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Clinicopathological features of infection related glomerulonephritis in adult

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Abstract
Post infectious glomerulonephritis, an immunologic response of the kidney to infection, commonly triggered by streptococci. Besides this common infection other organism may incite the pathophysiology. However, clinicopathological features of infection related glomerulonephritis in adults are less elucidated particularly in our perspective.
Objective: The objective of the study was to determine the clinicopathological features of infection related glomerulonephritis patients admitted in a tertiary care hospital.
Methods: This prospective study was conducted at the department of Nephrology in Dhaka Medical College and Hospital, from January 2018 to July 2019 following ethical approval. Total 71 infection related glomerulonephritis cases were included in this study after renal biopsy. Informed written consent was ensured for all participants. Collected data were focused on demographic profile, site of infection and relevant investigations. Data collection was carried out by the investigator herself. Data analysis were done SPSS 22 windows 7 version.
Results: Mean age of all study subjects was 41.61±15.35 SD (years) with slightly male predominance (M: F-1.27:1). Skin infection and URTI were the two most common site of infection found among the patients (46.50%). Unknown site of infection was found in a large portion of the population (36.60%). Nephritic presentation was the most common presentation. Oedema was the most prominent features of the patient (90.1%) but oliguria and hypertension were also present in larger amount. Forty one patients had endocapillary proliferation, twenty three patients had endocapillary & mesangial proliferation and seven had mesangial proliferation. On IF, all staining was seen with C3 with or without presence of staining of other immunoglobulins.
Conclusion: Endocapillary, endocapillary & mesangial and mesangial proliferation were the three histological pattern observed in infection related glomerulonephritis in our perspective which most commonly present with oedema and oliguria

Keywords: glomerulonephritis, Infection, Infection related glomerulonephritis renal biopsy

Introduction

Glomerulonephritis refers to an inflammation of the glomerulus. It is classified into several different pathological patterns, which are broadly grouped into non-proliferative or proliferative types. Primary causes are intrinsic to the kidney. Secondary causes are associated with certain infections (bacterial, viral or parasitic pathogens), drugs, and systemic disorders (SLE, vasculitis) [1]. Infection related glomerulonephritis (IRGN) by non-renal infections is an immune-mediated glomerulonephritis caused. It includes post- infectious glomerulonephritis (PIGN), which develops after complete resolution of the infection and an infection- free latent period, as well as glomerulonephritis associated with an ongoing infection. Infection might be acute or chronic in both cases. Incidence of post infectious glomerulonephritis is declining in industrialized countries but still it is a burden for some developing countries. In the past, most cases occurred in childhood following streptococcal upper respiratory tract or skin infection and were called post infectious GN. But in modern era, the spectrum of causative pathogen, sites and duration of infection differ in adult compared with children. A significant proportion of cases affects adults, particularly the elderly or immune compromised in developed countries [2], In adult not only streptococcus but also other bacterial infections are common. Other pathogens include viral, fungal, protozoal and parasitic infections though these are rare. Adult infection is usually ongoing at the time glomerulonephritis is diagnosed, the term infection-related glomerulonephritis (IRGN) has been proposed [3]. The sites of adult infection are more diversed, including skin, upper respiratory tract, lung, heart, oral mucosa/teeth, and urinary tract.[2] The age predominance in IRGN has been changed. Four decades ago, <6% of affected adults were elderly [4], compared with 34% in a recent report [5]. This change is likely due to improved life expectancy, higher frequency and

severity of infections in the elderly population, and higher prevalence of diabetes. A male predominance was found in adult IRGN after 1990, with male: female ratio ranging from 1.4:1 to 3:1. The clinical presentation of IRGN varies widely, from asymptomatic microscopic haematuria incidentally detected on routine urinalysis to a rapidly progressive glomerulonephritis with acute kidney injury requiring emergent dialysis [2]. Typical histological findings are diffuse end ocapillary proliferation accompanied by infiltration of neutrophils within the capillary lumen on light microscopy, C3-dominant granular deposits with or without IgG co-deposition on immune flurescence and characteristics subepithelial hump shaped deposits on electron microscopy. It is known to have a favourable prognosis of PIGN in children. But a significant proportion of adults do not recover renal function. 8-54% of patients develop persistent renal dysfunction and 4-33% progress to ESRD. The best prognosis appears to be in young adults without underlying conditions. In a Chinese study of 64 predominantly young adults (median age 29 years, only 3% >64 years) without underlying conditions, 86% of patients had complete renal recovery [6]. Much worse prognosis has been reported in elderly patients and those with underlying diabetic glomerulosclerosis. In North American study of 109 elderly patients, 22% patients had complete recovery of renal function, 44% had persistent renal dysfunction, and 33% progressed to ESRD. The independent poor prognostic factors in adult IRGN include older age [5], higher serum creatinine at biopsy **[2, 5]**, more tubulointerstitial scarring 2 and the presence of underlying conditions [6, 7]. Diffuse crescent formation is also a poor prognostic indicator in IRGN [8, 9]

Objectives

General objective

To determine the clinic opathological features of infection-related glomerulonephritis

Specific objectives

- To observe the clinical features of infection-related glomerulonephritis
- To find out the histological pattern of infection-related glomerulonephritis
- To determine the frequency of IRGN among patients presented with features of glomerulonephritis

Materials and Methods

It was a prospective study conducted in the Department of Nephrology, Dhaka Medical College Hospital from January 2018 to July 2019. A total of 732 patients presented with features of GN among them 96 patients were suspected as IRGN based on clinical or laboratory evidence of infection preceding the GN, low complement levels (C3) at presentation, active urinary sediments (red blood cells RBCs, RBC cast and white blood cell casts). A purposive sampling technique were followed for sample selection. Ethical clearance had been taken from the Ethical Board from DMCH. In all patients urine routine microscopic examination, 24 hour urinary total protein, serum creatinine, complete blood count, serum albumin, HBsAg, Anti-HCV, complement level (C3, C4) were done. In some cases ASO titre, chest X-ray, urine and blood for culture and sensitivity was done to identify infection. ANA, anti-ds DNA antibody, anti-neutrophil cytoplasmic antibodies, electrocardiogram and X-ray KUB were done when needed.

76 patients along with any of the following criteria: requirements of dialysis at presentation, progressive renal impairment, and persistent proteinuria of > 1gm per day or nephrotic range proteinuria at presentation underwent percutaneous renal biopsy after all prebiopsy work up. Two biopsy sample were sent to the department of pathology in 2 separate test tube. Renal biopsy was done by following procedure. Patients were positioned in prone with a pillow under the abdomen to straighten the spine. Left kidney was identified by ultrasonography. An indelible pen mark was used to indicate the point of entry of the biopsy needle. Local anaesthetic was infiltrated into the skin at the point previously marked. A stab incision was made through the dermis to ease passage of the biopsy needle. Once sufficient renal tissue obtained, the skin was dressed and the patient rolled in supine position and followed up. Biopsy sample was analyzed by single renal histopathologist for light microscopy using Hematoxylin and Eosin stain, Periodic acid Schiff stain (PAS), Silver stain and immunofluorescence study. Finally 71 patients were confirmed to have IRGN and selected as sample population of the study. Statistical analysis were done by using SPSS software version 22.0. Chi-square test was performed to compare between groups and ANOVA test was performed to compare the mean age and proteinuria of groups. Confidence interval will be considered at 95% level. P value of <0.05 was considered statistically significant.

Results

Among 732 patients presented with features of GN, 96 patients were suspected as IRGN. 71 patients were confirmed to have IRGN and included in final analysis

Table 1: Frequency of IRGN patient among total GN patient (732)

Glomerulonephritis	Frequency (n)	Percentage (5)
IRGN	71	9.7%

Table 1 showed distribution of IRGN among total Glomerulonephritis. 9.7% cases had IRGN

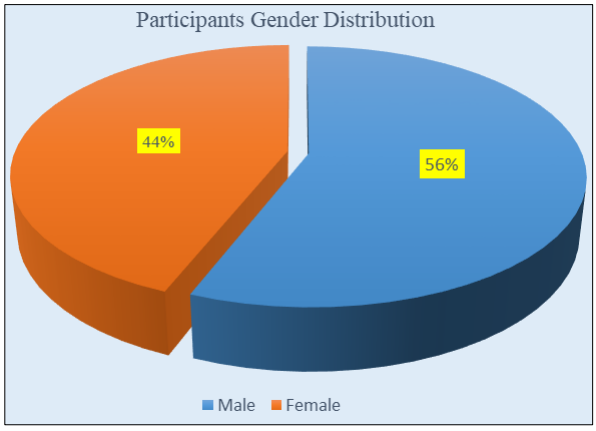

Fig 1: Gender distribution of study population (N=71)

Figure I showed among 71 study population, 40(56%) were male and 31(44%) were female. Male and female ratio was 1.27:1.

Table 2: Age distribution of study population (N=71)

Age (years)	Frequency (n)	Percentage (%)
≤ 20 yrs.	11	15.5
21- 40 yrs.	20	28.2
41 - 60 yrs.	35	49.3
>60 yrs.	5	7.0
Mean ± SD	41.6 ± 15.4	
Min - Max	18 -65	

Table 2 showed, among the study population maximum 35(49.30%) cases were in 41-60 years age group, 20 (28.20%) were in 21 - 40 years age group, 11(15.5%) were in ≤20 years age group and 5(7.0%) were in >60 years age group. The mean age of the patients was 41.61±15.35 years.

Table 3: Site of infection preceding IRGN (N=71)

Site of infection	Frequency (n)	Percentage (%)
Unknown	26	36.6
URTI	19	26.8
Skin	14	19.7
Lung	10	14.1
LUTI	7	9.9
>1 sites	5	7.0

Table 3 showed, among the study cases maximum 26 (36.6%) patients had an unknown site of infection, 19 (26.8%) cases had URTI, 14(19.7%) cases had skin infection, 10(14.1%) cases had lung infection, 7(9.9%) cases had LUTI and 5 (7.0%) cases had more than one site of infection.

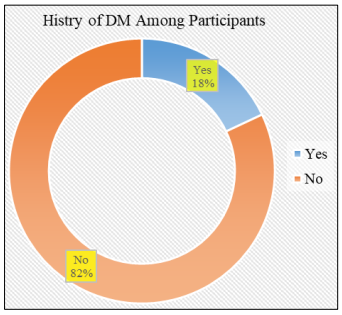

Fig 2: History of DM among study population (N=71)

Figure II showed, among study population, previous history of DM was present in 13(18%) cases. Rests 58 (82%) cases had no history of DM.

Table 4: Clinical features of study cases (N=71)

Clinical features		Frequency (n)	Percentage (%)
Oliguria	Yes	51	71.8
	No	20	28.2
Hypertension	Yes	50	70.4
	No	21	29.6
Haematuria (Gross)	Yes	14	19.7
	No	57	80.3
Oedema	Yes	64	90.1
	No	7	9.9
Fever	Yes	43	60.6
	No	28	39.4
Renal failure requiring dialysis	Yes	11	15.5
	No	60	84.5

Table 4 showed, among the study cases oliguria, hypertension, gross haematuria, oedema and fever was present in 71.80%, 70.40%, 19.70%, 90.10% and 60.60% cases respectively. 11 (15.5%) cases required dialysis due to renal failure.

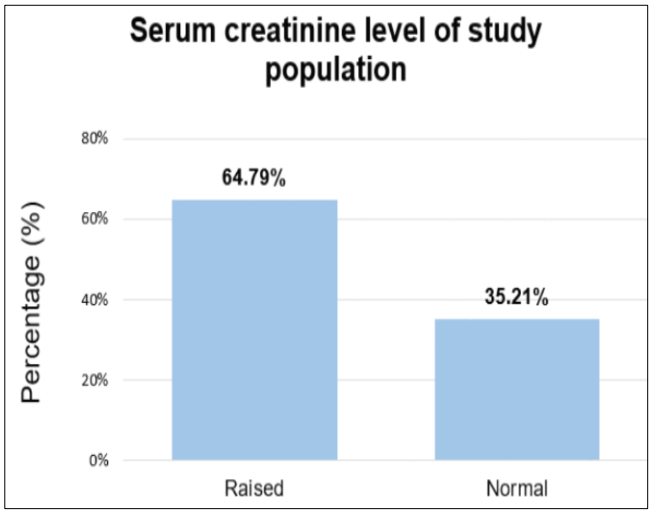

Fig 3: Serum creatinine level of study population (N=71)
Among the study cases 46(64.8%) cases had raised serum creatinine level and 25(35.2%) cases had normal serum creatinine

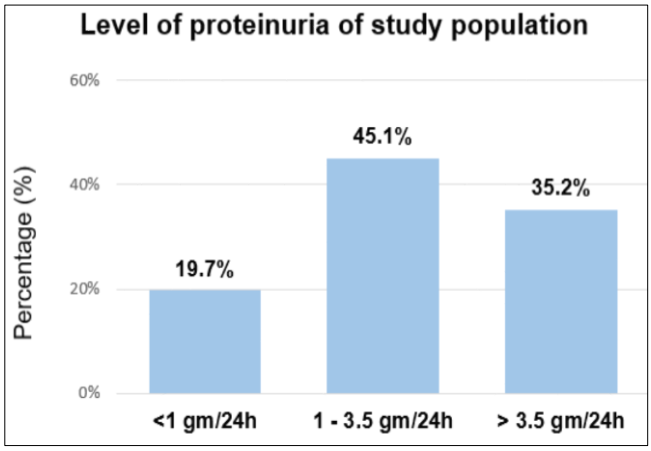

Fig 4: Level of proteinuria among the cases (N=71)

Among the study cases <1gm/24h proteinuria was in 14 (19.7%) cases, 1-3.5 gm/24h proteinuria was in 32 (45.1%) of cases and >3.5gm/24h proteinuria was in 25 (35.2%) cases.

Table 5: Histological pattern of glomerulonephritis among IRGN patients (N=71)

Light microscopy	Frequency (n)	Percentage (%)
Endocapillary proliferation	41	57.7
Endocapillary and mesangial proliferation	23	32.4
Mesangial proliferation	7	9.9
Cellular crescents	33	46.48
IF findings	Frequency (n)	Percentage (%)
C3 and IgG	44	62.0
C3 and IgA	9	12.7
C3 and others	18	25.3

Table 5 showed, on light microscopy, most common histological pattern was endocapillary proliferation (57.7%) followed by endocapillary and mesangial proliferation (32.4%), and mesangial proliferation (9.9%). 46.48% patients having glomerular crescent formation.In immunofluorescence study revealed C3-dominant or co-dominate glomerular staining in 100% cases. IgG was most frequent found in 62% and IgA found in 12.70% cases

Table 6: Clinical and biochemical presentation of different histological pattern in IRGN (N=71)

Presentation	Endocapillary proliferation (n=41)	Endocapillary and mesangial proliferation (n=23)	Mesangial proliferation (n=7)	Total (N=71)	p- Value
Age	41.46±15.16	44.41±13.11	38.43±20.35	41.61±15.35	0.660**
HTN	28(68.30%)	17(73.90%)	5(71.40%)	50(70.40%)	0.991*
Proteinuria (gm/24h)	3.4±2.55	3.26±2.35	2.33±1.40	3.40±2.55	0.676**
Dialysis support	6(14.6%)	4(17.39%)	1(14.30%)	11(15.49)	0.784*

*Chi-Square test (χ^2) was performed to compare between groups
** ANOVA test was performed to compare the mean age and proteinuria of groups

Table 6 showed within the different histopathological pattern there had no significant difference regarding mean age, HTN, mean proteinuria and dialysis support (p=0.660, 0.991, 0.676, 0.784 respectively).

Table 7: Histological features in different pattern of IRGN (N=71)

Histological features	Endocapillary proliferation (n=41)	Endocapillary and mesangial proliferation (n=23)	Mesangial proliferation (n=7)	Total (N=71)	p- Value
Glomerular crescents	18(37.5)	12(44.44)	3(37.5)	33(46.48)	0.813
Glomerular neutrophil infiltration	25(52.08)	13(48.15)	3 (37.5)	41(57.75)	0.607
IgA deposition	5(10.42)	2(7.41)	2(25.6)	9(12.68)	0.515

Chi-Square test (χ^2) was performed to compare between groups

Table 7 showed within the different histopathological pattern there had no significant difference regarding glomerular crescents, glomerular neutrophil infiltration and IgA deposition (p=0.813, 0.607, 0.515 respectively).

Discussion

Infection related glomerulonephritis is one of the renal problems that have encountered in nephrology ward. The spectrum of the disease has changed. It is important to understand the clinic opathological features of infection-related glomerulonephritis to combat the disease. Among the 732 patients presented with features of glomerulonephritis, 71(9.7%) cases were finally diagnosed as infection related glomerulonephritis. In this study mean age of the patients was 41.61±15.35 years. Maximum patients were 35(49.30%) between 41-60 years followed by 20(28.2%) between 21-40 years, 11(15.5%) 20 years and below and 5(7%) over 60 years respectively. This finding is similar to the findings of Sakthirajan and associates [10]. They also found the mean age of IRGN cases 42±13.5 years. Among their 47 cases maximum 18 (38.9%) cases aged between 40-60 years which is consistent to the findings of this study. Another study conducted by Handa and associates found the mean age of their Infection related glomerulonephritis cases 51±17 years [11]. Another study conducted by Srisawat and associates found the mean age of their IRGN cases 43.89 years [12]. Regarding gender, 56% cases were male and 44% were female. Male to female ratio was 1.27:1. This finding is almost similar to the findings of Natarajan and co-researchers [13]. Among their 102 infection related glomerulonephritis cases 56 (54.9%) were male and 46(45.09%) were female. Study conducted by Murmu and associates and Marques and associates [14, 15] and Dhanapriya and associated [16]. Among the study population in 36.60% cases site of infection was unknown. In this study, most common site of infection was upper respiratory tract in 26.8% cases, followed by skin in 14(19.7%) cases, lung in 10(14.1%) cases, lower urinary tract in 7(9.9%) cases and more than one site of in 5(7%) cases. Among the study population history of DM was present in 13(18%) cases. Among their study cases 17% cases had DM which is consistent to the findings of this study. Among their 82 study cases 100% cases had oedema, hypertension was present in 86.6% cases, haematuria was found in 26.8% cases. According to Trivedi and associates, among their IRGN cases hypertension was present in 81.7% cases, oliguria was present in 83.2% cases, haematuria was present in 15.2% cases and dialysis was required in 17.5% cases which is consistent to the findings of this study.[17] Regarding clinical features like HTN and dialysis support there had no significant difference within different histological pattern of glomerulonephritis (p=0.991 and 0.784 respectively). Regarding laboratory findings of the study population revealed that, 46(64.8%) cases had raised serum creatinine level, 14(19.7%) cases had proteinuria <1gm/24h, 32(45.1%) cases had proteinuria 1-3.5 gm/24h and 25(35.2%) cases had proteinuria >3.5gm/24h. The mean proteinuria was 3.40±2.55 gm/24 h. According to Satoskar and colleagues endocapillary proliferation was the commonest histological pattern of infection related glomerulonephritis [18]. Consistent to their finding this study revealed similar result. Endocapillary proliferation, endocapillary and mesangial proliferation and mesangial proliferation was present in 57.70%, 32.4% and 9.90% cases respectively. Resolution stage of PIGN may show mesangial proliferation. In his study endocapillary proliferative glomerulonephritis was present in 65% cases, glomerular crescents were present in 45% cases and glomerular neutrophil infiltration was present in 55% cases. In immunofluorescence study revealed C3 staining with or without immunoglobulin in 100% cases. Among co deposition of immunoglobulin IgG was

maximum 62% and IgA was found in 12.7% cases. Therefore, this study revealed infection related glomerulonephritis was more common in male and in 41-60 years age group. Nephritic presentation was common. Maximum cases had increase serum creatinine level (64.8%). Nephrotic range proteinuria was present in 35.2%. Endocapillary proliferation was the commonest histological pattern of infection related glomerulonephritis.

Limitations of the study

The study was a single center study. Organism specific glomerular changes and its association was not evaluated. Electron microscopic examination was not done because of lack of facilities.

Conclusion and Recommendation

In this study, it is observed that IRGN was more in male patient in 41-60 years age group. Oedema (90.1%) was the commonest presentation that was present among the cases. Respiratory tract and skin were two most common site of infection. A large portion of study population site of infection could not be identified. Maximum cases had renal impairment (64.8%). Predominant histopathological pattern was endocapillary proliferation. Further studies with follow up of the patients are recommended

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