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Research Article

Comparative Analysis Of Hypoalbuminemia And Anemia Across Varying Proteinuria Levels In Nephrotic Syndrome Patients Versus Healthy Controls

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Abstract:
Background: Nephrotic syndrome (NS) is a renal disorder characterized by the loss protein urine, hypoalbuminemia, and edema. Hypoalbuminemia and low hemoglobin levels are the common complications of NS which are associated with the adverse clinical outcomes as well. Proteinuria is the presence of excessive protein in urine and a clinical manifestation indicative of various underlying health conditions. This research article aims to provide a comprehensive outcome of proteinuria- its causes, diagnostic methods and the management strategies. Through an extensive knowledge on review of current literature and clinical studies, this study explains how low albumin levels and hemoglobin levels are correlated. These are the diagnostic and the management approaches to nephrotic syndrome Protein urine is one of the crucial parameter for the effective diagnosis and the management of NS and associated clinical conditions.
Materials and method: The study was approved by the institutional ethics committee. This study was conducted to know the status of hypoalbuminemia, proteinuria, and anemic status in patients with NS at diagnosis, after follow-up and healthy control. Serum albumin levels and the urine proteins were measured in VITROS 5600 by using the biuret method and hemoglobin concentrations were assessed in D10. We evaluated and compared the levels of serum albumin, hemoglobin concentration, and urinary protein concentration in patients with nephrotic syndrome at initial diagnosis and after the follow-up of three months and with healthy control with different levels of proteinuria noticed in NS.
Conclusion: This study explains the role of biochemical changes along with periodic medications in managing the disease. Our current study highlighted the importance of proteinuria, hypoalbuminemia, and anemia in NS and disease management. Management of these parameter values could have more importance in taking timely interventions and management aspects.

Keywords: Nephrotic syndrome, Hypoalbuminemia, Anemia, Proteinuria

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Introduction:

Nephrotic syndrome (NS) is a group of heterogeneous, glomerular disorders in which there is an increased permeability in glomerular - leading to a massive proteinuria, edema, and hypoalbuminemia [1]. Hypoalbuminemia can be defined as the levels of serum albumin is below 3.5 gm/dL, which is a current diagnostic feature of NS which in turn results in increased loss of urinary protein and the impaired synthesis of hepatic proteins [2]. Addition to this there is low hemoglobin levels can be seen, which is termed as nephrotic anemia. This is a common complication seen in NS patients which will contribute to an adverse clinical outcome [3]. Even with the advances in the medical technologies and management of NS, challenges in low hemoglobin concentration, hypoalbuminemia and proteinuria remains as a significant challenge. There is a need of further study on the prevalence and the clinical implications in NS. The structural and functional alterations in glomerular filtration rate barrier causes proteinuria, hypoalbuminemia and low hemoglobin concentration in patients with NS, which in turn leads to increased permeability in the kidney cells and causes the loss of proteins in the urine (4).

Lower hemoglobin concentration in NS: lower levels of hemoglobin which is called as anemia, are frequently noted in patients with NS. This anemia can cause the further clinical manifestations and complications in the later stage. The cause for anemia in NS can be multifunctional which can be due to various mechanism, for example due to decreased production in the erythropoietin levels, deficiency of iron, hemodilution due to the fluid retentions and suppression in the bone marrow concentrations [5]. Addition to it, proteinuria can be consisting of loss of transferrin and heptoglobin in the urine which will leads to impaired metabolism of iron and causes hemolysis [6]. There is an association of anemia in NS with the increased mortality and morbidity and with the mortality. This signifies the importance of detection of anemia in early stage and in the management of complications [7].

Materials and Methods:

The Institutional Ethical Committee was obtained for the conducted study. The Yenepoya Ethical Committee-1 approval number was YEC-048/2021. The study was in compliance with the ethical principles in accordance with the Declaration of Helsinki for medical research of human samples. The study was conducted in a medical college hospital laboratory, which is accredited by NABL. This cross sectional study enrolled initial diagnosed NS patients and followed up at Yenepoya Medical College Hospital. Demographic and clinical data, including serum albumin levels, hemoglobin concentrations, proteinuria, renal function, and relevant comorbidities, were collected from medical records. Serum albumin levels and urine proteins were measured using biuret method in VITROS 5600 and hemoglobin concentrations were assessed using Sahli's method. Clinical outcomes, including disease progression, hospitalizations, and mortality, were recorded during follow-up visits.

Statistical Analysis:

Data was coded in MS Excel and all statistical analysis were carried out using IBM SPSS 27 software. Shapiro-Wilk test was used to check the normality of continuous data. The summary of continuous variables was presented using mean and standard deviation. The summary of categorical variables was reported in terms of frequencies, percentage and charts. Pearson correlation coefficient was computed to test the correlation between two continuous variables. A p value <0.05 was considered as significant.

Results:

A total of 38 study samples were taken for the study - 38 NS patients (mean age 31.29 years) at initial diagnosis and three months of follow up and healthy controls of 38 subjects were included in the study. At diagnosis, the prevalence of hypoalbuminemia (serum albumin <3.5 g/dL) was 100%, and low hemoglobin levels (hemoglobin <10 g/dL) were observed in 75% of patients. The mean value of serum albumin and hemoglobin was found to be 2.23mg/dL and 10.0 g/dL. During the follow-up of three months, there was a modest improvement was seen in the serum albumin levels, with 35% of patients achieving normalization. However, the low hemoglobin levels persisted in 70% of patient's despite of the treatment. Hypoalbuminemia and low hemoglobin were associated with the increased risk of disease progression, hospitalizations, and the mortality ($p<0.05$).

Table 1& 2 and Figure 1- shows the frequency and percentage of gender and age distribution during the study. The mean age of the population was 31.29 years. The average distribution of gender as- 61% males and 39%were included in the study who are diagnosed with nephrotic syndrome and the same patient's samples were collected for study after three months of follow up.

Table no. 1: The frequency and percentage of gender distribution of sample collected during the study

Table no. 1 shows the frequency and the percentage of gender distribution				
	Nephrotic syndrome		**Healthy control**	
	Frequency	Percent	Frequency	Percent
Female	15	39.5	15	39.5
Male	23	60.5	23	60.5
Total	38	100.0	38	100.0

Figure 1: The distribution of frequency and percentage of gender during the study

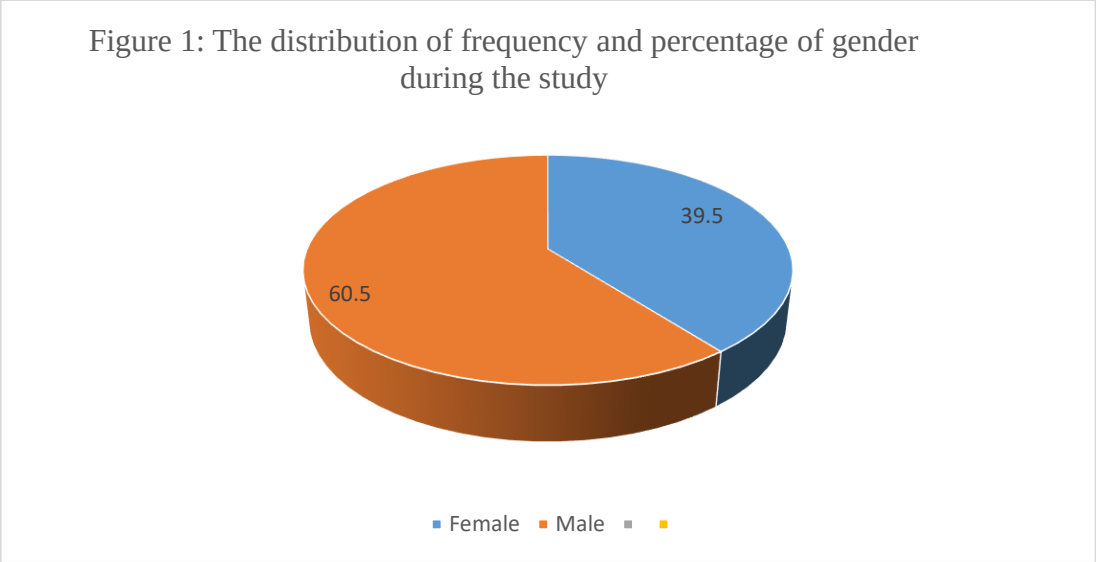


Table 2: The frequency and percentage of distribution of age of the subjects taken for the study

Table 2: The frequency and percentage of distribution of age of the subjects taken for the study (in years)					
Nephrotic syndrome					
	n	Minimum	Maximum	Mean	Std. Deviation
AGE	38	8	68	30.42	16.957
Healthy control					
AGE	38	11	68	31.29	16.096

Table 3 shows the correlation of Hb values of patients with Nephrotic syndrome at diagnosis, after three months of follow up and healthy control. The p value for the Hb levels were shown less than <0.001 which indicates that there is a highly significant correlation between the subjects.

Table 3: Correlation of Hb values –Nephrotic syndrome at diagnosis, after three months of follow up and healthy control

Table 3: Correlation of Hb values –Nephrotic syndrome at diagnosis, after three months of follow up and healthy control				
	Pearson Correlation	p value	95% Confidence Intervals (2-tailed)	
			Lower	Upper
Hb_control - Hb	-0.124	0.458	-0.427	0.204
Hb_control - Hb_followup	-0.068	0.684	-0.380	0.257
Hb_followup - Hb_NS	0.907	<0.001	0.827	0.951

Table no.4 shows the correlation of serum albumin values in patients with Nephrotic syndrome at diagnosis, after three months of follow up and healthy control. The p value for the albumin levels were found to be 0.01 & 0.037 respectively, which indicates that there is a significant correlation between three groups.

Table 4: Correlation of serum albumin values- Nephrotic syndrome at diagnosis, after three months of follow up and healthy control

Table no.4: Correlation of serum albumin values- Nephrotic syndrome at diagnosis, after three months of follow up and healthy control				
	Pearson Correlation	p value	95% Confidence Intervals (2-tailed)	
			Lower	Upper
SR_ALBUMIN_control - SR_ALBUMIN_NS	-0.129	0.440	-0.431	0.199
SR_ALBUMIN_control - SR_Albumin_followup	-0.414	0.010	-0.648	-0.109
SR_Albumin_followup - SR_ALBUMIN_NS	0.340	0.037	0.023	0.595

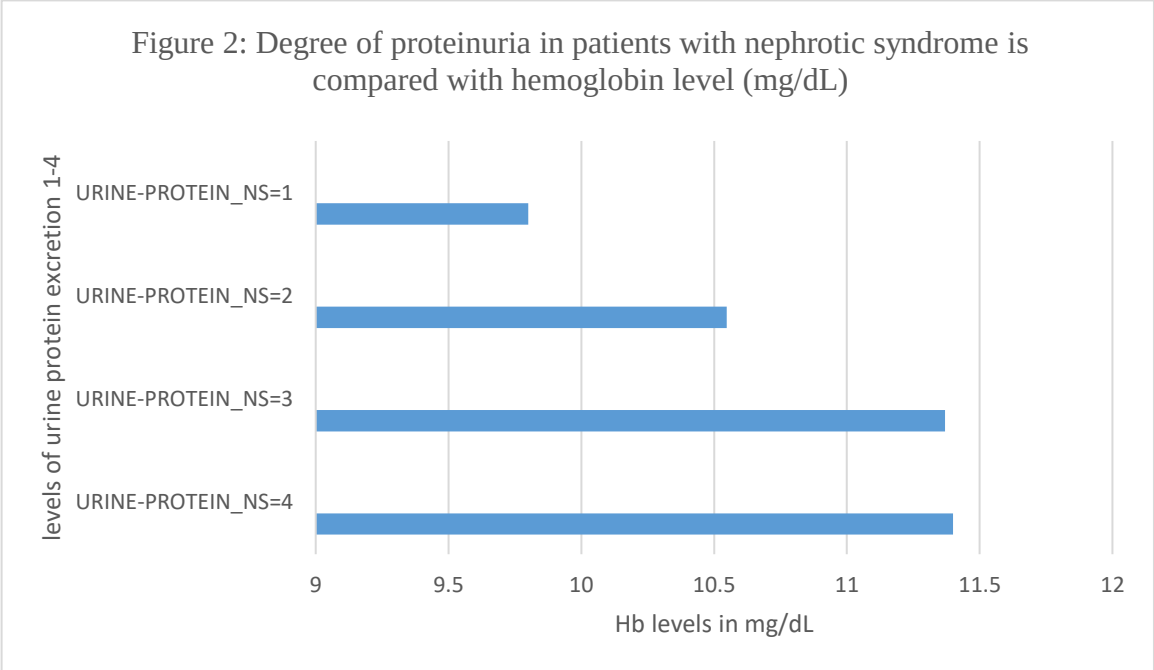
Table 5 shows the correlation of urine protein concentration in patients with Nephrotic syndrome at diagnosis and after three months of follow up. The p value for the urine protein levels were found to be 0.009

which indicates that there is a strong significant correlation between the two groups.

Table 5: Correlation of urine protein- Nephrotic syndrome at diagnosis and after three months of follow up

Table 5: Correlation of urine protein- Nephrotic syndrome at diagnosis and after three months of follow up				
	Pearson Correlation	p value	95% Confidence Intervals (2-tailed)	
			Lower	Upper
URINE_PROTEIN_NS - URINE_PROTEIN_followup	0.418	0.009	0.114	0.651

Figure 2 & 3 explains the degree of proteinuria in patients with nephrotic syndrome is compared with hemoglobin level and serum albumin levels. This explains that the increased in the urinary protein shows that there is decreased in the hemoglobin concentration and the levels of serum albumin.



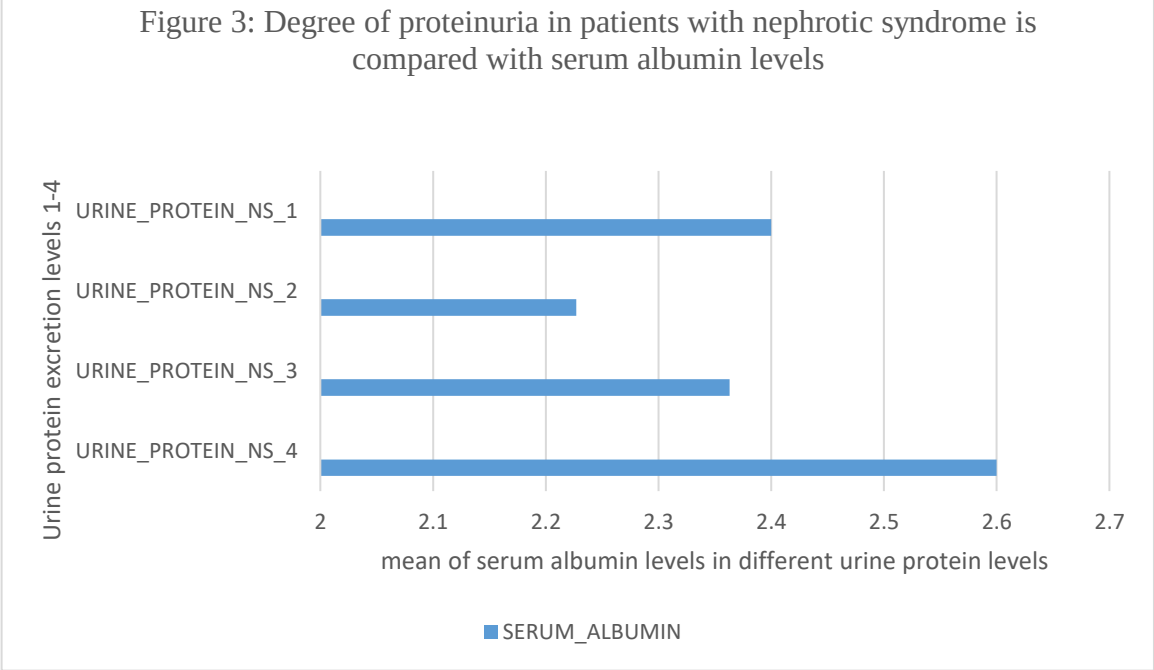


Figure 3: Degree of proteinuria in patients with nephrotic syndrome is compared with serum albumin levels

Table no 6—9 explains the distribution of levels of hemoglobin, serum albumin and protein levels with respect to different levels of urine proteins from levels 2-4.

Table No. 6 shows the descriptive Statistics of Hb. Serum protein and albumin levels in NS patients with urine protein level-2					
	n	Minimum	Maximum	Mean	Std. Deviation
Hb	13	8.9	12.7	10.492	1.2413
SR. PROTEIN	13	5.1	7.1	5.662	.5363
SR.ALBUMIN	13	2.1	2.7	2.246	.1761
URINE PROTEIN = 2					

Table No. 7 shows the descriptive Statistics of Hb. Serum protein and albumin levels in NS patients with urine protein level-3					
	n	Minimum	Maximum	Mean	Std. Deviation
Hb	17	8.4	13.0	11.065	1.2952
SR. PROTEIN	17	5.0	7.3	5.547	.5222
SR.ALBUMIN	17	2.0	2.8	2.335	.2262
URINE PROTEIN = 3					

Table No. 8 shows the descriptive Statistics of Hb. Serum protein and albumin levels in NS patients with urine protein level-3					
	n	Minimum	Maximum	Mean	Std. Deviation
Hb	3	10.3	12.9	11.400	1.3454
SR. PROTEIN	3	5.1	5.9	5.533	.4041
SR.ALBUMIN	3	2.4	2.7	2.600	.1732
URINE PROTEIN = 4					

Table NO. 9 shows the frequency of the respondents with different levels of Urine Protein				
Parameters	Urine protein levels	2	3	4
	Number of Patients	13	17	3
Mean of the different measurements with different levels of Urine Protein				
Hb		10.492	11.065	11.400
SR. PROTEIN		5.662	5.547	5.533

Table no 6-9 shows that the urine level 2 has higher distribution of nephrotic syndrome than level urine protein.

Discussion:

Our findings confirm the high prevalence of hypoalbuminemia and low hemoglobin in NS patients and highlight their significant clinical implications. Lower serum albumin levels reflect in the severity of the disease which in turn associated with the increased morbidity and mortality of renal and cardiovascular disease [8]. Lower concentration of hemoglobin leads to nephrotic anemia, fatigue, dyspnea and in the reduced quality life [9]. Timely management and the interventions strategies targeting the low hemoglobin levels and albumin levels are necessary for improving the patient's outcome in NS.

There are several studies explained the interplay between loss of protein in urine, low hemoglobin level and hypoalbuminemia in patients with NS along with pathophysiological aspects.

Vestergaard SV et al. (2021) studied on comparison of laboratory-recorded nephrotic hypoalbuminemia and proteinuria with the hospital recorded NS. This study explains the correlation between urinary proteins and hypoalbuminemia in NS. This study explained a strong association between the severity of hypoalbuminemia and the degree of proteinuria. This signifies the importance of hypoalbuminemia due to protein loss in urine. This study shows the importance of monitoring the loss of protein in urine as a surrogate biomarker for the disease progression and therapeutic interventions [10].

In a study by Mahajan V et al. (2023) studied the prevalence of anemia in nephrotic syndrome children, with its etiology, and the correlation with severity of the disease duration and response to steroids. explained the prevalence of anemia in patients with NS and the relation of anemia with the proteinuria. This study showed the higher levels of prevalence of anemia in NS patients. Proteinuria is the only independent factor for low levels of hemoglobin. This study does not explain the multifactorial role of anemia in NS, indicates only iron deficiency anemia as a significant marker with the heme levels. This study finding indicates the importance of anemia-early detection and the management in patients with NS to prevent the adverse clinical complications [11].

Hilmanto D et al. (2022) in their systemic review about the systemic complications in NS children along with the disease-associated complications. The study explains the etiology and management of anemia in NS, explained the various mechanism of hematological and other complications. This study signifies the importance of

proteinuria, hypoalbuminemia and the impaired iron metabolism in relation to the pathogenesis of anemia in NS patients. This study also highlights the challenges which are associated in the management of complications associated in patients with NS. This signifies the multifactorial targets required for targeting the causes for anemia and requirement of iron supplement and the erythropoietin stimulating factor [12].

Mähr N et al. (2005) conducted a literature review where they explained the mechanism of low hemoglobin levels in NS. This study gives a complete picture how proteinuria disrupts the metabolism of iron which leads to hemolysis and causing anemia in NS. This study explains that there are lower levels of Hb in NS women when compared to NS men. This study does not explain the management of proteinuria and hypoalbuminemia in anemia in patients with NS [13].

Wang CS et al. (2019) the study explained the effect of anemia in the NS patient's outcome. This study explains the significant of corticosteroids and the association with anemia and adverse effect of complications - morbidity and mortality in NS. The study shows the significance of lower level of hemoglobin levels and in interventions to come up the levels of hemoglobin in NS and to a need to improve the patient outcome [14].

Summary to these studies, explains the role of proteinuria, hypoalbuminemia and low hemoglobin levels in patients with NS are interrelated. Understanding with this mechanism and the clinical implications, there is a need of novel therapeutic targets and to optimize the patient care outcome in NS.

Conclusion:

The present study provides the prevalence and the clinical implications like hypoalbuminemia, lower levels of hemoglobin and excretion protein in urine in NS patients and the healthy control. The study findings state the significance of serial monitoring of serum albumin levels, urinary proteins and hemoglobin concentration could be used as a marker to prevent the serious kidney cells damage in the early stage. in our study. Proteinuria is the common clinical parameter which is associated with the renal and various systemic disorders. This can be used as a systematic approach for the diagnosis and the management of the disease. Understanding with the disease pathophysiology, etiology, diagnosis, and the therapeutic aspects, clinicians can be able to identify and address the proteinuria effectively. This can improve the patient care outcomes and can reduce the burden of further complications. There is a need of further research which elucidates the mechanism in proteinuria and exploring with the novel therapeutic targets which are needed for the advanced clinical aspects and which in turn enhances the quality of patient life. Further more research is required in identifying the novel therapeutic markers and management strategies for NS patients.

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Conflict of Interest:

Authors have no conflicts of interest

Author contributions:

Rahinaz Usman Bedrabettu: Designing, investigation, validation, analyzing the data and writing the paper. Dr Santhosh Pai B H guiding and recruiting the sample and supervision. Dr Anuradha Rao C K- supervision, writing review and editing the paper. Dr Ranajit Das and Dr Harsha in the statistical analysis. Authors names on this submission have contributed sufficiently to the scientific work. This study was performed at Yenepoya Medical College Hospital, Deralakatte.

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Consent for publication:

Consent to submit has been received from all coauthors, as well as from the responsible authorities.

Conflict of interest:

Authors have no conflict of interest for the present study.

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