ORIGINAL ARTICLE

CLINICAL PRESENTATIONS OF NEPHROTIC SYNDROME IN PATIENTS OF A TERTIARY CARE HOSPITAL AT PESHAWAR

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Background: Nephrotic syndrome (NS) is manifested by presence of pitting oedema, profound proteinuria in excess of 3.5 g/day, serum albumin levels of less than 3.0 g/dL and hypercholesterolemia.1,2 The prevalence of proteinuria is high, mainly due to its frequency in diabetic patients. The etiological causes of NS are however miscellaneous, ranging from primary renal diseases to systemic illnesses with various histo-pathological presentations. The renal diseases presenting with NS must be precisely characterized, since many therapeutic strategies and specific treatments exist and must be evaluated in each case. Independently of the underlying disease, urinary protein loss may lead to several complications either due to toxic effects of proteinuria on renal tubules, or due to plasma depletion of specific proteins.3 NS may result from a variety of disease processes having the capacity to damage the basement membrane of the glomerulus. Between 70–75% cases of NS result from different forms of glomerulonephritis. Nephrotic range proteinuria also may arise as a consequence of diabetes mellitus, systemic lupus erythematosus, neoplasms, or reactions to drugs or toxins. The disease is occasionally idiopathic in origin.4

NS has an incidence of three new cases per 100,000 each year in adults. It is a relatively common way for kidney disease to manifest compared with reduced kidney function or micro-albuminuria as a complication of systemic diseases, such as diabetes and raised blood pressure.5 It is estimated to have an approximately overall prevalence rate of 2–5 cases per 100,000 children with the cumulative prevalence of 15.5 cases per 100,000 during childhood.6 In few local studies NS was reported with the frequency of 50–70%, which was the common indications for renal biopsy.7,8

Apart from oedema, hypo-albuminemia, and hyperlipidemia some patients may present with complications of the nephrotic syndrome as their initial manifestation like thromboembolism, infections, malnutrition, anaemia, and hypocalcaemia.9 The purpose of this study was to determine clinical presentations of NS. The rationale behind doing this study is that owing to high frequency of nephrotic syndrome certain recommendation will be suggested to combat the situation.

INTRODUCTION

Nephrotic syndrome (NS) is the presence of pitting oedema, profound proteinuria in excess of 3.5 g/day, serum albumin levels of less than 3.0 g/dL and hypercholesterolemia.1,2 The prevalence of proteinuria is high, mainly due to its frequency in diabetic patients. The etiological causes of NS are however miscellaneous, ranging from primary renal diseases to systemic illnesses with various histo-pathological presentations. The renal diseases presenting with NS must be precisely characterized, since many therapeutic strategies and specific treatments exist and must be evaluated in each case. Independently of the underlying disease, urinary protein loss may lead to several complications either due to toxic effects of proteinuria on renal tubules, or due to plasma depletion of specific proteins.3 NS may result from a variety of disease processes having the capacity to damage the basement membrane of the glomerulus. Between 70–75% cases of NS result from different forms of glomerulonephritis. Nephrotic range proteinuria also may arise as a consequence of diabetes mellitus, systemic lupus erythematosus, neoplasms, or reactions to drugs or toxins. The disease is occasionally idiopathic in origin.4

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MATERIAL AND METHODS

This cross-sectional study was conducted in the Nephrology Unit, Khyber Teaching Hospital Peshawar from Mar-Nov, 2012. Patients with complaints of peri-orbital or generalized swelling and proteinuria on urine examination above 12 years of age of both genders were included in the study through emergency or out-patient department. A detailed history of the presenting complaints including age at onset and duration of symptoms, facial or generalized swelling, profound proteinuria in excess of 3.5 g/day, serum albumin levels of less than 3.0 g/dL and hypercholesterolemia.1,2 The prevalence of proteinuria is high, mainly due to its frequency in diabetic patients.

This cross-sectional study was done from March to November, 2012 (for 9 months). Patients with complaints of peri-orbital or generalized swelling, and proteinuria on urine examination were included in the study through emergency or outpatient department. Results: Out of 360 suspected cases, nephrotic syndrome was found with a frequency of 67.05%. Among these patients, 69.55% were male and 30.45% female. Majority (65.85%) were between 41–60 years with mean age of 40.36±15.93 years. All (100%) patients had oedema, 43.20% had oliguria, 17.28% presented with abdominal tenderness, 15.22% patients had fever, 13.16% showed hematuria, 10.28% patients had uremia and 2.5% of the patients had thrombosis. The majority of patients (56.80%) were diabetic, and 43.20% patients had hypertension. In 23.86% patient’s high blood urea alone was recorded and 17.28% showed high serum creatinine along with raised blood urea. Rest of patients had normal renal function at the time of presentation. Conclusion: Frequency of nephrotic syndrome was 67.05%. Among these majorities were males. Oedema was the commonest presenting complaint while oliguria, abdominal tenderness, fever, hematuria, uremia and thrombosis were found in descending orders. Diabetes mellitus was leading cause in majority of patients, followed by hypertension, high blood urea, and high serum creatinine.

Keyword: Nephrotic syndrome; presenting features; diabetes mellitus; hypertension

oliguria were recorded along with history of fever, vomiting, number of remission and relapses. Family history of renal disease and previous medications especially steroids, diuretics and antibiotics were also noted. Apart from the routine investigations, i.e., haemoglobin, total and differential Leukocyte Count, erythrocyte sedimentation rate, Chest X-ray, routine urine examination especially for protein and red blood cells, 24 hours urinary proteins and single urine sample (early morning voided) for protein to creatinine ratio was done to exclude other proteinuria causes. Renal biopsy was also done in few specific cases in which primary renal pathology was suspected. All the data was recorded on a pro forma and analysed using SPSS-12.

RESULTS
A total of 360 patients clinically suspected for nephrotic syndrome were admitted to the Nephrology Unit, Khyber Teaching Hospital Peshawar during the study period. Out of 360 patients clinically suspected for nephrotic syndrome, 243 (67.05%) had nephrotic syndrome with male to female ratio of 2.28:1. Data about age and sex is given in Table-1. Age ranged from 2 to 60 years with mean of 40.36±15.93 years.

Among the presenting complaints, all patients of nephrotic syndrome had oedema, among these 139 (57.20%) had generalized oedema, 76 (31.30%) had peri-orbital and 28 (11.50%) had only scrotal edema. Presenting complaints are shown in Table-2, which also gives account of physical and laboratory findings.

Table-1: Frequency and various characteristics of patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Frequency of Nephrotic syndrome among clinically suspected patients:</td>
<td>243/360</td>
<td>67.05</td>
</tr>
<tr>
<td>Sex:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>169/243</td>
<td>69.55</td>
</tr>
<tr>
<td>Female</td>
<td>74/243</td>
<td>30.45</td>
</tr>
<tr>
<td>Age:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–20 years</td>
<td>52</td>
<td>21.40</td>
</tr>
<tr>
<td>21–40 years</td>
<td>31</td>
<td>12.75</td>
</tr>
<tr>
<td>41–60 years</td>
<td>160</td>
<td>65.85</td>
</tr>
</tbody>
</table>

Table-2: Findings of presenting complaints, clinical and physical examination of patients (n=243)

<table>
<thead>
<tr>
<th>Findings</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presenting complaints:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oedema</td>
<td>243</td>
<td>100</td>
</tr>
<tr>
<td>Oliguria</td>
<td>105</td>
<td>43.20</td>
</tr>
<tr>
<td>Abdominal tenderness</td>
<td>42</td>
<td>17.28</td>
</tr>
<tr>
<td>Fever</td>
<td>37</td>
<td>15.22</td>
</tr>
<tr>
<td>Hematuria</td>
<td>32</td>
<td>13.16</td>
</tr>
<tr>
<td>Uraemia</td>
<td>25</td>
<td>10.28</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>5</td>
<td>02.50</td>
</tr>
<tr>
<td>Physical and Laboratory:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>138</td>
<td>56.80</td>
</tr>
<tr>
<td>Hypertension</td>
<td>105</td>
<td>43.20</td>
</tr>
<tr>
<td>High blood urea</td>
<td>58</td>
<td>23.86</td>
</tr>
<tr>
<td>High serum creatinine</td>
<td>42</td>
<td>17.28</td>
</tr>
<tr>
<td>Normal renal function</td>
<td>42</td>
<td>17.28</td>
</tr>
</tbody>
</table>

DISCUSSION
The NS is a condition characterized by oedema, proteinuria, hypo-albuminemia, and hyper-triglycerideridemia. It is caused by glomerular diseases which cause urinary loss of more than 3.5 g of albumin per day. Some of the secondary diseases include infectious diseases, collagen vascular diseases, malignancies and drugs. Sometimes, no primary disease is found, and the condition is called idiopathic nephrotic syndrome. Generalized oedema is one of the most important complications in these patients which could sometimes cause critical conditions like pulmonary oedema, heart failure and hypertension. Aetiology of the oedema includes possible decrease in glomerular filtration rate (GFR), inadequate excretion of sodium in distal tubules and hypo-albuminemia.10

Nephrotic syndrome may result from either primary glomerular or systemic disease leading to renal insult. Aetiologies of nephrotic syndrome vary depending on the patient’s age. Among secondary causes, type I or II diabetes remain the most frequent aetiology in adults, although approximately 10% of nephrotic syndrome cases in diabetes are due to other renal diseases. Other systemic diseases, such as systemic lupus erythematosus (SLE), amyloidosis, hepatitis B and C, HIV, neoplasms or hematologic diseases may also be associated with glomerular disorders causing nephrotic syndrome. Finally, drugs or toxic substances must also be considered (bisphosphonates, NSAIDs, heavy metals etc).11 Frequency of nephrotic syndrome in this study was 67.05%, which is comparable to the published data in the country in which nephrotic syndrome was reported with the frequency of 50% to 70%.7,8

In our present study there were majority (65.85%) of male patients in the age range of 41–60 with mean age of 40.36±15.93 years. In one similar study there were 64.9% males and 35.1% were female patients. Average age was (33.14±11.70) years.12 While in a local study of the 200 patients, 74 (37%) were children (<18 years) and 126 (63%) adults (<19 years). The mean age of children was 11.34±4.85 years (range 3–18 years) and that of adults was 35.44±11.4 years (range: 19–70 years). Of children, 38 (51.4%) were males and 36 (48.6%) females (M:F ratio: 1.65:1). Among adults, 75 (59.5%) were males and 51 (40.5%) females (M:F ratio: 1.47:1).2 Male majority is also reported in some other studies. Results of a study showed that mean age of the 51 eligible patients was 52 years, with 39 men.13 Another study showed that they included a total of 83 patients (50 males, 33 females, age range 18–79 years) with NS.14 Some analyzed 289 consecutive patients with NS, who were aged >18
years (59% men; mean age 42 years). Reasons of male preponderance in our and other studies could be due to the fact that our society is male oriented and female patients are not allowed to seek medical treatment from male doctors and they are restricted in the homes due to local, traditional, social and tribal rules and customs.

At the time of presentation in this study, 100% patients of nephrotic syndrome had oedema, among these, generalized oedema was present in 57.20% cases, 31.30% presented with peri-orbital oedema and only 11.50% had scrotal oedema. Our findings are in agreement with national and international literature. In our study Oliguria was recorded in 43.20% patients of NS. Similar results are also reported by a local study in which Oliguria was found in 40% patients and anuria in 4% patients. These findings were not associated with marked abnormalities of renal functions. Blood urea was raised in 23.86% patients in our study and serum creatinine was raised in 17.28% patients. These results are in agreement in one local study that showed that the blood urea was raised in 24% of patients but the serum creatinine was high only in 4% patients, which in fact is more sensitive indicator of impaired renal status.

Diabetes mellitus is the most common secondary cause of the NS in adults. Moreover, it is the leading cause of end-stage renal disease in Western societies and is responsible for more than 30% of cases of end-stage renal disease requiring dialysis. Diabetic nephropathy complicates 30% of cases of type 1 diabetes mellitus and up to 50% of cases of type 2 diabetes mellitus. In the present study a majority of patients (56.80%) was diabetic either type I and II.

A local study reported that hypertension was noted in 18% cases, which is consistent with literature. The landmark for diastolic blood pressure was more than 90 mm Hg. Other 82% patients were normotensive. Only small percentage of children with minimal change disease has haematuria or hypertension. These abnormalities when present are invariably transient in children with minimal disease. While in our study hypertension was noted in 43.20% patients, which is higher than the study quoted above.

In one local study abdominal tenderness was present in 16% patients. Except one patient who had primary peritonitis, rest of the patients had no proved abdominal infection or other cause except ascites, which may be wrongly interpreted by patient as abdominal tenderness. This is due to hypovolemia and circulatory collapse, since fluid shifts from intravascular to extra-vascular space. Our results also showed that there were 17.28% patients presented with abdominal tenderness.

Results of our present study showed that fever was recorded in 15.22% patients may be due to chest or throat infection, while a local study showed that 10% of their patients presented with fever. The nephritic syndrome is associated with haematuria and proteinuria and abnormal kidney function and carries poorer prognosis and is typically associated with hypertension.

At the time of presentation 13.16% patients in our study were having haematuria. In a similar local study haematuria was found in 10% patients. Out of these 5 patients, one patient had gross haematuria which later on changed to microscopic haematuria. Rest of the patients had microscopic haematuria (Red cells field). But in some studies high incidence of hypertension (42%) and microscopic haematuria (60%) is noted. Differences in various incidences may be due to different epidemiological and clinico-pathological characteristics of NS. The patients who had turned out to be steroid resistant in some studies also initially had haematuria and high blood pressure.

Venous thrombosis is common in NS, but portal vein thrombosis has a relatively low incidence in patients with NS. In the presence of newly diagnosed NS of minimal change disease, thrombus formation can occur and should be noted, particularly when it occurs, in rare sites. The recognition in NS complicated with portal, splenic and superior mesenteric vein thrombosis should be emphasized. After infections, thromboembolism is considered by many experts to be the most significant life-threatening complication of NS. Children (2.8%) are less likely than adults (26.7%) with NS to develop thromboembolism. However, infants and children aged >12 years are at much greater risk. Membranous histologic changes increase thromboembolic risk at all ages; in particular, adults with membranous nephropathy have the highest reported risk (37.0%) and children with membranous histology have a rate (25%) that approaches the overall adult rate. Patients with NS are at risk of developing thrombosis in both veins and arteries. Various manifestations in different organs have been reported.

A local study reported that no patient presented to them or had any features of thrombotic complication during one year study period. The incidence of thromboembolic complications in children with severe NS is very high. In contrast to this, our study showed that there were 2.5% patients who had presented with thrombosis.

Results of a study reported that male gender, heavy proteinuria, low serum albumin level, and high serum creatinine level were significant determinants.
in poor response by 6 month of therapy. Renal function, systolic and diastolic blood pressure remained stable. Renal impairment (>30% rise of serum creatinine), secondary infection, hypertension, gingival hyperplasia and liver impairment occurred in many patients.13

CONCLUSIONS
Frequency of NS was high with male gender preponderance. Oedema was the commonest presenting complaint followed by oliguria, abdominal pain, fever, haematuria, uraemia and thrombosis. Diabetes mellitus and hypertension are risk factors.

REFERENCES

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