New Onset Nephrotic Syndrome

Inpatient, Outpatient, Urgent Care & Emergency Department

Nationwide Children's — When your child needs a hospital, everything matters.

Center for Clinical Excellence

Inclusion Criteria

Patients < 21 years of age with pitting edema and proteinuria ≥ 3+ (> 300mg/dL) on urine dipstick or urine protein/creatinine ratio ≥ 2mg/mg

Exclusion Criteria

- Prior episodes of nephrotic syndrome
- Concern for heart failure
- Congenital Heart Disease
- Malignancy
- Known autoimmune disease
- Chronic kidney disease

Criteria for direct admission

- Hemodynamically stable
- Not hypertensive for age
- Normal mental status
- Afebrile
- Headache not present
- Serum sodium > 129 (if available)
- No respiratory distress

Clinical manifestations* of possible new onset nephrotic syndrome?

No → **Off Pathway** Consider Differential Diagnosis

Yes → **Obtain urine dipstick**

Proteinuria ≥ 3+ on urine dipstick and edema?

No → **Off Pathway** Consider Differential Diagnosis

Yes → **Consult Nephrology**

Is patient in Primary Care Clinic or Urgent Care?

Yes → **Does patient meet criteria for direct admission?**

Yes → **Admit All Patents with New Onset Nephrotic Syndrome to Nephrology Service**

Labs to be obtained as inpatient

Inpatient Management

No → Refer / Transfer to Main Campus ED

No → **Place IV**

Obtain labs

- CMP
- Urinalysis (UA) *if not already obtained*
- Lipid panel
- C3/C4
- CBC
- Urine protein to creatinine ratio
- Serum 25 hydroxy vitamin D
- TSH, Free T4

CMP and formal UA are the only labs that need to be resulted prior to admission

Admit All Patents with New Onset Nephrotic Syndrome to Nephrology Service

Inpatient Management

***Clinical Manifestations**

- Non-erythematous, soft, pitting edema (typically periorbital edema noticed first) that is gravity dependent
- Anasarca (generalized and massive edema)
- Non-specific symptoms including headache, irritability, malaise, fatigue

Definitions & Diagnosis

Complications of nephrotic syndrome

Definitions & Diagnosis

- **Nephrotic range proteinuria:** Protein to Creatinine Ratio (PCR) ≥2mg/mg (or urine protein dip at least 3+ dipstick)
- **Hypoalbuminemia:** serum albumin < 3.0 g/dL
- **Nephrotic Syndrome:** Nephrotic range proteinuria and either hypoalbuminemia or edema (when albumin is not available)

Typical Urine dipstick results are expressed semi quantitatively as follows, or as stated by manufacturer:

- Negative: 0 to < 15 mg/dL
- Trace: 15 to < 30 mg/dL
- 1+: 30 to < 100 mg/dL
- 2+: 100 to < 300 mg/dL
- 3+: 300 to < 1000 mg/dL
- 4+: ≥ 1000 mg/dL

Initial Evaluation

Inpatient Management

Differential Diagnosis

Alternate causes of edema
- Heart failure
- Angioedema
- Lymphatic dysfunction/obstruction
- Medications: Calcium channel blockers, Minoxidil
- Hypothyroidism

Alternate causes of hypoalbuminemia
- Liver disease
- Protein losing enteropathy
- Severe malnutrition

Increased capillary permeability

Initial Evaluation

Inpatient Management

Inpatient Management

Standard Evaluation

Infection:
- Quantiferon-TB Gold
- Hep B/C antibodies panel
- HIV 1 & 2 Ab/Ag screen

Renal function:
- Blood CMP (Q AM)
- Urine Na, K, Cr, NGAL

Imaging:
- Kidney US

Renal biopsy indications

< 6 months old or concern for autoimmune disease?

Yes

Additional Evaluation for Special Populations

< 6 months old:
- CMV PCR, Quantitative
- EBV PCR, Quantitative
- RPR
- Prevention Genetics Nephrotic Syndrome Panel (test code 10417)

Additional history for < 6 month old:
- Maternal creatinine and maternal UA for proteinuria (if obtained during pregnancy)
- Family history
- Infant birthweight and length
- Gestational age
- Placental abnormalities

Concern for Autoimmune Disease:
- ANA
- Crithidia
- ENA (SSA-SSB)
- ENA (sm, RNP) (aka SMITH)

No

Standard Management

- Initiate vaccine series if under vaccinated prior to immunosuppression
  - Influenza
  - Pneumococcal 13/15 and/or 23 valent
  - Consider COVID vaccination
- Prednisone 2 mg/kg (max 60 mg/dose) PO Q day **OR** Methylprednisolone 2 mg/kg (max 60 mg/dose) IV Q day
- Low sodium diet
- Daily weights
- Daily urine testing
- Consider GI prophylaxis with famotidine 0.5 mg/kg IV/PO BID (max 20 mg/dose)

Optional Management

25% albumin IV (0.5-1 gram/kg) max 50 grams **&**
IV furosemide 1-2 mg/kg (max 40 mg)

Consults
- Clinical Nutrition
- Social work
- Psychology
- Nephrology Research Team
- Nephrology nurses for nephrotic syndrome teaching
- Partners for Kids (care coordination consult)

Discharge Criteria
- Testing and education completed
- Tolerating oral steroids
- Patient has stabile weight and is not symptomatic from edema.

Symptoms related to edema include: difficulty ambulating, extremity pain, genital pain, labored breathing.

Discharge Instructions, Medications & Follow-up

Epic Tools

- ED/UC Order Panel/Order Set
- AMB Smart Set
- IP Order Set

Initial Evaluation

Inpatient Management

Indications for Renal Biopsy

- New onset nephrotic syndrome ≥ 12 years of age
- High index of suspicion for a different underlying pathology (macroscopic hematuria, extra-kidney symptoms, hypocomplementemia)
- AKI at onset not related to hypovolemia

Initial Evaluation

Inpatient Management

Complications of Nephrotic Syndrome

Infection

Increased risk of developing serious bacterial infection, especially with encapsulated bacteria:

- Pneumonia
- Empyema
- Peritonitis
- Sepsis (see Sepsis Clinical Pathway)
- Meningitis
- Cellulitis

Increased risk for more severe common viral infections

Varicella may be observed in patients receiving immunosuppressive therapy

Thromboembolism

Patient with nephrotic syndrome are hypercoagulable and at risk for:

- Pulmonary Embolism (see Pulmonary Embolism Clinical Pathway)
- Renal Vein Thrombosis
- Sagital Sinus Thrombosis
- DVT
- Catheter-associated thrombosis

Renal insufficiency due to hypovolemia, acute kidney injury or underlying glomerular pathology

Intravascular Depletion / Hypovolemia despite an increase in extracellular fluid volume

Hypertension

Fluid overload

- Pleural effusions
- Pulmonary edema
- Anasarca

Electrolyte abnormalities

- Hyponatremia
- Hypocalcemia (ensure to correct for level of serum albumin)

Initial Evaluation

Inpatient Management

Discharge

Medications:
- Prednisone 2 mg/kg (max 60 mg) daily x 6 weeks, then 1.5 mg/kg (max 40 mg) QOD x 6 weeks
- Famotidine 0.5 mg/kg BID (max 20 mg/dose)
- Albustix Reagent Misc Strip – Dispense 1 bottle
- Dispense 3 urine cups
- Oral Lasix if needed

Nursing follow-up:
Nephrology clinic nurses to call family weekly while on daily Prednisone dosing and every 2 weeks while on alternate day treatment

Clinic follow-up:
- 1-2 weeks after hospital discharge – coordinate nutrition consult with this visit
- 6-7 weeks after hospital discharge
- 12-13 weeks after hospital discharge

Family instructions:
- Continue Prednisone as prescribed until next clinic visit
- Test urine daily at home and record urine protein
- Record daily weight
- Call nephrology nurse when urine protein is negative or trace x 3 days
- Call nephrology nurse if your child develops fever (≥ 38.0 / 100.4), abdominal pain, blood in urine, trouble breathing, severe headache, worsened swelling, vision changes, or decreased urinary output (no urine output in 24 hours)

Initial Evaluation

Inpatient Management

Quality Measures

Goals:
- Decrease annual nephrotic syndrome relapse rates.
- Reduce complications of nephrotic syndrome.
- Decrease repeat hospitalizations after initial diagnosis.

Process Measures:
- Use of ED/UC Order Panel/Order Set
- Use of AMB Smart Set
- Use of IP Order Set

Outcomes Measures:
- ED/UC LOS
- IP LOS
- Minimize annual nephrotic syndrome relapse rates

Balancing Measure:
7 and 30 day readmission rates

Initial Evaluation

Inpatient Management

References

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Initial Evaluation

Inpatient Management

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Clinical Pathway Development

This clinical pathway was developed using the process described in the NCH Clinical Pathway Development Manual Version 6, 2022. Clinical Pathways at Nationwide Children's Hospital (NCH) are standards which provide general guidance to clinicians. Patient choice, clinician judgment, and other relevant factors in diagnosing and treating patients remain central to the selection of diagnostic tests and therapy. The ordering provider assumes all risks associates with care decisions. NCH assumes no responsibility for any adverse consequences, errors, or omissions that may arise from the use or reliance on these guidelines. NCH's clinical pathways are reviewed periodically for consistency with new evidence; however, new developments may not be represented, and NCH makes no guarantees, representations, or warranties with respect to the information provided in this clinical pathway.

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