Open Access

Original Article

Clinicopathological Analysis of Biopsy-Proven Glomerulonephritis in the Pediatric Patients : A Study from Tertiary Care Centre

Rabia Saleem Safdar, Afsheen Asghar Khan, Muhammad Faisal Mehar, Shazia Riaz, Nusrat Hussain, Kiran Abbas*

Nishtar Medical University, Multan Pakistan, *Jinnah Postgraduate Medical Center, Karachi Pakistan

ABSTRACT

Objective: To evaluate the clinic-pathological characteristics and their association with biopsy-proven glomerulonephritis in pediatric patients.

Study Design: Prospective longitudinal study.

Place and Duration of Study: Pediatric Department, Nishtar Medical University, Multan Pakistan, from Jan 2014 to Dec 2019.

Methodology: During the study, a total of 211 renal biopsy reports of different age groups were studied and analyzed for clinic-pathological features and patterns of direct immunofluorescence.

Results: The mean age of 8.6±3.25 years was observed. The most common pathology was focal segmental glomerulo-sclerosis in 86 (40.76) of the patients, followed by mesangio-proliferative glomerulonephritis in 41 (19.43) of the patients. Minimal change disease was seen in 26 (12.32) cases. It was observed that the majority of the patients with diffuse proliferative glomerulonephritis were younger than 11 years old, whereas; 10 (11.2), patients with lupus nephritis, 11 (15.1) and membranous nephropathy, 10 (12.2) were comparatively older.

Conclusion: Glomerulonephritis presents a diversified group of diseases with overlapping clinic-pathological features. The present study has reported many significant characteristics which could help diagnose a particular disorder among the pediatric population.

Keywords: Focal Segmental Glomerulo-sclerosis (FSGS), Glomerulonephritis, Nephropathy, Pediatric.

How to Cite This Article: *Safdar RS, Khan AA, Mehar MF, Riaz S, Hussain N, Abbas K. Clinicopathological Analysis of Biopsy-Proven Glomerulonephritis in the Pediatric Population of Pakistan: A Study from Tertiary Care Centre. Pak Armed Forces Med J 2022; 72(4): 1283-1286.*

DOI: https://doi.org/10.51253/pafmj.v72i4.5828

INTRODUCTION

Glomerulonephritis is defined by a range of immune-mediated kidney diseases associated with inflammation within the glomerulus and other kidney parts.[1] There are two proposed mechanisms via which the disease causes inflammation of the glomerulus. Firstly, the production of the patient's antibodies attacking the glomerular basement membrane (GBM) and the patient's antibodies attacking the non-glomerulus endogenous or exogenous antibodies in the patient's circulation.[2] This results in either a severe, rapidly progressive, destructive disease or a mild, slowly developing disorder, depending upon the amount of antigen-antibody interaction and the category and number of mediators involved in the process.[3]

The aetiology of glomerulonephritis is generally confusing because the term glomerulonephritis defines a constellation of different renal diseases that may share overlapping pathogenesis.[4] Glomerulonephritis manifests the autoimmune reaction to a patient's antigens or is caused by a secondary reaction to endogenous or exogenous antigens, infections, malignant, or metabolic diseases.[5,6]

To the best of our knowledge, most renal disease literature focuses on adult patients, and only a few retrospective reports are based on the pediatric population.[7-9] Renal diseases in children are on the rise. The glomerulonephritis is associated with severe clinical course and morbidity among pediatric patients. The scarcity of data from a local setting was severely felt. Therefore, the present study analyzed the clini-copathological pattern of renal diseases in the pediatric population based on fully worked-up renal biopsies. The study aimed to evaluate the clinical and histo-pathological characteristics of glomerulonephritis in pediatric patients in our local setting.

METHODOLOGY

A prospective longitudinal study was conducted from January 2014 to December 2019 for six years at the Pediatric Department, Nishtar Medical University, Multan Pakistan. Ethical approval was obtained from the Institutional Review Board of Nishtar Medical University, Multan prior to the study (Reference #

Correspondence: Dr Rabia Saleem Safdar, Pediatric Department, Nishtar Medical University, Multan, Pakistan.

Received: 06 Dec 2019; revision received: 20 Jun 2021; accepted: 24 Jun 2021

5226/NMU&H). A non-probability convenience sampling technique was used to select patients in the study.

For sample size calculation, the OpenEpi calculator was used. Shiva ad Behjati revealed acute glomerulonephritis prevalence of 75 in children aged between 6-15 years.[7] By keeping a confidence level of 90 and a margin of error of 5, a sample size of 203 was obtained. A total of 211 renal biopsy reports of different age groups were collected, studied, and included in this study.

Inclusion Criteria: Renal tissue from all patients with suspected nephropathy, kidney injury, proteinuria, and hematuria was sent for histopathological analysis.

Exclusion Criteria: Patients with debilitating illness or pregnant women, were also excluded from the study.

Comorbidities were classified as none, cardiovascular, diabetes mellitus and hypertension. The biopsy procedure was based on standard international protocols.

Informed written consent from the guardian of the children was obtained prior to the biopsy. In addition, they were informed of the procedure and the risk involved. Before the biopsy, each patient was assessed for vitals, haemoglobin levels, liver function tests, and coagulopathy profiles.

Desmopressin 0.4ug/kg was administered two hours before the kidney biopsy to the patient whose urea was more than 50 mg/dl. Ultrasound Kidneys were also a prerequisite to check the size of the kidney, cortical thickness, parenchymal changes and pelvicalyceal system. During the biopsy, the patient had to lie prone during the procedure. Two core samples were taken during the procedure. After the completion of the procedure, the patients were advised to have bed rest in a supine position at least for thirty to sixty minutes, and their vitals, including blood pressure, heart rate and rhythm and urine output, were regularly checked as per the standard protocol of the hospital to prevent hypotensive crisis or shock.

The patients were cleared after 8-12 hours post-procedure observation. The patients were advised to rest for the next 24 hours and to avoid physical activities for the next 24-48 hours. Biopsies were conducted with core biopsy instruments of 16 and 18 gauge. Two core samples were taken for light microscopy and immunofluorescence. An experienced histopathologist who was blinded to the objectives of the study prepared the tissue sectioning and paraffin embedding. These entire specimens were analyzed by microscopy using hematoxylin and eosin, Periodic acid Schiff, Jones silver methenamine, Congo red and Gamoretrichome stains. Immunofluorescence studies were performed using anti-human immunoglobulin, protein C complements, and kappa and lambda light chains. The biopsy-proven renal disease diagnosis was made per standard diagnostic criteria for each disease. The Haas grading was followed to categorize the type of glomerulonephritis.

The statistical analysis was done using the Statistical Package for the Social Sciences (SPSS) version 24.0 and Microsoft Excel. The continuous variables, including the patients' age, laboratory values, etc., were represented as mean plus standard deviation. In addition, the occurrence of glomerulonephritis was presented in frequency and percentage along with other clinicopathological characteristics.

RESULTS

A total of 211 cases were included in the study with the mean age of 8.6±3.25 years with a range of 13 years was reported with the youngest child of one-year old and the oldest child of fourteen years old. There were 102 (48.6) female and 109 (51.5) male patients. The most common pathology was focal segmental glomerulosclerosis (FSGS) in about two-fifths of the patients, followed by Mesangial proliferative glomerulonephritis in one-fifth of the patients. Minimal change disease was seen in 26 (12.32) patients (Table-I).

Table-I: Histopathological Characteristics of Glomerulonephritis Lesions in our study (n=211)

Histopathological Characteristics	n (%)
Diffuse proliferative glomerulonephritis	10 (4.74)
Focal segmental glomerulosclerosis	86 (40.76)
Lupus nephritis	15 (7.11)
Minimal Change Disease	26 (12.32)
Membranous nephropathy	22 (10.43)
Mesangial proliferative glomerulonephritis	41 (19.43)
Membranoproliferative glomerulonephritis	11 (5.21)
Immunofluorescence Results	
Negative	140 (66.35)
C1q Positive	2 (0.95)
C3 Positive	14 (6.64)
IgA Positive	5 (2.37)
IgG Positive	20 (9.48)
IgM Positive	30 (14.22)

The mean age among female children was significantly higher than male patients (female; 9.49±2.92 years and male; 7.93±3.37 years) with a *p*-value of <0.001. In addition, it was observed that most

patients with diffuse proliferative glomerulosclerosis were younger than ten years old, whereas patients with lupus nephritis and membranous nephropathy were comparatively older. However, the change was insignificant (p=0.556) (Table-II).

Table-II Association of factors with the IgA Nephropathy(n=211)

Parameters	Study Groups n (%)			*p*-value
	Group A (5 years or younger) (n=78)	Group B (6-10 years) (n=82)	Group C (11 years or Older) (n=51)	
Gender, n(%)				
Male	48 (61.54)	30 (36.59)	31 (60.78)	0.002
Female	30 (38.46)	52 (63.41)	20 (39.22)	
Diagnosis, n(%)				
Diffuse proliferative Glomerulosclerosis	5 (5.6)	5 (5.6)	1 (0.7)	0.554
Focal Segmental Glomerulosclerosis	15 (32.6)	39 (46.9)	28 (38.8)	
Lupus nephritis	0(0)	4 (3.7)	11 (15.1)	
Minimal Change Disease	9 (17.4)	8 (8.0)	12 (15.1)	
Membranous nephropathy	2 (3.5)	12 (13.6)	10 (12.2)	
Mesangioproliferative glomerulonephritis	13 (30.2)	13 (15.4)	12 (16.5)	
Membranoproliferative glomerulonephritis (MPGN)	4 (7.0)	6 (6.8)	2 (1.4)	

DISCUSSION

The incidence of renal disorders, both acquired and congenital, has increased substantially in recent years, which has stressed the health care sector globally.[10]

Glomerulonephritis is a group of renal disorders encompassing a minimal change from disease to rapid proliferative glomerulonephritis with severe symptoms and risk of end-stage renal disease.[11] Improper or delayed diagnosis can lead to an increased risk of morbidity and mortality. It is crucial to diagnose the disease and provide treatment to prevent progression to chronic kidney disease that will cause huge patient disability, requiring either regular dialysis or kidney transplantation.[12,13]

In the present study, we found that out of the approximately two hundred biopsies, the most common nephropathy found was the FSGS, i.e., almost 40 percent of cases. FSGS is a progressive inflammatory disease-causing detrimental damage to a portion of the glomerulus of the kidney resulting in sclerosis.[14] In contrast to a previous 20-year-long study, we found a higher prevalence of FSGS in the pediatric population in our study.[15] The multicenter study from Saudi Arabia reported that among the several glomerulonephrites, FSGS was most frequent, with an average prevalence of 21.2 in the last 20 years.[15]

In a similar study by Mubarak *et al.* mean age of 9.79±4.59 years was reported, which WAS greater than the current study. A much higher occurrence of minimal change disease, i.e., 43.8, was observed compared to the 12.32 occurrence in our study. The incidence of focal segmental glomerulosclerosis (FSGS) was 38.14 compared to the current study.[16] An Iranian study by Madni *et al.* in 2003 reported the FSGS and MCD incidence of 25.2 and 27.2, respectively.[17] This indicates that since the year 1996, the pattern of glomerulonephritis has greatly altered and evolved, with a much lower incidence of MCD and a higher incidence of FSGS being observed in neighbouring countries.[18] The exact reason for this upward trend in FSGS lesions among the pediatric population is unknown. Nevertheless, we can attribute it to a true rise in the occurrence of FSGS and the increased awareness and attention towards this lesion, making it easier to detect and diagnose histopathology.

In 2018, a six-year-long study was conducted, evaluating the prevalence and clinicopathological features of membranoproliferative glomerulonephritis (MPGN) among the pediatric Pakistani population. MPGN was reported among 63 (7) children out of the 890 pediatric kidney biopsies observed in the study.[9] In contrast, we found a relatively lower frequency, i.e., 11 (5.21) of the pediatric population diagnosed with MPGN in our setting.

In our study, immune complexes were detected using direct immunofluorescence. Most of the patients were negative for antibodies seen under direct immunofluorescence. Only a minority had IgM, IgG, and IgA complexes and complement components. In contrast to our findings, Haas *et al.* reported that out of the

126 biopsies they observed, about one-half had glomerular immune complex deposits detectable on electron microscopy; moreover, under direct immuno-fluorescence, there were up to 87 of cases that came up positive for at least one immunoglobulin or complement component, even though in most cases the staining was comparatively mild.[19]

LIMITATIONS OF STUDY

We could not include the electron microscopy findings, and the data was from a single centre with limited and restricted demographics. Nevertheless, to the best of our knowledge, this was one of the few studies to report the frequency and the clinico-pathological features of pediatric glomerulonephritis from our region. Further large-scale research should be conducted.

CONCLUSION

The present study reported focal segmental glomerulonephritis (FSGN) as the most frequently occurring glomerulonephritis among the pediatric population in Pakistan. However, only a minority of the patients had positive immune deposits and complemented as seen with direct immunofluorescence.

Conflict of Interest: None.

Author's Contribution

RSS: Study Design, AAS:, SR: Draft writing, data acquisition, MFM: Data acquisition, NH: Critical approval, KA: Draft writing, statical analysis.

REFERENCES

1. Chadban SJ, Atkins RC. Glomerulonephritis. Lancet 2005; 365(9473): 1797-806. doi: 10.1016/S0140-6736(05)66583-X.
2. Dixon FJ. The pathogenesis of glomerulonephritis. Am J Med 1968; 44(4): 493-498. doi: 10.1016/0002-9343(68)90050-8.
3. Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2020; 395(10225): 709-733. doi: 10.1016/S0140-6736(20)30045-3
4. Kambham N, Troxell M. Glomerulonephritis Associated with Other Bacterial Infections. In Bacterial Infections and the Kidney. Springer, Cham 2017; 2(1): 63-85).
5. Rafik H, El Amrani M, El Kabbaj D. Membranoproliferative glomerulonephritis associated with a human immunodeficiency virus infection. Ind J Nephrol 2017; 27(4): 319-320. doi: 10.4103/0971-4065.202838.
6. Akhtar SZ, Adeeb H, Bibi H, Ullah I. Glomerulonephritis; Distribution of Biopsy Proven Glomerulonephritis In Khyber Pakhtunkhwa Province of Pakistan, A Single Centre Study. Prof Med J 2019; 26(5): 44-50.
7. Shiva F, Far RR, Behjati MR. Acute glomerulonephritis in children. J Pak Med Assoc 1994; 44(5): 116-118.
8. Malik SI, Idrees MK, Naseem K, Sadiq S, Raza SH. Pattern of biopsy-proven kidney diseases: experience of a teaching hospital in Bahawalpur, Pakistan. Saudi J Kidney Dis Transpl 2019; 30(5): 1144-1150. doi: 10.4103/1319-2442.270271.
9. Khatri S, Bajeer IA, Tresa V, Hashmi S, Mubarak M, Lanewala AA. Short-term outcome of clinical and histopathologic variants of mesangiocapillary glomerulonephritis in children: A retrospective analysis from a tertiary care center. J Pak Med Assoc 2018; 68(1): 1199-1204.
10. Saran R, Robinson B, Abbott KC, Agodoa LY, Bhave N, Bragg-Gresham J, et al. US renal data system 2017 annual data report: epidemiology of kidney disease in the United States. Am J Kidney Dis 2018; 71(3 Suppl-1): A7-A10. doi: 10.1053/j.ajkd.2018.01.002.
11. Wenderfer SE. Glomerular diseases in children. Adv Chronic Kidney Dis 2017; 24(6): 364-371. doi: 10.1053/j.ackd. 2017.09.005.
12. Gebreyesus LG, Aregay AF, Gebrekidan KG, Alemayehu YH. Factors associated with treatment outcome of acute post streptococcal glomerulonephritis among patients less than 18 years in Mekelle City, Public Hospitals, North Ethiopia. BMC Res Notes 2018; 11(1): 693-698. doi: 10.1186/s13104-018-3794-7.
13. Nataprawira HM, Sapartini G, Indriani K. Delayed Diagnosis of Tuberculoma in a Child with Nephritis due to Systemic Lupus Erythematosus. Turk Thorac J 2018; 19(3): 153-155.
14. Nagata M, Kobayashi N, Hara S. Focal segmental glomerulosclerosis; why does it occur segmentally?. Eur J Appl Physiol 2017; 469(7-8): 983-988. doi: 10.1007/s00424-017-2023-x.
15. AlFaadhel T, Alsuwaida A, Alsaad K.. Prevalence and 20-year epidemiological trends of glomerular diseases in the adult Saudi population: a multicenter study. Ann Saudi Med 2019; 39(3): 155-161. doi: 10.5144/0256-4947.2019.155.
16. Mubarak M, Lanewala A, Kazi JI, Akhter F, Sher A, Fayyaz A, et al. Histopathological spectrum of childhood nephrotic syndrome in Pakistan. Clin Exp Nephrol 2009; 13(6): 589-593. doi: 10.1007/s10157-009-0216-0
17. Madani A, Fahimi D, Esfehani ST. Glomerular diseases in Iranian children: clinico-pathological correlations. Pediatr Nephrol 2003; 18(9): 925-928. doi: 10.1007/s00467-003-1166-5.
18. Trivedi M, Pasari A, Chowdhury AR, Abraham-Kurien A, Pandey R. The spectrum of focal segmental glomerulosclerosis from Eastern India: Is it different? Indian J Nephrol 2018; 28(3): 215-219. doi: 10.4103/ijn.IJN_115_17.
19. Haas M. Immune complex deposits in ANCA-associated crescentic glomerulonephritis: a study of 126 cases. Kidney Int 2004; 65(6): 2145-2152. doi: 10.1111/j.1523-1755-2004.00632.x.