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Research Article

Histopathological Features and Clinical Implications of Obesity-Associated Glomerulopathy in Children

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ABSTRACT

Background: Childhood obesity has emerged as a major public health concern worldwide and is increasingly associated with obesity-associated glomerulopathy (OAG), a renal disorder characterized by glomerular hypertrophy, focal segmental glomerulosclerosis (FSGS), proteinuria, and progressive decline in renal function. Early detection of obesity-related renal injury is crucial to preventing progression to chronic kidney disease (CKD).

Objective: To evaluate the histopathological features and clinical implications of obesity-associated glomerulopathy among obese pediatric patients presenting to tertiary care hospitals in Islamabad, Pakistan.

Methods: A cross-sectional study was conducted at tertiary healthcare centers in Lahore and Hyderabad, Pakistan, from January 2023 to December 2025. A total of 120 obese children aged 6–16 years with persistent proteinuria were enrolled. Clinical assessment included body mass index (BMI), blood pressure, serum creatinine, estimated glomerular filtration rate (eGFR), urinary protein excretion, lipid profile, and fasting blood glucose levels. Renal biopsy was performed in patients with persistent proteinuria (>1 g/day) and/or declining renal function. Histopathological evaluation was carried out using light microscopy and immunofluorescence techniques.

Results: The mean age of participants was 11.8 ± 2.7 years, and 61.7% (n = 74) were male. The mean BMI was 31.4 ± 3.8 kg/m². Proteinuria was present in 78.3% of participants, while hypertension was identified in 34.2%. Renal biopsy was performed in 42 patients. Histopathological examination revealed glomerulomegaly in 83.3%, podocyte hypertrophy in 57.1%, focal segmental glomerulosclerosis in 45.2%, and mesangial expansion in 38.1% of biopsy specimens. The mean urinary protein excretion among biopsy-positive patients was 1.82 ± 0.64 g/day. BMI demonstrated a significant positive correlation with the degree of proteinuria ($r = 0.49$, $p < 0.001$). Patients with FSGS exhibited significantly lower eGFR values compared with those without FSGS (89.4 ± 12.6 vs. 104.8 ± 14.3 mL/min/1.73 m², $p = 0.002$).

Conclusion: Obesity-associated glomerulopathy is an emerging cause of renal injury in Pakistani children. Glomerulomegaly and secondary FSGS were the predominant histopathological findings and were significantly associated with increased proteinuria and reduced renal function. Early screening, lifestyle modification, and timely intervention may help mitigate progression to chronic kidney disease and reduce the long-term burden of obesity-related renal complications.

Keywords: Obesity-Associated Glomerulopathy, Childhood Obesity, Focal Segmental Glomerulosclerosis, Proteinuria, Chronic Kidney Disease, Pediatric Nephrology, Pakistan.

INTRODUCTION

Childhood obesity has emerged as one of the most significant global public health challenges of the 21st century. The prevalence of overweight and obesity among children and adolescents has increased dramatically worldwide, affecting both developed and developing countries. According to recent estimates, more than 390 million children and adolescents aged 5–19 years were overweight

in 2022, highlighting the growing burden of obesity-related complications in younger populations [1]. Obesity is now recognized as a chronic multisystem disorder associated with metabolic, cardiovascular, endocrine, and renal complications that often persist into adulthood [1].

Among the less recognized but increasingly important complications of pediatric obesity is obesity-associated glomerulopathy (OAG), also known as obesity-related glomerulopathy. OAG represents a distinct form of kidney injury characterized by glomerular hypertrophy, glomerulomegaly, proteinuria, podocyte dysfunction, and focal segmental glomerulosclerosis (FSGS) [2,3]. Progressive renal injury resulting from these pathological alterations may ultimately lead to chronic kidney disease (CKD) and end-stage kidney disease if left untreated [2].

The pathophysiology of OAG is multifactorial and involves complex interactions among hemodynamic, metabolic, inflammatory, and hormonal pathways. Excess adiposity promotes glomerular hyperfiltration, activation of the renin–angiotensin–aldosterone system, insulin resistance, oxidative stress, chronic low-grade inflammation, and adipokine dysregulation [3,4]. These mechanisms contribute to podocyte injury, mesangial expansion, and progressive glomerulosclerosis. Recent evidence suggests that obesity-related renal injury may begin during childhood, long before clinically overt kidney disease becomes apparent [2,4].

Histopathologically, OAG is characterized by enlarged glomeruli, podocyte hypertrophy, segmental sclerosis, and varying degrees of tubulointerstitial fibrosis. Glomerulomegaly is considered the hallmark lesion, while secondary FSGS represents a marker of disease progression and poorer renal outcomes [3,5]. These structural alterations are believed to reflect adaptive responses to increased metabolic demand and hyperfiltration associated with obesity [5].

Growing evidence indicates that obese children may exhibit early markers of renal injury, including microalbuminuria, proteinuria, reduced estimated glomerular filtration rate (eGFR), hyperuricemia, and hypertension [4,6]. Such findings emphasize the importance of early screening and timely intervention to prevent irreversible nephron loss and progression to CKD. Furthermore, childhood obesity frequently persists into adulthood, increasing the lifetime risk of obesity-related kidney disease and cardiovascular morbidity [6,7].

Recent studies have highlighted the role of obesity-induced alterations in renal structure and function, including nephron hypertrophy, glomerular enlargement, and activation of pro-inflammatory pathways that accelerate kidney damage [7,8]. The increasing prevalence of pediatric obesity has therefore raised concerns regarding the future burden of CKD and end-stage renal disease worldwide [8].

Despite increasing international recognition of OAG, data from South Asian countries, particularly Pakistan, remain limited. The rising prevalence of childhood obesity in Pakistan necessitates a greater understanding of obesity-related renal complications and their histopathological correlates [8,9]. Evaluating the structural renal changes associated with obesity may facilitate earlier diagnosis and guide preventive strategies aimed at reducing the future burden of CKD.

Therefore, the present study aimed to evaluate the histopathological features and clinical implications of obesity-associated glomerulopathy among obese pediatric patients presenting to tertiary care hospitals in Islamabad, Pakistan [9].

METHODOLOGY

This cross-sectional study was conducted at tertiary healthcare centers in Lahore and Hyderabad, Pakistan, from January 2023 to December 2025. The study included obese children aged 6–16 years who presented to pediatric nephrology clinics with persistent proteinuria and fulfilled the eligibility criteria. Childhood obesity was defined according to age- and sex-specific body mass index (BMI) percentiles recommended by the World Health Organization and Centers for Disease Control and Prevention, with obesity classified as a BMI at or above the 95th percentile for age and sex. A total of 120 participants were recruited through non-probability consecutive sampling after obtaining informed consent from parents or legal guardians.

Detailed demographic and clinical information, including age, sex, duration of obesity, family history of obesity, hypertension, diabetes mellitus, and kidney disease, were recorded using a structured data collection form. Anthropometric measurements including weight, height, BMI, and waist circumference were obtained using standardized techniques. Blood pressure was measured using an appropriately sized cuff, and hypertension was

defined according to age-, sex-, and height-specific pediatric guidelines.

Laboratory investigations included fasting blood glucose, serum creatinine, blood urea nitrogen, lipid profile, serum albumin, urinary protein excretion, and urinary albumin-to-creatinine ratio. Estimated glomerular filtration rate (eGFR) was calculated using the updated Schwartz formula. Persistent proteinuria was defined as protein excretion exceeding 150 mg/day or a positive urinary protein test on at least two occasions separated by three months. Renal biopsy was performed in selected patients exhibiting persistent proteinuria greater than 1 g/day, nephrotic-range proteinuria, declining renal function, or unexplained urinary abnormalities. Renal tissue specimens were processed according to standard histopathological protocols and examined using light microscopy and immunofluorescence. Histopathological parameters assessed included glomerulomegaly, focal segmental glomerulosclerosis (FSGS), mesangial expansion, podocyte hypertrophy, tubular atrophy, and interstitial fibrosis. Histological findings were reviewed independently by experienced renal pathologists to ensure diagnostic accuracy.

Data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 27.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. The association between clinical parameters and histopathological findings was assessed using the independent-samples t-test, chi-square test, and Pearson correlation coefficient where appropriate. A p-value of less than 0.05 was considered statistically significant.

Ethical approval was obtained from the Institutional Review Board/Ethics Committee of the participating institutions prior to study commencement. All procedures were conducted in accordance with the principles of the Declaration of Helsinki, and confidentiality of participants' information was strictly maintained throughout the study.

RESULTS

A total of 120 obese children with persistent proteinuria were enrolled in the study. The demographic and baseline clinical characteristics of the participants are presented in Table 1. The mean age was 11.8 ± 2.7 years, with males comprising 61.7% of the study population. The mean body mass index (BMI) was 31.4 ± 3.8 kg/m². Proteinuria was detected in 78.3% of participants, while hypertension was observed in 34.2%. The mean serum creatinine and estimated glomerular filtration rate (eGFR) were 0.91 ± 0.24 mg/dL and 99.4 ± 15.8 mL/min/1.73 m², respectively. Renal biopsy was indicated and performed in 42 (35.0%) children based on persistent proteinuria and/or declining renal function.

The histopathological findings of renal biopsy specimens are presented in Table 2. Glomerulomegaly was the most common lesion, occurring in 83.3% of biopsy samples. Other important findings included podocyte hypertrophy (57.1%), focal segmental glomerulosclerosis (FSGS) (45.2%), mesangial expansion (38.1%), tubular atrophy (23.8%), and interstitial fibrosis (19.0%). These findings suggest that glomerular enlargement and progressive structural damage are common pathological features of obesity-associated glomerulopathy in children.

A comparison of renal function between children with and without FSGS is shown in Table 3. Children diagnosed with FSGS had significantly lower eGFR values (89.4 ± 12.6 vs. 104.8 ± 14.3 mL/min/1.73 m²; $p = 0.002$) and significantly higher urinary protein excretion (1.82 ± 0.64 vs. 1.18 ± 0.43 g/day; $p < 0.001$) than those without FSGS, indicating greater impairment of renal function in the presence of glomerulosclerosis.

The correlation analysis presented in Table 4 demonstrated a significant positive association between BMI and urinary protein excretion ($r = 0.49$, $p < 0.001$), systolic blood pressure ($r = 0.41$, $p < 0.001$), and serum creatinine ($r = 0.34$, $p = 0.001$). Conversely, BMI showed a significant negative correlation with eGFR ($r = −0.38$, $p < 0.001$), indicating that increasing obesity was associated with progressive deterioration in renal function.

The relationship between histopathological abnormalities and clinical parameters is summarized in Table 5. Children with FSGS and podocyte hypertrophy exhibited significantly higher levels of proteinuria and lower eGFR compared with those without these lesions. Similarly, patients with glomerulomegaly and mesangial expansion demonstrated evidence of greater renal dysfunction. These findings highlight the close association between the severity of histopathological changes and adverse clinical outcomes in obesity-associated glomerulopathy.

Table 1. Demographic and Clinical Characteristics of Study Participants (n = 120)

Variable	Value
Age (years), mean ± SD	11.8 ± 2.7
Male, n (%)	74 (61.7)
Female, n (%)	46 (38.3)
BMI (kg/m²), mean ± SD	31.4 ± 3.8
Systolic BP (mmHg), mean ± SD	122.6 ± 11.5
Diastolic BP (mmHg), mean ± SD	76.8 ± 8.3
Hypertension, n (%)	41 (34.2)
Serum Creatinine (mg/dL), mean ± SD	0.91 ± 0.24
eGFR (mL/min/1.73 m²), mean ± SD	99.4 ± 15.8
Proteinuria, n (%)	94 (78.3)
Urinary Protein Excretion (g/day), mean ± SD	1.32 ± 0.71
Renal biopsy performed, n (%)	42 (35.0)

Table 2. Histopathological Findings in Renal Biopsy Specimens (n = 42)

Histopathological Finding	N (%)
Glomerulomegaly	35 (83.3)
Podocyte hypertrophy	24 (57.1)
Focal Segmental Glomerulosclerosis (FSGS)	19 (45.2)
Mesangial expansion	16 (38.1)
Tubular atrophy	10 (23.8)
Interstitial fibrosis	8 (19.0)

Table 3. Comparison of Renal Function According to Presence of FSGS

Variable	FSGS (n = 19)	No FSGS (n = 23)	p-value
eGFR (mL/min/1.73 m²)	89.4 ± 12.6	104.8 ± 14.3	0.002
Urinary Protein Excretion (g/day)	1.82 ± 0.64	1.18 ± 0.43	<0.001
Serum Creatinine (mg/dL)	1.08 ± 0.19	0.82 ± 0.17	<0.001

Table 4. Correlation between BMI and Clinical Parameters

Variable	Correlation Coefficient (r)	p-value
Urinary protein excretion	0.49	<0.001
Serum creatinine	0.34	0.001
eGFR	–0.38	<0.001
Systolic blood pressure	0.41	<0.001

Table 5. Association between Histopathological Findings and Clinical Variables

Histopathological Finding	Mean Proteinuria (g/day)	Mean eGFR (mL/min/1.73 m²)	p-value
Glomerulomegaly	1.56 ± 0.58	95.6 ± 14.8	0.021
Podocyte hypertrophy	1.71 ± 0.61	92.8 ± 13.6	0.008
FSGS	1.82 ± 0.64	89.4 ± 12.6	0.002
Mesangial expansion	1.64 ± 0.55	93.7 ± 15.2	0.017

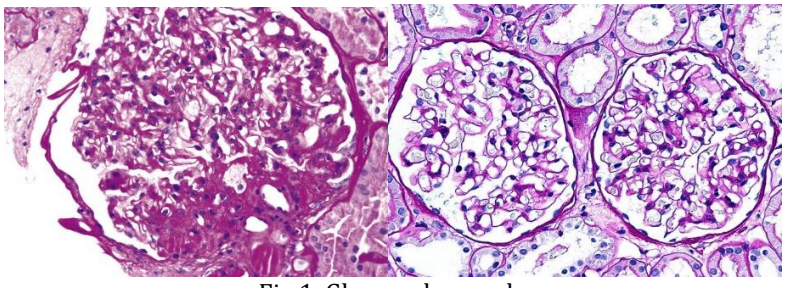

Fig 1. Glomerulomegaly

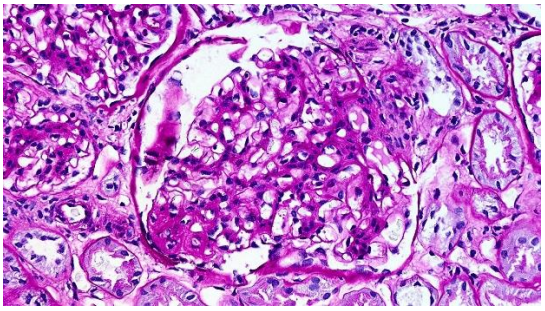

Fig 2. Focal Segmental Glomerulosclerosis

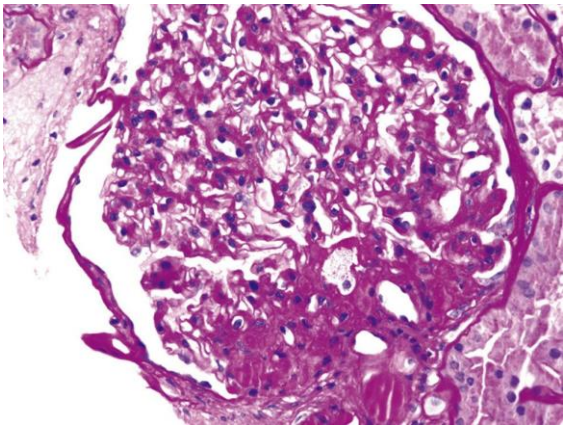

Figure 3: Podocyte Hypertrophy and Mesangial Expansion

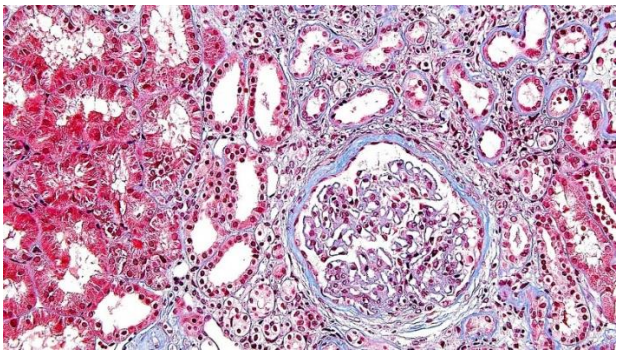

Figure 4: Tubulointerstitial Changes

DISCUSSION

The present study demonstrated that obesity-associated glomerulopathy (OAG) in children is characterized by significant histopathological alterations, with glomerulomegaly being the most prevalent lesion, followed by podocyte hypertrophy and focal segmental glomerulosclerosis (FSGS). These findings are consistent with recent studies that identify glomerulomegaly as the hallmark pathological feature of OAG, resulting from sustained glomerular hyperfiltration and adaptive nephron hypertrophy in response to increased metabolic demand [10,11].

A substantial proportion of our participants exhibited persistent proteinuria and hypertension, indicating early renal involvement in obese children. Similar observations have been reported in recent pediatric studies, suggesting that obesity induces structural and functional renal changes long before overt chronic kidney disease develops [12,13]. The significantly lower eGFR observed among children with FSGS further supports the concept that progressive glomerular injury is associated with deterioration of renal function and may accelerate the transition to chronic kidney disease if not recognized early [10,14].

The positive correlation between BMI and urinary protein excretion observed in this study highlights the adverse impact of increasing adiposity on renal health. Excess adipose tissue promotes activation of the renin–angiotensin–aldosterone system, insulin resistance, oxidative stress, chronic inflammation, and

adipokine dysregulation, ultimately leading to podocyte injury and glomerulosclerosis [11,15]. These pathophysiological mechanisms explain the close association between obesity severity and worsening renal function demonstrated in our study.

The findings emphasize the importance of routine renal screening in obese children, particularly those with persistent proteinuria or hypertension. Early identification of obesity-associated renal injury, coupled with lifestyle modification, weight reduction, and appropriate pharmacological interventions, may slow disease progression and reduce the future burden of chronic kidney disease [12,16]. Given the rising prevalence of childhood obesity in Pakistan, early preventive strategies and multidisciplinary management involving pediatricians, nephrologists, pathologists, physiologists, and public health professionals are essential to minimize long-term renal complications.

Authors' Contribution

Concept & Design of Study: Asma Niaz Khan, Aamir Nazir, Safiya Javed
Drafting: Faseela Amjad, Nosheen Niazi
Data Analysis: Aneeqa Adnan, Aamir Nazir
Critical Review: Aamir Nazir, Asma Niaz Khan, Safiya Javed
Final Approval of Version: All authors approved the final version.

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