Section: Pediatrics

Original Research Article

STUDY OF URINARY INDICES IN CASES OF FIRST EPISODE AND RELAPSE OF NEPHROTIC SYNDROME

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Keywords: FENa =Fractionated excretion of sodium, KI= Potassium index, UI = Urinary indices, INS=Idiopathic Nephrotic Syndrome.

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Abstract

Background: With prevalence of 2-7 new cases per 100,000 children, nephrotic syndrome one of the most prevalent renal disease in children. Sodium retention in nephrotic syndrome could be secondary to activation of renin–angiotensin–aldosterone axis or due to intrinsic activation of Na+ K+ ATPase in the cortical collecting duct. (UK+/UK+ + UNa+) is surrogate marker for aldosterone activity and can be useful in differentiating primary sodium retention from secondary sodium retention in children with INS. FENa and KI can be used as marker to detect hyperaldosteronism in nephrotic syndrome. The aim of study is to evaluate urinary indices (UI) in cases of first episode or relapse of childhood nephrotic syndrome and to study their correlation with Blood Urea Nitrogen/Creatinine ratio. **Methods:** cross sectional study done on nephrotic cases admitted in pediatrics department for 1 year fulfilling inclusion criteria. Samples collected, urinary sodium potassium sent. Serum urea creatinine sent. FENa and KI calculated. Statistical significance calculated by chi square test and by t test. Results: there is primary sodium retention in 56% of first episode versus 18% in relapse but was not statistically significant. **Conclusion:** Urinary Indices can be used to identify sodium retention in case of nephrotic syndrome and further classifying them into primary and secondary categories.

INTRODUCTION

Nephrotic syndrome is one of the most prevalent types of renal disease in children. Nephrotic syndrome (NS) is characterized by the triad of proteinuria, hypoalbuminaemia, and edema. Many glomerular disorders in childhood present with nephrotic syndrome, however, the vast majority are Idiopathic Nephrotic Syndrome (INS).

In recent years, the classic hypothesis of sodium retention due to hypovolemia and activation of the renin-angiotensin-aldosterone pathway causing secondary sodium retention has been questioned. In nephrotic syndrome, there is augmenting evidence of increased Na+ K+ ATPase activity, which leads to sodium retention (primary retention) in the cortical collecting duct. Secondary sodium retention occurs when proteinuria is severe enough to produce hypovolemia, which happens in only a small percentage of individuals. In contrast, children with nephrotic syndrome frequently have extensive proteinuria, making them more susceptible to secondary salt retention.[1]

Sodium retention with features of stimulated rennin production, such as increased aldosterone bioactivity, is seen at the beginning of a relapse in a phase of incipient proteinuria. This sodium retention is measured by an index called Potassium Index (KI) which is calculated by urine potassium/urine potassium + urine sodium ($UK^+/UK^+ + UNa^+$), which measures the enhanced Na^+/K^+ exchange. Without symptoms of hypovolemia, edema formation does not involve enhanced vasoactive hormones or subsequent salt retention, but rather points to a basic tubular malfunction. Children who are in the early stages of full-blown nephrosis may have hypovolemic symptoms.[2]

Trans tubular potassium gradient (TTKG), UK+/UNa+, and other indices shows varying relationships with serum aldosterone, and KI. Assuming that Na^+/K^+ exchange occurs in the cortical collecting duct and is promoted by aldosterone in hypovolemic individuals with nephrotic syndrome, KI has been used as a marker for aldosterone activity.[3]

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FENa< 1% and KI < 60% would favour primary sodium retention, whereas FENa< 1% and KI > 60% is linked to secondary sodium retention.

$$FENa=\frac{UNa\ X\ Sr}{\frac{cr}{Ucr}Sr\ Na\ X}$$

$$KI=\frac{UK^{+}}{UNa^{+}+UK^{+}}$$

$$BUN=\frac{Serum\ urea}{2.14}$$

Nephrotic patients with edema may have variable volume status i.e. hypo, hyper or normovolemia. Volume expanded patients may benefit with diuretics while volume-contracted patients need volume expansion, as shown in the study by Iyengar *et al.*[4]

Urinary Indices can be used to identify sodium retention in case of nephrotic syndrome and further classifying them into primary and secondary categories.

Aims and Objectives

To evaluate urinary indices in cases of first episode and relapse of childhood nephrotic syndrome

MATERIALS AND METHODS

The study is a hospital based cross sectional study, done in the department of Pediatrics, Assam Medical college and Hospital, Dibrugarh Assam (tertiary care centre) over a period of one year from 1st June 2021 to 31st May 2022. All patients of nephrotic syndrome fulfilling the inclusion criteria are included in our study.

Inclusion Criteria

Children with 1st episode and relapse of nephrotic syndrome, aged 1–12 years, admitted
in the Pediatrics department of AMCH.

Exclusion Criteria

Children with severe systemic illness (severe pneumonia, spontaneous bacterial peritonitis, meningitis). children with secondary Nephrotic Syndrome (secondary to systemic disease or drugs) and those children receiving diuretics or immunosuppressant in last 2 weeks.

Ethical Clearance

It was taken from Institutional Ethics Committee (H) of Assam Medical College & Hospital, Dibrugarh

Methodology

A total of 50 children with nephrotic syndrome were included in the study. Written informed consent taken from parents and guardian and ethical clearance was taken from ethical clearance committee. A thorough clinical history and clinical examination was performed. All data was documented in a pre-structured proforma. All patients with nephrotic syndrome admitted to the Paediatrics ward of AMCH during the study period and who met the inclusion and exclusion criteria were chosen, and a thorough history of facial puffiness, abdominal distension, symptoms of respiratory tract infections, skin infections, and previous medications was obtained. Blood tests were done as mentioned below. All data were documented in a pre-structured proforma.

All children were allowed to have a normal diet and amount of liquids.

Blood Sample
Collection and Urine
Sample Collection
Blood and Urine
collection is done as
per protocol

Statistical Analysis

All the data is compiled in MS- Excel 2010 spread sheet. Qualitative variable is presented as frequency and percentage while quantitative variables in terms of mean and standard deviation. Statistical significance is calculated by chi square test for categorical variables and by student t test for continuous variable. P value less than 0.05 is considered statistically significant.

RESULTS

The study was carried out in the Department of Pediatrics, Assam Medical College and hospital, Dibrugarh for the duration of one year from 1st June 2021 to 31st May 2022. The results have been divided in following categories

1. Demographic.
2. Clinical.
3. Laboratory parameters of urine and serum.
4. Correlation between various parameters.

Table 1: Age Wise Distribution of Patients

Age Distribution	Number (N)	Percentage (%)
<2 yrs	2	4
2 to <6 yrs	24	48
6 to <8 yrs	12	24
8 to 12yrs	12	24
Total	**50**	**100**
Mean±SD	**5.52±2.69**	

In our study we found maximum number of nephrotic syndrome patients are from the age

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group from 2 yrs to 6 yrs which constitute 48% of all cases and minimum in the age group of less than 2 years.

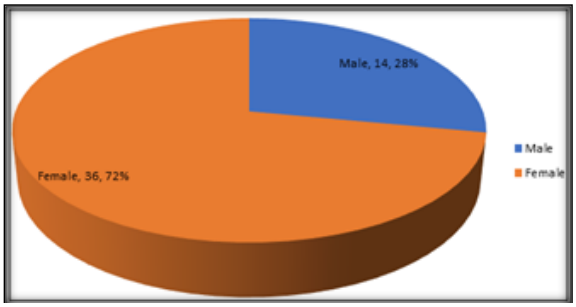

Figure 1: Sex Distribution of the Patients

Here we found that maximum number of cases are of female which constitute about 72% cases while male children are 28% cases.

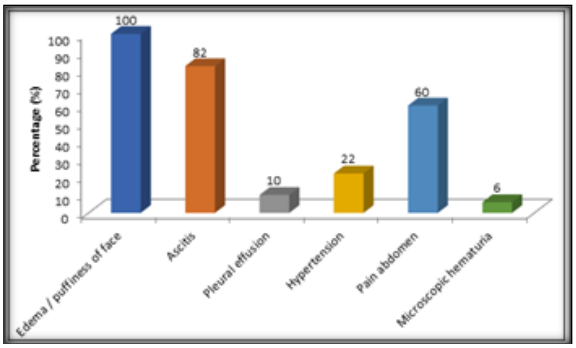

Figure 2: Clinical Presentation

All the participants have edema / puffiness (100%) followed by ascites (82%), while very less number of cases (only 6%) has microscopic hematuria.

Table 2: First Episode and Relapse

Event	Number	Percentage (%)
First episode	37	74
Relapse	13	26

In the study we found that out of 50 cases of nephrotic syndrome, 37 cases are of 1st episode (74%), while rest 13 are of relapse (26%).

Table 3: Steroid Responder and Resistance

	1st episode		relapse	
	Frequent	infrequent	frequent	infrequent
Steroid responder	7	26	2	5
Steroid resistance	2	2	2	4

In our study we found that 40 are steroid responder and 10 are steroid resistance

Table 4: Fena IN 1ST Episode and Relapse

FENa	MEAN	SD	Pvalue
1st episode	1.85	2.64	0.001
relapse	6.25	4.78	

We found FENa is less in 1st episode with an average of 1.85 and more in relapse which is 6.25

Table 5: KI in 1st Episode and Relapse

	MEAN	SD	P value
1st episode	28.83	15.41	0.18
relapse	22.36	12.64	

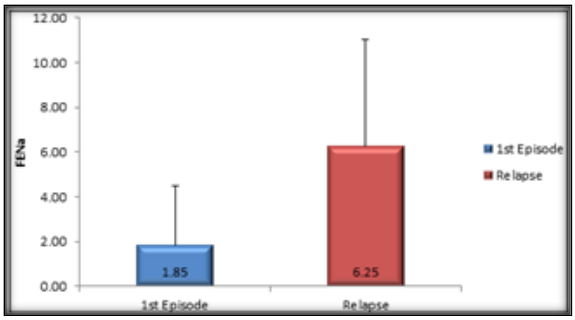

Figure 3: Relationship of FENa with 1st Episode and Relapse

Potassium index is more in first episode. Mean is calculated by t square test. Mean for 1st episode is 28.83, and in relapse it is 22.36.

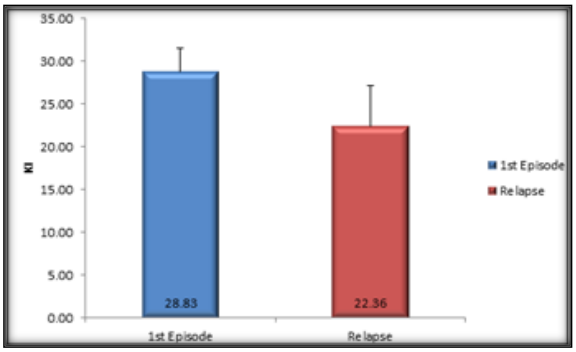

Figure 4: Relationship of KI with 1st Episode and Relapse

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DISCUSSION

Maximum numbers of nephrotic syndrome patients are from the age group from 2 to 6 years which constitute 48% of all cases and minimum in the age group of less than 2 years. In a cross-sectional study by Christopher *et al*.[5] in 2020, Similar findings are found in an observational study conducted by Anita Mehta *et al*.[9] in 2016 in UP, India, it was found that among 124 patients of nephrotic syndrome, the mean age was 4.32 years ± 2.25 which is comparatively lesser than our study. Arumugan *et al*.[10] in their analytical study among 50 patients conducted in New Delhi in 2014 stated that the mean age was 4.52 years ± 3.429, which is lesser than ours. Maximum number of cases are female which makes 72% (n=36) and male 28% (n=14). In a retrospective study done by Chaubey *et al*.[6] in 2020, male prepondence was observed.

In clinical features maximum cases had swelling of face, followed by ascites which constituted 100% and 82% respectively and least number of cases (6%) have microscopic hematuria. In a study done by Andolino TP *et al*.[7]

Mean fractionated excretion of sodium (FENa) is less in 1st episode with mean of 1.85 and in relapse with mean of 6.25. In a study done by Vande Walle *et al*.[8] with an average FENa of 0.7%, sodium retention was noticed at early onset of incipient proteinuria during a relapse with an average FENa of 0.2%. But no similar studies are found as of our knowledge showing FENa with 1st episode and relapse as of now.

According to a very recent study done by Niaudet P *et al*.[11] they found 90% of cases had edema and almost 20% had microscopic hematuria, the findings of which is similar to our study where microscopic hematuria (6%) is the least common and edema/puffines (100%) is most common clinical features.

Mean potassium index is 28.83 in first episode and 22.36 in relapse. We also found that KI is >60 in 1st episode (14%) than relapse (2%). In a study done by Ayenger *et al*.[8] there was no significant difference in the median KI in relapse and remission.

Limitations

The sample size is small. A larger sample size would have given a stronger result. It is a time limited study. Because of COVID pandemic, less number of cases was enrolled.

CONCLUSION

Based on urinary indices sodium retention, and whether it is primary or secondary sodium retention is calculated. We found that Primary sodium retention is more in first episode of nephrotic syndrome as compared to relapse. Sodium retention is seen in 56% cases of first episode of nephrotic syndrome.

Since edema is a common symptom of nephrotic syndrome often requires judicious use of diuretics in active management. Knowledge of primary sodium retention and secondary sodium retention can help clinicians to use diuretics judiciously for edema control.

REFERENCES

1. METCOFF J, RANCE CP, KELSEY WM, NAKASONE N, JANEWAY CA. Adrenocorticotrophic hormone (ACTH) therapy of the nephrotic syndrome in children. Pediatrics. 1952 Nov;10(5):543-66
2. Dodge WF, Daeschner Jr CW, Brennan JC, Rosenberg HS, Travis LB, Hopps HC. Percutaneous renal biopsy in children: I. General considerations. Pediatrics. 1962 Aug;30(2):287-96.
3. Dorhout EJ, Roos JC, Boer P, Yoe OH, Simatupang TA. Observations on edema formation in the nephrotic syndrome in adults with minimal lesions. Am J Med. 1979 Sep;67(3):378-84
4. Vande Walle JG, Donckerwolcke RA. Pathogenesis of edema formation in the nephrotic syndrome. Pediatr Nephrol. 2001 Mar;16(3):283-93.
5. Esezobor CI, Solarin AU, Gbadegesin R. Changing epidemiology of nephrotic syndrome in Nigerian children: a cross-sectional study. Plos one. 2020 Sep 21;15(9):e0239300.
6. Chaubey S, K SV, Singh P, Mittal M, K SA, Kushwaha KP. A study on intima- media thickness of carotid artery in children with nephrotic syndrome : a cross sectional study. J Pediatr Rev. 2017;4 (02):89–99
7. Andolino TP, Reid-Adam J. Nephrotic syndrome. Pediatrics in review. 2015 Mar;36(3):117-26.
8. Vande Walle JG, Donckerwolcke RA. Pathogenesis of edema formation in the nephrotic syndrome. Pediatr Nephrol. 2001 Mar;16(3):283-93.
9. Mehta A, Mishra S, Ahmad K, Tiwari HC, Singh V, Singh A. Carotid intima media thickness in children with nephrotic syndrome: an observational case control study. Sudan J Paediatr. 2019;19(2):110-116.

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