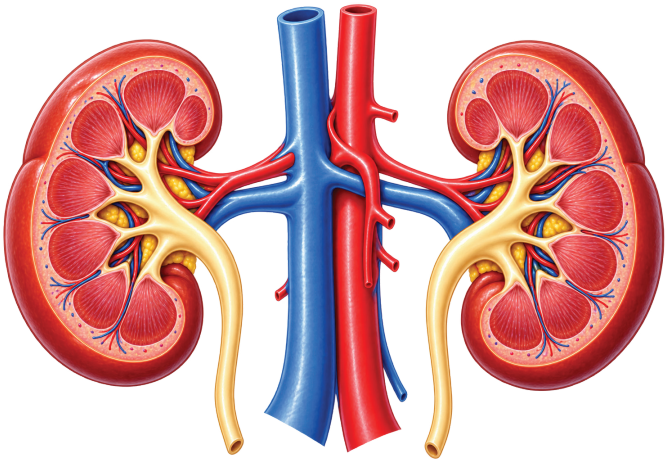
Nephrotic Syndrome

STG-020

Standard Treatment Guideline (STG)



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Rationale for Developing Standard Treatment Guidelines for Paediatric Nephrology

Standard Treatment Guidelines (STGs) for Paediatric Nephrology are essential to ensure safe, evidence-based, ethical, and standardized care for children with kidney and urinary tract disorders in Nepal. Variations in healthcare infrastructure, human resources, diagnostic facilities, and access to specialized nephrology services across the country necessitate nationally standardized clinical guidance.

These guidelines will provide a practical framework for paediatricians, paediatric nephrologists, medical officers, residents, nurses, and other healthcare professionals to make timely, consistent, and appropriate clinical decisions, particularly in resource-limited settings. They will promote standardized approaches to early recognition, diagnosis, risk assessment, stabilization, management, referral, and follow-up of paediatric renal conditions.

The STGs will reinforce adherence to the Nepal Medical Council's Code of Ethics and Professional Conduct by promoting professional competence, patient safety, informed consent, appropriate documentation, communication, and accountability. Nationally accepted standards will help reduce unwarranted variations in practice, prevent avoidable errors, support defensible clinical decision-making, and promote rational utilization of available resources.

As practical bedside and training resources, the guidelines will strengthen multidisciplinary communication, clinical training, quality assurance, clinical audit, and continuing professional development. Their adoption will strengthen clinical governance, promote equitable access to quality paediatric nephrology services, facilitate timely referral, and ultimately improve outcomes and reduce preventable morbidity and mortality among children with kidney diseases.

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Introduction and Definition

- **Nephrotic syndrome**: Nephrotic range proteinuria and either hypoalbuminaemia (serum albumin <3g/dL) or oedema (in case serum albumin level is not available).
- **Nephrotic range proteinuria**:
  - Spot urine protein-to-creatinine ratio ≥ 2 mg/mg or urine protein ≥ 3+ in the first morning void urine sample; or
  - 24-hour urine protein ≥40 mg/m^2/hour or ≥1000mg/m^2/day

Evaluation at initial episode

- Urine analysis (protein, RBC, WBC)
- Spot urine protein-to-creatinine ratio (PCR) or 24-hour urine protein
- Serum albumin
- Urea, creatinine, Na^+, K^+
- Complete blood counts
- Tuberculin test
- Serum total cholesterol
- Chest x-ray*
- Renal ultrasonography*
- Serum complement C3*, C4*, Antinuclear antigen (ANA)*
- HBsAg*, HCV*
- Anti-streptolysin O titre (ASO)*

*Additional investigations depending on clinical scenario.

Definitions

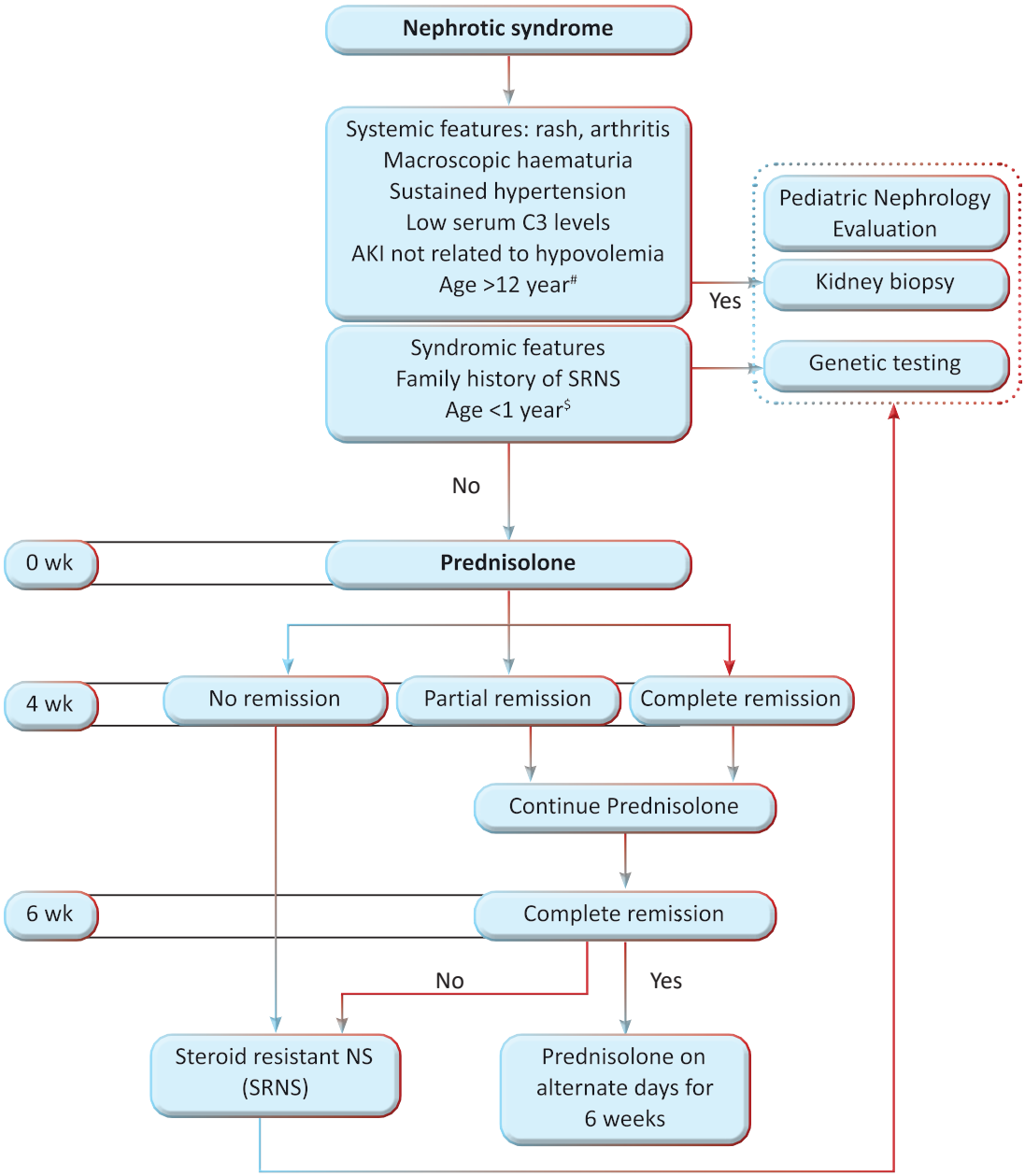
- **Complete Remission**: Spot urine protein-to-creatinine ratio <0.2 mg/mg based on first morning void urine specimens, or 24-hour urine protein <100mg/m^2/day, respectively OR urine protein is nil or trace based on first morning void urine specimens on three or more consecutive days.
- **Partial Remission:** Spot urine protein-to-creatinine ratio > 0.2 mg/mg but < 2 mg/mg based on first morning void urine, or 24-hour urine protein >100mg/m^2/day but <1000mg/m^2/day, and serum albumin ≥ 3 g/dL.
- **Steroid sensitive nephrotic syndrome:** Complete remission within 4 weeks of prednisolone at standard dose (60 mg/m^2/day or 2 mg/kg/day, maximum 60 mg/day).

- **Steroid sensitive nephrotic syndrome late responder:** A patient achieving complete remission during the confirmation period (i.e. between 4 and 6 weeks of prednisolone at standard dose) for new onset nephrotic syndrome.
- **Steroid resistant nephrotic syndrome:** Lack of complete remission within 4 weeks of treatment with prednisolone at standard dose, OR lack of complete remission by 6 weeks in children who had achieved partial remission at 4 weeks with prednisolone at standard dose.
- **Relapse**: Urine dipstick ≥ 3+ or spot urine protein-to-creatinine ratio ≥ 2 mg/mg based on first void urine specimens, with or without oedema for 3 consecutive days, having been in complete remission previously
- **Infrequent relapses**: < 2 relapses in the 6 months following remission of the initial episode or fewer than 3 relapses in any subsequent 12-month period
- **Frequent relapses**: ≥ 2 relapses in the first 6-months following remission of the initial episode or ≥ 3 relapses in any 12-month period
- **Steroid dependence**: A patient with SSNS who experiences 2 consecutive relapses during recommended prednisolone therapy for first presentation or relapse, or within 14 days of its discontinuation.
- **Sustained remission**: No relapses over 12 months with or without therapy.
- **Steroid toxicity:**
    - New or worsening obesity/overweight, sustained hypertension, hyperglycaemia
    - Behavioural/psychiatric disorders, sleep disruption
    - Impaired statural growth (height velocity < 25th percentile and/or height < 3rd percentile) in a child with normal growth before start of steroid treatment
    - Cushingoid features, striae rubrae/distensile, glaucoma, cataract, avascular necrosis
- **Complicated relapse**: A relapse requiring hospitalization due to one or more of the following: severe oedema, symptomatic hypovolemia or AKI requiring IV albumin infusions, thrombosis, or severe infections (e.g., sepsis, peritonitis, pneumonia, cellulitis).
- **Difficult-to-treat steroid sensitive disease:** Both of the following i) frequent relapses, or significant steroid toxicity with infrequent relapses, and ii) failure of ≥ 2 steroid sparing agents.

Treatment of first episode of nephrotic syndrome:

Prednisolone at a dose of 60 mg/m^2/day (2 mg/kg/day, maximum 60 mg in 1–2 divided doses) for 6 weeks; followed by 40 mg/m^2 (1.5 mg/kg, maximum 40 mg as single morning dose) on alternate days for the next 6 weeks

Figure 1: Treatment algorithm for children with nephrotic syndrome



[#] In children of age >12 years, treatment with prednisolone may be initiated in absence of atypical features. However, kidney biopsy is recommended in the presence of atypical features or steroid resistance.

[$] Genetic testing primarily (if available) or kidney biopsy (if genetic testing not available) is recommended in age <3 months; and an individualized approach in genetic testing and/or kidney biopsy should be considered in age 3–12 months age.

Treatment of relapses:

Prednisolone at 60 mg/m^2/day (2 mg/kg/day; maximum 60 mg) in single or divided-doses until remission; followed by 40 mg/m^2 (1.5 mg/kg, maximum 40 mg) on alternate days for 4 weeks.

Infections should be screened and treated if present before initiating prednisolone during relapses.

Treatment of frequently relapsing or steroid dependent nephrotic syndrome

Frequent relapses or steroid dependent nephrotic syndrome are treated as outlined in Figure 2 and Table 1.
However, the choice of drugs should be guided by *availability*, *tolerability, affordability* and *patient preferences*.

Figure 2: Treatment algorithm for children with frequent relapses or steroid dependence

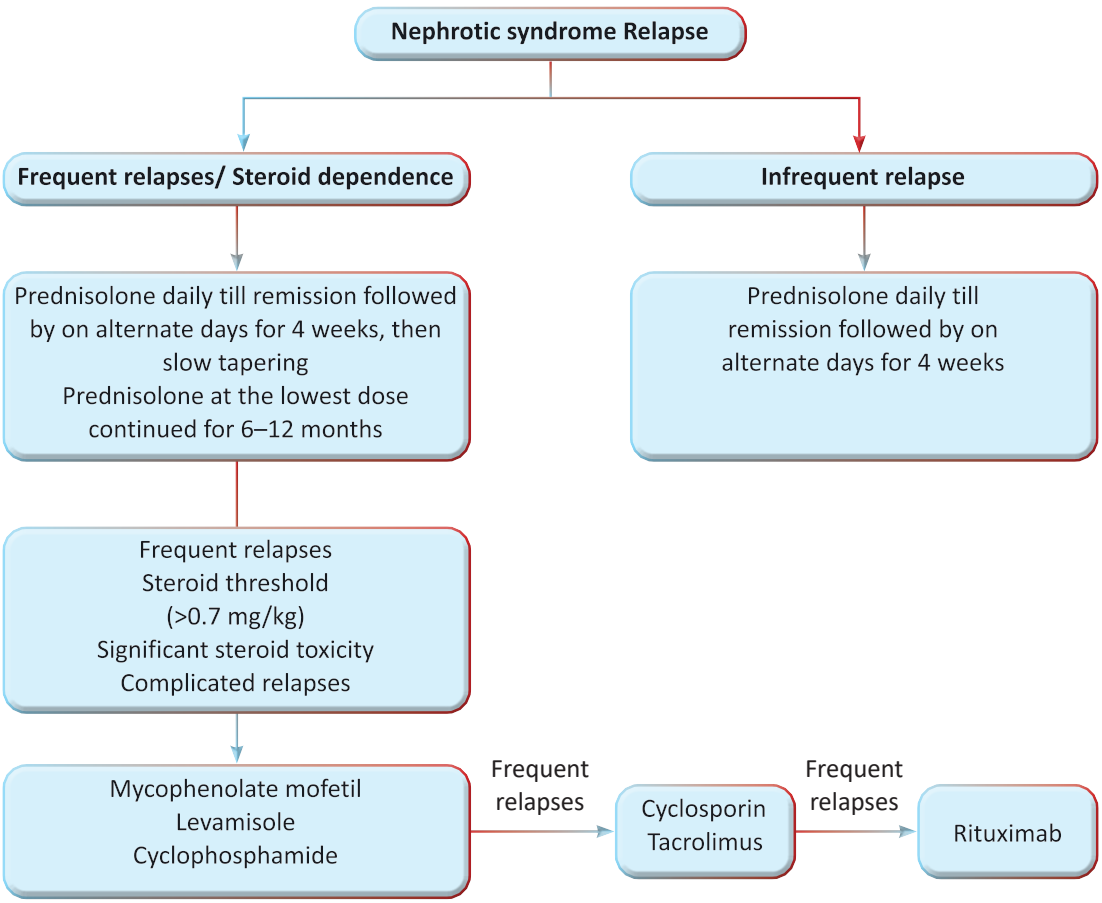


Table 1: Drugs used to treat frequent relapses or steroid dependence

Drug	Dose	Duration
Prednisolone	0.5–0.7 mg/kg on alternate days; oral	6–12 months
Levamisole	2–2.5 mg/kg on alternate days; oral	2–3 years
Cyclophosphamide	2–2.5 mg/kg/day; oral	8–12 weeks
Mycophenolate mofetil	600–1200 mg/m^2/day in divided doses; oral	2–3 years
Cyclosporin	4–5 mg/kg/day in divided doses; oral	2–-3 years
Tacrolimus	0.1–0.2 mg/kg/day in divided doses; oral	2–3 years
Rituximab	375 mg/m^2; slow IV infusion	2 doses, 1 week apart

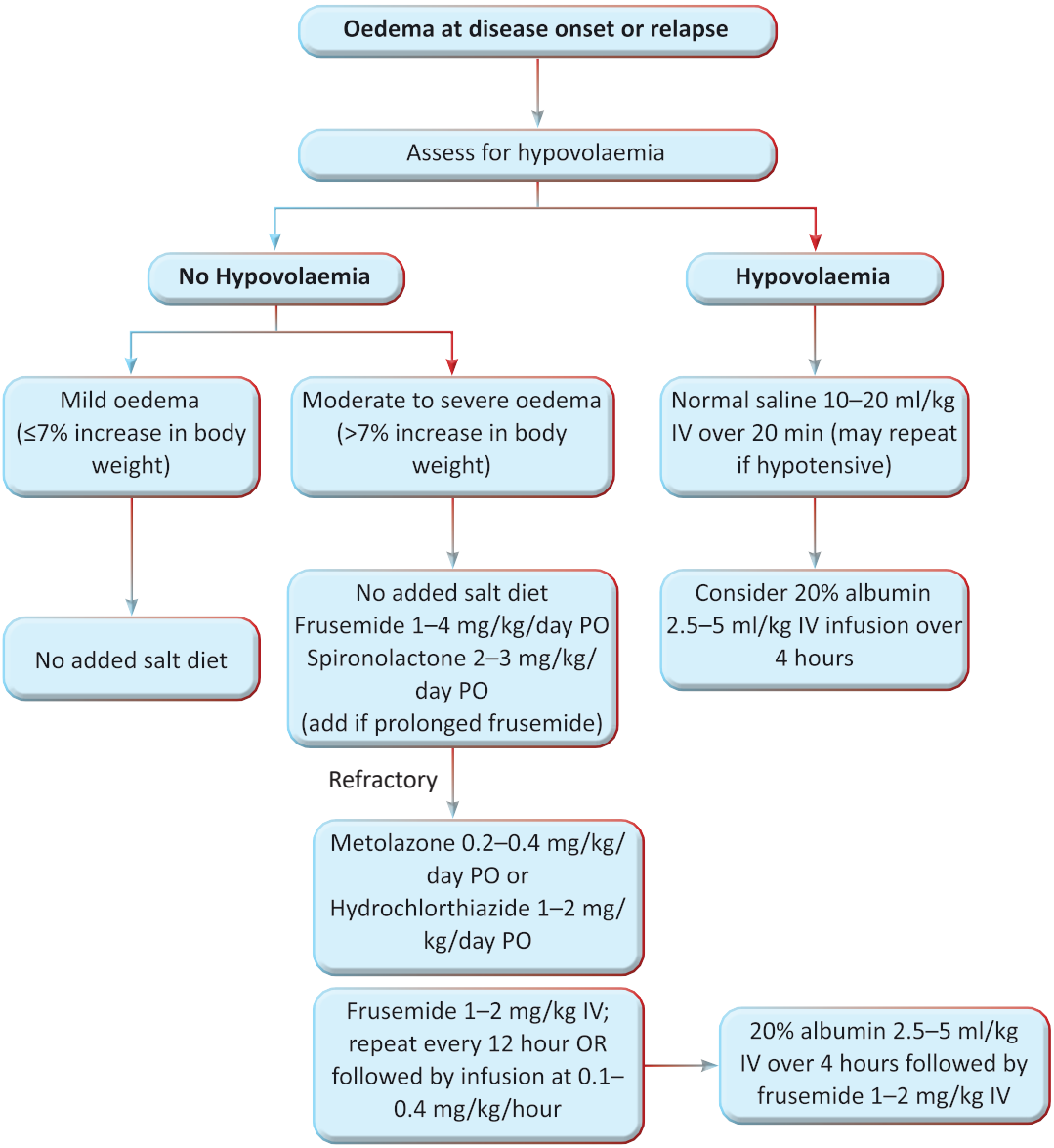
Short course steroid for prevention of relapses at onset of infection

- Routine use of short course of daily steroid therapy is not recommended at onset of infections if child is not on steroid therapy.
- Consider use of a short course of steroid (low daily dose prednisolone 0.5 mg/kg) at onset of an upper respiratory tract infection in selected children who have repeated infection-associated relapses.

Management of oedema

Figure 3: Management algorithm for treatment of oedema

(adapted from Reference 1)



Immunization

Refer to recommendations as per NEPAS Immunization guidelines.

Prevention of thrombosis

- Avoid immobilization and maintain intravascular volume during acute nephrotic state.
- Preventive anticoagulation routinely is not recommended.

Referral to Paediatric nephrology

Referral to a paediatric nephrologist is recommended in case of:

- Presence of atypical features not consistent with idiopathic nephrotic syndrome (microscopic or macroscopic haematuria, sustained hypertension, AKI not attributable to hypovolemia, systemic features)
- Congenital or infantile onset nephrotic syndrome
- Positive family history of nephrotic syndrome
- Age at onset of nephrotic syndrome >12 years
- Secondary nephrotic syndrome
- Steroid resistant nephrotic syndrome
- Steroid sensitive nephrotic syndrome late responder
- Frequently relapsing or steroid dependent nephrotic syndrome
- Steroid sensitive nephrotic syndrome with drug toxicities or complicated relapse

References

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2. Tautmann A, Boyer O, Hodson E, et al. IPNA clinical practice recommendations for the diagnosis and management of children with steroid-sensitive nephrotic syndrome. Pediatric Nephrology. 2023;38: 877-919.
3. Kidney Disease: Improving Global Outcomes (KDIGO) Nephrotic Syndrome In Children Work Group; Floege J, Gibson KL, Vivarelli M, Liew A, Radhakrishnan J, Rovin BH. KDIGO 2025 Clinical Practice Guideline for the Management of Nephrotic Syndrome in Children. Kidney Int. 2025;107(5S):S241-S289.