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Original Article

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Kidney Biopsy Findings and Management of Kidney Diseases in Patients with Class III Obesity: A Single-Center Experience

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ABSTRACT

Background: Class III obesity, formerly known as morbid obesity, is a known risk factor for chronic kidney diseases. Due to outdated information suggesting that morbid obesity is a contraindication for kidney biopsy and the misconception that proteinuria in obese patients is solely related to hyperfiltration, necessiating only conservative treatment, the vast majority of primary glomerulonephritis in these patients remains undiagnosed and untreated. Here, the clinical characteristics, treatments and results of patients who had class III obesity and needed a kidney biopsy are presented.
Methods: Two hundred thirty-one native kidney biopsies conducted between 2015 and 2021 were retrospectively reviewed, identifying 12 patients with a body mass index ≥40 kg/m^2.
Results: Ten patients presented with nephrotic syndrome, 8 of these patients underwent immunosuppressive therapy. Membranous nephropathy and focal segmental glomerulosclerosis were the most common diagnoses. Seven patients went into remission during follow-up. Our results indicated that class III obesity alone is not a detrimental morbidity when it comes to diagnosing and treating glomerular diseases.
Conclusion: If a primary glomerulonephritis is diagnosed through a safe biopsy procedure, there is no reason to avoid considering immunosuppressive therapy for these patients.
Keywords: Glomerulonephritis, kidney biopsy, morbid obesity, obesity

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INTRODUCTION

Class III obesity, previously termed morbid obesity, is a chronic condition characterized by a body mass index (BMI) of 40 kg/m^2 or higher, with detrimental effects on metabolic health. Obesity is a known risk factor for chronic kidney disease (CKD) and its prevalence is increasing worldwide.[1,2] Primarily, it affects the kidney by exacerbating diabetes, hypertension, and atherosclerosis.[3] Alterations in hemodynamics and inflammation signaling have a major role in hyperfiltration and glomerular damage as a result.[4] Obesity related glomerulopathy (ORG), characterized by glomerulomegaly and/or focal segmental glomerulosclerosis, is considered the culprit for the proteinuria and kidney damage in patients with obesity. However, in biopsy studies, this entity is reported to be relatively rare and it can not fully explain the pathophysiology of CKD in this population.[5,6] The management of obesity primarily involves of conservative measures, including weight loss and lifestyle changes.[3] This understanding contributes to the underestimation of proteinuria in individuals with obesity. However, there is a hidden burden of primary glomerular diseases in obese patients. Additionally, there is evidence that obesity alone might not be associated with progression to kidney failure in patients with primary glomerular diseases.[7] On top of these, there are many drawbacks of performing kidney biopsy and there is a lack of experience when it comes to treating kidney

diseases in obese patients.[8] Hence, it is essential to investigate primary glomerulonephritis within the obese patient group. These studies will help dispel any prevailing biases on this subject and ensure that patients receive the necessary treatment they require. We frequently diagnose and treat primary glomerulonephritis at our tertiary hospital and have observed that obesity is not uncommon among this specific patient population. Given the significance of the coexistence of class III obesity and primary glomerulonephritis, we aimed to share our experience and insights on this subject matter. Here, the clinical characteristics, treatments and results are presented for the 12 patients who had class III obesity and needed a kidney biopsy.

MATERIAL AND METHODS

We conducted a retrospective review of 231 patients who underwent a native kidney biopsy, with recorded BMI, between January 2015 and August 2021 at our institution. This study was approved by Ankara University School of Medicine Ethics Committee for Clinical Studies (Approval Date/Number: 14.04.2021/I4-259-21). Written informed consents had been obtained from all patients before kidney biopsy. Class III obesity was defined as BMI $\geq$ 40 kg/m^2. There were 12 patients who had class III obesity. Medical records were reviewed for demographic information, history of diabetes and/or hypertension (defined as >130-80 mm Hg or use of an antihypertensive drug), indications for kidney biopsy, medication use, follow-up laboratory results, and treatment responses. Serum creatinine (mg/dL), eGFR (estimated glomerular filtration rate, mL/min/1.73m^2, measured by Chronic Kidney Disease Epidemiology Collaboration equation[9]), serum albumin (g/L), proteinuria (measured by a 24-hour urine collection or spot urine protein–creatinine ratio), hematuria (defined as >5 red blood cells on a microscopic examination), serologic tests were also noted. Nephrotic syndrome was defined as a 24-hour protein excretion >3.5 g/day or as a urine protein/creatinine ratio of >3.5 g/g combined with hypoalbuminemia and edema. Remissions and relapses were defined according to Kidney Disease: Improving Global Outcomes (KDIGO) guidelines.[10]

Kidney biopsies were ultrasonography guided and were performed via a 16G needle. Eleven biopsies were performed by a nephrologist, while 1 was performed by an interventional radiologist. All kidney biopsies were evaluated by the same pathologist using the standard techniques in routine diagnosing procedure.

Statistical analysis was performed using IBM SPSS 23 (IBM SPSS v.23, Armonk, NY, USA). Clinical and laboratory data are expressed as percentages, means ($\pm$ SD) or medians [interquartile range (IQR)], as appropriate.

RESULTS

The charts of 231 patients, with recorded body weight and height data, were reviewed. There were 12 patients, 9 of whom were female, with a mean age of 51 $\pm$ 1 years and a BMI of 40 or higher. Seven patients had a diagnosis of diabetes mellitus and 8 had hypertension. Ten patients (83%) had a nephrotic syndrome at presentation (Figure 1). At the time of the biopsy, median (minimum–maximum) proteinuria, eGFR, and serum albumin were 10.4 g/day (1869-28588); 77.5 mL/min/1.73 m^2 (17-123); 22.5 mg/L (1.3-4.7), respectively.

There were no biopsy-related complications, except for 1 case of macroscopic hematuria, which resolved within hours. There were no inadequate kidney biopsies according to the pathologist (median glomeruli number of 14 [minimum–maximum: 6-40)]. Clinicopathological diagnoses of the patients were as follows: 4 (33%) membranous nephropathy, 4 (33%) focal segmental glomerulosclerosis, 1 (8%) benign nephrosclerosis, 1 (8%) AA amyloidosis with acute tubulointerstitial nephritis (ATIN), 1 (8%) minimal change disease, 1 (8%) diabetic nephropathy with ATIN. By light microscopic examination, histologic features of diabetic glomerulopathy (Kimmelstiel–Wilson nodules, microaneurysms, and fibrin cap) were demonstrated only in

MAIN POINTS

- Class III obesity, with a BMI of 40 kg/m^2 or higher, is associated with chronic kidney disease (CKD). Contrary to common misconceptions, primary glomerular diseases are a significant diagnosis in patients with class III obesity.
- The study challenges the notion that obesity-related glomerulopathy (ORG) is the primary cause of proteinuria in obese patients. Findings indicate a diverse spectrum of glomerular diseases, with primary glomerular diseases being more prevalent than ORG.
- Patients diagnosed with primary glomerulonephritis and class III obesity demonstrated positive outcomes with immunosuppressive therapy. Remissions were achieved in a significant percentage of cases, emphasizing the importance of considering immunosuppression as a viable treatment option for this patient population.

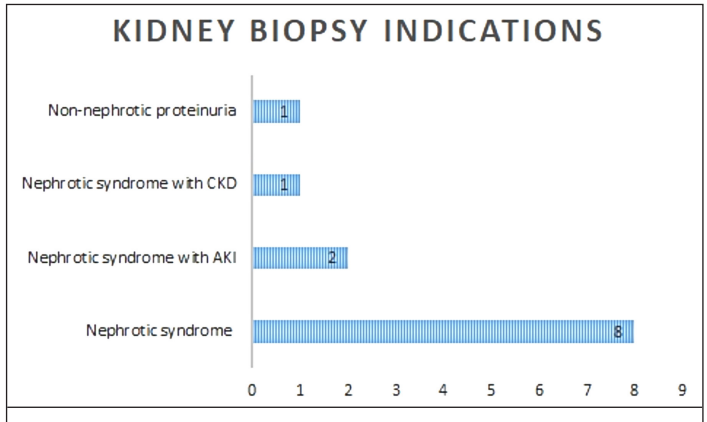

Figure 1. Kidney biopsy indications.

Table 1. Clinical Characteristics of the Patients

	Age/ Gender	BMI (kg/ m²)	DM/ HT	Cause of Biopsy	Pathological Diagnosis	Proteinuria at Presentation (mg/day)	Serum Creatinine (mg/dL)/eGFR (mL/ min/1.73m²)/serum albumine (g/L) at presentation	Microscopic Hematuria at Presentation	Immunosuppressive Therapy	Remission	Follow-Up Time (Months)
Patient 1	46/M	40	–/–	Nephrotic syndrome	Membranous glomerulonephritis (aPLRA2+)	10367	2.08/37/19	+	RTX	–	9
Patient 2	42/M	40.12	–/–	Nephrotic syndrome	FSGS	13400	0.88/106/19	+	Steroids, MMF	CR	6
Patient 3	74/F	40.23	+/+	Nephrotic syndrome	Membranous glomerulonephritis (aPLRA2+)	8558	0.80/73/2.4	+	–	–	–
Patient 4	49/M	41.67	+/+	Nephrotic syndrome with CKD	Benign nephrosclerosis	4005	1.45/56/31	–	–	–	21
Patient 5	43/F	41.9	+/+	Nonnephrotic range proteinuria	FSGS and ORG	1869	0.66/92/47	–	Steroids	CR	60
Patient 6	62/F	42	+/+	Nephrotic syndrome	AA Amyloidosis with ATIN	10504	2.82/17/23	+	Steroids	–	24
Patient 7	49/F	42.97	–/+	Nephrotic syndrome	MCD	11656	0.56/121/13	–	Steroids, AZA→MMF	CR	72
Patient 8	48/K	42.98	–/+	Nephrotic syndrome, with AKI	FSGS	28588	2.00/82/16	+	Steroids, CYC→ AZA→MMF→TAC→RTX	CR	36
Patient 9	43/F	43.06	+/–	Nephrotic syndrome	Membranous glomerulonephritis	8950	0.45/123/22	–	RTX	–	4
Patient 10	45/F	43.4	–/–	Nephrotic syndrome	Membranous glomerulonephritis (aPLRA2-)	6860	0.64/108/25	–	–	PR	4
Patient 11	47/F	46	+/+	Nephrotic syndrome	Diabetic nephropathy with ATIN	11904	1.30/49/29	–	–	PR	18
Patient 12	65/F	55.36	+/+	Nephrotic syndrome with AKI	FSGS	14240	2.34/21/17	–	Steroids, CSA	CR	28

aPLRA2, phospholipase A2 receptor antibody; AKI, acute kidney injury; ATIN, acute tubulointerstitial nephritis; AZA, azathioprine; BMI, body mass index; CKD, chronic kidney disease; CR, complete remission; CSA, cyclosporine; CYC, cyclophosphamide; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; F, female; FSGS, focal segmental glomerulosclerosis; HT, hypertension; M, male; MCD, minimal change disease; MMF, mycophenolate mofetil; ORG, obesity related glomerulopathy; PR, partial remission; RTX, rituximab; TAC, tacrolimus.

1 patient's biopsy and the biopsy was diagnosed as diabetic nephropathy. Other diabetic patients' biopsies revealed primary diagnoses other than diabetic nephropathy such as MGN, FSGS and amyloidosis; and the light microscopy and immunofluorescence findings were not sufficient to suggest a diabetic nephropathy in the background.

Median follow-up time of the patients was 21 (IQR 6-36) months. All the patients had a renin–angiotensin–aldosterone system (RAAS) blockade therapy. Alongside this, 8 (66%) of the patients also had immunosuppressive therapy. Seven of the patients who had an immunosuppressive drug went into remission. Three of the remitted patients experienced relapses and they went into remission again after the second or third line therapy. The most common treatment agent was steroids (Table 1).

DISCUSSION

We observed that if severe proteinuria is present, primary glomerular diseases are the major diagnosis in patients with class III obesity. Our case series stands out due to a few matters which are not frequently taken into consideration when it comes to glomerular diseases in people with obesity.

The spectrum of kidney disease in patients with obesity might be more diverse than typically recognized. It is an accepted knowledge that obesity increases the risk of a chronic kidney disease and albuminuria.[11] In addition to this, obesity had its own pathological entities in kidney. Choung et al[6] showed, in their series, that only 11.6% of 248 morbidly obese patients had ORG. The rest of the patients had glomerular diseases other than ORG and, interestingly, in 49% of the patients, biopsy led to a change in treatment. They stated that, if eGFR <30 mL/min/1.73 m^2, and/or if a nephrotic syndrome or an acute kidney injury are present, the likelihood of non-ORG lesions increases. Similarly, none of our patients had a diagnosis of ORG alone, and the primary glomerular disease was predominated. Remarkably, in patient 5, kidney biopsy indicated both ORG (glomerulomegaly) and FSGS. After being treated with steroids for lichen planus, her proteinuria resolved and did not return. Electron microscopy was unavailable during the study making it unclear if podocyte foot process effacement was partial or total. This information might have helped differentiate between primary and secondary FSGS, including ORG. Based on the clinical findings, we initially presumed it was primary FSGS. An interesting finding of our study, emphasizing the importance of performing a kidney biopsy in suspected cases, was the coexistence of ATIN in 2 patients whose proteinuria decreased after steroids.

As it was seen in our study, the success rate and safety of a kidney biopsy in patients with class III obesity seems to be sufficient enough to have a specific diagnosis without major biopsy-related complications.[6,8] It is stated that a transjugular and percutaneous kidney biopsy had similar complication and success rates.[12] We only saw 1 case of macroscopic hematuria and there were no inadequate biopsies.

The fear of the complications in biopsies or the prejudice that biopsy results would not change the patient management would prevent these patients from being diagnosed with a curable kidney disease. With the data obtained from the biopsy, therapeutic options such as bariatric surgery, RAAS blockade, lifestyle changes can be recommended more confidently, even in patients with ORG alone.[13] All patients received a RAAS-blockade therapy during the follow-up period. On top of it, 8 of our patients had immunosuppressive therapy alongside the conservative treatment according to the biopsy results.

Obesity is evaluated as an additional risk factor for progression of diverse kidney diseases such as IgA nephropathy or diabetic nephropathy.[3,14] However, the vast majority of the patients with morbid obesity who were diagnosed with a glomerular disease and had an immunosuppressive therapy could achieve remission. In our study, 66% of the patients were diagnosed with a primary glomerular disease and they were treated with an immunosuppressive therapy. Seven out of 8 cases went into remission; however, 3 cases recurred after weaning off the treatment. These 3 patients were remitted again after changing the treatment or after increasing the dose of the immunosuppressive treatment. Elyan et al[7] found no relation between BMI and progression to end stage kidney disease (ESKD) or mortality in their retrospective cohort study of primary glomerular diseases. Seven of our patients who had immunosuppressive treatment achieved remission, which implies that, with appropriate treatment, ESKD may be prevented in these patients. Although our study has a limited follow-up time for making broad-scale conclusions, no patients progressed to end-stage kidney disease.

In conclusion, all patients with an unexplained kidney failure, clinically significant hematuria and/or proteinuria should undergo a kidney biopsy without hesitation. Additionally, if a primary glomerulonephritis is diagnosed via biopsy, an immunosuppression therapy is not a treatment to be shied away from when it comes to patients with class III obesity.

Ethics Committee Approval: This study was approved by Ankara University School of Medicine Ethics Committee for Clinical Studies (Approval date/Number: 14.04.2021/I4-259-21).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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Declaration of Interests: The authors have no conflict of interest to declare.

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