

AsPNA Clinical Practice Guidelines for the Management of Infection Related Glomerulonephritis

Jitendra Meena¹, Aditi Sinha¹, Sudarsan Krishnasamy², Agnes A. Alba³, Madiha A Aziz⁴, Afroza Begum⁵, Eugene Yu-hin Chan⁶, Jameela A Kari⁷, Anirut Pattaragarn⁸, Inoka Perera⁹, Qian Shen¹⁰, Geetika Singh¹¹, Arvind Bagga^{1,12}; on behalf of the Glomerular Disease Working Group, Asian Pediatric Nephrology Association

¹Division of Nephrology, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India

²Pediatric Nephrology Services, Department of Pediatrics, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India

³Section of Nephrology, Institute of Pediatrics, The Medical City, Meralco Avenue, Pasig City, Philippines

⁴Department of Pediatric Nephrology, Sindh Institute of Urology & Transplantation, Karachi, Pakistan

⁵Department of Pediatric Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

⁶Department of Pediatrics, The Chinese University of Hong Kong, Hong Kong.

⁷Pediatric Nephrology Center of Excellence, Department of Pediatrics, King Abdulaziz University Hospital, Jeddah, Kingdom of Saudi Arabia

⁸Division of Nephrology, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

⁹Sirimavo Bandaranayake Specialized Children's Hospital, Peradeniya, Sri Lanka

¹⁰Department of Nephrology, Children's Hospital of Fudan University, National Key Laboratory of Kidney Diseases, National Children's Medical Center, Shanghai, China

¹¹Department of Pathology, All India Institute of Medical Sciences, New Delhi, India

¹²Department of Pediatrics, Indraprastha Apollo Hospitals, Delhi, India

Correspondence Arvind Bagga, Division of Nephrology, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India; email: arvindbagga@hotmail.com

Supplementary Material

Supplementary Table S1. Search strategy

Database	Search terms	Number of results
PubMed	((((((((((children[MeSH Terms]) OR (child[MeSH Terms])) OR (pediatrics[MeSH Terms])) OR (adolescent[MeSH Terms])) OR (adolescent[Title/Abstract])) OR (child*[Title/Abstract])) OR (pediatric*[Title/Abstract])))) OR (paediatric*[Title/Abstract])) AND (((((((("Infection related glomerulonephritis"[Title/Abstract]) OR ("Postinfectious glomerulonephritis"[Title/Abstract])) OR ("Post-infectious glomerulonephritis"[Title/Abstract])) OR ("Infection-related glomerulonephritis"[Title/Abstract])) OR ("post-streptococcal glomerulonephritis"[Title/Abstract])) OR ("poststreptococcal glomerulonephritis"[Title/Abstract])) OR ("Infection-related glomerulonephritis"[Title/Abstract])) OR (IRGN[Title/Abstract])) OR (PIGN[Title/Abstract])) OR ("staphylococcal glomerulonephritis"[MeSH Terms]))	882
EMBASE	'postinfectious glomerulonephritis'/exp OR 'postinfectious glomerulonephritis' OR 'infection-related glomerulonephritis':ti,ab,kw OR 'infection related glomerulonephritis':ti,ab,kw OR 'post-streptococcal glomerulonephritis':ti,ab,kw OR 'post streptococcal glomerulonephritis':ti,ab,kw OR 'poststreptococcal glomerulonephritis':ti,ab,kw OR 'staphylococcal glomerulonephritis':ti,ab,kw OR irgn:ti,ab,kw OR pign:ti,ab,kw OR 'post-infectious glomerulonephritis':ti,ab,kw OR 'postinfectious glomerulonephritis':ti,ab,kw) AND ('child'/exp OR child OR pediatrics:ti,ab,kw OR 'children'/exp OR paediatric:ti,ab,kw OR adolescent:ti,ab,kw OR infant:ti,ab,kw OR toddler:ti,ab,kw	906

Supplementary Table S2. Agreement on various guideline statements among 38 experts during Delphi survey

	Recommendation	Agreement proportion (%)
1	We suggest that the diagnosis of acute glomerulonephritis (GN) be considered in patients presenting with hematuria and proteinuria, along with oliguria, edema or hypertension, and without prior clinical or histological evidence of kidney disease. (2C)	94
2	We suggest that the diagnosis of postinfectious GN (PIGN) be considered in patients with acute GN who show transient depletion of serum C3 and/or evidence of preceding streptococcal or staphylococcal infection. (2B)	92
3	We suggest that the diagnosis of rapidly progressive GN (RPGN) be made in patients with rapid and severe loss of kidney function over days to weeks, if accompanied by features of acute GN (hematuria, proteinuria, oligoanuria, edema and/or hypertension). (2C)	92
4	We suggest the following evaluation at presentation in all patients with acute GN: (i) urinalysis, including dipstick and microscopy, (ii) serum creatinine, electrolytes and albumin; (iii) complete blood counts; (iv) complement C3 level; and (v) ultrasound scan of kidneys, ureters and bladder. (2C)	94
5	We suggest performing kidney biopsy in the following patients with acute GN at presentation: (i) rapidly progressive GN; (ii) systemic features (e.g., fever, skin rash or joint pains); (iii) nephrotic state (nephrotic range proteinuria and hypoalbuminemia); and (iv) normal complement C3 level. (2D)	94
6	We suggest performing kidney biopsy in the following patients with acute GN, during follow-up: (i) oliguria and/or severe AKI persisting beyond 7–10 days; (ii) persistence of gross hematuria beyond 2–4 weeks; (iii) persistence of nephrotic range proteinuria beyond 2–4 weeks; (iv) hypocomplementemia persisting beyond 12 weeks; (v) proteinuria (Up/Uc >0.5 mg/mg) persisting beyond 6 months; and (vi) microscopic hematuria persisting beyond 12 months. (2D)	92
7	We recommend that all kidney biopsy specimens are assessed by light microscopy and immunofluorescence. (1C)	97
8	We suggest that an attempt should be made to evaluate all kidney biopsy specimens with electron microscopy. (X)	86
9	We suggest that the presence of crescent (s) be considered evidence of severe glomerular injury. (2B)	86
10	We recommend hospital admission for patients with significant edema, severe AKI, or stage 2 hypertension. (X)	92

Recommendation	Agreement proportion (%)
11 We recommend monitoring of blood pressure, urine output, and serum creatinine in all patients hospitalized with acute GN. (X)	92
12 We recommend salt and fluid restriction in patients with edema and/or hypertension. (X)	97
13 In patients with acute GN with hypertension and either fluid overload or edema, we suggest using furosemide as the first antihypertensive agent. We suggest using calcium channel blockers in patients with stage 2 hypertension. (2B)	100
14 In patients with crescentic GN, we suggest induction therapy with IV methylprednisolone and IV cyclophosphamide. (2C)	100
15 We suggest maintenance therapy with oral prednisolone with mycophenolate mofetil or azathioprine for 6-12 months in patients with crescentic GN. (2D)	92
16 In patients presenting with RPGN and diffuse proliferation without crescents on light microscopy, we suggest treatment with IV methylprednisolone with or without IV cyclophosphamide, followed by oral prednisolone for 6–12 months. (X)	86
17 We suggest not administering antibiotic therapy in patients without evidence of active infection. (2B)	86
18 We suggest that all patients with PIGN be followed up long-term, with monitoring of serum creatinine, proteinuria, microscopic hematuria, and hypertension. (X)	97
19 We suggest that the diagnosis of staphylococcus-associated GN (SAGN) be based on: (i) evidence of ongoing staphylococcus infection, (ii) severe acute kidney injury, (iii) glomerular hematuria and nephrotic range proteinuria, and (iv) proliferative glomerulonephritis with C3 with or without IgA deposits on immunofluorescence microscopy. (2C)	89
20 We recommend that patients with SAGN receive antibiotic therapy to eliminate the underlying infection. (1B)	94
21 We suggest not to use immunosuppressive medications during active infection in patients with SAGN. (2C)	86

Supplementary Table S3. Comparison of histological features among various entities presenting as acute glomerulonephritis (GN) in childhood

Disease	Light microscopy	Immunofluorescence	Electron microscopy
Post-infectious (post streptococcal) GN	Diffuse proliferation, neutrophilic exudation, endocapillary and mesangial hypercellularity; crescents may be seen	IgG with C3 deposits (lumpy-bumpy, coarse granular or garland pattern [Fig. 3; 4 (a,b)])	Large, multiple subepithelial humps; few subendothelial electron dense deposits
C3 glomerulopathy	Membranoproliferative pattern is most common; diffuse proliferative or mesangioproliferative pattern of injury and crescents may be seen; focal necrotizing pattern is rare	C3 predominant (2 or more orders on immunofluorescence) deposits with weak or absent IgG [Fig. 4 (c,d)]	<i>C3 glomerulonephritis</i> : Mesangial and subendothelial deposits <i>Dense deposit disease</i> : Intensely osmiophilic, intramembranous deposits
IgA-dominant IRGN	Diffuse proliferation, neutrophilic exudation, endocapillary and mesangial hypercellularity; crescents may be seen	C3 with IgA deposits; C3 usually more than IgA	Mesangial and subendothelial deposits are usual; subepithelial humps may be seen
Staphylococcus associated GN	Endocapillary proliferation (may be segmental); segmental necrotizing lesions and crescents may be seen	C3 with IgA deposits; in some, C3 predominates over IgA; IgA deposits may be absent	Mesangial deposits most common; few small subendothelial deposits; subepithelial humps may be seen but are not characteristic
IgA nephropathy	Mesangial hypercellularity; segmental endocapillary hypercellularity and crescents may be seen	IgA deposits stronger than C3	Chiefly mesangial deposits; no subepithelial humps
Lupus nephritis	Variable endocapillary and mesangial hypercellularity; wire loop lesions or hyaline thrombi may be seen, depending on nephritis class	‘Full house’ pattern	Mesangial, subendothelial and subepithelial deposits, depending on the class of lupus nephritis
Infective endocarditis related GN	Variable patterns; endocapillary pattern most common; focal crescents and necrotizing lesions may be seen	C3 predominance with or without IgG deposits; few cases have IgA deposits	Small mesangial and capillary wall deposits; subepithelial humps are rare
Shunt nephritis	Diffuse proliferative or membranoproliferative pattern; crescents may be seen	Immunoglobulins with C3 deposits; may appear ‘full house’	Scattered mesangial and few subendothelial electron dense deposits
Ig immunoglobulin; IRGN infection related glomerulonephritis			