Nephrotic Syndrome

Purpose
It is aimed at providing medical and nursing staff who are presented with a child with nephrotic syndrome an up to date, evidenced based information to help guide management. This ensures consistency in the management of every case.

This guideline is aimed at management of Childhood nephrotic syndrome

Intended Audience
All doctors and nursing staff providing care to children who present to the emergency department, AAU and the medical ward.
1. Introduction

Nephrotic syndrome is characterised by massive proteinuria, hypoalbuminemia and oedema. Although uncommon, it is the commonest glomerular disorder of childhood with a UK incidence of 2/100000. It is more common in children of Asian descent.

There are many causes of nephrotic syndrome which can be divided into primary and secondary causes. Majority of cases are primary (>90%) with 80% of these cases caused by minimal change disease (MCD).

Although thought to be a relatively benign condition, its mortality rate remains between 0.5-1%.

2. Intended Audience

All doctors and nursing staff providing care to children who present to the emergency department, AAU and the medical wards.
3. Guideline Content

DEFINITION:

Nephrotic syndrome is characterised by

1. Massive proteinuria (3+ on dipstick or urine protein/creatinine ratio >200mg/mmol)
2. Hypoalbuminemia (<25g/l)
3. Oedema

- Other useful/related definitions:
  - Remission
    - proteinuria trace/negative on dipstick for 3 consecutive days
  - Relapse
    - proteinuria 3+ or more on dipstick for 3 consecutive days
    - +/- oedema
  - Frequent relapse
    - 2 or more relapses within the first 6 months of initial response
    - 4 or more relapses in any 12 month period
  - Steroid sensitive nephrotic syndrome
    - Complete remission within the initial 4 weeks of steroid therapy
  - Steroid dependent nephrotic syndrome
    - Relapse during steroid therapy or within 2 weeks of discontinuing steroids
  - Steroid resistant nephrotic syndrome
    - Failure to achieve remission after 4 weeks on high dose steroids (i.e. 60mg/m²/day)

CLASSIFICATION:

Nephrotic syndrome can be classified

- Primary glomerular disease /Idiopathic – causes include
  - Minimal change disease (80-90%)
  - Membranoproliferative glomerulonephritis
  - Focal segmental glomerulosclerosis
  - Congenital Nephrotic Syndrome
Secondary disease/ Non idiopathic
- HSP
- SLE

Majority of the cases of nephrotic syndrome are idiopathic of which approximately 80-90% are due to minimal change disease.

Approximately 80% of the cases of MCD would respond to steroid therapy but 75-85% would develop a relapse and 50% will go on to have frequent relapses.

The typical age group affected is 1 – 10 years with 2 years the most common age at presentation.

CLINICAL ASSESSMENT
Features and points in History to consider:
- Length of history, any known precipitating factors eg URTIs
- Atopy
- Any relevant drug history eg penicillamine
- Any symptoms to suggest underlying glomerulonephritis – see guideline on Acute glomerulonephritis (ref: 1912)
- Immunisations and childhood infections (particularly varicella zoster)
- Family history (particularly renal and thrombophilia)

Features to assess on examination:
- Weight and height, extent of oedema, presence of ascites, scrotal / vulval oedema, pleural effusions
- Signs of hypovolaemia - low JVP, poor peripheral circulation (assess capillary refill), postural hypotension
- Measure blood pressure - assess for hypovolaemia; 10-15% of those with steroid sensitive nephrotic syndrome (SSNS) have mild hypertension but severe hypertension suggests underlying glomerulonephritis
- Signs of specific complications - infection (cellulitis, peritonitis, septicaemia), thrombosis (especially renal vein)
- Signs of underlying disease, especially vasculitis, glomerulonephritis, connective tissue disorder

INVESTIGATIONS
- Urine
  - Urine dipstick for protein and blood
  - Urine Protein/creatinine ratio (early morning sample if possible)
  - Urine microscopy – if significant haematuria, to differentiate between primary nephrotic syndrome and glomerulonephritis (see table 1)
  - Culture – if UTI suspected
Blood
- FBC – haematocrit helps in general assessment and monitoring of hypovolaemia if needed
- Urea, creatinine and electrolytes, bone profile, albumin
- Varicella titres

NB: Femoral stab should be avoided due to the risk of thrombosis, a known complication.

TYPICAL VERSUS ATYPICAL NEPHROTIC SYNDROME

Children with atypical features of nephrotic syndrome should be discussed with Nephrology SPIN Paediatrician / paediatric nephrologist before commencing treatment as they are less likely to have MCD and may not respond to steroids.

Table 1

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Typical nephrotic syndrome</th>
<th>Atypical nephrotic syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1-11 years</td>
<td>&lt;1 or &gt;11 years</td>
</tr>
<tr>
<td>Renal function</td>
<td>Normal creatinine</td>
<td>Elevated creatinine</td>
</tr>
<tr>
<td>Haematuria</td>
<td>Microscopic may occur</td>
<td>Macroscopic</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Usually normotensive</td>
<td>Elevated</td>
</tr>
<tr>
<td>Family history of nephrotic syndrome</td>
<td>Usually absent</td>
<td>May be present</td>
</tr>
</tbody>
</table>

Indications for discussion with SPIN Paediatrician or Paediatric nephrologist at presentation
- Atypical features (as above)
- Suspicion of hypovolaemia or elevated haemoglobin/urea
- Before administering albumin infusion

Indications for Renal biopsy
- Age at onset <12 months or > 12 years
- Initial macroscopic haematuria
- Persistent hypertension and /or microscopic haematuria and /or low C3
- Renal failure not related to hypovolaemia
- Clinical evidence of systemic disease
- Steroid resistant

MANAGEMENT

a. Establish diagnosis of nephrotic syndrome.
b. Determine if there are any features which would suggest that the diagnosis is other than 'minimal change disease' (MCD) and that a renal biopsy should be performed / considered **BEFORE** steroid treatment is started.

c. At diagnosis, children should be admitted to the ward, even if there is not significant oedema, at least for a few days; to teach the child and their parents about nephrotic syndrome. Most children will be in hospital for several days having daily thorough assessment of their fluid status which should include an accurately completed fluid balance chart, regular blood pressure monitoring and daily weights. They should be examined daily for extent of oedema and signs of hypovolaemia.

d. **Corticosteroid therapy**

For initial presentation of nephrotic syndrome, if classical presentations with no atypical features give standard regimen of steroid:

   a. Prednisolone 60mg/m$^2$/day in single morning dose (maximum 80mg/day) for 28 days. (Intravenous Methylprednisolone can be used in a child with vomiting at a dose of 48mg/m$^2$/day)

   b. Then reduce dosage to 40mg/m$^2$/alternate day (maximum 50mg/alternate day) given once daily, for 28 days and then stop without tapering.

For relapses the following regimen should be used

   a. Prednisolone 60mg/m2 /day (maximum 80mg/day) in single morning dose until remission (negative or trace proteinuria for 3 consecutive days) is induced

   b. Decrease to Prednisolone 40mg/m2 /alternate day (maximum 50mg/alternate day) given as single morning dose. Stop after 28 days.

   c. Known nephrotic patients under the renal team in relapse, do not need to be reviewed in hospital with every relapse, if the parents are happy and report the child is well. Parents overtime become very knowledgeable and pre relapses very early before the child gets unwell or significantly oedematous. Useful questions to ask the parents when they call would include:

      - If the child is well?
      - If puffy? Where? – face, legs, abdomen, genitalia?
      - Abdominal pain?
      - Vomiting?

   d. The child needs review in hospital if parents report child looks unwell, has generalised oedema, persistent abdominal pain or vomiting.
Nephrotic Syndrome

e. It is safe to start the child on Prednisolone as above. Use the last weight in clinic which would be a more appropriate weight (without oedema).

f. Email Nephrology SPIN consultant (grace.ehidiamhen@nhs.net) and renal secretary (Hayley.downes1@nhs.net). We would liaise with the family on our return with further plan on weaning the steroid.

e. Other management

a. **Fluid balance** - whilst in hospital keep accurate fluid input/output charts and weigh daily. Moderate fluid restriction may be needed on occasion if fluid intake is excessive. Suggested fluid intake

   i. < 5 years =750ml

   ii. >5 years = 1 litre

b. **Diuretics** - may be required to control oedema whilst steroids are taking effect. These should only be used in severe and worsening oedema/ascites in the absence of hypovolaemia. Initially furosemide may be tried alone but if oedema severe it can be used in conjunction with spironolactone.

   Use Furosemide 1 - 2mg/kg/day +/- Spironolactone 2mg/kg/day, usually in two divided doses.

   If oedema still persists a thiazide diuretic can be used, only after discussion with a paediatric nephrologist.

c. **Blood pressure** - measure 4 hourly whilst in hospital, more frequently if appropriate. Hypertension may be due to hypervolaemia, or occasionally due to extreme hypovolaemia or associated glomerulonephritis and needs to be carefully assessed. Persistent hypertension may need drug treatment.

d. **Diet** - healthy diet advised with 'no-added' salt and avoidance of salty foods. Arrange for dietician to see patient.

e. **Antibiotic prophylaxis** - at increased risk of pneumococcal infection and others eg. E. coli. Benefits of antibiotics debated; in practice give oral Penicillin V in prophylactic dosage whilst oedematous.

f. **Gastroprotection**: Few children develop gastritis on high doses of steroids. If necessary children can be administered gastroprotection whilst on high dose steroids (rani tidine or lansoprazole)

g. **Pneumococcal immunisation**: All children should receive a dose of 23 valent Pneumococcal polysaccharide vaccine. This can be given from 2 years of age.

h. **Albumin infusion** - only rarely needed, indicated only for symptomatic hypovolaemia or severe diuretic resistant oedema. Only use after discussion
Nephrotic Syndrome

with Consultant. If used needs extremely careful monitoring, give during 'daylight hours' and stop immediately if signs of respiratory distress develop (pulmonary oedema can be induced). Give 1g/kg of 20% albumin solution over 4 hours with 1 - 2mg/kg Furosemide IV half way through infusion.

i. **Monitoring** - Once daily dipstick of first morning urine needed to monitor progress of proteinuria, daily weight with accurate input / output charts.

**DISCHARGE**

This is a significant diagnosis and it must be explained to the family.

Information booklet on “Nephrotic Syndrome” and Nephrotic diary can be obtained from Dr Grace Ehidiamhen via her secretary;

Signposting to the infoKID website ([www.infokid.org.uk](http://www.infokid.org.uk)) would also be useful for the family. It can also serve as the written information for the family..

They need to be taught how to test urine with albustix, be provided with a diary to keep record of results and treatment and how to detect relapse

**Discharge Checklist**

Before discharge, parents/carers should know

- How to dipstick early morning urine and record the result in the daily diary
- How to recognise a relapse
- Whom to contact for advice
- Appropriate fluid and dietary advice
- Steroid and immunosuppression advice.
FOLLOW UP – All patients should be followed up for a minimum of 6 months

At discharge initial diagnosis of nephrotic syndrome

Review in 1 week in MDC or renal nurse led clinic (GAEFT). Check
- BP
- Weight
- Urinalysis
- Signs of oedema and other complications
- Check medication compliance

No Concerns

Follow up before **Day 28** of treatment by General Paediatrician/SPIN Nephrologist (Grace Ehidiamhen - GE)

No concerns

Review in clinic before Day 56

Follow up routinely for 6 months
If relapse refer to SPIN nephrologist (GE)

Yes Concerns

Discuss with Consultant on call /SPIN Nephrologist (GE)

Yes Concerns

Discuss with /Refer to SPIN Nephrologist (GE)/Paediatric Nephrologist
Newly diagnosed nephrotic patients can be followed up by the admitting General Paediatrician or Nephrology SPIN Paediatrician. Referral to SPIN Nephrology Paediatrician (GE) is required if they relapse at any point.

Cortisol level or Synacthen test is not required before stopping steroids in the standard treatment regime.

ROUTINE IMMUNISATIONS IN NEPHROTIC SYNDROME

Children with nephrotic syndrome should receive routine vaccinations according to the schedule

Live vaccines should not be administered to children who are immunosuppressed as defined below. These are children who are receiving or have received in the last 3 months

- a. Prednisolone 2mg/kg/day for >1 week
- b. Prednisolone 1 mg/kg/day (40mg/m² alternate days) for 1 month
- c. Lower doses of prednisolone combined with cytotoxic drugs
- d. Long term lower dose immunosuppression

**Chicken pox contact**

- a. All children with nephrotic syndrome who are varicella non immune should be vaccinated against chicken pox at the first opportunity of their being non immunosuppressed

- b. Non-immune children who have close contact with chicken pox (household or same school) may require post exposure treatment with Acyclovir – “For those identified as susceptible, and who would otherwise be offered VZIG, antivirals (oral aciclovir or valaciclovir) should be given from day 7 to day 14 after exposure. The day of exposure is defined as the date of the rash if the index is a household contact and date of first or only contact if the exposure is on multiple or single occasion(s) respectively” – PHE Aug 2018.

- c. If the patient presents after day 7 of exposure, a 7 day course of antivirals can be started up to day 14 after exposure, if necessary.
4. References


7. Nottingham University Hospital Clinical guideline for the Management of Nephrotic Syndrome. Revised September 2017

8. Public Health England - Updated restrictions on use of Varicella Zoster Immunoglobulin (VZIG) during supply shortage: advice to health professionals. August 2018