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Pediatric steroid dependence nephrotic syndrome: A case series

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Abstract
Pediatric nephrotic syndrome is defined by the presence of nephrotic range proteinuria, hyperlipidemia, and hypoalbuminemia. It is the commonest glomerular disease and 15 times more common in children than adults. The incidence is popular in Asian population than Europeans with 9-16 per 1,00,000. Here we reported 3 cases of steroid dependence nephrotic syndrome under 10 years of age. All the three cases having the classical features of nephrotic syndrome like facial puffiness, pedal edema and proteinuria. Corticosteroid is the drug of choice for nephrotic syndrome. So it is necessary to counsel the patient caregivers about need of proper follow up, weight checkup, growth measurement etc.

Keywords: Corticosteroid, nephrotic syndrome, proteinuria, oliguria

1. Introduction
Pediatric nephrotic syndrome is defined by the presence of nephrotic range proteinuria, hyperlipidemia, and hypoalbuminemia [1]. Nephrotic syndrome is the main manifestation of many different glomerular diseases. Leakage of massive amount of serum protein in to the urine leads to hypercoagulable state, a higher rates of infectious disease and the dysregulation of fluid balance [2]. The estimated annual incidence range of nephrotic syndrome from 2 to 7 new cases in children under 16 years per 1,00,000 total population, leading to a cumulative prevalence of 15.7 per 1,00,000 due to the chronic nature of the disease [3]. Nephrotic syndrome generally divided into primary, secondary and congenital. Primary nephrotic syndrome also called idiopathic nephrotic syndrome, is associated with glomerular disease intrinsic to the kidney which includes minimal change nephrotic syndrome (MCNS), focal segmental glomerulosclerosis (FSGS), membraneous neuropathy (MN), membrane proliferative glomerulonephritis (MPGN), C3 glomerulonephritis (C3 GN), Ig A nephropathy and others[4]. Secondary nephrotic syndrome refers to an etiology intrinsic to the kidney includes autoimmune and vasculitic disease, infectious disease, malignancy, diabetes mellitus etc. Congenital nephrotic syndrome is defined as heavy proteinuria starting before the age of 3 months and may be associated with congenital infections (such as syphilis, toxoplasmosis or Cyto Megalo Virus) [1].
Consequently, a clinically useful classification of nephrotic syndrome is that of steroid sensitive and steroid resistant nephrotic syndrome. Nephrotic syndrome is 15 times more common in children than in adult. Most frequent type of idiopathic nephrotic syndrome is minimal change neprotic syndrome, and more than 95% minimal change neprotic syndrome well respond to the steroid therapy [4]. Idiopathic nephrotic syndrome is a chronic relapsing disease and frequency is variable. In some patients relapses are infrequent (≤3) whereas others have frequent relapse [5].

2. Case Report
2.1 Case no.1
A 5 year old boy with history of Nephrotic syndrome since 2 years has presented with puffiness of face, periorbital swelling, oliguria, abdomen distension, fever and dysuria. At the time of admission all the vitals were normal. He had abdominal tenderness and pedal edema. He stopped taking Prednisolone 10 mg, four weeks prior to the admission in hospital. On laboratory examination hemoglobin level was slightly reduced (10g/dl). The boy had hypoalbuminemia (2.1g/dl; normal value: 3.8-5 g/dl) with 3 + albumin in urine. The protein level in the blood was reduced at the level of 3.5 mg/dl (normal level 6-8 mg/dl). Urine analysis showed the presence of bacteria in the urine and pus cells of 2-3/HPF. He was diagnosed with steroid dependent nephrotic syndrome and urinary tract infection. Antibiotic Cefotaxime 500 mg was given for bacterial infection. Prednisolone 20 mg was restarted with fluid restricted diet.

2.2 Case no: 2
A 9 year old female child admitted with complaints of facial puffiness, oliguria, pedal edema, nausea and vomiting. She was a known case of nephrotic syndrome on regular treatment since the age of 7. At the time of admission all vitals were normal. On laboratory examination albumin in urine was 3 + and showed the presence of pus cells 4-6/HPF. Urine spot protein and creatinine ratio was 1618 mg/mmol. She was advised with fluid restricted diet and Prednisolone10 mg three times a day.

2.3 Case no: 3
A 7 year old male child was admitted at pediatrics department with the complaints of puffiness around eyes, swelling of face, olyguria and dysuria. He was a known case of nephrotic syndrome and under regular treatment with steroids. On physical examination pedal edema and pallor was present. His blood reports revealed that there was a severe hypoalbuminemia, serum albumin level 1.6gm/dl with albuminuria 3+ and normal urea and creatinine level (19mg/dl and 0.8mg/dl respectively). Serum cholesterol was about 280mg/dl (normal value: upto 200 mg/dl). Urine culture showed a significant presence of bacteria in the urine and given Cefixime 60mg/day to treat infection. He was also given with prednisolone 10 mg two times a day with restricted oral fluids and fluid restricted diet.

3. Discussion
Here we reported 3 cases of steroid dependence nephrotic syndrome under 10 years of age. It is the commonest glomerular disease and 15 times more common in children than adults [6]. The incidence is popular in Asian population than Europeans with 9-16 per 1,00,000. All the three cases having the classical features of nephrotic syndrome like facial puffiness, pedal edema and proteinuria [7]. Claudi *et al.* explained that proteinuria is connected to alteration of the slit diaphragm, a structure fundamental in forming a barrier for the passage of plasmatic protein at the level of the glomerular capillary wall [8]. Proteinuria results in hypoalbuminemia, which lead to the malnutrition. Edema formation can be defined by two hypothesis underfill hypothesis and overfill hypothesis. Underfill hypothesis is that decrease in plasma oncotic pressure, causing an extravasation of plasma water into the interstitial space and resulting contraction in plasma volume which leads to stimulation of the renin-angiotensin-aldosterone axis and antidiuretic hormone. The resultant retention of sodium and water by the renal tubules contributes to the extension and maintenance of edema. Overfill hypothesis postulates that a primary defect in renal sodium handling which increases in renal sodium reabsorption leads to net salt and water retention and subsequent edema [1]. Treatment of nephrotic syndrome is complex and should be tailored to the individual patient [9].

Arniel first proposed the use of prednisolone in children with nephrotic syndrome [10]. Subsequently the International Study of Kidney Disease in Children (ISKDC) proposed 60mg/m^2/dayof prednisolone for induction of remission of nephrotic syndrome which has seen accepted as the standard treatment [11]. Prednisolone is started at a dose of 2mg/kg (maximum dose 60mg) once daily for 6 weeks, then tapered to 1.5mg/kg (maximum dose of 40mg) on alternate days for another weeks. Infrequent relapses are treated with prednisolone 2mg/kg daily until urine is negative for protein at least 3 days; then prednisolone is changed to 1.5mg/kg on alternative days for 4 weeks [12]. In our study all the three cases are steroid dependent and one patient relapse after stopping the drug. All patients' caregivers hould be trained to moniter first morning urine protein at home using urine dipstick method and weight should be checked every morning.

4. Conclusion
Corticosteroid is the drug of choice for nephrotic syndrome. There was a positive correlation between the side effects and cumulative dose of steroids in children. Obesity, hirsutism, arterial hypertension and psychological disturbances are usually reversible after cessation of steroid therapy. Growth failure was also observed in children with prolonged use of daily steroid therapy, while alternate days were not associated with significant impairment. So it is necessary to counsel the patient caregivers about need of proper follow up, weight checkup, growth measurement etc.

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