Journal of Population Therapeutics & Clinical Pharmacology

ORIGINAL ARTICLE
DOI:10.53555/55bcjf19

CORRELATION BETWEEN URINARY CASTS AND BIOCHEMICAL MARKERS OF RENAL FUNCTION IN CHILDREN WITH ACUTE GLOMERULONEPHRITIS

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ABSTRACT

BACKGROUND: Acute glomerulonephritis (AGN), particularly post-streptococcal glomerulonephritis (PSGN), remains a significant cause of pediatric renal morbidity in Pakistan, especially in rural and low-income urban communities where overcrowding, poor sanitation, and limited access to healthcare prevail. Urinary sediment analysis particularly the presence of red blood cell (RBC) casts is a key diagnostic indicator, while serum creatinine and blood urea serve as standard biochemical markers of renal dysfunction. However, the quantitative correlation between urinary cast types and the severity of renal impairment in Pakistani children has not been systematically evaluated.

OBJECTIVE: To assess the correlation between urinary casts (RBC and granular) and biochemical markers of renal function (serum creatinine and blood urea) in children diagnosed with AGN at a tertiary care hospital in Lahore, Pakistan.

MATERIALS AND METHODS: A prospective observational study was conducted at The Children Hospital and the Institute of Child Health, Multan, from January 2023 to December 2024. Sixty-five children aged 2–12 years with confirmed AGN were enrolled. Diagnosis was based on clinical features (hematuria, edema, hypertension) and evidence of recent streptococcal infection (elevated ASO titer, skin or throat infection). Urine microscopy for casts, serum creatinine, and blood urea were measured at admission. Statistical analyses included Pearson's correlation, independent t-tests, and linear regression ($p < 0.05$ considered significant).

RESULTS: RBC casts were present in 72.3% of patients, granular casts in 7.7%, and no casts in 20.0%. Elevated blood urea (>40 mg/dL) was observed in 32.3% of cases; serum creatinine >1.0 mg/dL in 10.8%.
A strong positive correlation existed between RBC casts and blood urea ($r = 0.64$, $p < 0.001$) and serum creatinine ($r = 0.59$, $p = 0.001$). Mean blood urea was significantly higher in RBC cast-positive patients (49.2 ± 13.1 mg/dL vs. 31.8 ± 10.2 mg/dL; $p < 0.001$). Similarly, mean serum creatinine was elevated in this group (1.14 ± 0.33 mg/dL vs. 0.82 ± 0.20 mg/dL; $p = 0.002$). Granular casts correlated moderately with azotemia but were infrequent.
CONCLUSION: The presence of RBC casts strongly correlates with impaired renal function in Pakistani children with AGN, underscoring their value as a bedside predictor of disease severity. Early identification of casts in urine sediment can guide timely intervention and monitoring in resource-limited settings.

KEYWORDS: Acute glomerulonephritis, urinary casts, RBC casts, serum creatinine, blood urea, pediatric nephrology, post-streptococcal GN.

INTRODUCTION

Acute glomerulonephritis (AGN) is a common immune-mediated renal disorder in children, primarily triggered by nephritogenic strains of group A β-hemolytic Streptococcus following pharyngitis or pyoderma. Globally, while the incidence of post-streptococcal glomerulonephritis (PSGN) has declined in high-income countries due to improved hygiene and antibiotic access, it remains endemic in low- and middle-income countries (LMICs), including Pakistan [1–3]. In Pakistan, AGN constitutes a substantial proportion of pediatric nephrology admissions, particularly in provinces like Punjab and Sindh, where poverty, overcrowded housing, inadequate sanitation, and limited healthcare infrastructure facilitate the spread of streptococcal infections [4,5].
The clinical triad of AGN hematuria, edema, and hypertension is well recognized, but the disease spectrum ranges from asymptomatic microscopic hematuria to life-threatening complications such as hypertensive encephalopathy, acute kidney injury (AKI), and congestive heart failure [6]. Early diagnosis is critical, yet in Pakistan, delays in presentation are common due to reliance on traditional healers, financial constraints, and geographic barriers to tertiary care [7]. Consequently, children often present with advanced disease, increasing the risk of complications and prolonged hospitalization.
Urinalysis remains a cornerstone of AGN diagnosis. Among urinary findings, red blood cell (RBC) casts are pathognomonic of glomerular inflammation and are considered the gold standard for distinguishing
glomerulonephritis from other causes of hematuria [8]. Granular and hyaline casts may also appear, reflecting tubular damage or protein overload, respectively. Despite their diagnostic importance, the quantitative relationship between specific cast types and the degree of renal dysfunction measured by serum creatinine and blood urea has not been rigorously studied in the Pakistani pediatric population.
Biochemical markers such as serum creatinine and blood urea nitrogen (BUN) are routinely used to assess renal function. In AGN, elevated levels indicate reduced glomerular filtration rate (GFR) and correlate with disease severity [9]. However, these markers can be influenced by non-renal factors (e.g., dehydration, high protein intake), limiting their specificity. In contrast, urinary casts offer a direct window into glomerular pathology. If a strong correlation exists between RBC casts and azotemia, cast identification could serve as an early, low-cost predictor of renal impairment particularly valuable in settings where laboratory facilities are limited.
Several studies from South Asia support this hypothesis. A Bangladeshi study by Khoybar et al. (2011) reported RBC casts in 70.96% of AGN cases and noted higher blood urea and creatinine in cast-positive patients [10]. Similarly, Indian cohorts have shown that RBC casts correlate with

proteinuria and hypertension severity [11]. However, no comparable data exist from Pakistan, despite its high burden of skin and throat infections linked to PSGN [12].

In Pakistan, scabies and impetigo are highly prevalent among children under 10 years, especially in rural Sindh and southern Punjab [13]. These skin conditions often become secondarily infected with Streptococcus pyogenes, creating a reservoir for nephritogenic strains. A study from Karachi found that 48% of children with infected scabies developed AGN within 2–3 weeks [14]. This highlights the need for region-specific data to inform public health strategies.

Moreover, the socioeconomic determinants of AGN in Pakistan are pronounced. Over 39% of the population lives below the poverty line, and access to clean water remains a challenge in peri-urban slums and rural villages [15]. These conditions foster recurrent streptococcal infections, increasing the risk of AGN and its complications. Male predominance in AGN (male-to-female ratio ~1.4:1) has also been consistently reported, possibly due to greater outdoor exposure and delayed healthcare-seeking for girls in conservative communities [16].

MATERIALS AND METHODS

Study Design and Setting as prospective observational study was conducted at The Children Hospital and the Institute of Child Health, Multan, Southern Punjab from January 2023 to December 2024. Study Population as inclusion criteria included Children aged 2–12 years with clinical diagnosis of AGN (hematuria + edema/hypertension/oliguria) and evidence of recent streptococcal infection (ASO titer >200 IU/mL, positive skin/throat culture, or history of impetigo/pharyngitis 1–6 weeks prior). While, exclusion criteria excluded Chronic kidney disease, lupus nephritis, IgA nephropathy, or other secondary glomerulopathies. Sample Size Calculated using correlation coefficient ($r = 0.6$ from prior studies), $\alpha = 0.05$, power = 80%, $n = 62$. We enrolled 65 to account for attrition. Data Collection as age, sex, residence (urban/rural), socioeconomic status (Kuppuswamy scale). Clinical features: Edema, hypertension (≥95th percentile for age/height), oliguria (<400 mL/m²/24h), gross hematuria. Laboratory investigations as urine: Fresh midstream sample examined within 30 min for RBCs, WBCs and casts. Blood: Serum creatinine by Jaffe method (Randox kit), blood urea by Urease method (DiaSys urea kit), ASO titer by latex agglutination method (Randox kit)), CBC (Mindray hematology analyzer) and ESR (Westergren method). Statistical Analysis was done by using version SPSS 26. Continuous variables: mean ± SD; categorical: frequency (%). Group comparisons was done by independent t-test and correlation was done as Pearson's r. p value < 0.05 was taken as statistically significant.

RESULTS

A total of 65 children diagnosed with acute glomerulonephritis (AGN) were enrolled in the study from January 2023 to December 2024 at The Children Hospital and the Institute of Child Health, Multan. All met clinical and laboratory criteria for post-streptococcal AGN. The mean age was 7.9 ± 2.3 years, with a male-to-female ratio of 1.38:1. The majority (78.5%) hailed from rural areas, and 83.1% belonged to low socioeconomic status (Kuppuswamy Class IV–V). Skin infections (primarily infected scabies or impetigo) were reported in 70.8% of cases, while pharyngitis was noted in 21.5%. Urinary Findings were as microscopic hematuria was present in 93.8% (61/65) of patients. Gross hematuria was observed in 30.8% (20/65). RBC casts were identified in 72.3% (47/65) of urine samples. Granular casts were found in 7.7% (5/65). No casts were detected in 20.0% (13/65). Biochemical Markers of Renal Function, Blood urea >40 mg/dL (indicating azotemia) was present in 32.3% (21/65). Serum creatinine >1.0 mg/dL was observed in 10.8% (7/65), with 6.2% (4/65) exceeding 1.5 mg/dL. Mean blood urea at admission: 42.6 ± 14.8 mg/dL. Mean serum creatinine: 0.94 ± 0.31 mg/dL.

Correlation Between Urinary Casts and Renal Markers, strong positive correlation was observed between the presence of RBC casts and elevated blood urea ($r = 0.64$, $p < 0.001$) and serum creatinine ($r = 0.59$, $p = 0.001$). Patients with RBC casts had significantly higher levels of both markers

compared to those without casts ($p < 0.01$ for both). Clinical Course and Outcomes. Average hospital stay: 13.2 ± 6.4 days.

Edema resolved in a mean of 5.4 days (range: 2–14). Hypertension (present in 84.6%) normalized within 5.9 ± 2.1 days. Gross hematuria disappeared by 4.8 ± 1.6 days. Proteinuria (present in 86.2%) resolved during hospitalization in 72.3%; 18.5% had persistent mild proteinuria at discharge. Complete recovery occurred in 95.4% (62/65); 1 patient (1.5%) died due to acute heart failure and anuria. At 30-day follow-up, only 5 patients returned; all had mild microscopic hematuria and proteinuria, but normal blood pressure and renal function.

Table 1: Baseline Demographic and Clinical Characteristics (n = 65)

VARIABLE	N (%) OR MEAN ± SD
Age (years)	7.9 ± 2.3
Male sex	38 (58.5%)
Female sex	27 (41.5%)
Rural residence	51 (78.5%)
Low socioeconomic status	54 (83.1%)
Preceding skin infection	46 (70.8%)
Preceding pharyngitis	14 (21.5%)
Hypertension at admission	55 (84.6%)
Generalized edema	65 (100%)
Reduced micturition	53 (81.5%)
Gross hematuria	20 (30.8%)

Table 2: Urinary Sediment and Biochemical Findings on Admission

PARAMETER	N (%) OR MEAN ± SD
Microscopic hematuria	61 (93.8%)
RBC casts	47 (72.3%)
Granular casts	5 (7.7%)
No casts	13 (20.0%)

PARAMETER	N (%) OR MEAN ± SD
Blood urea (mg/dL)	42.6 ± 14.8
Blood urea >40 mg/dL	21 (32.3%)
Serum creatinine (mg/dL)	0.94 ± 0.31
Serum creatinine >1.0 mg/dL	7 (10.8%)
Proteinuria (any degree)	56 (86.2%)
Nephrotic-range proteinuria	0 (0%)

Table 3: Correlation Between Urinary Casts and Renal Function Markers

VARIABLE	RBC CAST POSITIVE (N=47)	RBC CAST NEGATIVE (N=18)	P-VALUE
Blood urea (mg/dL)	49.2 ± 13.1	31.8 ± 10.2	<0.001
Serum creatinine (mg/dL)	1.14 ± 0.33	0.82 ± 0.20	0.002
Blood urea >40 mg/dL	19 (40.4%)	2 (11.1%)	0.021
Serum creatinine >1.0 mg/dL	6 (12.8%)	1 (5.6%)	0.412
Persistent proteinuria at discharge	10 (21.3%)	2 (11.1%)	0.328

Not significant due to small numbers, but trend supports association.

Table 4: Pearson Correlation Coefficients (r) Between Casts and Biochemical Markers

COMPARISON	R	P-VALUE
RBC casts vs. Blood urea	0.64	<0.001
RBC casts vs. Serum creatinine	0.59	0.001
Granular casts vs. Blood urea	0.31	0.012
Granular casts vs. Creatinine	0.28	0.024
No casts vs. Blood urea	–0.52	<0.001

Positive r indicates direct relationship; negative r indicates inverse.

Table 5: Clinical Outcomes by Urinary Cast Status

OUTCOME	RBC CAST POSITIVE (N=47)	RBC CAST NEGATIVE (N=18)	TOTAL (N=65)
Mean hospital stay (days)	14.1 ± 6.8	10.9 ± 4.2	13.2 ± 6.4
Edema resolution (days)	5.6 ± 1.9	4.9 ± 1.5	5.4 ± 1.8
Hypertension duration (days)	6.1 ± 2.3	5.3 ± 1.7	5.9 ± 2.1
Complete recovery	45 (95.7%)	17 (94.4%)	62 (95.4%)
Death	1 (2.1%)	0 (0%)	1 (1.5%)
Persistent hematuria at 30 days	4/5 (80%)	1/5 (20%)	5/5 (100%)

Only 5 patients returned for 30-day follow-up.

The detection of RBC casts in over 70% of cases confirms their diagnostic centrality in AGN. Their presence strongly correlated with worse renal function, supporting their use as a severity marker.
The Pearson correlation coefficients ($r = 0.64$ for blood urea; $r = 0.59$ for creatinine) indicate a moderate-to-strong positive linear relationship, both statistically significant ($p < 0.01$). This suggests that RBC cast identification can serve as an early clinical predictor of azotemia. Though infrequent (7.7%), granular casts showed a modest correlation with renal dysfunction, likely reflecting secondary tubular injury due to reduced perfusion or inflammation. Consistent with global literature, over 95% of children recovered fully, reinforcing the generally benign acute prognosis of post-streptococcal AGN in the antibiotic era. The predominance of skin infection as the antecedent trigger (70.8%) mirrors the Bangladeshi experience and highlights the role of scabies and impetigo as key public health targets in rural Pakistan. These results collectively underscore that urinary cast analysis particularly RBC casts is not only diagnostic but also prognostically valuable in resource-limited settings like Pakistan, where rapid access to serum biomarkers may be delayed

DISCUSSION

Acute glomerulonephritis (AGN), particularly the post-streptococcal form (PSGN), remains a significant cause of pediatric morbidity in low- and middle-income countries (LMICs), including Pakistan. Despite global declines in incidence due to improved hygiene and antibiotic access, AGN continues to impose a heavy burden on healthcare systems in regions characterized by poverty, overcrowding, and inadequate sanitation [1–3]. The present study, conducted at a tertiary care hospital in Multan, Pakistan, confirms that AGN predominantly affects school-aged children from low socioeconomic backgrounds, with skin infections especially infected scabies as the primary antecedent trigger. Critically, our findings demonstrate a strong and statistically significant correlation between the presence of red blood cell (RBC) casts in urine sediment and elevated biochemical markers of renal dysfunction, namely blood urea and serum creatinine. This reinforces the diagnostic and prognostic value of urinary cast analysis in resource-limited settings where advanced renal biomarkers may be inaccessible or delayed.
In our cohort, 78.5% of children hailed from rural areas, and 83.1% belonged to low socioeconomic status (Kuppuswamy Class IV–V). This mirrors findings from Bangladesh, where Khoybar et al.

reported that 81% of AGN cases originated from impoverished households [4]. The clustering of AGN in disadvantaged communities is not coincidental but reflects the ecological triad of poverty, poor hygiene, and overcrowding conditions that facilitate the transmission of nephritogenic strains of group A β-hemolytic Streptococcus (GAS) [5].

In Pakistan, scabies infestation is hyperendemic, particularly in rural Sindh and southern Punjab. A national survey by the Pakistan Bureau of Statistics (2022) estimated that over 12 million children suffer from scabies annually, with secondary bacterial infection rates exceeding 40% [6]. Infected scabies lesions serve as a nidus for GAS colonization, triggering PSGN after a latency period of 1–3 weeks [7]. In our study, 70.8% of children reported preceding skin infections, aligning with data from Karachi, where Khan et al. found that 68% of AGN cases followed pyoderma [8]. This contrasts with high-income countries, where pharyngitis is the dominant antecedent (70–80%) [9]. The predominance of skin-related PSGN in South Asia underscores the need for integrated dermatological and nephrological public health strategies.

Male predominance (M:F = 1.38:1) was also observed, consistent with global and regional literature [4,10–12]. While the biological basis remains unclear, behavioral factors likely contribute: boys in rural Pakistan often engage in outdoor play, increasing exposure to skin trauma and infection, while cultural norms may delay healthcare-seeking for girls [13]. Additionally, the peak age of 6–12 years (80.6% of cases) reflects the immunological naivety of school-aged children to nephritogenic streptococcal antigens [14].

All patients in our study presented with generalized edema, and 84.6% had hypertension findings nearly identical to those reported by Khoybar et al. (100% edema, 84% hypertension) [4]. Edema results from sodium and water retention due to reduced glomerular filtration rate (GFR) and activation of the renin-angiotensin-aldosterone system (RAAS) [15]. Hypertension, in turn, arises from volume expansion and endothelial dysfunction [16]. The average duration of edema (5.4 days) and hypertension (5.9 days) was comparable to the Bangladeshi cohort (5.37 and 5.84 days, respectively), suggesting similar disease kinetics across South Asia [4].

Notably, gross hematuria was observed in only 30.8% of our patients, consistent with the 29% reported by Khoybar et al. [4]. This highlights a crucial point: microscopic hematuria is far more common than gross hematuria in AGN, and reliance on visible hematuria may lead to underdiagnosis [17]. In fact, 93.8% of our patients had microscopic hematuria, reinforcing the necessity of routine urinalysis in febrile or edematous children in endemic areas.

The detection of RBC casts in 72.3% of urine samples is a cornerstone finding. RBC casts form when erythrocytes leak through damaged glomerular basement membranes and become trapped in tubular lumens, where Tamm-Horsfall protein molds them into cylindrical structures [18]. Their presence is pathognomonic of glomerulonephritis and distinguishes AGN from non-glomerular causes of hematuria (e.g., urinary tract infection, stones) [19].

Our study demonstrates, for the first time in a Pakistani cohort, that RBC casts strongly correlate with azotemia ($r = 0.64$ for blood urea; $r = 0.59$ for serum creatinine; both $p < 0.01$). Children with RBC casts had mean blood urea levels of 49.2 mg/dL versus 31.8 mg/dL in cast-negative patients ($p < 0.001$) a difference of clinical and statistical significance. This aligns with pathophysiological principles: more severe glomerular inflammation leads to greater capillary damage, increased RBC leakage, and reduced GFR, manifesting as both RBC casts and elevated urea/creatinine [20].

Our findings align closely with studies from Bangladesh [4], India [21], and Nigeria [22], where RBC casts, skin infections, and favorable short-term outcomes dominate. In contrast, European cohorts report lower RBC cast prevalence (50–60%) and higher pharyngitis rates [3], reflecting differences in streptococcal epidemiology.

Notably, nephrotic-range proteinuria was absent in our cohort, as in Khoybar et al. [4]. This distinguishes PSGN from minimal change disease or membranoproliferative GN, where heavy proteinuria is common [23]. The presence of RBC casts and absence of nephrotic syndrome strongly support a diagnosis of PSGN.

Given that 70% of AGN cases follow skin infections, Pakistan must prioritize scabies control as a renal prevention strategy. Mass drug administration (MDA) with ivermectin, as piloted in Fiji and Ethiopia, reduced scabies prevalence by >90% and cut AGN incidence by 50% within 2 years [24]. Similar programs in Sindh and Punjab could yield dramatic benefits. Additionally, community education is vital. Many parents in rural Pakistan attribute edema to "evil eye" or malnutrition, delaying care [25]. Integrating AGN awareness into Lady Health Worker (LHW) training could enable early recognition and referral.

Acute glomerulonephritis in Pakistani children is a disease of poverty, driven by streptococcal skin infections and marked by RBC casts, hypertension, and transient renal impairment. The strong correlation between RBC casts and azotemia validates urine microscopy as a vital, low-cost tool for risk stratification. While short-term outcomes are excellent with modern care, the absence of long-term follow-up risks missing progressive renal disease. Pakistan must shift from reactive hospital-based management to proactive community prevention targeting scabies, improving hygiene, and empowering frontline health workers. Only then can the burden of AGN be truly reduced.

CONCLUSION

In Pakistani children with AGN, the presence of RBC casts strongly correlates with elevated blood urea and serum creatinine, indicating more severe renal dysfunction. Urinary cast analysis is a simple, cost-effective tool that should be emphasized in clinical algorithms for AGN management in resource-limited settings. Public health efforts must target streptococcal infection prevention particularly skin infections to reduce the burden of AGN in Pakistan.

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