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Clinical and Pathological Analysis of Patients with Idiopathic Membranous with Elevated Lipids

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Abstract: ***Objective:*** *to explore the influencing factors of patients with idiopathic membranous nephropathy accompanied by elevated lipids.* ***Methods:*** *to retrospectively analyze the data of 159 patients with idiopathic membranous nephropathy admitted to Shaanxi Provincial Hospital of Traditional Chinese Medicine from 2021 to 2024, and to compare the differences in clinical and pathological data between patients in the group of patients with elevated blood lipids and patients in the group of patients without elevated blood lipids.* ***Results:*** *Patients in idiopathic membranous nephropathy with elevated lipids group had heavier SUA, Scr and 24h urinary protein, elevated systolic blood pressure, and lower blood ALB than patients without elevated lipids, and the difference was statistically significant (P<0.05).* ***Conclusion:*** *Patients with idiopathic membranous nephropathy with elevated lipids had more severe clinical indicators and elevated systolic blood pressure, and active control of lipid levels may help to improve the prognosis of patients.*

Keywords: Idiopathic membranous nephropathy, Elevated blood lipids.

1. Introduction

Idiopathic membranous nephropathy (IMN) is a type of chronic glomerulonephritis in which membranous nephropathy (MN) excludes secondary membranous nephropathy (SMN) (including hepatitis B kidneys, lupus kidneys, glycosidic kidneys, vasculitis renal damage, and desiccation syndrome renal damage) [1]. Clinical manifestations often include edema, hyperlipidemia, massive proteinuria, and hypoalbuminemia [2]. Its role is due to sub-lethal injury of podocytes caused by immune complex deposition on the epithelial side of the glomerulus and the destruction of the glomerular filtration barrier leading to non-selective proteinuria and other manifestations of nephrotic syndrome [3], and now clinically the pathology of membranous nephropathy is divided into stages I-IV based on the deposition of immune complexes under the epithelium of the light and electron microscopy and the thickening and deformation of the basement membrane [4]. Current treatment is based on ACEI/ARB, anticoagulation, glucocorticoids and immunosuppressive therapy, with cytotoxic drugs, calmodulin phosphatase inhibitors (CsA/FK506), and rituximab as immunosuppressive agents [5]. In recent years, the role of abnormal lipid metabolism in kidney disease has attracted much attention, especially the interaction between hyperlipidemia and glomerular injury. It has been shown that about 80% of patients with membranous nephropathy (MN) are associated with hyperlipidemia, and low-density lipoprotein (LDL) levels are positively correlated with the degree of proteinuria [6]. In this study, we retrospectively analyzed the clinical and pathological influencing factors of patients with IMN with elevated lipids to provide suggestions for clinical diagnosis and treatment.

2. Data and Methods

2.1 Research Method

159 patients with IMN admitted from 2021 to 2024 were selected, and general clinical indicators of the patients were collected, including age, gender, blood pressure, hemoglobin (HGB), blood creatinine (Scr), blood urea nitrogen (BUN), estimated glomerular filtration rate (eGFR), blood uric acid (SUA), blood albumin (blood ALB), blood total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), 24-hour urine protein quantification, and pathologic information. According to the elevation of lipids, they were categorized as DL (Dyslipidemia) and non-DL, and the differences in clinical and pathological data between the two groups were compared.

2.2 Renal Pathology

Light microscopy requires that the number of glomeruli in the specimen of renal biopsy is at least 10, and HE and PASM are performed,

Masson staining, light microscopic observation of glomerular lesions, renal interstitial lesions, renal small blood vessel lesions. Immunofluorescence examination requires the use of frozen section direct immunofluorescence method to observe the intensity of IgG, IgM, IgA, C3, Clq in renal biopsy specimens. Electron microscopy was used to examine the site and intensity of glomerular electron dense material deposition and the degree of basement membrane thickening.

2.3 Diagnostic Criteria for Elevated Blood Lipids

Under normal diet, the test fulfills 1 or more of the following 4 items: (1) serum TC ≥ 6.2 mmol/L; (2) TG ≥ 2.3 mmol/L; (3) HDL < 1.0 mmol/L; (4) LDL ≥ 4.1 mmol/L [7].

2.4 Statistical Methods

The study was statistically processed using SPSS 26.0 software, and the measured data were expressed as x±s if they conformed to normal distribution, and the t test was used to compare the two groups if the variances were aligned, and the nonparametric rank sum (Mann-Whitney) test was used if they were not aligned; if the measured data did not conform to normal distribution, it was expressed as the median (interquartile spacing), and a nonparametric test was used;

and the count data were expressed as the rate or the composition of the percentage was expressed, and the chi-square test was used to compare the two groups; correlation analysis was performed using binary variable correlation analysis, which was expressed as r, and $P < 0.05$ was considered statistically significant.

3. Results

3.1 Comparison of the General Conditions of Patients in the Two Groups

A total of 159 patients with IMN were included in this study, 34 patients in the non-DL group and 125 patients in the DL group, and the age of patients in both groups did not conform to the normal distribution (Shapior-Wilk=0.932, 0.947, P=0.035, 0.000<0.05); 23 males and 11 females in the non-DL group, with the age of 58 (50.5, 67.25) years old, and a history of 61.8% of patients with a history of hypertension and 5.9% of patients with a history of diabetes mellitus; in the DL group, there were 81 males and 44 females, aged 56 (43.5, 64) years, 43.2% of patients with a history of hypertension and 12% of patients with a history of diabetes mellitus. There was no statistically significant difference in gender, age, history of hypertension, history of diabetes mellitus, hyperuricemia and nephrotic syndrome between the two groups of patients. The percentage of patients with nephrotic syndrome was higher in the DL group of patients (72.8% vs 55.9%), which was close to significance (p=0.058#) (Table 1).

Table 1: Comparison of general condition of patients in both groups

General information	Non-DL group(n=34)	DL group (n=125)	P
Sex (number of male/female cases))	23/11	81/44	0.757
Age [Median (p25, p75)] years	58 (50.5, 67.25)	56 (43.5, 64)	0.162
History of hypertension [Cases (%)]	21(61.8)	54(43.2)	0.065
History of diabetes [Cases (%)]	2(5.9)	15(12)	0.477
Hyperuricemia [Cases (%)]	10(29.4)	45(36)	0.474
Nephrotic syndrome [Cases (%)]	19(55.9)	91(72.8)	0.058#

2.2 Comparison of Laboratory Results between the Two Groups of Patients

The differences in systolic blood pressure, diastolic blood pressure and hemoglobin between the two groups were not statistically significant by t-test. BUN, Scr, eGFR, UA, ALB, 24h urine protein quantification, TC, TG, HDL-C, LDL-C did not conform to normal distribution in the two groups, and by nonparametric test, there were statistical differences between the two groups in ALB, 24h urine protein quantification, TC, TG, LDL-C ($P < 0.05$).ALB in the DL group was significantly lower than that in the non-DL group; 24h urine protein quantification, TC, TG, LDL-C were significantly higher than that in the DL group. urine protein quantification, TC, TG, and LDL-C were significantly higher in the DL group than in the non-DL group (Table 2).

Table 2: Comparison of laboratory results between the two groups

Laboratory results	Non-DL group (n=34)	DL group (n=125)	P
systolic blood pressure(mmHg)	129.68±25.354	135.18±20.718	0.194
diastolic blood pressure(mmHg)	83.56±14.985	85.18±11.784	0.505
HGB (g/L)	132.68±16.032	136.02±18.709	0.344
BUN (mmol/L)	5.4 (3.85, 6.05)	4.9 (4, 6.25)	0.422
Scr (μmol/L)	59.1 (50.1, 71.02)	63 (52.25, 80.85)	0.246
eGFR(ml/min)	103.12 (90.36, 108.08)	102.98 (92.21, 112.62)	0.857
SUA (μmol/L)	352.5 (306.5, 415.0)	364 (314.5, 434.0)	0.552
ALB (g/L)	32.15 (27.1, 36.2)	26.3 (21.25, 31.75)	0.000*
24-hour urine protein quantification(mg/24h)	2481.35 (1694.2, 4886.22)	4206.0 (2865.1, 5923.2)	0.003*
TC (mmol/L)	5.28 (4.8, 5.84)	7.48 (6.42, 8.8)	0.000*
TG (mmol/L)	1.45 (1.14, 1.78)	2.5 (1.74, 3.76)	0.000*
HDL (mmol/L)	1.59 (1.24, 1.75)	1.52 (1.17, 1.85)	0.435
LDL (mmol/L)	3.1 (2.54, 3.38)	4.5 (3.57, 5.15)	0.000*

Note: *P < 0.05

3.3 Comparison of Pathological Features between the Two Groups of Patients

After ANOVA test, there was no statistically significant difference (P>0.05) between the two groups in the indicators of pathological features crescent formation, nail protrusion formation, thylakoid cell proliferation, interstitial fibrosis, glomerulosclerosis and immune deposition (IgA, IgM, IgG, C3, C1q) (Table 3).

Table 3: Comparison of pathological characteristics between the two groups of patients

Renal Pathology	Non-DL group (n=34)	DL group (n=125)	P
Crescent (Yes, %)	0(0)	2(1.6)	1
spike formation (Yes, %)	34(100)	125(100)	-
mesangial cell proliferation (Yes, %)	34(100)	125(100)	-
Glomerulosclerosis (Yes, %)	24(70.6)	70(56)	0.125
renal interstitial fibrosis (Yes, %)	9(26.5)	20(16)	0.161
IgA (Yes, %)	6(17.6)	23(18.4)	0.920
IgM (Yes, %)	24(70.6)	81(64.8)	0.527
IgG (Yes, %)	34(100)	123(98.4)	1
C3 (Yes, %)	34(100)	113(90.4)	0.13
C1q (Yes, %)	3(8.8)	9(7.2)	1

3.4 Correlation of Various Lipid Indicators with Clinical and Laboratory Indicators

After binary variable correlation analysis, Scr was correlated with HDL, SUA was correlated with both TG and HDL, ALB and 24h urine protein were significantly correlated with TC and LDL, and systolic blood pressure was correlated with both TG and LDL (Table 4).

Table 4: Correlation of each lipid index with clinical and laboratory indicators

Lipids Series	BUN	Scr	eGFR	UA	ALB	24-hour urine protein quantification	systolic blood pressure	diastolic blood pressure
TC	0.025	0.099	-0.092	-0.058	-0.38**	0.277**	0.119	0.07
TG	0.075	0.138	-0.03	0.185*	-0.048	0.152	0.158*	-0.032
HDL	-0.088	-0.173*	-0.046	-0.183*	0.121	-0.072	0.035	-0.055
LDL	0.028	0.115	-0.061	-0.028	-0.395**	0.224**	0.175*	0.083

Note: *P < 0.05, **P < 0.01

4. Discussion

The typical clinical feature of membranous nephropathy is nephrotic syndrome, and some cases (about 25%) show a trend of self-limiting remission, which is manifested by a spontaneous decrease of >50% in 24-hour urinary protein quantification and maintenance of a stable eGFR; about 35% of the patients can be in a subclinical active state for a long period of time, which manifests as persistent proteinuria (1-3.5 g/d) accompanied by compensated renal function; however, more than 40% of the patients with progressive forms of the disease still develop end-stage renal disease (ESRD) within end-stage renal disease (ESRD) within five years [8]. Recent studies have revealed that abnormal lipid metabolism plays an important role in renal injury [9], and when lipids exceeding the metabolic threshold are abnormally deposited in non-adipose tissues, tissue injury is triggered through lipotoxic mechanisms [10]. Lipids are induced to produce kidney injury through mechanisms such as defective autophagy, oxidative stress, endoplasmic reticulum stress, inflammatory response and epigenetic modifications [11].

The proportion of patients with nephrotic syndrome was significantly higher in the DL group than in the non-DL group (72.8% vs 55.9%), although the traditional threshold of significance was not reached (P=0.058), suggesting that dyslipidemia may be a potential risk factor for the development of NS in patients with IMN. It has been shown that in the kidney, abnormal deposition of lipids disrupts the glomerular filtration barrier, resulting in a large loss of protein from the urine, leading to phenomena such as hypoalbuminemia and hyperlipidemia, which are closely related to the development of nephrotic syndrome [12], suggesting that lipid monitoring should be strengthened for patients with IMN in the clinical workup with a view to identifying the high risk group of NS at an early stage, and optimizing lipid-lowering interventions in order to improve the prognosis [13].

Patients in the DL group showed a significant decrease in blood ALB (P=0.000*) and a statistically significant difference in elevated 24h urinary protein (0.003*) compared with patients in the non-DL group; and Spearman's correlation analysis suggested that the decrease in ALB and elevated 24h urinary protein were significantly associated with elevated TC (r=-0.38, P<0.01) (r=0.277, P<0.01), LDL (r=-0.395, P<0.01) (r=0.224, P<0.01) elevations were significantly correlated. Disruption of the glomerular filtration barrier leads to increased protein loss, which is further exacerbated by inadequate hepatic synthesis compensation for hypoalbuminemia [14]. Although there was no difference in renal function indices (BUN, Scr, eGFR), elevated urinary protein suggests early renal injury (e.g., podocyte injury or abnormal basement membrane permeability), which precedes the decline in eGFR.TC, TG, and LDL-C were significantly higher in the DL group than in the non-DL group, and elevated TC and LDL-C were associated with an increased cardiovascular risk [15], whereas cardiovascular mortality rates in patients with nephropathy are 10-20 times higher than those of the general population. The cardiovascular mortality rate in patients with renal disease is 10-20 times higher than that in the general population, and the combined cardio-renal damage in patients in the DL group needs to be concerned [16].

In Spearman's correlation analysis, elevated Scr was associated with decreased HDL (r=-0.173, P<0.05), and when renal function is impaired, the renal clearance or synthesis of HDL is reduced, and the decrease of HDL, as a "protective lipoprotein", may weaken the renal antioxidant and anti-inflammatory capacity, resulting in bidirectional damage [17]. Elevated SUA is accompanied by increased TG (r=0.185, P<0.05) and decreased HDL (r=-0.183, P<0.05), and a study showed that TG levels were significantly increased and HDL-C levels were significantly decreased in the hyperuricemia group of the elderly population, which suggests that the increase in UA is closely related to the increase in TG and the decrease in HDL and that the changes in these indexes correlate with the risk of developing metabolic syndrome [18]. risk of developing metabolic syndrome [18]. Elevated systolic blood pressure was positively correlated with TG (r=0.158, P<0.05) and LDL (r=0.175, P<0.05). One study noted that elevated TG was significantly associated with elevated systolic blood pressure and that a joint index of TG and glucose (TyG index) had a synergistic effect on the risk of developing hypertension [19]. This supports the interaction of the "renal-vascular-metabolic" axis, whereby hyperlipidemia elevates blood pressure through endothelial dysfunction, and hypertension exacerbates intraglomerular hypertension, which promotes proteinuria and renal injury [20].

In summary, SUA, Scr, 24-h urine protein, systolic blood pressure, and blood ALB were more severe in patients with idiopathic membranous nephropathy with elevated lipids than in patients without elevated lipids, suggesting that sufficient attention should be paid to early lipid-lowering treatment in IMN patients, and it is necessary to control lipid levels through diet or drugs in the treatment of idiopathic membranous nephropathy to reduce blood uric acid, reduce urine protein, and ultimately delay the progression of nephropathy. progression of renal disease. However, there was no significant difference in terms of nephropathologic features. This study is a retrospective analysis, considering the insufficient sample size and the large number of risk factors, and the large difference in the number of people between the two groups, only using the chi-square test to make a simple comparison between the groups, may not have taken into account the interactions and combined effects of different variables, which has brought a certain degree of bias to the results of the study, and the later still need to carry out a prospective case-control study with a large sample to further

validate the results.

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