STUDY OF URINARY INDICES IN CASES OF FIRST EPISODE AND RELAPSE OF 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 Idiopatic 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. 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 vasooactive 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. 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.
FENa< 1% and KI < 60% would favour primary sodium retention, whereas FENa< 1% and KI > 60% is linked to secondary sodium retention.

\[
\text{FENa} = \frac{U\text{Na} \times S\text{r}}{\text{Pr}\text{Sr} \times N\text{a} \times X}
\]

\[
\text{KI} = \frac{U\text{K}^+ + U\text{Na}^+ + U\text{K}^+}{\text{Serum urea} \times 2.14}
\]

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 1\(^{st}\) June 2021 to 31\(^{st}\) May 2022. All patients of nephrotic syndrome fulfilling the inclusion criteria are included in our study.

**Inclusion Criteria**

Children with 1\(^{st}\) 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 spreadsheet. 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.
group from 2 yrs to 6 yrs which constitute 48% of all cases and minimum in the age group of less than 2 years.

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

![Figure 1: Sex Distribution of the Patients](image)

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

![Figure 2: Clinical Presentation](image)

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 2: First Episode and Relapse](table)

<table>
<thead>
<tr>
<th>Event</th>
<th>Number</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First episode</td>
<td>37</td>
<td>74</td>
</tr>
<tr>
<td>Relapse</td>
<td>13</td>
<td>26</td>
</tr>
</tbody>
</table>

Table 3: Steroid Responder and Resistance

<table>
<thead>
<tr>
<th>Event</th>
<th>Frequent</th>
<th>Infrequent</th>
<th>Relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroid responder</td>
<td>7</td>
<td>26</td>
<td>2</td>
</tr>
<tr>
<td>Steroid resistance</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

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

![Table 4: Fena IN 1ST Episode and Relapse](table)

<table>
<thead>
<tr>
<th>FENa</th>
<th>MEAN</th>
<th>SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st episode</td>
<td>1.85</td>
<td>2.64</td>
<td>0.001</td>
</tr>
<tr>
<td>relapse</td>
<td>6.25</td>
<td>4.78</td>
<td></td>
</tr>
</tbody>
</table>

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](table)

<table>
<thead>
<tr>
<th>Event</th>
<th>MEAN</th>
<th>SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st episode</td>
<td>28.83</td>
<td>15.41</td>
<td>0.18</td>
</tr>
<tr>
<td>relapse</td>
<td>22.36</td>
<td>12.64</td>
<td></td>
</tr>
</tbody>
</table>

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.
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.\[^1\] in 2020, Similar findings are found in an observational study conducted by Anita Mehta et al.\[^8\] 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.\[^11\] 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 preponderance 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.\[^9\]

Mean fractionated excretion of sodium (FENa) is less in 1\[^{st}\] 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 1\[^{st}\] episode and relapse as of now. According to a very recent study done by Niiaudet P et al.\[^10\] 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.\[^26\] 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