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Case Series

Paediatrics Section

Interpretation of 24-hour Urinary Protein Level for Diagnosis of Nephrotic Syndrome in Marked Hypoalbuminemia

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ABSTRACT

Nephrotic syndrome is a common renal problem in childhood and is characterised by generalised oedema, massive proteinuria, hypoalbuminemia and hyperlipidemia. There are various laboratory methods to quantify proteinuria. Among them the 24-hour urinary protein estimation is considered to be a gold standard for diagnosis of nephrotic syndrome. Nephrotic range proteinuria is considered when 24-hour urinary protein is more than 40 mg/m^2/hr. There is limited literature available regarding the changes in quantitative proteinuria when there is marked hypoalbuminemia (serum albumin less than 2.5 gm/dL). This series is about three patients of nephrotic syndrome (6-years-old, 4-year-old and 5 year-old male), having marked hypoalbuminemia and their 24-hour urinary protein level resulted into non-nephrotic range. All the patients underwent relevant physical, clinical examinations and laboratory blood and urine investigations (Haemoglobin, Mantoux test, chest x-ray, urine routine, urine culture and sensitivity, lipid profile, serum albumin and 24 hour urinary protein). All the cases were managed with Prednisolone and diuretics like Furosemide and were followed up till the subside of proteinuria and oedema conditions.

Keywords: Mantoux test, Oedema, Proteinuria quantitative, Urine culture

INTRODUCTION

Nephrotic syndrome affects 2-7 per 100000 children annually [1]. Nephrotic syndrome in children is one of the most common renal conditions encountered in clinical practice. It is mainly characterised by massive proteinuria, oedema, hypoalbuminemia and hyperlipidemia. Various methods of quantification for proteinuria are done and one of them is estimation of 24-hour urinary protein. Although it is taken as a gold standard for diagnosis of nephrotic syndrome, its interpretation is not well described in literature when the level of serum albumin is markedly low (<2.5 gm/dL).

This series is reported with the aim that these three cases had marked hypoalbuminemia in nephrotic syndrome in children as a common occurrence, so clinicians should keep in mind that in these situations 24-hour urinary protein may not reflect in the nephrotic range. These cases were admitted in the pediatric ward having characteristics features and laboratory parameters, suggestive of diagnosis of nephritic syndrome except 24-hour urinary protein that resulted into non-nephrotic range proteinuria (<40 mg/m^2/hr).

CASE SERIES

Case 1

A six-year-old male child presented with complain of swelling all over his body for last 10 days, decreased urine output for eight days, fever and abdominal pain for last six days. Patient was apparently well 10 days back when he developed swelling around his eyes and face which gradually progressed to the whole body. The mother noticed decreased urine output two days later. Previously, he had to urinate 7-8 times per day and now only 3-4 times per day. He had continuous fever for last six days which was not associated with chills and rigor. Abdominal pain was located in the mid upper abdomen, moderate to severe in intensity and non-radiating. Patient had history of similar complaints two year back and was treated in the local hospital and got relieved. Documents were not available. No other history was found significant.

Vitals were within normal limits. Mild pallor was present. On systemic examination, abdomen was distended, umbilicus was everted, dilated veins were visible and fluid thrill was present. Bowel sounds were normally heard. Other systemic examinations were within normal limits. In view of history and clinical examination, patient was provisionally diagnosed as steroid sensitive nephrotic syndrome with relapse.

Further investigations that were planned were Complete Blood Count (CBC), Mantoux test, chest X-ray, routine examination of urine and urine culture and sensitivity, lipid profile, serum albumin and 24 hour urinary protein as per unit protocol. CBC was within normal limit except Haemoglobin (Hb) which was 11.2 gm/dL. Urine albumin had variable results from 1+ to 4+ in consequent three days, pus cells ranged between 4-6 cells/hpf on centrifused urine. Serum albumin was 0.8 gm/dL on the first day. Urine culture was sterile. Total cholesterol was 430 mg/dL, 24 hr urinary protein was 0.24 gm. Mantoux test result was negative.

After getting the urine culture report as sterile, Prednisolone 2 mg/kg/day was started, divided in three doses as per unit protocol. He was advised to take a high protein diet (3-4 gm/kg/day). The child also needed short term diuretic for two days (Furosemide in dose 1 mg/kg/day) reduce oedema. After eight days of prednisolone therapy, proteinuria started decreasing and child went into remission after 13 days of therapy. Then the patient was discharged. On weekly regular follow-ups the child was in remission and was doing well.

Case 2

A four-year-old male child presented with generalised swelling all over the body for 15 days, decreased urine output for 13 days. He was apparently well 15 days back when he developed swelling around the eyes and that gradually progressed and involved the whole body. He had complaints of decreased urine output. Patient was diagnosed with nephrotic syndrome one year ago. Detailed treatment history was not available.

On examination, vitals were found within normal limits. On general examination, there was pallor and pedal and scrotal oedema. On systemic examination, fluid thrill was present and other systems were within normal limits. On the basis of history and clinical examination, patient was provisionally diagnosed with relapse of nephrotic syndrome.

On routine urine examination, urinary albumin was 4+, RBC were 10-12 per HPF and pus cells were 20 to 25 per HPF. Urine culture

was sterile. Total cholesterol was 567 mg/dL. Serum albumin was 1.4 gm/dL and 24 hour urinary protein result was 0.32 gm. Renal function tests were within normal limits and Hb was 10.1 gm/dL. Mantoux test was negative and chest X-ray was normal. Ascitis was present on ultrasonography of abdomen.

The child was treated with prednisolone 2 mg/kg/day divided into three doses till the patient went into remission. Then the dose was tapered to 1.5 mg/kg/day as a single dose. He was also advised a high protein diet 3-4 gm/kg/day. The patient was discharged after remission and on the last follow-up he was doing well and was in remission.

Case 3

A five-year-old male child came with generalised swelling of the whole body for the last 10 days that started from the face and gradually progressed to the whole body. The mother also noticed decreased urine output since last three days. The child had no similar history in the past.

On examination, the child appeared pale and on abdominal examination fluid thrill was present, Other systemic examination were found within normal limits. It was provisionally diagnosed as first episode of nephrotic syndrome and further investigations were done.

On routine examination of urine, the urinary albumin varied between 3+ to 4+, RBCs and pus cells were within normal units. Serum albumin was 1.3 gm/dL. Total protein was 3.5 gm/dL. Renal function tests were within normal limits. Total serum cholesterol was 396 mg/dL. The 24 hr urinary protein was 0.42 gm. Ultrasonography of abdomen was showing fluid in peritoneal cavity and both kidney sizes were within normal limits.

The child was treated as first episode of nephrotic syndrome. He was given prednisolone 2 mg/kg/day divided into three doses for six weeks and then 1.5 mg/kg/day as a single dose for another six weeks with other supportive treatments such as high protein diets and diuretics for three days (furosemide). Child achieved remission after ten days of prednisolone and on follow-up after seven days, he was still in remission.

DISCUSSION

Normal protein excretion in children between 4-40 mg/m^2/hour is considered normal and any value above this is considered as nephrotic range proteinuria [2-4]. Two most commonly used tests for quantification of urinary protein is dipstick test and 24 hour urinary protein. The 24 hour urine collection is still the gold standard for quantification of urinary protein [5]. Dipstick test primarily detects albumin and does not detect low molecular weight protein and is graded as trace <20 mg/dL, 1+ (30 mg/dL), 2+ (100 mg/dL), 3+ (300 mg/dL) and 4+ (>2000 mg/dL) [4,5]. Marked hypoalbuminemia is considered when serum albumin level is less than 2.5 gm/dL [6].

All the above cases had 24-hour urinary protein less than nephrotic range proteinuria (<40 mg/m^2/hour) although all these patients had clinical symptoms, signs and investigations reports like serum albumin, total cholesterol suggestive of nephrotic syndrome. These patients were treated with steroids as per standard protocol and well responded. From these three cases it can be observed that when there is marked hypoalbuminemia in nephrotic syndrome, their 24 hours urinary protein may not reflect in nephrotic range.

A 24-hour urinary protein estimation test is cumbersome in clinical practice as it needs to collect 24 hour urine which is specially difficult in young children [7,8]. Spot urine sampling is an another reliable method of testing protein in urine and is not affected by hydration status of the patient. The protein and creatinine concentration in urine are measured and protein-creatinine ratio is calculated. The protein creatinine ratio of the spot urine of morning sample is preferred as urinary protein values vary significantly during the day hours. Its sensitivity is 87.8%, specificity 89.3% positive predictive value 29.3% and negative prediction value 96.2% [9]. If the ratio is more than 2 then it is taken as nephrotic range proteinuria and if between 0.2 to 2 then it is advisable to obtain 24 hour urine collection for estimation of 24-hour urinary protein [10]. In these situations, urinary protein/creatinine ratio can be an alternative method but it needs to be further studied for its validity.

The aim to report these cases in view that marked hypoalbuminemia in nephrotic syndrome in children as a common occurrence, so clinicians should keep in mind that in these situations 24-hour urinary protein may not reflect in the nephrotic range, secondly this may motivate for further research in this direction so that a relation could be established.

CONCLUSION(S)

The 24-hour urinary protein level for diagnosis of nephrotic syndrome in children may not reflect the level of nephrotic range proteinuria when there is marked hypoalbuminemia but it needs further research to establish this relation. In future, further research in this direction can be done so that a relation could be established.

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