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Prevalence of Post Infectious Glomerulonephritis (PIGN) and Associated Complication

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ABSTRACT

Introduction

Post infectious glomerulonephritis (PIGN) is the most common renal disease in children causing significant morbidity. The affected children present with features of acute nephric syndrome (hematuria, hypertension, edema and oliguria. The objective of this study was to determine the prevalence, clinical characteristics, complications, and outcomes of children presenting with post infectious glomerulonephritis in paediatric ward of tertiary care hospital.

Methods

This was a prospective observational study conducted at a tertiary care hospital in Chitwan, Nepal from March 1st 2020 to February 28th 2021. Children aged 4 – 15 years satisfying 2 out of 4 features of acute nephritic syndrome were included in the study. After discharge, patients were followed up at 4 weeks and 8 weeks. Data entry was done in statistical packages for the social science version 20.

Results

Among 46 children recruited with acute nephritic syndrome, 73% had Post infectious glomerulonephritis. The most common etiology of PIGN was Post streptococcal glomerulonephritis (63%). The mean age of children was 11.2 (±3.2) years. Males to females' ratio was 1.5:1. The most common presenting feature was edema (100%). The most common complication was acute kidney injury (41.3%).

Conclusions

Post infectious glomerulonephritis was the most common cause of acute nephritic syndrome in children. High incidence of life-threatening complications like CCF, retinopathy, encephalopathy and renal insufficiency occur that require close monitoring and timely intervention to prevent morbidity and mortality.

Keywords: Post infectious glomerulonephritis, PIGN, GAS,

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INTRODUCTION

Post infectious glomerulonephritis (PIGN) is the most common renal (Glomerular) disease in children that results from reactive immunological process triggered by bacterial, viral, protozoal and fungal infections. Post-streptococcal glomerulonephritis (PSGN), a prototype of PIGN, is a non-suppurative complication of Group A beta haemolytic Streptococcus (GAS) infections that occurs 1 – 4 weeks after the infection. The incidence of PIGN has reduced dramatically in developed nation.[1] However it is still common in developing countries with median incidence of 24.3 cases per 100,000 person-years.[2 – 4] The affected children present with features of acute nephritic syndrome (hematuria, hypertension, edema and oliguria). It causes significant morbidity; sometimes serious and life threatening complications that requires immediate interventions. Acute cerebral complications include headaches, seizures, mental status changes, visual changes. Dyspnoea may occur due to congestive cardiac failure.[5] Other potential complications include rapidly progressive glomerulonephritis (RPGN), dyselectrolytemia and acidosis. One percent patient develop chronic kidney disease.[6] In Nepal, there is paucity of data on this subject. Hence, this study was conducted to describe the clinical characteristics, complications and outcomes of PIGN.

METHODS

A prospective observational study conducted from March 1st 2020 to February 28th 2021 in the Pediatric ward of College of Medical Sciences, Bharatpur, Chitwan after obtaining ethical clearance from Institute Review Committee (Ref No. COMSTH-IRC/2020-064). Data was collected by using convenience sampling technique. Children with age one to 15 year age with the diagnosis of PIGN were prospectively recruited for the study after taking informed consent from the guardian. PSGN was defined in the presence of following criteria: a) features of acute nephritic syndrome, and b) evidence of recent streptococcal infection (pyoderma, or pharyngitis with positive ASO titres or anti-DNAse B titres*). and c) Low C_3, with normalisation of C3 levels in 8 weeks follow up.[7-8] Hypertension was defined as systolic and/or diastolic blood pressure values exceeding the 95th percentile for age, sex and height on three or more occasion.[9] Hyperkalemia was defined as serum potassium > 5.0 mmol/L.[10] Microscopic hematuria was defined as more than 5 red cells/high power field on a centrifuged urinary specimen.[11] Nephrotic range proteinuria was defined as urinary protein: urinary creatinine ratio >2. Acute kidney injury was defined as an abrupt rise in serum creatinine > 0.3 mg/dL or a percentage increase in serum creatinine more than 1.5 fold high than baseline.[12] Stage 1 AKI was defined as increase in serum creatinine of more than or equal to 0.3 mg/dl (≥ 26.4 μmol/l) or increase to more than or equal to 150% to 200% (1.5- to 2-fold) from baseline. Stage 2 AKI was defined as increase in serum creatinine to more than 200% to 300% (> 2- to 3-fold) from baseline. Stage 3 AKI is defined as increase in serum creatinine to more than 300% (> 3-fold) from baseline.[12] Rapidly Progressive glomerulonephritis (RPGN) was defined as rapid decline in renal function within few days to weeks, with extensive crescent formation (involving more than 50% of glomeruli) in children presenting with acute nephritic syndrome.[8] The patients were followed up daily in the ward. Input/output chart was maintained daily. In the patients with deranged renal function, urine abnormalities and electrolytes, these investigations were repeated daily till normalization/discharge. Renal biopsy was done if indicated. Complete remission is defined as absence of edema, hypertension and normal renal function (absence of proteinuria and normal serum creatinine for age) at discharge. Partial remission is defined as presence of any of following – edema, hypertension, proteinuria or abnormal serum creatinine for age at

discharge.[7,11,13] After the discharge, patients were followed up at 4 weeks and 8 weeks. In each follow up, patients were inquired about the colour and amount of urine; Physical examination was done to look especially for edema and hypertension; certain investigation like urine routine examination and RFT were done. Serum C_3 was repeated in 2nd follow up (8 weeks). The data was entered and analysed in Statistical Package for Social Sciences (SPSS) 20.0. In the descriptive statistics, frequency, percentage were calculate for categorical variable while for continuous variable mean and standard deviation (SD) were calculated while in the inferential statistics, chi-square was used for qualitative variables and unpaired T- test for quantitative variables. P-value <0.05 was considered statistically significant.

RESULTS

Age of the patients ranged from 4 to 15 years with mean age 11.2 ±3.2 years. Majority of the patients (54.3%) were from 10 – 15 years age group. Male to female ratio was 1.5:1. (Table 1)

Table 1. Demographic characteristics

Demographic Characteristics	Number of cases (%) (n = 46)
Age (years)	
<5	1 (2.2)
5 – 10	12 (26.1)
10 – 15	25 (54.3)
15	8 (17.4)
Mean±SD	11.2 ±3.2 years
Sex	
Male	28 (60.9)
Female	18 (39.1)
Residence	
Hill	23 (50)
Mountain	8 (17.4)
Outer Terai	8 (17.4)
Inner Terai	7 (15.2)
Season	
Spring	6 (13)
Summer	15 (32.6)
Fall (Autumn)	17 (37)
Winter	8 (17.4)

Clinical Characteristics of PIGN

The most common presenting feature was edema (100 %) followed by hypertension (89.2%). (Table 2).

Table 2. Symptoms and signs of PIGN

Symptoms	Number (%) (n=46)
Edema	46 (100)
Decreased urine output	29 (63)
Red coloured urine	27 (58.7)
Shortness of breath	22 (47.9)
Palpitation	11 (23.9)
Headache	11 (23.9)
Blurred vision	4 (8.7)
Vomiting	8 (17.4)
Seizure	2 (4.3)
Fever	10 (21.7)
Pain abdomen	1 (2.2)
Cough (productive)	1 (2.2)
Signs	
Hypertension	41 (89.2)
Stage 1	9 (19.6)
Stage 2	32 (69.4)
Tachycardia	10 (21.7)
Tachypnea	24 (52.2)
Fever	4 (8.7)
Healing rashes of pyoderma	12 (26.1)
Hypertensive changes in eye	1 (2.2)
Altered sensorium	1 (2.2)
Hepatomegaly	7 (15.2)
Wheeze/crepitation	6(13.2)
Gallop rhythm	1(2.2)

Etiology (based on history):

Majority of the cases of PIGN were preceded by pyoderma (37%) followed by pharyngitis (26%). No etiology could be identified in 30.4% cases. Pyoderma and sore throat preceded the PIGN by mean interval of 17 and 20.29 days respectively. (Table 3)

Table 3. Etiology of PIGN

Etiology	Number (%)(n=46)
Pyoderma associated	17 (37)
Pharyngitis associated	12 (26)
Mumps	2 (4.3)
Pneumonia	1 (2.2)
Unknown	14(30.4)

Laboratory features

Microscopic hematuria was the most common laboratory feature (78.2%). Serum C3 was normal at presentation in 2 cases. (Table 4).

Table 4. Laboratory features

Laboratory features	Number (%) (n=46)
Microscopic hematuria	36 (78.2)
Proteinuria	31 (67.3)
Nephrotic range proteinuria	5 (10.9)
Pyuria	17 (37)
Hyperkalemia	15 (32.6)
Deranged creatinine as per age	20 (43.47)
ASO titre (> 200 IU/ml)	23 (50)
Low C_3 (< 0.3 g/dl)	44 (95.7)

Complications

Most common complication was AKI in 20 (41.3%) followed by CCF in 8 (17.4%). (Table 5)

Table 5. Complications of PIGN

Complications	Number (%) (n=46)
Congestive cardiac failure	8 (17.4)
Encephalopathy	3 (6.5)
Hypertensive retinopathy	1 (2.2)
RPGN	1 (2.2)
AKI	19 (41.3)
Stage 1	11 (57.9)
Stage 2	5 (26.3)
Stage 3	3 (15.8)

A. Outcome at discharge

Most 39(85%) of the children had complete remission at discharge, 7(15%) had partial remission. (Fig.1).

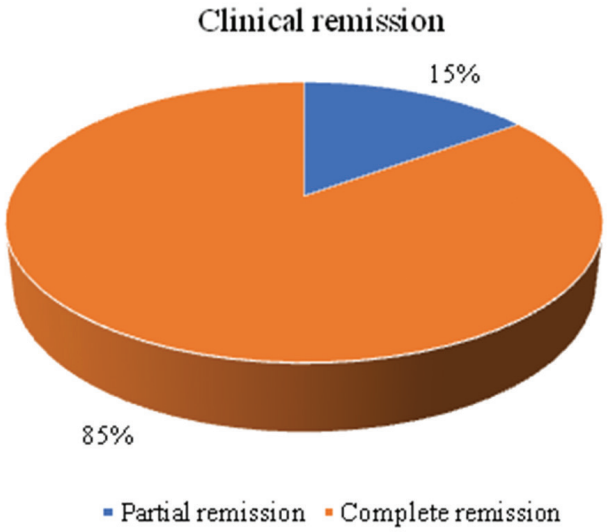

Figure 1. Clinical remission

Laboratory features at follow up

Out of 46 children diagnosed with PIGN, 10 children were lost to follow up at 4 weeks and 10 children did not follow up at 8 weeks. Hence 36 children were followed up both at 4 weeks and 8 weeks of discharge. There was persistence of microscopic haematuria, proteinuria and abnormal creatinine in 17.4%, 8.7%, and 8.7% at 4 weeks and 10.9%, 8.3% and 4.4% cases respectively at 8 weeks follow up.

DISCUSSION

Sixty-three children presenting with the features of acute nephritic syndrome were prospectively recruited. Out of these, 73% were

diagnosed as PIGN. Renal diseases such as Lupus nephritis, IgA nephropathy, RPGN and MPGN were encountered in 27% cases. It is therefore imperative that diagnosis other than PIGN be searched for, whenever a child presents with features of acute nephritic syndrome. Similarly, although PSGN constituted most of the PIGN cases, few cases were due to mumps and pneumonia (6.5%), emphasizing the need to recognize acute nephritic syndrome as the potential complication of these tropical diseases. In this study, etiology could not be established in 30% cases. This may be partly due to inability to perform Anti-DNAse B test, which is expensive, and majority of patients could not afford it. The mean age of children presenting with PIGN was 11.2 years with 97.8% of them being above 5 years. This observation is in accordance with other studies in which age at presentation of childhood PIGN is 5 – 12 years.[1] The rarity of PSGN in very young children is attributed to the low rate of streptococcal pharyngitis in this age group and an immature immune (or antibody) response.[5] The majority of the children in this study were male with the male to female ratio of 1.5: 1 and this finding also matches with the other studies; the reason for this is unknown. [5] About 70% admissions were during the summer and fall. In geographical areas having distinct seasons, pyoderma-associated cases tend to occur in the late summer or early fall months, while in regions with a constant tropical climate cases occur year round. [5, 14] Majority of the PSGN followed pyodermas (58.6%), which is common in developing countries.[1, 5] The most common presentation was edema which was present in 100% cases which is also the most common presenting feature in several other studies. [5] In this study, 41(89.2%) cases had hypertension and among them, stage 2 hypertension was present in 32(78%) cases. The proportion of patients presenting with hypertension is high in other studies also.[7,11,15] Serious and life-threatening complications attributed to hypertension were congestive cardiac failure, encephalopathy, and retinopathy seen in 17.4, 6.4, and 2.2% respectively. The number of children presenting with these complications were high in comparison to one recent study done in India where the incidence were 12.3, 4.6, and 1.5% respectively.[7] The incidence of cerebral complication like headache, altered mental status, and seizures are reported as high as 35% in some studies.[5] Therefore, the need to treat and monitor these hypertensive patients, is of utmost importance to prevent these complications. The glomerular filtration rate is often decreased in acute phase of PIGN. In present study, 41.3% of children with PIGN were diagnosed with acute kidney injury and this percentage is very high when compared with other studies where AKI was seen in 23 and 29%. [7,11] When further classified as per the Acute Kidney Injury Network (AKIN), 15.8% cases were in stage 3 which was less (<20%) as compared to the recent Indian study. Only one patient (2.2%) developed rapidly progressive glomerulonephritis, however dialysis was not required as the patient improved on supportive therapy and received cyclophosphamide pulse therapy for 6 months. In spite of all these complications, none of the patients required intensive care admission and none of them died. This might be due to timely therapeutic intervention in these patients. Among 46 cases of PIGN, no deaths were recorded. One patient was complicated by crescentic glomerulonephritis, however the patient improved on supportive treatment and dialysis was not required. The ASO titre was positive (>200IU/ml) in large proportion of patients (50%) as compared to other study, where ASO titre was elevated in 4.2% cases only.[7] In pharyngitis associated PSGN, ASO titres are usually high in contrast to pyoderma associated PSGN, where anti-DNAse B titres are high.[5] In present study also, ASO titre was elevated in 58% of patients with history of pharyngitis while it was elevated in only 41% of patients with pyoderma. Anti-DNAse B was not done because of financial issue, so its association

with pyoderma couldn't be elicited. Hence, in this study, the patients were diagnosed as PSGN based on the history of pyoderma or pharyngitis along with features of acute nephritic syndrome and low Complement 3 (C_3) with normalization of C_3 at 8 weeks follow up. The sudden decrease of serum C_3 concentration of PSGN with return to normal levels is of foremost diagnostic value in absence of renal biopsy.[5] In present study, 4.2% of cases of PIGN, serum C_3 was normal at presentation. A study from Cincinnati Children's Hospital showed that 10% of children with PSGN had normal serum C_3 concentration at clinical onset.[16] This was confirmed after renal biopsy in these patients. The limitations of this study are that it is hospital based study with small sample size. Also, there is possibility of recall bias, however enough time was given to them to recall the events. Although most of the patients recovered completely at discharge, some patients did not appear for follow up and hence residual renal disease might have been missed. Long term follow up is also needed in the patients having partial remission at discharge as PIGN and AKI are the well known risk factors for developing hypertension and chronic kidney disease later in life.[5,17,18] The strength of this study are its prospective design, well defined criteria for the complications and outcomes, and its location in southern central Nepal in contrast to many other studies.

CONCLUSIONS

PIGN was the most common cause of morbidity in children with acute nephritic syndrome. Edema was the most common clinical feature and AKI is the most common complication. High incidence of hypertension related life-threatening complications like CCF, retinopathy, encephalopathy and renal insufficiency occur that require timely intervention to prevent morbidity and mortality. Long term follow up is also needed in the patients having partial remission at discharge as PIGN and AKI are the known risk factors for CKD.

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