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A STUDY OF INFECTION-RELATED GLOMERULONEPHRITIS(IRGN) FROM A TIER-2 CITY IN SOUTHERN TAMILNADU

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ABSTRACT

Infection-related glomerulonephritis(IRGN)/ Postinfectious glomerulonephritis (PIGN) is an immune-mediated glomerulonephritis caused by non-renal bacterial viral infections.In children it usually follows skin or pharyngeal infection followed by acute Nephritic syndrome.However in adults IRGN presentation more often in an atypical way .This study was done in a retrospective manner wherein we had analysed the way of presentation of those cases whose kidney biopsy was suggestive of IRGN. RPGN ,Acute Nephritic syndrome or Nephrotic syndrome with or without renal failure or Renal failure with Subnephrotic proteinuria are the various presentations we have seen in our study popuation. Many of them had diabetes ,Preexisting kidney disease .Most of them had renal failure on presentation . Nearly half of them needed dialysis in the shortterm. A significant percentage had progresssion to CKD over a period of time . IRGN in adults is not as benign a disease as in children

INTRODUCTION

Postinfectious glomerulonephritis (PIGN) is an immune-mediated glomerulonephritis caused by non-renal bacterial ,viral infections. In the past, most cases occurred in childhood and followed streptococcal upper respiratory tract or skin infections, and hence were called 'post-streptococcal glomerulonephritis (PSGN)'. The past 3 decades have witnessed a major shift in epidemiology and outcome. The spectrum of causative pathogens and the sites and duration of infection differ in adults compared with children.. Because infection is usually ongoing at the time GN is diagnosed, the term infection-related glomerulonephritis (IRGN) has been proposed[2] The sites of adult infection are more heterogeneous, including skin, upper respiratory tract, lung, heart, oral mucosa/teeth, and urinary tract. In contrast to childhood PSGN and epidemic PSGN, which usually resolve, sporadic adult IRGN has a guarded prognosis, with a significant proportion developing chronic kidney disease or end-stage renal disease (ESRD)[1].

MATERIALS AND METHODS;

This was a retrospective study conducted from two hospitals in a Madurai Tamilnadu. We had taken records of patients whose kidney biopsy report shows IRGN(Diffuse Endocapillary Proliferative exudative Glomerulonephritis). The patient's clinical presentation and laboratory investigation reports were analysed .Their short term & outcome at 1 year were analysed. Indication for kidney biopsies

1. Presentation as RPGN(Rapidly Progressive Glomerulonephritis)
2. Adult onset Nephrotic syndrome with/without renal failure.
3. Acute Nephritic Syndrome without preceding obvious infections/ASO neg/C3 ,C4 normal
4. Need for RRT on presentation with normal sized kidneys & Proteinuria.

All the biopsies were performed under ultrasound guidance using Bard® Max-Core® disposable core biopsy instrument. .All renal biopsy samples were processed according to the standard techniques of LM and IF. For each patient, six slides, which were stained with hematoxylin and eosin, Masson's trichrome, periodic acid-Schiff, and Jones methenamine silver were reviewed. Systematic analysis on the morphologic changes of glomeruli, tubules, interstitium, and vessels was done according to the practical standardization in renal biopsy reporting. IF staining was performed on 3 µm cryostat sections using polyclonal fluorescein-isothiocyanate-conjugated antibodies to IgG, IgM, IgA, C3, C1q, C4, kappa and lambda . The intensity of IF staining was graded on a scale of 0 – 3+. The histopathological LM diagnosis of IRGN was made by the presence of typical endocapillary or endocapillary with mesangial proliferation with or without the presence of neutrophilic infiltration depending on the stage of the disease when the patient underwent the biopsy. This was coupled with the IF findings of typically high-intensity staining for C3 with or without the presence of staining for other Igs.
The In hospital ethical clearance were obtained.

RESULTS

All the patients whose kidney biopsy was suggestive of IRGN were included .

27 patients whose kidney biopsies showed Diffuse proliferative and exudative GN with abundant intracapillary neutrophils suggestive of IRGN were included in the study
11 female ; 16 male patients
Age group ; Mean age 46.44 yrs

Male	Female
46.6 yrs	46.5 yrs

Age group distribution

SEX AGE	M	F
20 TO 40	3	3
40 TO 60	12	6
>60	1	2

There is a slight male predominance of patients & in 40-60 age group(66,6%).

IRGN-preexisting Diabetes

sex	NON- DM	DM
M	9	8
F	8	2

37 % patients had underlying Diabetes mellitus.
IRGN- Hypertension

	NON-HTN	HTN
M	7	10
F	1	9

19 patients (70.3%) patients had hypertension on presentation
IRGN Underlying CKD

CKD	CKD	NON- CKD
M	3	14
F	1	9

4 (14.8%) patients had preexisting CKD.On Presentation almost all the patients had edema .Their renal function on admission based on S.creatinine

S.Creatinine	<1.3 mg/dl	1.4-4 mg/dl	4.1-7 mg/dl	> 7mg/dl
20-40 years	0	6	1	0
41-60 years	0	8	2	5
>60 years	0	2	2	1

1 patient had anuria for one month recovered later.(reached normal

creatinine after 45 days).7(25.9%) patients had oliguria which improved. Majority patients had proteinuria >2+/spot PCR >3.Two patients had gross hematuria/others had microscopic hematuria.ASO level was elevated in 5/27 patients(18.5%). Complement C3 &C4 levels were low in 77.7% & 3.7% respectively.

C3 level (90-180)	Normal	Low
Patients	7	20
C4 level (10-40)	Normal	Low
Patients	26	1

Histopathological features on light microscopy/IF study of renal biopsy of patients with infection-related glomerulonephritis

S.No	Light Microscopy	IF	No of Patients
1	DPGN	C3 +IgG	17
2	DPGN/CRESCENTS	C3+IgG,C3	4
3.	DPGN+DIAB.NEPHROPATHY	C3+IgG,C3	3
4	FPGN	C3+IgG	1
5	DN+CRESCENTS	C3	1
6.	MES.PGN.+ATN	C3+IgG	1

Kidney biopsy showed DPGN(Diffuse Proloferative Glomerulonephritis), DPGN with crescents , DPGN with ATN ,Focal Proliferative Glomerulonephritis,Diabetic nephropathy with crescents

Site of infection	No.
Skin	16
Unknown	11
Blood culture positive	2
Urine culture positive	5

There is a known source of infection in 16/27(60%) either in the form of cellulitis,Furuncle Herpes Zoster Or ulcer whereas in others the site of infection was not clear. In the remaining 11 patients two patients had grown Staphylococcus Aureus in Blood culture,.Five had urine culture positive (E.Coli,Klebsiella,CONS). . Eleven (40.7%) patients needed hemodialysis on admission. Of the patients whom dialysis was initiated 6/11(55%) had recovery of renal function whereas 5/11(45%) had either partial or non recovery or progression to CKD.Two (7.4%) patients had died in the study period .We had two patients who tested positive for ANA & ANCA each respectively.

S.NO	Dialysis at admission		Recovered		Non recovery/ Progression to CKD	
	Male	Female	Male	Female	Male	Female
1.	7	4	4	2	3	2

Immunosuppression in the form of Steroids was used in those who presented as RPGN or Progressive Renal failure in many cases even before biopsy diagnosis is available.Nearly 21/27 (77.7%) had received steroids.

Treatment	Steroids	
	Yes	No
Patients	21	6

DISCUSSION

This study was unique in that we had a look back at varied clinical presentation of a common pathological entity (Diffuse proliferative and exudative GN with abundant intracapillary neutrophils/ IRGN) in adults. Our patients presented either as Rapidly Progressive Glomerulonephritis(RPGN), Anuric Renal failure or Nephrotic syndrome or acute Nephritic syndrome. Clinical clues to diagnosis of IRGN/PIGN in these adults was lacking due to lack of typical presentation as in children. ASO titre & complements levels were not helpful & hence all of our patients underwent kidney biopsy. Most reported series of IRGN from around the world report male predominance with male:female ratio ranging from 1.4:1 to 3:1[1,2]. Our population had a slight male predominance with the male:female ratio at 1.45:1. In the pediatric age group, the sites of infection are usually the throat or skin; however, the adult population shows a much-varied site of preceding infection including upper respiratory tract, skin, lung, heart, urinary tract, teeth/oral mucosa, bone, and deep-seated visceral, or somatic abscesses[1].In our series, the most common infection was a skin infection(pyoderma) or cellulitis. In our study there was a significant proportion of patients for whom site of primary infection is not obvious11/27(40%).Of the 11 patients 2/27(7.4%) patients had grown Staphylococcus Aureus in Blood culture,5/27(18.5%) had urine culture positive (E.Coli, Klebsiella, CONS). Its likely that Urinary tract,Blood borne infection could be triggering immune response. In one study of 109 elderly patients from the United States, the four most common sites were skin (28%), lung (16%), urinary tract (13%), and upper respiratory tract (10%). Of note, in a minority of adult cases, the infection is not clinically evident and some patients with clinically evident infection may have negative cultures, especially following antibiotics[5,6] In contrast to children in whom the latent period between infection and onset of renal disease is typically 1–6 weeks, in a significant percentage of adults and particularly elderly patients the infection is only discovered at the time of IRGN diagnosis, indicating that the infection may go unrecognized for some time.[2] .Hypertension is present in majority of adult patients of IRGN at presentation.[3-5] In our study 19/27 patients(70.3%) had hypertension. We also had 10/27 patients(37%) who had pre-existing Diabetes. Renal biopsy showed DPGN superimposed on diabetic nephropathy in 3 patients(11.1%) & Crescents with DN changes in 1 patient(3.7%).The degree of proteinuria varies from 1-3 g/day, with a 25%–30% of patients presenting as a nephrotic syndrome. Almost all adult of IRGN patients have microhematuria, and gross hematuria occurs in 17%–56% of patients.[3,5] .In our patient series majority had micro-hameturia and only two had macro haemuturia. ASO was positive only in 5/27 patients (18.5%). Hypocomplementemia is usually seen in 35%–80% of adult patients and in 90% of the children[3] .In most patients, C3 is depressed with a normal level of C4. In our series,77.7% of patients had low C3 at presentation . The most common LM finding on renal biopsy is diffuse proliferative and exudative GN with abundant intracapillary neutrophils[1] In one study of 86 patients, this pattern was seen in 72% of patients, followed by focal endocapillary proliferative GN in 12% and mesangial proliferative GN in 8%[3] y represent milder disease or a resolving phase. Crescentic and necrotizing glomerulonephritis with >50% crescents is rare, and affected only 5% of cases in the above study, although focal crescents involving o20% of glomeruli are encountered in up to a quarter of cases[2] In our series, the most common LM pattern was the typical endocapillary proliferative GN seen in 77.7% of the patients. The next most common pattern seen was a diffuse endocapillary with crescents (<50%) seen in 14.8% of the patients. Crescentic GN with ATN >50% crescents was seen in one (3.7%).Focal proliferative GN was seen in one patient (3.7%).We had underlying Diabetic Nephropathy in 4/27 (14.8%) biopsy specimens. We also had 4 patients (14.8%) who had underlying kidney dysfunction superimposed on which IRGN occurred resulting in worsening of Renal failure. 2/4 (50%) of this population had progression to ESRD over a period 1-2 years after the episode of IRGN. In our series majority of patients had renal failure(> 90%) on presentation, and it is higher in elderly patients than younger adults. In contrast to children in whom the need for dialysis for severe acute renal failure is uncommon, close to a half of elderly patients require dialysis at the initial presentation for uremic symptoms and/or fluid overload.[1,7] .In our study 11/27 (40.7%) needed dialysis. Of the patients whom dialysis was initiated 6/11(55%) had recovery of renal function whereas 5/11(45%) had either partial or non recovery or progression to CKD. One patient had Anuria for one month from which she recovered completely after 45 days. Her renal functions are normal in the followup period of 1 year. Our study was conspicuous by the absence of IgA dominant Postinfectious GN exact cause of which is not known.We had treated 77.7% of patients with steroids as they had presented as RPGN,Acute nephritic Syndrome with severe renal failure.This cohort of adult patients who had severe form of presentation of IRGN,hence there is more need of RRT and need for immunosuppression.

CONCLUSION ;

IRGN in adults is common in developing countries like India. It can have varied presentation in adults & elderly in the form of either RPGN,Acute nephritic syndrome, Anuric renal failure or

Subnephrotic proteinuria with renal failure. Clinical clues to diagnosis may be lacking in adults & older patients. Primary site of infection may not be obvious or it may be ongoing.IRGN can present as more severe renal impairment and need for dialysis in adults.They can have worsening of pre-existing renal function ,Hypertension or cardiac failure. Kidney Biopsy is needed in cases where the diagnosis is not obvious or RPGN like presentation or severe renal failure.Some adults and elderly patients may have irreversible damage in kidney function.

Limitations of study:
Small sample size

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