

Original Article

The Epidemiology, Presentation, and Outcome of Acute Post-infectious Glomerulonephritis in North East India: A Single Centre Experience



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ABSTRACT

Background and Aim: Acute post-infectious glomerulonephritis (PIGN) can occur due to various etiologies. Among these, post-streptococcal glomerulonephritis is the common cause. Though the burden has drastically decreased over the years in developed nations, it remains a reason for concern in developing countries. This study aimed to document the burden, clinical presentation, etiology, and outcome of PIGN referred to a tertiary care center in a developing country.

Methods: This retrospective study was conducted in a tertiary care teaching hospital in northeast India. All cases diagnosed with acute PIGN were included in the study. Cases with an alternate diagnosis and cases with incomplete records were excluded from the study. Data on relevant clinical, demographic, and laboratory variables were extracted from the case records and discharge summary. Simple descriptive statistics, such as frequency and proportion were used.

Results: A total of 202 cases of PIGN were included in the study. The Mean±SD annual admission rate was 22.4±6.1 per year. The Mean±SD age at presentation was 10.0±3.9 years and the male to female ratio was 1.2 to 1. The most common clinical features at the time of presentation were hypertension in 183 patients (90.59%), edema in 168(83.16%), history of oliguria in 146(72.27%), and hematuria in 168 patients (83.2%). Proteinuria was present in 95 cases (47.03%). Either clinical or serological evidence of preceding streptococcal infection was observed in 160 children (83.2%). Two cases had scrub typhus and one case had hepatitis B seropositivity. Hypertensive encephalopathy and left ventricular failure were observed in 20(9.90%) and 44 children (21.78%), respectively. Admission to the pediatric intensive care unit was required in 28.21%. No mortality was observed.

Conclusion: PIGN constitutes a significant burden in this part of India. The incidence of complications was high but the outcome was good with adequate acute care.

Keywords: Post-infectious glomerulonephritis (PSGN), Hypertensive encephalopathy, Streptococcal infection, Hematuria

Introduction

Acute glomerulonephritis (AGN) is characterized by a relatively abrupt onset of variable degrees of hematuria, edema, and hypertension [1]. It can occur due to a non-infectious etiology or may follow various infections. In the latter case, it is called post-infectious glomerulonephritis (PIGN). Among the PIGNs, post-streptococcal glomerulonephritis (PSGN) accounts for a major share [2]. It is usually a self-limiting disease with an excellent outcome. However, it may cause significant morbidity in children [3, 4]. Though the burden of PSGN has drastically decreased over years in developed nations, it remains a reason to worry in developing countries and certain aboriginal populations [5, 6]. However, very few recent reports exist from developing countries including India to document the burden.

Meghalaya is a tribal province in the northeast of the country with limited resources. In this area, PIGN is common in clinical practice and is the most common cause of pediatric kidney-related hospital admission [7]. With this background, this study aimed to document the burden, clinical presentation, etiology, and outcome of PIGN in this area.

Materials and Methods

All cases admitted between January 2010-December 2018 with a diagnosis of acute glomerulonephritis, PIGN, or post-streptococcal glomerulonephritis were identified, and their discharge summaries and inpatient charts were retrospectively reviewed. Institute ethics committee approval was obtained for the study (NEIGR/IEC/M6/F10/18 dated October 4, 2018). Cases with an alternate diagnosis and cases with incomplete records were excluded from the study. For this purpose, all cases with an acute presentation with all three facial edema, hypertension, sub-nephrotic proteinuria, and hematuria with low C3 at the time of presentation in the absence of an alternate diagnosis were included in the study. Patients with normal complement levels were included only if biopsy confirmed PIGN, or were excluded otherwise. All clinical or serological cases of preceding glomerulonephritis were called PSGN, and the rest was called PIGN. Data on relevant clinical, demographic, and laboratory variables were extracted from the case records and discharge summary.

Blood pressure was graded based on the normative distribution of BP according to age, sex, and height percentile [8]. Hematuria was defined as 5 red blood

cells/high power field on a centrifuged urinary specimen. Proteinuria was defined as sub-nephrotic urinary protein, urinary creatinine ratio between 0.2 and 2 or 1-2+ on the dipstick and as nephrotic range proteinuria if urinary protein, urinary creatinine ratio >2 or >2+ on the dipstick [9]. Acute kidney injury was defined using the acute kidney injury network (AKIN) criteria [10]. A single anti-streptolysin O (ASLO) titer of >200 Todd's unit was considered positive. C3 level of <90 mg/dL was considered low.

Simple descriptive statistics, such as frequency and proportion were used.

Results

Figure 1 shows details of inclusion, exclusion, and etiology in the flow chart. Out of the 202 cases, the number of male patients was 112(55.5%) and the total number of female patients was 90(44.5 %). The male to female ratio is 1.2 t 1. The mean age at the time of presentation was 10.0±3.9 years. Table 1 presents the demographic data of the study group.

Healed impetigo and infected scabies were considered clinical evidence. History of sore throat in absence of an elevated ASLO titre is classified as an unconfirmed etiology due to the significant overlap of symptoms with other etiologies of sore throat.

Presenting features

The most common clinical features at the time of presentation were hypertension in 90.6%, edema in 83.2%, and a history of oliguria in 72.3% of cases. Hematuria was present in 83.2% of patients, of which gross hematuria was observed in 79 cases (39.1%) and only microscopic hematuria was observed in 89 cases (44.1%). Proteinuria was observed in 95 cases (47.03%), of which 70 cases (34.65%) had nephritic range proteinuria and 25 cases (12.37%) had nephrotic range proteinuria. Children with nephrotic range proteinuria were evaluated for serum albumin and cholesterol to rule out nephrotic syndrome. C3 level was low in all but 3 children who underwent a biopsy to confirm the diagnosis.

A renal biopsy was performed on 6 children to confirm the diagnosis. The indications were persistent nephrotic range proteinuria with stage 3 acute kidney injury (AKI) in two, antinuclear antibody (ANA) positivity with nephrotic range proteinuria in one, and normal C3 level in three. The biopsy of all these children showed features of exudative proliferative glomerulonephritis, suggestive of

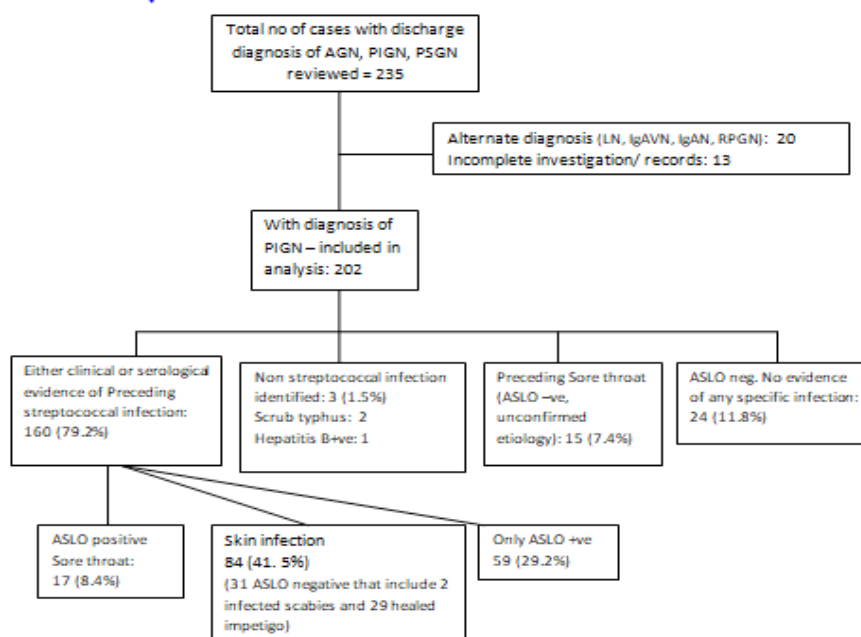


Figure 1. Study flow chart showing inclusion, exclusions, and major etiological findings of the study

PIGN. Another child with nephritis with low titer ANA positivity refused biopsy and was followed up clinically. The nephritis resolved spontaneously in this child and the C3 level returned to normal range on follow-up. Both the children with a positive ANA had a negative double-stranded DNA (dsDNA) and did not have other clinical features of systemic lupus erythematosus.

Complications and outcome

Out of the 183 children who were referred with hypertension, 119 children (58.9%) had stage 2 hypertension, and 64 patients (31.7%) had stage 1 hypertension. A total of 20(9.9%) patients presented with features of hypertensive encephalopathy. This included features, such as seizures 11(5.5%), headache 4(1.9%), vomiting 3(1.4%), blurring of vision 1(0.5%), and altered sensorium 5(2.3%).

Left ventricular failure was observed in 44 patients (21.8%), of which 3 (1.5%) had to be ventilated for pulmonary edema. The average time of ventilation for these patients was about 72 h. Repeat 2D (2 dimensional) echocardiography on follow-up in these patients showed normal left ventricular ejection fraction.

According to the acute kidney injury network (AKIN) criteria, a total of 40 people (19.8%) had AKI. Nineteen patients (9.4%) had stage 1, 16 patients (7.9%) had stage 2, and 5(2.5%) had stage 3 AKI, of whom 2 patients required hemodialysis. Both these children spontaneously

recovered without the need for immunosuppressant and were biopsied to exclude crescentic nephritis and other alternate diagnoses.

Antecedent infection

We found that 160 children (79.2%) had clinical (healed or active pyoderma) and or serological evidence of streptococcal infection. This included 17 cases (8.4 %) with a sore throat (with positive ASLO) and 81 cases (40.1%) with a skin infection and 59 cases (29.7%) with positive ASLO titer only. Two children tested positive for scrub typhus and one was hepatitis B surface antigen positive. In 24 cases (11.8%), no specific preceding infection was found while 15 cases (7.4%) had a history of preceding sore throat but ASLO was negative, hence classified as unconfirmed etiology (Figure 1).

Temporal and seasonal trend

The annual Mean±SD admission rate of PIGN in our institute was 22.4±6.1 cases per year. This accounted for 1.0%-2.6% of total admissions. There didn't seem to be any decreasing trend over the years (Figure 2). More patients were admitted during the autumn and winter season compared to a lower rate of admission in spring and monsoon (Figure 3).

Outcome

Fifty-seven children (28.2%) required pediatric intensive care unit (ICU) admission and the rest were man-

Table 1. Clinical characteristics and complications of children with post-infectious glomerulonephritis (PIGN)

Clinical Characteristics and Complications		No. (%)
Edema		168(83.2)
History of oliguria		146(72.3)
Hematuria		168(83.2)
Gross		79(39.1)
Microscopic only		89(44.1)
Proteinuria		95(47.03)
Nephrotic range		25(12.4)
Sub-nephrotic range		70(34.7)
Hypertension		183(90.59)
Stage I		64(31.7)
Stage II		119(58.9)
Evidence of preceding streptococcal infection		160(79.2)
History of sore throat (ASLO +ve)		17(8.4)
History of pyoderma		84(41.5)
Only ASLO positive		59(29.2)
Complications		104(51.5)
a) Hypertensive encephalopathy		20(9.9)
b) Left ventricular failure		44(21.8)
c) AKI		40(19.8)
Stage	1	19(9.4)
	2	16(7.9)
	3	5(2.5)

ASLO: Anti-streptolysin O; AKI: Acute kidney injury.

aged in the pediatric ward. According to unit policy, patients were discharged if they were no longer oliguric, blood pressure was in the normal range, gross hematuria had resolved and serum creatinine had reached baseline. All patients except 3 patients were discharged against medical advice before meeting the discharge criteria. No mortality was observed.

Discussion

It is widely acknowledged that PSGN cases have decreased in the past several decades [5]. However, PIGN (including PSGN) continues to be a significant burden in developing countries and certain aboriginal populations

[11-13]. Population studies show a median incidence of post-streptococcal nephritis of 24.4 cases per 1,000,000 person-years in developing countries versus about 0.64 cases per 1,000,000 person-year in developed countries [14, 15].

PIGN is associated with a wide range of bacteria, viruses, and protozoa [15]. Among post-infectious GN, streptococcal glomerulonephritis is a common cause, accounting for more than 85% of the cases. Gunasekaran et al from south India have made similar observations where 90% of PIGNs documented clinic-serological evidence of streptococcal infection [11]. Though post-streptococcal etiology is the most common and almost

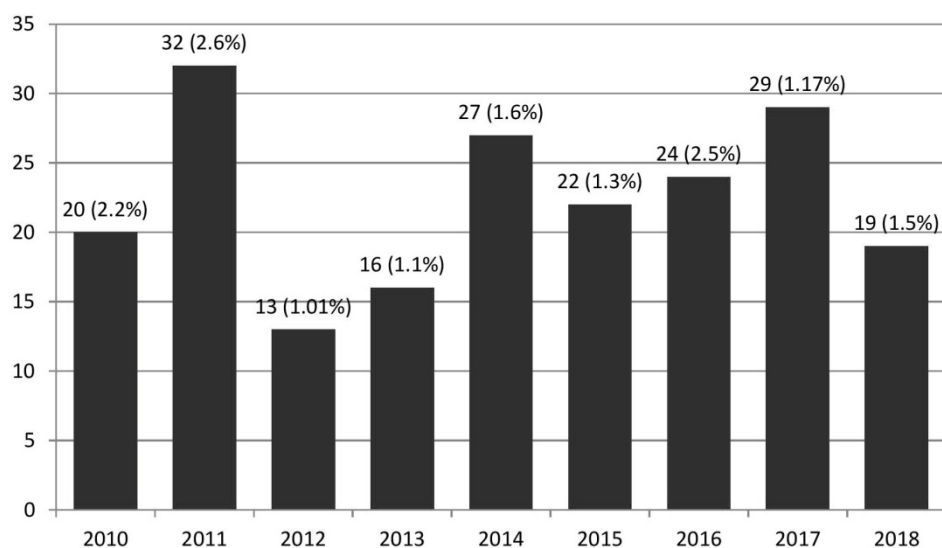


Figure 2. The trend of the number of children admitted with PIGN over the study period (the figure in the bracket indicate the proportion of total admission in that year)

exclusive cause of PIGN in certain areas, it should be realized that other infections causing PIGN do occur and should always be considered.

Our area is a resource-poor area of a developing country and PIGN is a common cause of hospitalization [7]. In absence of a population-based study, it is difficult to compare the burden among different areas. However, an annual number of incident cases in an area may provide a fair, albeit imprecise way of comparing with another area. A relatively recent series from Florida reports 6.4 annual admissions with PSGN, compared to the annual mean of 15.7 to 50 cases from India and other developing countries [4, 11, 12, 14]. Sepahi et al reported 94 cases of admissions in 6 years (2000-2006) from central Iran with an annual mean of 15.6 cases [4]. Gunasekaran et al (2013-2014) from a high-volume center in southern

India reported 72 cases recruited over 18 months (annual mean 48 cases) [11]. Bhalla et al., (2019) reported 50 cases in one year from their center in northern India. Barrios et al have shown that their center in Chile changed from an annual mean of 37.5 cases (1980-1983) to an annual mean of 15.7 cases from 1990 to 1999 [16]. In our series, we saw an annual mean of 22.4 admissions of PIGN per year (range 13-32 cases per year) in the last 9 years and there seems to be no decreasing trend over the years (Figure 1). It is evident that centers from India including ours, have a higher admission rate for PIGN compared to centers in the Middle East, North, and South America. Our institute is situated in a tribal hilly province with a lower population density whereas the other two centers are higher volume centers catering to a larger population.

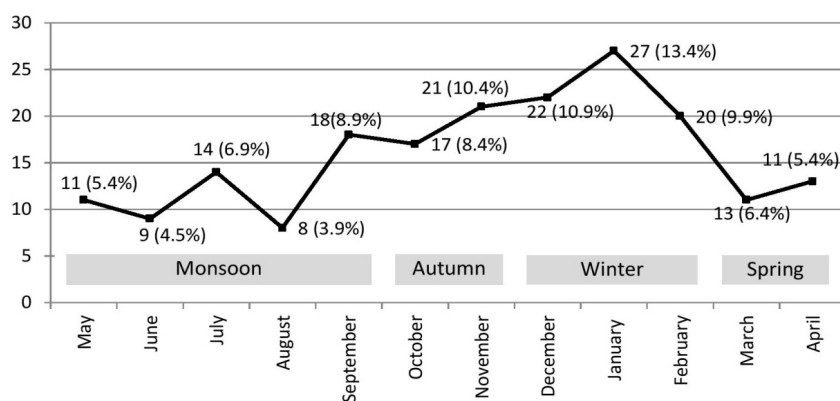


Figure 3. Seasonal trend in the admission of children with PIGN in the study

Most children in our series encountered edema, hypertension, and hematuria. Our findings were comparable to published literature regarding the age of presentation, the presenting symptoms as well as the seasonal variation [1, 9-13, 17-19]. Microscopic hematuria is regarded as a universal finding in post-infectious nephritis. But, in our series, 17.8% of children did not show microscopic hematuria, which is higher compared to most published series. It is known that post-streptococcal nephritis can demonstrate a variable degree of urinary abnormalities, and occasional urine analysis may not show a significant abnormality [1, 20, 21]. A large series reported for Chile did not find hematuria in 10% of their cases [15]. Our finding that microscopic hematuria was absent in most cases could be partly due to a false negative due to inadvertent delay in urinalysis [22].

The proportion of children with hypertensive complications in our series was similar to a recent series from south India but was much higher compared to most studies [11, 18, 19]. This may reflect referral bias or poor health-seeking behavior. This may indicate a, 'tip of the iceberg phenomenon' suggesting that there may be a larger number of non-sick children with PIGN in the community not reaching the hospital.

Skin infection was found to be the most common cause of the preceding infection. This is in sync with the trend in India and other developing countries and in contrast to recent trends from developed countries [17]. In the western world, there has been a drastic decrease in PSGN caused by skin infection, but subsequent pharyngitis remains stable. This offers an optimistic outlook that factors, such as improving socioeconomic status may lead to decreased burden in developing countries.

The study had certain limitations inherent to its study design. This is a retrospective study, and data quality issues and other unnoticed biases cannot be denied. Also, as we included PIGN requiring hospitalization, asymptomatic and minimally symptomatic PIGN are missed out thereby reflecting only the tip of the iceberg. This underestimates the true incidence. A C3 value was available at admission but no subsequent C3 measurement was available to demonstrate a return to normal value. In most cases that were negative for microscopic hematuria at admission, repeat urinalysis was not available to rule out a pre-laboratory error. Streptococcal seropositivity in our series could be underestimated using ASLO because anti-deoxyribonuclease (DNAase) B was not performed.

Conclusion

We conclude that this part of India has a significant burden of PIGN and post-streptococcal nephritis accounting for most of it. The possibility of PIGN after infections other than streptococcal infection should be considered. A significant proportion of PIGN can be associated with complications, but the outcome is usually favourable if adequate acute care is provided.

Ethical Considerations

Compliance with ethical guidelines

The study was approved by the Institutional Ethics Committee of [North Eastern India Gandhi Regional Institute of Health and Medical Sciences](#) (NEIGR/IEC/M6/F10/18 dated October 4, 2018).

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Authors' contributions

Conceptualizing the study and reviewing the literature: Himesh Barman and Lima Sangla; Collecting data: Lima Sangla and Biswajit Dey; Drafting the manuscript: Lima Sangla, Biswajit Dey, and Wihiwot Valarie Lyngdoh; Data analysis: Himesh Barman, Rosina Ksoo and Manisha De. Final approval: All authors.

Conflict of interest

The authors declare no conflict of interest.

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