Editorial Address

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Original Articles

279 Anthropometric Study of the Relationship between Tibia Length and Height of the Ethnic Papuans

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There was a relationship between tibia length and height with the results of the Pearson test obtained p value = <0.001.

283 Gait Analysis of Ankle Joints of Indonesians at Low, Medium and High Speeds

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Indonesians have a range of maximum dorsiflexion values for low, medium, and high speeds of 7.9°, 8.3°, 8.9° and maximum plantar flexion for low, medium, and high speeds of: 13.4°, 20.6°, 26°. There is a difference between the normal gait of the ankle joint of Indonesians and Europeans.

289 Differences in the Degree of Spasticity in Post-Haemorrhagic and Non-Haemorrhagic Stroke Patients Based on the Modified Ashworth Scale

Ifandias Gian Abhista[1], Maria Belladonna Rahmawati Sugianto[2], Tanti Ajoe Kesoema[3,4], Trianggoro Budisulistyo[2,4]
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There is no difference in the degree of spasticity in post-stroke patients between hemorrhagic and non-hemorrhagic stroke types.

295 Correlation between Urine Albumin Creatinin Ratio (UACR) Value to Urine Osmolality Value and Estimate Glomerular Filtration Rate (EGFR) Value on Patient with Kidney Failure

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The results of this study showed no correlation between UACR value to urine osmolality value and EGFR value in patients with kidney failure.

300 Platelet to Lymphocyte Ratio (PLR) Value in Normotency, Preeclampsia and Severe Preeclampsia

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The PLR value was significantly lowest in the severe preeclampsia group.

306 Effect of Vitamin D Administration on Interleukin–6 (IL-6) Levels in Peritoneal Fluid in Endometrioma Patients

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Vitamin D supplementation in endometrioma patients is not associated with peritoneal fluid interleukin-6 (IL-6) levels.

312 The Effectiveness of Cognitive Behavior Therapy in Enhancing Self-Esteem among Schizophrenia Patients at Dr. Soeharto Heerdjan Psychiatric Hospital, Jakarta in 2024

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Cognitive behavior therapy is effective for patients with low self-esteem because it can increase self-esteem and abilities in patients with schizophrenia.

Editorial

At the end of this year, Indonesia go though various events. In politic, the country successfully carried out the democratic election. Indonesia is also ahead at many sport events, sustainable infrastructure development and also in the world of science. How about in the fields of medicine and education? Many government programs have been implemented, i.e. scholarship and vaccination programs, examination facility for triple elimination program for expectant mothers. The problem now is that the rate of medical technology development is extremely rapid thus forces this country to keep up with the rest of the world. For this to happen, we need high quality, capable, steadfast and resilient human resources. The growth of technology can be followed and even implemented in Indonesia, the benefit of which can be reaped by our citizens to improve their quality of life. The evident proof this is the sprout of many articles based on research on medical technology. There are plenty of excellent quality articles on which the medical service process in Indonesia can be based on.

In this edition, there is a rising spirit in the published articles from many fields. From the perspective of medical science, research methodology, statistical analysis, and the results from various research, all show that Indonesia as a country refuses to be left behind.

In the matter of improving the quality of medical service, how exactly can civitas hospitalia show their progress? Of course based on what is written of the research done.The field of research in Indonesia undergoes significant improvement lately, proven from the quantity & quality of medical articles. The world of medicine is fast advancing, and the proof is in the medical experiences and research.

Keep researching.

The Effect of Feeding Process Stimulation on Oral Preparedness Readiness in Premature Infants

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Abstract

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Background : Most preterm infants do not have proper sucking, swallowing, and breathing coordination which caused delay in oral feeding readiness. The objective of this study was to analyze the influence of feeding stimulation on the readiness of premature infant's oral feeding.

Methods : This study was a true experimental study that involved 44 preterm infants born between 32–34 weeks of gestational age, devided in two groups. Twenty two infants in the intervention group received positioning (mid-line control symmetric) and oral feeding stimulation, while the control group received only positioning intervention. Oral stimulation was given 8 times a day for 7 days, before starting the oral feeding program. Oral feeding readiness was measured by using a modified early feeding scale (EFS) instrument on the first and the seventh days. Data analysis using t-test dependent, independent t-test, and Mc Nemar test.

Results : The results showed that there was a significant effect of the intervention on EFS score (p <0.001) and also on preterm infant's oral feeding readiness (p = 0.002). The results also showed that there was an effect of intervention on the length of stay (p=0.001).

Conclusion : Early oral feeding stimulation improves the infant's oral feeding readiness and shortens the infant's length of stay. Researchers recommend stimulation of the feeding process as an independent nursing intervention in caring for premature infants.

Keywords : Lenght of stay, oral feeding stimulation, oral feeding readiness, preterm infant

INTRODUCTION

A Preterm infant is an infant born alive at 37 weeks gestational age or pregnancy.[1] The immature gestational age causes various malfunction and poor coordination between body systems. This condition may threat premature infant life, therefore, premature infants required special care.[2]

A new concept of special care for premature infant is developmental care.[3] Spesial control care in infants may aid the infant's external environment to resemble the infant's internal environment related nesting and flexion positions. Developmental care has both short and long-term impacts. Short-term effects of developmental care shorten the use of endotracheal tubes thus rapid extubation, and long-term effects may support children's development.[2] The extubation gives the opportunity for oral feeding in infant. Premature infants are usually experience many problems including hypothermia, respiratory distress syndrome, intracranial hemorrhage, hyperbilirubinemia and hypoglycemia due to weak suctioning power lead inadequate intake.[4]

Oral feeding in premature infants are complex process. Oral feeding requires good coordination between the nervous and oral motor systems be able to suck, swallow, and breathe at the same time. A problem that often arises in premature infants are the immaturity of the respiratory and oral motor central nervous systems. Clinical manifestations of the problem of oral feeding can be in the form of three symptoms: aspiration, regurgitation, and desaturation.[5] Premature infants who experience desaturation are in difficult situations that can be life-threatening. Oral motor stimulation can increase the power of sucking premature infants, thereby reducing the risk of aspiration and desaturation.[6]

Premature infant care in the perinatology ward at Dr. Cipto Mangunkusumo National General Hospital has implemented positioning and oral motor stimulation in the expectation the premature infant' oral drinking readiness will be better. Good drinking readiness is one indicator of the infant's readiness to return home. Infant who are not ready to drink will be referred to the Medical Rehabilitation Unit for medical rehabilitation measures. Some of these premature infants have problems in readiness to drink orally. Based on medical record from Cipto Mangunkusumo Hospital, the data showed that 885 premature babies were treated in the perinatology ward. Some of these premature babies had issues with oral feeding readiness. A total of 231 premature babies (26.1%) were referred to the URM due to problems with feeding readiness.

This data shows that there is still a problem with premature infant' readiness to drink, even though they have received standard oral motor stimulation treatment. Thus, the objective of this study is to analyze whether there is an influence of stimulation of the feeding process on the readiness to drink orally in premature infant.

METHODS

The research was a true experimental study. This research obtained approval and was ethically reviewed by the Faculty of Nursing, University of Indonesia, with the number: 329/UN2.F1/ETIK/2017. This study consisted of two groups: an intervention group and a control group. Subjects were divided into an intervention group and a control group. The intervention group received stimulation feeding process (oromotor stimulation and positioning), while the control group received standard care consisting of positioning. In the intervention group, the EFS assessment was conducted initially before the feeding process stimulation and after the feeding process stimulation on the 7th day. In the control group, the EFS assessment was conducted before and after the standard oromotor stimulation. The difference in oral feeding readiness of premature babies before and after the intervention in both the intervention and control groups was then analyzed.

The target population of this study is all premature infants. The populations were premature infants who were treated in the Perinatology ward and respondents were obtained using a randomized sampling technique. Samples in this study are 50 premature infants, 25 were intervention group and 25 were control group. Data collection for this study was conducted in 2017. Given the rapid advancements in health science and the potential for changes in clinical practice, it is important to assess whether the findings from 2017 remain relevant for reference in 2024. Although the data continues to be utilized as the standard operating procedure at RSCM, it is recommended to review recent literature and updates in clinical guidelines to confirm that the 2017 results still hold true and are applicable in the current context. The length of the day of care is calculated from the time the infant first enters the treatment room until the infant leaves the hospital and goes home. Statistical analysis was performed using an independent t-test.

The intervention was carried out for 7 days. The intervention was carried out for 7 days according to the study conducted by Lesson which recommends promoter stimulation for premature babies.[1] Oral stimulation program improved oromotor skills and growth rate in premature babies aged 28–32 weeks.[7] There was a reduction in the transition time from tube feeding to oral feeding. Another study that oromotor stimulation before feeding can improve feeding performance, shorten hospital stays for premature neonates, and increase breastfeeding rates.[8]

Premature infant's drink preparation can be assessed objectively with various instruments, one of which is the assessment of early feeding skills for premature infant (EFS). EFS assesses the infant's

readiness and drinks tolerance as well as the development of the infant's drink skills. EFS is a checklist sheet that can be filled out by nurses or mothers who have premature infant. This research was conducted in the Perinatology Room at Dr Cipto Mangunkusumo National Hospital. Statistical analysis will use the McNemar and Chi Squre tests.

RESULTS

The characteristics of the intervention group and the control group consisting of age, gender, and weight of the infant was presented in Table 1.

Based on the Table 1, the average age in both intervention and control group were 32.8 weeks. In the intervention group, there were 9 males (40.9%), and in the control group, there are 12 males (54.5%). The average birth weight in the intervention group was 1565.7 kg, and in the control group, was 1587.7 kg.

After the intervention in seven days, we assessment the EFS score in first day for pre test and in seventh day for post-test. Table 2 showed there were differences in EFS scores before and after intervention in the intervention group ($p = 0.006$).

Table 3 showed that there was no significant difference in EFS scores before and after the intervention in the control group ($p = 0.71$). After comparing the average EFS scores on the seventh day between the intervention group and the control group, the analysis results indicated that there was no significant difference.

There was a significant effect of the feeding process on the readiness for oral feeding in preterm infants ($p = 0.001$). The mean EFS score showed a mean difference of 0.74, with a 95% confidence interval ranging from 3.89 to 6.93 points ($t = 7.261$).

Table 5 showed that there was an effect of stimulation of the researchers classify the value of EFS scores into two categories. The researchers categorized ready to feeding infants if the EFS scores was .>10 and the infant was not ready to feeding if the EFS score was <10. The result Table 5 of the analysis showed that there was a statistically significant effect of the stimulation of the feeding process on oral readiness for feeding in preterm infants ($p = 0.002$).

TABLE 1
Characteristic of respondents

Characteristic of Respondents	Group	
	Intervention (n=22)	Control (n=22)
Age (week); mean ± deviation standard	32.8 ± 1.2	32.8 ± 1.3
Gender, n (%)		
Male	9 (40.9)	12 (54.5)
Female	13 (59.1)	10 (45.5)
Birth weight (in gram): mean± Deviation standard	1565.7 ± 394.9	1587.7 ± 365.9

TABLE 2
Difference of EFS score in intervention group before and after treatment

Variabel	Mean (SD)	t	p
EFS Score	3.45 (5.32)	-3.05	0.006

TABLE 3
Difference EFS score in control group
The Effect of Feeding Process for the Readiness of Oral Feeding in Preterm Infants

Variabel	Mean (SD)	t	p
EFS Score	-0.27 (3.35)	-0.381	0.71

TABLE 4
Difference EFS score in intervention group and control group
The Effect of Feeding Process for the Readiness of Oral Feeding in Preterm Infants

Variabel	*Mean* (SD)	*Mean Difference* (95%CI)	t	*p*
EFS Score	–	0.74 (3.89 – 6.93)	7.261	0.001

TABLE 5
The Effect of Feeding Process for the Readiness of Oral Feeding in Preterm Infants

Oral feeding readiness before intervention	Oral feeding readiness after Intervention		Total	P
	Ready	Not Ready		
Ready	17	0	17	0.002*
Not Ready	10	17	27	
Total	27	17	44	

TABLE 6
The Effect of Stimulation of The feeding on The Length of Care for Premature Infants

Variabel		*Mean*	*Standard Deviation*	t	*p*
EFS Score	Intervention	3.45	2	7.261	<0.0001*
	Control	0.27	3.35		
Length of stay	Intervention	21.7	9.4	3.5	0.001*
	Control	33.9	–		

The analysis showed there are differences in mean length of stay (LOS) or length of days treatment for preterm infants who received stimulation of the feeding process with premature infants who received standard care. The result of the analysis is shown in Table 6.

The result showed that there was a difference in feeding stimulation on the length of stay of preterm infants (p = 0.001). Early oral feeding stimulation improves the infant's oral feeding readiness and shorten the infant's length of stay.

DISCUSSION

There was a significant difference in oral feeding ability in premature infants aged less than three weeks and four weeks with premature infants over thirty-four weeks.[6] The ability to coordinate breathing at the time of feeding is fully achieved at the age of thirty-six weeks. Feeding ability includes the ability to coordinate breathing by swallowing. Good feeding ability shows readiness to feeding per oral infant. Oromotor stimulation before feeding can improve feeding performance, shorten hospital stays for premature neonates, and increase breastfeeding rates.[8] The appropriate positioning is the first step when the infant is ready to start the process of oral feeding. Appropriate position during oral feeding initiation is to maintain the midline control position. This midline position is the physiological position of the fetus in the uterus so that the infant becomes more comfortable.[9] The infant's comfort will support the infant to focus more on his motor movements. The infant's dissection in the flexion and midline position can reduce the gross motor movement of the infant so that the infant becomes more focused on fine motor activities namely sucking, swallowing, and breathing.

The rapid increase in feeding readiness was seen in one of the intervention group respondents. EFS score before receiving feeding stimulation shows a score of 0. A score of 0 illustrates the condition of a infant who does not have good oral motor muscle strength so the infant unable to suck properly. Infants do not have enough energy, so in one burst they cannot produce a short

suction of more than seven suction. Infants also seem to stop sucking and preparing their breath before sucking again which indicates that the infant has not been able to coordinate the breathing process, sucking and swallowing at one time. The EFS 0 score shows that the infant is not ready for oral feeding. Infant's EFS score after seven days of stimulation of the feeding process changes. The EFS score becomes 10 from the score of 0. The infant has been able to maintain the strength of the oral motor muscle to suck and push the liquid to swallow together with the breathing process. The EFS 10 score shows the infant is ready for oral feeding.

Oral motor intervention can improve feeding readiness per oral premature infant.[10] Massage in the perioral area can remind the infant to suck and push the tongue in motion for feeding. Stimulation of the muscles in the perioral area helps infant strengthen muscle strength thereby increasing their suction ability. A strong tongue pushes the fluid towards the back to improve the ability to swallow premature infants. The midline position maintained by dissection helps the infant concentrate on fine and respiratory motor movements. This combination of sucking power, ability to swallow, and ability to maintain breathing is what increases the readiness of feeding per oral premature infant.[11] Oral stimulation impacts the oral structures as a crucial component in the oral stimulation program and can enhance the strength of the oral muscles for effective sucking. Oral stimulation using a pacifier (non-nutritive sucking) as another component of this program can also improve the efficiency and endurance of the oral structures in the sucking process. Overall, this program can enhance the maturity of the central or peripheral nervous system structures, improve sucking ability, and coordinate the sucking-swallowing-breathing process.[12]

Oral motor intervention or oral stimulation is defined as sensory stimulation on the lips, jaw, tongue, soft palate, pharynx, larynx, and respiratory muscles that affect the oropharyngeal mechanism. Sensory stimulation on these oral structures can enhance the ability of the oral structures in the sucking and swallowing processes.

The combination of positioning and oral motor stimulation was used to intervene in preterm infants in the intervention group while infants in the control group received intervention in the form of treatments that became the standard treatment procedure in the room, and the combination was called feeding as stimulation process. The results showed that infants who were fed stimulation were more ready to feed than infants who did not receive stimulation of the feeding process.

Readiness to feeding premature infants supports adequate nutritional intake so that enough energy to improve health status. The infant's health status is well characterized by good clinical and weight gain. Infants with good health status will be allowed to go home so that

their health status is related to the length of stay. The results showed a mean difference in length of stay between preterm infants who received stimulation of the feeding process with infants who received standard room care (21.7 + 9.4 vs 33.9 + 13.4). The results showed that there was a stimulation effect on the feeding process for the length of stay ($p = 0.001$). Infants who get a feeding process are 12.2 days faster than infants who receive standard room care.

The length of stay for infant who received oral motor stimulation was 2.6 days shorter than infant who did not receive oral motor stimulation. Oral motor stimulation which part of the stimulation of the feeding process helps strengthen the oral motor muscles and comfort the infant so that the infant is able to strengthen the strength of suction and the swallowing-breathing process. This condition benefits the infant due to nutrition is better and energy needs are sufficient. Energy is stored in the form of fat reserves that can be stored.

Limitations

The results showed that there was an effect of stimulation of the feeding process on readiness to feeding per oral premature infant. The research did not examine the progress of the volume of feeding per oral infant. The Research examined body weight as the final result of the progress of oral feeding.

CONCLUSION

Oral feeding in premature infants is a complex task because it requires good coordination between sucking, swallowing, and breathing simultaneously. This study shows a statistically significant effect of feeding process stimulation on oral feeding readiness in premature infants, but the researchers faced a limitation in not measuring the progress in oral feeding volume. Researchers recommend that future studies investigate the effect of feeding process stimulation on the progress of oral feeding in premature infants.

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Original Article

The Effect of Core Stability Exercise on Decreasing Angle of Trunk Rotation Degree in Idiophatic Scoliosis

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Abstract

Background : Scoliosis is a group of conditions consisting of changes in the shape and position of the spine on the lateral side that may be accompanied by rotation caused by various etiologies. Core stability exercise is a form of exercise that can be used to reduce the degree of scoliosis curve. This study aims to determine the effect of core stability exercise on junior high school student (JHS).

Methods : This study used one group pre and post test with control design involving 32 students of SMP 2 Wonosari Klaten who were divided into 2 groups, using the blind randomized control trial method. 16 subjects as intervention group given treatment of core stability exercise and a control group 16 subjects as control group without any treatment. The intervention was carried out for 5 weeks with a frequency of 3 times a week. Measuring the degree of the scoliosis curve using a scoliometer. The pre-test trunk rotation angle (ATR) value for the treatment group was found to be an average of 5.06° and a post-test ATR value of 4.75°. Meanwhile, in the control group, there was no change in the ATR value during the pre-test or post-test, which was 5.43°.

Results : Statistical test of differences in pre-post test of treatment groups using the Wilcoxon test obtained a value of $p = 0.025$ ($p < 0.05$).

Conculsion : There is an effect of core stability exercise on reducing the scoliosis curve in junior high school student.

Keywords : angle of trunk rotation, core stability exercise, idiopatic skoliosis, skoliosis

INTRODUCTION

Scoliosis is a general term for a group of conditions consisting of changes in the shape and position of the spine, chest, and trunk. Changes in the anatomical structure are characterized by curvature of the spine to the lateral side accompanied by rotation.[1] The causes of scoliosis are divided into congenital, neuromuscular and idiopathic.[2] Idiopathic scoliosis is a lateral curvature of the spine of 10 degrees or more of unknown etiology without any underlying congenital or neuromuscular abnormalities.[3]

According to the SOSORT Consesus 2016, idiopathic scoliosis based on age is classified into: infant (0 to 2 years), juvenile (3 to 9 years), adolescent (10 to 17 years) and adult (18 years and more). Idiopathic scoliosis can develop at any time during childhood or adolescence.[4]

Research conducted by Baswara *et al.*, indicated that the criteria for moderate scoliosis were most often found in females in the juvenile age group 13 students and in adolescents group was 18 students, meanwhile according to the severe risk scoliosis criteria, only one case was found in the juvenile age group of male students and in the adolescent age group, the same number was found in 3 students, men and women.[5] The prevalence of idiopathic scoliosis has increased among school-age children aged 10 to 15 years.[6] In Asia, 0.4 to 7% suffer from idiopathic scoliosis.[7] Research conducted by Komang-Agung *et al*. (2017) in Surabaya revealed that the prevalence rate of idiopathic scoliosis in the age group of 9 to 16 years among males (0.51%) was lower than that of females (2.42%) with a ratio of 1:4.7.[8] From the above data, we can conclude that many adolescents suffer from idiopathic scoliosis. Various interventions have been proposed to treat cases of idiopathic scoliosis. The type of scoliosis treatment depends on the severity of the scoliosis curve and includes exercises, bracing, and surgery.[9]

Core stability exercise is a form of exercise that activates the internal core muscles synergistically. Core stability exercise is one of the exercise interventions that can be used by physical therapists to treat idiopathic scoliosis in mild and moderate degrees. An imbalance in postural muscle activity results in unilateral compensatory postural muscle movement. Core stability exercises can increase postural stability and reduce postural imbalances by involving local muscle stability training (transvesus abdominis, multifidus and diaphragm) and global muscle stability training (psoas major, quadratus lumborum and pelvic floor).[10]

Research conducted by Qi *et al*. showed that core stability exercises resulted in a statistically significant reduction in cobb angle from before to after treatment in subjects aged 13 years with a 12-week exercise dose with a frequency of 3 times a week.[11] Research by Weng & Li shows that core stability exercises can significantly reduce the cobb angle in idiopathic scoliosis and improve the poor body posture of scoliosis patients.[12] According to research by Kocaman *et al.*, shows that the results in reducing the degree of scoliosis curve in the mild category are more effective using scroth exercises rather than using core stability exercises.[13] A systematic study conducted by Khaledi *et al.*, shows that core stability exercises are safe, easy to perform, and effective in improving the degree of idiopathic scoliosis curve, but there is insufficient evidence to support this hypothesis, so additional research evidence quality is still necessary to draw definitive conclusions and make clinical decisions.[14]

However, there are several fundamental differences between this research and research conducted by Weng & Li and conducted by Qi *et al.*, namely the implementation time and the number of movement exercises.[11,12]

Based on the above data, researchers were prompted to conduct research on the effect of core stability exercises on reducing the degree of spinal curvature in idiopathic scoliosis patients with mild degrees. of scoliosis in junior high school adolescents (JHS) aged 12 to 14 years. This research will be conducted to find out whether core stability exercises can reduce the degree of scoliosis curve in JHS.

METHODS

This research uses a type of randomized controlled trial research, 2 groups namely one group of research subjects as the treatment and another group as the control group. The sampling technique used blind allocation with randomized, using simple random sampling subjects choosed in the form of random lottery numbers in the container provided. If they got an odd number, the subject became the treatment group and if they got an even number the subject became the control group. The initial examination using the APECS application and then the protocol for measuring the degree of the ATR curve using a scoliometer will be carried out separately for male and female students. The research location is at SMP 2 Wonosari Klaten in June–July 2023. Core stability training was provided to the treatment group in 15 sessions at a frequency of 3 times per week for 5 weeks. The control group only received training on how to maintain correct body posture.

The research design is described as follows:
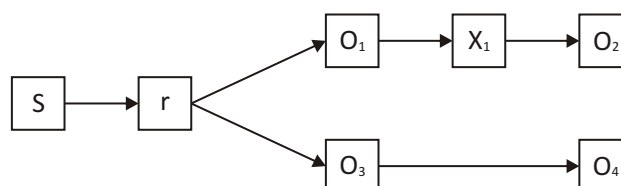
The explanation :

S : Subject

r : Randomized

O_1 : Examination of scoliosis using the APECS application and measurement of the ATR (Angle of Trunk Rotation) value of the degree of spinal curvature using a scoliometer measuring instrument before treatment in group 1.

X_1 : Providing core stability exercise treatment

O_2 : Measurement of ATR value for scoliosis degree curve using scoliometer measuring instrument after treatment in group 1.

O_3 : Examination of scoliosis using APECS application and measurement of ATR value of degree of spinal curvature using scoliometer measuring instrument before treatment in group 2.

O_4 : Measurement of the ATR value of the scoliosis degree curve using a scoliometer measuring instrument after treatment in group 2.

The inclusion criteria for this study were (1) the subject was a junior high school adolescent aged 12 to 14 years, (2) idiopathic scoliosis detected, (3) an ATR value of 4° to 6° detected on the basis of the measurement results. with a scoliometer, (4) understood the instructions given and are able to communicate well, (5) willing to respond and complete informed consent.

The exclusion criteria for this study were as follows: (1) junior high school adolescents who have congenital scoliosis or congenital spinal defects, (2) experienced spinal fractures, surgery spinal cord, have congenital spinal disorders, (3) have limb disorders. upper or lower movements, (4) have a history of diseases related to rheumatology, neuromuscular, cardiovascular, respiratory or renal problems, (5) the respondent is currently participating in a scoliosis therapy program or participating in other research.

Inspections and measurements are carried out to collect initial data. The initial examination to determine whether or not there is scoliosis is done using the APECS (AI Posture Evaluation and Correction System) application and the instrument to measure the degree of spinal curvature in scoliosis in this study is a scoliometer. The scoliometer is a tool used to measure ATR which is applied simultaneously with the forward bend test and has a good correlation with the gold standard (cobb angle).[15]

APECS is software created to assess posture through non-invasive photogrammetry techniques, to correct and prevent postural deformities with various exercises.[16] APECS was used at the beginning of the study for screening or early detection by analyzing the anterior and posterior shoulder height level, trunk position and waist line.

The Pearson correlation coefficient between the APECS application and the gold standard (X-ray) was 0.9874 (98.74% correspondence). The agreement between plain radiographs and average APECS Pro measurements from all examiners (including right and left sides) was 94.64% (kappa = 0.8323; p = 0.001), indicating an excellent result.[17]

Data analysis used SPSS version 26.0. Data analysis included descriptive analysis and difference testing. The normality test uses the Shapiro-Wilk test and the homogeneity test uses the levene's test. The pre-test and post-test data of the treatment group and the control group were analyzed using the Wilcoxon rank-sum test. Post-test data on scoliosis curve degree in the treatment group and control group were analyzed using the Mann Whitney test. The basis for drawing conclusions is that if the $p\text{-}value$ <0.05, then there is an effect after treatment with core stability exercises. But if the $p\ value$ is ≥ 0.05, there is no effect after the intervention.

All research procedures have been approved with the issuance of ethical clearance number 1.116/VI/HREC/2023 from the Health Research Ethics Commission (KEPK) RSUD Dr. Moewardi. Research subjects received an explanation regarding the aims, objectives, benefits, and research protocol and completed a questionnaire and informed consent letter before the intervention was performed. Each subject in the treatment group received training on how to exercise and follow-up in the form of participation in training according to a predetermined schedule.

The basic stability exercises applied in this study were curls up, hundreds pattern, diafragmatic breathing, bird dog, face down, and sitting in a crossed leg position. This exercise aims to activate the posture muscles so that the degree of the scoliosis curve decreases. The training dose given for each movement is 8 repetitions for 3 sets with a rest of 30 seconds for each set. Each movement has a hold time of 5 seconds.

RESULTS

The subjects of this research were middle school students aged 13 to 14 years old. The subjects were students who met the inclusion criteria and whose their parents were willing to sign informed consent.

The research subjects consisted of 32 people, the research subjects were divided into 2 groups. Group I consisted of 16 subjects who received treatment in the form of core stability exercises and Group II consisted of 16 subjects constituting the control group. During the research process, no subjects withdrew or dropped out, so the number of subjects in this study did not change, which was 32 people.

Table 1 shows the subject characteristics. The results of subject characteristics based on gender in the treatment group and control group showed data on the frequency of 10 female subjects and 6 male subjects. Most of the subjects were girls. In this study, the age of the treatment group was obtained with a mean age of 13.93

TABLE 1
The Subject characteristics by gender and age

Variabel	Treatment Group (n=16)	Control Group (n=16)
Sex		
Men	6	6
Women	10	10
Age	13.93 (0.250)	13.81 (0.403)
Weight	45.87 (8.89)	46.5 (7.10)
Height	155.25 (8.22)	154.62 (6.97)

Values listed are in the form of mean or mean and (standard deviation)

TABLE 2
ATR scoliometer values before and after treatment

Value	Treatment Group (n=16)	Control Group (n=16)	(p)
Scoliometer (ATR value)			0.002
Pre Test	5.06° (0.573)	5.43° (0.512)	
Post Test	4.75° (0.577)	5.43° (0.512)	
(p)	0.025	1.00	

Values listed are in the form of mean or mean and (standard deviation)

and a standard deviation of 0.250. Meanwhile, the control group obtained age data with a mean of 13.81 and a standard deviation of 0.403. Body weight in the treatment group had a mean of 45.87 and a standard deviation of 8.89, while in the control group it had a mean of 46.5 and a standard deviation of 7.10. Body height in the treatment group has a mean of 155.25 and a standard deviation of 8.22, while in the control group it has a mean of 154.62 and a standard deviation of 6.97.

Table 2 presents the ATR scoliometer values before and after treatment. In the pre-test measurement of the ATR value for the treatment group, the result was a mean of 5.06 and a standard deviation of 0.5737, while in the control group the result was a mean of 5.43 and a standard deviation of 0.5123. In the post-test measurement of the treatment group, the results obtained were a mean ATR value of 4.75 and a standard deviation of 0.5773. Meanwhile, in the control group, the average ATR value was 5.43 and the standard deviation was 0.5123.

The effect of core stability exercise on reducing the degree of scoliosis curve is known through hypothesis testing. Hypothesis testing in the treatment group, namely the pre and post-test difference between the treatment groups using the Wilcoxon test, showed a value of $p=0.025$ ($p<0.05$) meaning that there was a significant influence between before and after being given the core stability exercise. Hypothesis testing in the control group, namely the pre- and post-test difference test for the treatment group using the Wilcoxon test with a scoliometer, showed a value of $p=1.00$ ($p \geq 0.05$), which means that there is no significant effect (Table 2).

The results of the post-test difference in the ATR degree of scoliosis curve in the treatment group and the control group using the Mann Whitney test obtained a value of $p=0.002$ ($p<0.05$), which means that there is a difference in influence between the two groups (Table 2).

DISCUSSION

Postural stability can be achieved through good coordination of core muscles and regulation of intra-abdominal pressure (IAP) by the central nervous system. IAP regulation and the Integrated Spinal Stabilization System (ISSS) play an important role in spinal stabilization. The cause of the increase in IAP is the work of the diaphragm muscle. Activation of the diaphragm muscle can stimulate the pelvic floor muscles, transverse abdominis muscles, multifidus and balanced activation between spinal flexor and extensor muscles in the thorax region to increase IAP and ensure postural stability.[18]

Hypothesis testing of the data was performed and the results show that core stability exercise has an effect on reducing the ATR degree of the scoliosis curve.

Hypothesis testing in the treatment group, namely the pre- and post-test difference between the treatment groups using the Wilcoxon test, showed a value of $p = 0.025$ meaning that there was a significant influence between before and after being subjected to core stability exercise treatment, as evidenced by a decrease in the mean ATR value of 0.31°. Hypothesis testing in the control group, namely the pre and post-test difference between the control group using the Wilcoxon test, showed a result of $p = 1.00$ ($p ≥0.05$), which means there is no significant effect.

This is consistent with research by Weng & Li, showing that core stability exercises can significantly ($p<0.01$) reduce Cobb angle in idiopathic scoliosis and improve poor body posture in older people. scoliosis patients with a total of 31 subjects after receiving treatment for 12 weeks. The decrease in Cobb angle was 2.74° in the group that received core stability exercises.[12]

However, there are several fundamental differences between this research and the research conducted by Weng & Li, that is the implementation time and the number of movement exercises. The research conducted by Weng & Li required a 12-week treatment period, whereas this research was only conducted for 5 weeks. The number of movement exercises applied in Weng & Li research was 7 movements, while this study only implemented 6 types of movements of core stability exercises.[12] However, this difference is not an inhibiting factor to prove that providing core stability exercises to adolescents with idiopathic scoliosis can reduce the degree of the scoliosis curve.

Another study whose results were consistent with this research and became the basis for it was conducted by Qi *et al.*, and involved 38 subjects aged 12 to 14 years old, divided into two groups. Group I received a treatment of core stability exercises and group two received no treatment. The exercise was applied for 12 weeks with an intensity of 3 times per week. In addition to having results consistent with this research, the research conducted by Qi *et al.*, had the same number of basic stability exercise movements, i.e. 6 movements. The research results of Qi *et al.*, showed that there was a decrease in the mean value of scoliosis degree after undergoing core stability exercise intervention with a decrease in the mean value of Cobb angle, namely 3, 76°.[11]

The above two studies had statistical analysis results of $p = 0.01$ ($p < 0.05$), which means that there was a significant influence between before and after core stability exercise treatment basic. Meanwhile, this study has a value of $p=0.025$ ($p<0.05$), which means that it also has an effect on providing core stability exercises on reducing the ATR value for the degree of scoliosis.

Thus, this does not exclude the possibility that just 5 weeks, 3 times a week and 6 types of core stability exercises can reduce the degree of idiopathic scoliosis curve in junior high school adolescents. This is proven by

the results of the statistical analysis, the value of $p = 0.025$ ($p<0.05$), which means that there is an influence between before and after the treatment of core stability exercises and a decrease in the average ATR value of 0.31°.

Activating the core muscles as the stabilizing muscles of the spine will relax the surrounding muscles that were previously in spasm. The coordinated and simultaneous contraction of these muscles will provide rigidity to support the trunk. As a result, intradiscal pressure is reduced and will reduce the workload of the lumbar muscles, so lumbar muscle tension is thereby achieved.[19]

CONCLUSION

This research proves that providing core stability exercises for 5 weeks can reduce the degree of scoliosis curve in junior high school adolescents.

Based on the above research results, suggestions that can be made to future researchers should increase the number of research subjects from multiple regions in order to describe the results of the population as a whole. Future researchers can also compare types of core stability training with other types of training.

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Original Article

The Relationship between Family Support and Quality of Life in Elderly with Dementia

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Abstract

Background : The growing number of elderly individuals can result in a decline in physical and mental functioning, which in turn affects the quality of life of the elderly. The family serves as the primary support system for the elderly in maintaining their health. Effective family support can enhance the quality of life of the elderly, enabling them to enjoy a fulfilling life in their later years. This study was aimed to determine the relationship between family support and quality of life in elderly people with dementia.

Methods : This is a quantitative-correlative study design with a cross-sectional design. The analysis test used is chi-square. A total of 73 respondents were sampled for the purposes of data collection. This was achieved by administering two questionnaires: one pertaining to family support and the other to quality of life (Short Form 12).

Results : The results of this study indicate that the majority of elderly individuals aged 6074 (69.9%), females (53.4%), reside in the same household as their children (53.4%), work as farm laborers (69.9%), have basic education (72.6%), and have moderate levels of dementia. (50.7%). Having family support shows the moderate category (91.8%), while the quality of life is mostly good (58.9%), with a significance p-value of 0.033.

Conclusion : There is a significant relationship between family support and quality of life in elderly people with dementia.

Keywords : Dementia, elderly, family support, quality of life

INTRODUCTION

In both developed and developing countries, there is an increasing number of elderly people due to declining birth (fertility) and death (mortality) rates. This trend is impacting life expectancy and changing the overall population structure. China, India, the United States, Japan, and Indonesia are among the five countries with the largest elderly populations in the world. As a developing country, Indonesia has the fourth largest population in the world.[1] The life expectancy of the Indonesian population has increased from 68.6 years in 2014 to 72 years in 2015. This upward trend is projected to continue. Based on the 2014 National Census, the number of elderly people in Indonesia reached 20.24 million, which is approximately 8.03% of the entire population. This is an increase from the 2013, which reported 18.1 million elderly people, accounting for 7.6% of the total population.[2]

The province with the highest proportion of elderly population in Indonesia is the Special Region of Yogyakarta (DIY), that is (14.5%).[3] DIY has four districts and one provincial capital, that are Sleman, Gunung Kidul, Bantul, Kulonprogo, and the provincial capital Yogyakarta. Sleman District has the highest proportion of elderly people among the five districts. According to data provided by the Sleman Regency government, the number of residents aged 60 years and over in Sleman Regency is 104,380, which represents the elderly population; Gunung Kidul is 103,000 people; Bantul is 90,928 people; Kulon Progo is 56,550 people; and Yogyakarta City is 31,559 people. Data from Sleman Regency shows that Sleman consists of 17 sub-districts; administratively, Cangkringan sub-district consists of 5 villages, that are Argomulyo, Wukirsari, Glagaharjo, Kepuharjo, and Umbulharjo villages; it also consists of 73 padukuhan, 151 Rukun Warga (RW), and 307 Rukun Tetangga (RT).[4]

The growing number of elderly individuals can potentially lead to challenges in the aging process.; the tendency for decreased physical and mental function in the elderly is a common problem, one of which is dementia.[5] Dementia is a disease characterized by decreased cognitive function, which can interfere with daily activities. Elderly people need to have a sufficient level of knowledge to know what diseases can occur to them and the signs and symptoms of disease, especially dementia. A person's knowledge and attitudes influence dementia prevention behavior.[6] According to the World Health Organization and the Alzheimer's Disease International Organization, the total number of people with dementia worldwide is estimated to reach 47.5 million in 2015, with as many as 22 million of them in Asia.

A projection indicates that the global population of individuals aged 65 and over with dementia is expected to reach 75.6 million in 2030 and 135.5 million in 2050.[7] Developed countries such as the United States currently have more than 4 million elderly people experiencing Alzheimer's dementia. This figure is expected to increase by almost four times by 2050. Among the elderly, 58% live in low- and middle-income countries, and this proportion is expected to increase to 71% by 2050. Every year, the worldwide number of new dementia cases is almost 7.7 million, which means that every 4 seconds, there is 1 new case of dementia.

In 2016, an estimated 1.2 million people in Indonesia suffered from dementia. This number is projected to increase to 2 million by 2030 and 4 million by 2050.[2] The prevalence of dementia in elderly people aged more than 60 years in DIY reached 20.1%. As the elderly age, the prevalence rate of dementia also increases. At the age of 60, 1 in 10 DIY seniors experiences dementia. Compared with the prevalence at the global level, the prevalence of dementia in DI Yogyakarta is much higher.[4] This condition can have an impact on the quality of life of older people.

Health problems that arise in the elderly can affect their quality of life. The consequences of decreased cognitive function in the elderly can cause dependence on carrying out daily activities and affect the quality of life.[8] The concept of quality of life (QOL) encompasses both positive and negative dimensions. QOL is understood to be a multifaceted construct that encompasses various aspects of well-being, including happiness, life satisfaction, and subjective well-being. These dimensions are not independent of one another but rather exhibit a complex interdependence, influencing one another in ways that contribute to an overall perception of QOL.[9] According to the research, the quality of life of the elderly may decline due to physical changes, which often decrease and affect health. The deterioration of cognitive function in older adults can have a deleterious effect, impinging upon their autonomy in activities of daily living. As a result, close supervision from family and others may be necessary.[10,11] The quality of life of the elderly individuals is affected by various factors, with family support being a significant one. Family support encompasses different types of assistance provided by family members, such as information, assessment, appreciation, practical help, and emotional support. Families play a crucial role in helping the elderly maintain their health.[12,13]

The family has a very important role in caring for elderly people with dementia at home. Special preparation is needed to live with an elderly person who has dementia.[14,15] Preparations that can be made are mental and environmental. Mentally, the family must be able to adapt to the changes that occur in elderly people with dementia, and the family is expected to be able to provide a supportive environment for the elderly, namely an environment that makes the elderly feel

comfortable, so that the family can provide optimal care for the elderly.[12,13] The objective of this study is to examine the relationship between family support and quality of life in elderly individuals with dementia.

METHODS

This study involves quantitative-correlational research using a cross-sectional research approach. Sampling was carried out using the total sampling method. A sample of 73 elderly individuals with dementia was obtained from three hamlets in Cangkringan, Sleman district, Yogyakarta: Ngemplak, Kregan, and Salam. The research instrument that was used is a family support questionnaire, which consisted of 16 question items regarding family support. To assess the quality of life of the elderly, the SF-12 (Short Form-12) questionnaire was used with 12 question items regarding the quality of life of the elderly. The Short Portable Mental Status Questionnaire (SPMSQ) is used to measure the intellectual function of the elderly. The validity and reliability of these three instruments have been thoroughly tested. This research has also undergone an ethical test with ethical test number 282.3/FIKES/PL/VIII/2019 from the Health Research Ethics Commission of Respati University, Yogyakarta.

RESULTS

The following table provides data on the characteristics of elderly respondents in Ngemplak, Kregan, and Salam Hamlets.

The data provided, it is evident that 69.9% (51 respondents) of the participants fall within the age group of 60–74 years, gender is dominated by women by 53.4% (39 respondents), the majority of elderly who live with their families are supported by their children, accounting for 53.4% (39 respondents), the majority of occupations are landless laborers 69.9% (51 respondents), the majority of basic education (Elementary junior high school) is 72.6% (53 respondents), with a moderate level of dementia category, namely 50.7% (37 respondents), moderate family support at 91.8% (67 respondents), and good quality of life at 58.9% (43 respondents).

The relationship between family support and quality of life for the elderly in Ngemplak, Kregan, and Salam Hamlets is presented in Table 2.

The results of the Chi-Square Test indicate a significant relationship between family support and quality of life in the elderly, with a ρ-value of 0.033, which is less than 0.05.

DISCUSSION

Characteristics of respondents
The research results showed that most of the participants were between 60 and 74 years old. The results of this study are in accordance with life expectancy in Indonesia, that is 72 years.[1,16] Based on gender, there were more female elderly respondents than male elderly respondents. Statistics in Indonesia also state that the elderly population over 60 years old is dominated by women. Women have a higher life expectancy compared to men; this can be seen by the existence of a larger female elderly population.[1,2]

TABLE 1
Characteristics of respondents (n=73)

Characteristics	f	Percent
Age (69.3 ± 7.69)		
60–74 years old	51	69.9
75–90 years old	22	30.1
Gender		
Man	34	46.6
Woman	39	53.4
Family members live at home		
Husband	20	27.4
Wife	14	19.2
Child	39	53.4
Occupations		
Not employed	22	30.1
Landless laborer	51	69.9
Education level		
Not in school	4	5.5
Elementary – junior high school	53	72.6
Senior high school	16	21.9
Level of dementia		
Mild	34	46.6
Moderate	37	50.7
Severe	2	2.7
Level of family support		
Medium	67	91.8
High	6	8.2
Quality of life		
Poor	30	41.1
Good	43	58.9
Total	73	100

TABLE 2
The relationship between family support and quality of life in the elderly (n=73)

Categories	Quality of life		Total	X^2	p-value
	Bad	Good			
Level of Family Support					
Medium	30	37	67	4.561	0.033
High	0	6	6		
Total	30	43	73		

The results indicated that elderly individuals who resided with their biological children received greater family support, but the support of family support from husbands and wives was not as much as support from children, according to research,[13,14] stated that individuals who are married have a higher quality of life compared to those who are not. The results showed that the majority of the elderly had jobs as landless laborers. Other research said that a People who are employed generally have a better quality of life compared to those who are not.[17,18]

The results of this study also show that most of the elderly have a low education level. Statistical data mention low education because more than half of the elderly population in Indonesia has never been to school and did not graduate from elementary school.[19] The majority of family support for elderly people with dementia is in the moderate category, namely 67 people (91.8%). Family support is a crucial factor that can influence a person's behavior, lifestyle, and ultimately their health and quality of life. If the elderly receive sufficient support from the family, they will be motivated to change their behavior to live a healthy lifestyle optimally to improve health and quality of life.[12-14]

The majority of elderly people with dementia have a good quality of life, specifically 43 people (58.9%). Previous research also states that The quality of life of the elderly is rated as moderate. The quality of life of the elderly is influenced by many factors, such as physical, environmental, social, and psychological factors.[10]

The relationship between family support and quality of life

The study's findings suggest a significant correlation between elderly quality of life and family support. Other studies mention the importance of family in caring for the elderly, including maintaining and improving their mental status, providing support, and facilitating their spiritual needs. If family support is strong, it can enhance quality of life and even reduce morbidity and mortality rates in the elderly.[20] Previous similar research also mentioned that providing family support interventions can improve the quality of life for the elderly.[21]

The family's approach to caring for the elderly reflects the cultural values within the family, highlighting the importance of respecting, valuing, and providing proper care for the elderly as parental figures. Furthermore, the elderly contribute significantly to the family unit, offering unique advantages and a wealth of experience. The input of the elderly is still required in the decision-making process and can serve as a source of guidance for their children.[22] Furthermore, offering family support, such as information and emotional support, can make the elderly feel less anxious and more secure and comfortable.[23]

CONCLUSION

Family support has an impact on the elderly's quality of life. The family is the primary support system for the elderly. Family support can be in the form of physical, social, psychological, and informative support. This support can improve the elderly's health, independence, and quality of life. More research is needed on other aspects, such as culture, that can influence the quality of life of the elderly.

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Original Article

Effects of α-Mangostin-Loaded Self-Nanoemulsion (MG-SNE) and Physical Exercise on The Reduction of Waist Circumference in Wistar Rats

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Abstract

Background : Waist circumference (WC) is a marker of intra-abdominal adipose tissue and a risk factor for cardiometabolic disease. A higher risk of coronary heart disease was associated with an increased WC. Garcinia mangostana Linn's anti-inflammatory activity would reduce abdominal fat deposition and WC. Additionally, Garcinia mangostana Linn's potential would increase in nanotechnology. This study was aimed to demonstrate that WC in Wistar rats induced by an atherogenic diet can be decreased by α-Mangostin-loaded self-nanoemulsion (MG-SNE) treatment combined with physical activity.

Methods : Experimental research with Randomized Control Trial design using a total sample of 15 male white rats *(Rattus novergicus strain Wistar)* weighing 300 grams and aged between 6 and 8 weeks, split into 3 groups given physical exercise for 8 weeks along with 3 different doses of medication (group K received Atorvastatin 1.44 mg once; group P1 received Garcinia mangostana Linn pericarp extract, at a dose of 800 mg/kg, divided into 3 administrations; and group P2 received MG-SNE 50 mg/kg once). Waist circumference was measured using a metline, before and after treatment.

Results : WC decreased in Groups K, P1, and P2, with deltas of -5.00±21.21 mm, -12.50±24.75 mm, and -17.50±12.58 mm. The greatest decrease in WC was P2. There was no significant difference, according to the paired test between the pre-test and posttest in all groups. The p value >0.05 was determined to indicate that there were no significant differences between the groups.

Conclusion : WC in Wistar rats induced by an atherogenic diet can be decreased by MG-SNE treatment combined with physical exercise.

Keywords : Garcinia mangostana Linn, α-Mangostin self-nanoemulsion, Physical exercise, Waist Circumference

INTRODUCTION

Waist circumference (WC) can be more reliable as a general indicator of body size compared to body mass index (BMI). A risk factor for metabolic syndrome is obesity, with a waist circumference of at least 102 cm (40 inches) for males and at least 88 cm (35 inches) for females. The measurement of waist circumference raises the risk of cardiometabolic disease and can be used as an indicator of intra-abdominal adipose tissue. The primary cause of death worldwide, coronary heart disease (CHD), is one of the cardiovascular diseases that is more likely to occur in people with metabolic syndrome. According to WHO data, the number of deaths from CHD rises annually. The CHD death rate increased from 8.9 million in 2019 to 11.1 million in 2020, or over two million deaths. CHD is the cause of up to 30% of deaths worldwide, with developing nations accounting for 80% of these cases. Even though the death rate from CHD has decreased in developed countries, it still causes one-third of deaths in the over-35 age range.[1–3]

The effects of mangosteen peel *(Garcinia mangostana Linn)* on obesity, atherosclerosis, and lowering blood sugar levels have been the subject of numerous studies on the use of herbs in medicine in Indonesia.[2,3] Long-term consumption of Garcinia mangostana Linn does not adversely affect immunity, liver, or renal functions. Instead, it has a significant anti-inflammatory and antioxidant effects.[4] Garcinia mangostana Linn has a wide safety index and does not cause death.[5]

From research conducted on mice with diet-induced metabolic syndrome, which increases sugar and saturated fat levels and causes obesity, hypertension, left ventricular stiffness, dyslipidemia, and a fatty liver, it was determined that Garcinia mangostana Linn has anti-inflammatory effects. Garcinia mangostana Linn pericarp supplementation with 5% of diet-induced metabolic syndrome rats' diet, or 168 mg/kg/day α-mangostin, 355 mg/kg/day procyanidins, 3.9 mg/kg/day thocyanin, and 11, 8 mg/kg/day of hydroxycitric acid, for 8 weeks, can reduce body weight, alter mice's physiology and metabolism, and decrease the amount of waist fat deposition, waist circumference, and total body fat mass.. According to the study's findings, chronic Garcinia mangostana pericarp consumption can lessen inflammatory cell infiltration in mice with diet-induced metabolic syndrome, which in turn can lessen the symptoms of metabolic syndrome, liver problems, and cardiovascular disease.[5,6]

A recent advancement in nanotechnology allows for the transportation of drugs, proteins, peptides, and particles in structures as small as 0.1 to 100 nm.[7] The pericarp extract (MPE) of Garcinia mangostana Linn was successfully synthesized using polyvinylpyrrolidone (PVP) nanofiber mats, which increased the activity of the antioxidant release rate. However, further in vivo research is required to confirm the MPE's potential for anti-inflammatory and antioxidant effects.[8]

Another study was similarly successful in determining that the therapeutic efficacy of α-Mangostin (MG) microemulsion can be increased. The Alpha (α)-Mangostin-loaded self-microemulsion (MG-SME) has the potential to be a drug loading system characterized by encapsulation efficiency, size distribution, and morphology, resulting in high performance in terms of pharmacokinetics and tissue distribution.[9]

As a nano-sized delivery system, aqueous MG-SNE's spherical particles with an average diameter of 24.6 nm and an encapsulation efficiency of 87.26% effectively promote absorption in the digestive tract and alter its distribution in tissues. Specifically, the alteration of nanomicelles enhanced the solubility of α-mangostin by a factor of more than 10,000. Furthermore, polymeric nanoparticles allowed for targeted delivery and greatly improved the bioavailability of MG-SNE.[9] The purpose of this study is to demonstrate that waist circumference in Wistar rats with atherogenic diets can be decreased by MG-loaded self-nanoemulsion therapy in addition to physical activity.

METHODS

This research is an experimental study with a randomized pre- and post-test control trial (RCT) design. The research was conducted for 9 weeks, consisting of 1 week of acclimatization and 8 weeks of treatment. Male *Rattus norvegicus Wistar* strain mice, aged 6 to 8 weeks, who were active, met the inclusion criteria for this study. Meanwhile, mice who appeared unwell or crippled met the exclusion criteria for this study. This study reports changes in waist circumference in male Wistar rats given an atherogenic diet for eight weeks that included high fat (2023% by weight; 40–45% kcal from fat), saturated fatty acids (>60% of total fatty acids), milk fat or butterfat, sucrose (34% by weight), and cholesterol (0.2% total) in order to induce atherosclerosis. The animal model was treated with physical exercise combined with the administration of statins, *Garcinia mangostana Linn pericarp extract*, and MG-loaded self-nanoemulsion. Physical training was carried out by running 60 minutes at a speed of 12 m/minute, 5 days per week, for 8 weeks on a special rodent treadmill set at an incline of 0.

In total, 15 samples were used in this study, which were divided into 3 groups: 5 samples were used as the control group, which received treatment for 8 weeks consisting of parenteral administration of Atorvastatin 1.44 mg and physical exercise; 5 samples were used as treatment group 1 (P1), which received parenteral administration of Garcinia mangostana Linn pericarp extract at a dose of 800 mg/kg, divided into

3 administrations, along with physical exercise; and 5 samples were used as treatment group 2 (P2), which received parenteral administration of MG-loaded self-nanoemulsion 50 mg/kg once, along with physical exercise. Then, both before and after therapy, the research subjects' waist circumference was measured using a metline. The research was conducted at the Biomolecular Laboratory of Sultan Agung Islamic University The study adhered to national criteria for the care and use of laboratory animals and was authorized by the Faculty of Medicine, Diponegoro University's Health Research Ethics Committee (approval number: 51/EC/H/FK-UNDIP/VI/2022).

RESULTS

The average (mean) waist circumference of the mice was 201.43 ± 7.27 mm prior to treatment, according to the data collected. Following the course of treatment, there was a decrease in waist circumference, with a mean measurement of 186.88 ± 11.00 mm (see Table 1, Figure 1).

The results of the normality test of waist circumference data using Saphiro-Wilk showed a $p>0.05$ value in groups K and P1 before treatment. Meanwhile, in group P2, there was no normality test value because the waist circumference before treatment in group P2 was the same at 200 mm. Meanwhile, after treatment, groups K and P1 could not be tested for normality of data because,

at the end of the treatment, there were only 2 rats left. In group P2, after treatment, a $p>0.05$ was obtained, so it can be concluded that the data was normally distributed (Table 2).

Based on the results of the average waist circumference data before and after treatment obtained, it was found that the largest waist circumference difference was obtained in group P2, which received *MG-loaded self-nanoemulsion* 50 mg/kg once administered per round and physical exercise for 8 weeks (Figure 2).

Furthermore, a paired t-test was conducted using a paired T-Test for pre-test and post-test data. At the same time, a one-way ANOVA was used to compare treatment groups.

The results of the paired t-test between the Pre-test and the post-test Waist Circumference in groups K, P1, and P2 showed that the p-value was > 0.05, so there was no significant difference.

From the results of the unpaired t-test between groups K-P2 before treatment, no significant difference was found ($p>0.05$), with the Levene test $p<0.05$, so it can be concluded that the data obtained is not homogeneous. Meanwhile, waist circumference after treatment showed a value of $p>0.05$, and the Levene test $p>0.05$, so it can be concluded that there was no significant difference in waist circumference between groups, and the data obtained was homogeneous. Likewise, the delta WC obtained between groups showed a value of $p>0.05$ and

TABLE 1
Mean and Median Waist Circumference of the Rats

Variable	Mean ± SD (mm)	Median (min – max) (mm)
Pre-test	201.43 ± 7.27	200 (190 – 421)
Post-test	186.88 ± 11.00	185 (170 – 200)
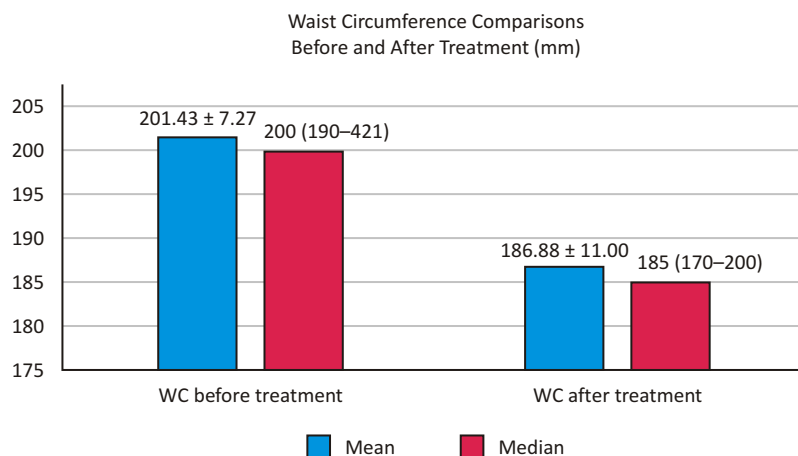
Figure 1. Difference between the mice's mean and median waist circumferences before and after treatment

TABLE 2
Descriptive and normality tests for waist circumference

WC	Groups	N	Mean ± SD (mm)	Median (min – max)	p
Pre-test	K	5	200.00 ± 10.00	200 (190 – 210)	0.119*
	P1	5	203.33 ± 10.33	200 (190 – 220)	0.473*
	P2	5	200.00	200,00	–
Post-test	K	2	190.00 ± 14.14	190 (180 – 200)	–
	P1	2	192.50 ± 3.54	192,5 (190 – 195)	–
	P2	4	182.50 ± 12.58	180 (170 – 200)	0.406*
Delta	K	2	-5.00 ± 21.21	-5 (-20 – 10)	–
	P1	2	-12.50 ± 24.75	-12,5 (-30 – 5)	–
	P2	4	-17.50 ± 12.58	-20 (-30 – 0)	0.406*

Details: * Normal ($p > 0.05$)
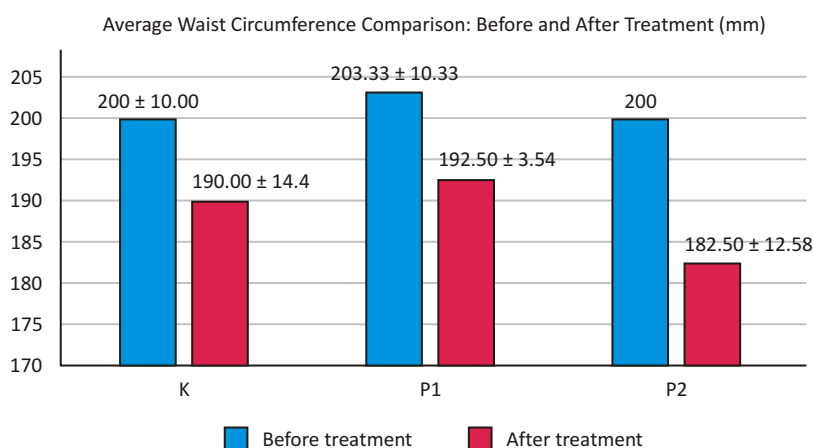
Figure 2. Average waist circumference comparison graph pre- and post-treatment

the Levene test $p>0.05$, so it can be concluded that there was no significant difference between groups, and the data variance was homogeneous (Table 3).

DISCUSSION

Waist circumference indicates intra-abdominal adipose tissue and increases the risk of cardiometabolic disease.[10,11] Based on the Cross-Sectional Study by Badrooj *et al.* in 2022, the potential for inflammatory processes can also be seen from anthropometry, one of which is waist circumference. The study also mentioned that a Pro-inflammatory Diet will increase Waist Circumference, including poor anthropometric measurements. An increase in waist circumference will increase metabolic risk, so it is recommended to provide cardioprotective drug therapy.[12]

Previous studies have found that mangosteen contains xanthone, a substance with anti-inflammatory

and antioxidant activity from mangosteen peel isolation. The compound α-mangosteen has been found to have a variety of biological activities, with anti-inflammatory, anti-tumor, cardioprotective, antidiabetic, antibacterial agents, antifungal, antiparasitic, antioxidant, and anti-obesity. This supports the results of research that α-mangosteen compounds have activity as cardioprotective and can reduce waist circumference.[12]

Based on a study by Ibrahim MY *et al.* in 2016, the compound α-mangostin induces apoptosis of 3T3-L1 preadipocytes by inhibiting fatty acid formation and can suppress intracellular lipid accumulation in differentiated adiposity and stimulation of lipolysis in mature adipocytes. The study further explained that the inhibition of fatty acid formation by α-mangosteen is due to a stronger effect on the ketoacyl formation domain and a weaker effect on the acetyl/malonyl transferase domain. So, based on these studies, the compound α-mangostin is useful in the therapy or prevention of
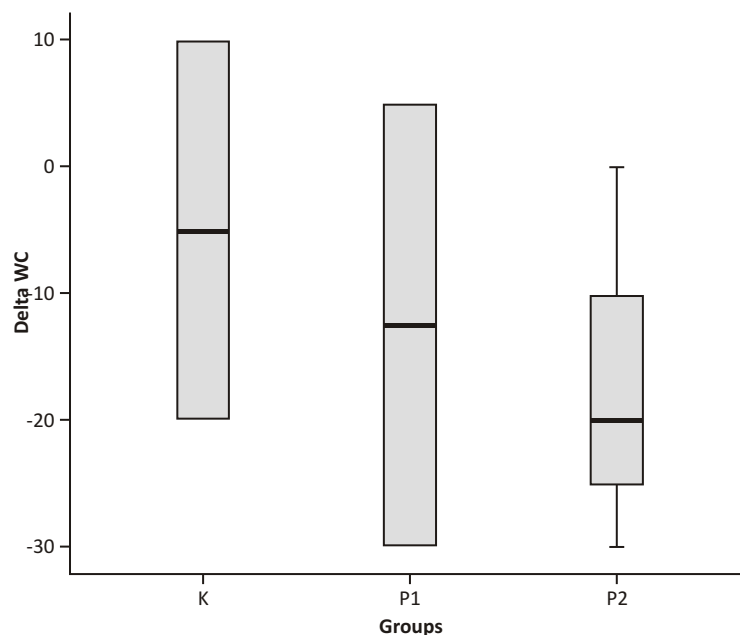
Figure 3. Waist circumference delta amongst groups K, P1, and P2.
There is no significant difference between treatment groups

TABLE 3
Waist Circumference (WC) Difference Test Results

Groups	WC		p	Delta WC
	Pre test	Post test		
K	200.00 ± 10.00	190.00 ± 14.14	0.795[¶]	-5.00 ± 21.21
P1	203.33 ± 10.33	192.50 ± 3.54	0.605[¶]	-12.50 ± 24.75
P2	200.00	182.50 ± 12.58	0.069[¶]	-17.50 ± 12.58
p	0.753[§]	0.594[§]	−	0.727[§]
Lavene	0.018	0.426**	−	0.264**

Details : * Significant ($p < 0.05$); ** Homogen ($p > 0.05$); ¶ Paired t; § One Way Anova

obesity.[13]

A significant relationship exists between increased waist circumference and the prevalence of abdominal obesity. Where an increase in waist circumference can also increase the risk and prevalence of abdominal obesity. Based on the research by Robert Ross in 2020, an increase in waist circumference is also a major cause of increased risk factors for cardiometabolic events. Thus, decreasing waist circumference will also reduce the risk of cardiometabolic events.[14]

Based on the results of the study, it was found that there was a decrease in waist circumference in the control group who received treatment with Atorvastatin 1.44 mg once administered per round and physical exercise for 8 weeks; treatment group 1 (P1) which was given *Garcinia mangostana Linn pericarp extract*, at a dose of 800 mg / kgbb, divided by 3 times administration, per round, and

physical exercise for 8 weeks; and treatment group 2 (P2) which was given MG-loaded self-nanoemulsion 50 mg/kg once administered, per round, and physical exercise for 8 weeks. This is based on the research of Oliver *et al.*, where it was found that supplementation of *Garcinia mangostana Linn pericarp* as much as 5% of the diet of rats with diet-induced metabolic syndrome, or a dose of 168 mg/kg/day α-mangosteen, 355 mg/kg/day procyanidins, 3.9 mg/kg/day thocyanin and 11.8 mg/kg/day hydroxy citric acid, for 8 weeks, can reduce body weight, change the physiology and metabolism of rats, reduce waist fat deposition, reduce waist circumference and whole body fat mass.[6]

A crucial factor in determining how well drug molecules move through pharmacological phases including biopharmaceutics, pharmacokinetics, and pharmacodynamics is drug bioavailability. One of the
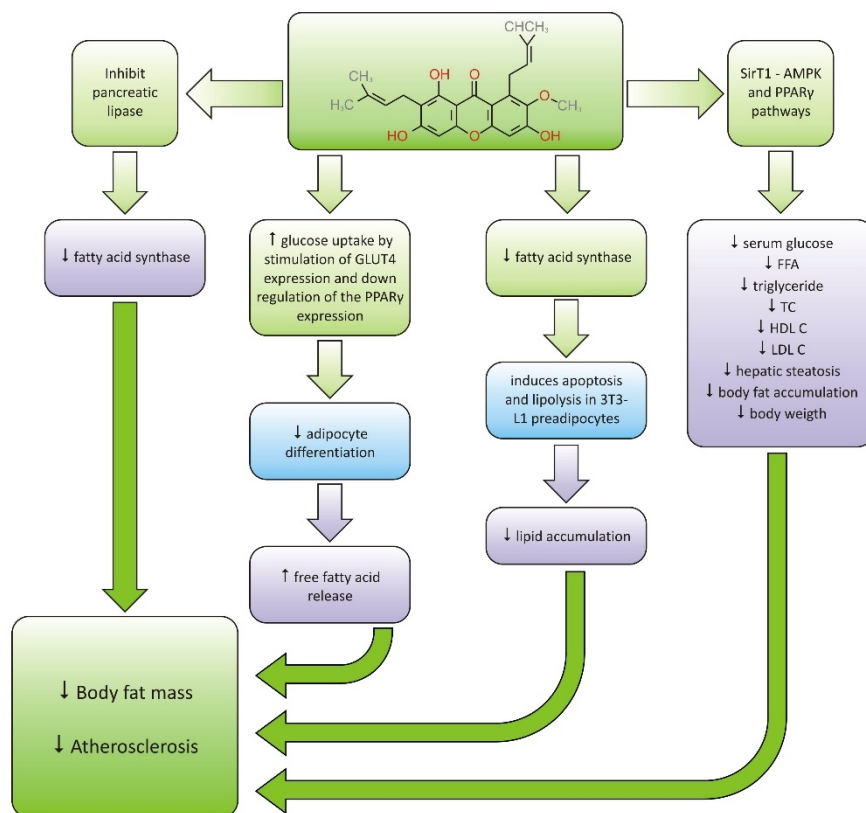
Figure 4. Diagram illustrating the method by which α-mangostin reduces body fat mass.
GLUT4: Glucose transporter type 4; PPARγ: peroxisome proliferator-activated receptor-γ; SirT1: Sirtuin 1;
AMPK: 50 AMP-activated protein kinase; FFA: free fatty acids; TC: total cholesterol;
HDL: high density lipoprotein; LDL: low density lipoprotein.[1]

main characteristics that can boost a drug's bioavailability to the maximum is its solubility in water. At the moment, the most widely utilized method for treating diseases with nanomedicine is the utilization of drug delivery systems based on nanoparticles. Based on a study by Tri Rizki in 2023, nanoemulsion is an emulsion system with a particle size between 10 and 100 nm, with very small droplet size characteristics. The principle of nanoemulsion synthesis uses a high-energy method by dispersing the material using high energy to produce a small-sized suspense so that it will shorten the homogenization cycle by providing an attraction that expands the surface of the material that interacts with the homogenizer.[15]

According to the study results, rats in group P2 who received MG-loaded self-nanoemulsion 50 mg/kg once administered per round and physical exercise for 8 weeks experienced the greatest decrease in waist circumference. This is possible because nanoemulsions can increase the potential for clinical efficacy due to improved pharmacokinetic performance of the drug loading system, encapsulation efficiency, size distribution, morphology, and tissue distribution. Furthermore, the nano-sized delivery system will efficiently improve gastrointestinal absorption.

A study by Belalcazar *et al.* 2013 found that research subjects given statins only experienced weight loss but no decrease in waist circumference. Meanwhile, this study found a decrease in waist circumference in the P1 group who received Atorvastatin 1.44 mg once administered per round and physical exercise for 8 weeks. This is not show by previous studies. The decrease in waist circumference in group P1 may be due to physical exercise performed by rats.[16]

Based on the research results by Sinha *et al.* in 2020, it was stated that treadmill exercise for 12 weeks can reduce central obesity.[17] Physical exercise reduces body weight, waist circumference, fat mass (especially visceral fat), blood pressure, and inflammation. Physical exercise can also improve insulin sensitivity.[18–20] In addition, based on research by Pons *et al.* in 2013, physical exercise has a cardioprotective effect, especially in cases of obesity.[21]

CONCLUSION

According to the results of this study, waist circumference in Wistar rats that have been given an atherogenic diet can be decreased by administering an MG-loaded self-nanoemulsion along with physical activity.

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Original Article

Comparison Between Robotic Finger Therapy Exercise and Conventional Exercise on the Range of Motion of the Metacarpophalangeal Joints: Study of Post-stroke Patients at Diponegoro National Hospital

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Abstract

Background : Metacarpophalangeal (MCP) joints range of motion (RoM) exercise can be done using either conventional exercise or robotic finger therapy. This study aimed to compare MCP joints RoM improvement between conventional exercise and robotic finger therapy exercise in post-stroke patients.

Methods : This study was a randomized controlled trial pre and post test controlled group design. The data were taken from individuals aged 45–65 years with a history of stroke undergoing medical rehabilitation at the Diponegoro National Hospital before and after intervention (robotic finger therapy exercise vs conventional exercise) for 6 weeks. MCP joints RoM was measured using goniometer before and after the intervention. Datas were analysed using SPSS ver 20.0. Normality of data distribution would be assessed using the Shapiro-Wilk test. Differences in the RoM of MCP joints before and after treatment in each group were tested using paired t-test. Group differences were tested using unpaired t-test.

Results : There was significant RoM improvement in each MCP joint in each group before and after the treatment ($p < 0.05$). There was no significant difference in RoM improvement between groups ($p > 0.05$).

Conclusion : Both robotic and conventional therapy significantly improve MCP joints RoM in post-stroke patients. There was no significant difference in MCP joints RoM improvements between robotic finger therapy and conventional exercise.

Keywords : conventional exercise, robotic finger therapy, metacarpophalangeal joints range of motion.

INTRODUCTION

The number of individuals suffering from stroke continues to increase. Based on *Riset Kesehatan Dasar* (RISKESDAS), the prevalence of stroke is currently 10.9%, increasing from the data in 2013.[1,2] In post stroke patients, metacarpophalangeal (MCP) joints range of motion (RoM) decreased due to spasticity of flexor synnergic pattern.[3]

Stretching is a general term used to describe any therapeutic maneuver designed to increase soft tissue elongation, thereby increasing flexibility by lengthening structures that have been shortened. Stretching exercises are very effective in reducing spasticity through tissue extensibility.[4] The elongation of collagen tissue can be maintained due to changes in the organization of collagen fibers and by changes in the viscoelasticity of collagen fibers that occur after continuous stretching.[5] Conventional exercise by repetitively moving joints through their full RoM aims to improve their RoM, but requires an one-on-one session with a therapist which limits its own availability (therapists as human resources).[6]

According to the American College of Sports Medicine, the recommended stretching exercise prescription for stroke patients is as follow. Type of exercise is passive static flexibility, with frequency of ≥ 2–3 times/ week, mild to intensity discomfort is felt in the stretched joint. Hold the stretch for 10–30 seconds, 2–4 repetitions for each stretch exercise.[7]

Robotic finger therapy is classified as therapeutic device meaning that the robotic device is expected to exert therapeutic effects. Robotic finger therapy is also classified as exoskeleton robotic device. To exert its therapeutic effect, robotic device needs to be secured around certain points on the body parts, hence the name exoskeleton. Robotic finger therapy can also be implemented to improve joint RoM by using same mechanism of action but without conventional exercise's limitation in human resource (therapist) availability.[6,8,9]

Currently there is no research comparing robotic therapy and conventional exercise in improving MCP RoM of post-stroke patients. This research aimed to determine the effectiveness and compare MCP joints RoM improvements between robotic finger therapy and conventional exercise in post-stroke patients at Diponegoro National Hospital.

METHODS

This study was carried out at Diponegoro National Hospital and was carried out from February to May 2023. This study was a randomized controlled trial pre test and post test controlled group design to determine the effect of finger therapy equipment training on the RoM of MCP joints in post-stroke patients. Participants in the intervention group performed robotic exercises 3 times a week for 6 weeks. The control group received conventional exercise 3 times a week.

The target population was individuals with a history of stroke. Inclusion criteria were as follows: (1) age 45–65 years; (2) diagnosed with stroke 6 months ago or more (chronic stroke) with weakness on one side; (3) Elbow flexor muscle strength with MMT > 3; and (4) Spasticity in the elbow joint (Tardieu scale <3). Exclusion criteria were as follows: (1) other neuromuscular diseases that can affect muscle tone; (2) systolic blood pressure > 160 mmHg and/or diastolic >100 mmHg; (3) there are contractures in the upper extremities, history of musculoskeletal injuries in both upper extremities; (4) there is dislocation or subluxation of the shoulder; (5) INA MoCA score < 26; (6) currently on antispastic therapy or other drugs that can affect muscle tone in the last 3 months; and (7) have uncorrected visual impairment. Drop out criteria were as follows: (1) failure to show to the therapy schedule more than 3 times non-consecutive or 2 times consecutively; and (2) did not come at the beginning and end of the research assessment. Subjects were recruited using consecutive sampling method then randomized into robotic therapy and
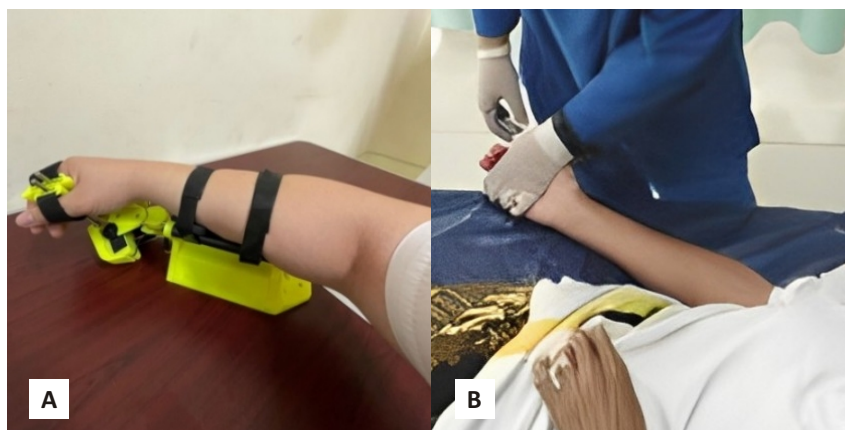
Figure 1. (A) Robotic finger therapy; (B) Conventional therapy
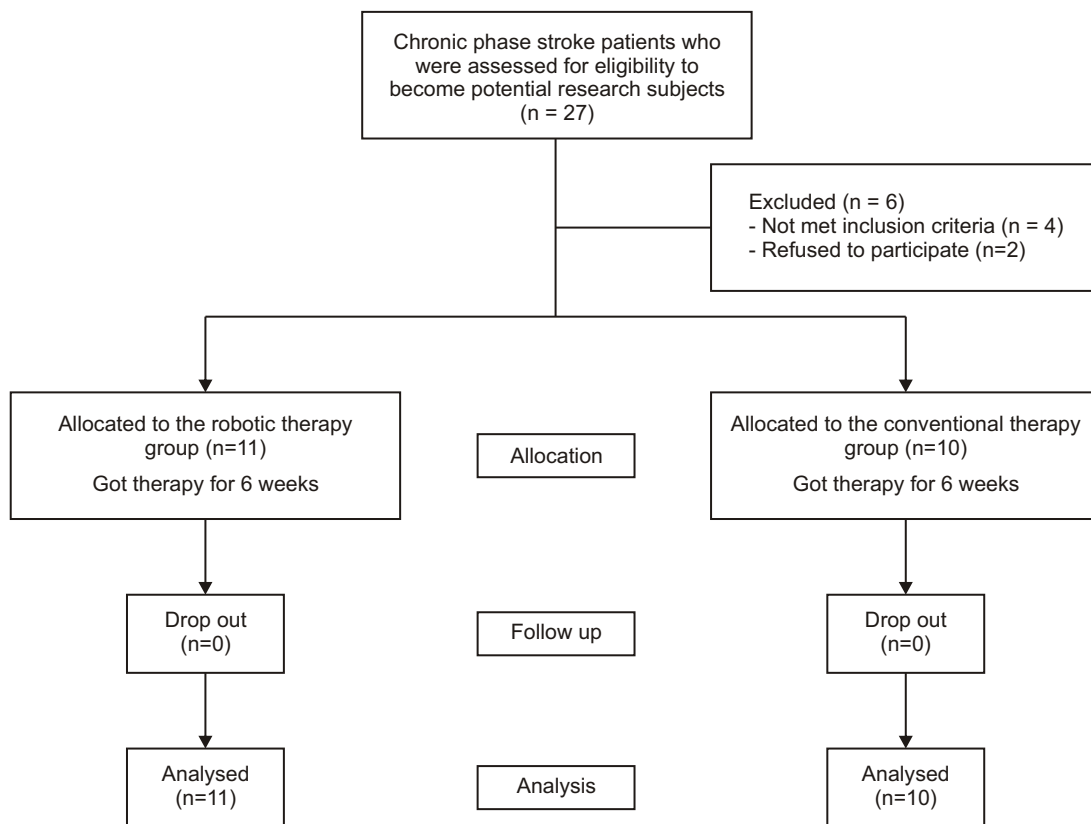
Figure 2. Consort diagram of data sample selection

conventional therapy group.

Robotic finger therapy has static part to support patient's lower arm and secure it with velcro. The moving (dynamic) part was the hand part. On the hand part there are two iron rods where plastic supports were installed. One plastic support would support digits II–V then tightened with velcro. The other plastic support would support digit I with the same mechanism. After the robotic device was turned on, the two plastic supports would move away from each other so that they provided an extension effect on the MCP I–V joints. Robotic finger therapy was given 3 times/week, with intensity until strech was felt on MCP joints (00 extension). 80 repetitions of extension were given with intervention time about 10 minutes.

Conventional therapy was carried out by therapist. Stretching exercise was given 3 times/week, with intensity until the strech was felt on MCP joints (00 extension). Each stretch was held for 10 seconds, then repeated stretch 10 times to conclude a set. A total of 2 sets were given in one therapy session.

MCP joints RoM was measured using goniometer before and after the intervention. MCP joints RoM was measured by same instrument and by principal investigator & research team. Data was collected in data collection sheets and coded, tabulated in the computer. Data analysis included descriptive analysis and hypothesis testing. Normality of data distribution was assessed using the Shapiro-Wilk test. P value of ≥ 0.05 showed that data was normally distributed.

The differences in the RoM of the MCP joints based on goniometer measurements before and after exercise in each group were tested using the paired t-test for data that was normally distributed and Wilcoxon test for data that was not normally distributed. The differences in the RoM of the MCP joints based on goniometer measurementus between groups that received robotic therapy and conventional therapy were tested using the unpaired t-test for data that was normally distributed and Mann-Whitney test for data that was not normally distributed. All data was processed with the help of a computer using SPSS® software ver 20.0. Significance in this study was obtained with a p value <0.05.

This study has been reviewed and approved by the Health Research Ethics Commission (KEPK), Faculty of Medicine, Diponegoro University with Document No. 123/EC/KEPK/FK-UNDIP/IV/2023.

RESULTS

Twenty seven datas of post-stroke patients were gathered. Six out of 27 were excluded due to failure to meet the exclusion criteria (n=4) and refusal to participate (n=2). The consort diagram of data sample selection was

shown in Figure 2.

Baseline characteristics of both groups were shown in Table 1. The table showed the results of the homogeneity test of baseline characteristics consisting of age, sex, duration from stroke onset, and stroke type. There was no significant difference between the robotic therapy group and conventional therapy group, with p-value >0.05. Demographic characteristics in both groups were homogenous.

Descriptive table and normality of MCP joints RoM before therapy were shown in Table 2. The table showed the results of the homogeneity test of RoM of MCP I-V before therapy in each group. There was no significant difference between of RoM of MCP I-V joints before therapy in conventional therapy group, with

p-value >0.05. In robotic therapy group, significant differences were found for MCP II-IV joints, but no significant difference was found for MCP I & V joints.

The analysis of MCP I joint RoM improvement before and after therapy in each group and between group were shown in Table 3. Improvement of MCP I joint RoM before and after therapy both in robotic and conventional therapy group were found to be both significantly different (p<0.05). Improvement of MCP I joint RoM before and after therapy between robotic and conventional therapy group (improvement delta) was found to be not significantly different (p = 0.952).

The analysis of MCP II-V joint RoM improvement before and after therapy in each group and between groups were shown in Table 4–7. Improvement of MCP

TABLE 1
The baseline characteristics of data subjects

Variable	Group		p
	Robotic Therapy (11)	Conventional Therapy (10)	
Age (years)	57.27 ± 4.98	59.40 ± 6.08	0.217[‡]
Sex			0.562[¥]
Male	7 (50%)	7 (50%)	
Female	1 (25%)	3 (75%)	
Duration from stroke onset (months)	13.91 ± 5.30	20.30 ± 8.08	0.044[§*]
Stroke type			0.124[¥]
Hemorrhagic stroke	3 (100%)	0 (0%)	
Non hemorrhagic stroke	8 (44.4%)	10 (55.6%)	

*Significant (p<0.05); [¥]Chi square; [§]Independent t; [‡]Mann Whitney

TABLE 2
Normality of MCP joints RoM before therapy

Joint RoM	Group	Mean ± SD	Median (min–max)	p
MCP I (degree)	Robotic therapy	22.27 ± 12.72	20 (5–45)	0.345*
	Conventional therapy	26.50 ± 14.15	25 (10–55)	0.304*
MCP II (degree)	Robotic therapy	34.55 ± 30.29	25 (10–110)	0.008
	Conventional therapy	75.80 ± 24.83	77.5 (45–120)	0.499*
MCP III (degree)	Robotic therapy	39.55 ± 28.94	30 (20–115)	0.001
	Conventional therapy	81.00 ± 27.06	87.50 (40–120)	0.509*
MCP IV (degree)	Robotic therapy	40.45 ± 29.70	30 (15–120)	0.003
	Conventional therapy	77.00 ± 29.83	80 (30–120)	0.808*
MCP V (degree)	Robotic therapy	41.82 ± 24.73	40 (15–100)	0.156*
	Conventional therapy	76.00 ± 31.07	80 (20–120)	0.305*

*Normal (p > 0.05); [£]Shapiro–Wilk

TABLE 3
Analysis of MCP I joint RoM

MCP I RoM	Group		p
	Robotic Therapy (11)	Conventional Therapy (10)	
Pre test (degree)	22.27 ± 12.72	26.50 ± 14.15	0.480[§]
Post test (degree)	39.55 ± 8.50	44.00 ± 9.37	0.267[§]
P	<0.001[¶*]	<0.001[¶*]	
Delta (degree)	17.27 ± 7.20	17.50 ± 9.79	0.952[§]

*Significant (p < 0.05); [§]Independent t; [¶]Paired t

TABLE 4
Analysis of MCP I joint RoM

MCP II RoM	Group		p
	Robotic Therapy (11)	Conventional Therapy (10)	
Pre test (degree)	34.55 ± 30.29	75.80 ± 24.83	0.007[‡*]
Post test (degree)	51.82 ± 24.73	94.00 ± 24.47	0.002[‡*]
P	0.001[¶*]	0.002[¶*]	
Delta (degree)	17.27 ± 12.32	18.20 ± 13.59	0.871[§]

*Significant (p < 0.05); [§]Independent t; [‡]Mann Whitney; [¶]Paired t

II-V joint RoM before and after therapy both in robotic and conventional therapy group were found to be both significantly different (p<0.05). Improvement of MCP II-V joint RoM before and after therapy between robotic and conventional therapy group (improvement delta) was found to be not significantly different. Improvement delta p values were 0.871, 0.359, 0.586, and 0.573 for MCP II–V respectively.

DISCUSSION

This study showed that there were significant improvements in MCP I–V joints RoM in both robotic and conventional therapy group before and after therapy. In the robotic therapy group, RoM increased by 17.27 ± 7.20, 17.27 ± 12.32, 18.18 ± 12.30, 17.27 ± 11.70, and 18.64 ± 12.06 for MCP I–V respectively. In conventional therapy group, RoM increased by 17.50 ± 9.79, 18.20 ± 13.59, 13.00 ± 12.95, 14.50 ± 11.17, and 15.50 ± 13.01 for MCP I–V respectively.

Underlying pathology in post-stroke spasticity showed that there was decrease hyaluronic in acid turnover, increase in intramuscular connective tissue deposition, and increase in extracellular connective tissue viscosity. Those three mechanisms will in turn reduce the threshold for stimulation of spindle in the muscle and decrease golgi tendon organ function leading to spasticity. In time, increase in viscosity of the loose connective tissue may cause decreased gliding between the layers of collagen fibers, which may be perceived by patients as stiffness.[10] Another mechanism of spasticity relates to postactivation depression. Postactivation depression is a phenomenon that controls the excitability of the stretch reflex acting at the spinal level without depending on supraspinal control. It appears to be independent of the influences exerted by rostral centres. In stroke patients, postactivation depression decreases due to limb immobilization.[11] Mechanisms behind stretching and mobilization can reduce spasticity are that the increased extracellular connective tissue spasticity can be counteract by stretching and limb mobilization can restore post active depression.[10,11]

There were no significant differences in RoM improvements between robotic and conventional therapy group for each MCP joint. Comparing MCP I RoM improvements between robotic and conventional therapy group yielded p-value of 0.952. P-values were 0.871, 0.359, 0.586, and 0.573 for MCP II-V RoM improvements between robotic and conventional therapy group respectively.

Those findings were in conjunction with some previous studies. The study by Francisco J Valero-Cuevas in 2016 showed inconclusive result comparing robot-assisted vs. conventional therapy in 77 patients who had had chronic motor impairment after a cerebrovascular

TABLE 5
Analysis of MCP III joint RoM

MCP III RoM	Group		p
	Robotic Therapy (11)	Conventional Therapy (10)	
Pre test (degree)	39.55 ± 28.94	81.00 ± 27.06	0.004[‡*]
Post test (degree)	57.73 ± 26.30	94.00 ± 25.69	0.005[§*]
P	0.001[¶*]	0.011[¶*]	
Delta (degree)	18.18 ± 12.30	13.00 ± 12.95	0.359[§]

*Significant ($p < 0.05$); [§]Independent t; [‡]Mann Whitney; [¶]Paired t

TABLE 6
Analysis of MCP IV joint RoM

MCP IV RoM	Group		p
	Robotic Therapy (11)	Conventional Therapy (10)	
Pre test (degree)	40.45 ± 29.70	77.00 ± 29.83	0.009[‡*]
Post test (degree)	57.73 ± 26.40	91.50 ± 29.54	0.018[‡*]
P	0.001[¶*]	0.003[¶*]	
Delta (degree)	17.27 ± 11.70	14.50 ± 11.17	0.586[§]

*Significant ($p < 0.05$); [§]Independent t; [‡]Mann Whitney; [¶]Paired t

TABLE 7
Analysis of MCP V joint RoM

MCP V RoM	Group		p
	Robotic Therapy (11)	Conventional Therapy (10)	
Pre test (degree)	41.82 ± 24.73	76.00 ± 31.07	0.011[§*]
Post test (degree)	60.45 ± 26.78	91.50 ± 27.79	0.017[§*]
P	0.001[¶*]	0.004[¶*]	
Delta (degree)	18.64 ± 12.06	15.50 ± 13.01	0.573

*Significant ($p < 0.05$); [§]Independent t; [‡]Mann Whitney; [¶]Paired t

accident.[12] Study by Cora Carrillo in 2023 revealed that the effects of robotic therapy and conventional therapy were similar, and that robotic therapy combined with conventional therapy was not superior to conventional therapy alone.[13]

The absence of significant differences between RoM improvements between robotic and conventional therapy group for each MCP joint can be explained by lack of therapy intensity, frequency and duration, especially for the robotic therapy group. The study by Nero Singh in 2021 comparing robotic and conventional groups for post-stroke rehabilitation, the protocol for the robotic group was 45-minute of individual sessions perday for 20 therapy sessions (5 days a week for 4 weeks). In this study, comparing active RoM improvements between robotic-therapy and control group, the difference was significant with p-value of 0.02.[14] Systematic review and meta-analysis by Lee Bih-O in 2023 evaluating robotic arm use for upper limb rehabilitation after stroke, the duration of the intervention varied from 3 to 5 times per week for 30 to 120 min per session. The duration of the intervention ranged from 3 to 12 weeks.[15]

However, there are some other aspects in which robot are better than conventional therapy. Robots can enhance existing conventional therapy by delivering a

precise and consistent therapy of highly repetitive movements. Robot assisted physiotherapy could facilitate the effectiveness of unsupervised rehabilitation and thus, may reduce the cost and duration of therapist-assisted rehabilitation.[16] Additionally, robotic rehabilitation can potentially increase patient motivation and engagement. It is worthy to note that the use of robotics for rehabilitation is viewed as acceptable, useful, and beneficial by patients and healthcare professionals.[17] This study had some limitations that might affect the study results. Sample size was relatively small, and protocols implemented in this study lacked in intensity, frequency, and duration.

CONCLUSION

Both robotic and conventional therapy significantly improve MCP joints RoM in post-stroke patients. There were no significant differences in MCP joints RoM improvements between robotic finger therapy and conventional exercise.

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Original Article

Perineal Laceration in Primipara in Association with Perineal Length, Fetal Head Circumference, and Fetal Weight

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Abstract

Background : Perineal laceration is one of the risk and complication of spontaneous labour resulting intervention in short-term and long-term quality of life. Lack of research on perineal length in Indonesia, fetal birth weight and fetal head circumference and its impact on spontaneous labour and perineal laceration gave rise to the idea of research in order to minimize the occurrence of complications from perineal laceration in spontaneous labour. The aims of this study was to know find out the association between perineal length, fetal head circumference, and fetal weight with degree of perineal laceration in primiparous women.
Methods : Observational cross sectional multi-center study conducted between August 2023 until October 2023 in which all subject that delivered vaginally within inclusion criteria was measured. All data will be further analized to determine the significant predictor of perineal tear.
Results : The result of this study has indicated that there is no significant association of perineal length with the degree of spontaneous primiparous perineal laceration. While there is an association of fetal head circumference and fetal weight with the degree of spontaneous primiparous perineal laceration in aterm pregnancy. Based on further analysis, fetal head circumference greater than 325 mm increases the risk of severe perineal laceration 4.4 times (PR=4.4; 95% CI=1.4–13.9) and Fetal weight greater than 3097.5 grams increases the risk of 2.7 times (PR=2.7; 95% CI=1.1–6.4) the occurrence of severe perineal laceration.
Conclusion : There is an association of fetal head circumference and fetal weight with the degree of spontaneous primiparous perineal laceration.

Keywords : Fetal head circumference, Fetal weight, Perineal laceration, perineal length, Spontaneus labour.

INTRODUCTION

Perineal laceration is one of the risk and complication of spontaneous labour resulting intervention in short-term, i.e perineal pain; sexual dysfunction, and long-term quality of life i.e fecal incontinence, rectovaginal fistula, and psychological trauma. Based on the data from 2013 at Dr. Cipto Mangunkusumo Hospital, prevalence of perineal laceration in spontaneous labour reached 74.1% with 8.2% prevalence of anal sphincter injury.[1]

Severe perineal laceration risk factor during labour can be caused by multiple risk factors. Perineal length and elasticity, body mass index, age and number of parities may contributes due to compliance of the tissue. Fetal risk factors like head circumferences, malposition, and shoulder dystocia may disrupt the descent. Meanwhile for obstetric risk factors such as birth attendant, labour duration, instrumental delivery, and selective episiotomy may have a share in severe perineal laceration. Perineal body, head circumference and fetal weight are non modifiable factors in labour and delivery which have a great impact on perineal laceration severity. Lack of research in Indonesia gave rise to the idea of research in order to minimize the occurrence of complications from perineal laceration in spontaneous labour.[2,3]

METHODS

This study conducted between August 2023 until October 2023, consecutive nulliparous women whom underwent spontaneous labour in 5 Center Hospitals that considered eligible for the study gave a written informed consent. Inclusion criteria were : 1) All nulliparous women in labour with aterm pregnancy, 2) above 20 years old, 3) single fetus, cephalic presentation, 4) without prior vaginal and/or anal surgery was recruited. Exclusion criteria were : All delivery in which ending in caesarean section, assisted delivery with episiotomy, and instrumental delivery was excluded. Ethical Clearance obtained from each center. Characteristic of each participants were collected.

Measurement of perineal length obtained during the first stage of labour by appointed birth attendant with a POP-Q ruler. Perineal laceration severity will be classified with WHO classification by the same birth attendant. While other data such as duration of second stage of labour, fetal head circumference, fetal birth weight, and degree of laceration was obtained after the delivery of fetus.

Statistical analysis was performed with SPSS ver 24.0 with cross sectional methods. Univariate analysis used to present the characteristics, while bivariate using Chi-Square was used for correlation between each criteria. Logistic regression analysis was used to determine significant factor of perinal laceration. While ROC curve analysis was displayed to procure a cut off point.

RESULTS

During the study period, 75 out of 152 patients met the inclusion criteria; their characteristic are shown on Table 1. Among 75 spontaneous labour, 18 suffered third degree perineal laceration (24%), while the mean of perineal length is 30.81±8.39 mm, fetal head circumference 326.27±17.28 cm, and fetal weight of 3020.1±400.8 grams.

On bivariate analysis based on perineal length, fetal head circumference, fetal weight, second stage of labour duration, and IMT, there are significant correlation between fetal head circumference and fetal weight with $P<0.05$, and IMT was found as a confounding factors in determining degree of perineal laceration with $P<0.25$ (Table 2–6).

Based of logistic regression analysis, it was concluded that fetal head circumference is the most significant factor in determining the degree of perineal laceration during spontaneous labour (Table 7).

In ROC curve was analyzed for cut off point of each risk factors, in which the result can be seen in Table 8.

Based on the cut off points, on each variable was analyzed and thus determined the prevalence ratio of variables in which associated with perineal laceration severity was fetal head circumference > 325mm followed by fetal weight >3097.5 gram.

DISCUSSION

Characteristics of Research Subjects

Total of 75 subjects in this study, the age range of primiparas was 20 to 39 years old, with the largest age range being 25 to 29 years old, 34 subjects (45.3%). In spontaneous labor, the most common laceration was second degree perinal laceration involving the vaginal mucosa and perineal muscles without sphincter anal injury, was found in 47 subjects (62.7%). Obesity was found in 56 subjects (74,7%).

Relationship between Research Variables and the Degree of Laceration

The mean perineal length of primiparas in this study was 31 mm with the lowest range of 23 mm and the highest of 50 mm. This finding resembles a study in Vietnam with a mean length of 3.4 cm and previous research in Indonesia with a mean perineal length of 3.3 cm.[1,3,4] Based on statistical analysis, there was no significant association between perineal length in primiparas and the degree of perineal laceration in spontaneous labor. This is different from the results of previous studies which stated that

TABLE 1
Characteristics of the study population

Characteristics	Frequency n = 75	%	Mean ± SD	Median (min – max)
Age				
20–24	33	44.0		
25–29	34	45.3		
30–34	6	8.0		
35–39	2	2.7		
Education				
Elementary	4	5.3		
Middle School	14	18.7		
High School	36	48.0		
University	21	28.0		
Occupation				
Homemaker	52	69.3		
Enterpreneur	23	30.7		
IMT				
Underweight	2	2.7		
Normoweight	6	8.0		
Overweight	11	14.7		
Obesity	56	74.7		
Gestational Age			38.76 ± 1.26	39 (37 – 42)
Oxytocin Usage				
Yes	47	62.7		
No	28	37.3		
Second Stage of labour duration			30.81 ± 8.39	30 (5 – 100)
Perineal length			31.28 ± 5.62	30 (23 – 50)
Head Circumference			326.27 ± 17.28	330 (290 – 390)
Fetal Birth Weight			3020.1 ± 400.8	3000 (2020 – 4300)
Degree of perineal laceration				
Intact	3	4.0		
First	7	9.3		
Second	47	62.7		
Third	18	24.0		
Degree of perinal laceration				
Mild	57	76.0		
Severe	18	24.0		

TABLE 2
Differences of perineal length in each degree of perineal laceration

Degree of laceration	Perineal length		p
	Mean ± SD	Median (min – max)	
Mild	31.23 ± 5.52	30 (23 – 40)	0.881
Severe	31.44 ± 6.08	30 (25 – 50)	

TABLE 3
Differences of fetal head circumference in each degree of perineal laceration

Degree of laceration	Fetal Head Circumference		p
	Mean ± SD	Median (min – max)	
Mild	323.68 ± 17.87	320 (290 – 390)	0.009
Severe	334.44 ± 12.47	330 (310 – 360)	

TABLE 4
Differences of fetal weight in each degree of perineal laceration

Degree of laceration	Fetal Weight		p
	Mean ± SD	Median (min – max)	
Mild	2941.05 ± 370.11	2950 (2020 – 4050)	0.002
Severe	3270.56 ± 400.62	3200 (2655 – 4300)	

TABLE 5
Differences of second stage of labour duration

Degree of laceration	Second stage of Labour duration		p
	Mean ± SD	Median (min – max)	
Mild	30.05 ± 19.13	30 (5 – 100)	0.331
Severe	33.22 ± 16.08	31.5 (10 – 60)	

there was a significant difference from the length of the perineum to the degree of perineal laceration.[3,5,6] This difference can be caused by differences in research subjects, namely in this study only observing the length of the perineum of primigravida patients did not performed episiotomy nor instrumental delivery. The elasticity factor of the birth canal that can affect the labour process has not been assessed in this study. In further assessment, elasticity examination with sonoelastography may be performed to assess the elasticity of the birth canal.[6]

This study found that patients with a mean fetal weight of 2941.05 ± 370.11 grams had mild laceration and 3270.56 ± 400.62 grams had severe laceration. The findings of this study are similar to previous studies conducted in Indonesia which stated that the birth weight of babies over 3150 grams had perineal lacerations of degree III–IV.[3] The greater the fetal weight, the greater the dimensions of the fetal body size, this will be related to the head circumference, chest circumference, and fetal body length which in the process of labor will be one of the factors that determine the strain on the mother's birth canal.[7]

TABLE 6
Differences of IMT

| IMT | Perineal Laceration | | | | p |
| | Severe | | Mild | | |
	n	%	n	%	
Underweight	1	50	1	50	0.176
Normoweight	1	16.7	5	83.3	
Overweight	0	0	11	100	0.881
Obesitas	16	28.6	40	71.4	

TABLE 7
Logistic regression analysis

Variabel	p	OR	95% CI
BMI	0.969	1.207	0.020 – 10.594
Head Circumference	0.007	6.400	1.667 – 24.576
Fetal Birth Weight	0.126	2.531	0.771 – 8.305
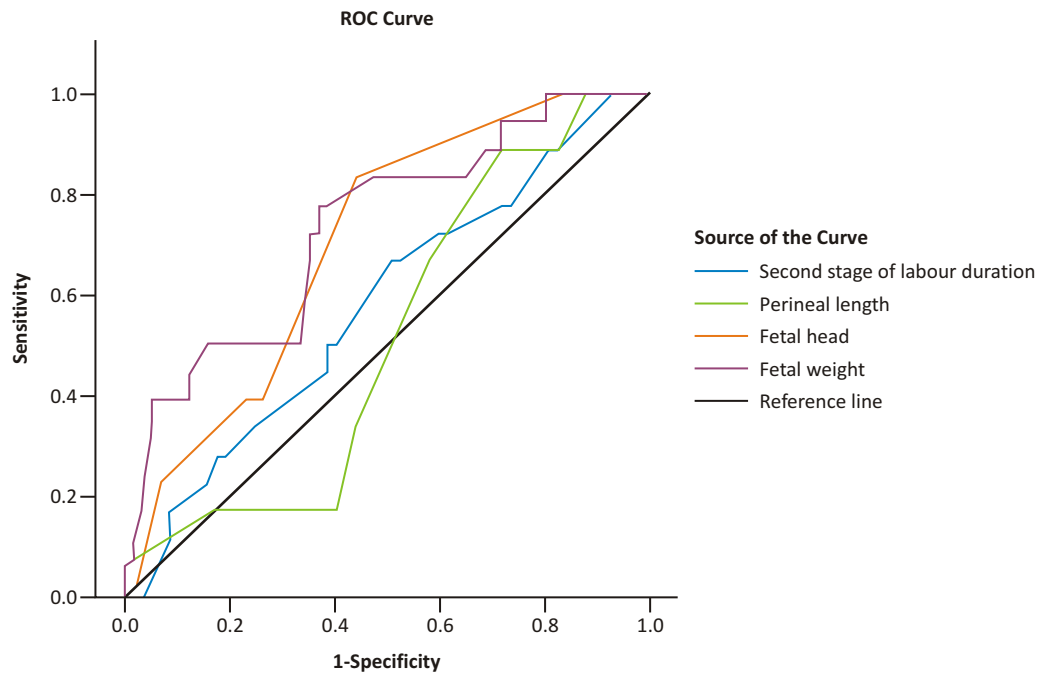
Figure 1. ROC based on variables

A fetal birth weight of more than 3000 grams results in an approximately twofold increased risk of third and fourth degree tears for every additional 500 grams, likely due to the greater increase in biomechanical stress on the vulva, due to the larger size of the newborn with a larger head circumference diameter.[8]

Other studies have also shown that birth weight greater than 3500 grams has been established as a risk factor for severe lacerations. Increased infant weight is associated with a higher risk of shoulder dystocia, greater bleeding volume and perineal laceration. Macrosomia is associated with an increased risk for cesarean delivery

TABLE 8
ROC from outcome variable

Variabel	AUC	Cut of point
Second Stage of Labour duration (minutes)	0.576	31.00
Perineal Length (mm)	0.512	30.50
Fetal Head Circumference (mm)	0.701	325.00
Fetal Weight (gram)	0.731	3097.50

TABLE 9
Correlation between second stage of labour duration and degree of perineal laceration

Second stage of labout duration	Degree of laceration, n (%)		p-value	Prevalence Ratio (95% CI)
	Severe	Mild		
≥31 minutes (n=32)	9 (28.1)	23 (71.9)	0.654	1.3 (0.6 – 3.0)
<31 minutes (n=43)	9 (20.9)	34 (79.1)		

TABLE 10
Correlation between perineal length and degree of perineal laceration

Perineal length	Degree of laceration, n (%)		p-value	Prevalence Ratio (95% CI)
	Severe	Mild		
<30.5mm (n=44)	12 (27.3)	32 (72.7)	0.606	1.4 (0.3 – 1.7)
≥30.5mm (n=31)	6 (19.4)	25 (80.6)		

and birth canal trauma. Several studies have proposed that macrosomia is associated with higher rates of injury during labor. There were twice as many patients with an anal sphincter tear in the macrosomia group.[8,9]

Fetal head circumference with a value of 334.44 ± 12.47 mm was at risk for severe laceration and was the dominant factor influencing the incidence of perineal laceration. This result is in accordance with previous studies in Indonesia which stated that there was a significant difference in infant head circumference with the incidence of perineal laceration.[1,3] This is related to the stretching of the perineum and vagina during labour, where the mother's birth canal will stretch to accommodate the fetal head circumference. This head circumference is the largest hard diameter of the fetal part. In this study, it was found that there was a relationship between the baby's head circumference and the degree of perineal laceration.

The mean duration of the second stage in this study was 30.81 ± 18.39 minutes. The results of this study are still in accordance with the specified period of waiting time of the second stage in nulliparous patients which is 120 minutes. A short period of time is known to give the perineum insufficient time to stretch, resulting in prematurity in the head extension process, causing a bigger anteroposterior diameter and increasing the likelihood of obstetric trauma.[6]

In the results of the ROC table, the highest value of sensitivity is the head circumference and birth weight of the baby, so that if the head circumference was found to exceed 325 mm accompanied by the baby's birth weight above 3097.5 grams, there is a 66.7% chance that the patient can experience severe perineal laceration. From the AUC it can be concluded that with the results of 0.701 in head circumference and 0.731 in baby's birth weight, statistically, these two measuring values have a fairly good accuracy value for the risk of perineal laceration during spontaneous labor.

Strategies that can be done to minimize the occurrence of perineal laceration are identifying risk factors and modifiable actions. Modifiable factors are labor with maternal actions or positions during labor that increase the flexibility of the sacrum such as the lithotomy position. Non-modifiable risk factors include old age,

TABLE 11

Correlation between Fetal Head Circumference and degree of perineal laceration

Fetal Head Circumference	Degree of laceration, n (%)		p-value	Prevalence Ratio (95% CI)
	Severe	Mild		
≥325mm (n=40)	15 (37.5)	25 (62.5)	0.008	4.4 (1.4 – 13.9)
<325mm (n=35)	3 (8.6)	32 (91.4)		

TABLE 12

Correlation between fetal weight and degree of perineal laceration

Fetal Weight	Degree of laceration, n (%)		p-value	Prevalence Ratio (95% CI)
	Severe	Mild		
≥3097.5 gram (n=32)	12 (37.5)	20 (62.5)	0.037	2.7 (1.1 – 6.4)
<3097.5 gram (n=43)	6 (14.0)	37 (86.0)		

post-term pregnancy, infant birth weight, perianal edema, and prolonged second stage of labour.[10,11]

Based on further analysis, fetal head circumference greater than 325 mm increases the risk of severe perineal laceration 4.4 times and Fetal weight greater than 3097.5 grams increases the risk of 2.7 times the occurrence of severe perineal laceration.

From the findings of this study further research is needed regarding the elasticity of the female soft birth canal with tolerance and the occurrence of the degree of perineal laceration in spontaneous labour in primiparas and excluding the factor of external assistance on perineal stretching.

In the combination of fetal weight is more than equal to 3097.5 grams and head circumference (HC) is more than equal to 325 mm, primiparous women should consider the risk of having a severe degree perineal laceration thus deliberately considering labour and delivery in hospital with adequate resources, while the mode of delivery should be still based on obstetrics consideration and indications.

Strengths and Limitations of the Study

The strength of this study is the prospective data collection and assessment of various risk factors. This study also used a validated protocol for documentation of perineal tears to provide more comprehensive information on perineal tears as well as a more homogenous study sample.

Limitations of the application of perineal stretching assistance in Normal Labor Care such as the use of antenatal perineal massage as a protective factor was not included because these variables were not included in the study protocol.[12] Birth canal elasticity assessment was not performed due to the wider coverage of sampling in some areas that did not have adequate tools for assessing the elasticity of the perineum, so the assessment of birth canal elasticity was not included in the research protocol. In this multicenter study, diverse birth attendant could affect the outcome of the degree of perineal laceration even when Indonesia has been carried an all compassing normal labour care for midwives and general practitioner.

CONCLUSION

Based on this study there is no significant association of perineal length with the degree of spontaneous primiparous perineal laceration in aterm pregnancy. While there is an association of fetal head circumference and fetal weight with the degree of spontaneous primiparous perineal laceration in aterm pregnancy.

Further research to determine the predictive factors of estimated fetal weight and ultrasound measurement in third trimester in relation to the perineal laceration may be conducted to give a more predictive risk in spontaneous labour.

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Original Article

Anthropometric Study of the Relationship between Tibia Length and Height of the Ethnic Papuans

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Abstract

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Background : Height is an important main characteristic in the forensic anthropological identification process to determine the identity of a person. Estimating height based on the length of long bones such as the tibia, fibula, ulna, and humerus is one method that is widely used because it has a good correlation. This study was conducted to determine the relationship between tibia bone length and height of students of the Medical Education Study Program, Faculty of Medicine, Cenderawasih University who are indigenous Papuans.

Methods : This study applied correlative analytic method with a cross sectional approach. The research sample was students of the Medical Education Study Program at Cenderawasih University in 2020-2023. The tibia bone length was measured using a metline and height was measured using a microtoise directly on the research subject. Data was analysed with Pearson test.

Results : Fifty-five subjects (25 males, 30 females), found male height of 161.060 cm, a female height of 153.000 male tibia bone length of 26.620 cm, and female of 34.170 cm.

Conclusion : There was a relationship between tibia length and height with the results of the Pearson test obtained p value = <0.001.

Keywords : Height, Ethnic Papuans, Length of tibia bone

INTRODUCTION

The National Disaster Management Agency (BNPB) in its report stated that in 2023 there were 4,940 cases of natural disasters in Indonesia,[4] the impact of these resulted in 267 people dying and 33 people missing.[2] In 2018 there was a huge flood and tsunami in Palu that caused many casualties.[3] Papua has also experienced floods with considerable impact, one of which was the 2019 flood in the Sentani Jayapura district.[6] Some casualties have been successfully evacuated even though their bodies are no longer intact.[8] Evacuation of some body parts has also been carried out; head, feet, hands, and several long bones.[11] Thus, forensic identification is needed to identify the victims.[5] Forensic anthropology is a specific branch of biological anthropology based on human anatomy and bones for identification.[12] The difference between one victim and another can be known through the identification process.[15] In the process, bones are often used by experts in identifying individuals, such as height, gender, race, time of death, age, and cause of death.[10]

The identification process was based on a number of key characteristics, one of which is height.[9] Various purposes including data collection and investigation required height.[17] The method that was often applied in an effort to estimate height was to use certain bones because the correlation was good.[18] The objective of this study was to determine the relationship between tibia length and height in students of the Medical Education Study Program at Cenderawasih University.[11]

METHODS

This study was correlative analytic research with a cross-sectional design.[13] The subjects of this study were students of the Medical Education Study Program at Cenderawasih University and met the research criteria.[14] The research period was June 11–13, 2024. Sampling was done by probability sampling.[16] Inclusion criteria included subjects aged 19–23 years, two generations above the subject was of indigenous Papuan ethnicity without mixed marriages and willing to participate in the study. Exclusion criteria consisted of a history of foot surgery, dislocation or fracture of bones that affect height and deformity of the leg or vertebral columna. Measurement of tibia length was measured with a metline and height was measured with a microtoise directly on the research subject.[7] Data analysis was conducted using the Pearson test with SPSS 26.

This study has obtained permission and ethical approval from the Jayapura Health Research Ethics Committee with ethical approval letter number EC32.43-0524.

RESULTS

Fifty-five research subjects who met the inclusion criteria were students of the Medical Education Study Program at Cenderawasih University in 2020–2023. Subject characteristics can be seen in Table 1.

DISCUSSION

The sample in this study was dominated by women (54.5%) by the age of 19 years. Based on the results of the study, the average height of men was 161.060 cm and women 153.00 cm. The average length of the tibia bone in men was 36.620 cm and women 34.170 cm. From the results of this study, it can be seen that the length of the tibia bone of men was much longer than women, thus causing the height of the male sample to be higher than women. This was in accordance with the previous study conducted by medical students at the Muslim University of Indonesia in the Bugis tribe.[7]

Overall, based on the results of the Pearson correlation test, it can be stated that there was a significant correlation between the tibia bone length and height in men (r=0.909) and women (0.751) with strong to very

TABLE 1
Subject Characteristics

Variable		Positive	
		N	**%**
Gender	Male	25	45.5%
	Female	30	54.5%
Age	19 years old	19	34.5%
	20 years old	13	23.6%
	21 years old	18	32.7%
	22 years old	4	7.3%
	23 years old	1	1.8%

TABLE 2
Measures of Height and Tibia Length

Variable		Height Mean ± SD	Height Mean ± SD
Gender	Male	160.98 ± 5.839	36.62 ± 1.823
	Female	153.00 ± 7.241	34.17 ± 1.594
Total		156.63 ± 7.704	35.28 ± 2.087

TABLE 3
Relationship between tibia length and height

Variable		N	r	p
Gender	Male	25	0.909	0.001
	Female	30	0.751	
Total		55	0.864	

strong correlation and positive correlation direction. This indicated that the longer the tibia bone, the higher their height will also be. This study was in line with previous studies conducted by the medical students at Sam Ratulangi University in the Sangihe tribe.[1]

There are various causes of differences in height and bone length of an individual, one of which is ethnicity. Different ethnicities certainly have differences in height and bone length that are different from other ethnicities. In addition, there are also genetic and environmental factors that are quite influential in the process of physiological development of a person.

The results of this study when compared with previous studies on indigenous Papuans have a longer tibia bone length so that when referred to base on the results, it was found that indigenous Papuans, especially in men, had a high enough height.

CONCLUSION

From this study, it was found that there was a significant relationship between the length of the tibia bone and the height of indigenous Papuan ethnic students at the Medical Education Study Program of Cenderawasih University in 2020–2023.

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Gait Analysis of Ankle Joints of Indonesians at Low, Medium and High Speeds

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Abstract

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Background : Amputation is a loss of body part, and most amputations are lower extremity amputations. The most common is transtibial amputation. After an amputation a person will need a prosthesis. However, up to now there has been no functional prosthesis specifically made for Indonesians who undergo transtibial amputation because the ankle joint gait data that are currently used are European gait data. So it is necessary to measure the normal gait data of Indonesians' ankle joint. The aims of this study was to measure the normal gait data of the ankle joint of Indonesian population

Methods : The Research sample is Indonesians aged 18–26 years with normal gait measured by the 2DMA (two-dimensional motion analyzers) at low, medium and high speeds. The resulting data is searched for the mean and standard deviations and then an independent t-test is performed between normal gait data of Indonesians and Europeans

Results : Indonesians have a range of maximum dorsiflexion values for low, medium, and high speeds of : 7.9°, 8.3°, 8.9° and maximum plantar flexion for low, medium, and high speeds of 13.4°, 20.6°, 26°. In the comparison test there was a significant difference between the maximum plantar flexion angle of Indonesians and Europeans.

Conclusion : Indonesians have a range of maximum dorsiflexion values for low, medium, and high speeds of 7.9°, 8.3°, 8.9° and maximum plantar flexion for low, medium, and high speeds of: 13.4°, 20.6°, 26°. There is a difference between the normal gait of the ankle joint of Indonesians and Europeans.

Keywords : Ankle joints; dorsiflexion; gait analysis; plantar flexion

INTRODUCTION

Amputations of all parts of the body, and 85% of amputation procedures are lower extremity amputations. Every year 150,000 people undergo lower extremity amputations in the United States. The most common lower extremity amputation is transtibial amputation / below knee amputation.[1,2] A 2019 cross sectional study in Malaysia involving 170 patients who had undergone surgical intervention for diabetic foot infections at three district hospital revealed that of 170, a total of 21 patients undergone major amputations of lower limbs (15 transtibial and 6 transfemoral).[3]

Transtibial/below knee amputation is an amputation that involves removal of the foot (pedis), ankle joint, distal tibia and fibula and surrounding tissue.[4] Ideally, within four to eight weeks, the limb stump is healed enough so that an amputee can go on to have a prosthesis with addition to limb physiotherapy. So mobility and prosthesis play a significant role in the rehabilitation of patients after undergoing transtibial amputation.[5] The ankle joint or articulatio talocrural is a joint formed from the lower part of the tibia and fibula bones with the upper part of the talus and its main motion is plantar-flexion and dorso-flexion.[6] The ankle joint connects the crus with the pedis, thereby enabling a kinetic connection between the lower extremities and the ground, which is a prerequisite for the formation of a gait cycle or cycle of walking and other activities of daily living.

Gait can be assessed and compared from one person to another using gait analysis. Gait analysis is a set of procedures that function to observe, measure, interpret and analyse how to move.[7,8] Deviations in gait, especially those involving the ankle joint can affect the walking cycle and cause certain compensation.[9]

There are several approaches to gait analysis such as vision-based (including direct using markers such as three-dimensional motion analysis, and non-direct/without markers), sensor based (using Ground Reaction Force Plates, electromyography), a combination of the two, and approaches using tools. such as an electrogoniometer.[10] Gait analysis is performed by observing joint movement and then comparing it with certain gait parameters. One of the parameters used is the kinematic parameter. This parameter assesses changes in body segments regardless of the forces acting. One example of the kinematic parameters being assessed is the change in the degree of angle at each joint followed during a walking cycle.[11] The data obtained is then used to determine the range of motion in the prosthesis to be made.

However, currently there has been no functional prosthesis made sperifically for Indonesians after undergoing transtibial/below knee amputation due to the normal ankle joint gait data currently used are European gait data. Previous study comparing the gait of different races (African American's and White American's) shown that there are differences in kinematics parameter between the two, including ankle joint kinematics.[12] Currently, there are no database of ankle joint kinematics of Indonesians. Racially, and by leg length, weight and height between Indonesians and Europeans are different, so it is suspected that it can affect the results of gait analysis, including the ankle joint. The reference data for normal ankle joint gait at various speeds are expected to be a reference for the manufacturer of a prosthesis that can approach a physiological gait for Indonesians after undergoing transtibial/below knee amputation.

METHODS

This study took place at UNDIP CBIOM3S Laboratory, Semarang, Indonesia. The subjects were Indonesian people aged 18–26 years with normal gait qualitatively with observations in the city of Semarang and has been approved by Health Research Ethics Committee Diponegoro University (No. 215/EC/KEPK/FK-UNDIP/VI/2021). The study subjects that were involved in this study needed to meet inclusion criteria such as: a qualitatively normal gait of vision which was carried out by one orthopaedic specialist and one general practitioner. Gait is normal, indicated by a regular and symmetrical gait cycle without any additional movement and without any complications in complex gait maneuvers such as stopping, turning around, jumping on one or two legs and walking backwards; have a complete number of limbs; can walk on a treadmill smoothly; willing to be a research subject and follow research procedures; Indonesian people aged 18–26 years who do not have a mixture of genes from outside Indonesia; not currently suffering from illness characterized by fever and fatigue/malaise. Subjects who have a walking disorder and difficulty; have a history of head trauma that causes neurological symptoms; have had lower limb surgery; have experienced trauma that causes changes in the form or function of the lower limbs were excluded. This age group was chosen because in this age category no degenerative changes related to aging are present, and this age group express mature gait, with less variability compared to children.[13,14] Study sampling by simple random method, with Confidence Interval 95% and absolute error value of 10%, the sample size of this study was 44 subjects which were divided into 22 males and 22 females. The research sample used leggings and socks and then was given a marker in the form of coloured paper at the ankle joint (*malleolus lateralis, metatarsal lateralis* and superior and parallel to the *malleolus lateralis*) as shown in Figure 1. The markers are affixed to the right foot outside. Figure 2 presented the method with which the gait assessment is done.

Figure 1. Marker Placement
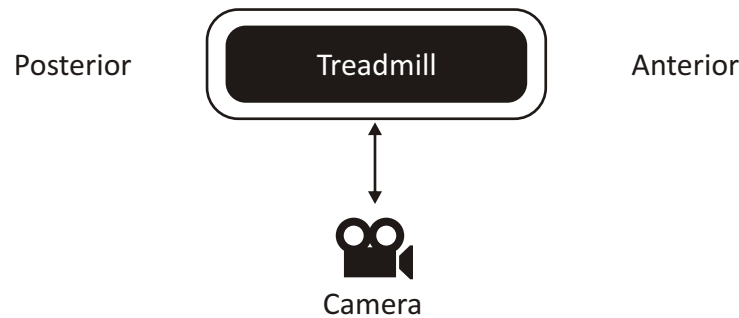
Figure 2. Camera placement

The study sample walked on a treadmill at low, medium, and high speeds for 10 phases of walking for each speed. The different speeds were used on this research because different walking speeds affect the ankle kinematics.[14] The walking will be recorded using 1 camera located on the right side of the treadmill. The point 0° when the ankle joint was in the anatomical position, formed an angle of 90° and was perpendicular to the plane. In this study, point 0° was determined by measuring the anatomical position using software and then averaged over the entire sample. (Software measurement produces raw data which must be reduced by the value of 0). Of the 10 moving phases at each speed, the angle of the ten running phases was assessed, then the average value and standard deviation were sought.

The kinematic parameters were tested using an unpaired T test to determine the comparison between the reference standard of normal gait of the ankle joint of Europeans with data obtained from the gait of Indonesians being studied. Pearson's correlation analysis was performed for leg length relationship to ankle joint angle size and body mass index relationship to ankle joint angle size. Spearman correlation test was performed for walking speeds relationship to ankle joint angle size.

RESULTS

Research subjects had an average body mass index of $22.22 \pm 4.74 \, \text{kg}/\text{m}^2$, average leg length 86.95 ± 4.90 cm and average height 164.23 ± 8.39 cm. Subject characteristic are shown in Table 1.

At low speed, male subjects had a maximum dorsiflexion angle of $5.86 \pm 4.41°$ and a maximum plantar flexion of $14.81 \pm 5.26°$. Female subjects had a maximum dorsiflexion angle of $10.09 \pm 4.27°$ and a maximum plantar flexion of $12.02 \pm 5.22°$. There is a significant difference in the maximum plantar flexion angle between research subjects compared to European literature studies on male subjects ($p<0.001$) and female subjects ($p<0.001$) (Table 2).

At medium speed, male subjects had a maximum dorsiflexion angle of $5.37 \pm 3.47°$ and a maximum plantar flexion of $21.88 \pm 7.83°$. Female subjects had a maximum dorsiflexion angle of $11.28 \pm 4.72°$ and a maximum plantar flexion of $19.41 \pm 8.21°$. There is a significant difference in the maximum plantar flexion angle between research subjects compared to European literature studies on male subjects ($p=0.026$) and female subjects ($p=0.018$) (Table 2).

At high speed, male subjects had a maximum dorsiflexion angle of $6.44 \pm 3.13°$ and a maximum plantar flexion of $25.33 \pm 7.40°$. Female subjects had a maximum

TABLE 1
Characteristics of the study subjects

Variable		Mean ± SD	Median (Min – Max)
Gender	Male n=22 (50%)	–	–
	Female n=22 (50%)	–	–
BMI (kg/m²)		22.221 ± 4.744	20.9 (15.8 – 36.1)
Leg length (cm)		86.95 ± 4.904	87 (77 – 100)
Height (cm)		164.23 ± 8.397	165 (140 – 182)

TABLE 2
Ankle joint angle analysis subjects

Ankle Joint Analysis at Different Speeds	Literature	Male	Female	*p*-value - male	*p*-value - female
Maximum dorsiflexion, LS	8.2°	5.864° ± 4.412°	10.098° ± 4.278°	0.612	0.669
Maximum plantar flexion, LS	38.6°	14.810° ± 5.267°	12.025° ± 5.222°	0.000	0.000
Maximum dorsiflexion, MS	9.1°	5.372° ± 3.470°	11.285° ± 4.727°	0.305	0.656
Maximum plantar flexion, MS	41.0°	21.885° ± 7.803°	19.415° ± 8.216°	0.026	0.018
Maximum dorsiflexion, HS	10.8°	6.448° ± 3.134°	11.310° ± 4.387°	0.189	0.910
Maximum plantar flexion, HS	45.0°	25.335 ° ± 7.403°	26.720° ± 7.787°	0.017	0.032

Gender Relationship to Ankle Joint Angle Size	Male	Female	*p*-value	
Maximum dorsiflexion	5.405° ± 3.472°	11.285° ± 4.727°	0.000	
Maximum plantar flexion	21.885° ± 7.803°	19.415° ± 8.216°	0.313	

LS ; Low Speed, MS ; Medium Speed, HS ; High Speed

dorsiflexion angle of 11.31 ± 4.38° and a maximum plantar flexion of 26.72 ± 7.78°. There is a significant difference in the maximum plantar flexion angle between research subjects compared to European literature studies on male subjects (*p*=0.017) and female subjects (*p*=0.032) (Table 2).

There was a significant difference between the maximum dorsiflexion angle between men and women (*p*<0.001) but there was no significant difference in the maximum plantar flexion angle (Table 2).

Based on the relationship analysis, it was found that walking speed had a connection with the maximum plantar flexion angle (*p*<0.001) with a unidirectional relationship and moderate correlation strength (r=0.592) (Table 3). There is a connection between leg length and the maximum dorsiflexion angle (*p*=0.034) with the opposite relationship and the strength of the weak correlation (r= -0.321) (Table 3). However, there is no connection between body mass index and the maximum

dorsiflexion angle and maximum plantar flexion (Table 3).

DISCUSSION

The purpose of this study is to provide a reference of normal gait data of Indonesian people and to investigate whether racial diffrences exist in kinematics gait analysis. The knowledge of kinematics data of the ankle joint, is one of the fundamentals for making a prosthesis for the lower limb. Espescially ankle-foot prosthesis.[15] Knowing the difference between kinematics data of Indonesians and Europeans will provide a better functional prosthesis made specifically for Indonesians. A 2017 systematic review of 12 studies found that walking with a prosthesis was the most notable factor that influenced quality of life of people who underwent lower extremity amputation.[5] Kinematics data provided can also be utilize to aid gait

TABLE 3
Different factors relations to the ankle joint angle size

Walking Speeds	Correlation Coefficient	p-value
Maximum dorsiflexion	0.074	0.397
Low Speed		
Medium Speed		
High Speed		
Maximum plantar flexion	0.592	0.000
Low Speed		
Medium Speed		
High Speed		
Leg length		
Maximum dorsiflexion	-0.321	0.034
Maximum plantar flexion	0.060	0.699
Body mass Index		
Maximum dorsiflexion	-0.097	0.530
Maximum plantar flexion	0.148	0.339

analysis done by clinician with providing an objective data, and thus helping the clinician to assess patient's gait. The normal gait range of the Indonesians' ankle angle during maximum dorsiflexion is 7.9°, 8.3° and 8.9° at low, medium, and high speeds. At maximum plantar flexion, the ankle angles were 13.4°, 20.6° and 26° at low, medium, and high speeds.

At maximum dorsiflexion angle, whether at low, medium, or high speeds, there was no significant difference between the ankle joint of Indonesians and Europeans. But at the maximum plantar flexion angle, at low, medium and high speeds there were significant diffrences between the two groups. The mechanisms for these diffrences remain untested, perhaps we can suggest that due to the range of motion of ankle joint during dorsiflexion are smaller than when performing plantar flexion.[6] This can provide a "similar" comparison between the two groups. And for the plantar flexion angle which shows significant diffrences between the two groups might be because the ankle joint has a greater range of motion during plantar flexion compared to when performing dorsiflexion movements. Apart from that Europeans need a greater maximal plantar flexion to propel a body with greater mass than of Indonesians.

In male and female subjects, a significant difference was found in the maximum dorsiflexion angle, in which the dorsiflexion of female subjects is greater than that of male subjects. This finding is in line with several previous studies that yielded the same conclusion, where female subjects had larger angles than men at the same speed. This happens because to travel the same speed as male subjects, it takes more effort.[16]

Based on research data, leg length affects the movement of the ankle joint. Especially at the maximum dorsiflexion angle where a significant and opposite relationship is obtained, which means that the longer a person's leg length, the smaller the maximum dorsiflexion angle will be. This can be explained based on previous studies that assessed the relationship between height and the length of one gait cycle (leg length is a component that plays a role in determining a person's height). Several previous studies have stated that the longer the leg length of a person, the faster the gait cycle will be.[17,18] The faster gait cycle will certainly lead to a narrowing of the gait phases, including the terminal stance phase, the phase where the ankle joint reaches its maximum dorsiflexion angle.[11] Before the ankle joint can reach the maximum dorsiflexion angle, due to the rapid phase the ankle joint is ready to perform a swing phase to push the body forward before reaching the maximum dorsiflexion angle. The method in which the gait analysis is done in three different speeds hopefully can provide a more "real-world" data. In which in our daily life, we do not walk at the same constant speed. And speed influence the gait kinematics of ankle joint, like what is proven in this study, and also previous studies.[14,19,20] Thus ensuring the data can be utilized to produce a prosthesis that can be used at different speeds is important.

This study has several limitations first, the camera used are limited to 60 fps video recording. While the use of this camera can represent the data, the use of 120 fps camera will reduce the blur effect thus providing more data to the motion analyzer, and preventing re-recording due to blurry video quality in certain frames. Second, this study only compares walking in a flat and smooth surface, while in the real-world situation, a person might walk in an ascending descending surfaces and also uneven surface.

CONCLUSION

There is a difference between the normal gait of the ankle joint of Indonesians and Europeans at low, medium, and high speeds. Especially at the maximum plantar flexion angle which shows a significant difference. The higher the walking speed, the greater the maximum plantar flexion angle. The longer, the length of a person's limbs, the smaller the maximum dorsiflexion angle. Gender affects ankle joint gait, especially at the maximum dorsiflexion angle where female subjects have a greater maximum dorsiflexion angle than male subjects.

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Original Article

Differences in the Degree of Spasticity in Post-Haemorrhagic and Non-Haemorrhagic Stroke Patients Based on the Modified Ashworth Scale

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Abstract

Background : Stroke is a brain function disorder caused by vascular disturbances with manifestations ranging from paralysis to death. Stroke is a health issue with high incidence and mortality rates. Furthermore, post-stroke patients can experience various residual symptoms such as spasticity, which can lead to decreased productivity and socio-economic impacts. Spasticity is a common symptom in stroke survivors, with a prevalence ranging from 30% to 80%. This symptom typically appears several weeks after a stroke and can persist for up to 12 months, causing reduced productivity and socio-economic challenges. Hemorrhagic strokes result from blood vessel rupture, while non-hemorrhagic strokes are caused by ischemia. Both types can damage motor pathways, leading to spasticity. Understanding the differences in spasticity severity between stroke types may guide targeted rehabilitation strategies. The aimsof ths study was to determine the difference in the degree of spasticity in post-stroke patients between hemorrhagic and non-hemorrhagic strokes based on the Modified Ashworth Scale.

Methods : An analytical observational study with a cross-sectional design was conducted. The study included 33 post-hemorrhagic stroke patients and 33 post-non-hemorrhagic stroke patients. The degree of spasticity was measured using the Modified Ashworth Scale. Statistical analysis was performed using the Chi-Square test.

Results : The Chi-Square test for the variable "stroke type" and "degree of spasticity" yielded a p-value of 0.428 ($p > 0.05$). The Chi-Square test is considered significant when the p-value is < 0.05.

Conclusion : There is no difference in the degree of spasticity in post-stroke patients between hemorrhagic and non-hemorrhagic stroke types.

Keywords : Haemorrhagic Stroke, Non-Haemorrhagic Modified Ashworth Scale, Stroke, Spasticity.

INTRODUCTION

Stroke is a collection of symptoms with manifestations ranging from paralysis to death due to a disruption in brain function that lasts for more than 24 hours.[1] The collection of symptoms arises from vascular causes and is not caused by other factors.[2] There are two main classifications of stroke, namely hemorrhagic and non-hemorrhagic. Hemorrhagic stroke accounts for 15% of stroke cases, while non-hemorrhagic stroke accounts for 85%.[3] Globally, stroke is the second leading cause of death.[4] In Asia itself, Indonesia has the highest incidence of stroke and ranks third in terms of mortality in Indonesia, following cancer and heart disease.[5]

In addition to high incidence and mortality rates, stroke survivors who successfully pass the critical period may experience functional impairments leading to a decline in productivity.[6] Patients who have experienced a stroke may undergo nerve changes due to damage to upper motor neurons, resulting in muscle stiffness (spasticity), characterized by a decrease in range of motion and an increase in muscle tone. As a result, stroke survivors may become dependent on others for their daily activities.[7–9] Post-stroke spasticity can occur between 19% and 92%, especially in the first year after a stroke. Estimates of prevalence vary widely due to differences in spasticity measurement instruments and the onset of stroke.[9]

Previous studies indicate that spasticity is a common symptom after a stroke, with a prevalence ranging from 30% to 80% among stroke survivors.[10] It is a persistent symptom in post stroke patients and can lead to disabilities. Spasticity begins to emerge around the second week and reaches its maximum level in the third week after an ischemic stroke.[11] In another study, it is mentioned that spasticity can persist for up to 12 months, even with the administration of physiotherapy.[11,12] However, to date, there is no research on the differences in the degree of spasticity in post-stroke patients between hemorrhagic and non-hemorrhagic types.

The fundamental difference between hemorrhagic and non-hemorrhagic strokes lies in the fact that hemorrhagic stroke involves the rupture of blood vessels in the brain, leading to the accumulation of blood in the intracranial space. This accumulated blood can rapidly and extensively damage the brain, as it quickly disrupts neurons. Meanwhile, non-hemorrhagic stroke occurs when blood flow to certain parts of the brain is insufficient, resulting in ischemia. This type of stroke is not as dangerous as hemorrhagic stroke because the extent of damage is smaller, and the onset is not as rapid as in hemorrhagic strokes.[13] Brain damage due to stroke can affect the pyramidal and extrapyramidal tracts, leading to the development of spasticity.[10] Based on this premise, researchers are interested in investigating the differences in the degree of spasticity in hemorrhagic and non-hemorrhagic stroke patients. Understanding the differences in spasticity severity between stroke types may guide targeted rehabilitation strategies.

The degree of spasticity in this study will be measured using the Modified Ashworth Scale. The Modified Ashworth Scale (MAS) is a scale commonly used to assess increased muscle tone manifested by increased joint resistance during passive movement. Increased muscle tone is often exhibited in pathological conditions such as stroke, multiple sclerosis, spinal cord injury, traumatic brain injury, cerebral palsy, and other neurological conditions that result in damage with upper motor neuron (UMN) lesions.[14] The Modified Ashworth Scale is determined manually by passively moving the patient's extremities and sensing the resistance and reduction in range of motion (ROM).

METHODS

The research was conducted in June–July 2023 using an analytical observational approach with a cross-sectional design. 66 samples were included 33 post-hemorrhagic and 33 post-non-hemorrhagic stroke patients at Dr. M. Ashari Regional General Hospital, Pemalang, selected through purposive sampling. Inclusion criteria included patients aged 45 years and above, those who had experienced a stroke at least 3 months prior, and those who had not undergone physical therapy for at least 1 week before participation. Exclusion criteria involved patients with neurological or musculoskeletal disorders affecting range of motion.

Subjects underwent spasticity assessment using the Modified Ashworth Scale (MAS) for both upper and lower extremities, with the highest spasticity value recorded. The classification of stroke type (hemorrhagic or non-hemorrhagic) was confirmed using medical records.

The data collected included primary data (spasticity degree obtained through direct examination by the researcher) and secondary data (stroke type and gender from medical records). Since the researcher collected all data independently, no inter-rater reliability test was conducted.

Confounding Factors: Duration since the stroke (minimum 3 months) was evaluated as a potential confounding factor; Gender data was also collected to analyze potential differences between male and female subjects.

Data analysis involved hypothesis testing to evaluate differences in spasticity degree between stroke types. Spasticity was categorized into two groups: mild spasticity (MAS 0, 1, and 1+) and moderate-to-severe spasticity (MAS 2, 3, and 4). A Chi-Square test was used, with a p-value of <0.05 considered statistically significant.

RESULTS

Characteristics of research subjects

Further details on the characteristics of the research subjects can be found in the Table 1.

From the data collected, which met the inclusion and exclusion criteria, the study included 66 patients. The sample was evenly divided between those with hemorrhagic and non-hemorrhagic stroke. Just over half of the participants were female. Most of the patients were aged 60 and above, and a majority had been experiencing post-stroke symptoms for six months or more, while a smaller group was within six months after their stroke. The degree of spasticity ranged from normal to severe, with most patients exhibiting mild to moderate levels of

TABLE 1
Characteristics of research subjects

Characteristic	Category	n	%
Type of Stroke	NHS	33	50%
	HS	33	50%
Gender	Male	31	47%
	Female	35	53%
Age	<60 Years	29	43.9%
	≥60 Years	37	56.1%
Onset of Stroke	<6 Months	11	16.7%
	≥6 Months	55	83.3%
Degree of Spasticity	0 (Normal)	16	24.2%
	1 (Very mild)	19	28.8%
	1+ (Mild)	10	15.2%
	2 (Moderate)	10	15.2%
	3 (Moderately severe)	5	7.6%
	4 (Severe)	6	9.1%
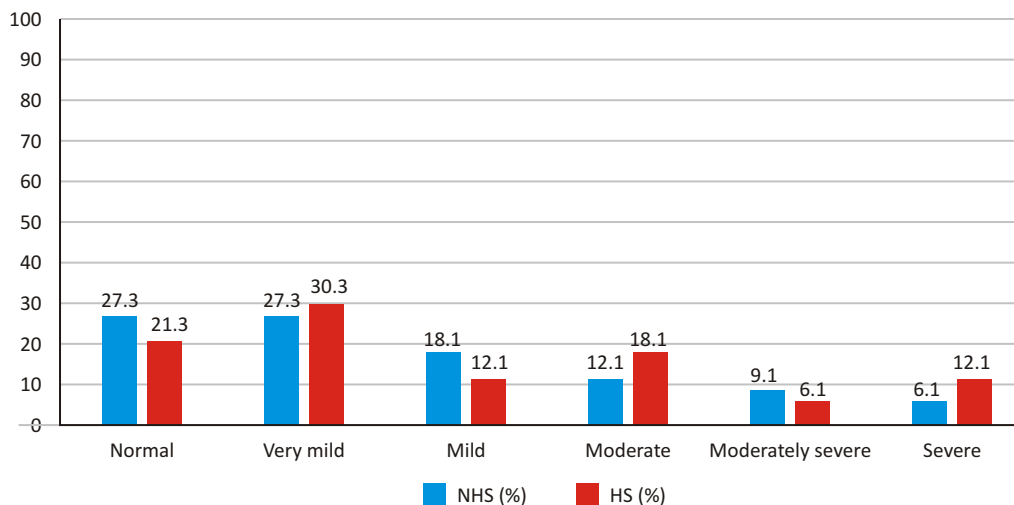
Figure 1. Distribution of the degree of spasticity based on the type of stroke.

spasticity.

The degree of spasticity in patients was assessed using the Modified Ashworth Scale (MAS). The results showed that most patients had normal to very mild spasticity, while fewer exhibited moderate to severe spasticity. Further analysis was conducted to examine the distribution of spasticity levels for each type of stroke.

The degree of spasticity for each type of stroke is as follows: for non-hemorrhagic stroke, there are 9 patients with normal spasticity, 9 patients with very mild spasticity, 6 patients with mild spasticity, 4 patients with moderate spasticity, 3 patients with moderately severe spasticity, and 2 patients with severe spasticity. For hemorrhagic stroke, there are 7 patients with normal spasticity, 10 patients with very mild spasticity, 4 patients with mild spasticity, 6 patients with moderate spasticity, 2 patients with moderately severe spasticity, and 4 patients with severe spasticity (Figure 1).

Hypothesis Testing

The degree of spasticity will be divided into two main groups: the mild spasticity group (MAS normal, very mild, and mild) and the moderate-severe spasticity group (MAS moderate, moderately severe, and severe).

Based on Table 2, the p-value for the variable type of stroke with the degree of spasticity is p=0.428 (p >0.05). The Chi-Square analysis shows that there is no significant difference in the distribution of spasticity degrees (mild vs. moderate-severe) between hemorrhagic stroke (HS) and non-hemorrhagic stroke (NHS) patients (χ^2 = 0.626, df = 1, p=0.428). Therefore, it can be concluded that there is no significant difference in the degree of spasticity between patients with hemorrhagic stroke and non-hemorrhagic stroke.

Based on Table 3, the p-value for the variable age group with the degree of spasticity is p = 0.140 (p > 0.05). The Chi-Square analysis shows that there is no significant difference in the distribution of spasticity degrees (mild vs. moderate-severe) between patients aged < 60 years and those aged > 60 years (χ^2 = 2.175, df = 1, p = 0.140). Therefore, it can be concluded that there is no significant difference in the degree of spasticity between the two age groups.

TABLE 2
Chi-Square test between the type of stroke and the degree of spasticity

Type of Stroke	Degree of Spasticity		Total	*p*
	Mild	Moderate–Severe		
NHS (%)	24 (72.7)	9 (27.3)	33 (100)	
HS (%)	21 (63.6)	12 (36.4)	33 (100)	0.428
Total (%)	45 (68.2)	21 (31.8)	66 (100)	

TABLE 3
Chi-Square test between age and the degree of spasticity

Age	Degree of Spasticity		Total	*p*
	Mild	Moderate–Severe		
<60 years (%)	17 (58.7)	12 (41.3)	29 (100)	
≥60 years (%)	28 (75.7)	9 (24.3)	37 (100)	0.140
Total (%)	45 (68.1)	21 (31.9)	66 (100)	

TABLE 4
Chi-Square test between the onset of stroke and the degree of spasticity

Onset of stroke	Degree of Spasticity		Total	*p*
	Mild	Moderate–Severe		
<6 months (%)	9 (81.9)	2 (18.1)	11 (100)	
≥6 months (%)	36 (65.5)	19 (34.5)	55 (100)	0.287
Total (%)	45 (68.2)	21 (31.8)	66 (100)	

Based on Table 4, the *p*-value for the variable onset of stroke with the degree of spasticity is p=0.287 (p >0.05). The Chi-Square analysis shows that there is no significant difference in the distribution of spasticity degrees (mild vs. moderate-severe) between patients with a stroke onset of < 6 months and those with an onset of > 6 months (χ^2 = 1.135, df = 1, p=0.287). Therefore, it can be concluded that there is no significant difference in the degree of spasticity between the two onset groups.

DISCUSSION

The result of this study is no differences were found in the severity of spasticity between post-hemorrhagic and post-non-hemorrhagic stroke patients, all with a duration of more than 3 months.

Spasticity more frequently occurs in hemorrhagic strokes, as indicated by the research results, with the number of patients who are normal (without spasticity) being nine in post-non-hemorrhagic stroke patients, whereas in post-hemorrhagic stroke patients, it is seven. This is in line with the study by Hualing *et al.*, which stated that hemorrhagic strokes have a higher prevalence of spasticity.[12,15] This is because the damage in hemorrhagic strokes is more extensive due to direct bleeding affecting brain parenchymal tissue. However, the more frequent occurrence of spasticity does not necessarily mean a greater severity. Although the difference in the proportion of the presence or absence of spasticity appears slight, this can be explained by the study by Katoozian *et al.*, which states that post-stroke spasticity more frequently occurs in hemorrhagic stroke patients, with the onset of spasticity most common in the first month post-stroke.[16] Considering that this study includes post-stroke patients with a duration of more than 3 months, it is not impossible that many non-hemorrhagic stroke patients have already developed spasticity.

The findings in this study align with research by Hualing *et al.*, which observed that hemorrhagic strokes have a higher prevalence of spasticity due to more severe brain damage from direct bleeding into the parenchyma. In the current study, post-hemorrhagic stroke patients showed a slightly lower proportion of normal (spasticity-free) patients compared to post-non-hemorrhagic stroke patients (7 vs. 9). This finding supports Hualing *et al.*'s conclusion that hemorrhagic stroke is more likely to result in spasticity. However, Katoozian *et al.* note that spasticity tends to manifest within the first month post-stroke, particularly in hemorrhagic stroke patients, which may explain why, after 3 months, both groups in this study showed similar levels of spasticity. The longer duration post-stroke in this study (over 3 months) likely allowed for the development of spasticity in non-hemorrhagic stroke patients as well.

The degree of spasticity, for which differences were sought in this study, was divided into two groups: post-non-hemorrhagic stroke patients and post-hemorrhagic stroke patients. However, no significant difference was found in the severity of spasticity. This is because the severity of spasticity is determined by many factors, including lesion location, age, history of hypertension, history of diabetes, stroke severity, management in the acute phase, and individual responses to nerve damage.[17] In some cases, spasticity may be more severe in hemorrhagic strokes, while in other cases, the degree of spasticity may be more severe in non-hemorrhagic stroke patients. Therefore, to determine whether there is a difference in the degree of spasticity in post-stroke patients between hemorrhagic and non-hemorrhagic types, many other factors need to be considered, and the type of stroke alone is not sufficient to be the determinant of spasticity severity.[18]

Schinwelski *et al.* emphasize that spasticity severity is influenced by numerous factors beyond stroke type. These include lesion location, patient age, comorbidities (such as hypertension and diabetes), initial stroke severity, acute-phase management, and individual variability in nerve damage response. This complexity explains why no significant difference in spasticity severity was observed between hemorrhagic and non-hemorrhagic strokes in this study. The type of stroke alone does not adequately predict spasticity outcomes; rather, a multifactorial approach is required to fully understand the variability in spasticity severity. Future studies should take these additional factors into account to provide a more comprehensive understanding of spasticity in post-stroke patients.

CONCLUSION

Based on the results of the research and discussion, it can be concluded that there is no difference in the degree of spasticity in post-stroke patients between hemorrhagic and non-hemorrhagic types at RSUD Dr. M. Ashari Pemalang.

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Correlation between Urine Albumin Creatinin Ratio (UACR) Value to Urine Osmolality Value and Estimate Glomerular Filtration Rate (EGFR) Value on Patient with Kidney Failure

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Abstract

Background : Kidney failure is one of the causes of death in the world. Laboratory tests related to kidney function are very important in the management of patients with kidney failure because they are useful in identifying any decline in kidney function, monitoring treatment and progression of kidney disease. The urine albumin creatinine ratio (UACR): is related to assess the protein filtration function in the glomerulus. The urine osmolality is to assess pre-renal, renal and post-renal hemodynamic status. The estimated glomerular filtration rate (EGFR) is to assess overall glomerular function. EGFR is the gold standard. The aim of this research is to determine 1). The correlation between UACR value to urine osmolality value, 2). The correlation between UACR value to EGFR value. Patient with kidney failure is the independent variable, meanwhile UACR value, urine osmolality value and EGFR value are dependent variables..

Methods : This study is a quantitative study with analytical observations through a cross sectional design using 30 sample patients with kidney failure either acute kidney injury (AKI) or chronic kidney disease (CKD). This study was conducted from May to June 2024 at the Central Laboratory Installation of Dr. Saiful Anwar Hospital, East Java Province. UACR and EGFR examination used the principle of photometric test while urine osmolality examination used the principle of electrical conductivity. The data were analyzed using the Shapiro-Wilk normality test and the Spearman non-parametric correlation test through SPSS 27.

Results : In the normality test results, it was found that UACR and EGFR values were not normally distributed (p = <0.001) while urine osmolality values were normally distributed (p = 0.523). Spearman's non-parametric correlation test showed that there was no correlation between UACR to urine osmolality (p = 0.342) and EGFR value (p = 0.481).

Conclusion : The results of this study showed no correlation between UACR value to urine osmolality value and EGFR value in patients with kidney failure.

Keywords : EGFR, Kidney Failure, UACR, Urine Osmolality

INTRODUCTION

Kidney failure is a significant contributor to mortality worldwide. Based on the 2018 data from the World Health Organization (WHO), over 10% of the global population suffers from chronic kidney disease (CKD). It is predicted that between 5 to 10 million individuals die annually owing to CKD, while roughly 1.7 million patients succumb to acute kidney injury (AKI) each year.[1] According to the 2018 National Riskesdas Report, there are 713,783 Indonesians aged ≥ 15 years who suffer from chronic kidney disease. Additionally, 113,045 individuals in East Java also experience chronic kidney disease.[2]

Screening for kidney function is crucial in the care of patients who have kidney failure or reduced kidney function. Kidney function screening is valuable for detecting any deterioration in kidney function, monitoring the effectiveness of treatment, and tracking the advancement of kidney disease. One of the laboratory tests used to assess kidney health is the estimate glomerular filtration rate (EGFR), which is considered the most reliable measure of glomerular function.[3] The estimate glomerular filtration rate (EGFR) is a laboratory test used to assess the function of glomerular filtration.[4] When assessing EGFR, serum creatinine levels are necessary. However, adjustments for race, gender, and age are required when utilising serum creatinine.[3] The proteinuria (albuminuria) examination is also important thing to know the kidneys function. Albuminuria is employed as a diagnostic tool to identify early-stage kidney disease in individuals with diabetes mellitus. It serves as a reliable indicator for cardiovascular illness, indicating higher levels of endothelial permeability. Additionally, it is also an indicator for chronic kidney problems. If albuminuria is seen in two separate examinations and urinary tract infection is ruled out, it suggests malfunction of the glomeruli.[3] Albuminuria is a significant indicator of chronic kidney disease and highly anticipates end-stage renal disease. Albuminuria can be assessed by conducting a urine albumin creatinine ratio (UACR) test utilising a sample of urine obtained during a single instance of urination.[5] UACR represents the quotient obtained by dividing the concentration of albumin in urine (mg/dl) by the concentration of creatinine in urine (g/dl).[6]

A study conducted by Megumi Oshima, *et al* revealed a substantial association between changes in albuminuria and EGFR during a 2-year period and the likelihood of future kidney failure in patients with type 2 diabetes mellitus. The findings indicate that tracking albuminuria and EGFR over a period of time can effectively identify persons with diabetes mellitus who are at a significant risk of kidney failure. It also helps identify those who need careful monitoring to initiate timely preventative and therapeutic measures.[7] Nevertheless, Andrew S. Levey, *et al* stated that EGFR

alterations are more effective in detecting the beginning stage of CKD compared to albuminuria changes, as albuminuria changes are specific to diseases characterised by albuminuria. However, when it comes to therapy effects, albuminuria changes are more effective than EGFR alterations.[8]

In addition to EGFR and UACR, urine osmolality is a crucial factor in assessing kidney function since it reflects the kidney's ability to either dilute or concentrate urine. Urine osmolality is a more precise measure for assessing kidney function compared to urine specific gravity. Urine osmolality refers to the level of concentration of all dissolved particles present in urine.[9] Dong-Won Yoo, *et al* stated that decreased urine osmolality can result from elevated water consumption, vasopressin insufficiency, or diabetes mellitus. High urine osmolality frequently arises under hypovolemic conditions, such as dehydration, resulting in decreased blood supply to the kidneys and injury to renal tubular cells, thereby hindering the kidney's capacity to concentrate urine.[10] Nevertheless, a separate study indicated that low urine osmolality is a distinct prognostic marker for unfavourable kidney outcomes in individuals with chronic kidney disease. However, its predictive capability did not surpass that of EGFR.[11] Boonsong K. Kitiwan, *et al*. discovered that there was no significant correlation between quartiles of urine osmolality and reduced EGFR and/or albuminuria. Nevertheless, there was a notable correlation between higher urine osmolality and lower estimated glomerular filtration rate (EGFR) in people with an EGFR of 60 mL/min/1.73 m^2 or higher. Conversely, there was a positive correlation between urine osmolality and improved kidney function in people with an estimated glomerular filtration rate (EGFR) of 60 mL/min/1.73 m^2.[12]

Considering the information provided and multiple studies, urine osmolality has not yielded significant insights regarding kidney function due to inconsistent outcomes in urine osmolality results. Consequently, additional research is required to investigate the correlation between urine albumin creatinin ratio (UACR) value to urine osmolality value and estimate glomerular filtration rate (EGFR) value in patients with kidney failure. This research is expected to aid in the early detection of abnormalities associated with declining kidney function. Furthermore, if there is a correlation between the urine albumin creatinin ratio (UACR) value and the urine osmolality value, the urine osmolality parameter can be included as a reportable parameter on the Sysmex UF-4000 equipment utilised in this investigation.

METHODS

This research has been approved by the Ethics Committee

of Dr. Saiful Anwar Hospital, East Java Province, with the reference number 400/120/K.3/102.7/2024. It was conducted during a period of 2 months, from May to June 2024, at the Central Laboratory Installation of Dr. Saiful Anwar Hospital, East Java Province.

The study employed a quantitative research design, analytic observations within a cross-sectional design.[13] The study population consisted of patients diagnosed with kidney failure at Dr. Saiful Anwar Hospital, East Java Province. A nonprobability sampling method called purposive sampling was used to select a sample of 30 in patients. The inclusion criteria include patients diagnosed with kidney failure, either Acute Kidney Injury (AKI) or Chronic Kidney Disease (CKD), aged 18–74 years, with urine samples collected using spot urine. Meanwhile, the exclusion criteria include patients aged less than 18 years and more than 74 years. The patients were both male and female. They underwent UACR, routine urinalysis, and serum creatinine examinations.

The UACR examination is conducted using the Cobas c-503 instrument, which employs a photometric test concept. In this process, urine albumin is checked using an immunoturbidimetric test principle, while urine creatinine is examined using an enzymatic test principle.

The UACR value is derived by calculating the ratio of urine albumin to urine creatinine using the formula :[6]

$$\frac{\text{Urine albumin (mg/dl)}}{\text{Urine creatinine (g/dl)}} = \text{ACR (mg/g)}$$

The Sysmex UF-4000 equipment is used for routine urinalysis examination. It employs the idea of Urine Flowcytometry with Blue Semiconductor. The device reports urine osmolality values as research parameters. Urine osmolality is determined by measuring electrical conductivity. The urine osmolality value is determined by performing the following calculation :[10]

$$\text{Osmo. [mOsm/kg]} = 34.294x$$
(where x is the urine conductivity level)

The Cobas c-503 device is utilised for serum creatinine examination, employing a photometric test principle. This examination measures serum creatinine levels through an enzymatic test. The EGFR value is then calculated using the CKD-EPI (Chronic Kidney Disease – Epidemiology Collaboration) 2021 equation, which excludes race as a factor :[14]

$\text{EGFR}_\alpha = 142 \times \min(S_\alpha/\kappa, 1)^a \times \max(S_\alpha/\kappa, 1)^{-1,200} \times 0.9938^{\text{Age}} \times 1.012$ [if female]

Description:

κ : 0.7 for females or 0.9 for males

a : -0.241 for females or -0.302 for males

S_α : serum creatinine (mg/dL); divided by 88.4 for serum creatinine (µmol/L)

min : minimum for S_α/κ or 1

max : maximum for S_α/κ or 1

Age : age in years

The UACR and EGFR findings were obtained via the laboratory information system (LIS), whereas the urine osmolality results were obtained from the Sysmex UF-4000 equipment. In addition, the collected data were subjected to statistical analysis using IBM SPSS Statistics 27. The statistical analysis commenced with a normality test using the Shapiro-Wilk test due to the sample size being less than 50.[15] In addition, the Spearman non-parametric correlation test was conducted due to the non-normal distribution of the data.[13]

RESULTS

The normality test revealed that the UACR values were not normally distributed, as indicated by the significance value of < 0.001 (< 0.05). On the other hand, the urine osmolality values were found to be normally distributed, with a significance value of 0.523 (> 0.05). Similarly, the EGFR values were also not normally distributed, with a significance value of < 0.001 (< 0.05).

Table 1 is a descriptive analysis of 30 aged from 18 to 74 years old. Found 3 (10%) aged 11 to 20 years old, 8 (26.67%) aged 21 to 30 years old, 5 (16.67%) aged 31 to 40 years old, 6 (20%) aged 41 to 50 years old, 7 (23.33%) aged 51 to 60 years old, 1 (3.33%) aged 61 to 70 years old. However, there is no one aged 71 to 80 years old. In general, 10 males (33.33%) and 20 females (66.67%) of the total. 14 (46.67%) included acute kidney injury (AKI), 16 (53.33%) chronic kidney disease (CKD).

Shows that: 1). Median UACR ranged from 39.74 to 14766.46 mg/g was (Median ± SD: 1574.91000 ± 3840.948458; 2). Mean urine osmolality 129 to 576 mOsm/kg (Mean ± SD: 295.26667 ± 98.076302); 3). Median EGFR 1.322 to 37.966 mL/minute/1.73 m² (Median ± SD: 6.84350 ± 11.071225).

The data outcomes of the study were analysed using Spearman's non-parametric correlation test. Table 2 shows that the correlation test between UACR value and urine osmolality value resulted in a significance value (2-tailed) of 0.342 (>0.05), indicating that there is no correlation between UACR value and urine osmolality value. Similarly, the correlation test between UACR value and EGFR value yielded a significance value (2-tailed) of 0.481 (>0.05), indicating no correlation between UACR value and EGFR value.

TABLE 1
Descriptive Analysis of Research Sample

Characteristics	Total (n=30)	Percentage
Age		
11 – 20 years old	3 people	10 %
21 – 30 years old	8 people	26.67 %
31 – 40 years old	5 people	16.67 %
41 – 50 years old	6 people	20 %
51 – 60 years old	7 people	23.33 %
61 – 70 years old	1 person	3.33 %
71 – 80 years old	0 people	0 %
Gender		
Male	10 people	33.33 %
Female	20 people	66.67 %
Diagnosis		
Acute Kidney Injury (AKI)	14 people	46.67 %
Chronic Kidney Disease (CKD)	16 people	53.33 %

TABLE 2
Spearman Correlation Test Results

Variables	UACR Value	Urine Osmolality Value	p-value
UACR value	–	0.342*	0.481*
Urine osmolality value	0.342*	–	–
EGFR value	0.481*	–	–

*p-value

DISCUSSION

The correlation test study between UACR value and urine osmolality value, as well as EGFR value, in patients with kidney failure indicates a lack of association between UACR value and either urine osmolality value or EGFR value. This discrepancy arises due to the differing diagnoses observed in this study, specifically between acute kidney injury (AKI) and chronic kidney disease (CKD). According to the RIFLE criteria, patients with AKI are classified into five categories based on the decline in kidney function, with each category having a distinct diagnostic significance.[16] Meanwhile according to KDIGO, patients with CKD are classified based on a decrease in kidney function, measured by a decrease in GFR, and an increase in albuminuria. The decrease in GFR is divided into six categories, while the increase in albuminuria is divided into three categories and each category also has different diagnostic implications.[17]

Currently, the most reliable method for examining urine osmolality is the freezing point drop method.[18] However, in this study, the urine osmolality value was estimated using the principle of electrical conductivity.[10] Research conducted by Matthijs Oyaert, *et al* has shown that the principle of electrical conductivity still needs further investigation before it can be used to accurately report urine osmolality in routine clinical practice.[19]

There is no correlation between UACR value and EGFR value in patient with kidney failure. According to a study conducted by Andrew S. Levey, *et al*, changes in albuminuria are more effective indicators of therapy outcomes in individuals with chronic kidney disease (CKD) than changes in estimated glomerular filtration rate (EGFR).[8] It is unclear in this study which samples

have undergone medication that alters the UACR value while the EGFR value remains low. This can result in the absence of an expected correlation.

Furthermore, Boonsong K. Kitiwan, *et al* discovered in their research that the correlation between urine osmolality and EGFR exhibited a non-linear pattern. After controlling for demographic, social, cardiovascular, and dietary risk factors, there was no statistically significant relationship found between quartile urine osmolality and the decline in kidney function and/or the presence of albuminuria. Kidney function decline was defined as having estimated glomerular filtration rate (EGFR) values below 60 mL/min/1.73 m^2, and albuminuria was defined as having urine albumin creatinine ratio (UACR) values equal to or greater than 30 mg/g.[12]

CONCLUSION

There was no correlation between the urine albumin creatinin ratio (UACR) value and the urine osmolality value (p = 0.342) or the estimate glomerular filtration rate (EGFR) value (p = 0.481) in individuals diagnosed with kidney failure. The findings of this investigation cannot be utilized to establish the urine osmolality parameter as a reportable parameter on the Sysmex UF-4000 equipment employed in this study. In future research, there is an expectation for a more even distribution of samples, particularly in terms of patient diagnoses and the forms of therapy received by kidney failure patients included in the study. Furthermore, the evaluation of urine osmolality should employ the method of freezing point depression.

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Platelet to Lymphocyte Ratio (PLR) Value in Normotency, Preeclampsia and Severe Preeclampsia

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Abstract

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Background : Hyperactivation of the inflammatory response in preeclampsia causes a significant increase in the number of leukocytes. Platelet to Lymphocyte Ratio (PLR) has been known as a marker of systemic inflammatory response. In preeclampsia, the role of PLR markers is still uncertain regarding the ability of clinical evaluation, differential diagnosis and evaluation of patient prognosis. The aims of this study was to analyze differences in platelet to lymphocyte ratio (PLR) values in normotensive, preeclampsia, and severe preeclampsia pregnancies

Methods : Analytical observational study with cross sectional design with 90 samples consisting of 30 normotensive, 30 preeclampsia and 30 severe preeclampsia pregnancies. Evaluation was carried out on the platelet to lymphocyte ratio (PLR) value. Analysis was carried out using the SPSS 32 edition application. Results are significant if $p<0.05$.

Results : Comparison between the normotensive versus preeclampsia versus severe preeclampsia group showed that platelet levels decreased but not significantly ($p=0.081$), lymphocyte levels increased significantly ($p<0.001$) and PLR values decreased significantly ($p<0.001$) as the degree of severity increased preeclampsia. In the severe preeclampsia group, the lowest platelet levels, the highest lymphocyte levels and the lowest PLR values were obtained. Patients with a PLR value of < 104.62 have an 8.43x (OR 8.43; CI95% 3.12–22.78) higher risk of experiencing severe preeclampsia compared to subjects with a PLR value > 104.62.

Conclusion : The PLR value was significantly lowest in the severe preeclampsia group.

Keywords : preeclampsia, severe preeclampsia, platelet to lymphocyte ratio

INTRODUCTION

One form of hypertension during pregnancy that is dangerous is preeclampsia (PE). Preeclampsia (PE) affects approximately 2–8% of all pregnancies worldwide and remains one of the leading causes of maternal morbidity and mortality.[1] In severe cases, preeclampsia can lead to maternal organ dysfunction, systemic diseases such as HELLP syndrome (hemolysis, elevated liver enzymes, low platelets), poor maternal clinical outcomes, and poor perinatal clinical outcomes such as early and late intrauterine growth retardation.[2]

Studies show that hyper-reactivation of inflammatory cells and immunological response of neutrophils and lymphocytes occurs by releasing inflammatory cytokines and autoantibodies that cause endothelial dysfunction. The clinical manifestations of PE are associated with widespread endothelial dysfunction, leading to vasoconstriction and end-organ ischemia.[2] The enhancement of inflammatory and immune responses that occurs in preeclampsia significantly increases white blood cell count and modulates white blood cell function, leading to the production of more superoxide than nitric oxide, leading to damage and dysfunction. endothelium.[3]

Platelet to Lymphocyte Ratio (PLR) has been known as a marker of systemic inflammatory response. It is considered to have diagnostic significance in many systemic and local inflammatory diseases. In PE, abnormal changes are also observed in leukocytes. However, the role of these systemic inflammatory markers remains unclear in the clinical assessment, differential diagnosis, and prognostic assessment of PE. This study was conducted to analyze the differences in platelet to lymphocyte ratio (PLR) values as predictors of normotensive pregnancies, preeclampsia and severe preeclampsia.

METHODS

Analytical observational study with cross sectional design of 90 samples consisting of 30 normotensive 30 preeclampsia and 30 severe preeclampsia pregnancies. Evaluation was carried out on the platelet to lymphocyte ratio (PLR) value. Sampling was carried out using consecutive sampling, namely selecting research subjects based on research criteria and subjects signing an agreement to participate in the research.

The study was conducted from May to November 2023 in RSUP dr. Kariadi Semarang. Inclusion criteria include 1) pregnant women with gestational age >20 weeks, 2) singleton pregnancies, 3) patients diagnosed with normotensive pregnancy (Systolic blood pressure (SBP) <140 mmHg and diastolic blood pressure (DBP) <90 mmHg) or preeclampsia (SBP ≥140 mmHg and/or DPB ≥90 mmHg with target organ damage) or severe preeclampsia (SBP ≥160 mmHg and/or DPB

≥110 mmHg with target organ damage). Exclusion criteria include 1) pregnant women with platelet disorders such as ITP, HELLP syndrome, 2) premature rupture of membranes, 3) multiple pregnancies, and 4) patients with uncontrolled comorbidities.

1) Individuals who met the inclusion and exclusion criteria and agreed to take part in the research were used as research subjects. Explanations were given directly by researchers, medical personnel or residents who were on duty in the Polyclinic or in the emergency installation.

2) Anamnesis was performed on the research subjects. Their name, age, address, parity, first day of last menstruation, gestational age, current complaints, general condition and vital signs were checked.

3) Every pregnant woman studied continued to undergo pregnancy checks according to the specified schedule. At each routine visit, blood pressure measurements, obstetric examinations (uterine fundal height, gestational age, fetal heart rate) and laboratory examinations (routine blood and proteinuria) were carried out.

4) The research subjects had 3 mL of venous blood drawn. For patients who were planned to receive antenatal corticosteroids, samples were taken before administration of antenatal corticosteroids.

5) Blood samples were sent to the laboratory of RSUP Dr. Kariadi for routine blood and absolute lymphocyte tests. Blood samples from the community health center were taken by midwives/ nurses, then the blood samples along with the research sample form were submitted to the laboratory section of RSUP Dr. Kariadi. Blood samples could be sent directly or stored in a cool box at a temperature of 40oC for a maximum of 12 hours before being sent to the laboratory at RSUP Dr. Kariadi.

6) Absolute platelet and lymphocyte values were collected and recorded from prints of the hematoanalyzer results of research samples. The PLR value was obtained from the platelet count divided by the absolute lymphocyte count, then the data was analyzed statistically

Tests for differences in platelet levels and PLR values between the three research groups were carried out using Kruskal Wallis because the data had an abnormal distribution. The test for differences in lymphocyte levels between the three research groups was carried out using one way ANOVA because it has a normal data distribution. ROC curve analysis was carried out to determine the best cut off value in estimating the incidence of severe preeclampsia in research subjects. Analysis of the risk of preeclampsia based on the PLR value was carried out using the Chi-Square test. Analysis was carried out using the SPSS 32 edition application. Results were said to be significant if the p value <0.05. Ethical approval was obtained from The Health Research Ethics Committee RSUP Dr. Kariadi Semarang no.

1465/EC/KEPK-RSDK/2023.

RESULTS

Analysis of platelet levels, lymphocyte levels and PLR values was carried out in the three research groups so that the following results were obtained.

There was no significant difference in the distribution of platelet levels between study groups (p=0.081). There was a significant difference in the distribution of lymphocyte levels between the study groups (p<0.001), where the highest lymphocyte levels were found in the severe preeclampsia group. There was a significant difference in the distribution of PLR values between study groups (p<0.001), where the lowest PLR value was found in the severe preeclampsia group.

There were significant differences in the distribution of PLR values between study groups, where the lowest PLR values were found in the severe preeclampsia group. There is a correlation between the PLR value and preeclampsia status with a moderate and inverse correlation level. This means that the more severe the preeclampsia status will be correlated with a decrease in the PLR value.

The PLR value (AUC: 0.826) with a cut off <104.62 had a sensitivity of 78.3% and a specificity of 70% in assessing the incidence of severe preeclampsia in research subjects.

Subjects with a PLR value ≤104.62, were 21 subjects with PEB and 13 subjects with PE-normal. Subjects with PLR values > 104.62, were 9 subjects with PEB and 47 subjects with PE-normal. There was a relationship between the PLR value and the incidence of PEB (p<0.001) where subjects with a PLR value ≤104.62 had an 8.43x (OR 8.43; CI95% 3.12–22.78) higher risk of experiencing PEB than subjects with a PLR value > 104.62.

The analysis found a correlation between platelet levels and systolic blood pressure (p=0.035) and diastolic blood pressure (p=0.031) with a weak and inverse correlation level, a correlation between lymphocyte levels and systolic blood pressure (p<0.001) and diastolic blood pressure (p<0.001) with a moderate and unidirectional

TABLE 1

Platelet to Lymphocyte Ratio based on the blood pressure status of pregnant women

Variable	Normotensive (n=30)	Preeclampsia (n=30)	Severe Preeclampsia (n=30)	*P*
Platelet	309.300 ± 53.138; 308.000 (203.000–395.000)	222.100 ± 55.103; 227.000 (109.000–358.000)	199.866 ± 86.260; 217.000 (12.000–326.000)	0.081‡
Lymphocyte	1.703 ± 457.76; 1.665 (1.000–2.910)	2.305.33 ± 641.01; 2.305 (1.040–3.950)	2.373.73 ± 713.78; 2.295 (1.140–3.910)	<0.001†
PLR	195.31 ± 63.32; 185.76 (102–310)	106.53 ± 44.35; 104.76 (37.45–191.34)	84.98 ± 33.45; 88.45 (9.23-133.33)	<0.001‡

†One-way ANOVA; ‡Kruskal wallis; significant *p*<0.05
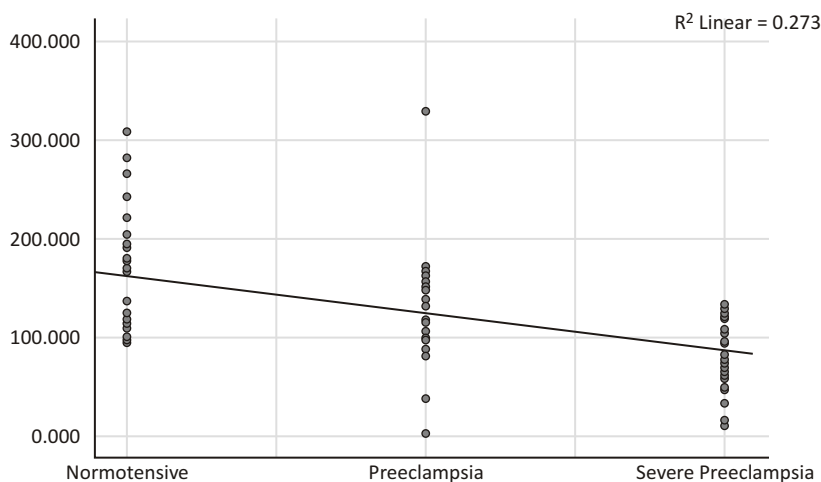
Figure 1. Scatter plot curve of platelet levels based on preeclampsia status
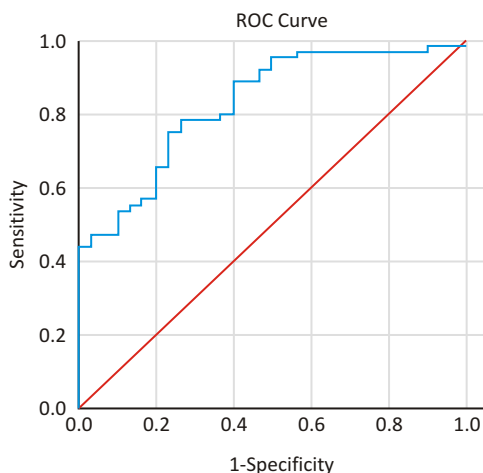
Figure 2. ROC curve analysis of PLR values on the incidence of severe preeclampsia
(severe preeclampsia vs preeclampsia–normal)

TABLE 2
The risk of preeclampsia based on the PLR value

| Variable | | Preeclampsia | | p | OR (CI95%) |
		Severe Preeclampsia	Preeclampsia-Normal		
PLR	≤ 104.62	21	13	<0.001	8.43 (3.12–22.78)
	> 104.62	9	47		

Chi-Square; significant $p<0.05$

TABLE 3
Correlation test between PLR and systolic and diastolic blood pressure

| Variable | Systolic Blood Pressure | | Dystolic Blood Pressure | |
	p	r	p	r
Platelet	0.035	-0.222	0.031	-0.227
Lymphocyte	<0.001	0.408	<0.001	0.441
PLR	<0.001	-0.522	<0.001	-0.564

Spearman; significant $p<0.05$

correlation level and a correlation between PLR values and systolic blood pressure ($p<0.001$) and diastolic blood pressure ($p<0.001$) with a moderate and inverse correlation level. This means that higher systolic blood pressure or diastolic blood pressure will correlate with decreased platelet levels, increased lymphocyte levels and decreased PLR values.

DISCUSSION

Cui H. found that PLR values were lower in PEB cases than in controls.[4] Toptas *et al*. also found that PLR values were comparable between PE pregnancies and normal pregnant women. In addition, patients with PEB had lower PLR values compared with PE.[5]

Melekoglu R *et al*. grouped preeclampsia cases as PE and PEB and reported that the sensitivity, specificity and AUC of PLR for diagnosing PEB were 45.9%, 78.1% and 0.573, respectively.[6] In two trials, the accuracy of PLR in identifying PEB reported the sensitivity, specificity and AUC of 49.6%, 74.7%, 0.639 and 55%, 50%, 0.554.[7,8] Mahmoud AGE, *et al* stated that the PLR value with a cut off 8.07 can be used as a predictor of preeclampsia with a sensitivity of 81.1%, specificity of 95.1%, PPV 28.6% and NPV 64.6%.[9] This study has a higher PLR cut-off value compared to other studies, allegedly caused by the

research subjects who had a gestational age of >20 weeks, while in the study of Mahmoud AGE, *et al* used subjects with a gestational age of 7–14 weeks and then followed until delivery. Research by Cha HH, *et al* has shown that the PLR value increases with increasing gestational age. So it is not surprising that the PLR cut-off value of this study is higher than the study of Mahmoud AGE, *et al* because of the difference in maternal gestational age.[10]

Severe preeclampsia shows hyperinflammatory activation which causes a decrease in PLR, compared with normal pregnancy. Preeclampsia develops due to defects in placentation, excessive innate/adaptive immune activation, and inflammation at the maternal-fetal interface. In preeclamptic patients, there is a shift from Th2 to Th1 lymphocytes, with reduced immune tolerance.[11] In severe preeclampsia the coagulation system is directly attacked, and the number of platelets reaches a much lower level than in normal pregnancy.[12]

Fluid retention occurs during pregnancy due to sodium and water retention caused by the effects of the estrogen and progesterone, which causes hemodilution or pseudo-thrombocytopenia. Presumably, increased vascular tone during pregnancy causes platelet destruction and coagulation defects also occur. In addition, increased serum levels of platelet-associated IgG may occur in some pregnant women suffering from hypertension. However, elevated immunoglobulins are nonspecific and do not indicate the presence of immunologically mediated thrombocytopenia.[13] Additionally, contact of platelets with damaged endothelium stimulates the coagulation cascade, which can increase platelet consumption and production in the bone marrow.[14]

Thrombocytopenia in preeclampsia is due to various causes including increased platelet consumption due to disseminated intravascular coagulopathy and/or immune mechanisms. The attachment of platelets to areas of damaged vascular endothelium can also result in secondary destruction of platelets.[15]

Prostacyclin is an important eicosanoid that has a strong inhibitory effect on platelet aggregation. Eicosanoids are continuously available in the blood vessels thereby maintaining circulating platelets in a dispersed form. Low levels of prostacyclin can cause circulating platelets to be increasingly susceptible to aggregation. Removal of platelet aggregates from the body's circulatory system is thought to be responsible for the occurrence of thrombocytopenia which often occurs in cases of hypertension during pregnancy. Platelets from patients with severe preeclampsia also showed a lower response than normal pregnancies to various aggregation agents suggesting that platelets may have undergone prior aggregation in the microcirculation.[15]

Recent studies have found that elevated plasma levels of the soluble vascular endothelial cell growth factor (VEGF) receptor sFlt1 type 1 as well as endoglin, an endothelial cell-derived member of the tumor growth factor receptor-2 (TGF-2) family, are present in patients thought to be will experience preeclampsia at the end of the first trimester. Increased levels of soluble fms-like tyrosine kinase-1 (sFlt1) and endoglin mRNA were found in the placenta of preeclamptic patients, indicating that this is the main cause of preeclampsia. sFlt1 is known to bind and inactivate VEGF and placental growth factor (PLGF), the levels of which usually increase during pregnancy, while endoglin blocks the binding of TGF-2 to endothelial cells.[16]

Preeclampsia is characterized by higher levels of superoxide and markers of systemic inflammation.[17] Lymphocytes have pro- and anti-inflammatory effects associated with pregnancy phenotypes. Anti-inflammatory T regulatory cells (Tregs) are known to suppress the maternal immune system response against fetal tissues, and T-helper 17 (Th17) cells promote inflammation, autoimmunity and transplant rejection in humans. Significant increases in Th17 cells and/or decreases in Treg numbers have been reported in severe obstetric complications. Identification of lymphocytes would be informative, but a decrease in total lymphocyte numbers in PE suggests that inflammatory features may play an important role in the maintenance of obstetric complications, such as PE.[18]

There are differences in lymphocyte levels in preeclampsia patients compared to normal pregnancies between several studies, it is suspected that one of the influencing factors is gestational age. Research that assessed the lymphocyte levels of preeclampsia patients between preterm births compared to term births found that the mean lymphocyte levels were significantly higher in preterm births (2.25 vs 2.07; $p<0.001$).[19]

This study has several limitations, including 1) the enforcement of PE and PEB criteria did not use other laboratory markers, 2) in eliminating exclusion criteria only using patient's history data and, 3) The gestational age range used as inclusion criteria was too broad (>20 weeks), but it is known that lymphocyte levels will normally change with changes in gestational age. It has been mentioned that lymphocyte levels decrease during the 1st and 2nd trimesters, then increase in the 3rd trimester.[20] Therefore, further research should conduct analysis based on the trimester of pregnancy.

CONCLUSION

The PLR value was significantly lowest in the severe preeclampsia group. Evaluation of low PLR values (<104.62) in pregnant women is at risk of developing severe preeclampsia

CONFLICTS OF INTEREST

There is no conflict of interest in this research.

ACKNOWLEDGMENT

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Original Article

Effect of Vitamin D Administration on Interleukin–6 (IL-6) Levels in Peritoneal Fluid in Endometrioma Patients

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Abstract

Background : An endometrioma is a cyst that occurs when endometrial tissue grows on the epithelium of the ovary. Vitamin D is a steroid hormone that can be extracted from commonly available foods and can be synthesized by humans when exposed to sunlight. Vitamin D deficiency has been reported to be associated with various pathologies, including endometrioma. Vitamin D has been reported to have anti-angiogenic effects that may inhibit the growth of endometriotic implants.The aimsof this study was to proving the effect of vitamin D administration on interleukin 6 (IL-6) levels in peritoneal fluid in patients with endometrioma.

Methods : Experimental research with two groups, post-test only design with single blind that was carried out at Central General Hospital (RSUP) Dr. Kariadi Semarang. The research subject was 50 patients with endometrioma of the ovary. The definite diagnosis of endometrioma was made based on histopathological examination of tissue samples after the patient went surgery. Patients would be divided into 2 groups, namely the vitamin D3 supplementation and placebo groups. The intervention was carried out by providing vitamin D3 50,000 IU/week for a month. Evaluation of serum vitamin D levels were obtained using venous blood samples immediately when the patient was undergoing surgery. Interlukin-6 levels were obtained using peritoneal fluid samples obtained when the patient underwent surgery. Statistical analysis was carried out using the Independent T Test, Mann-Whitney U, Dependent T Test and Wilcoxon. Results are significant if $p < 0.05$. Statistical analysis was carried out using SPSS edition 26.

Results : Peritoneal fluid interleukin-6 (IL-6) levels between the vitamin D supplementation group and the placebo group did not show a significant difference (p=0.554).

Conclusion : Vitamin D supplementation in endometrioma patients is not associated with peritoneal fluid interleukin-6 (IL-6) levels.

Keywords : Endometrioma, interleukin 6, peritoneal fluid, vitamin D

INTRODUCTION

Endometrioma is a benign gynecological disease that often occurs in women. It is estimated that 10–15% of women of childbearing age worldwide suffer from endometrioma, and 30–40% of them have the potential to experience infertility.[1–3] Localized pelvic inflammatory disease, accompanied by changes in immune-related cell function and changes in cytokine levels in the abdominal cavity, is associated with the presence of endometrioma. Many studies have shown that the peritoneal fluid of women with endometriomahas significantly increased levels of activated macrophages, produces more cytokines, including IL-6, and increases angiogenesis.[4–6] This has also been proven by several studies reporting increased levels of pro-inflammatory cytokines such as IL-6 in the peritoneal fluid of women with endometrioma.[7,8] It is known that there are several potential stimuli for IL-6 production in the abdominal cavity, one such stimulus being retrograde menstruation, a reported etiology of endometrioma.[6] High levels of IL-6 are associated with the severity of endometrioma and have been used as a marker of endometrioma.[9]

Vitamin D is a steroid hormone that can be extracted from commonly available foods such as egg yolk, marine fish, and liver, which humans can synthesize through exposure to sunlight. Vitamin D comes in different forms, the most common of which is vitamin D3, which is produced in the epidermis by UVB rays. However, it has been reported that more than one billion people suffer from vitamin D deficiency, of which 36–69.9% are of reproductive age. Vitamin D deficiency has been reported to be associated with various pathologies such as musculoskeletal disorders, recurrent miscarriages, and endometrioma.[10,11]

Vitamin D is a powerful antioxidant with anti-inflammatory and immunomodulatory properties that affect both the innate and adaptive immune systems.[12–14] Vitamin D is known to strengthen immunity by suppressing immune reactions. Several studies have shown that vitamin D3 can influence the local activity of immune cells, which have an important pathogenic role in the development of endometrioma. It has been reported that vitamin D administration can significantly reduce IL-1β and IL-8 levels.[15,16] In addition, vitamin D has also been reported to have anti-angiogenic effects that can inhibit the growth of endometriotic implants in mice. These properties support vitamin D as an effective adjuvant therapy with minimal side effects.

This research was conducted to prove the effect of vitamin D administration on interleukin 6 (IL-6) levels in peritoneal fluid in patients with endometrioma.

METHODS

This research is an experimental research with two group, post-test only design with single blind that was carried out at Central General Hospital (RSUP) Dr. Kariadi Semarang. The research sample was 50 patients with endometrioma, and the selection of research subjects would be carried out using consecutive sampling, namely the selection of research subjects based on research criteria and the subjects signing an agreement to participate in the research. Patients would be divided into 2 groups, namely the vitamin D3 supplementation group and placebo. The intervention was carried out by providing vitamin D3 50,000 IU/week for a month.

The diagnosis of endometrioma was established in two stages. The first stage was based on the suspicion of endometrioma through physical and ultrasound (USG) examinations. In the second stage, a definite diagnosis was made based on histopathological examination of tissue samples after the patient went surgery. The inclusion criteria in this study were 1) female, 2) aged 15–45 years, 3) patients diagnosed with endometrioma on ovary, 4) vitamin D deficiency with a 25 (OH)D concentration <20 mg/mL, 5) indicated to undergo laparoscopy surgery. The exclusion criteria in this study were 1) patients with a history of consuming vitamin D 6 months before surgery, 2) patients with systemic diseases (hypertension, diabetes, coronary heart disease, kidney and liver disease), 3) patients with malignancies, 4) menopausal patients, 5) patients undergoing hormonal therapy, including oral contraceptives in the last 6 months.

Vitamin D serum levels were obtained using venous blood samples immediately when the patient was undergoing surgery. Interlukin-6 levels were obtained using peritoneal fluid samples obtained when the patient underwent surgery. The data that has been obtained is entered in the form of a master table using the SPSS statistical data processing software program. The data was tested for normality of data distribution using the Shapiro-Wilk test, where the data distribution is said to be normal if $p>0.05$. For numerical variables (ratios and intervals), if the data distribution was normal, the analysis was carried out using the independent T-test (for unpaired data) or dependent T-test (for paired data), but if the data distribution was not normal then the analysis was carried out using the Mann Whitney U test (for unpaired data) or Wilcoxon test (for paired data). Results are significant if $p<0.05$. Before the research was carried out, the researcher submitted an ethical clearance to the Health Research Ethics Commission (KEPK) of the Faculty of Medicine, Diponegoro University no 1457/EC/KEPK-RSDK/2023.

RESULT AND DISCUSSION

Endometrioma often occurs in women of reproductive age, but not in postmenopausal women due to the lack of estrogen hormone. Hormonal changes can affect the

TABLE 1
Vitamin D levels based on vitamin D supplementation

Variable	Vitamin D Supplementation		Placebo		*p*
	n (%)	Mean ± SD; Median (min–max)	n (%)	Mean ± SD; Median (min–max)	
Vitamin D pre		14.54 ± 3.27; 14.6 (8.8–20)		15.73 ± 3.56; 15.7 (10.2–24)	0.224[†]
Deficiency	24 (96)		21 (84)		
Insufficiency	1 (4)		4 (16)		
Normal	0 (0)		0 (0)		
Vitamin D post		28.54 ± 12.80; 23.9 (12.1–55.5)		14.34 ± 4.32; 13.3 (8.8–28.8)	<0.001[†]
Deficiency	9 (36)		23 (92)		
Insufficiency	7 (28)		2 (8)		
Normal	9 (36)		0 (0)		
p		<0.001[¶]		0.034[¶]	
Δ Vitamin D	–	13.99 ± 12.60; 9.4 (0.7–43)	–	-1.38 ± 3.08; -0.5 (-8.8–4.8)	<0.001[†]

[†]Independent T test; [¶]Dependent T test; significance *p*<0.05

TABLE 2
IL-6 levels based on vitamin D supplementation

Variable	Vitamin D Supplementation		Placebo		*p*
	n (%)	Mean ± SD; Median (min–max)	n (%)	Mean ± SD; Median (min–max)	
Interleukin 6	–	19.03 ± 35.93; 1.9 (0.02–105)	–	19.92 ± 36.69; 1.6 (0.02–105)	0.554[‡]

[‡]Mann Whitney U; significance *p*<0.05

proliferation of endometrial cells attached to the mesothelium. This supports the idea that endometrioma is an estrogen-dependent condition.[17] In addition, domestic work largely dominates among female employees in the private sector. This contrasts with outdoor workers who are exposed to more sunlight than indoor workers. Vitamin D3 levels were significantly lower in patients with severe endometrioma compared to normal controls and patients with mild endometrioma. Vitamin D is produced in the body from food and supplements and from sunlight on the skin.[18]

Assessments carried out between initial vitamin D and final vitamin D levels showed that there was a significant difference in the vitamin D supplementation group (*p*<0.001) and the placebo group (*p*=0.034), whereas, in the vitamin D supplementation group, there was a significant increase in vitamin D levels whereas in the placebo group experienced a significant decrease in vitamin D levels.

Khodadadiyan A *et al.*, in a systematic review and meta-analysis regarding the effect of vitamin D supplementation on serum vitamin D levels, found a significant change in 25(OH)D (SMD: 2.2, I2: 92.3, 95% confidence interval (CI): 1.38–3.02, *p*-value: 0.048) and 1.25(OH)2D (SMD: 1.23, I2: 86.3, 95% CI: 0.01–2.44, *p* value < 0.010) was affected by vitamin D intervention.[19] Best CM *et al.*, in an experimental study of 161 adults supplemented with 2,000 IU/day of vitamin D3, obtained results that initially showed a positive, non-linear relationship between total vitamin D intake. in serum and total 25(OH)D in serum. concentration. The modulating effect of supplementation was an increase in serum vitamin D to 29.2 (95% CI: 24.3, 34.1) nmol/L and an increase in serum vitamin D 25(OH)D to 33.4 (95% CI: 27.7, 39.2) nmol/L.[20]

The response of 25(OH)D to a given dose of vitamin D varies widely among individuals. A systematic review explained approximately 50% of the interindividual variation in response to body weight, age, type of supplement (vitamin D2 or D3), concomitant use

TABLE 3
Vitamin D levels based on interleukin-6 levels

Variable	IL-6 <0.36 pg/mL		IL-6 > 0.36 pg/mL		*p*
	n (%)	Mean ± SD; Median (min–max)	n (%)	Mean ± SD; Median (min–max)	
Vitamin D pre		15.85 ± 3.75; 16.45 (10.4–24)		14.74 ± 3.24; 14.75 (8.8–20.5)	0.278[†]
Deficiency	15 (83.3)		30 (93.8)		
Insufficiency	3 (16.7)		2 (6.3)		
Normal	0 (0)		0 (0)		
Vitamin D post		22.70 ± 9.32; 21.55 (10–43)		20.73 ± 13.17; 16.1 (8.8–55.5)	0.130[‡]
Deficiency	8 (44.4)		24 (75)		
Insufficiency	6 (33.3)		3 (9.4)		
Normal	4 (22.2)		5 (15.6)		

[†]Independent T test; ‡Mann Whitney U; significance *p*<0.05

of calcium supplements, and baseline serum 25(OH)D concentrations. More recent evidence emphasizes the contribution of genetic variation.[21] For example, variants of the GC gene encoding the vitamin D binding protein (DBP) are strongly associated with the 25(OH)D response.[22] Although not confirmed, this may be related to genetic differences in serum DBP concentrations, which also vary depending on clinical status, sex, and life stage.

In the vitamin D supplementation group, the mean IL-6 level was 19.03 pg/mL with a standard deviation of 35.93 pg/mL, the median value was 1.9 pg/mL with the smallest value being 0.02 pg/mL, and the largest value being 105 pg/mL. In the placebo group, the mean IL-6 level was 19.92 pg/mL with a standard deviation of 36.69 pg/mL, the median value was 1.6 pg/mL with the smallest value being 0.02 pg/mL and the largest value being 105 pg/mL. There was no significant difference in the distribution of interleukin-6 levels between study groups (*p*=0.554).

Ashtari F, *et al* in their research found the same thing that there was no correlation between vitamin D levels and IL-6 levels (*p*>0.05).[15] El-Hajj C, *et al* who conducted an RCT study by providing cholecalciferol supplementation of 30,000 IU/week obtained similar results that there was no significant difference (*p*=0.1) in IL-6 levels between the vitamin D supplementation group and the control group.[23]

IL-6 is a pleiotropic cytokine that plays a role in stimulating inflammation. IL-6 is produced by lymphocytes and non-lymphocytes and activates the innate immune system during infection or trauma.[24] Through membrane receptors, IL-6 activates the non-receptor tyrosine kinase JAK2, which induces the JAK2/STAT3 cascade, leading to angiogenesis and tumor

mass growth as it regulates cell cycle progression. This mechanism is very important in cachexia, tumor cell migration and cancer development.[25,26] Chronic inflammation is also found in a quarter of cancer cases.[27]

In this study, there was no correlation between vitamin D supplementation and IL-6 levels, presumably due to the dose of vitamin D given to research subjects was too low so it could not have a significant effect on the body's pro-inflammatory cytokines. Another factor that is thought to be able to cause this was too fast a period of vitamin D supplementation. That was too fast, thus those was no time for the immune system to adjust to the factors produced during the inflammatory process so that there were no significant changes in IL-6 levels in research subjects.

Evaluation of serum vitamin D levels showed that there was no significant difference in pre (*p*=0.278) and post vitamin D levels (*p*=0.130) between endometrioma patients who had peritoneal fluid IL-6 levels <0.36 ng/mL versus >0.36 ng/ mL.

Vitamin D is the main regulator of the immune system and inflammation.[28] Numerous studies demonstrate the impact of vitamin D on innate and adaptive immune system cells. Various lines of evidence indicate that vitamin D levels are important for an optimal anti-inflammatory response of monocytes. By lowering the expression of many pro-inflammatory cytokines, such as tumour necrosis factor (TNF) and IL-6, vitamin D exerts an anti-inflammatory effect on monocytes. Numerous immune system cells, including human regulatory T cells, B cells, neutrophils, lymphocytes, and macrophages, have been discovered to contain vitamin D (VDR). By attaching VDR to the immune system, vitamin D can lower inflammatory and immunological responses.[29]

It is believed that vitamin D's inhibition of cell expression is the biochemical mechanism behind the relationship between vitamin D and IL-6.[30] This mechanism involves the pro-inflammatory transcription factors NFkB and MAPK phosphatase-1 (MKP-1). The last target of NF-KB activation, the pro-inflammatory cytokine IL-6, has been found to be regulated by vitamin D. Animal studies indicate that VDR deletion may contribute to increased NFkB transcriptional activity and increased circulating IL-6. This indicates that binding of vitamin D to VDR in the immune system may cause a decrease in circulating IL-6 levels.

The absence of a relationship between serum vitamin D levels and peritoneal fluid IL-6 levels in this study is thought to be due to other factors related to endometriomas that cannot be assessed but can influence IL-6 levels, including the number of endometriomas and endometrioma size. An increase in the number of endometriomas and endometrioma size is thought to be related to an increase in the degree of inflammation that occurs in patients. However, in this study it was not possible to evaluate these two factors due to limited data.

CONCLUSION

Vitamin D supplementation is not associated with peritoneal fluid interleukin-6 (IL-6) levels in endometrioma patients.

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Original Article

The Effectiveness of Cognitive Behavior Therapy in Enhancing Self-Esteem among Schizophrenia Patients at Dr. Soeharto Heerdjan Psychiatric Hospital, Jakarta in 2024

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Abstract

Background : Schizophrenia patients often experience low self- esteem which require modality therapy. One of modality therapy for patients with mental disorders is cognitive behavioral therapy (CBT). The aim of this research is to determine the effectiveness of cognitive behavior therapy in increasing self-esteem. and abilities in Schizophrenia patients.

Methods : This research method is quasi-experimental. The data was analyzed by Paired *t* test. The research was conducted in one hospital on 50 control patients and 50 intervention patients.

Results : The research results showed that cognitive behavior therapy significantly reduced signs and symptoms in clients with low self-esteem (*P*-value ≤0.05). The comparison of self-esteem scores in the intervention group was significantly higher compared with that in the control group (*P*-value ≤ 0.05).

Conclusion : Cognitive behavior therapy is effective for patients with low self-esteem because it can increase self-esteem and abilities in patients with schizophrenia. Future researchers should conduct research using cognitive behavior therapy without providing psychotherapy.

Keywords : Cognitive Behavior Therapy, low self-esteem, Schizophrenia

INTRODUCTION

Schizophrenia is a mental disorder that must be treated carefully. Schizophrenia has symptoms such as disturbances in consciousness and cognition, psychological symptoms in motor behavior, psychological symptoms in thought processes, perception disturbances related to cognitive impairments, and perception disturbances related to conversion and dissociation phenomena.[1] Schizophrenia patients need to be given modality therapy. One form of modality therapy for patients with mental disorders is cognitive behavior therapy.

Cognitive behavior therapy (CBT) focuses on problems, is outcome oriented and experiences problems here and now.[2] The purpose of CBT is to change irrational beliefs, faulty reasoning, and negative self-statements that underlie behavior.[2] In general, the implementation of CBT is as follows: a) to increase activity, b) to reduce maladaptive behaviors, c) to increase desired behaviors, d) to increase satisfaction, e) to achieve social skills.

The process of CBT is implemented across four sessions, each lasting for 30 to 45 minutes.[3] The first session, identifying events that lead to negative automatic thoughts and behaviors, and practicing techniques to counter the first negative automatic thought. The second session, practicing techniques to counter the second negative automatic thought and behavior, reviewing the exercises from the first session, and continuing to work on countering the second negative automatic thought. The third session, practicing to utilize the support system and the fourth session, evaluating the benefits of countering negative thoughts.

Research has shown that CBT can significantly reduce symptoms of chronic low self-esteem and violent behavior, with a P-value ≤0.05. Another study demonstrated that CBT could improve low self-esteem in gifted students.[4] Low Self-Esteem is a condition when someone feels that they are no longer valuable, useless and inferior for a long time or continuously.[5] Signs and symptoms of patients with low self-esteem are feeling inferior to others, criticizing themselves and others, difficulty in relationships, excessive self-importance, feelings of inadequacy, disturbances in relationships, and pessimistic outlook on life. One of the negative impacts of low self-esteem is feeling unworthy of achieving one's desires, becoming isolated from environment and group. Low self-esteem can lead to social isolation, withdrawal and violent behavior.[6]

Based on observations at Dr. Soeharto Heerdjan Mental Hospital, many patients suffer from low self-esteem. According to inpatient care data in 2022, 95 patients were diagnosed with low self-esteem as a primary nursing problem and had already received generalist therapy for low self-esteem. However, upon observation during outpatient care, it was found that many patients still exhibited low confidence, struggled to socialize, express opinions, or work effectively. If left unaddressed, these issues could worsen their chronic low self-esteem. Given this context, the researcher is interested in conducting a study titled "The Effectiveness of Cognitive Behavior Therapy on Improving Self-Esteem in Patients with Low Self-Esteem at Dr. Soeharto Heerdjan Mental Hospital, Jakarta."

METHODS

This study is a quantitative research project with a quasi-experimental design. The research was conducted at Dr. Soeharto Heerdjan Mental Hospital, Jakarta, from July to December 2024. The study population consists of all patients with low self-esteem in the Inpatient and Rehabilitation Units of Dr. Soeharto Heerdjan Mental Hospital. Total sample size of 100 respondents will be selected using non-probability sampling with a purposive sampling technique.

The instruments used in this study include a demographic data questionnaire, an evaluation instrument to assess signs and symptoms of chronic low self-esteem (CLSE), and an instrument to evaluate the clients' ability to cope with chronic low self-esteem. This research had received research ethics permission from the Soeharto Heerdjan Hospital research ethics commission number KH.03.02/D.XXXVIII.2/2563/2024 on January 10th, 2024.

RESULTS

Based on Table 1, the characteristics of respondents in both the intervention and control groups reveal no significant differences in gender distribution, with males accounting for 50% of the intervention group and 56% of the control group. The majority of respondents aged 31–60 years (60%), and most had a high school education (46%). The intervention group had a higher proportion of respondents with a Diploma/Bachelor's degree (16%) compared to the control group (6%).

Regarding marital status, 46% of the respondents were single, with the intervention group having a higher percentage of married respondents (50%) and the control group having a higher percentage of widow respondents (22%). The majority of respondents (60%) in both groups were unemployed. In terms of illness duration, 36% of respondents had been ill for 2–4 years, with most respondents in the control group had illness duration for more than 1 year (38%) while those in the intervention group have duration of illness of 5–8 years (30%).

Table 2 illustrates the changes in low self-esteem symptoms in both the intervention and control groups before and after the intervention. Both groups showed a reduction in cognitive, affective, physiological, behavioral, and social symptoms. The intervention group

TABLE 1
Demographic Data of Intervention and Control (n=100)

Characteristics	Intervention n (%)	Control n (%)	Total n (%)
Gender			
Male	25 (50)	28 (56)	53 (53)
Female	25 (50)	22 (44)	47 (47)
Age			
20–30 Years	19 (38)	21 (42)	40 (40)
31–60 Years	31 (62)	29 (58)	60 (60)
Education			
No Formal Education	1 (2)	2 (4)	3 (3)
Elementary School	7 (14)	5 (10)	12 (12)
Middle School	11 (22)	17 (24)	28 (28)
High School	23 (46)	23 (46)	46 (46)
Diploma/Bachelor's	8 (16)	3 (6)	13 (13)
Marital Status			
Married	25 (50)	16 (32)	41 (41)
Single	23 (46)	23 (46)	46 (46)
Widow	2 (4)	11 (22)	13 (13)
Occupation			
Housewife	8 (16)	6 (12)	14 (14)
Private Employee	1 (2)	7 (14)	8 (8)
Entrepreneur	14 (28)	3 (6)	17 (17)
Civil Servant	1 (2)	0 (0)	1 (1)
Others	26 (52)	34 (68)	60 (60)
Duration of Illness			
<1 Year	6 (12)	10 (20)	16 (16)
>1 Year	7 (14)	19 (38)	26 (26)
2–4 Years	22 (44)	14 (28)	36 (36)
5–8 Years	15 (30)	2 (4)	17 (17)

had a higher average reduction in affective symptoms (24.27), physiological symptoms (23.14), and social symptoms (18.87). However, respondents in the control group had a slightly higher average reduction in cognitive (24.54) and behavioral (23.42) symptoms compared with those in the intervention group

Further analysis demonstrated that Cognitive Behavior Therapy (CBT) in the intervention group and general therapy in the control group had a significant effect on reducing symptoms of low self-esteem (p-value <0.05). The intervention group showed a greater overall reduction in symptoms compared with the control group did

Table 3 shows the changes in respondents' ability to cope with low self-esteem. Before therapy, the control group had a higher score (31.75%), but after the intervention, the intervention group greater improvement (99%). Analysis confirmed that both

TABLE 2
Distribution of Low Self-Esteem Symptoms Before and After Intervention

Variable	Group	n	Pre-Test	Post-Test	Negative Mean Rank	*p*-value
Cognitive	Intervention	50	197 (65.7%)	97 (32.3%)	22.20	0.000
	Control	50	179 (59.7%)	81 (27.0%)	24.54	0.000
Affective	Intervention	50	207 (69.0%)	84 (28.0%)	24.27	0.000
	Control	50	218 (72.7%)	173 (57.7%)	17.95	0.037
Physiological	Intervention	50	149 (49.7%)	39 (13.0%)	23.14	0.000
	Control	50	124 (41.3%)	71 (23.7%)	19.91	0.000
Behavioral	Intervention	50	307 (55.8%)	143 (26.0%)	23.24	0.000
	Control	50	309 (56.2%)	196 (35.6%)	23.42	0.000
Social	Intervention	50	100 (66.7%)	43 (28.7%)	18.87	0.000
	Control	50	100 (66.7%)	68 (45.3%)	14.62	0.000

TABLE 3
Distribution of Ability to Cope with Low Self-Esteem Before and After Intervention

Variable	Group	n	Pre-Test	Post-Test	Negative Mean Rank	*p*-value
Client's Ability	Intervention	50	102 (25.5%)	396 (99.0%)	25.50	0.000
	Control	50	127 (31.75%)	81 (73.25%)	23.50	0.000

groups demonstrated a significant improvement in coping ability post-therapy (*p*-value <0.05), with the intervention group exhibited higher improvement in coping ability (25.50) compared to that in the control group.

DISCUSSION

Based on the results of the respondent characteristics, there is no significant difference between the intervention and control group. The number of male and female respondents are almost equal. The age range of respondents is between 31 and 60 years. The majority of respondents have a high school education. The average marital status of respondents is single. Most respondents are jobless, and the average duration of illness 2 to 4 years.

The majority of respondents are in the age range of 31 to 60 years. The most common age range is between 31 and 60 years. This age range marks the onset of a crucial psychosocial stage, where the key focus is on establishing good relationships with society, work relationships, and intimate relationships with others. If this is not achieved, individuals may struggle to build relationships.[7] Meanwhile, for the optimal achievement of self-esteem, individuals need to experience a sense of worth, meaning they feel valued and are able to appreciate others. They also need to feel capable, which is the feeling of being able to achieve desired outcomes, and feel accepted. The feeling of being accepted is when individuals feel valued and accepted for who they are and treated as part of a group.

The majority of respondents have been ill for more than 1 year, which may contribute to the development of low self-esteem in patients. One of precipitating factors of low self-esteem is the transition of roles from health to illness, as a result of the shift from a healthy state to an illness state. Additionally, patients with psychotic disorders often experience low self-esteem. This is associated with the development and duration of psychotic symptoms and poor clinical outcomes.[8]

Based on the results of the decrease in signs and symptoms of low self-esteem feelings in the intervention group receiving CBT and the control group receiving general therapy, data showed a decrease in symptoms in both groups. The decrease occurred in the cognitive, affective, physiological, behavioral, and social aspects. However, the decrease in symptoms of low self-esteem in the intervention group was higher on average compared to the control group, with the highest decreases in the

affective symptoms (24.27), physiological symptoms (23.14), and social symptoms (18.87). Based on the effects of CBT therapy in the intervention group and general therapy in the control group, both had an impact on the decrease of signs and symptoms of low self-esteem, with p-value of 0.000 (P-value <0.05).

International guidelines suggest that CBT is effective in improving self-esteem among patients with mental disorders. It was mentioned that after CBT intervention, patients in the CBT group showed improvement in terms of positive self-beliefs and self-esteem.[8] This perspective is supported by Sasmita (2010), indicating that Cognitive Behavioral Therapy significantly improves the cognitive and behavioral abilities of clients with low self-esteem, particularly among clients receiving CBT. This is because CBT is a form of psychotherapy that can enhance self-esteem of schizophrenia patients.[9] Another study also reported a significant improvement (p <0.05) in self-esteem following CBT sessions.

The decrease in signs and symptoms of low self-esteem also occurred in the control group, which received general therapy, and it was found that general therapy decreased signs and symptoms of low self-esteem (P-value ≤0.05). This is supported by previous, which mention that patients experienced an increase in self-esteem after receiving positive skills training. Positive skills training was shown to improve the self-esteem of patients with low self-esteem and poor self-concept.[10]

From the case study results in the implementation of therapeutic communication using low self-esteem strategies, it was found that general therapy could address nursing problems in schizophrenia patients with low self-esteem after five days of treatment. The evaluation after five days of care showed that the patient was able to improve their self-esteem, there was eye contact, the patient was able and willing to interact with others, and the patient was very cooperative.[11]

CONCLUSION

Cognitive behavior therapy is effective for patients with low self-esteem because it can increase self-esteem and abilities in patients with schizophrenia. Cognitive behavior therapy also reduces signs and symptoms of low self-esteem affectively, physiologically, behaviorally and socially. Patients with low self-esteem need psychotherapy and cognitive behavior therapy.

RECOMMENDATIONS

Cognitive Behavior Therapy has proven to be an effective intervention for patients with low self-esteem (P-value ≤ 0.05) and can be employed to enhance self-esteem in patients with schizophrenia, whether they are undergoing inpatient care or outpatient treatment at mental health facilities. This therapy can also be implemented in primary healthcare centers or other mental health services. Future researchers should conduct research using cognitive behavior therapy without providing psychotherapy.

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Original Article

The Association between Waist-Hip Ratio and Body Fat Composition, and Metabolic Syndrome: A Study at RSUP Dr. Kariadi

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Abstract

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Background : Metabolic syndrome, which is a collection of symptoms which are usually include of hypertension, hyperglycemia, dyslipidemia, and central obesity, has various fatal complications. Fat composition is known to have a close relationship with complications of metabolic syndrome. However, measurement of fat usually requires expensive tools and methods. Meanwhile, anthropometric indicators such as waist-to-hip ratio (WHR) have links with metabolic syndrome and central obesity. This study examines whether there is a significant relationship between WHR and body fat composition in patients with metabolic syndrome. This study examined relationship between WHR and body fat composition as described in fat percentage, fat mass, visceral fat rating, and degree of obesity in patients with metabolic syndrome.

Methods : Cross-sectional observational analytic study was conducted on 51 metabolic syndrome patients at Endocrine Polyclinic, RS dr. Kariadi. Respondents filled out informed consent and questionnaires and measured WHR and body fat composition using Tanita scales. Data analysis was performed by univariate test and bivariate test (Pearson test, Spearman test, or Mann-Whitney test).

Results : There is a weak significant negative correlation between WHR and body fat percentage ($p = 0.023$; $r = -.0.318$). There is no correlation between WHR and fat mass ($p=0.312$). There is a weak positive significant correlation between WHR and visceral fat rating ($p=0.001$; $r=0.441$). And there is no correlation between WHR and the degree of obesity ($p=0.785$).

Conclusion : WHR has a weak significant correlation with body fat percentage and visceral fat rating in NCEP ATP III metabolic syndrome patients.

Keywords : Waist to hip ratio, body fat composition, metabolic syndrome.

INTRODUCTION

World Health Organization defines metabolic syndrome as a pathological condition characterized primarily by central obesity, hypertension, insulin resistance, and hyperlipidemia.[1] Metabolic syndrome has various definitions depending on the criteria used, WHO, National Cholesterol Education Program (NCEP) ATP III, European Group for the Study of Insulin Resistance (EGIR), and International Diabetes Federation (IDF) criteria.[2,16] The impact/complications caused by metabolic syndrome can be fatal to health and life-threatening, such as sudden cardiac death and other atherosclerotic cardiovascular diseases,[3] as well as cerebrovascular diseases like stroke.[4] Central obesity, which is the accumulation of fat in the visceral area, is closely related to metabolic syndrome.[5] Therefore, studies on body fat in patients with metabolic syndrome need to be developed with the hope of finding variables that can be used as predictors to predict the risk of metabolic syndrome and its complications earlier. Meanwhile, body fat composition is described both as the degree of fat cells present in the body, which can be illustrated in body fat percentage, total body fat mass, visceral fat rating, and degree of obesity. Excess fat in the body is closely related to complications of metabolic syndrome, such as atherosclerotic cardiovascular disease.[6] Therefore, early detection of changes in body fat composition is expected to indicate the complications, such as cardiovascular diseases, complications in patients with metabolic syndrome as early as possible.

There are several methods of measuring body fat composition that are considered valid. For this research, the researchers used the bioelectrical impedance analysis (BIA) method because this technique is known to be quite fast, simple, inexpensive, and easy to perform.[15] However, not all healthcare facilities have body composition measurement tools like BIA. In addition to fat composition measurement techniques like BIA, there are several anthropometric indicators that are believed to have a strong correlation with metabolic syndrome, such as the waist-to-hip ratio (WHR).[9] Anthropometric measurement techniques like WHR have several advantages, such as simple, inexpensive, and easy to perform without requiring special skills. This study was conducted on patients with metabolic syndrome with the aim of assessing the correlation between WHR and body fat composition measured by the BIA technique. It is hoped that WHR measurement can become an alternative method that is simple, accurate, inexpensive, and easy for measuring body fat composition in patients with metabolic syndrome, if BIA is not feasible. With the discovery of an alternative method that is cheaper and easier to perform, it is hoped that fat composition screening and the prediction of related complication risks in patients with metabolic syndrome can be done as early as possible.[9]

METHODS

This research is an observational analytic study with a cross-sectional design involving samples of metabolic syndrome patients according to the NCEP ATP III criteria with Asian modifications at the Endocrine Clinic of Merpati at Dr. Kariadi Hospital. The study was conducted at the Endocrine Clinic of Merpati, Dr. Kariadi Hospital, from September to October 2022. The samples in this study were metabolic syndrome patients according to the NCEP ATP III criteria with Asian modifications at the Endocrine Clinic of Merpati, Dr. Kariadi Hospital, who met the inclusion criteria (aged 25–65 years and agreed to participate in the study) and exclusion criteria (pregnant or postpartum, using hormonal contraception, consuming alcohol, having conditions that prevent direct measurement, or choosing not to continue to participate in the study). Sample collection was carried out using consecutive sampling, and 51 samples that met the inclusion and exclusion criteria including already assigning informed consent were obtained.

The independent variable in this study was the waist-to-hip ratio based on the measurement guidelines from the Centers for Disease Control and Prevention (CDC). The dependent variable in this study was body fat composition. The components of body fat composition measured include body fat percentage, body fat mass, visceral fat rating, and degree of obesity. Data analysis consists of univariate and bivariate tests.

The univariate test was used to determine the general characteristics of respondents and the distribution of each variable studied, including age, gender, smoking history, nutrition, physical activity, resting metabolic rate, waist-to-hip ratio, body fat percentage, body fat mass, visceral fat rating, and degree of obesity descriptively in the form of frequency and percentage tables.

The bivariate or hypothesis test aims to determine the relationships between variables. The Pearson test was used to analyze the relationship between WHR, age, and resting metabolic rate variables (numeric ratio scale) and the dependent variables such as body fat percentage, body fat mass, visceral fat rating, and degree of obesity (numeric ratio). Prior to this, a normality test was conducted using the Kolmogorov-Smirnov test. The Spearman test was used to analyze the relationship between fat consumption and physical activity (ordinal categorical scale) and the dependent variables such as body fat percentage, body fat mass, visceral fat rating, and degree of obesity (numeric ratio). The Mann-Whitney-test was used to analyze the relationship between gender and smoking history variables (nominal categorical variables) and the dependent numerical

variables such as body fat percentage, body fat mass, visceral fat rating, and degree of obesity.

The study was conducted after obtaining ethical clearance from the Health Research Ethics Committee of the Faculty of Medicine, Diponegoro University, under approval number 299/EC/KEPK/FK-UNDIP/VIII/2022. In addition, this study had got the ethical clearance from Dr. Kariadi Hospital's ethics committee. Participants who agreed to take part in the study provided their consent by signing an informed consent form.

RESULTS

General Characteristics of the Sample

The researchers collected data from 51 samples of patients with metabolic syndrome NCEP ATP III criteria at the Endocrine Polyclinic Merpati, Dr. Kariadi Hospital. The distribution of the population characteristics shown at Table 1.

Based on Table 1, the most prevalent component was excessive waist measurement or central obesity (96.1%); the second most prevalent was hyperglycemia (86.3%); hypertension was in the third place at 78.4%; low HDL stands at 58.8%; and the least prevalent component was high triglycerides at 43.1%. General characteristics of other variables can be observed in the Table 2.

Based on Table 2, out of 51 respondents, only 1 (2%) had a normal WHR, while the remaining 50 (98%) had an excessive WHR or above the cut off. In terms of age, the study was participated by 2 (3.9%) early adulthood respondents, 12 (23.5%) late adulthood respondents, 17 (33.3%) early elderly respondents, and 20 (39.2%) late elderly respondents. Regarding gender, the study was participated by 16 (31.4%) male samples and 35 (68.6%) female samples. Therefore, the number of

female samples exceeds male samples by more than twice. Among the 51 samples, only 9 individuals (17.6%) had a history of smoking, whether active or passive, while the remaining 42 individuals (82.4%) did not have a smoking history. In terms of physical activity, there were 13 (25.5%) samples classified as light physical activity, 13 (25.5%) as moderate physical activity, and 25 (49%) as heavy physical activity. Meanwhile, in terms of fat consumption category, out of 51 samples, 2 (3.9%) were classified as severe deficit, 7 (13.7%) as moderate deficit, 5 (9.8%) as severe deficit, 10 (19.6%) as normal category, and 27 (52.9%) as excess fat category. In terms of RMR, 21 (41.2%) respondents had RMR in the low range, while 30 (58.8%) respondents had RMR in the medium range.

Regarding body fat composition variables such as fat percentage showed that 12 (23.5%) respondents had normal values or below the cutoff, while 39 (76.5%) respondents had excessive values. In terms of fat mass, 23 (45.1%) respondents had normal fat mass values, while 28 (54.9%) respondents had excessive values. In terms of visceral fat rating, 34 (66.7%) respondents had normal or below cut off values, while 17 (33.3%) respondents had excessive values. Finally, in terms of the degree of obesity (DO), 7 (13.7%) respondents were in the normal category, 32 (62.7%) were in the overweight category, and 12 (23.4%) were in the obesity category.

Relationship between General Characteristics and Body Fat Composition

Based on Table 3, the relationship between age and fat percentage resulted in a *p*-value of 0.152 (*p*>0.05), indicating that the two variables were not significantly related. The relationship between age and fat mass resulted in a *p*-value of 0.097 (*p*>0.05), indicating no significant relationship between the two variables. Spearman's test between age and VFR resulted in a

TABLE 1
Characteristics of Patients with Metabolic Syndrome

NCEP ATP III Criteria for Metabolic Syndrome	Sample that meets the criteria
Fasting blood glucose	44 (86.3%)
Blood pressure	40 (78.4%)
Triglycerides	22 (43.1%)
HDL	30 (58.8%)
Waist measurement	49 (96.1%)

*Criteria for metabolic syndrome based on modified NCEP ATP III for Asians are as follows:
a. Fasting blood glucose ≥ 100 mg/dL
b. Blood pressure ≥ 130/85 mmHg
c. Triglycerides ≥ 150 mg/dL
d. HDL ≤ 50 mg/dL in females dan ≤ 40 mg/dL in males
e. Waist measurement ≥ 80 cm in females dan ≥ 90 cm in males

TABLE 2
General Characteristics of Variables

Variables		Frequency	Percentage (%)
Waist-Hip Ratio	Normal	1	2
	Excessive	50	98
Age	Early Adulthood	2	3.9
	Late Adulthood	12	23.5
	Early Elderly	17	33.3
	Late Elderly	20	39.2
Gender	Female	35	68.6
	Male	16	31.4
Smoking History	No	42	82.4
	Yes	9	17.6
Physical Activity Score	Light	13	25.5
	Moderate	12	23.5
	Heavy	26	51.0
Fat Consumption Score	Mild Deficit	2	3.9
	Moderate Deficit	7	13.7
	Severe deficit	5	9.8
	Normal	10	19.6
	Excessive	27	52.9
Resting Metabolic Rate	Low	21	41.2
	Medium	30	58.8
	High	0	0
Fat Percentage	Normal	12	23.5
	Excessive	39	76.5
Fat Mass	(No universal category)	–	–
Visceral Fat Rating (VFR)	Normal	34	66.7
	Excessive	17	33.3
Obesity Degree (OD)	Normal	7	13.7
	Overweight	32	62.7
	Obesity	12	23.5

p-value of 0.010 ($p<0.05$), indicating a significant relationship with r=0.360, implying a weak positive correlation. Meanwhile, age with obesity degree (OD) resulted in a p-value of 0.374 ($p>0.05$), indicating no significant relationship between the two variables.

The relationship between gender and fat percentage resulted in a p-value of <0.001 ($p<0.05$), indicating a significant relationship between the two variables. The relationship between gender and fat mass resulted in a p-value of 0.008 ($p<0.05$), indicating a significant relationship between the two variables. The test of the relationship between gender and VFR resulted in a p-value of <0.001 ($p<0.05$), indicating a significant relationship. Meanwhile, gender with OD resulted in a

TABLE 3
Relationship between General Characteristics and Body Fat Composition

Variables		Fat Percentage	Fat Mass	VFR (Visceral Fat Ratings)	OD (Obesity Degree)
Age	p	0.152[a]	0.097[a]	0.010[b]*	0.374[a]
	r	-0.204[a]	-0.235[a]	0.360[b]	-0.127[a]
Gender	p	<0.001[c]*	0.008[c]*	<0.001[c]*	0.903c
Smoking History	p	0.648c	0.739c	0.970c	0.408c
Physical Activity Score	p	0.105[b]	0.195[b]	0.625[b]	0.522[b]
	r	0.230[b]	0.184[b]	-0.070[b]	0.092[b]
Fat Consumption Score	p	0.699[b]	0.936[b]	0.505[b]	0.339[b]
	r	0.055[b]	0.011[b]	0.096[b]	0.137[b]
RMR	p	0.039[b]*	0.413[b]	<0.001[b]*	0.009[b]*
	r	-0.290[b]	0.117[b]	0.720[b]	0.362[b]

Notation:
a : Pearson Test
b : Spearman Test
c : Mann-Whitney Test
* : Significant Relationship ($p<0.05$)

TABLE 4
Relationship between WHR and Body Fat Composition

Variables		Fat Percentage	Fat Mass	VFR (Visceral Fat Ratings)	OD (Obesity Degree)
WHR	p	0.023[a]*	0.312[a]	0.001[b]*	0.785[a]
	r	-0.318	-0.145	0.441	0.039

Notation:
a : Pearson Test
b : Spearman Test
* : Significant relationship ($p<0.05$)

p-value of 0.903 ($p>0.05$), indicating no significant relationship between the two variables.

The relationship between smoking history and fat percentage resulted in a p-value of 0.648 ($p>0.05$), indicating that the two variables were not significantly related. The relationship between smoking history and fat mass resulted in a p-value of 0.739 ($p>0.05$), indicating a non-significant relationship between the two variables. The test of the relationship between smoking history and VFR resulted in a p-value of 0.970 ($p>0.05$), indicating a non-significant relationship. Meanwhile, smoking history with OD resulted in a p-value of 0.408 ($p>0.05$), indicating no significant relationship between the two variables.

The relationship between physical activity and fat percentage resulted in a p-value of 0.105 ($p>0.05$), indicating that the two variables were not significantly related. The relationship between physical activity and fat mass resulted in a p-value of 0.195 ($p>0.05$), indicating a non-significant relationship between the two variables. The test of the relationship between physical activity and VFR resulted in a p-value of 0.625 ($p>0.05$), indicating a non-significant relationship. Meanwhile, the test of the relationship between physical activity and OD resulted in a p-value of 0.522 ($p>0.05$), indicating no significant relationship between the two variables.

The relationship between fat consumption and fat percentage resulted in a p-value of 0.699 ($p>0.05$), indicating that the two variables were not significantly related. The relationship between fat consumption and fat mass resulted in a p-value of 0.936 ($p>0.05$), indicating a non-significant relationship between the two variables.

The test of the relationship between fat consumption and VFR resulted in a p-value of 0.505 ($p>0.05$), indicating a non-significant relationship. Meanwhile, fat consumption with OD resulted in a p-value of 0.339 ($p>0.05$), indicating no significant relationship between the two variables.

The relationship between RMR and fat percentage resulted in a p-value of 0.039 ($p<0.05$), indicating a significant relationship between the two variables. However, the value of r=-0.290 indicates a very weak negative correlation. The relationship between RMR and fat mass resulted in a p-value of 0.413 ($p>0.05$), indicating a non-significant relationship between the two variables. The test of the relationship between RMR and VFR resulted in a p-value of <0.001 ($p<0.05$), indicating a significant relationship with r=0.720, indicating a strong positive correlation. Meanwhile, RMR with OD resulted in a a p-value of 0.009 ($p<0.05$), indicating a significant relationship between the two variables with r=0.362, indicating a weak positive correlation.

Relationship between WHR and Body Fat Composition

The relationship between WHR and fat percentage resulted in a p-value of 0.023 ($p<0.05$), indicating a significant relationship between the two variables. This relationship has an r-value of -0.318, indicating a weak negative correlation. The relationship between WHR and fat mass resulted in a p-value of 0.312 ($p>0.05$), indicating no significant relationship between the two variables. The Spearman test between RLPP and VFR resulted in a p-value of 0.001 ($p<0.05$), indicating a significant relationship with an r-value of 0.441, implying a weak positive correlation. Meanwhile, RLPP with OD resulted in a p-value of 0.785 ($p>0.05$), indicating no significant relationship between the two variables.

DISCUSSION

The Pearson test shows a significant relationship between WHR and fat percentage ($p=0.023$) with a weak negative correlation (r=-0.318). This result aligns with Verma et al.' (2017) study, which also found a significant relationship between WHR and fat percentage ($p=0.01$) but with a very weak positive correlation (r=0.075).[7] This may be due to the majority of respondents being female (68.6%). Theoretically, in females, excess fat tends to accumulate in the hip and thigh areas, while in males, it tends to accumulate in the abdominal area.[10] This may explain the significant negative correlation between WHR and fat percentage in the population of metabolic syndrome patients.

The Pearson test shows no significant relationship between WHR and fat mass ($p=0.312$). Previous studies specifically examining the relationship between WHR and absolute body fat mass were not found. The non-

significant result may be due to variations in fat distribution in the body. The majority of respondents in this study were females, who genetically and hormonally tend to accumulate fat in the hip and thigh areas. In contrast, in males, fat is more likely to be distributed in the abdominal or waist area.[11] Therefore, excess fat mass in an individual may not necessarily be distributed in the waist area, leading to an increase in WHR.[8] However, why does this result differ from the relationship between WHR and fat percentage? Fat mass represents the absolute mass of fat in the body, whereas fat percentage was obtained by dividing fat mass by total body mass. This difference may explain why fat mass does not have a significant relationship with WHR as fat percentage does.[12]

The Spearman test shows a significant relationship between WHR and VFR ($p=0.001$) with a weak positive correlation (r=0.441). This result was consistent with Gadekar et al.'s (2018) study, which found a significant strong relationship between WHR and visceral fat score ($p<0.05$; r=0.920) in adults in India.[9] Many factors can cause an increase in WHR, one of which was the accumulation of fat in the visceral area. With this result, WHR can be used as an indicator of visceral fat level in the population of metabolic syndrome patients.

The Pearson test shows no significant relationship between WHR and OD ($p=0.785$). Previous research on the relationship between OD and WHR was not found. However, there was research on the relationship between BMI and RLPP, where BMI was a value that also indicates whether someone was obese or not (Basically, OD was a value that indicates how far someone was from the BMI value of 22). Previous research by Doustjalali (2020) found a significant relationship between BMI and WHR ($p\le0.01$; r=0.498) in a population of elementary school students. This can happen for several reasons. First, the variables used were not exactly the same, where this study uses OD while previous research uses BMI. Second, the sample in this study consists of metabolic syndrome patients with a range of ages from adults to the elderly, while previous research was conducted on elementary school students. The non-significant result may also be due to the fact that the OD value indicates how far someone was from the BMI value of 22. The BMI value does not fully indicate whether someone with a high BMI has more fat than someone with a low BMI (an athlete can have a high BMI due to high muscle mass).[13,14] Moreover, each person's fat distribution was different, especially since the majority of respondents were females whose fat distribution tends to be in the hip and thigh areas.[8] Therefore, someone's high OD because of fat or other substances may not necessarily increase their WHR. Although the research results were not significant, further research is needed to further confirm the relationship between WHR and OD.

Based on the correlation tests between WHR and

body fat composition variables, significant results were found between WHR and fat percentage and VFR. However, between WHR and fat mass and OD, non-significant relationships were found. Therefore, among the tested body fat composition parameters, only fat percentage and VFR can be described with WHR. Although further research is needed, WHR can be considered to represent fat percentage and VFR in the population of metabolic syndrome patients.

This study has several strengths, including its focus on a well-defined patient population of metabolic syndrome patients using the NCEP ATP III criteria with Asian modifications, ensuring relevance to the targeted demographic. Additionally, the inclusion of comprehensive variables, such as waist-to-hip ratio and detailed body fat composition metrics, provides a holistic understanding of the relationships being studied. However, the study has some limitations. Its cross-sectional design restricts the ability to establish causal relationships. Some variables, such as nutrition and physical activity, rely on self-reported data, which may be subject to recall bias. Furthermore, being a single-center study conducted at one clinic, the findings may not be fully generalizable to other populations or settings.

CONCLUSION

WHR has a weak but significant relationship with body fat percentage and visceral fat rating in patients with NCEP ATP III metabolic syndrome at the Endocrine Polyclinic Merpati, dr. Kariadi Central General Hospital, Semarang. However, the WHR does not have a significant relationship with body fat mass and the degree of obesity in this sample. Therefore, since the relationship between the WHR and body fat percentage was negative, it can be concluded that the WHR is not a good tool for describing body fat percentage. However, it can still be relied upon to describe visceral fat rating.

DECLARATION OF INTERESTS

The authors declare no conflict of interest

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Original Article

The Effect of Standardized Mangosteen Peel Extract, Nano-emulsion, Nano-chitosan and Treadmill Exercise on Atherogenic Rat Model

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Abstract

Background : Atherosclerosis, the most common cause of CVD, is associated with oxidative stress and cholesterol. Antioxidant and regular physical exercise have been considered as interventions to dampen the process. The mangosteen peel *(Garcinia mangostana Linn)* is known for containing a high amount of xanthones including α-mangostin with antioxidant effects. The current study investigates the anti-atherogenic potential of mangosteen peel extract in nano-emulsion and nano-chitosan formulations, singly and in combination with treadmill exercise, versus the statin, Atorvastatin.

Methods : A randomized controlled trial was conducted on 30 male Wistar rats, divided into six groups: normal diet control (C1), atherogenic diet control (C2), and four treatment groups receiving an atherogenic diet plus treadmill exercise combined with Atorvastatin (T1), standardized mangosteen extract (T2), mangosteen nano-emulsion (T3), or mangosteen nano-chitosan (T4). The aortic tunica intima and tunica intima-media thickness were measured histologically after 56 days.

Results : The aortic intimal thickness was noticeably higher in the atherogenic diet group (C2: 12.13±1.87 mm) compared to the normal diet group (C1: 4.27±0.75 mm). In the treatment groups, the intimal thickness ranged from 2.97±0.45 mm to 4.17±1.70 mm and showed no significant differences from the normal diet group. A similar pattern was seen in the intima-media thickness, with 145.63±17.12 mm recorded in the normal diet group and values ranging from 106.90±10.41 mm to 135.90±12.63 mm in the treatment groups, and 106.90±10.41 mm to 135.90±12.63 mm in the treatment groups suggesting no significant difference. Survival analysis using Kaplan-Meier curves showed obvious differences between groups ($p < 0.001$). The untreated atherogenic diet group (C2) had the poorest survival, with no rats survived until the end of the study. In contrast, survival improved in all treatment groups, with the Mangosteen Nano-chitosan (T4) group and the normal diet group (C1) achieving the best outcomes, as all rats in these groups survived.

Conclusion: Mangosteen peel extracts, whether in nano-emulsion or nano-chitosan forms, combined with treadmill exercise, showed significant differences in maintaining the survivability of rat with atherogenic-induced diet despite no significant differences in preventing atherogenesis compared to Atorvastatin or a normal diet. Further research is needed to confirm these potential therapeutic effects.

Keywords : Mangosteen skin, nano-emulsion, nano-chitosan, treadmill exercise, atherogenesis

INTRODUCTION

Atherogenesis is the pathobiological process underlying atherosclerosis in cardiovascular disease.[1] Atherosclerosis is a chronic immunoinflammatory, fibroproliferative disease of large and medium-sized arteries initiated by increasing lipids.[2] It is the most common cause of cardiovascular disease, which is the major cause of mortality and morbidity worldwide.[3] In 2016, the global prevalence of coronary artery disease (CAD) was 154 million, accounting for 32.7% of the global cardiovascular disease burden and 2.2% of the overall global disease burden.[4] Atherogenesis consists of three stages, initiation, progression, and complication.[5] The initiation stage is characterized by the recruitment of mononuclear leukocytes to the intimal layer of the vessel wall, induced by oxidized lipoprotein.[5] The progression stage is marked by the accumulation of smooth muscle cells that elaborate extracellular matrix macromolecules.[5] The complication stage is the progression of thrombosis.[5] This disease may progress when the atherothrombotic plaque ruptures, leading to coronary artery occlusion, reduced blood flow, and myocardial ischemia.[6] The main risk factor for atherosclerosis is high plasma cholesterol levels, particularly low-density lipoprotein (LDL), which plays a crucial role in atherogenesis, from plaque formation to plaque destabilization.[6]

The atherogenesis process involves oxidative stress, particularly the oxidation of low-density lipoprotein (LDL), so administering antioxidants[7] and engaging in physical training[8] may reduce oxidative stress and attenuate atherosclerosis formation. Therefore, the administration of anti-oxidants might reduce oxidative cardiovascular injury in atherosclerosis.[9] *Garcinia mangostana Linn* pericarp, usually known as the mangosteen skin, is a tropical fruit that is usually used as a medicinal plant among the people of Southeast Asia.[10] Mangosteen is rich in phenol components, such as xanthone, tannins, and anthocyanins.[11] Xanthone has an antioxidant property to overcome the oxidative stress.[11] The xanthone component comprises α-mangostin, β-mangostin, and γ-mangostin.[12] Predominantly, the α-mangostin, and γ-mangostin, has anti-inflammatory properties.[13] It can decrease the thickness of aortic perivascular adipose tissue, therefore reducing the thickening of the intima media layer, increasing the HDL C levels, and lowering the LDL-C levels, along with the Triglyceride and Total Cholesterol.[14] It was proven to inhibit atherosclerosis by inhibiting LDL oxidation and decreasing ROS in endothelial cells.[15] Drug bioavailability is an important parameter to determine how successful drug molecules pass through pharmacological phases and give the expected effect.[16] Drug bioavailability is primarily influenced by drug solubility, and nanoparticle drug delivery systems, such as nano-emulsions and nano-chitosan, enhance solubility due to their large surface areas.[16] Besides antioxidants, physical exercise is one alternative treatment to reduce the risk factor of atherosclerosis and has the advantage of being cost-effective.[17] The protective effects of physical exercise against coronary disease may involve mechanisms such as improved endothelial function, reduced plaque progression, enhanced collateral formation, and decreased release of inflammatory mediators.[18] Physical exercise can induce cardiac preconditioning, providing sustainable protection against cardiac injury.[19] Regular aerobic exercise can reduce the progression of coronary lesions.[20] Regular aerobic exercise, such as treadmill workouts, improves endothelial function and helps prevent atherosclerosis progression.[21] The primary outcome of this study is to compare the effectiveness of several mangosteen skin extract preparations, which are standardized, nano-emulsion, and nano-chitosan preparations and treadmill exercise for preventing atherogenesis in atherogenic rats. Meanwhile, the secondary outcome of this study is to compare the effectiveness of various preparations of mangosteen peel extract with Atorvastatin, the commonly used drug of choice, in combination with treadmill exercise for inhibiting atherogenesis in rats.

METHODS

A true experimental with randomized control trial was conducted. This study was conducted at the Biomolecular Laboratory of Universitas Islam Sultan Agung Semarang from February to May 2022 for sample maintenance, treatment, and examination. Paraffin block preparation and HE (Hematoxylin-Eosin) staining of histopathologic samples were performed at the Anatomical Pathology Laboratory of Diponegoro University. Ethical clearance was granted by the Ethical Commission for Health Research, Faculty of Medicine, Diponegoro University (No. 51/EC/H/FK-UNDIP/VI/2022).

This study used 30 male Wistar *(Rattus norvegicus)* rats as subjects. The inclusion criteria were healthy male rats, aged 6–8 weeks with active movement. The exclusion criteria were rats that have defects, appeared sick (standing fur, mushy feces), and were dead before the study period. All subjects were simply randomized into six groups and given an adaptation period of wheel and treadmill running at a speed of 12 m/min for 56 days (8 weeks). Five rats were selected randomly and received a standard diet (standard AD-2 pellets and drinking water in bottles orally) for 56 days as the control group 1 (C1). The rest 25 rats were induced with purified atherogenic diet patented product (Envigo®) with high-fat diet formulation (20–23 % BW; 40–45 % kcal from fat), saturated fatty acids (SFA > 60% of total fatty acids), milkfat or butterfat, sucrose (34% by weight), cholesterol (0.2% total), and tap drinking water for 56 days (24–30). Control group 2 (C2) received no additional treatment.

Treatment group 1 (T1) received atorvastatin at a human-adjusted dose of 80 mg/day (1.44 mg/0.5 mL), once daily for 58 days. Treatment group 2 (T2) received mangosteen peel extract (Mastin®) at 800 mg/kgBW/day (0.2 mL), three times daily for 56 days. Treatment group 3 (T3) was given MG-loaded self-nanoemulsion (MNE) at 50 mg/kgBW (4 mL), once daily for 56 days. Treatment group 4 (T4) received MG-loaded self-nanochitosan (MNC) at 50 mg/kgBW (4 mL), once daily for 56 days. Treatment was done individually.

At the end of Day 56, surviving rats were terminated, and their aortic arch and aortic sinus were collected for histopathologic examination, including paraffin blocking, HE staining, and outcome interpretation by two independent blinded anatomic pathologists. For each sample, observations were done four times in four different quadrants. The thickness of the intima and media layers was measured using an oculo-micrometer, with a digital microscope at the Pathology Anatomy Laboratory, Faculty of Medicine, Diponegoro University. Statistical analysis was done with one-way ANOVA with post hoc Tukey Test using Graph pad prism 9.

RESULTS

The flow of study participants is depicted in Figure 1. A total of 30 male Wistar rats were recruited based on the inclusion and exclusion criteria, with all meeting the eligibility requirements. The rats were then randomly divided into six groups: two control groups (C1: normal diet control; C2: atherogenic diet control) and four treatment groups (T1: treadmill exercise with Atorvastatin; T2: treadmill exercise with Mangosteen Extract (ME); T3: treadmill exercise with Mangosteen Nano-emulsion Extract (MNE); T4: treadmill exercise
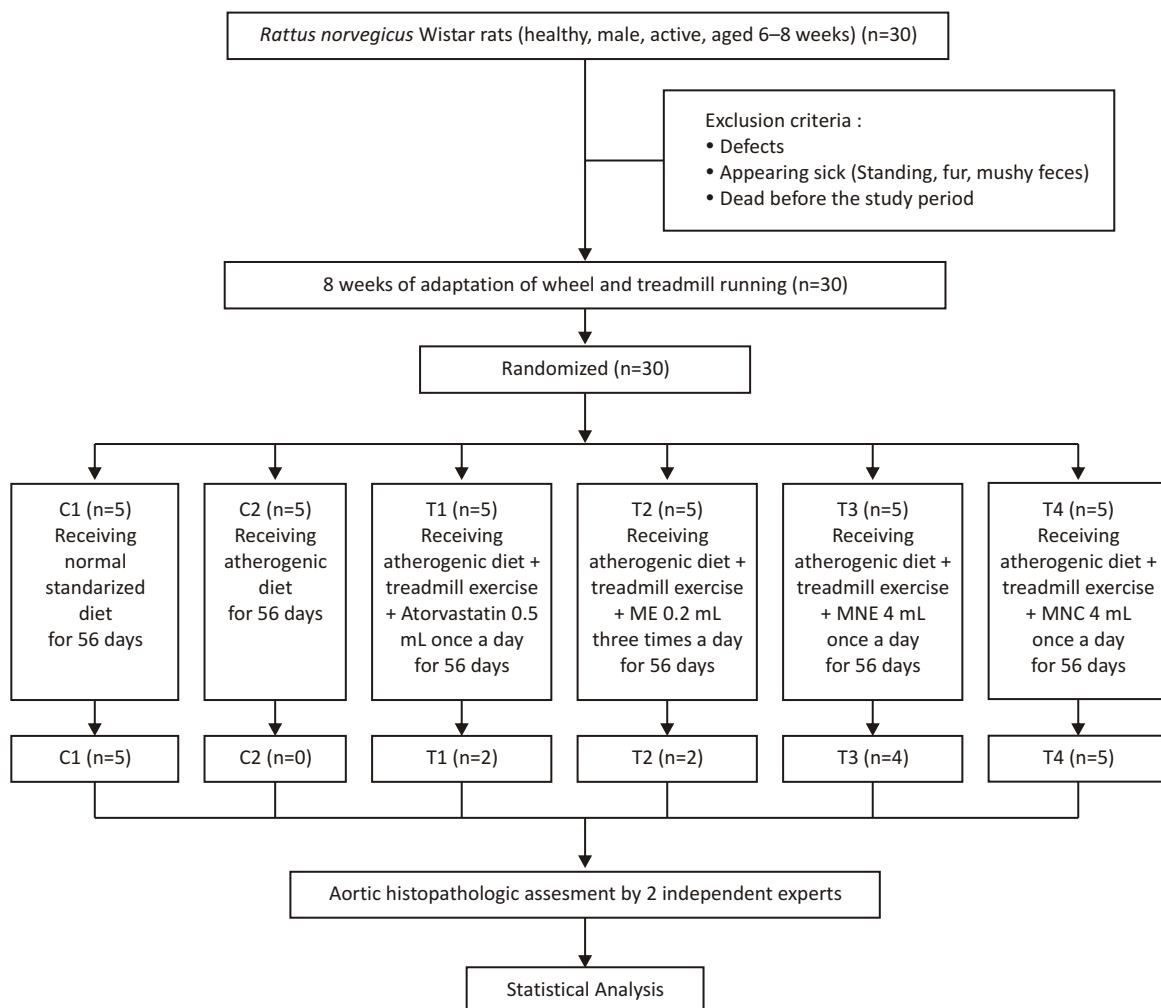
Figure 1. Consort flowchart depicting the progression of the study. Thirty Wistar rats were screened according to inclusion and exclusion criteria, and then randomly allocated into control and intervention groups. The rats were terminated on Day 56 and examined for aortic tunica intima and intima-media thickness through histopathological analysis.
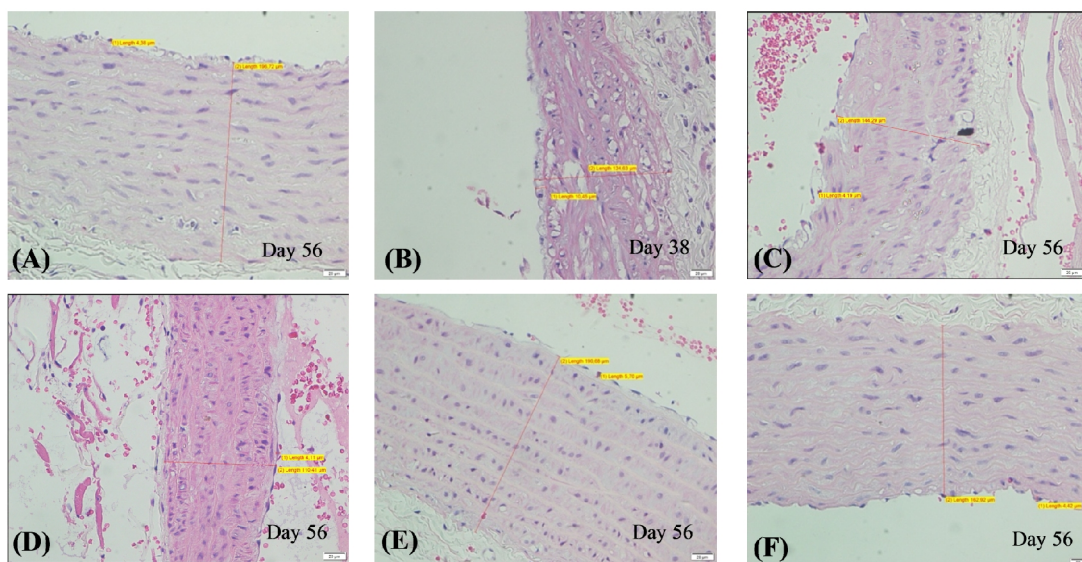
Figure 2. Histopathologic examination of aortic section with HE staining in 400x magnification. Male wistar rats treated with (A) Normal diet, (B) Atherogenic diet, (C) Atherogenic diet + treadmill exercise + Atorvastatin, (D) Atherogenic diet + treadmill exercise + ME, (E) Atherogenic diet + treadmill exercise + MNE, and (F) Atherogenic diet + treadmill exercise + MNC.
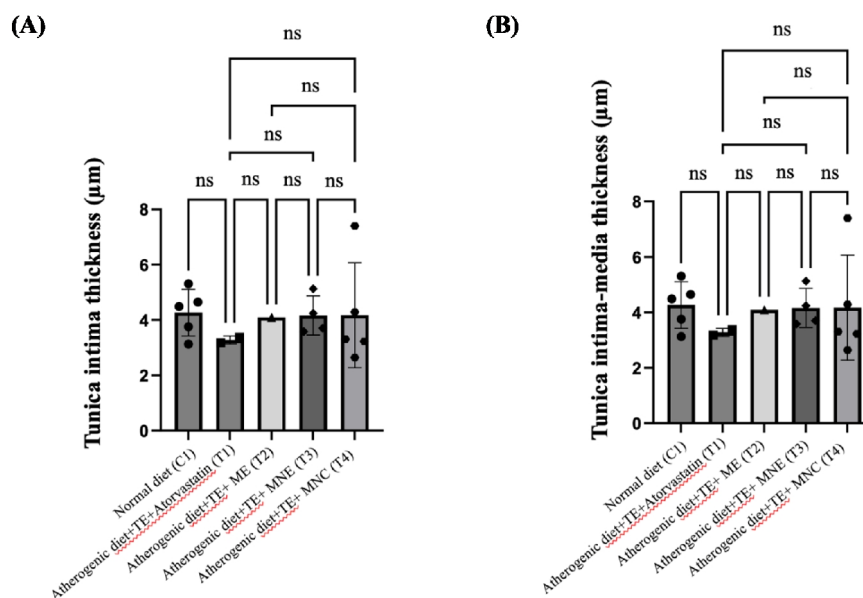
Figure 3. The effect of mangosteen peel extract (ME), mangosteen nano-emulsion extract (MNE), and mangosteen nano-chitosan extract (MNC) on the aortic wall thickness of Wistar rats. (A). Quantitative analysis of aortic tunica intima thickness. (B). Quantitative analysis of aortic tunica intima-media thickness. Wistar rats were given an atherogenic diet and the combination of treadmill exercise (TE) and atorvastatin (n=2) or mangosteen peel extract in ME (n=1), MNE (n=4), MNC (n=5). The thickness of each sample (A and B) was measured from aortic tissue histopathology examination, with averaged data from 4 different fields of view. Results are presented as Mean±SD; scale bar =100 μm.

with Mangosteen Nano-chitosan Extract (MNC)). Each group was monitored over a 56-day period, during which the intervention groups received their respective treatments as described in the methods section.

Survival outcomes varied by group. All rats in the normal diet control group (C1) survived till the end of the study (n=5), whereas none of the rats in the untreated atherogenic diet group (C2) survived (n=0) at the end of the study. Among the treatment groups, two rats survived in both the T1 (n=2) and T2 (n=2) groups, while
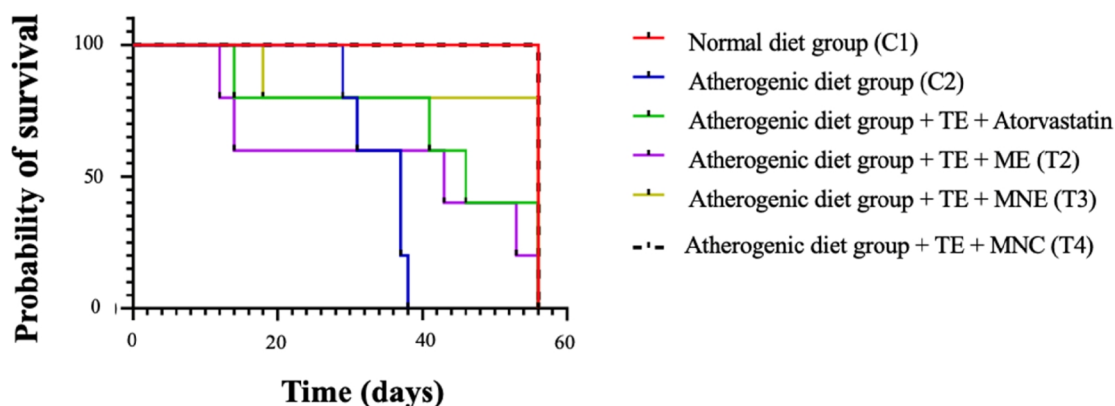
Figure 4. Kaplan-Meier Survival Curves for Rats Undergoing Different Diet Treatments. Kaplan-Meier survival curves were plotted to depict the survival of rats following various dietary interventions. Groups of rats were given either a standard diet or an atherogenic diet, in association with treadmill exercise and diverse therapeutic combinations, namely, atorvastatin, T1; mangosteen extract, ME, T2; mangosteen nano-emulsion extract, MNE, T3; mangosteen nano-chitosan extract, MNC, T4. These Kaplan-Meier survival curves give the probability of survival over time for each respective group, with observation from the lowest to the highest median survival are atherogenic diet grup (C2), followed by atherogenic + ME (T2), atherogenic + atorvastatin, atherogenic + MNE (T3), atherogenic + MNC (T4) and normal diet grup (C1). Log-rank test Mantel-Cox was performed to compare the survival distributions among the groups. *P*-value is less than 0.001, indicating a significantly different survival among the diet treatment groups.

four survived in the T3 group (n=4). The T4 group demonstrated the highest survival rate, with all rats completing the study period (n=5).

The histopathologic examination of male Wistar rats with various interventions is detailed in Figure 2. This analysis was conducted by two independents, blinded anatomical pathologists, ensuring an unbiased assessment. This examination specifically focused on measuring the aortic thickness of the tunica intima and the tunica intima-media across study groups. It was done after 56 days using HE staining, but in rats who died before the study period, the aortic thickness of tunica intima and tunica intima-media was counted before 56 days.

The mean aortic tunica intima thickness in Wistar rats on a normal diet (C1) is 4.27±0.84 μm (Figure 3A) and on an atherogenic diet (C2) is 12.13±2.10 μm (data is not shown in Figure 3 because it was taken before the study period ended). For the groups given an atherogenic diet, all subjects were treated with treadmill exercise with different interventions regarding the group. The rats were terminated and examined by histopathologist after the study endpoint (56 days), showing the tunica intima thickness was as follows: 3.28±0.14 μm in the group treated with Atorvastatin (T1) 4.10 μm in the group treated with ME (T2), 4.16±0.71 μm in the group treated with MNE (T3), and 4.17±1.90 μm in the group treated with MNC (T4). At the study endpoint, the number of study subjects differs, but as compared to the results, statistical analysis showed no significant difference between the normal diet control group (C1) and the

atherogenic diet intervention groups treated with treadmill exercise and Atorvastatin (T1), ME (T2), MNE (T3), and MNC (T4) as shown in Figure 3A.

Our observation on the same group as previously mentioned showed that aortic tunica intima-media thickness in Wistar rats with a normal diet (C1) is 145.63±19.14 μm. In the group treated with Atorvastatin (T1) is 107.03±4.66 μm, in the group treated with ME (T2) is 115.56 μm, in the group treated with MNE (T3) is 147.67±13.03 μm, and in the group treated with MNC (T4) is 135.9±14.12 μm (Figure 3B). Statistical analysis showed no significant difference between the normal diet control group (C1) and the atherogenic diet intervention groups treated with treadmill exercise and Atorvastatin (T1) (*p*=0.0660), ME (T2) (*p*=0.4171), MNE (T3) (*p*=0.9996), and MNC (T4) (*p*=0.8469).

Several study subjects died before the study ended. All rats died in the atherogenic diet group (C2) died with a median survival of 37 days. In a group receiving an atherogenic diet, combined with treadmill exercise and Atorvastatin (T1), three rats died, with a median survival of 46 days. Additionally, in the group receiving an atherogenic diet, treadmill exercise and ME (T2), four rats died, with a median survival of 43 days. In contrast, no deaths were observed in the normal diet group (C1), or in the atherogenic diet groups receiving treadmill exercise combined with MNE (T3) or MNC (T4). These findings are illustrated in Figure 4, which represents the Kaplan-Meier Survival Curves for the study groups.

DISCUSSION

Our study aims to evaluate the effectiveness of mangosteen peel *(Garcinia mangostana linn pericarp)* extract in nano-emulsion and nano-chitosan formulations for preventing atherogenesis, which is measured from the thickness of aortic tunica intima and tunica intima-media thickness. In this study, there is no significant difference in both aortic tunica intima and tunica intima-media thickness between rats receiving a normal diet (C1) and rats receiving an atherogenic diet in combination with treadmill exercise and Atorvastatin (T1), mangosteen peel extract (T2), mangosteen nano-emulsion extract (T3), and mangosteen nano-chitosan extract (T4).

Our study shows a direct relationship between mangosteen peel extracts administration and atherogenesis by examining tunica intima and media of rat aorta. We found that rats receiving an atherogenic diet, treadmill exercise, and various preparations of mangosteen peel extracts (standardized mangosteen extract 800 mg/kgBW/day; Mangosteen Nano-emulsion Extract 50 mg/kgBW; Mangosteen Nano-chitosan Extract 50 mg/kgBW) didn't show statistically significant differences in aortic tunica intima and tunica intima-media thickness compared to the normal diet group. Additionally, we compared the effects of Atorvastatin, a widely used lipid-lowering agent,[22] with various mangosteen skin extract preparations, including standardized herbal medicine (Mastin®), nano-emulsion extract (MNE) and nano-chitosan extract (MNC). We observed that the administration of Atorvastatin didn't result in significant differences in tunica intima and tunica intima-media thickness compared to the various preparations of mangosteen peel extracts. Our findings suggest that these mangosteen preparations do not significantly differ from Atorvastatin in their impact on atherogenesis, highlighting its potential as an adjuvant therapy for patients at risk of atherosclerosis. However, this result had to be interpreted carefully and further evidences are needed to confirm this effect.

Other than involvement in preventing atherogenicity, the effect of mangosteen peel extract on lipid profiles and oxidative stress markers was reported. In one study investigating the effect of mangosteen peel ethanolic extract on hypercholesterol diet-fed Wistar rats found that mangosteen peel ethanolic extract 200 mg/kgBW didn't produce significant results, while at the dose of 400 mg/kgBW, mangosteen extract can lower total cholesterol level and raise HDL level. The most effective dose is 800 mg/kgBW, where at this dose, mangosteen extract improves lipid profile, decreasing H_2O_2 level, NF-KB and iNOS.[23]

The mean aortic tunica intima thickness in Wistar rats on an atherogenic diet (C2) was significantly higher than the normal diet group (C1), confirming the successful induction of atherogenicity. We expected that all rats would survive throughout the study period. However, all the rats in the C2 group died before the end of the study and were therefore excluded from the analysis. It suggests the death of the rats is due to the progression of the disease, which is a total blockage in the aorta following the atherogenesis induction with a high-fat diet, as illustrated in Figure 4, representing the Kaplan-Meier survival curve. This is supported by another study stating that a high-fat diet can induce remarkable cardiotoxicity by promoting cardiac injury.[24] Our study examines a relatively new and understudied drug packaging method which is in nanoparticle size expected to improve drug absorption. However, we acknowledge that our study's limitations include the small number of study subjects and the loss of subjects before the end of the study period. Therefore, the result of our study needs to be interpreted carefully.

CONCLUSION

Our study concludes that atherogenesis in rats receiving the combination of mangosteen peel extracts in any preparations (Mastin®, nano-emulsion, nano-chitosan) along with treadmill exercise didn't differ significantly from rats on a normal diet. Furthermore, when compared to Atorvastatin, a commonly prescribed medication for lowering lipid profiles, no significant atherogenesis changes were found between the Atorvastatin group and mangosteen peel extracts in any preparations (Mastin®, nano-emulsion, nano-chitosan), Suggesting potential usage of mangosteen peel extracts in the prevention of atherogenicity.

Our study warrants further study to explore the potential effect of mangosteen peel extracts in atherosclerotic disease.

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A Clinical Dilemma of Bilateral Hematosalpinx in Ectopic Pregnancy: Case Report

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Abstract

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Background : Blastocyst implantation outside the uterine cavity leads to ectopic pregnancy. About 96% of ectopic pregnancies occur in the fallopian tubes, where it most frequently occurs; the fimbrial end accounts for 11% of all ectopic pregnancies. There was an uncommon type of ectopic pregnancy called bilateral tubal ectopic pregnancy. Bilateral tubal ectopic pregnancy is estimated to affect 1 out of 725 – 1580 ectopic pregnancies or 1 out of 200,000 live births. However, the villi quickly penetrate the endosalpinx once the implantation of the ectopic pregnancy has occurred before reaching the tubal wall and peritoneum. Vascular growth and a peritubal hematoma or hematosalpinx, which frequently involves the contralateral tubal section, are also present with this penetration. The purpose of this article is to report on the dilemmas that often occur in the case of bilateral hematosalpinx in ectopic pregnancy.

Case Description : In this report, we discuss a 33-year-old woman with a positive pregnancy test and transvaginal ultrasound result that was suggestive of ectopic pregnancy in a stable hemodynamic state. The patient underwent an exploratory laparotomy, which showed bilateral hematosalpinx with right ectopic pregnancy with damaged fimbria. The left fallopian tube had a blue-purple bulge that suggested hematosalpinx secondary to ectopic pregnancy rather than bilateral ectopic pregnancy condition. The decision for definitive management was made, right salpingectomy puncture and drainage of the hematosalpinx were performed without complication. The final diagnosis was confirmed on pathology examination that showing chorionic villi within the right damaged fimbria, focal decidua, a few trophoblast-like cells that indicated ectopic pregnancy in the left tubal cavity.

Conclusion : This approach encourages both shared decision-making and preparedness, both of which are required to provide patient-centered and comprehensive caremanagement such as bilateral hematosalpinx in ectopic pregnancy case, that must always be individualized, and patient's desire for future conception must be taken into account.

Keywords : ectopic pregnancy, hematosalpinx, clinical dilemma, fallopian tube

INTRODUCTION

Ectopic pregnancy is a medical emergency that occurs when a fertilized egg implants outside the uterus, usually in the fallopian tube. It is a life-threatening condition that accounts for 6–16% of women who present to the emergency room. Ectopic pregnancy is a rare complication, affecting only 2% of all pregnancies, but it is responsible for about 4% of all pregnancy-related deaths. The fallopian tubes are the most common site of ectopic pregnancy, accounting for 96% of cases occurring in these tubes. The fimbrial end of the fallopian tube, which is the closest part to the ovary, is the most frequent site of ectopic implantation, accounting for 11% of all ectopic pregnancies. If left untreated, ectopic pregnancy can cause life-threatening complications such as internal bleeding and shock. Therefore, early diagnosis and prompt management are crucial to prevent serious complications.[1,2] Bilateral tubal ectopic pregnancy (BTP) is a type of ectopic pregnancy that occurs when both fallopian tubes are affected. It is considered a rare condition, estimated to affect only about 1 out of 725 – 1580 ectopic pregnancies or 1 out of 200,000 live births. In a BTP, the fertilized egg implants itself in one of the fallopian tubes, and then another egg implants itself in the other fallopian tube. This condition is dangerous and requires immediate medical attention, as it can lead to severe complications such as hemorrhage, shock, and even death. Early diagnosis and treatment are essential for the best possible outcome, and women who experience symptoms such as abdominal pain, vaginal bleeding, and shoulder pain should seek immediate medical attention to rule out the possibility of BTP.[3] Most cases of bilateral tubal ectopic pregnancy are only discovered during surgery, and they are clinically indistinguishable from unilateral tubal ectopic pregnancy. There is currently no management policy that is supported by evidence.[3–6] The purpose of this article is to report dilemmas that often occur in the case of bilateral hematosalpinx in ectopic pregnancy.

CASE REPORT

A 33-year-old woman from a level 3 hospital was admitted to the emergency room for chief complaint of missing lower abdominal pain, brownish-red vaginal bleeding, and being late for menstruation. G4P3A0H2's obstetric history includes 10 years of normal childbirth and secondary infertility. The patient has been complaining of intermittent yellowish discharge with a slight smell over the past five years, along with less low back pain. All examination data and published data have received consent from the patient (without mentioning real identity).

The patient appeared moderately ill, with normal vital signs. The pregnancy test showed a positive reading without providing any quantitative data. An ultrasound examination revealed a suspicion of an ectopic pregnancy, as the image of the uterine cavity appears inhomogeneous, suspected *pseudosac*, and the posterior part of the uterus appeared hyperechoic, suspected hematocele. blood tests were within normal limits, but because of the absence of laparoscopic facilities, informed consent was seek for diagnostic exploration laparotomy as a diagnosis of ectopic pregnancy, with differential diagnosis of pregnancy of unknown location.

Preparation for surgery was carried out by administering medications for stabilizing and maintaining the patient's hemodynamics. During the exploratory laparotomy, which is a surgical procedure to examine the abdominal organs, it was discovered that there was approximately 100 ml of of blood in the peritoneal cavity, specifically in the pouch of douglas, located in the lower part of the pelvis. Additionally, there was blood in both fallopian tubes as shown in Figure 1. There was suspicion of an ectopic pregnancy, with
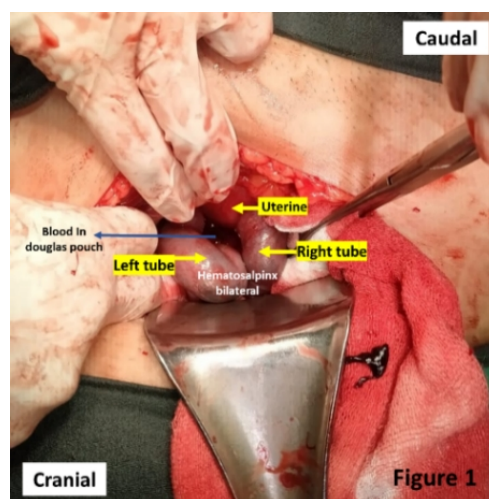
Figure 1. Hematosalpinx in both tubes
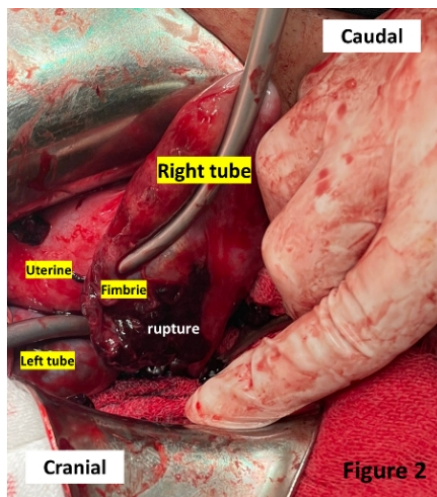
Figure 2. Rupture of the right pars fimbrie fallopian tube

Figure 3. Rupture of the right pars fimbrie fallopian tube

rupture of the right pars fimbriae fallopian tube, as shown in Figure 2. Therefore, it was decided to perform a dextral salpingectomy, which is the surgical removal of the affected fallopian tube. After undergoing the necessary procedure, a subsequent ultrasound examination was conducted to assess the progress.

The results showed that there was no free fluid present in the pelvic cavity, indicating that the procedure was successful. Further examination of the patient's histopathological findings revealed the presence of bilateral ectopic pregnancy, which is a rare type of pregnancy where the fertilized egg implants outside of the uterus, typically in the fallopian tubes. Additionally, the histopathological findings also showed the presence of focal decidua, which is a type of tissue lining that develops in the uterus during pregnancy. This detailed assessment provides crucial insights into the patient's condition, allowing for better treatment and management.

After the surgical procedure, patients receive postoperative care for 48 hours, both within and outside the hospital. During this time, the healthcare professionals kept a close monitoring on the patient's condition to ensure that they are recovering well. Following this, a follow-up ultrasound was conducted to examine pelvic cavity for any sign of free fluid. The results of the ultrasound showed that no free fluid presents in the pelvic cavity, indicating that the patient is healing well. The patient's histopathological findings revealed bilateral ectopic pregnancy. The left fallopian cavity shows showed focal decidua and trophoblast-like cells, which are indicative of ectopic pregnancy. On the other hand, the right damaged fimbrialpresented chorionic villi, which is another sign of ectopic pregnancy. This detailed information about the patient's condition is essential for the healthcare professionals to provide appropriate treatment and care to the patient.

DISCUSSION

Ectopic pregnancies is a potentially life-threatening condition that occurs when a fertilized egg implants itself outside of the uterus, often present with ipsilateral hematosalpinx, which refers to the presence of blood in the fallopian tube on the same side as the affected ovary. However, the association between ectopic pregnancies and contralateral hematosalpinx, which occurs when blood is found in the fallopian tube on the opposite side, is uncommon and typically relates to assisted reproduction methods. Peritubal hematomas or hematosalpinx, which refer to the accumulation of blood in the fallopian tube, may result from the penetration of the villi into the blood vessels and the resulting vascular proliferation. Villi are finger-like projections that grow from the surface of the early placenta and are responsible for the exchange of nutrients and waste products between the mother and the developing embryo. It grows into the blood vessels, they can cause bleeding, and the resulting blood may accumulate in the fallopian tube as a hematoma or hematosalpinx. This phenomenon has been well-documented in numerous medical studies.[3–4]

When a pregnancy occurs outside the uterus, it is called an ectopic pregnancy. In cases of chronic ectopic pregnancies, where the pregnancy has not been naturally aborted or surgically removed, the presence of hematosalpinx can be observed. Hematosalpinx refers to bleeding that occurs inside the fallopian tube. If bleeding occurs in the uterine tubes, despite no rupture or abortive phase, it is an indication that the pregnancy is ectopic. In such cases, the fertilized egg has implanted outside the uterus, which can lead to dangerous complications if left untreated. In situations where there is a hematocele in the pelvic cavity, which is a collection of blood within the pelvic region, secondary hematosalpinx can occur. This happens when the bleeding accumulates inside the fallopian tube itself, forming hematosalpinx without communicating with the peritoneal cavity. Therefore, the presence of hematosalpinx can be a significant indicator of an ectopic pregnancy, and timely medical intervention is crucial to avoid potentially life-threatening complications.[4–6]

Following a dextra salpingectomy, the palpation of the right tube is considered a potential rupture in the pars fimbria tuba. Aspiration was conducted, which revealed blood-filled fluid that raised the possibility of hematosalpinx. Similarly, palpation of the left tubal uncovered a liquid without any solid component. It is worth noting that a dextra salpingectomy is a surgical procedure that involves the removal of a fallopian tube. Any discomfort or pressure felt in the area after the operation should be viewed with suspicion, as there is a risk of developing a rupture in the pars fimbria tuba. The aspiration procedure involves the removal of fluid from the fallopian tube. The presence of blood-filled fluid in

this case raises the possibility of hematosalpinx, a medical condition characterized by the accumulation of blood in the fallopian tube. The presence of a liquid within the left fallopian tube is of particular concern. Liquids within the fallopian tube can interfere with fertility and increase the risk of ectopic pregnancy if they grow large enough to obstruct the passage of a fertilized egg.[4–6] Bilateral hematosalpinx-complicated tubal ectopic pregnancy is uncommon and can present a treatment dilemma. To avoid inappropriate treatment, such as the removal of the contralateral tube, careful preoperative and intraoperative evaluation is required. The possibility of bilateral ectopic pregnancy ought to be ruled out simultaneously. Despite this, it might be misleading. In this instance, the scan does not assess the left-side ectopic pregnancy and instead shows the exact ectopic pregnancy, which is actually hematosalpinx.[5–7] Pathologies that indicated focal decidua and some trophoblast-like cells indicating ectopic pregnancy in the left fallopian cavity and chorionic villi in the right damaged fimbrial confirmed the final diagnosis.

Bilateral tubal ectopic pregnancy is a rare form of ectopic pregnancy, and it is regarded as the rarest form when there has been no prior use of ART, as in this instance.[5,6] There is no difference between unilateral and bilateral tubal ectopic pregnancy in terms of the clinical presentation. The majority of ectopic pregnancies do not progress beyond this point, and the evaluation of the contralateral tubes does not guarantee that bilateral tubal ectopic pregnancy will be correctly identified. Instead of being accurately diagnosed prior to surgery, bilateral tubal ectopic pregnancy is frequently diagnosed during surgery.[5–7]

More than 200 cases have been reported in the literature, but only three of them were diagnosed with bilateral tubal ectopic pregnancy prior to surgery using ultrasound. There is insufficient data to suggest that additional imaging modalities should be used to diagnose Bilateral tubal ectopic pregnancy.[3,6] In the context of investigating adnexa and providing preoperative counseling, it is imperative to consider the possibility of bilateral tubal ectopic pregnancy, particularly among patients who express a desire to conceive in the future. This medical condition arises when the fertilized egg implants outside the uterine cavity, usually within the fallopian tubes.[7–9] As such, it is essential to manage such cases with a high degree of caution and diligence, given the potential implications for future fertility.[8–14] Thus, it is incumbent upon healthcare providers to undertake a comprehensive and meticulous examination of the patient's medical history, as well as to conduct a thorough physical and diagnostic evaluation. By doing so, they can establish a clear and accurate diagnosis and develop an appropriate course of treatment, taking into account the patient's individual needs and circumstances.[15–17] In summary, when dealing

with patients who are either experiencing symptoms of adnexal disease or who are seeking guidance on future fertility, healthcare providers must be mindful of the potential for bilateral tubal ectopic pregnancy. By adopting a methodical and informed approach to diagnosis and treatment, they can help ensure the best possible outcomes for their patients.[18–21]

CONCLUSION

A clinical problem arises when ectopic pregnancy and hematosalpinx occur simultaneously. To address this issue and lessen the likelihood of a delayed or missed diagnosis. The ideal treatment plan for bilateral tubal ectopic pregnancy would be one based on evidence; However, due to the low incidence of bilateral tubal ectopic pregnancy and the poor presurgical diagnosis, such a protocol must be adapted to each individual case from published case reports. In order to provide comprehensive and patient-centered care, this strategy encourages preparedness and shared decision-making. Lastly, a thorough preoperative examination of the bilateral adnexa and an intraoperative pelvic examination may reduce the likelihood of a persistent ectopic pregnancy and its complications.

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Oropharyngeal Dysphagia as The Presenting Symptom of Myasthenia Gravis with Diabetes Mellitus

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Abstract

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Background : Oropharyngeal dysphagia may caused by a variety of causes. Myasthenia gravis is a common autoimmune disease affecting the neuromuscular junction. While ocular symptoms are common in myasthenia gravis, bulbar symptoms such as dysarthria and dysphagia are less common. The aims of this study was to present the importance of recognizing atypical presentations of myasthenia gravis and utilizing electromyography in diagnosis when AChR antibody testing is unavailable.

Case Presentation : A 57-year-old woman was referred because of progressive dysphagia for both solid and liquid food. She also experienced weight loss, heaviness of the right eyelid, drooling, and chewing difficulty. Medical history revealed diabetes. Vital signs were stable. Physical examination revealed right ptosis without any other neurological deficits. Wartenberg test and dysarthria counting test were positive. Laboratory examination revealed a blood glucose level of 270 mg/dL and an HbA1c level of 9.4%. The barium swallow study revealedno abnormalities. Esophagogastroduodenoscopy revealed esophageal candidiasis. Electromyography showed more than 20% decremental response of the orbicularis oculi muscle. This result is suggestive of neuromuscular junction disorder. Improvement of the condition was achieved after the administration of intravenous steroids and oral pyridostigmine combined with therapeutic plasma exchange.

Discussion : Oropharyngeal dysphagia accompanied by ptosis and positive Wartenberg & dysarthria counting test is suggestive of myasthenia gravis. Although an AChR antibody test cannot be performed, significant electromyography alongside relevant clinical presentation is sufficient to diagnose myasthenia gravis.

Conclusion : It is crucial to recognize the accompanying signs and symptoms of oropharyngeal dysphagia. EMG may be used to diagnose MG in the appropriate clinical context.

Keywords : Dysphagia, Myasthenia Gravis, Oropharyngeal

INTRODUCTION

Dysphagia is a complaint that is frequently encountered in the daily practice. Oropharyngeal dysphagia (OD) may caused by a variety of causes, including structural and neurological issues.[1,2]

Myasthenia Gravis (MG) is a common autoimmune disease affecting the neuromuscular junction with an estimated incidence rate of 150 to 200 per million people.[3] Bulbar symptoms such as dysarthria and dysphagia are less common. MG with predominantly bulbar weakness can present a diagnostic challenge for non-neurologists, as its symptoms may be confused with those of other more common medical conditions. However, this subtype of MG can lead to significant morbidity if not promptly recognized and treated, due to potential complications such as aspiration and respiratory muscle weakness.[4] We present a case of myasthenia gravis with predominant symptoms of oropharyngeal dysphagia.

CASE ILLUSTRATION

A 57-year-old woman was referred to our hospital because of progressive dysphagia for the last 2 months. Initially, she experienced swallowing difficulty with solid food without any problems with liquid. Her swallowing difficulty worsened over time. She has experienced swallowing difficulty with solid and liquid food for the last 1 month and an inability to initiate swallowing any food for the last 1 week. She also reported a 7-kilogram weight loss during the previous 2 months, heaviness of her right eyelid for the last 2 weeks without any vision problems, drooling, and chewing difficulty during the previous 1 week. She experienced neither fever, slurredspeech, sore throat, hoarseness, nausea, vomiting, shortness of breath, chest pain, or hemiparesis. Medical history revealed diabetes in the last 5 years with routine glimepiridemedication.

Upon admission, she was hemodynamically stable. Physical examination revealed right ptosis without any other neurological deficits. During the water drinking test, she was unable to swallow the water, which collected in her oral cavity. Wartenberg test and dysarthria counting test were positive. Laboratory examination was normal, except for a blood glucose level of 270 mg/dL and an HbA1c level of 9.4%. ECG showed normal sinus rhythm. Chest X-ray showed no abnormalities.

The barium swallow study did not show any abnormalities. Esophagogastroduodenoscopy revealed esophageal candidiasis with erosive gastritis. Subsequent gastric biopsy showed no *Helicobacter pylori* infection.

Myasthenia gravis (MG) was suspected. Acetylcholine receptor antibodies (AChRantibody) examination, which is the gold standard for MG diagnosis was not available. Electromyography (EMG) showed more than 20% decremental response to 1 Hz, 3 Hx, and 20 Hz stimulation to the orbicularis oculi muscle which is considered suggestive of neuromuscular junction disorder. Stimulation of the abductor digiti minimi muscle at 3 Hz, 20 Hz, and 50 Hz showed a decremental response of more than 10%.

Intravenous methylprednisolone at a dose of 125 mg/8 hours and oral pyridostigmine bromide at a dose of 60 mg/8 hours are administered. The dose of
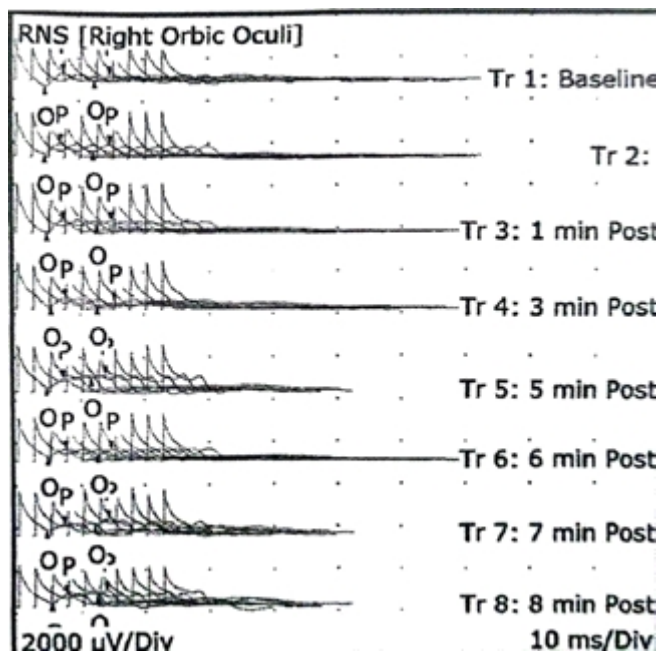
Picture 1. EMG of Orbicularis Oculi Muscle
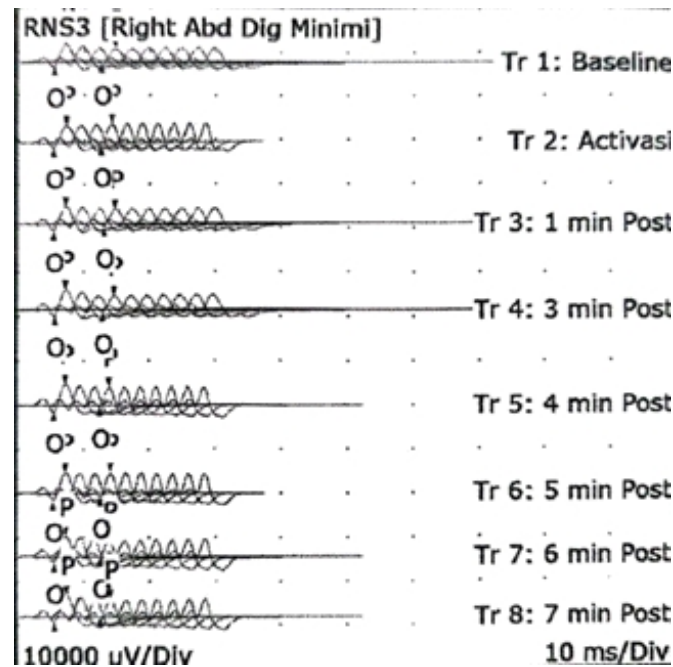
Picture 2. EMG of Abductor Digiti Minimi Muscle

methylprednisolone was reduced gradually and stopped on the 15th day of hospitalization. Fluconazole at a dose of 200 mg/24 hours was administered in intravenous. Blood glucose level was maintained by insulin and glimepiride. A therapeutic plasma exchange program was performed. After 4 cycles of therapeutic plasma exchange, ptosis and dysphagia resolved, and she was able to swallow solid and liquid food. The patient was then discharged while still being given pyridostigmine bromide.

One week after discharge, she came to the outpatient department. She had no complaint. Pyridostigmine bromide 60 mg/8 hours orally was continued.

DISCUSSION

This patient experienced oropharyngeal dysphagia, resulting in difficulty directing water from the oral cavity. The barium swallow study and electromyography examinations confirm the absence of any structural abnormalities. Oropharyngeal dysphagia, along with ptosis and positive results on the Wartenberg and dysarthria counting tests, strongly suggests a diagnosis of Myasthenia gravis (MG).

Myasthenia gravis (MG) is an autoimmune condition characterized by weakness in skeletal muscles. It arises due to the presence of autoantibodies targeting the postsynaptic membrane at the neuromuscular junction, including acetylcholine receptor (AChR) antibodies, muscle-specific kinase (MuSK) antibodies, and low-density lipoprotein receptor- related protein 4 (LRP4) antibodies.[4]

Most patients experience some level of generalized weakness, while a smaller proportion present only with ocular symptoms. While ocular symptoms are frequently observed in individuals with myasthenia gravis, bulbar symptoms such as dysarthria and dysphagia are less common and rarely occur as isolated symptoms.[1] Dysphagia is observed in 15–40% of cases with the generalized form of MG. However, it serves as the initial presenting symptom in only 6% of MG patients.[5,6]

It is essential to test for antibodies such as AChR, MuSK, or LRP2 to confirm the diagnosis of MG.[4] Unfortunately, we were unable to perform these antibody tests in this case due to the unavailability of necessary reagents at our facility.

However, electrodiagnostic studies, particularly with slow repetitive nerve stimulation, serve as the primary diagnostic approach in acute settings or when antibody testing is unavailable.[4]

In MG, with low stimulation rates, the physiological reduction in end-plate potential (EPP) amplitudes can reach a level where the EPP falls below the threshold needed to activate muscle fibers. With continuous stimuli, an increasing percentage of muscle fibers experience blockage. This leads to a reduction in the amplitude and area of the compound muscle action potential (CMAP) with repeated stimuli, resulting in an observable abnormal decrement. The threshold for an abnormal decrement is set at 10% of the initial amplitude or area. However, with precise recording, any decrement displaying the characteristic pattern warrants further investigation.[7]

The physical examination and EMG findings are

consistent with a diagnosis of Myasthenia Gravis in our patient. As a result, the patient was diagnosed with MG and started on treatment with steroids, pyridostigmine bromide, and therapeutic plasma exchange. The patient's improvement following treatment with steroids, pyridostigmine bromide, and therapeutic plasma exchange further supports the diagnosis of MG. Diabetes Mellitus (DM) is a metabolic disease characterized by high blood sugar due to either insulin deficiency or insulin resistance. It is one of the known risk factors of esophageal candidiasis. Esophageal candidiasis is the most common cause of infectious esophagitis. Esophageal candidiasis can be diagnosed by the presence of erythematous, pseudomembranous, and plaque-like changes. The most common species causing esophageal candidiasis is *Candida albicans* (71%), while the most common non-*Candida albicans* species is *Candida dubliniensis*.[8,9]

A study by Yu-Dong Liu *et al* showed that patients with type 2 diabetes (T2DM) had a higher risk of MG than patients without T2DM. The mean onset age of MG patients with diabetes was significantly higher than that of MG patients without diabetes. This indicates that the clinical type of MG patients with diabetes is mostly late-onset myasthenia gravis (LOMG).[10]

CONCLUSION

Myasthenia gravis may present as oropharyngeal dysphagia, making the recognition of accompanying signs and symptoms crucial. EMG may be used to diagnose MG in the appropriate clinical context. A multidisciplinary team, consisting of neurologists, internists, and other disciplines is needed to achieve the best outcome and avoid unnecessary management.

INFORMED CONSENT

The patient provided written consent for the publication of this case report and any related photographs. Under privacy protection guidelines, all identifiable information has been anonymized.

CONFLICT OF INTEREST

The authors wish to disclose that they have no conflicts of interest related to this work.

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A Case Report of Female Systemic Lupus Erythematosus and Cerebral Lupus as The Complication : Diagnosis and Treatment

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Abstract

Background : Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that affects multiple systems in the body. Because clinical manifestations can appear in different organs, the complications are diverse and can be quite severe, one of which is cerebral lupus or neuropsychiatric systemic lupus erythematosus (NPSLE). It includes neurological and psychiatric syndromes in SLE patients where other causes have been ruled out. We reported a case of SLE manifestation with cerebral complication involvement. This case report aims to provide insights and expect to offer an understanding into the clinical presentation, diagnosis, and management of a patient with cerebral lupus.

Case Presentation : 18-year-old Indonesian woman with complaint of sudden seizure was referred to the Emergency Unit of Dr. Ramelan Naval Central Hospital Surabaya. She had previously been diagnosed with SLE back in 2022 and consistently does a monthly checkup in the internal medicine clinic at Dr. Ramelan Naval Central Hospital Surabaya. Initial examinations revealed signs of infection, slight electrolyte imbalances, and a flare phase of SLE, but no abnormalities in imaging tests. She received initial treatments of loading phenytoin along with mecobalamin injection, vitamin B6, methamizole, and cefobactam. Over the course of her hospital stay, with no further seizures, she was discharged with medication for continued treatment and a scheduled follow-up.

Conclusion : This case of cerebral lupus is rare. SLE can damage the blood brain barrier (BBB), causing neuropsychiatric complications.

Keywords : Autoimmune diseases, Neuropsychiatric Systemic Lupus Erythematosus, Systemic Lupus Erythematosus.

INTRODUCTION

Systemic Lupus Erythematosus (SLE) can be defined as a chronic, multi-system autoimmune disease with various systemic manifestations that involve almost all tissues and organs.[1,2] The annual incidence of SLE in Asia ranges from 2.8 to 8.6 per 100,000 people per year, with the prevalence varying from 26.5 to 103 per 100,000 individuals.[3] Several classification criteria has been developed over time. there are three classification criteria for SLE that can be used: ACR 1997, SLICC 2012, and EULAR/ACR 2019.[4,5] Because clinical manifestations can occur in various organs, complications of SLE are diverse and can be severe, one of which is cerebral lupus or neuropsychiatric systemic lupus erythematosus (NPSLE).

Cerebral lupus encompasses various psychiatric and neurological manifestations due to SLE involvement in the nervous system, where other causes have been excluded.[6–9] Neuropsychiatric manifestations of SLE range from mild symptoms such as headaches, anxiety, depression, psychosis, and pseudodementia, to more severe conditions such as seizures, stroke, or coma.[6,7,10] These manifestations usually occur early in the course of SLE, with a higher incidence in young women.[11] Cerebral lupus presents unique challenges in diagnosis.[8,9] There are no specific criteria for diagnosing NPSLE, but they can be assisted by using clinical, serological, immunological, electrophysiological, and neuroimaging studies to eliminate other comparative diagnoses.[12,13]

We present a case of a patient with Systemic Lupus Erythematosus (SLE) complicated by cerebral lupus. Additionally, this case report is expected to offer an understanding of the clinical characteristics, diagnosis, and treatment of patients with SLE complicated by cerebral lupus.

CASE PRESENTATION

18-year-old Indonesian woman was brought to the emergency department of RSPAL Dr. Ramelan Surabaya with the chief complaint of seizure that lasted about 5 minutes, 30 minutes before she was admitted to the hospital. It occured throughout the whole body, with stiffening and jerking, without a foamy mouth nor bed wetting. She was unconscious right after the seizure stopped, then regained consciousness again. She had a history of frequent headeche (migraines), nausea, and vomiting. While in the emergency room, the patient experienced repeated seizures for the second time – a similar one, which was a tonic clonic for about 15 seconds.

The history of seizures was denied, but she has suffered from Systemic Lupus Erythematosus (SLE) for a year, as confirmed by Antinuclear Antibody (ANA) test, which resulted in a strong positive 161 units. The medication has been taken since that day, and the latest medications were Kamyfet 2 x 500mg, Fenofibrat 1 x 100mg, Folic acid 2 x 1 mg, Inpepsa 3 x 1 C, and Omeprazole 1 x 20mg which were routinely taken and controlled.

Upon arrival, her general appearance was weak, with blood pressure of 104/79 mmHg, heart rate of 120/min, temperature of 36,4°C, respiratory rate of 20 breaths per minute, and oxygen saturation of 97% free air. General status within normal limits. Normal neurological examination (no lateralization and meningeal sign was normal), psychiatric disorders were absent.

To establish the diagnosis in this patient, it is necessary to carry out several supporting examinations to exclude the possibility of other diagnoses that result in seizures. The results of the laboratory examination found leukopenia, neutrophilia, lymphocytopenia, anemia,

Figure 1. Past history of ANA Test result

TABLE 1
Laboratory test result

Laboratory Test	Patient Test Results	Normal Range
Complete Blood Count		
Leucocytes (10^3/μL)	3.38 (L)	4.00 – 10.00
Eosinophils (%)	1.40	0.5 – 5.0
Basophils (%)	0.4	0.0 – 1.0
Neutrophils (%)	82.50 (H)	50.0 – 70.0
Lymphocytes (%)	12.50 (L)	20.0 – 40.0
Monocytes (%)	3.20	3.0 – 12.0
Haemoglobin (g/dL)	7.70 (L)	12 – 15
Hematocrit (%)	23.20 (L)	37.0 – 47.0
Erythrocytes (10^6/μL)	2.73 (L)	3.50 – 5.00
MCV (fmol/cell)	84.9	80 – 100
MCH (pg)	28.4	26 – 34
MCHC (g/dL)	33.4	32 – 36
Trombosit (10^3/μL)	143.00 (L)	150 – 450
MPV (fL)	12.5 (H)	6.5 – 12.0
PDW (%)	16.8	15 – 17
PCT (10^3/μL)	1.780 (H)	0.108 – 282
Electrolytes		
Calsium (mg/dL)	9.9	8.8 – 10.4
Natrium (mEq/L)	149.00 (H)	135 – 147
Kalium (mmol/L)	2.95 (L)	3.0 – 5.0
Chlorida (mEq/L)	111.4 (H)	95 – 105
Chemical Chemistry Analyzer		
Random Blood Sugar (mg/dL)	120	< 200
Quantitative CRP (mg/dL)	127.0 (H)	< 10
Procalcitonin (PCT) (mg/dL)	0.62 (H)	< 0.5
Blood Gas Analysis (BGA) of Artery		
pH	7.345 (L)	7.35 – 7.45
pCO2 (mmHg)	34.9 (L)	35 – 45
PO2 (mmHg)	290.6 (H)	80.0 – 100.0
HCO3 Act (mEq/L)	18.8	–
HCO3 Std (mEq/L)	19.2	22 – 26
BE (ecf) (mmol/L)	-7.1	-2 s/d +2
BE (B) (mmol/L)	-6.5	–
ctCO2 (mmol/L)	19.9	–

TABLE 1. *Continued...*

Laboratory Test	Patient Test Results	Normal Range
O2 SAT	99.6	>95
O2CT(mL/dL)	15.1	–
pO2/FI02	4.84	–
pO2(A-a)(T) (mmHg)	115.6	–
pO2(A/a)(T) (mmHg)	0.72	–
Temp (C)	36.0	–
ctHb (g/dL)	10.2	–
FIO2 (%)	61.0	–
Renal Function Test		
Creatinin (mg/dL)	1.8 (H)	–
BUN (mg/dL)	41 (H)	–
Culture Test		
Left blood culture + Antibiotic sensitivity test	No bactery growth	
Right blood culture + Antibiotic sensitivity test	No bactery growth	
Urinalysis		
URO	Normal	Normal
BLD	3+	Negative
BIL	Negative	Negative
KET	Negative	Negative
GLU	Negative	Negative
PRO	2+	Negative
pH	7.5	5.0 – 7.5
NIT	Negative	Negative
LEU	2+	0 – 5
CRE	0.1	Negative
ALB	Over	≤ 0.02
P/C	2+	<0.15
A/C	2+	< 30
S.G	1.005	1.015 – 1.025
COLOR	Yellow	–
CLOUD	2+	Negative

thrombocytopenia, increased creatinine, increased Blood Urea Nitrogen (BUN) levels, hematuria, proteinuria, pyuria, slight hypernatremy, slight hypokalemia, hyperchloremia, high quantitative C-Reactive Protein (CRP), and increased procalcitonin (PCT). Chest X-ray and Magnetic Resonance Imaging (MRI) were within normal limits. Therefore, by using the SLICC (Systemic Lupus International Collaborating Clinics) damage index

Figure 2. Chest X-ray within normal limit
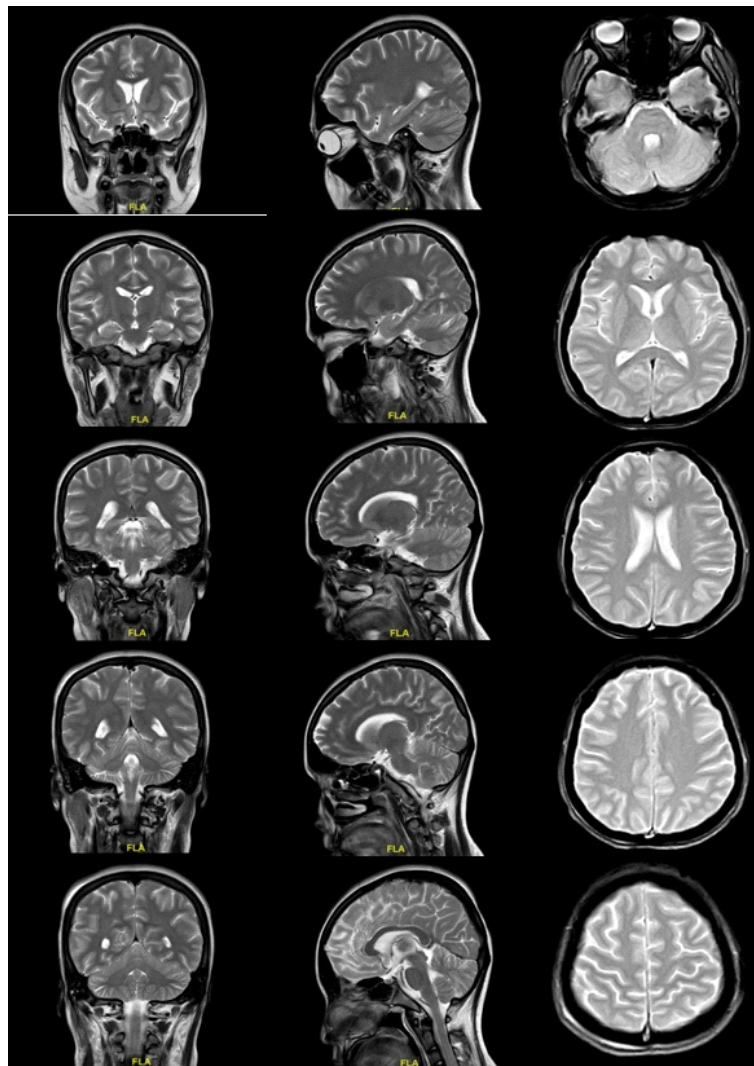
Figure 3. Magnetic Resonance Imaging (MRI) head/brain. Non-contrast MRI does not appear abnormality.
Brain parenchyme does not show abnormality, no visible infarct/bleeding

Entry criterion
Antinuclear antibodies (ANA) at a titer of ≥1:80 on HEp-2 cells or an equivalent positive test (ever)

↓

If absent, do not classify as SLE
If present, apply additive criteria

↓

Additive criteria
Do not count a criterion if there is a more likely explanation than SLE.
Occurrence of a criterion on at least one occasion is sufficient.
SLE classification requires at least one clinical criterion and ≥10 points.
Criteria need not occur simultaneously.
Within each domain, only the highest weighted criterion is counted toward the total score§.

Clinical domains and criteria	Weight	Immunology domains and criteria	Weight
Constitutional		*Antiphospholipid antibodies*	
Fever	2	Anti-cardiolipin antibodies OR	
Hematologic		Anti-β2GP1 antibodies OR	
Leukopenia	3	Lupus anticoagulant	2
Thrombocytopenia	4	*Complement proteins*	
Autoimmune hemolysis	4	Low C3 OR low C4	3
Neuropsychiatric		Low C3 AND low C4	4
Delirium	2	*SLE-specific antibodies*	
Psychosis	3	Anti-dsDNA antibody* OR	
Seizure	5	Anti-Smith antibody	6
Mucocutaneous			
Non-scarring alopecia	2		
Oral ulcers	2		
Subacute cutaneous OR discoid lupus	4		
Acute cutaneous lupus	6		
Serosal			
Pleural or pericardial effusion	5		
Acute pericarditis	6		
Musculoskeletal			
Joint involvement	6		
Renal			
Proteinuria >0.5g/24h	4		
Renal biopsy Class II or V lupus nephritis	8		
Renal biopsy Class III or IV lupus nephritis	10		

Total score:

↓

Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.

Figure 4. ACR/EULAR Criteria of SLE 2019[17]

to establish the diagnosis, where the ANA-IF test was positive as the immunologic criteria and for the clinical criteria in which, seizures, severe persistent headache, hematuria, proteinuria, pyuria, thrombocytopenia, and leukopenia were found, all indicated the activity of SLE in this case. Supported by neuropsychiatry systemic lupus erymathosus guidelines from American College of Rheumatology, we could diagnose that the seizures and severe persistent headache were caused by the NPSLE.

The patient was consulted to a neurologist who gave the advice of administering Phenytoin 100 mg x 7 ampoules using a syringe pump for 15 minutes; 3x1 ampoules were subsequently given; and if the seizures recur, Diazepam 1 ampoule was to be given slowly intravenously; as well as Mecobalamin injection of 500 mcg 1x1, Vitamin B6 per oral 1x1 tablet, and Metamizole 3 x 1000 mg IV for the headache complaints. Regarding the history of SLE, she was consulted to an internist who gave the advice of administering Methylprednisolone 250 mg in NaCl 0.9%. 100 cc used up in 1 hour for 3 days and Cefobactam 2x2 gr IV drip in NaCl 0.9% 100 cc used up in 1 hour. Because the results of the laboratory examination found that the potassium level was below normal, KCL 25 meq was given in NaCl 0.9% 500 cc (8 drops per minute). For complaints of nausea and vomiting, she was given omeprazole 2 x 40 mg IV and inpepsa 3 x 1 C.

On the 3rd day of hospitalization, the patient experienced an improvement in complaints, and there was no seizure period. The next day, she underwent an electroencephalogram (EEG) examination, and the results were normal recording of EEG. No epileptiform waves or abnormal slowdown. Some drugs were still given, but the dose was reduced or stopped. Methylprednisolone was given 1 x 125 mg IV until day 5, then lowered to 1 x 62.5 mg. Cefobactam was still given at

the same dose until day 10.

The patient's condition was stable when she was discharged from the hospital and given Phenytoin capsul 3x1, Vitamin B6 2x1 tabs, KSR 2x1 tabs, Omeprazole 2x 20 mg, Methylprednisolone 16 mg 1- 1-0, Kamyfet 3x 500 mg per oral, and Xepazym 2x1 tabs for home consumption. She was recommended to return for a control visit in the hospital a week later.

DISCUSSION

Cerebral lupus includes neurological and psychiatric syndromes observed in patients with SLE where other causes have been excluded. The manifestations usually occur at the beginning of the SLE journey, with a higher incidence in young women and is the leading cause of morbidity.[8] A three- year prospective study conducted by Magro-Checa *et al.*, 2023 of 370 SLE patients with no prior history of Central Nervous System (CNS) involvement determined that CNS involvement was rare in SLE patients, covering only 7.8 per 100 person-years.[11] It occurs because of the damage of the Blood Brain Barrier (BBB) so that the lymphocytes that are inflammatory cells enter the brain and produce cytokines (like IL-6) and autoimmune antibodies (anti-NMDAR and anti-RP) responsible for neuronal damage through signal pathway induction will worsen inflammation as well as initiate the entry of calcium that leads to apoptosis.[14]

According to a series of definitions of 19 Neuropsychiatric Systemic Lupus Erythematosus Syndrome (NPSLE) and its diagnostic criteria from the American College of Rheumatology (ACR), less than 40–50% of incidences are caused by the underlying CNS lupus activity. Further studies showed that Lupus CNS is

at least as common in children as it is in adults. A three-year prospective study of 370 SLE patients with no previous history of CNS involvement determined that clinically severe CNSparticipation is rare in patients with SLE, covering only 7.8 per 100 people-years.[11] Patients with cerebral lupus have varying clinical manifestations, making it a unique challenge in diagnosis enforcement. This disease affects the central nervous system, causing aseptic meningitis, seizures, anxiety syndrome, psychosis, or peripheral nervous systems, with myasthenia gravis, mononeuritis, autonomic neuropathy, or polyneuropathies.[15] These manifestations range widely from mild symptoms such as headaches, altered mental status, anxiety, depression, psychosis and pseudodementia, to more serious conditions such as seizures, strokes, or coma. These manifestations most often appear in the first year of SLE diagnosis.[6,7,10] Focal syndromes are mostly neurological, whereas diffuse syndrome is mostly psychiatric. Cerebrovascular disorders and epileptic seizures are found in 5–15% of NPSLE patients. Cognitive impairments, mood disturbances, state of acute confusion, or peripheral neuropathy are found only in 1–5% of patients, while psychosis, myelitis, unconscious movement of extremities and facial muscles, and aseptic meningitis are very rare.[16] As in this patient, we can find the clinical manifestations are more related to the focal manifestation in CNS which are seizures and severe headache.

Diagnosing NPSLE is often difficult because doctors have to rule out alternative causes, such as infections and tumors, before they can establish a diagnosis. There are no laboratory or radiological biomarkers to establish a diagnosis, but they can be assisted by using clinical, serological, immunological,

TABLE 2
SLICC (Systemic Lupus International Collaborating Clinics)[18]

Clinical Criteria	Immunologic Criteria
Acute cutaneous lupus	ANA
Chronis Cutaneous lupus	Anti-DNA antibodies
Oral or nasal ulcers	Anti-Sm antibodies
Non-scaring alopecia	Antiphospholipid antibody
Arthritis	Low complement (C3, C4, CG50)
Serositis	Direct Coombs' test
Renal	(do not count in the presence of hemolytic anemia)
Neurologic	
Hemolytic anemia	
Leukopenia	
Thromovytopenia (<100.000/mmc)	

TABLE 3

Neuropsychiatry manifestations in systemic lupus erymathosus; Adapted from Guidelines for the definition of neuropsychiatric nomenclature from American College of Rheumatology[16]

Clinical Criteria	Central Nervous System (CNS)	Peripheral Nervous System (PNS)
Diffuse manifefstation	Acute confusional state	–
	Anxiety disorder	
	Cognitive dysfunction	
	Mood disorders	
	Psychosis	
Focal manifestations	Aseptic meningitis	Guillain-Barre syndrome
	Cerebrovascular disease	Autonomic disorder
	Demyelinating syndrome	Mononeuropathy, single/multiple
	Headache	Myasthenia gravis
	Movement disorder	Neuropathy, cranial
	Myelopathy	Plexopathy
	Seizures	Polyneuropathy

electrophysiological, and neuroimaging studies to eliminate other comparative diagnoses because most of the outcomes of support examinations yield results without specific abnormalities.[12,13] Currently, serological tests are not accurate enough to establish the diagnosis of NPSLE and/or to assess the severity of the disease. Autoantibodies, which are a hallmark of lupus, may also be useful in functioning as biomarkers. In addition to autoantibodies, it is also possible to explore molecules, which circulate in blood and/or Cerebrospinal Fluid (CSF) but so far the findings of CSF are also non-specific and only serve to rule out other etiologies.[19] Neuroimaging can be used to identify CNS involvement in a noninvasive manner in SLE. Compared to CT, MRI is a more sensitive imaging modality to detect intracranial abnormalities and assess the chronicity and evolution of these abnormalities. MRI is the current gold standard of radiology used in assessing patients with SLE, but about 50% of NPSLE patients do not have detectable abnormalities.[8,12] As with patients in this case report, supporting examination results from MRI found normal results with no specific anomalies and laboratory examinations found no signs of infection which leading to infection of the central nervous system, no abnormalities for the EEG examination.

The European League Against Rheumatism (EULAR) issued a consensus recommendation for the management of NPSLE stating that neuropsychiatric manifestations in patients with SLE should be first assessed and treated in the same way as in patients without SLE, including routine symptomatic therapy and psychological interventions. Current practice is mostly symptomatic and includes the use of antipsychotic drugs, antidepressants, and anti-anxiety medications to treat psychiatric symptoms as well as antiepileptic drugs to treat seizures, and immunosuppressive agents (e.g., corticosteroids, cyclophosphamide, azathioprine, mofetil mycophenolate) to suppress the systemic inflammatory response.[17,20] As in this case, the patient was given therapy for seizures first before knowing the cause of the seizures due to the emergency state by giving Phenytoin 100mg x 7 ampoules using a syringe pump for 15 minutes; 3x1 ampoules were subsequently given. Regarding the SLE history, she was prescribed methylprednisolone as the immunosuppressive agent. Then other supportive therapy are also given based on the complaints experienced and the findings of the examination such as mecobalamin, vitamin B6, metamizole, cefobactam, KCL, omeprazole, and inpepsa.

CONCLUSSION

A case of coexistence of systemic lupus erythematosus (SLE) with involvement of the brain has been reported in 18-year-old female patient who has suffered from SLE for a year with the clinical manifestation of tonic clonic seizure. The diagnosis of this case was established after a series of examinations so we could exclude other possible diagnosis. The management in this case was the same as what is written in the guideline, the first therapy given was the emergency therapy for seizures accompanied by symptomatic and immunosuppressive therapy. The

patient's condition improved after therapy. Further research is needed to determine the vary clinical manifestations of cerebral lupus or NPSLE, further examination findings, and the therapy because single-case observations have limitations.

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Case Report : Rehabilitation Intervention in Improving Infant's Oromotor Skill and Body Weight

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Abstract

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Background : Preterm birth rates are still very high. Global data found that preterm babies occurred in 11% of all live births. A recent study showed that more than 25% of neonates baby born between 28 and 32 weeks of gestation, developed disorders condition at the age of two, and this ratio reached 40% at the age of ten. Preterm infants had higher risk of poor motoric skills, such as subtle deficits in eye-hand coordination, sensory-motor integration, manual dexterity, and gross motor skills that lead to poor feeding skills and neuromotor development delay. Therefore, interventions need to be done to optimize growth and development.

Case : A 10-day-old male infant consulted by the Medical Rehabilitation department due to feeding difficulty and low birth weight. At 10 days old, the patient weighs 1550 grams, length 44 cm, head circumference 31 cm, and the non-nutritive scoring (NNS) was 45. The patient was given proper positioning, oral motor stimulation (OMS) with the Fucile method for 1 week in the hospital and the treatment continue at home. After 2 weeks of intervention, the infant's body weight increased to 2010 grams, body length 45 cm, head circumference 32 cm, and the non-nutritive scoring (NNS) became 86.

Conclusion : Oral motor stimulation improves oral motor skills such as sucking and swallowing reflexes in infants without organ abnormalities thus optimized good oral feeding ability and weight gain acceleration.

Keywords : oral motor stimulation, body weight, oromotor skill, premature, infant

INTRODUCTION

Preterm infant birth is a condition of childbirth in less than 37 weeks gestation, with a baby weighed less than 2500 grams.[1] Based on the weight of the fetus at birth, preterm infants are divided into *low birth weight* (birth weight <2500 grams), *very low birth weight* (birth weight <1500 grams), and *extremely low birth weight (birth weight* <1000 grams).[2] Platt *et al.* (2014) highlighted that preterm birth is a common issue worldwide, estimated at 10% from all of births. Preterm infants are more prone to face short-term and long-term neurodevelopmental disorders due to intrauterine growth interruption and hospitalization in the neonatal intensive care unit (NICU).[3] A recent study showed that more than 25% of neonates, born between 28 and 32 weeks of gestation, developed disorders condition at the age of 2, and this ratio reached 40% at the age of 10.[4] Therefor infants without major neurodevelopmental delays are still have higher risk of poor motor outcomes, such as subtle deficits in eye-hand coordination, sensory-motor integration, manual dexterity, and poor motor skills.[5] One of the problems of preterm baby is eating difficulties due to anatomical disorders in mouth area, impaired sucking patterns, and impaired sucking-swallowing-breathing coordination. Early detection and medical rehabilitation are needed to overcome the disorder experienced by preterm infants. Sucking reflex disorder if not properly managed can lead to impaired growth and development. Therefor OMS should be performed for 2 weeks and evaluated through weight gain and *non-nutritive scoring* (NNS) to asses oral motor skills before and after the intervention. Currently, there are only few scientific evidences related to medical rehabilitation in preterm infant, so this report was created to have outcomes of medical rehabilitation in preterm infant with low birth weight.

CASE PRESENTATION

Newborn baby, on May 28, 2024, male, was born from P2A0 mother, 34 weeks gestation, by section cesarean on the indication of *impending eclampsia*. The baby was born with no immediate cry, and retraction was found. The baby's Apgar scores at 1, 5, and 10 minutes were 5, 6, and 7, respectively. The anthropometric status of the baby followed as: body weight in 1820 grams, body length in 44 cm, and head circumference in 31 cm. The baby was resuscitated and received oxygen therapy through *continuous positive airway pressure* (CPAP) with a PEEP setting of 7 cmH$_2$O and an oxygen fraction of 35%. On the seventh day, oxygen therapy through CPAP was stopped.

On the tenth day, the infant transferred to the

TABLE 1

NNS score before medical rehabilitation intervention in infants

Positive Items	Mark the suitable				Converted Values
Rooting reaction	Yes ( ) (4)	No (✓) (0)			0
Easy beginning of sucking	Yes ( ) (4)	No (✓) (0)			0
Labial sealing	Always ( ) (12)	most part (✓) (8)	sometimes ( ) (4)	never ( ) (0)	8
Tongue central groove	Always ( ) (9)	most part ( ) (6)	sometimes (✓) (3)	never ( ) (0)	3
Peristatic tongue movement	Always ( ) (9)	most part ( ) (6)	sometimes (✓) (3)	never ( ) (0)	3
Jaw raising and lowering movement	Always ( ) (9)	most part (✓) (6)	sometimes ( ) (3)	never ( ) (0)	6
Labial, tongue and jaw coordination	Always ( ) (15)	most part (✓) (10)	sometimes ( ) (5)	never ( ) (0)	10
Sucking strength	Always ( ) (12)	most part (✓) (8)	sometimes ( ) (4)	never ( ) (0)	8
Sucking rhythm	Always ( ) (12)	most part (✓) (8)	sometimes ( ) (4)	never ( ) (0)	8
Total positive items					

TABLE 1. *Continued...*

Negative Items	Mark the suitable				Converted Values
Bites	Always ( ) (-3)	most part ( ) (-2)	sometimes (✓) (-1)	never ( ) (0)	-1
Excessive jaw excursion	Always ( ) (-3)	most part ( ) (-2)	sometimes ( ) (-1)	never (✓) (0)	0
Stress signals	Always ( ) (-15)	most part ( ) (-10)	sometimes ( ) (-5)	never (✓) (0)	0
Total negative items					-1
TOTAL					45

TABLE 2
NNS score after medical rehabilitation intervention in infants

Positive Items	Mark the suitable				Converted Values
Rooting reaction	Yes (✓) (4)	No ( ) (0)			4
Easy beginning of sucking	Yes (✓) (4)	No ( ) (0)			4
Labial sealing	Always (✓) (12)	most part ( ) (8)	sometimes ( ) (4)	never ( ) (0)	12
Tongue central groove	Always (✓) (9)	most part ( ) (6)	sometimes ( ) (3)	never ( ) (0)	9
Peristatic tongue movement	Always (✓) (9)	most part ( ) (6)	sometimes ( ) (3)	never ( ) (0)	9
Jaw raising and lowering movement	Always (✓) (9)	most part ( ) (6)	sometimes ( ) (3)	never ( ) (0)	9
Labial, tongue and jaw coordination	Always (✓) (15)	most part ( ) (10)	sometimes ( ) (5)	never ( ) (0)	15
Sucking strength	Always (✓) (12)	most part ( ) (8)	sometimes ( ) (4)	never ( ) (0)	12
Sucking rhythm	Always (✓) (12)	most part ( ) (8)	sometimes ( ) (4)	never ( ) (0)	12
Total positive items					86

Negative Items	Mark the suitable				Converted Values
Bites	Always ( ) (-3)	most part ( ) (-2)	sometimes ( ) (-1)	never (✓) (0)	0
Excessive jaw excursion	Always ( ) (-3)	most part ( ) (-2)	sometimes ( ) (-1)	never (✓) (0)	0
Stress signals	Always ( ) (-15)	most part ( ) (-10)	sometimes ( ) (-5)	never (✓) (0)	0
Total negative items					0
TOTAL					86

Medical Rehabilitation department due to a lack of suction reflex, with status of the baby followed as: ten days old with a body weight of 1550 grams and a body length of 44 cm. Based on physical examination laboratory and x-ray, no abnormalities were found in the oromotor organ, lungs, and heart. Then, the baby was given medical rehabilitation interventions, such as oral motor stimulation four times a day for 10 minutes, tactile stimulation, proprioception, and vestibular stimulation once a day for 4 minutes, and *positioning* using swaddling with *midline* flexion and *nesting* positions during care. The intervention occurs for two weeks, with one week treatment at the hospital by a doctor and one week treatment at home by the parent. The intervention was monitored through communication via telephone and home visits. At post-intervention control, the baby was 24 days old, weighed 2010 grams, body length 45 cm, and head circumference 32 cm. In addition to anthropometric evaluation, patients were evaluated using the *non-nutritive scoring* (NNS) *system* to assess the ability of sucking in preterm infants before oral feeding. The NNS score was calculated before and after the medical rehabilitation intervention, as shown in Table 1.

DISCUSSION

In this case report, a baby was born from P2A0 mother, 36 weeks gestational age, by *section caesarian* on the indication of *impending* eclampsia. The baby was born with a body weight of 1820 grams, a body length of 44 cm, and a head circumference of 31 cm. Based on these two data, the preterm baby born in less than 37 weeks gestation, with the baby weighed less than 2500 grams.[1] Based on the weight of the fetus at birth, the baby is classified as low birth weight baby (LBW) or *low birth weight* because the baby's birth weighed between 1500 grams to 2500 grams.[2]

The baby in this case had respiratory distress at birth and an inadequate suction reflex. The infant was given oxygen therapy via *continuous positive airway pressure* (CPAP) with a PEEP setting of 7 cmH$_2$O and an oxygen fraction of 35%. On the seventh day, oxygen therapy through CPAP was stopped. Meanwhile, to improve the suction reflex, the infant was transferred to medical rehabilitation for further treatment Preterm babies experienced various disorders due to the immature development of the baby in the womb, but the baby has already been born due to multiple conditions. Babies born at 32–36 weeks gestation, as in this case, have an 8% risk of developmental disorders, such as neurosensory disorders, cognitive and language development disorders, motor disorders, neurobehavioral, socioemotional, and learning difficulties.[7]

Medical rehabilitation interventions are needed to optimize child development, catch up with developmental delays, and prevent further deterioration. Preterm infants have poor sensory processing and organization, poor muscle tone and motor coordination, resulting in limitations in daily life functions.[8] Various medical rehabilitation interventions can be given to preterm infants: therapeutic exercise, neuromotor and sensory-motor interventions, neuromuscular stimulation, joint mobilization, *positioning*, and orthosis. In this case, the medical rehabilitation interventions treatment were oral stimulation four times a day, proprioception and vestibular stimulation one time a day, and *positioning* using swaddling with *midline* flexion and *nesting* positions.[16]

The oral stimulation performed in this case refers to the method issued by Fucile *et al*.[8] The methods given such as, 15 minutes consisting of 12 minutes on the cheeks, lips, gums, and tongue area and 3 minutes for sucking exercises. During this stimulation, the position of the infant is supinated. This program was conducted for ten consecutive days, before each feeding time.[8] The oral stimulation method by Fucile *et al*[8] can be seen in Table 3.

Infants receiving oral stimulation could be fed orally faster, with a mean time of 11±4 days.[8] Meanwhile, infants who did not receive oral stimulation could be fed orally at 18±7 days. The difference was also found statistically significant (p=0.005). In addition, the overall intake of infants also increased significantly in infants who received oral stimulation (p=0.0002).[8] Similar results were also found by Pereira *et al*[9] that there was a significant difference in the time required to achieve oral feeding, which was 4 (3–11) days in the intervention group and 8 (7–13) days in the control group (p=0.003).[9]

The results of this study suggests that the provision of oral stimulation is also associated with better nutritional *intake*. Infants who receive oral stimulation, strengthen the muscles around the mouth so that they can suck adequately.[8] The stimulation also trains neuromuscular structures more efficiently and has greater endurance. This is related to the maturation of neural structures that were previously not optimally mature, especially related to the ability to suck and the coordination of sucking-swallowing-breathing. The findings prove that the concept of infant sucking maturation is not only depend on anatomical and physiological maturation but also learning experience that the learning process of oral stimulation may achieve.[10]

The Beckman method includes oral motor stimulation aims to improve the strength, flexibility, and control of the muscles around the mouth including the lips, tongue, cheeks, and jaw. It focuses on specific exercises for the muscles, such as movement of the lips jaw, and tongue which are beneficial for babies with muscle weakness or stiffness in the mouth area. This method uses gentle massage techniques used for children, while the Fucile method is more often used for

TABLE 3
Oral stimulation method based on Fucile _et al_[8]

Structure	Stimulation Steps	Purpose	Frequency	Duration
Cheek	1. Place index finger at the base of the nose. 2. Compress the tissue, move finger toward the corner of the corner of the lip (ie, C pattern). 3. Repeat for other side.	Improve range of motion and strength of cheeks, nad improve lip seal.	4x each cheek	2 min
Upper Lip	1. Place index finger at the corner of the upper lip. 2. Compress the tissue. 3. Move the finger away in a circular motion, from the corner toward the center and the other corner. 4. Reverse direction	Improve lip range of motion and seal.	4x	1 min
Lower Lip	1. Place index finger at the corner of lip. 2. Compress the tissue. 3. Move the finger away in a circular motion, from the corner toward the center and the other corner. 4. Reverse direction.	Improve lip range of motion and seal.	4x	1 min
Upper and lower lip curl	1. Place index finger at center of lip. 2. Apply sustained pressure, stretch downward toward the midline. 3. Repeat for lower lip-apply sustained pressure and stretch upward toward the midline.	Improve lip strength, range of motion and seal.	2x each lip	1 min
Upper gum	1. Place finger at the center of the gum, with firm sustained pressure slowly move toward the back of the mouth. 2. Return to the center of the mouth. 3. Repeat for opposite side.	Improve lip strength, range of motion and seal.	2x	1 min
Lower gum	1. Place finger at the center of the gum, with firm sustained pressure slowly move toward the back of the mouth. 2. Return to the center of the mouth. 3. Repeat for opposite side.	Improve range of motion of tongue, stimulate swallow and improve suck.	2x	1 min
Internal cheek	1. Place finger at inner corner of lip. 2. Compress the tissue, move back toward the molars and return to corner of lip. 3. Repeat for opposite side.	Improve cheek range of motion and lip seal.	2x each cheek	2 min
Lateral borders of the tongue	1. Place finger at the level of molar between the side blade of the tongue and lower gum. 2. Move the finger toward midline, pushing the tongue toward the opposite direction. 3. Immediately move the finger all the way into the cheek, stretching it.	Improve tongue range of motion and strength.	2x each side	1 min

TABLE 3. *Continued...*

Structure	Stimulation Steps	Purpose	Frequency	Duration
Midblade of the tongue	1. Place index at the center of the mouth 2. Give sustained pressure into the hard palate for 3 second. 3. Move the finger down to contact the center blade of tongue. 4. Displace the tongue downward with a firm pressure. 5. Immediately move the finger to contact the center of the mouth at the hard palate	Improve range of motion of tongue, stimulate swallow and improve suck.	4x	1 min
Elicit a suck	1. Place finger at the midline, center of the palate gently stroke the palate to elicit a suck.	Improve suck, and soft palate activation.	N/A	1 min
Pacifier	1. Place the pacifier in mouth	Improve suck, and soft palate activation.	N/A	3 min

infants as it relies on gentle touch. Newborns are very sensitive to touch, especially the face, hands, soles of the feet, and tummy.[8]

In addition to oral stimulation, patients are given proprioception and vestibular stimulation once a day, *positioning* using swaddling with *midline* flexion and nesting positions.[11] Previous studies have found that proprioceptive and vestibular stimulation can increase infant weight and activity and improve infant social-emotional abilities.[12] Proprioceptive-vestibular stimulation stimulates specific receptors that affect the center of the respiration system in the central nervous system. The previous research found a synchrony relationship between the extremities' breath rate and vibrational stimulation. Namely, proprioceptive receptors activate proprioceptive afferent pathways that improve human coordination between movement and respiratory rhythm.[13-15] Proper positioning of preterm infants can promote normal motor development and minimize the development of abnormal movement patterns. A systematic review study found that positioning of preterm infants, whether pronation, supination, or nesting, improved respiratory function, neuromotor development, gastrointestinal function, and sleep. The study also found that the supination position was more widely used because it was easier and could monitor the baby better.[16]

The medical rehabilitation intervention in this case showed success, characterized by an improvement in anthropometric status and NNS score. In this case, there was an increase in body weight and body length, indicating the effect of medical rehabilitation intervention on the growth of preterm infants. In addition, there was also an increase in NNS scores indicating the impact of medical rehabilitation intervention on the development of sucking ability of preterm infants. We recognized that this study has limitation given that it is based on single-case report. Therefore, future studies with observational studies or clinical trial design related to oral motor exercise are needed.

CONCLUSION

Oral motor stimulation improves oral motor skills such as sucking and swallowing reflexes in infant without organ abnormalities thus optimized good oral feeding ability and weight gain acceleration.

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AUTHOR GUIDELINE

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ORIGINAL ARTICLE

Research manuscript should adhere guidelines as follow:

Title:
1. Is neither too long nor too short, approximately 12–14 words
2. Describes research design
3. Contains no abbreviation unless standard

Abstract:
1. Is well structured (background, aim, method, result, conclusion)
2. Consists of maximum 250 words
3. Consists of 3-8 keywords
4. Is presented in English

Introduction:
1. Consists of 2 paragraphs/parts. The first paragraph consists of research background (research justification): what have been known and what need to be added. The second paragraph consists of hypothesis or research aim.
2. Is supported by relevant and strong references

Methods:
1. Explains research design, settings and time
2. Explains population and sample, sampling technique, sample size (equation doesn't need to be enclosed), inclusion and exclusion criteria.
3. For clinical trial, explains randomization and conceal allocation, and Kappa test if conducted and detailed investment
4. Thoroughly explains method, instrument, measurement technique and data collection
5. Explains data analysis with proper tests according to data, significance and confidence interval
6. Explains computer program (software) used
7. Explains ethical clearance and informed consent

Results:
1. Is presented in a logical sequence
2. Presents subject characteristics (in a table). For clinical trial, subject characteristic of each group before trial are presented
3. Explains subjects who drop out and the reasons. If possible, provides consort diagram
4. Maximum 3-4 tables
5. Provides hypothesis without commentary

Discussion:
1. Discusses all relevant findings and its association with practice. There is no redundant repetition of findings already presented in the results section.
2. Is compared with previous study findings.
3. Mentions research strengths/weaknesses and its impact on findings.

Conclusion:
1. Should answer research question
2. Should be based on research findings, not quotation
3. Can provide suggestion for future research

References:
1. Uses Vancouver style (see *Uniform Requirements for Manuscripts Submitted to Biomedical Journals*) www.icjme.org

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1. Present complete name of authors without academic title along with office/institution/work place address under the title
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   The main author provides a statement explaining that article has never been published nor sent for publication to other journals and has already been approved by all co-authors evidenced by a statement sheet. All sent articles are reviewed by profession groups (peer reviewers) and editors. All articles should provide ethical clearance issued by Ethical Review Board and 2 sheets of inform consent form already signed in "pdf" format.

CASE REPORT

Title :
1. Is neither too long nor too short, approximately 12-14 words
2. Contains no abbreviation unless standard

Abstract :
1. Is well structured (background, aim, case report, discussion, conclusion)
2. Consists of maximum 250 words
3. Consists of 3-8 keywords
4. Is presented in English

Introduction :
1. Consists of 2 paragraphs/parts. The first paragraph consists of research background (justification of the case report). The second paragraph consists of aim of case report emphasizing diagnose/pathogenesis/therapy.
2. Is supported by relevant and strong references

Case report :
1. Presents short case involving medical history, physical examinations, and investigations.
2. Stresses new or rare cases or new therapies or procedures
3. Provides patient's picture (if necessary), investigations such as radiology or laboratory or others as needed. Pictures/photos size minimum 300 dpi.
4. Obtains patients' or families' informed consent for publication for patients with easily identified features. Editors may conceal physical features considered unnecessary.
5. Contains maximum four photos/pictures for each article.

Discussion :
1. Provides epidemiology data showing that rare cases occur or new procedures are conducted.
2. Provides relevant discussion according to aim of the case report emphasizing diagnose/pathogenesis/therapy comparing/relating to other cases and providing LoE (Level of Evidence).

Conclusion and suggestion :
1. Are in line with the aim of case report.
2. Suggestion consists of improvement for case management.

Reference :
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SERTIFIKAT

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