Glomerulonephritis (acute) in Children



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Introduction and Who Guideline applies to

This guideline describes the assessment and management of children and young people presenting with acute glomerulonephritis

This guideline applies to Children and young people under 18 years of age with glomerulonephritis within the EMEESY Children's Kidney Network (East Midlands, East of England and South Yorkshire) being managed by the Leicester Children's Hospital and the Paediatric Emergency Department.

Other related guidelines include:

Hypertension UHL Childrens Medical Guideline UHL Trust ref: E8/2020 Abnormal Glomerular Filtration Rate UHL Childrens Medical Guideline E6/2020 Nephrotic Syndrome UHL Childrens Medical Guideline UHL Trust ref: E4/2019 Fluid Electrolyte Management UHL Childrens Hospital Guideline UHL Trust ref: C6/2015

This EMEESY network guideline has been developed by clinicians from Nottingham Children's Renal Unit with consultation across the network including from the Leicester Royal Infirmary and has been ratified by the Leicester Children's Hospital guideline process.

Glomerulonephritis (Acute)

| Title of Guideline (must include the word | | Guideline for the assessment and | | |
|---|--------------------|---|--|--|
| etc) | | children and young people | | |
| Contact Name and Job Title (author) | | Dr A Lunn. Consultant Paediatric Nephrologist, | | |
| Directorate & Speciality | | Directorate: Family Health – Children Speciality: | | |
| · · | | Renal | | |
| Date of submission | | November 2022 | | |
| Date on which guideline must be reviewed | (one | November 2027 | | |
| to five years) | | | | |
| Explicit definition of patient group to which | it | Children and young people under 18 years age | | |
| applies (e.g. inclusion and exclusion criteria | а, | with acute giomerulonephritis | | |
| diagnosis) | | This guideling describes the assessment and | | |
| ADSITACI | l | management of children and young people | | |
| | l | presenting with acute domerulonephritis | | |
| Kev Words | | Nephritic syndrome, glomerulonephritis. | | |
| | l | haematuria, renal, child, young person | | |
| Statement of the evidence base of the guid | leline - | - has the guideline been peer reviewed by | | |
| colleagues? | | | | |
| 1a meta analysis of randomised | | | | |
| controlled trials | | | | |
| 2a at least one well-designed | YES | | | |
| controlled study without | | | | |
| randomisation | | | | |
| 2b at least one other type of well- | | | | |
| designed quasi-experimental study | ── | | | |
| 3 Well – designed non-experimental descriptive studies (ie comparative / | | | | |
| correlation and case studies) | | | | |
| 4 expert committee reports or | | | | |
| opinions and / or clinical | | | | |
| experiences of respected | | | | |
| authorities | | | | |
| 5 recommended best practise based | | | | |
| on the clinical experience of the | | | | |
| guideline developer | | | | |
| Consultation Process | l | Paediatric Nephrologists, Paediatric Guidelines | | |
| | I | Group, Pharmacist, Microbiologist, | | |
| | I | Immunologist | | |
| | I | EMEESY guideline group – Leicester and | | |
| Targat audience | | Clinicians and healthcare professionals caring | | |
| Talger audience | I | for children and young people with acute | | |
| | alomerulonephritis | | | |
| This guideline has been registered with | the tru | ust However, clinical guidelines are | | |
| guidelines only. The interpretation and application of clinical guidelines will remain the | | | | |
| responsibility of the individual clinician. If in doubt contact a senior colleague or expert. | | | | |
| Caution is advised when using guidelines after the review date | | | | |

Glomerulonephritis (acute) in children

V2 approved by UHL Policy and Guideline Committee on 20 January 2023 Trust Ref: E5/2019 Next Review: April 2026 NB: Paper copies of this document may not be most recent version. The definitive version is held on InSite in the Policies and Guidelines Library

Document Control

| Version | Issue Date | Author | |
|---------|---------------|--|--|
| | November 2002 | | |
| | December 2004 | Dr M Christian | |
| | December 2007 | Dr J Evans | |
| V3 | March 2011 | Dr M Christian | |
| V4 | March 2013 | Dr C Langstaff | |
| V5 | May 2016 | Dr A Lunn | |
| V6 | July 2017 | Dr A Lunn | |
| V7 | May 2022 | Dr Hesham Shafik – Trust Grade Registrar | |
| | | Dr A Lunn – Consultant Nephrologist | |

Document Amendment Record

General Notes:

Summary of changes for the new version:

- 1. New time course of clinical manifestations of acute post-streptococcal glomerulonephritis.
- 2. Lifestyle modifications added as part of HTN management.
- 3. Modified the dose and use of Nifedipine for treating HTN as per the new HTN guideline.
- 4. Hint added about using ACEIs after referral to nephrology team.
- 5. Appendix added for other bacterial related GN.
- 6. References updated.

1. Background

Acute glomerulonephritis (GN) develops because of the abrupt onset of glomerular injury and inflammation that leads to a decline in glomerular filtration rate with sodium and water retention. Urinalysis usually reveals red blood cells (with red blood cell casts if the sample is very fresh) and sometimes low-level proteinuria.

Patients may present with:

- Macroscopic or microscopic haematuria
- Signs of fluid overload such as hypertension and oedema
- Renal dysfunction.

In the paediatric age group, the most common cause (about 80% of cases) is acute post-infection glomerulonephritis (APSGN). Streptococcal infections represent most of this post-infectious acute GN; other infections include Staphylococcus aureus or Staphylococcus epidermidis and gram-negative bacteria.

APSGN may occur at any age but is most common between the ages of 2 and 15 years (median age at presentation is 6 – 8 yrs. old).¹ APSGN typically follows either pharyngeal or, less commonly, skin infection with group A streptococcus. The symptoms usually develop:

- 1-2 weeks after a throat infection (Pharyngitis).
- Alternatively, 3 6 weeks after skin infection (Impetigo).

The prognosis for APSGN is good, with 95% of patients making a full recovery, with most clinical symptoms resolving spontaneously within 2 - 3 weeks after onset.²

Time course of clinical manifestations of acute post-streptococcal glomerulonephritis².



Other causes of acute glomerulonephritis have a less good prognosis and should be referred to a Paediatric Nephrologist. Criteria for referral can be found in section 2.3

See <u>appendix 2</u> for other bacterial related GN.

The differential diagnoses include^{2,3}:

| Disease | Associated features |
|--|---|
| IgA nephropathy | Normal C3 |
| Membranoproliferative | Persisting low C3 and proteinuria beyond |
| glomerulonephritis (MPGN) | 3 months |
| Vasculitides especially: | Often systemic symptoms e.g., General |
| | malaise, weight loss |
| IgA Vasculitis – see HSP | Purpuric rash especially on dependent |
| guideline, may not need referral | and pressure areas, arthropathy |
| to nephrologist | especially of the lower limbs |
| Systemic Lupus | Butterfly rash, photosensitive rash, |
| Erythematosus (SLE) | arthropathy, Raynaud's phenomenon, |
| | alopecia, pleuritis |
| ANCA positive vasculitis | Involvement of respiratory system e.g., |
| | Nasal ulceration, sinusitis, haemoptysis, |
| | cough |
| Alport Syndrome | May have a family history of deafness or |
| | renal disease (usually x-linked dominant) |

2. Management of Initial Episode

Most children will require admission to manage fluid overload, oliguria, hypertension or worsening renal dysfunction.

2.1. Clinical history

To include a history of:

- Recent throat or skin infection (up to 6 weeks previously)
- Previous episodes of macroscopic haematuria (IgA, Alport syndrome, MPGN, SLE, ANCA positive vasculitis)
- Joint pains and swelling (HSP, SLE, ANCA positive vasculitis)
- Family history of renal disease or deafness (Alport syndrome)

2.2. Clinical examination

To include:

- Height, weight, estimated body surface area (an estimate of dry weight will give a more accurate surface area estimate)
- Blood pressure
- Assessment of oedema (usually mild lower limb, sacral, ascites, scrotal, pleural effusions)
- Cardiovascular status and perfusion (volume status):
 - Indicators of fluid overload: tachycardia, hypertension, respiratory distress, warm peripheries, hepatomegaly, raised JVP
 - Indicators of hypovolaemia: tachycardia, hypotension, cool peripheries, delayed capillary refill time
- Examination of the whole body for rashes (esp. lower limbs for purpura of HSP and face for butterfly rash of SLE)

2.3. Investigations

(A) Urine for:

- Dipstick urinalysis
- Urine culture
- Urine microscopy for casts (often not seen unless extremely fresh specimen)
- Urine protein: creatinine ratio (confirm with early morning specimen)

(B) Blood for:

- Paediatric renal profile to include urea, electrolytes, creatinine, calcium, phosphate, chloride, bicarbonate, and albumin
- Full blood count
- Antistreptolysin titre (ASOT)
- Ask lab to store blood for Anti-DNase B titres if ASOT negative
- C3 and C4 levels
- Anti-nuclear antibody (ANA)

(C) Throat or skin (if infected) swab

(D) CXR if hypertensive or fluid overloaded

Discuss with Consultant Paediatric Nephrologist cases with:

- estimated GFR <90 ml/min/1.73m² see Appendix 1
- electrolyte imbalance (especially hyperkalaemia)
- hypertension
- nephrotic syndrome or protein: creatinine ratio >50 mg/mmol
- normal C3 and/or low C4 (low C3 would be consistent with PIGN)
- signs/results suggestive of systemic vasculitis (rash, arthralgia, other organ involvement, positive ANA)

Further investigations to consider after discussion:

- Renal Ultrasound
- Anti-neutrophil cytoplasmic antibody (ANCA), anti-glomerular basement membrane antibody (anti-GBM antibody) if renal dysfunction or signs suggestive of vasculitis
- General viral titres plus Hep B and C, HIV, Hantavirus
- C1q and C1q antibodies if SLE suspected
- Cryoglobulin titre (cryoglobulinemia is a small vessel vasculitis, rare in childhood, associated with chronic infections especially hepatitis C, autoimmune disorders, and B-cell lymphoproliferative diseases)

2.4. Management

Post streptococcal acute glomerulonephritis usually remits spontaneously and treatment is supportive only. Children without fluid overload, hypertension or electrolyte imbalance may be managed as outpatients providing they are reviewed frequently. Initially children should be followed up within a week after their initial presentation. Further follow up will depend on their clinical course.

Information for parents about glomerulonephritis, haematuria and HSP are available on the Infokid website from this link: <u>https://www.infokid.org.uk/conditions</u>

2.4.1. Antibiotics

This does not alter the natural history of the disease but prevents the spread of nephritogenic strains of group A streptococcus.

Phenoxymethyl Penicillin:

Doses are as follows:

1 – 5 yr. 125 mg four times a day for 10 days

6 – 11 yr. 250 mg four times a day for 10 days

12 - 17 yr. 500 mg four times a day for 10 days

If Pencillin allergic use Clarithromycin:

Doses are as follows:

1 month - 11 yr (body-weight up to 8kg) 7.5mg/kg twice daily for 10 days

1 month – 11 yr (body-weight 8-11kg) 62.5mg twice daily for 10 days

1 month – 11 yr (body-weight 12-19kg) 125mg twice daily for 10 days

1 month – 11 yr (body-weight 20-29kg) 187.5mg twice daily for 10 days

1 month – 11 yr (body-weight 30-40kg) 250mg twice daily for 10 days

12 - 17 yr. 250 mg twice daily for 10 days

2.4.2 Fluid Balance

- Fluid input and urine output should be closely monitored.
- All children should be weighed daily.
- All patients should be on a no added salt diet.
- If oliguric (<0.5 ml/kg/hr) restrict fluid input to replacement of insensible losses (400 ml/m²/day) plus
 previous days urine output
- If overloaded (i.e., Hypertensive, raised JVP, oedematous) give furosemide 1 2 mg/kg up to twice daily to induce a negative fluid balance.

2.4.3 Hypertension (i.e., BP > 95% centile - see hypertension guideline for normal ranges and further advice) – discuss with a paediatric nephrologist

- Treat fluid overload which is the usual cause (see above)
- If euvolemic, use Amlodipine (starting dose 100 200 mcg/kg once daily)

+/-Nifedipine PRN you immediate control of elevated BP if want (Up 250 microgram/kg Max 5mg). Note small frequent doses are safest. to Please also note that blood pressure may rebound after Nifedipine use, so not suitable for long term management.

Do not use ACE inhibitors as these can reduce renal function. ACEIs may be considered in special circumstances when proteinuria with HTN is present but this will be after a referral to the nephrology team. Beta-blockers can exacerbate hyperkalaemia.

2.4.4 Hyperkalaemia – see Fluid Electrolyte Management UHL Childrens Hospital Guideline

2.4.5 Lifestyle modifications – Employ these in all patients with GN as synergistic means for improving control of HTN and proteinuria.

- Restrict daily sodium no added salt
 - Normalize weight
 - Exercise regularly

3. Prognosis and follow up

3.1 Prognosis

95% of patients with post-streptococcal glomerulonephritis will make a complete recovery, however, a small proportion will develop rapidly progressive glomerulonephritis.³ If renal function is satisfactory and improving and the patient is normotensive, an early discharge should be possible with early and regular outpatient follow up.

3.2 Follow up pathway and indications for referral to paediatric nephrology service:



4. Audit points

- 1. Are investigations undertaken as per guidelines?
- 2. Are referrals made to paediatric nephrology appropriate and at the correct time?
- 3. Has the patient been offered written information about the condition?

5. Supporting References

1. Eison TM, Ault BH, Jones DP, Chesney RW, Wyatt RJ. (2011) Post-streptococcal acute glomerulonephritis in children: clinical features and pathogenisis. *Pediatric Nephrology*; **26**: 165 – 180

2. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases

3. Smith JM, Faizan MK, Eddy AA. The child with acute nephritic syndrome. In Webb NJA, Postlethwaite RJ, eds. Clinical Paediatric Nephrology (3rd Edition), pp 367-379. Oxford: Oxford University Press, 2003.

4. Vehaskari VM, Aviles DH. Acute glomerulitis and rapidly progressive glomerulonephritis. In Kher KK, Schnaper HW, Makker SP, eds. Clinical Paediatric Nephrology (2nd edition) pp. 145-154. Abingdon, Oxon: Informa Healthcare, 2006.

6. Key Words

EMEESY, Nephritic syndrome, haematuria, renal, child, young person

7. Education and Training

None

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.

As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

| CONTACT AND REVIEW DETAILS | | | | | |
|--|--------------|---|--|--|--|
| Guideline Lead (Name and Title) | | e) | Executive Lead | | |
| A Hall – Associate Specialist | | | Chief Medical Officer | | |
| Details of Changes made during review: | | | | | |
| Date | Issue Number | Reviewed By | Description Of Changes (If Any) | | |
| August 2022 | 2 | NUH Children's renal services EMEESY Children's Kidney Network UHL Children's Hospital clinical guidelines group UHL Antimicrobial working party | New time course of clinical manifestations of acute post-streptococcal glomerulonephritis. Lifestyle modifications added as part of HTN management. Modified the dose and use of Nifedipine for treating HTN as per the new HTN guideline. Hint added about using ACEIs after referral to nephrology team. Appendix added for other bacterial related GN. References updated. | | |

Appendix 1 – Estimated GFR

Estimated GFR is automatically reported in all in-patients in Nottingham Children's Hospital over 2 years of age.

Where automated GFR is unavailable use the formula (Schwartz Equation):

eGFR (ml/min/1.73m²) = k x height (cm) / serum creatinine (µmol/l)

In NUH k = 36 in males \geq 13 years of age and k = 30 in all other cases.

In UHL k = 40 for both sexes and all age groups.

If a locally validated k value has not been established, then k = 40 should be used.

An eGFR of less than 90 ml/min/1.73m² requires further clinical evaluation.

Limitations:

- 1. Hypoalbuminemia and NS may lead to overestimation of true GFR due to increased tubular creatinine secretion.
- 2. Low muscle mass overestimates GFR
- 3. AKI confounds all estimates, which are valid only in steady-state

Appendix 2 – Bacterial infection-related GN

- 1. Post-streptococcal GN (OR post-bacterial)
- 2. Shunt nephritis
- 3. Endocarditis related GN
- 4. IgA dominant infection-related GN (uncommon in children)

Shunt nephritis

- Risk is highest in ventriculoarterial shunts and least in ventriculoperitoneal shunts.
- Organism culture in blood, CSF, shunt tip (usually Staph epidermidis, Staph Albus or Staph aureus)
- Outcome is good with early diagnosis and treatment of infection
- Will mostly require shunt removal and replacement
- Kidney biopsy frequently demonstrates membranoproliferative glomerulonephritis
- ANCA may be positive (ANCA natural history is unclear and may need a follow up)
- C3 is low in 50%, C4 is low in 20-30%
- Some patients may be left with a residual CKD

Endocarditis related GN

- Risk factors, history, examination, and investigations as in endocarditis + GN
- Outcome is good with prompt infection eradication (Valve replacement may be needed)