Medica Hospitalia
Journal of Clinical Medicine
Med Hosp 2023; vol 10 (2) : 230–234

OPEN ACCESS

Original Article

Relationship between Serum Albumin Levels and Pulmonary Edema in Glomerulonephritis Patients

Nabilla Fikria Alviani[1], Dwi Lestari Partingrum[2], Lydia Purna Widyastuti Setjadiningrat Kuntjoro[3], Yurida Binta Meutia[3]

[1]Faculty of Medicine, Diponegoro University, Semarang, Indonesia
[2]Departement of Internal Medicine, Faculty of Medicine, Diponegoro University, Semarang, Indonesia
[3]Departement of Radiology, Faculty of Medicine, Diponegoro University, Semarang, Indonesia

p-ISSN: 2301-4369 e-ISSN: 2685-7898
https://doi.org/10.36408/mhjcm.v10i2.892

Accepted: December 29th, 2023
Approved: July 12th, 2023

Author Affiliation:
Faculty of Medicine, Diponegoro University, Semarang, Indonesia

Author Correspondence:
Nabilla Fikria Alviani
Prof. H. Soedarto Street, S.H Tembalang, Semarang, Central Java 50275, Indonesia

E-mail:
nabillafikriaalviani@gmail.com

Publisher's Note:
dr. Kariadi Hospital stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Copyright:
© 2023 by the author(s).
Licensee dr. Kariadi Hospital, Semarang, Indonesia. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution-ShareAlike (CC BY-SA) license (https://creativecommons.org/licenses/by-sa/4.0/).

Abstract

Background : Glomerulonephritis is an inflammatory disease of the glomerulus that causes changes in permeability, changes in kidney's structure, and function of the glomerulus. Hypoalbuminemia in glomerulonephritis can decrease oncotic pressure resulting in extravasation of fluid into the interstitium. In severe hypoalbuminemia, extravasation of fluid can result in pulmonary edema. The subjective of this study was to analyze the correlation between serum albumin and the incidence of pulmonary edema by chest x-ray in patients with glomerulonephritis.
Methods : The samples of this study were collected by purposive sampling using secondary data from the medical records of Dr. Kariadi Hospital in Semarang with a total of 46 subjects from January 2016–January 2021. The serum albumin was categorized as normal if serum albumin was >3,5 g/dL, mild hypoalbuminemia if serum albumin was 2.5–3.5 g/dL and severe hypoalbuminemia if serum albumin was <2.5 g/dL.
Results : Mann Whitney test showed a significant relationship between between serum albumin and the incidence of pulmonary edema by chest x-ray in patients with glomerulonephritis (p = 0.016). A higher mean rank was found in patients with pulmonary edema compared to patients without pulmonary edema.
Conclusion : There is a significant relationship between serum albumin and the incidence of pulmonary edema by chest x-ray in patients with glomerulonephritis. Patients with lower serum albumin have a greater tendency to develop pulmonary edema than patients with higher serum albumin.

Keywords : Chest X-Ray; Glomerulonephritis; Serum Albumin; pulmonary edema; Serum albumin

INTRODUCTION

Glomerulonephritis is an inflammatory disease of the glomerulus that causes changes in permeability, changes in kidney's structure, and function of the glomerulus. Kidneys have a vital function to regulate the volume and regulate chemical composition of blood by selectively excreting metabolic wastes and water. Therefore, if there is an abnormality, it can cause abnormalities in the volume and composition of blood and body fluids.

Classification of glomerulonephritis based on its etiology, divided into primary glomerulonephritis and secondary glomerulonephritis. Based on the histopathological lesion, glomerulonephritis is divided into non-proliferative and proliferative glomerulonephritis. Glomerulonephritis which included in the non-proliferative glomerulonephritis are minimal lesion glomerulonephritis, focal segmental glomerulosclerosis, and membranous glomerulonephritis, Which are often found with clinical manifestations of nephrotic syndrome. Meanwhile, proliferative glomerulonephritis includes proliferative membranous glomerulonephritis, crescentic glomerulonephritis, and mesango-proliferative glomerulonephritis.

Data from the Indonesian Nephrology Association (Pernefri) shows that glomerulonephritis is the cause of end-stage kidney disease undergoing hemodialysis with an incidence of 39% in 2000. Pulmonary edema that causes the sudden accumulation of fluid in the interstitial tissue and alveoli of the lungs. It is due to its high intravascular pressure or the increased permeability of its capillary membranes (non-cardiogenic pulmonary edema). That causes rapid extravasation of the liquid. Then a gradual change in respiration in the alveoli causes hypoxia.[5]

The incidence rate of primary glomerulonephritis worldwide ranges between 0.2–2.5/100.000 people/year. Glomerulonephritis IgA nephropathy is the most common type obtained by adults, as much as 2.5/100.000 people/year. For children, glomerulonephritis minimal type change disease has the highest incidence, 2/100,000 people/year. The primary and secondary glomerulonephritis incidence rate in the U.S is 57 and 134/100,000 people/year.[6]

Data on the epidemiology of glomerulonephritis in Indonesia is still very little. Several hypertension and kidney centers aim to report their study and becomes a report of every hypertension and kidney center. The study by Himawan S. *et al*. in Jakarta reported based on 729 renal biopsies of nephrotic syndrome patients, 276 cases (48.9%) were glomerulonephritis of minimal change type. Proliferative mesangial type glomerulonephritis and focal segmental glomerulosclerosis reported 81 (14.4%) and 62 cases (11%). From the data obtained, 36.5% showed manifestations of clinical nephrotic syndrome. 19.2% acute nephrotic syndrome, 3.9% rapid progressive glomerulonephritis, 15% with hematuria, 19.3% proteinuria, and 6.8% hypertension.[7]

This study aims to examine more deeply and find out about correlation between serum albumin and the incidence of pulmonary edema by chest x-ray in patients with glomerulonephritis at Dr. Kariadi Hospital Semarang

METHODS

The study was conducted after obtaining ethical approval and ethical clearance in the form of ethical clearance number 125/EC/KEPK/FK-UNDIP/IV/2021 from the Medical Health and Research Ethics Commission (KEPK) Faculty of Medicine, Diponegoro University.

This study was conducted with an analytic type of observational research. The design used was cross-sectional. The research location was in the Medical Record Installation section of RSUP Dr. Kariadi Semarang, during June 2021–July 2021. Inclusion criteria include: Glomerulonephritis patient age ≥18 years. They were female and men with proteinuria and hematuria. They performed a chest x-ray and serum albumin test. All patients were recieved the same therapy, with the same drug doses, and duration of therapy during therapy on the ward. The exclusion criteria were secondary glomerulonephritis patients due to multiple myeloma, Hodkin's lymphoma, other malignant diseases. Also, glomerulonephritis patients who had diabetes mellitus and a chronic renal failure concomitant disease.

The consecutive sampling method was to take samples where the data was available, and the criteria met were then inputted into the research until the subject needed was appropriate. According to the large formula of samples in the cross-sectional design, 46 samples as a minimum sample size. The serum albumin was categorized as normal if serum albumin was >3.5 g/dL, mild hypoalbuminemia if serum albumin was 2.5–3.5 g/dL and severe hypoalbuminemia if serum albumin was <2.5 g/dL.

The data that had been collected was analyzed using electronic statistical applications. Hypothesis testing in this study used the univariate test for descriptive data of each variable and the bivariate test in the form of the Chi-Square correlation test and Mann Whitney test, which showed a significant relationship if p-value <0.05.

RESULTS

The samples studied were glomerulonephritis patients who were receiving treatment at RSUP Dr. Kariadi Semarang. The number of male patients was 33, and the number of female patients was 13. References from the

study by Akirov *et al*.[8] divided hypoalbuminemia into mild hypoalbuminemia (2.5–3.5 g/dL) and severe hypoalbuminemia (<2.5 g/dL). The sampling used was consecutive. It means that this study included all medical record with selection criteria until the required sample size reached the minimum sample size for this study has been met.

TABLE 1
Characteristic Distribution of Research Subjects

Variables	F	%
Age		
18–33	30	65.2
34–49	8	17.4
50–65	7	15.2
≥66	1	2.1
Gender		
Male	33	71.7
Female	13	28.3
Glomerulonephritis		
Acute	26	56.5
Chronic	20	43.4
Serum albumin		
Hypoalbuminemia	42	91.3
Mild (2.5–3.5 g/dL)	9	21.4
Severe (<2.5 g/dL)	33	78.6
Normal	4	8.7
Pulmonary Edema		
Yes	35	76.1
No	11	23.9

According to the Table 1, the subjects studied are most in the range of 18–33 years (65.2%), where the youngest is 18 years, and the oldest is 68 years. The most studied subjects were male, namely 33 patients (71.7%), while female were 13 patients (28.3%).

According to the Table 1, 42 patients experienced hypoalbuminemia (91.3%), nine patients had mild (21.4%), and 33 patients had severe (78.6%), and four patients had normal albumin levels (8.7%) and there were 35 (76,1%) glomerulonephritis with pulmonary edema.

According to the Table 2, Mann-Whitney test showed a significant relationship beetwen incidence of pulmonary edema and serum albumin in glomerulonephritis patients, with p=0.016 ($p < 0.05$). It can be concluded that there is a significant relationship between pulmonary edema and serum albumin in glomerulonephritis patients in RSUP Dr. Kariadi Semarang in January 2016–January 2021.

From the mean rank above, it was also found that pulmonary edema (25.61) had a higher mean than non-pulmonary edema (16.77). Since the codes used for the statistical test were: normal (1), mild hypoalbuminemia (2) and severe hypoalbuminemia (3), higher rank indicate lower serum albumin. Thus, glomerulonephritis patients with lower serum albumin tend to have a higher tendency of pulmonary edema compared to patients with higher serum albumin.

DISCUSSIONS

According to medical records data studied in January 2016–January 2021, there were 46 glomerulonephritis patients. Most research subjects were from the 18–33 year-old group of 30 patients (65.2%). At the same time, the most gender percentage was male, 71.3% (33 patients).

Furthermore, the results also found that the incidence of pulmonary edema in glomerulonephritis patients was 35 patients (76.1%). It also obtained 42 patients with hypoalbuminemia (91.3%). Nine patients had mild hypoalbuminemia (21.4%), and 33 patients had

TABLE 2
Result of Correlation Test Between Serum Albumin and Pulmonary Edema

Variables	Pulmonary Edema				p value
	Yes		No		
	n	%	n	%	
Normoalbumin	1	25.0	3	75.0	0.016*[M]
Mild Hypoalbuminemia	6	66.7	3	33.3	
Severe Hypoalbuminemia	28	84.8	5	15.2	
Total	35	76.1	11	23.9	

*Significant [M]Mann-Whitney; Mean rank pulmonary edema 25.61; Non pulmonary edema 16.77

severe hypoalbuminemia (78.6%) and 4 patients had normal albumin levels (8.7%).

Based on the Mann-Whitney test between serum albumin and the incidence of pulmonary edema, it was found that the correlation level between these variables was significant ($p = 0.016$: $p < 0.05$). It is in line with that done in 2005 by Sudung O. Pardede *et al*.[9] In acute glomerulonephritis, patients found 87% of patients with clinical manifestations of edema and 14% of patients with pulmonary edema radiology. It follows Starling's laws, where several things, namely vascular permeability, influence the transfer of fluid from intravascular to interstitial space. Some pressures, such as intravascular hydrostatic, interstitial space hydrostatic, intravascular oncotic, and interstitial space oncotic.[10] Thus, hypoalbuminemia is the cause of pulmonary edema. This condition lowers the oncotic pressure in the blood so that intravascular fluid moves into the interstitial.[5] Thus, the condition of hypoalbuminemia is a cause of pulmonary edema because this condition lowers the oncotic pressure in the blood so that intravascular fluid moves into the interstitial.

Research conducted by Hassan *et al*. in 2005[11] also revealed that Pulmonary edema is associated with the accumulation of excess extracellular fluid after impaired excretion of fluids and solutes. Under normal conditions there is an exchange of fluids, colloids and solutes from the blood vessels into the interstitial space. Pulmonary edema occurs when there is a shift of fluid from the blood into the interstitial spaces or into the alveoli that exceeds the amount of fluid returned to the blood vessels and fluid flow to the lymphatic system.[12]

In this study, it was also found that glomerulonephritis patients with higher serum albumin had a lower tendency to develop pulmonary edema than glomerulonephritis patients with lower serum albumin. This is in accordance with the research of Feng Li *et al*. in 2015 who conducted a study with 220 hypoalbuminemia patients and this study stated that serum albumin was associated with the severity of disease and prognosis in hypoalbuminemia patients with pulmonary complications. In this study, it was found that the mortality rate increased by 89% with a decrease in serum albumin of 1 g/dL.[13] In a study conducted by Akirov *et al*. also stated that the lower the patient's serum albumin, the longer the length of stay in the hospital.[8] Likewise with the study by Bassoli *et al*. which found a negative correlation between serum albumin and disease severity with $p<0.0001$. This study also stated that in inflammatory conditions transcapillary leakage can occur which is stimulated by an increase in interleukin-2, interferon and interleukin-6. Damage to the vascular endothelium results in leakage of albumin into the interstitial space of the lung.[14]

However, our study's limitation is that the study was conducted with secondary data using medical records of patients with glomerulonephritis.. This study also only took chest X-ray samples and serum albumin at one time, namely when the first examination of the patient was performed. The cross-sectional method limited our study to analyze the correlation between serum albumin and the incidence of pulmonary edema after therapy. In this study also did not use other laboratory data such as protein, ureum, and serum creatinine.

CONCLUSION

There is a strong relationship between serum albumin and pulmonary edema in glomerulonephritis patients and in patients with severe hypoalbuminemia (serum albumin < 2.5 g/dL) have a greater tendency to develop pulmonary edema.

In future studies, researchers suggest using more variables to get better and more reliable results. Future research is necessary to do further research by considering the involvement of other factors that can affect the condition of pulmonary edema in glomerulonephritis such as hypertension, ureum, and serum creatinine.

ACKNOWLEDGEMENTS

We express our most thoughtful gratitude to the staffs at Medical Records Installations in Dr. Kariadi Hospital Semarang for their assistance and persmission to collect data.

REFERENCES

1. Satoskar AA, Parikh SV, Nadasdy T. Epidemiology, pathogenesis, treatment and outcomes of infection-associated glomerulonephritis. Nat Rev Nephrol [Internet]. 2020 [cited 2021 Jan 31] ;16(1):32–50. Available from: http://dx.doi.org/10.1038/s41581-019-0178-8
2. Perinandika T, Rachmadi D, Dwiyatnaningrum F. A Study of Hypoalbuminemia and Pleural Effusionin Pediatric Nephrotic Syndrome. Althea Med J. 2017;4(2):188–91.
3. Downie ML, Gallibois C, Parekh RS, Noone DG. Nephrotic syndrome in infants and children: Pathophysiology and management. Paediatr Int Child Health [Internet]. 2017 [cited 2021 Feb 3];37(4):248–58. Available from: http://doi.org/10.1080/20469047.2017.1374003
4. PERNEFRI. 11th Report of Indonesian Renal Registry 2018. Irr [Internet]. 2018 [cited 2021 Jan 31];1–46. Available from: https://www.indonesianrenalregistry.org/data/IRR2018.pdf
5. Gupta S, Pepper RJ, Ashman N, Walsh SB. Nephrotic syndrome: Oedema formation and its treatment with diuretics. *Front Physiol*. 2019;10(JAN):1–10.
6. Hizon MAP, LIM RS, Tan ZK, Yeo SC, Villanueva ART, Liew A. Sun-014 Epidemiology of Glomerulonephritis in Southeast Asia: the Gn-Special (Glomerulonephritis Singapore-Philippines Epidemiology Cohorts in Adults) Study. Kidney Int Reports [Internet]. 2019 [cited 2021 Mar 24] ;4(7):S158.

Available from: https://doi.org/10.1016/j.ekir.2019.05.408
7. Yusria R. Diagnosis dan Manajemen Glomerulonefritis Kronik. J Kedokt Muhammadiyah Surakarta. 2016;25972.
8. Akirov A, Masri-Iraqi H, Atamna A, Shimon I. Low Albumin Levels Are Associated with Mortality Risk in Hospitalized Patients. Am J Med [Internet]. 2017;130(12):1465.e11–1465.e19. Available from: https://doi.org/10.1016/j.amjmed.2017.07.020
9. Pardede SO, Trihono PP, Tambunan T. Gambaran Klinis Glomerulonefritis Akut pada Anak di Departemen Ilmu Kesehatan Anak Rumah Sakit Cipto Mangunkusumo, Jakarta. Sari Pediatr. 2016;6(4):144.
10. Woodcock TE. Plasma volume, tissue oedema, and the steady-state Starling principle. BJA Educ [Internet]. 2017 [cited 2021 Jan 31];17(2):74–8. Available from: http://dx.doi.org/10.1093/bjaed/mkw035
11. Salah I, Hassan A, Ghalib MB. of Kidney Diseases and Transplantation Editorial Lung Disease in Relation to Kidney Diseases Pulmonary edema in the setting of renal. 2005;16(3):282–7.
12 Polito C, Martin GS. Albumin: Physiologic and clinical effects on lung function. Minerva Anestesiol. 2013;79(10):1180–6.
13. Li F, Yuan MZ, Wang L, Wang XF, Liu GW. Characteristics and prognosis of pulmonary infection in patients with neurologic disease and hypoproteinemia. Expert Rev Anti Infect Ther. 2015;13(4):521–6.
14. Bassoli C, Oreni L, Ballone E, Foschi A, Perotti A, Mainini A, *et al*. Role of serum albumin and proteinuria in patients with SARS-CoV-2 pneumonia. Int J Clin Pract. 2021;75(4):15.