A review on nephrotic syndrome in children

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ABSTRACT

Nephrotic syndrome is a common pediatric kidney disease which is characterized by the leakage of the protein from the blood into urine through the damaged glomeruli. Nephrotic syndrome is characterized by heavy proteinuria, hypoalbunemia (serum albumin <2.5g/dl), hyperlipidemia (serum cholesterol >200mg/dl) and edema. Nephrotic range proteinuria is present if early morning urine protein is 3+/4+ (on dipstick test), spot protein/creatinine ratio >2mg/mg or >200mg/mmol urine albumin excretion >40 mg/m2 per hour. Precise quantitative measurement is necessary by 24 hour urine protein measurement. It occurs at all age groups but is most common in children of one year five months to six years, Boys>Girls, 2:1 ratio. It is higher in underdeveloped countries. The incidence rate worldwide is 2-7 cases per 100,000 children /year. Nephrotic syndrome happens when tiny structures in the kidneys called glomeruli stops working properly and allow too much protein into the kidneys. Signs of nephrotic syndrome may vary significantly from child to child, but similar symptoms such as: fatigue, malaise, decreased appetite, weight gain and facial swelling. A number of conditions can damage the glomeruli and cause nephrotic syndrome. In children, the most common cause is minimal change disease. The treatment's goal is to stop the loss of protein in the urine and increase the amount of urine passed from the body. Prednisolone is the first choice of drug given for this syndrome followed by immunomodulators; additional drugs like ACE inhibitors, diuretics, HMG COA inhibitors were also prescribed. Most children with nephrotic syndrome are characterized by minimal change disease. There may be primary and secondary causes associated with the occurrence of nephrotic syndrome. The most common symptoms include: fatigue and malaise, decreased appetite, weight gain and facial swelling. Nephrotic syndrome can be managed with the use of steroid therapy and immunomodulators along with additional drugs like ACE inhibitors, diuretics, HMG COA inhibitors.

Key words: Nephrotic syndrome, glomeruli, immunomodulators, ACE inhibitors, diuretics, HMG COA inhibitors.

INTRODUCTION

Nephrotic syndrome is a common pediatric kidney disease which is characterized by the leakage of the protein from the blood into urine through the damaged glomeruli. This is a syndrome caused by renal diseases that increase the permeability across the glomerular filtration membrane. Healthy kidneys help to retain proteins in the blood but damaged kidneys leaks proteins into urine, and as a result not enough protein is left in the blood to soak water. Both adults and children can be affected with nephrotic syndrome. Causes and treatment of nephrotic syndrome in children are different from adults. Childhood nephrotic syndrome is mostly characterized by minimal change disease.
disease. It can occur at any age but is most common between the age groups of 1 year 5 months and 6 years. It is more likely to affect boys more than girls (Srivastava et al., 1975; Kerlin et al., 2012).

A child with nephrotic syndrome has the following characteristics:

1. High levels of protein in urine, a condition called as proteinuria
2. Low levels of protein in blood
3. Swelling due to excess buildup of salt and water
4. Less frequent urination
5. Weight gain from excess water (Kerlin et al., 2012)

Nephrotic syndrome is characterized by heavy proteinuria, hypoalbuminemia (serum albumin <2.5g/dl), hyperlipidemia (serum cholesterol >200mg/dl) and edema. Nephrotic range proteinuria is present if early morning urine protein is 3+/4+ (on dipstick test), spot protein/creatinine ratio >2mg/mg or >200mg/mmol urine albumin excretion >40 mg/m² per hour. Precise quantitative measurement is necessary by 24 hour urine protein measurement as shown in Figure 1 (Kerlin et al., 2012; Lombel et al., 2013).

**EPIDEMIOLOGY**

This occurs at all age groups but most commonly in children of one year five months to six years Boys>Girls, 2:1 ratio. It is higher in underdeveloped countries. The number of incidence worldwide are 2-7 cases per 100,000 children/year (Lombel et al., 2013).

**Causes of nephrotic syndrome**

Most children with nephrotic syndrome have "minimal change disease". This means that their kidneys appear normal or nearly normal if a tissue sample is studied under a microscope. The cause of minimal change disease is unknown as shown in Figure 2. Nephrotic syndrome can sometimes occur as a result of a kidney problem or another condition as shown in Table 1, such as:

a) Glomerulosclerosis: when the inside of the kidney becomes scarred
b) Glomerulonephritis: inflammation inside the kidney
c) An infection: such as HIV or hepatitis lupus
d) Diabetes
e) Sickle Cell Anemia
f) In very rare cases, certain types of cancer – such as leukemia, multiple myeloma or lymphoma (Lombel et al., 2013; Niaudet, 2004)

**Pathophysiology**

The pathophysiology of nephrotic syndrome are shown in Figure 3.
**Figure 2**: Causes of nephrotic syndrome.

**Table 1**: Primary and secondary causes of nephrotic syndrome.

<table>
<thead>
<tr>
<th>PRIMARY CAUSES</th>
<th>SECONDARY CAUSES</th>
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</thead>
<tbody>
<tr>
<td>MINIMAL CHANGE DISEASE</td>
<td>SYSTEMIC LUPUS ERYTHEMATOUS</td>
</tr>
<tr>
<td>MEMBRANE GLOMERULONEPHRITIS</td>
<td>DIABETES MELLITUS</td>
</tr>
<tr>
<td>MEMBRANOPROLIFERATIVE</td>
<td>BACTERIAL INFECTION</td>
</tr>
<tr>
<td>GLOMERULONEPHRITIS</td>
<td>DRUGS LIKE NSAIDS</td>
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<tr>
<td>RAPIDLY PROGRESSIVE</td>
<td></td>
</tr>
<tr>
<td>GLOMERULONEPHRITIS</td>
<td></td>
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<tr>
<td>FOCAL GLOMERULOSCLEROSIS</td>
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**Laboratory investigations.**

The laboratory investigations carried out for the symptoms of nephrotic syndrome are shown in Table 2, they include urine analysis, urine sediment examination, 24 Hr urinary protein measurement, serum albumin, serological studies for infections, renal ultrasonography, renal biopsy, complete blood count; blood levels of albumin; urea; and creatinine, tuber test, electrolytes.

**Abnormality in laboratory values observed in children**

These are shown in Table 3.

**CLINICAL MANIFESTATIONS**

1. Most children with nephrotic syndrome have times when their symptoms are under control (remission), followed by times when symptoms return (relapses).
2. Some of the main symptoms associated with nephrotic syndrome are shown in Figure 4, they include:
3. Swelling – Swelling is usually first noticed around the eyes (peri orbital), then around the lower legs and the rest of the body.
4. Infections
5. Urine changes – occasionally, the high levels of protein being passed into the urine can cause it to become frothy. Some children with nephrotic syndrome may also pass less
Table 2: Laboratory investigations carried out for the symptoms of nephrotic syndrome.

1. Urinalysis
2. Urine Sediment Examination
3. 24 Hr Urinary Protein Measurement
4. Serum Albumin
5. Serological Studies For Infections
6. Renal Ultrasonography
7. Renal Biopsy
9. Tubercuin Test
10. Electrolytes

Table 3: Abnormality in laboratory values observed in children.

<table>
<thead>
<tr>
<th>Serum proteins</th>
<th>protein excretion greater than 3.5 g/24 hours</th>
</tr>
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<tbody>
<tr>
<td>Albumin</td>
<td>less than 3 g/dL or 30g/l</td>
</tr>
<tr>
<td>Lipids(serum cholesterol)</td>
<td>&gt;200mg/dl</td>
</tr>
<tr>
<td>Dipstick test</td>
<td>A 3+ reading represents 300 mg/dL of urinary protein or more, which correlates with a daily loss of 3 g or more and thus is in the nephrotic range.</td>
</tr>
<tr>
<td>spot protein/creatinine ratio</td>
<td>&gt;2mg/mg, &gt;200mg/mmol</td>
</tr>
<tr>
<td>urine albumin excretion</td>
<td>&gt;40 mg/m² per hour</td>
</tr>
</tbody>
</table>

Edema

Pitting edema is the presenting symptoms in about 95% of children with nephrotic syndrome. Edema is typically found in the lower extremities, face and peri orbital regions, scrotum or labia, and abdomen (ascites).
urine than usual during relapses.
6. Blood clots – important proteins that help prevent the blood clotting can be passed out in the urine of children with nephrotic syndrome. This can increase their risk of potentially serious blood clots.
7. Extreme tiredness (fatigue)
8. A general feeling of discomfort (malaise)
9. Decreased appetite.
10. Fluid buildup in the body (edema)
11. Fluid buildup in the belly area (ascites) (Lombel et al., 2013; Niaudet, 2004)

COMPLICATIONS

Infections: Prone to develop primary peritonitis and systemic infection due to urinary loss and inefficient production of immune globulins, defective cell mediated immunity and use of immune suppressive drugs.

Hyperlipidemia: It may occur due to increases in hepatic synthesis of lipoproteins secondary to hypoalbuminemia. Hyperlipidemia may lead to platelet aggregates and risk of renal vein thrombosis.

Electrolyte disturbances: Hyponatremia, hyperkalemia and hypocalcaemia. Hypocalcaemia occur as result of reduction of protein bound calcium secondary to hypoalbuminemia, urinary loss of D-binding globulin, 25-hydroxyvitamin D3 and is further aggravated by prolonged corticosteroids therapy.

Acute renal failure: It occurs due to intrinsic glomerular damage in atypical nephrotic syndrome. These patients are very sensitive to reduction of blood volume. As result of diarrhea, vomiting or rapid diuresis they can develop hypovolemic shock and pre renal azotemia promptly managed by administration of albumin or plasma to prevent renal dysfunction (Niaudet, 2004).

MANAGEMENT

Appropriate therapy at the first episode is an important determinant of the long term course of the disease.

Prednisolone is the drug of choice

It is given at a dose of 2 mg/kg per day (max 60 mg in single or divided doses) for 6 weeks, followed by 1.5 mg/kg (max 40 mg) as a single morning dose on alternate days for the next 6 weeks, therapy is then discontinued (Zhang et al., 2011; Gipson et al., 2009).

DISCUSSION

Nephrotic syndrome happens when tiny structures in the kidneys called glomeruli stop working properly and let too much protein enter the kidneys. Signs of nephrotic syndrome may vary significantly from child to child, but you or your child may notice: fatigue, malaise, decreased appetite, weight gain and facial swelling. A number of conditions can damage the glomeruli and cause nephrotic syndrome.
syndrome. In children, the most common cause is due to minimal change disease. The treatment’s goal is to stop the loss of protein in the urine and increase the amount of urine passed from the body. Prednisolone is the first choice of drug given followed by immunomodulators; additional drugs like ACE inhibitors, diuretics, HMG COA inhibitors are also prescribed (Gipson et al., 2009; Pediatr, 1981).

CONCLUSION

Most children having nephrotic syndrome are characterized by minimal change disease. There may be primary and secondary causes associated with the occurrence of nephrotic syndrome. Most common symptoms include: fatigue and malaise, decreased appetite, weight gain and facial swelling. Nephrotic syndrome can be managed with the use of steroid therapy and immunomodulators along with additional drugs like ACE inhibitors, diuretics, HMG COA inhibitors (Gipson et al., 2009; Pediatr, 1981;).

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REFERENCES