Nephrotic syndrome in children

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KPA Nephrology Precongress

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What is Nephrotic syndrome??

- Nephrotic syndrome is caused by renal diseases that increase the permeability across the glomerular filtration barrier.
  - Nephrotic range proteinuria — Urinary protein excretion greater than 50 mg/kg per day
  - Hypoalbuminemia — Serum albumin concentration less than 3 g/dL (30 g/L)
  - Edema
  - Hyperlipidemia

Why Nephrotic syndrome

- Nephrotic syndrome is the commonest diagnosis in the pediatric renal clinics at tertiary centres
- Also one of the commonest reason for pediatric nephrology consultation in the wards after acute kidney injury
- most guidelines on nephrotic syndrome renal biopsy based on studies done long ago, in continents far away from here and in populations different from ours
- Local data is scanty at best
- And thus…….

Classification

1. Age of onset
2. Aetiology
3. Histological
4. Response to steroids

Congenital & early onset nephrotic syndrome

- **Congenital** – presentation < 1 month
  (most commonly CNS of Finnish type)

- **Early onset** – can be from days to months
  (Heterogeneous group – diffuse mesangial sclerosis, MCNS)

Classification of congenital and early-onset nephrotic syndrome

Primary NS

- Congenital nephrosis of the Finnish type
- Isolated diffuse mesangial sclerosis
- Denys-Drash syndrome
- Congenital NS with brain and other malformations (Galloway – Mowat syndrome)
- FSGS
- Membranous glomerulosclerosis

Aetiological classification (early or late onset)

- Primary
- Secondary

  Infections

  - Congenital syphilis
  - Toxoplasmosis, rubella, CMV, Hepatitis, HIV
  - Malaria

  SLE

Histological classification

Four defined categories of primary podocytopathy:

1. Normal histology – minimal change nephropathy
2. Mesangial sclerosis – diffuse mesangial sclerosis
3. Segmental sclerosis – focal segmental glomerulosclerosis
4. Collapse of the glomerular basement membrane – collapsing glomerulopathy

Schnaper and colleagues

Response to steroids

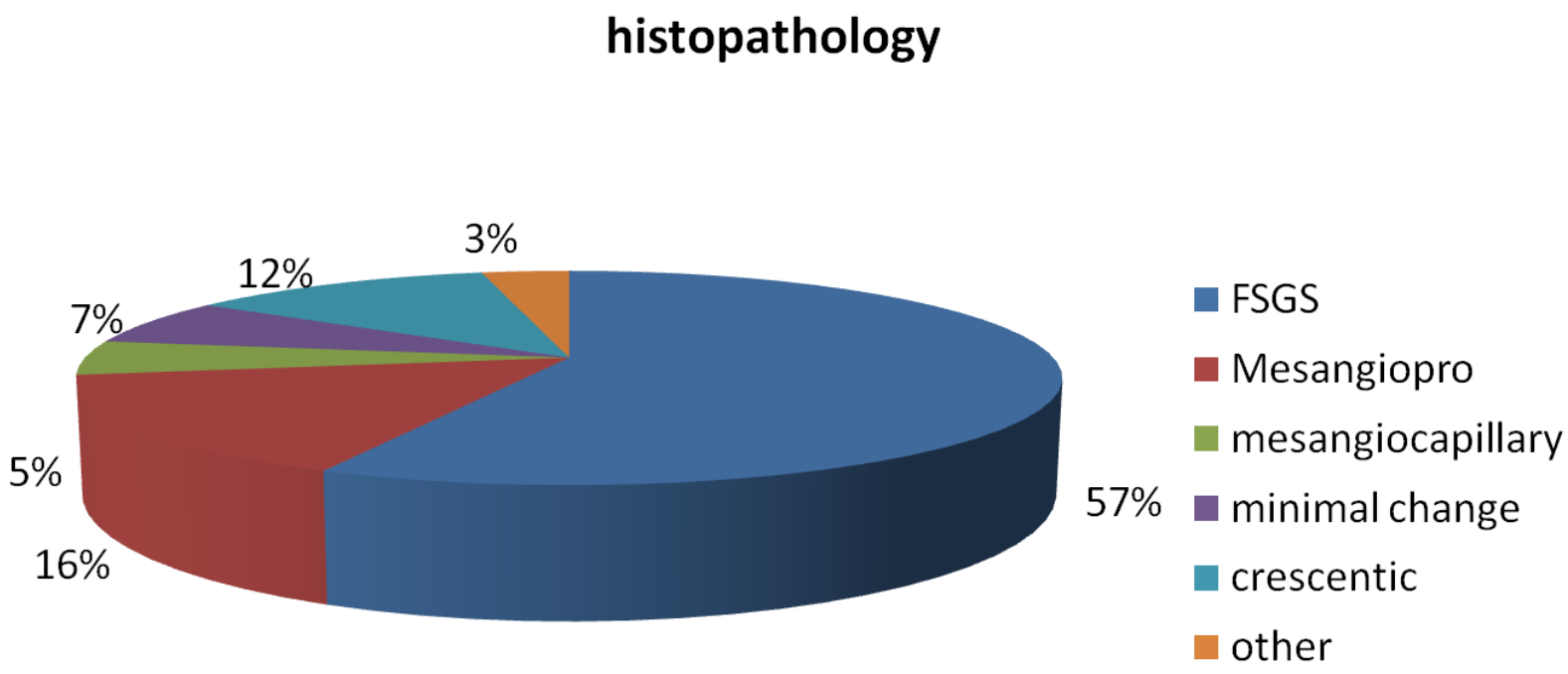
- Idiopathic NS has an estimated incidence of 20-30 per million children annually
- Of all treated patients
  - 1/3rd - no relapses
  - 1/3rd - infrequent relapses
  - 1/3rd - steroid dependent
  - 7% - steroid resistant – renal biopsy
- 93% steroid-responsive
  - Long-term outcome is excellent
  - Mortality (1%) mostly due to sepsis and thrombosis rather than renal failure

Etiology ?????

Renal biopsy findings in children at Kenyatta National Hospital

Kenyatta National Hospital

Histopathology



Histopathology

- ISKDC biopsies on 521 children in Europe, N America and Asia showed most children had minimal change (77%) FSGS (2%)
- South Nigeria in children with steroid resistance showed mesangiocapillary 43.5% FSGS 39.1% minimal change 4% (n=
- Study from Tunisia showed FSGS 50%mesangial proliferation 40%
- American canadian studies showing increasing incidence of FSGS

Nephrotic syndrome in children: prediction of histopathology from clinical and laboratory characteristics at time of diagnosis. A report of the International Study of Kidney Disease in Children. Kidney Int 1978; 13:159

Histopathology findings in children in southwestern Nigeria:Saudi J kidney disTransplant 2010 Sep;21(5):979-90

*Tunis Med:*2011 Mar;89(3):258-61

Bonilla-Felix, M, Parra, C, Dajani, T, et al. Changing patterns in the histopathology of idiopathic nephrotic syndrome in children. Kidney Int 1999; 55:1885.

Renal Biopsy Review
1990 – 1999 Cape town

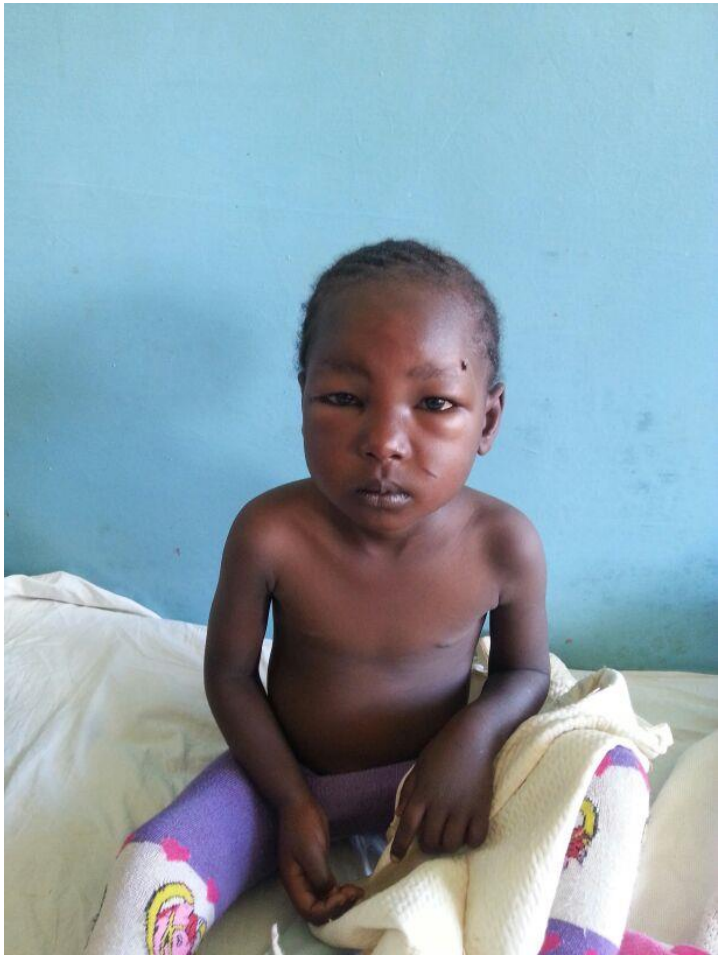
- *Mesangial Proliferation 36/96(37.5%)
- FSGS 9/96(9.4%)
- Mesangiocapillary 4/96(4.2%)
- Membranous 19/96(2.1%)
- Minimal Change Disease 2/96(2.1%)

Patient

- 7 year old girl first presentation
- Swelling of face and body – ascites +++
- Urine: protein 4+ Blood 2+
- BP 90/60 mmhg
- No impetigo or throat infections
- Clinically cool peripheries, HR 130b/min

  apex not displaced, HS normal

Chest Dull Left base



Clinical manifestations

- Pedal periorbital edema
- Ascites and pleural effusions.
- Infections like peritonitis. (may present as acute abdomen)

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- The likelihood of hypertension varies with the underlying cause of nephrotic syndrome.
  - Hypertension is common in patients with focal segmental glomerulosclerosis or glomerulonephritis, but is infrequent in MCD.
- Gross hematuria is most often seen in patients with glomerulonephritis

Complications

- Infection — Children with nephrotic syndrome have increased susceptibility to encapsulated bacterial infection, particularly peritonitis because of defects in humoral immunity.
    - Although antibiotics have reduced the mortality rate of nephrotic syndrome due to infection, infection still remains the main cause of death in children with nephrotic syndrome.
- Anasarca — Anasarca (generalized and massive edema) can cause
  - respiratory distress (eg, pulmonary edema or large pleural effusions),
  - skin breakdown with an increased risk of cellulitis,
  - increases the risk of bacterial peritonitis.

Complications

- Thrombosis
- Renal insufficiency.
- Hypovolemia

Diagnosis

- Urinalysis: protein > 3+, +/- blood
- Quantitative protein analysis
  - Total daily excretion >50mg/kg/day
  - Urine protein :creatinine ratio> 0.2gm/mmol
- Serum albumin<30g/dl
- Urea/electrolyte/creatinine
  - Calculate GFR height x coefficient/creatinine
- Lipid profile: hypercholesterolemia

Quantitative urine protein evaluation

- 24 hr urine collection is a myth in paediatrics!
- Nice to hear about it but not done world wide and difficult to do it for logistical reasons
- Spot urine protein: creatinine ratio valuable
- >0.02 g/mmol-proteinuria
- >0.2g/mmol nephrotic range
- Comparable results to 24 hr urine collection

Houser, M. Assessment of proteinuria using random urine samples. J Pediatr 1984; 104:845.

Houser, MT, Jahn, MF, Kobayashi, A, Walburn, J. Assessment of urinary protein excretion in the adolescent: effect of body position and exercise. J Pediatr 1986; 109:556.

Other tests

- Blood count
- Hepatitis B, HIV, VDRL
- Complement studies
- Antinuclear antibodies

CASE

INVESTIGATIONS

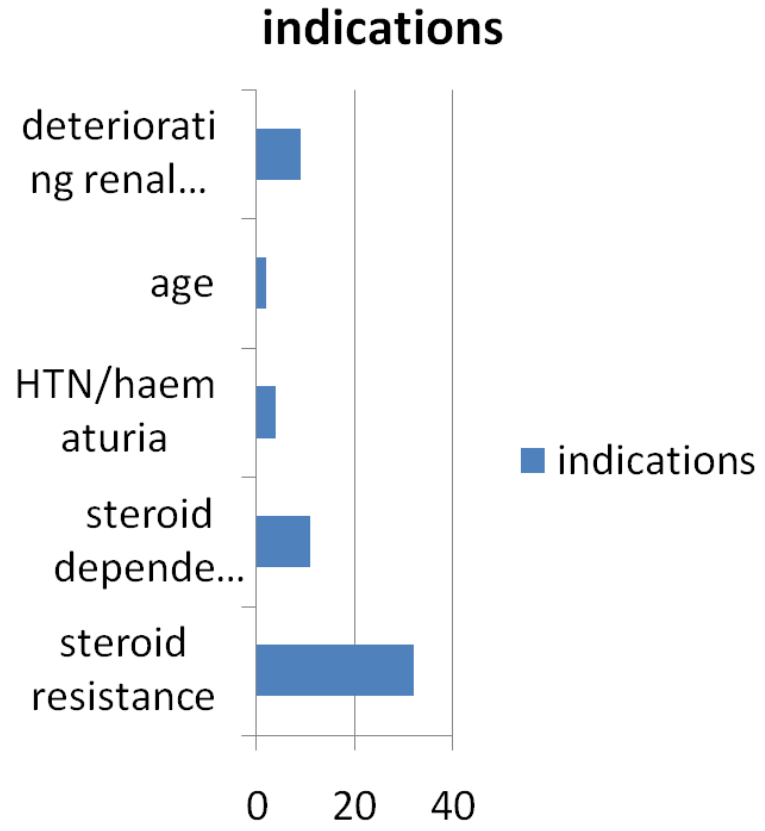
- Pr/Cr ratio 1.5 (N <0.02g/mmol)

- Urea 5 Creat 40 umol/l
- Protein 38 Alb 9 Cholesterol 10
- FBC normal, ESR 114
- RVD negative
- Hep B negative and VDRL negative
- Mantoux non-reactive
- CXR- rt pleural effusion

Indications for biopsy

- Indications:

1. Age <1 or >10 years
2. Steroid resistance
3. Steroid dependence or frequent relapse
4. HTN, gross haematuria
5. Deteriorating renal function



Nephrotic Syndrome Management

- Daily urine dipsticks
- Salt restriction
- No fluid restriction unless hypertensive or in renal failure
- Control severe oedema - IV albumin with diuretics
- Avoid diuretics on own – check perfusion.
- Prophylactic penicillin
- Aggressive treatment of infection

Treatment

- Prednisolone 2mg/kg/day for 6 weeks then 1.5 mg/kg alternate days for 6 weeks then taper off over 6 weeks (KDIGO)
- Most respond to treatment
- About 60% relapse
- Frequent relapsers are >2 relapse in 6 months
- Steroid resistance is proteinuria > 3 + at 4 weeks of treatment

Treatment

- Other modalities
  - Alkylating agents
    - Cyclophophamide, chlorambucil
  - Calcineurin inhibitors
    - Cyclosporin, tacrolimus
  - MMF, azathioprine
  - ACE inhibitors

Renal Biopsy findings at KNH

- FSGS and steroid resistance: 84.8% of biopsies with steroid resistance had FSGS v/s 23.6% if indication something else (p= 0.008)
- Mean age 9.34yrs those without 8.34yrs
- Other factors like gender not different

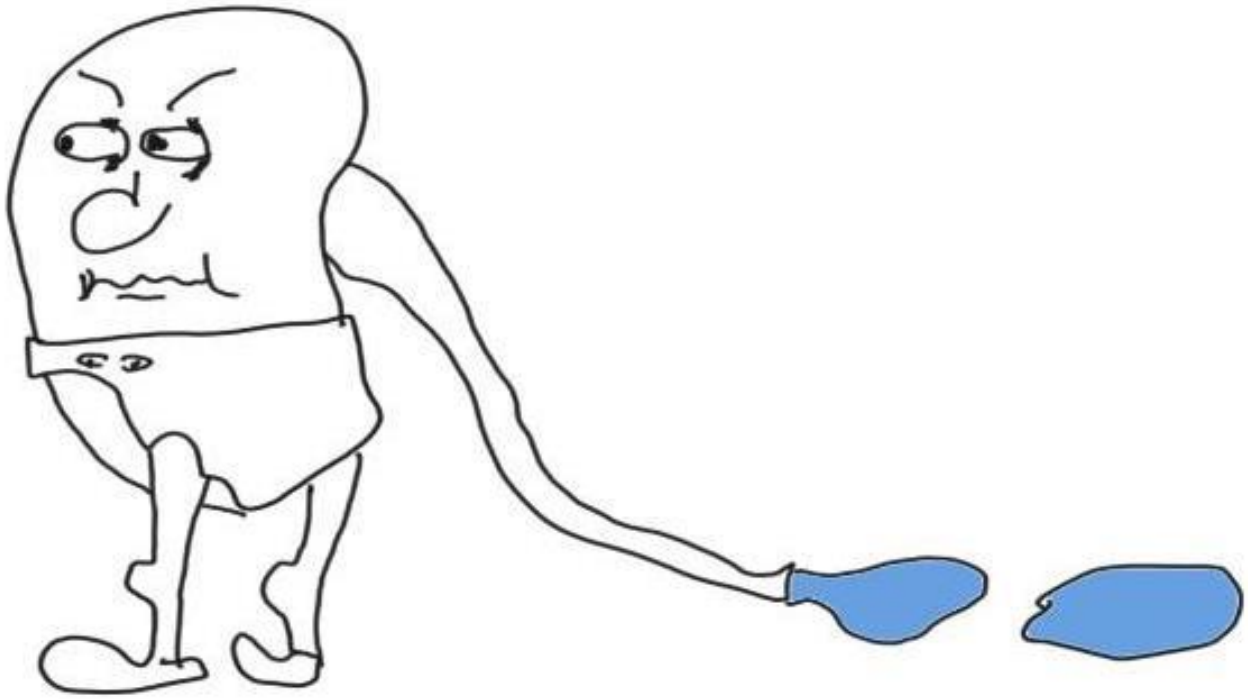
Treatment of steroid-resistant FSGS: Evidence-based recommendations

Treatment	Recommendation
Oral cyclophosphamide (12 weeks)	No benefit
Cyclosporin (at least 6 months)	**Beneficial**
IV methylpred and alkylating agents (6 months to 1 year)	Possible benefit
IV cyclophosphamide (monthly for 6 months)	Possible benefit
MMF	Case reports
Tacrolimus	Case reports
Plasmapharesis	Anecdotal reports
High dose Enalapril	Useful in reducing proteinuria

Summary

- Nephrotic syndrome is a common paediatric renal condition
- It is important to make the diagnosis based on proteinuria, hypoalbuminemia, oedema and hypercholesterolemia
- Initiate treatment with steroids at the right dose

- Refer at the earliest as these patients complicate fast



Some things just don't hold water...