Medica Hospitalia
Journal of Clinical Medicine
Med Hosp 2025; vol 12 (2) : 166–172

OPEN ACCESS

*Original Article*

# The Association between Monocyte-derived Macrophages TNF-α Expression and Anthropometrics Measures in Polycystic Ovary Syndrome

Naylah Muna[1,2], Oki Riayati[2], Heri Wibowo[3], Andon Hestiantoro[2,4,5]

[1]Master Programme in Biomedical Sciences, Faculty of Medicine, Indonesia University, Indonesia
[2]Human Reproduction, Infertility, and Family Planning Research Center,
Indonesian Medical Education and Research Institute (IMERI), Faculty of Medicine, Indonesia University, Indonesia
[3]Departement of Parasitology, Faculty of Medicine, Indonesia University, Indonesia
[4]Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology
Faculty of Medicine, Indonesia University, Indonesia
[5]Yasmin IVF Clinic, Dr. Cipto Mangunkusumo General Hospital Jakarta, Indonesia

p-ISSN: 2301-4369 e-ISSN: 2685-7898
https://doi.org/10.36408/mhjcm.v12i2.1224

**Accepted:** October 10th, 2024
**Approved:** July 08th, 2025

**Author Affiliation:**
Human Reproductive, Infertility,
and Family Planning Research Center,
Indonesian Medical Education and
Research Institute (IMERI),
Faculty of Medicine, Indonesia University,
Indonesia

**Author Correspondence:**
Naylah Muna
Salemba Raya Street No.16,
Jakarta, Indonesia, 10430

**E-mail:**
Naylah147@gmail.com



## Abstract

**Background :** Polycystic ovary syndrome (PCOS) is a female infertility disease that is often associated with low-grade chronic inflammation. This inflammation was suspected to correlate with certain body conditions, especially physical lipid composition that can be obtained under anthropometrics measurements. Monocytes and macrophages of PCOS patients were more susceptible to inflammation and contributed to this condition. Tumor Necrosis Factor-alpha (TNF-α), as one of the major inflammatory cytokines, holds an important role in the chronic inflammation of PCOS. This study aimed to evaluate the association of inflammatory cellular levels TNF-α in macrophage cells of women diagnosed with PCOS with physical anthropometrics.
**Methods :** Twenty PCOS women and ten healthy women as the control group were recruited in this study. Anthropometric data were measured. Peripheral blood was collected, mononuclear cells were isolated, and then cultured. Monocytes were selected and differentiated into macrophages. Macrophages were then exposed to oxidized Low-Density Lipoprotein (ox-LDL) and underwent flow cytometry to examine the level of TNF-α. Anthropometric data and TNF-α level were analyzed using Spearman-Rho Correlation test followed by a linear regression test.
**Results :** TNF-α expression was found to be statistically correlated with Body Mass Index (BMI), waist circumference (WC), waist-to-height ratio, visceral fat level, and muscle mass of arm (MMA) ($p$<0.05). However, only WC and MMA gave significant impact to macrophage TNF-α expression based on linear regression association test with equation -96.971 + 0.601*waist circumference + 2.665*MMA.
**Conclusion :** TNF-α was strongly associated with waist circumference and muscle mass percentage of arm in PCOS cases.

**Keywords :** Anthropometrics; Low-Grade Chronic Inflammation; PCOS; TNF-α.

## INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a multifactorial endocrine disorder that affects fertility in reproductive age women. The prevalence of women with PCOS in the world varies, which can reach 7–15%.[1] Based on the Rotterdam criteria, the occurrence of anovulatory disorders, the appearance of cysts in the ovarian morphology and hyperandrogenism both clinically and in biochemistry were three main symptoms in PCOS.[2] PCOS also has clinical implications from the accumulation of fatty tissue, such as type 2 diabetes, insulin resistance, and obesity.[1–3]

Several studies that have been conducted showed a link between cystic ovarian syndrome and low-grade chronic inflammation.[3–6] These studies found that there is not only a correlation but also a cause-and-effect relationship between chronic inflammation, obesity, and hyperandrogenism, which are the clinical manifestations of PCOS. Several inflammatory mediators, such as C Reactive Protein (CRP), Interleukin 1-β (IL-1β), Interleukin 6 (IL-6), and Tumor Necrosis Factor-α (TNF-α), were found to have higher levels in women with PCOS symptoms.[5] However, the chronic inflammation that occurs often only releases significant and permanent pro-inflammatory cytokines, but in low amounts that are difficult to detect in the blood circulation system.[7]

The exact pathophysiology and pathomechanism of the causal interaction between chronic low-grade inflammation and PCOS still need to be fully understood. Obesity and increased fat levels are thought to be one of the primary triggers for this condition.[8] An increase in fat levels will cause adipocyte cells in adipose tissue to increase size to accommodate and compensate for increased fat levels. The event of increasing the size of adipocyte cells is called hypertrophy.[9] When experiencing hypertrophy, adipocyte cells will experience hypoxia and release Nuclear Factor kappa B (NF-κB), which causes adipocytes to become more susceptible to inflammation, cell death by apoptosis mechanism, and release more fatty acids. The release of NF-κB, a transcription factor, will also cause an increase expression in MCP1 (Monocyte Chemoattractant Protein-1).[4,10]

MCP1 is a chemokine that attracts the chemotaxis of monocytes, neutrophils, and lymphocytes. MCP1 is also the main factor that regulates the migration and infiltration of monocytes from the endothelial tissue of blood vessels.[11] Increased MCP1 expression in PCOS cases causes the recruitment of more monocytes in adipose tissue. Meanwhile, immune cells in PCOS women, including monocytes, are thought to be more susceptible to inflammation and secrete more significant amounts of inflammatory cytokines.[12,13]

PCOS is strongly associated with obesity and therefore is also often linked to adipose tissue dysfunction. About 30–60% of PCOS women showed obesity characteristics, which could lead to metabolic complications.[9] Obesity is a surplus condition of energy uptake compared to metabolic needs. This condition might cause an imbalance in body fat and adipose tissue distribution inside the body. Adipose tissue is a dynamic organ that secretes adipokines, chemical molecules secreted by adipose, such as adiponectin, visfatin, and TNF-α.[8]

TNF-α is a member of the TNF superfamily.[14] This protein plays a vital role in inflammation reactions. Related to PCOS, TNF-α might induce high androgen secretion while decreasing SHBG (Sex Hormones Binding Globulin), thus manifesting hyperandrogenism. TNF-α is also suggested to have an association with obesity, infertility implications in PCOS, and other metabolic syndromes.[14,15]

Numerous studies found that there might be a mutual effect of obesity and increased inflammation condition in women suffering from PCOS. However, the exact pathomechanism is not fully understood. Fat and adipose tissue distribution might differ between lean, overweight, and obese individuals. Fat accumulation in certain parts of the body might cause some complications. This study wanted to examine the association between inflammation occurred in PCOS women through the level of TNF-α correlated with body fat distribution and presentation. TNF-α would be measured from monocyte cells as it was suspected that monocytes and macrophages in PCOS women were susceptible to inflammation compared to healthy women.

## METHODS

### Study design and subjects

This was a cross-sectional study. Samples were collected between February to May 2024 at Human Reproduction, Infertility, and Family Planning (HRIFP) Research Centre, IMERI FM UI. Twenty PCOS women were drawn as the case group, and ten healthy women were included as a control group. Purposive sampling technique was done under several inclusion criteria: Suspected PCOS and fulfilled 2 out of 3 Rotterdam criteria, irregular menstrual cycle, not a pregnant nor breast-feeding woman, in reproductive age (18–35 years old) and consented to participate in the research. Samples failed to blood collection, under PCOS medical treatment, or diagnosed with Atherosclerosis or type 2 Diabetes would be excluded. Subjects fasted for 8–10 hours prior to blood collection to obtain fasting glucose levels. After filling out the consent form, subjects were measured for their demographic and anthropometric data, and peripheral blood collection was performed. Seven milliliters of blood were collected in an anti-coagulant heparin tube. This study has passed ethical approval from The Ethics

TABLE 1
**Anthropometric measurements and mean levels of TNF-α expression**

| Parameter | PCOS (n=20) | Control (n=10) | *p* value |
|---|---|---|---|
| Age (years) | 31.1 ± 4.6 | 27.5 ± 2.1 | 0.053 |
| Body height (m) | 1.5 ± 0.1 | 1.6 ± 0.1 | 0.012* |
| Body weight (kg) | 68.3 ± 14.1 | 54.7 ± 5.1 | 0.819 |
| BMI (kg/m$^2$) | 27.7 ± 5.2 | 22.3 ± 0.6 | 0.000* |
| Waist circumference (cm) | 89.7 ± 10.3 | 78.4 ± 3.7 | 0.009* |
| Hip circumference (cm) | 103.3 ± 10.4 | 95.7 ± 4.1 | 0.000* |
| Waist to Hip Ratio | 0.87 ± 0.0 | 0.82 ± 0.0 | 0.993 |
| Waist to Height Ratio | 0.57 ± 0.0 | 0.50 ± 0.0 | 0.009* |
| Whole body fat (%) | 34.4 ± 4.5 | 31.3 ± 2.0 | 0.011* |
| Resting metabolism (kcal) | 1356 ± 187.4 | 1120 ± 92.5 | 0.091 |
| Visceral fat level (cm$^2$) | 8.2 ± 4.1 | 4.1 ± 0.9 | 0.000* |
| Whole body subcutaneous fat (WBSF) (%) | 31.2 ± 5.3 | 26.5 ± 1.7 | 0.001* |
| Subcutaneous fat of Trunk (SCFT) (%) | 27.1 ± 5.1 | 21.4 ± 1.8 | 0.000* |
| Subcutaneous fat of Arm (SCFA) (%) | 47.5 ± 6.0 | 44.0 ± 2.5 | 0.000* |
| Subcutaneous fat of Leg (SCFL) (%) | 44.1 ± 7.2 | 39.3 ± 2.4 | 0.001* |
| Whole body muscle mass (WMM) (%) | 39.2 ± 2.4 | 24.1 ± 1.8 | 0.037* |
| Muscle mass of Trunk (MMT) (%) | 18.2 ± 2.1 | 19.4 ± 0.8 | 0.000* |
| Muscle mass of Arm (MMA) (%) | 24.0 ± 4.3 | 27.5 ± 1.3 | 0.000* |
| Muscle mass of Leg (MML) (%) | 37.2 ± 1.8 | 37.3 ± 1.2 | 0.163 |
| TNF-α Expression (%) | 4.4 (1.0–27.7) | 0.5 (0.1–3.1) | 0.000* |

Data are expressed as mean ± SD or median (minimum–maximum).
*$p$<0.05 significant difference among the groups using independent T-test for normally distributed data and Mann-Whitney test for non-normally distributed data.

Committee of the Faculty of Medicine, Universitas Indonesia-Cipto Mangunkusumo Hospital with approval number KET-205/UN.2.F1/ETIK/PPM.00.02/2024.

**Demographic and anthropometric data collections**

Subjects who agreed to participate in the study were measured for demographic data and body composition analysis. This analysis was performed using Omron Karada Scan (Production Facility Omron Dalian Co., Ltd., Shanghai, China). Fat body composition, basal metabolic rate, visceral fat, and waist-hip circumference were obtained from the measurements. Fat body composition measured in this study were Whole Body Fat Percentage (WFP), Whole Body Subcutaneous Fat (WBSF), Subcutaneous Fat of Arm (SCFA), Subcutaneous Fat of Trunk (SCFT), Subcutaneous Fat of Leg (SCFL), Whole Body Muscle Mass (WMM), Muscle Mass of Arm (MMA), Muscle Mass of Trunk (MMT), and Muscle Mass of Leg (MML). This study also measured subjects' body weight and height then converted them to Body Mass Index (BMI). The waist and hip circumferences were also measured and calculated using the waist-to-hip and waist-to-height ratios.

**Macrophages culture**

Eight milliliters of peripheral blood was collected in a heparin tube. White blood cells containing monocytes were separated from other blood components using Ficoll-Paque (Cytiva, Uppsala, Sweden) gradient centrifugation. Isolated monocytes from buffy coat were then cultured using 1 mL complete medium (RPMI [Sigma Aldrich, MO, USA], FBS 10% [Gibco, PRF, USA], Pen-Strep 1% [Gibco, NJ, USA], Amphotericin-B 1%

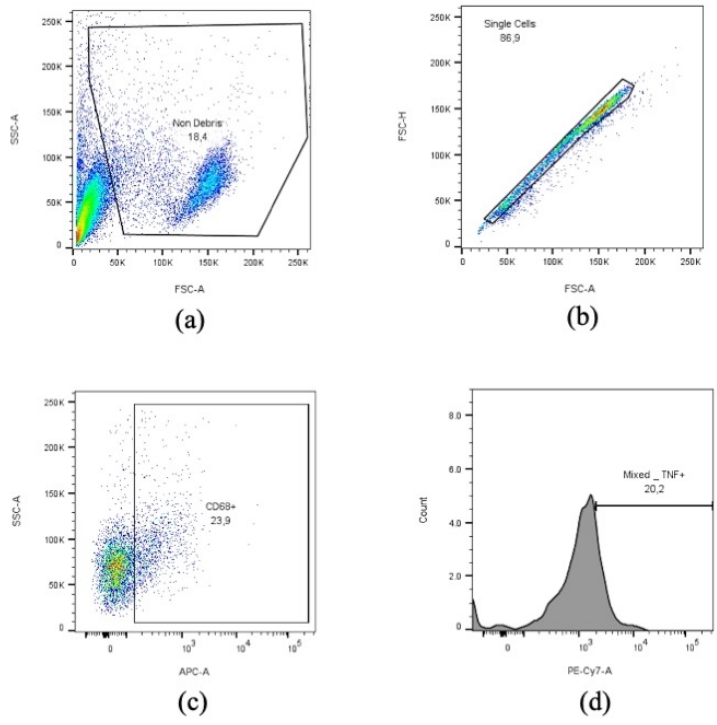


**Figure 1.** Flow cytometry to measure the levels of monocyte-derived macrophages TNF-α expression. (a) Non-Debris selection. (b) Single cells selection. (c) Macrophage selection with CD68+. (d) TNF-α expression.

[Gibco, NJ, USA]) under the influence of 50 ng/ml M-CSF growth factor (Sigma Aldrich, MO, USA) for 2 x 72 hours to differentiate into M0 macrophages. Suspected monocyte-derived macrophage was then exposed to oxidized LDL (Invitrogen, OR, USA) for 24 hours. After 24 hours, the macrophages were harvested using Trypsin EDTA (Sigma Aldrich, MO, USA) for 2 x 3 minutes.

**TNF-α flow cytometry measurement**

Harvested culture cells were washed using PBS (Gibco, NJ, USA) to remove the remaining culture media. After the wash, the cells were stained with allophycocyanin (APC)-conjugated CD-68 monoclonal surface antibody (Thermo Scientific, MA, USA) diluted in stain buffer to distinguish macrophage cells. Staining was then continued with phycoeritrin-Cyanine7 (PE-Cy7)-conjugated TNF-α monoclonal intracellular antibody (Thermo Scientific, MA, USA) staining to mark the TNF-α protein. Cell samples were then read using a BD FACS Canto II Flow Cytometry instrument (BD Biosciences, NJ, USA).

**Statisical analysis**

Statistical analysis in this study was performed with SPSS version 26 software. All tests were considered as two-sided, and a *p-value* < 0.05 was considered statistically significant. Variables were summarized as mean ± SD or median (minimum–maximum), according to the normality of data. The obtained TNF-α data was then tested for correlation with anthropometric data. Parameters that were proven to be statistically correlated were then tested with linear regression to determine the parameters that had the most influence on TNF-α.

## RESULTS

In this study, we collected twenty women diagnosed with PCOS and ten healthy subjects as a control group. TNF-α expression from monocyte-derived macrophages with CD68+ was also examined using BD FACS Canto II Flow Cytometry system (Figure 1). TNF-α and other anthropometric variables showed significant differences between PCOS group and the control group, except for age, body weight, waist-to-hip ratio, and Muscle Mass of leg (MML) (Table 1).

The Spearman test revealed statistical correlations between TNF-α expression to BMI, waist circumference, waist-to-height ratio, visceral fat level, and muscle mass of arm (MMA) (Table 2). The five correlations gave *p-values* under 0.05 with r 0.431, 0.459, 0.451, 0.431 and -0,271 respectively. From the correlation test, the statistic continued with multivariate linear regression to evaluate which factor(s) influence the change of TNF-α expression.

Multivariate linear regression analysis was carried out using the backward method. In this test, TNF-α acted as the dependent variable. In contrast, the independent

TABLE 2
**Correlation analysis summary of TNF-α expression as a dependent variable with anthropometrics data**

| TNF-α Expression to | r | *p* value |
|---|---|---|
| Age | 0.101 | 0.952 |
| Body weight | 0.368 | 0.064 |
| Body height | 0.001 | 0.981 |
| BMI | 0.431 | 0.019* |
| Waist circumference | 0.459 | 0.012* |
| Hip circumference | 0.311 | 0.111 |
| Waist-to-hip ratio | 0.363 | 0.631 |
| Waist-to-height ratio | 0.451 | 0.010* |
| Whole body fat | 0.219 | 0.262 |
| Resting metabolism | 0.073 | 0.337 |
| Visceral fat | 0.431 | 0.021* |
| Whole body subcutaneous fat (WBSF) | 0.350 | 0.073 |
| Subcutaneous fat of Trunk (SCFT) | 0.297 | 0.119 |
| Subcutaneous fat of Arm (SCFA) | 0.222 | 0.274 |
| Subcutaneous fat of Leg (SCFL) | 0.271 | 0.155 |
| Whole body muscle mass (WMM) | -0.110 | 0.560 |
| Muscle mass of Trunk (MMT) | -0.238 | 0.222 |
| Muscle mass of Arm (MMA) | -0.271 | 0.043* |
| Muscle mass of Leg (MML) | 0.069 | 0.721 |

*$p<0.05$ significant correlation Spearman test

variables were 11 factors that yielded p values under 0.25 in the Spearman test (Table 2), including body weight, BMI, waist and hip circumference, waist-to-height ratio, visceral fat level, whole body subcutaneous fat, Subcutaneous Fat of Trunk (SCFT), Subcutaneous Fat of Leg (SCFL), Muscle Mass of Trunk (MMT), and Muscle Mass of Arm (MMA). The regression test showed two variables significantly associated with TNF-α: waist circumference and MMA (Table 3). Thus, the linear regression equation for this model to predict TNF-α expression was -96.971 + 0.601*waist circumference + 2.665*MMA with *p value* 0.02. This equation can describe macrophage's TNF-α expression in 16.4%.

## DISCUSSION

TNF-α is a cytokine that holds a significant role in inflammation and acts as a pro-inflammatory messenger.[15] TNF-α, dominantly produced by monocytes and macrophages, regulates the transcription of other proteins, such as other cytokines, growth factors, and cell adhesion molecules.[16] Although its famous role as an inflammatory cytokine, TNF-α was not significantly higher in circulating serum of women with PCOS when compared to those of healthy women, conflicting with their low-grade chronic inflammation.[14]

This research sought to assess the expression of TNF-α in cellular macrophages among women with PCOS compared to healthy ones. Statistical tests revealed that TNF-α expression of monocyte-derived macrophage was higher in PCOS women. This result proved that at cellular levels, TNF-α as an inflammatory cytokine was produced higher by the immune cells, in this case, macrophage cells. This finding might explain chronic low-grade inflammatory conditions in women suffering from PCOS that were unable to be detected in circulating serum. A past study stated that the different levels of TNF-α expression might also be caused by a polymorphism in the gene promoter. The presence of GGCCT haplotype in the promoter region changed the susceptibility of the macrophages and monocytes that produce more inflammatory cytokines than anti-inflammatory mediators. This GGCCT haplotype was found to have a higher frequency in PCOS women,

TABLE 3
**A multiple linear regression analysis utilizing the backward method was conducted to examine TNF-α expression as the dependent variable, with independent variables including weight, BMI, waist circumference, hip circumference, waist-to-height ratio, visceral fat, total body subcutaneous fat, SCFT, SCFL, MMT, and MMA.**

| Model | Unstandardized coefficients | | Standardized coefficients | t | *p* value |
|---|---|---|---|---|---|
| | B | Standard error | Beta | | |
| Weight | -0.311 | 0.267 | -0.701 | -1.133 | 0.274 |
| BMI | 0.501 | 0.373 | 0.412 | 1.356 | 0.182 |
| Waist circumference | 0.608 | 0.231 | 1.022 | 2.701 | 0.010* |
| Hip circumference | 0.243 | 0.519 | 0.381 | 0.472 | 0.647 |
| Waist-to-height ratio | -66.751 | 705.172 | -0.669 | -0.111 | 0.932 |
| Visceral fat | 0.393 | 1.952 | 0.253 | 0.203 | 0.861 |
| Whole-body subcutaneous fat | 0.663 | 1.551 | 0.537 | 0.421 | 0.672 |
| Subcutaneous fat of Trunk (SCFT) | -0.267 | 4.631 | -0.239 | -0.061 | 0.951 |
| Subcutaneous fat of Arm (SCFA) | -0.419 | 0.828 | -0.461 | -0.509 | 0.623 |
| Muscle mass of Trunk (MMT) | -1.701 | 3.710 | -0.459 | -0.462 | 0.649 |
| Muscle mass of Arm (MMA) | 2.672 | 1.149 | 0.882 | 2.331 | 0.277* |

contributing to inflammatory conditions.[14]

TNF-α cytokine produced by immune cells suppresses the expression of SHBG (Sex Hormone Binding Globulin) protein, thus raising the level of free androgen in the circulating system.[11,13] This hyperandrogenism might worsen clinical and fertility issues in PCOS women. TNF-α is also associated with insulin resistance among PCOS, one suspected culprit in PCOS pathophysiology. Monitoring the levels of TNF-α could help predict the risk of inflammatory condition in PCOS.[10]

The rise of macrophage TNF-α expression is subject to which factors affect this condition in PCOS women. The linear regression analysis performed in this study indicated that two variables are significantly correlated with the expression of TNF-α: waist circumference (WC) and muscle mass of arm (MMA). In concordance with this result, Pedersen (2019) also stated that higher WC is associated with low-grade inflammation.[17] Training and physical activity are known to reduce body fat and WC.[17,18] This reduction in WC was then found to have a positive correlation with decreasing TNF-α levels.[17] Another previous research also stated that fatty acid levels correlate positively with the level of TNF-α circulating in the blood system.[19]

MMA was negatively correlated with TNF-α level, meaning that the level of MMA percentage counteracts TNF-α. Decreasing the percentage of MMA was usually followed by increasing the fat level.[18] Another past study might explain the association between TNF-α and the percentage of muscle mass of the arm (MMA). This research indicated that macrophages are more likely to exhibit pro-inflammatory behavior and less anti-inflammatory behavior in individuals with excess weight and body fat.[11] Fatty acid that was released in lipolysis interact with inflammation by altered methylation level of certain cytokine genes. This article also stated that macrophages from obesity patients still respond in a pro-inflammatory way even after being taken out from an obesity environment.[11]

Macrophages, the most abundant immune cells, are essential in preventing infections and maintaining tissue homeostasis.[20,21] In healthy women, the number of macrophages is balanced between pro- and anti-inflammatory cells to prevent inflammatory conditions. Meanwhile, the number of pro-inflammatory macrophages increases and releases more inflammatory cytokines in PCOS women, thus inflicting low-grade chronic inflammatory conditions.[22] The secretion of TNF-α by macrophages also influences the insulin signaling pathway, leading to the development of insulin resistance. The reciprocal and causal relationship between PCOS and low-grade inflammation makes determining the exact pathophysiology challenging.[22,23]

This study did not establish a correlation between TNF-α and other significant anthropometric variables;

however, these findings represent progress toward personalized medicine and the creation of a treatment model tailored to individual patients. The results regarding TNF-α expression may indicate additional approaches for managing and monitoring the inflammatory aspects associated with polycystic ovary syndrome. This research is also constrained by the criteria used for sample grouping. Further study should be subjected to BMI grouping, considering fat and obesity might vary the inflammatory condition. Moreover, grouping control and PCOS women based on their BMI categories might yield different results, considering that PCOS is a metabolic disorder.

## CONCLUSION

This study revealed that TNF-α expression in monocyte-derived macrophage was statistically associated with waist circumference and muscle mass of arm with regression equation as follows: -96.971 + 0.601*waist circumference + 2.665*MMA.

## REFERENCES


1. Febri RR, Wiweko B, Hanifah N, Sholihah AM, Iffanolida PA, Mutia K, *et al*. BAX/BCL-2 expression in granulosa cells was not altered in patients with polycystic ovary syndrome. In: J Phys: Conf Ser. Institute of Physics Publishing; 2018.
2. Wiweko B, Beelonie A, Asmarinah, Purwito N, Bowolaksono A, Hanifah N, *et al*. Correlation between anti-Müllerian hormone serum level and Bax/Bcl-2 mRNA expression ratio from granulosa cells in patients with PCOS. In: J Phys: Conf Ser. Institute of Physics Publishing; 2018.
3. Escobar-Morreale HF, Luque-Ramírez M, González F. Circulating inflammatory markers in polycystic ovary syndrome: A systematic review and metaanalysis. Fertil Steril. 2011 Mar 1;95(3).
4. Spritzer PM, Lecke SB, Satler F, Morsch DM. Adipose tissue dysfunction, adipokines, and low-grade chronic inflammation in polycystic ovary syndrome. Reproduction. 2015 May 1;149(5):219–27.
5. Popovic M, Sartorius G, Christ-Crain M. Chronic low-grade inflammation in polycystic ovary syndrome: is there a (patho)-physiological role for interleukin-1? Semin Immunopathol. 2019 Jul 1;41(4):447–59.
6. Rudnicka E, Suchta K, Grymowicz M, Calik□ksepka A, Smolarczyk K, Duszewska AM, *et al*. Chronic low grade inflammation in pathogenesis of pcos. Int J Mol Sci. 2021 Apr 1;22(7):112.
7. Vasyukova E, Zaikova E, Kalinina O, Gorelova I, Pyanova I, Bogatyreva E, *et al*. Inflammatory and Anti-Inflammatory Parameters in PCOS Patients Depending on Body Mass Index: A Case-Control Study. Biomedicines. 2023 Oct 1;11(10).
8. Durmus U, Duran C, Ecirli S. Visceral adiposity index levels in overweight and/or obese, and non-obese patients with polycystic ovary syndrome and its relationship with metabolic and inflammatory parameters. J Endocrinol Invest. 2017 May 1;40(5):487–97.
9. Perovic Blagojevic IM, Vekic JZ, MacUt DP, Ignjatovic SD, Miljkovic-Trailovic MM, Zeljkovic AR, *et al*. Overweight and obesity in polycystic ovary syndrome: Association with inflammation, oxidative stress and dyslipidaemia. Br J Nutr. 2022 Aug 28;128(4):604–12.
10. Zhai Y, Pang Y. Systemic and ovarian inflammation in women with polycystic ovary syndrome. J Reprod Immunol. 2022 Jun 1;151.
11. Boersema GSA, Utomo L, Bayon Y, Kops N, van der Harst E, Lange JF, *et al*. Monocyte subsets in blood correlate with obesity related response of macrophages to biomaterials in vitro. Biomaterials. 2016 Dec 1;109:32–9.
12. González F, Considine R V., Abdelhadi OA, Acton AJ. Lipid-induced mononuclear cell cytokine secretion in the development of metabolic aberration and androgen excess in polycystic ovary syndrome. Hum Reprod. 2020 May 1;35(5):1168–77.
13. Lima PDA, Niv*et AL*, Wang Q, Chen YA, Leader A, Cheung A, *et al*. Polycystic ovary syndrome: Possible involvement of androgen-induced, chemerin-mediated ovarian recruitment of monocytes/macrophages. Biol Reprod. 2018 Oct 1;99(4):838–52.
14. Bhatnager R, Jalthuria J, Sehrawat R, Nanda S, Dang AS. Evaluating the association of TNF α promoter haplotype with its serum levels and the risk of PCOS: A case control study. Cytokine. 2019 Feb 1;114:86–91.
15. Jang DI, Lee AH, Shin HY, Song HR, Park JH, Kang TB, *et al*. The role of tumor necrosis factor alpha (Tnf-α) in autoimmune disease and current TNF-α inhibitors in therapeutics. Int J Mol Sci. 2021 Mar 1;22(5):1–16.
16. Liu C, Chu D, Kalantar-Zadeh K, George J, Young HA, Liu G. Cytokines: From Clinical Significance to Quantification. Adv Sci. 2021 Aug 1;8(15).
17. Pedersen LR, Olsen RH, Anholm C, Astrup A, Eugen-Olsen J, Fenger M, *et al*. Effects of 1 year of exercise training versus combined exercise training and weight loss on body composition, low-grade inflammation and lipids in overweight patients with coronary artery disease: A randomized trial. Cardiovasc Diabetol. 2019 Oct 1;18(1).
18. Karam I, Yang YJ, Li JY. Hyperlipidemia Background and Progress. SM Atheroscler J [Internet]. 2017;1(1). Available from: https://www.researchgate.net/publication/319652957
19. Hussey B, Steel RP, Gyimah B, Reynolds JC, Taylor IM, Lindley MR, *et al*. DNA methylation of tumour necrosis factor (TNF) alpha gene is associated with specific blood fatty acid levels in a gender-specific manner. Mol Genet Genomic Med. 2021 Dec 1;9(12).
20. Zhang D, Yu Y, Duan T, Zhou Q. The role of macrophages in reproductive-related diseases. Heliyon. 2022 Nov 1;8(11).
21. Liu L, Stokes J V., Tan W, Pruett SB. An optimized flow cytometry panel for classifying macrophage polarization. J Immunol Methods. 2022 Dec 1;511:1–8.
22. Feng Y, Tang Z, Zhang W. The role of macrophages in polycystic ovarian syndrome and its typical pathological features: A narrative review. Biomed Pharmacother. 2023 Nov 1;167.
23. Aboeldalyl S, James C, Seyam E, Ibrahim EM, Shawki HED, Amer S. The role of chronic inflammation in polycystic ovarian syndrome––a systematic review and meta-analysis. Int J Mol Sci. 2021 Mar 1;22(5):1–31.