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ORIGINAL RESEARCH

Clinicopathological Analysis of Patients with Isolated Hematuria and/or Mild Proteinuria

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Objective: This investigation aimed to explore the clinicopathological features of patients with isolated hematuria and/or mild proteinuria in kidney disease.

Materials and Methods: We conducted a retrospective review of the clinical and pathological information of patients initially diagnosed with chronic nephritis syndrome in the Nephrology Department of Yuebei People's Hospital.

Results: In total, 227 participants were recruited for the study, including 79 patients (34.8%) in the group with isolated hematuria and/or mild proteinuria and 148 patients (65.2%) in the group with medium-large amounts of proteinuria. There were 29 cases (36.7%) of IgA nephropathy, seven cases (8.9%) of focal segmental glomerulosclerosis, six cases (7.6%) of membranous nephropathy, and six cases (7.9%) of acute renal tubular injury in the group with isolated hematuria and/or mild proteinuria. The common pathological types in the medium-large proteinuria group were membranous nephropathy in 68 cases (45.9%), minimal change nephropathy in 25 cases (16.9%), and IgA nephropathy in 20 cases (13.5%).

Conclusion: IgA nephropathy is the main pathological type in the group with isolated hematuria and/or mild proteinuria, while membranous nephropathy is the common pathological type in the group with moderate to severe proteinuria. There was a significantly stronger correlation between the level of hematuria/proteinuria and both BMI and MAP.

Keywords: isolated hematuria, proteinuria, renal biopsy puncture

Introduction

Performing a renal biopsy is indispensable for confirming the diagnosis of kidney diseases. The pathologic information provided by a renal puncture biopsy can help optimize treatment regimens in up to 74% of patients.[1] However, renal biopsy represents a potentially risky and invasive medical procedure. The decision on whether renal biopsy should be performed in patients with isolated hematuria and/or mild proteinuria is not clear. While some nephrologists are hesitant to recommend kidney biopsy for some renal diseases, considering that it does not significantly alter patient management or treatment success. Others enthusiastically endorse the procedure, believing that it greatly enhances diagnostic precision and prognostic clarity, ultimately guiding more effective therapeutic strategies.[2,3]

It is worth noting that body mass index (BMI), as an index to measure overweight or obesity, is closely related to metabolic disorder and renal function damage. At the same time, the increase of mean arterial pressure (MAP) has also been proved to be closely related to proteinuria. Therefore, maintaining a healthy weight and blood pressure level plays a vital role in preventing and controlling proteinuria.

In this article, we summarized the clinical and pathological information of renal biopsies from patients with kidney disease. The information was gathered spanning the entirety of the year 2021, from January 1st to December 31st. The patients were grouped according to the degree of hematuria and urinary protein, and the indications for renal biopsy were discussed. By analyzing these data, doctors can gain a deeper understanding of the renal pathology in patients with isolated hematuria and/or mild proteinuria, which helps improve the accuracy of diagnosis and enables the formulation of more suitable treatment plans for patients, thereby enhancing treatment effectiveness and patient prognosis.

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Materials and Methods

Study Participants

Patients who were hospitalized at the Department of Nephrology, Yuebei People's Hospital, and initially diagnosed with chronic nephritis syndrome based on clinical manifestations. The study included data collected between the dates of January 1st, 2021, and December 31st, 2021. The individuals were categorized into a group with isolated hematuria and/or mild proteinuria and a group with medium-large amounts of proteinuria, based on the severity of hematuria and proteinuria. The inclusion criteria were as follows: (1) isolated proteinuria; (2) isolated hematuria; (3) proteinuria and glomerular hematuria; (4) rapidly progressive glomerulonephritis; (5) renal parenchymal injury; (6) systemic diseases with abnormal urine analysis; (7) systemic disease with renal insufficiency and/or without abnormal urinalysis; (8) hereditary kidney disease. The exclusion criteria were as follows: isolated kidneys, significant bleeding tendency, severe hypertension, mental illness, poor positioning, kidney infection and tumor, renal hyperposition or wandering kidney, late-stage chronic kidney disease, incomplete clinical or pathological data, and loss to follow-up. All participants gave their voluntary and informed consent to participate in the study. This study was approved by the Ethics Committee of Yuebei People's Hospital.

Data and Methods

General information: In total, 227 patients (244 patients in total, excluding 17 patients with incomplete data) with nephropathy who were hospitalized in our department and underwent renal puncture biopsy from January 1, 2021, to December 31, 2021, were selected, and the sex, age, height, weight, MAP, Hb, serum albumin (ALB), serum creatinine (Scr), blood urea nitrogen (BUN), and data on the quantity of protein in a 24-hour urine sample were gathered. Within the group of patients included in the study, 127 were male (55.9%), and 100 were female (44.1%). The ages of the patients ranged from 12 to 82 years, and the mean age was 46.1 ± 15.4 years (Table 1).

Percutaneous renal biopsy under ultrasound: the whole operation was conducted under ultrasound guidance, using a special needle for renal biopsy. After routine disinfection, sterile hole towels were laid, and two qualified kidney tissues were punctured. After the puncture procedure was completed, the patients lay in bed for 24 h. The vital signs of the patients were monitored, and their urine color was observed. Patients who underwent renal biopsy did not experience hematuria or lumbar or abdominal pain.

Pathological examination: All renal biopsies were routinely examined via light microscopy, immunofluorescence, and electron microscopy. All renal tissues with glomerular membranous lesions were positive for the IgG subtype and PLA2R. All renal tissues were examined via light microscopy, electron microscopy, immunofluorescence, and immunohistochemistry. All renal tissues examined via electron microscopy and immunofluorescence contained >1 glomerulus, and all renal tissues examined via light microscopy contained >10 glomeruli. Congo Red dye was added to samples that were suspected of having renal amyloid. As per the WHO histological classification of glomerular diseases in 1995, the classification was performed based on clinical data, laboratory results, light microscopy results, and immunopathological characteristics. Pathologists who analyzed the data and diagnosed the patients were blind to the clinical outcome.

Statistical Methods

All data were analyzed using SPSS 21. For continuous measurement data, initially, a normality test was performed, and those conforming to a normal distribution were described by x ±s. We employed *t*-tests to ascertain the statistical significance of the parameter variations between the two groups. Count data were expressed as percentages, and the

Table 1 Clinical Characteristics of the Isolated Hematuria and/or Mild Proteinuria Group Versus Medium-Large Amounts of Proteinuria Group

Groups	Number	Gender (male)	Age (year)	MAP (mmHg)	BMI (kg/m^2)	GFR (mL/min)	Alb (g/l)	Hb (g/l)
A	79	35 (44.3%)	44.4±13.5	94.4±15.3	23.6±3.8	80.7±36.7	41.2±5.3	130.8±22.1
B	148	92 (62.2%)	47.0±16.2	101.1±17.3	25.4±5.4	80.3±31.9	25.7±8.4	126.9±26.9

Notes: A: isolated hematuria and/or mild proteinuria group; B: medium-large amounts of proteinuria group.

differences in parameters between the groups were determined by the $\chi 2$ test. For two-sided tests, the differences observed between groups were considered to be statistically significant at $P < 0.05$.

Results

In the isolated hematuria and/or mild proteinuria group, there are 79 individuals, with 35 being male (representing 44.3% of the group). The average age of this group is 44.4±13.5 years, the mean arterial pressure (MAP) is 94.4±15.3 mmHg, the body mass index (BMI) is 23.6±3.8 kg/m², the glomerular filtration rate (GFR) is 80.7±36.7 mL/min, the albumin (Alb) level is 41.2±5.3 g/l, and the hemoglobin (Hb) level is 130.8±22.1 g/l.

In the medium-to-large proteinuria group, there are 148 individuals, with 92 being male (representing 62.2% of the group). The average age of this group is 47.0±16.2 years, the MAP is 101.1±17.3 mmHg, the BMI is 25.4±5.4 kg/m², the GFR is 80.3±31.9 mL/min, the Alb level is 25.7±8.4 g/l, and the Hb level is 126.9±26.9 g/l (Table 1).

Renal pathology distribution: In total, 227 subjects were included in this study. The isolated hematuria and/or mild proteinuria group contained 79 patients, 35 of whom were male (44.3%) and 44 of whom were female (55.7%). Renal pathology revealed 29 (36.1%) cases of IgA nephropathy, seven (8.86%) diagnoses of focal segmental glomerulosclerosis, six (7.59%) diagnoses of membranous nephropathy, nine (11.39%) diagnoses of tubulointerstitial disease (six diagnoses of acute tubular injury and three diagnoses of chronic tubular injury), seven (8.86%) diagnoses of thin basement membrane nephropathy, three (3.80%) diagnoses of minimal change nephropathy, four (5.06%) diagnoses of renal arteriolar sclerosis with renal injury, two (2.53%) diagnoses of minimal change nephropathy with renal injury, three (3.80%) diagnoses of diabetic nephropathy, two (2.53%) diagnoses of tethered capillary glomerulonephritis, and two (2.53%) diagnoses of allergic violet glomerulonephritis. Two (2.53%) patients were diagnosed with allergic purpura nephritis, two (2.53%) patients were diagnosed with lupus nephritis, one (1.27%) patient was diagnosed with renal amyloidosis, one (1.27%) patient was diagnosed with C3 glomerulonephritis, one (1.27%) patient was diagnosed with anti-GBM nephropathy, and one (1.27%) patient was diagnosed with thrombotic microangiopathy. The medium-large proteinuria group had 148 patients, including 92 (62.2%) males and 56 (37.8%) females. Renal pathology revealed 65 (43.92%) diagnoses of membranous nephropathy, 24 (16.22%) diagnoses of minimal change nephropathy, 19 (12.84%) diagnoses of IgA nephropathy, 12 (8.11%) diagnoses of diabetic nephropathy, eight (5.41%) diagnoses of lupus nephritis, five (3.38%) diagnoses of focal segmental glomerulosclerosis, five (3.38%) diagnoses of membranous capillary glomerulonephritis, four (2.70%) diagnoses of renal amyloidosis, two (1.35%) diagnoses of renal arteriolar sclerosis with renal injury, one (0.68%) diagnoses of acute tubular injury, one (0.68%) diagnoses of minimal change nephropathy with renal injury, one (0.68%) diagnoses of anaphylactic purpura nephritis, and one (0.68%) diagnoses of diabetes combined with hypertension (Table 2).

Comparative Study of Clinical Data

The BMI of patients in the group with isolated hematuria and/or mild proteinuria was significantly reduction than that of the patients in the group with medium-large amounts of proteinuria, and the MAP of patients in the group with isolated hematuria and/or mild proteinuria was markedly higher than that of the patients in the group with medium-large amounts of proteinuria. The comparison of MAP and BMI between the two patient groups is statistically significant (P<0.05). The

Table 2 Distribution of Renal Pathological Types in Isolated Hematuria and/or Mild Proteinuria Group and Medium-Large Amounts of Proteinuria Group

Group	Number	Pathological Type (n%)												
		MN	MCD	IgA	DN	LN	FSGS	MPGN	RA	MPA	TIN	ANS	TBMN	Others
A	79	7.59	3.80	36.71	3.80	1.27	8.86	2.53	1.27	2.53	11.39	5.06	8.86	6.33
B	148	43.92	16.22	12.84	8.11	5.41	3.38	3.38	2.70	0.68	0.68	1.35	0	1.35

Abbreviations: MN, membranous nephropathy; MCD, minimal change nephropathy; IgA, IgA nephropathy; DN, diabetic nephropathy; LN, lupus nephritis; FSGS, focal segmental glomerulosclerosis; MPGN, membrano-proliferative glomerulonephritis; RA, renal amyloidosis; MPA, anaphylactic purpura nephritis; TIN, tubulointerstitial disease; TBMN, thin basement membrane nephropathy; ANS, renal arteriolar sclerosis with renal injury.

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difference in age, GFR, Hb, and other data between the two groups failed to reach statistical significance ($P>0.05$). The patients in the isolated hematuria and/or mild proteinuria group were mainly female, while all patients in the medium-large proteinuria group were mainly male. The gender data revealed a statistically significant distinction between the two groups ($P<0.05$). There is a significant difference in pathological composition between patients with isolated hematuria and/or mild proteinuria and patients with moderate to large proteinuria. ($P<0.05$)

Discussion

Hematuria and proteinuria are frequently observed as clinical manifestations of nephropathy. However, ascertaining the cause of kidney disease, the type of pathology, and the prognosis of the disease only based on hematuria and/or proteinuria is difficult. Renal biopsy can be used to determine the type of kidney injury and perform disease assessment, management, and disease diagnosis; thus, it can guide patient prognosis. Renal biopsy also contributes substantially in detecting disease recurrence.

Renal biopsy is an invasive procedure that has many contraindications and, thus, should always be performed under the supervision of a nephrologist. Simple tests involving Scr, blood pressure, urinary tract ultrasound, urine samples (eg, urine routine, Urine Protein-to-Creatinine Ratio, etc), and renal immunologic screening can help determine whether a renal biopsy is required.

No uniform standard is available for the indications of renal biopsy procedures in different countries or regions. This situation is especially pertinent to patients displaying isolated microscopic hematuria and mild proteinuria, accompanied by normal renal function and blood pressure levels. Among researchers, there exists uncertainty regarding the necessity of conducting a renal biopsy in instances of isolated, non-visible hematuria, which is unlikely to significantly impact treatment outcomes, given that these patients typically enjoy a favorable long-term prognosis.[2,4–7]

In stable transplant patients, biopsy results in a GFR loss of 0.77 mL/min,[8] which suggests that kidney biopsy is a safe diagnostic tool. Although the occurrence rate is relatively low, the persistent presence of microscopic hematuria in certain patients has been found to have a notable association with the course of progressing to end-stage kidney disease.[9–11] As renal biopsy contributes significantly to the diagnosis and treatment of patients with kidney disease, a patient-centered approach should be adopted to make a decision on whether a renal biopsy is required (eg, isolated non-macroscopic hematuria or elderly patients).[12] Age should not be considered an exclusion criterion for renal biopsy.[13] Renal biopsy is often suggested for patients with isolated hematuria and/or mild proteinuria and normal renal function and blood pressure levels if there are no contraindications.[3]

In this study, membranous nephropathy accounted for the highest proportion of renal biopsy patients (31.3%), which matched the findings of other studies.[14] In the isolated hematuria and/or mild proteinuria group, IgA nephropathy accounted for the highest proportion (36.7%). In total, 77.2% of patients in the isolated hematuria and/or mild proteinuria group did not change their treatment regimen after renal biopsy. However, nine patients who were concurrently diagnosed with tubulointerstitial diseases (six with acute tubular injury and three with chronic tubular injury), two with microscopic polyangiitis renal injury, two with allergic purpura nephritis, one with lupus nephritis, one with renal amyloidosis, one with C3 glomerulonephritis, one with anti-GBM nephropathy, and one with thrombotic microangiopathy (accounting for 22.8% of patients with renal biopsy) were diagnosed on time and recommended a change in treatment plan. These patients benefitted from renal biopsy.

Previous studies have shown that being overweight is linked with a decrease in kidney function and elevated risk for developing ESKD.[15–17] Metabolic factors associated with overweight, such as hypertension and insulin resistance, may mediate the relationship between overweight/obesity and renal risk.[18,19] The study also revealed that the MAP and BMI were significantly lower in patients with isolated hematuria and/or mild proteinuria than in patients with medium-large amounts of proteinuria, suggesting that controlling the weight and blood pressure can delay the progression of nephropathy.[20]

This study was based on data from a single-center medical institution. The sample size was limited, which might have introduced bias into the results. This study had certain limitations, and future studies need to include more samples.

The novelty of this article lies in its detailed retrospective review and analysis of the clinical and pathological information of patients with isolated hematuria and/or mild proteinuria. The study not only identifies the common

pathological types in these patient groups but also highlights the significant correlation between the level of hematuria/proteinuria and both BMI and MAP. This research provides a foundation for guiding the clinical diagnosis and management of individuals presenting with these symptoms.

To summarize, for patients with isolated hematuria and/or mild proteinuria, renal biopsy should be perfected as much as possible, to improve the early diagnosis and treatment of more diseases. Additionally, controlling weight and blood pressure has clinical significance in delaying disease progression and improving patient prognosis.

Data Sharing Statement

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethic committee of Yuebei People's Hospital. The written informed consent was obtained from the participants or their guardians.

Consent for Publication

The written informed consent was obtained from the participants or their guardians.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors declare that they have no conflict of interests.

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