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Association of Systemic Immune Inflammation Index and Pan-immune Inflammation Value with Prognosis in Idiopathic Membranous Nephropathy

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ABSTRACT

Idiopathic membranous nephropathy (IMN) presents a heterogeneous clinical course, with approximately 30% to 40% of patients experiencing spontaneous remission, while others respond poorly to treatment. This study aims to identify reliable biomarkers for risk stratification in IMN patients.

We conducted a prospective observational study involving 187 patients with IMN from February 2022 to February 2024. Patients were categorized into remission and non-remission groups based on clinical outcomes one year post-treatment. Comparative analyses revealed that the non-remission group exhibited significantly higher incidences of hypertension, elevated 24-hour urinary protein, higher serum creatinine levels, and increased inflammatory markers, including the systemic immune inflammation index (SII), systemic inflammation response index (SIRI), and pan-immune inflammation value (PIV). Conversely, the estimated glomerular filtration rate (eGFR) and lymphocyte-to-monocyte ratio (LMR) were lower in non-remission patients.

Spearman correlation identified hypertension, 24-hour urinary protein, and inflammatory indexes as positive correlates with non-remission, while eGFR showed a negative correlation.

Multivariate logistic regression confirmed hypertension, high 24-hour urinary protein, SII, SIRI, and PIV as independent risk factors for non-remission; eGFR was a protective factor. Receiver operating characteristic analysis revealed that SII and PIV effectively predicted non-remission (AUC=0.743 and 0.759, respectively). These findings underscore the potential of these indicators in assessing disease severity and guiding personalized treatment strategies.

Keywords: Idiopathic membranous nephropathy; Pan-immune inflammation value; Prognosis; Systemic immune inflammation index

INTRODUCTION

Idiopathic membranous nephropathy (IMN) is a common glomerular disease and accounts for approximately 30% of adult primary nephrotic syndromes.[1] The pathogenesis of IMN is mainly related to autoimmunity. Autoantibodies bind to antigens in the glomerular basement membrane to form immune complexes, which activate the complement system and lead to inflammatory reactions and damage to the

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glomerular filtration barrier.[2] The clinical manifestations of IMN are diverse, but it mainly presents as nephrotic syndrome, which includes massive proteinuria, hypoalbuminemia, edema, and hyperlipidemia. Some patients may also have hematuria, hypertension, and renal function impairment. Approximately 30% to 40% of patients with IMN achieve spontaneous remission, whereas many have suboptimal responses to treatment and eventually progress to end-stage renal disease.[3,4]

Current prognostic assessments in IMN predominantly rely on clinicopathological features and immune function markers. Several studies have identified specific pathological findings, such as grading of renal ectopic lymphoid tissue, as indicators of disease activity and severity.[5] Additionally, complement activation, as evidenced by elevated serum levels of complement factor B (CFB), has been associated with disease progression and treatment non-response[6]. However, these markers do not fully capture the complex inflammatory milieu and immune dysregulation inherent to IMN.

In this context, the systemic immune inflammation index (SII) and pan-immune inflammation value (PIV) have emerged as potentially valuable inflammatory biomarkers. IMN is characterized by the interplay of diverse immune cells and inflammatory mediators. SII integrates information about neutrophils, lymphocytes, and platelets, reflecting both the pro-inflammatory (neutrophils) and anti-inflammatory (lymphocytes) responses, as well as the potential role of platelets in thrombosis and inflammation. PIV, combining neutrophil, lymphocyte, monocyte, and platelet counts, provides an even more integrated assessment of immune cell populations, offering a more nuanced perspective on the immune-inflammatory balance.[7,8,9] By incorporating multiple cell types, SII and PIV offer a more holistic view of systemic inflammation than single-marker assessments, providing insights into the dynamic immune interactions that drive IMN pathogenesis.

However, there have been some limitations in current research. There are relatively few studies on the correlations between composite inflammatory indicators such as SII and PIV and the clinicopathological features and prognosis of patients with IMN, and no systematic understanding currently exists. Furthermore, differences in the selection of inflammatory indicators and research methods between studies have affected the comparability and consistency of results.[10,11] Further research is needed to determine how to comprehensively utilize multiple inflammatory indicators and clinicopathological factors to construct a more accurate prognostic prediction model. Therefore, the aim of this study was to investigate the characteristics of peripheral blood inflammatory indicators, including SII and PIV in patients with IMN and their correlations with pathological features and treatment prognosis.

MATERIALS AND METHODS

Participants

This study involved a prospective, observational, and open-cohort design. PASS 2023 was used to estimate the sample size by referring to the short-term non-remission rate of approximately 60% for IMN in previous studies and a confidence interval of 95%. The calculation indicated that at least 183 patients should be included. A total of 187 patients with IMN were admitted to our hospital from February 2022 to February 2024 and enrolled.

All included patients had to have a pathological diagnosis of IMN by renal biopsy. According to relevant pathological diagnostic criteria, immune complex deposition can be seen under the epithelium of the glomerular basement membrane, and other secondary factors are excluded. All patients were also between 18 and 75 years old and signed informed consent forms to voluntarily participate in the study.

Patients were excluded if they had diseases that could cause secondary membranous nephropathy, such as systemic lupus erythematosus, Sjogren's syndrome, hepatitis B virus infection, and malignant tumors. Furthermore, patients with any active infection or systemic inflammatory conditions, as indicated by clinical symptoms, elevated inflammatory markers (e.g., C-reactive protein, erythrocyte sedimentation rate), or treatment with antibiotics or anti-inflammatory drugs within the preceding month were also excluded. Patients were also excluded if they had severe complications such as acute infection, acute kidney injury, and heart failure or if they had been treated with immunosuppressants, glucocorticoids, or other drugs that may affect the immune-inflammatory state within the past 3 months. Lastly, patients were excluded if they had incomplete clinical data or if they were lacking key laboratory test data or pathological materials, which would have made comprehensive analysis and evaluation impossible.

Treatment Methods and Follow-up

All patients received individualized treatment plans that were formulated based on factors such as disease severity, renal function status, proteinuria level, and the presence of comorbidities. Non-specific treatment was mainly provided to low-risk patients (with normal renal function and urinary protein<4 g/d). The treatment included angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin II receptor blockers (ARBs) to reduce proteinuria; control blood pressure; reduce high pressure, high perfusion, and high filtration in the glomeruli; and delay the progression of renal function. Patients were advised to rest, avoid fatigue, and prevent infections.

Medium-risk patients (with normal renal function and urinary protein of 4–8 g/d) received glucocorticoid combined with immunosuppressant treatment in addition to conservative therapy. The commonly used regimen was glucocorticoid plus cyclophosphamide administrated as follows: intravenous infusion of 1 g of methylprednisolone for 3 days, followed by oral prednisone 0.4 mg/kg/d for 27 days, then oral cyclophosphamide at 2.5 mg/kg/d for 30 days. This treatment cycle was repeated 3 times for a total treatment duration of 6 months. Some patients also received a regimen of glucocorticoid combined with chlorambucil, given as: intravenous methylprednisolone 1 g/day for 3 days in months 1, 3, and 5, followed by oral prednisone 0.4 mg/kg/day for 27 days. In months 2, 4, and 6, prednisone was discontinued and replaced with oral chlorambucil 0.2 mg/kg/day. The total treatment duration for this regimen was also 6 months.

High-risk patients were characterized by decreased renal function, urinary protein>8 g/d, or severe complications such as hypertension and edema. These patients received new immunosuppressants such as cyclosporine A and tacrolimus in addition to the treatments given to patients with low and medium risk. The initial dose of cyclosporine A was 3-5 mg/(kg/d), which was taken orally in two divided doses. The dose was adjusted to maintain a drug's concentration in the blood at 100–200 ng/mL

The initial dose of tacrolimus was 0.05-0.1mg/(kg/d), administered orally in two divided doses, with target trough blood concentrations of 5–10 ng/mL. During the treatment process, the patients' vital signs, renal function, urinary protein, blood routine, blood biochemistry, and other indicators were closely monitored. Adverse drug reactions were observed and treated appropriately in a timely manner.

Follow-up began on the date of IMN diagnosis and combined outpatient visits with telephone follow-up. Outpatient reviews included questions about symptom changes, including edema, urine volume, and fatigue. A comprehensive physical examination was performed, and laboratory tests such as renal function indicators, 24-hour urinary protein, serum albumin, blood routine, and inflammatory indicator tests were carried out. Telephone follow-up mainly focused on understanding patients' daily life conditions, medication compliance, and the occurrence of new symptoms or complications. Follow-up concluded in February 2025 ensuring that all patients had at least 1 year of follow-up for assessment of treatment efficacy and prognosis.

Patient grouping

Based on the 1-year post-treatment outcomes, patients were classified into a clinical remission group (n=69) and a non-remission group (n=118). The criteria for clinical remission referenced the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines. Complete remission was defined as 24-hour urinary protein < 0.3 g or urinary protein-to-creatinine (T/Cr) < 0.3 mg/g with normal serum albumin levels and serum creatinine. Partial remission was defined as 0.3 g≤24-hour urinary protein<3.5 g or T/Cr 0.3–3.5 mg/g with a decrease of more than 50% compared to the baseline, an increase or normalization of serum albumin compared to the baseline value, and stable serum creatinine. Both patients with complete remission and those with partial remission were assigned to the clinical remission group; otherwise, patients were defined as having nonremission and included in the nonremission group.

Observation Indicators

General clinical data collected before treatment from the hospital's electronic medical record system, including age, gender, and body mass index (BMI). The patient's hypertension status was also recorded. Hypertension was defined as systolic blood pressure≥140 mmHg or diastolic blood pressure≥90 mmHg, or a history of hypertension and currently treatment with antihypertensive medications. The presence of diabetes was determined based on blood-glucose results with fasting blood glucose≥7.0 mmol/L,

2-hour postprandial blood glucose≥11.1 mmol/L, or a history of diabetes with current hypoglycemic therapy.

The presence of cardiovascular diseases, such as coronary heart disease and cardiomyopathy, was determined from the patient's medical history, electrocardiograms, echocardiograms, and other examination results. The duration from the onset of symptoms to the diagnosis of IMN was defined as the IMN course. Information was also obtained on whether the patient had a history of smoking (defined as smoking≥1 cigarette per day for≥1 year) or a history of drinking (defined as drinking≥2 times per week for≥1 year, with each drinking amount equivalent to≥15 g of pure alcohol).

All urine produced within 24 hours was collected and mixed evenly, and an appropriate aliquot was taken for testing. The 24-hour urinary protein was quantified by the pyrogallol red-molybdenum complex chromogenic method. Serum creatinine (Scr) was measured as a renal function indicator by the picric acid method. The estimated glomerular filtration rate (eGFR) was calculated using the simplified "Modification of Diet in Renal Disease" (MDRD) formula: eGFR (mL/min/1.73 m^2)=186×$(Scr)^{-1.154}$×$(age)^{-0.203}$×(0.742 if female). The degree of glomerular lesions was determined based on the pathological results of renal biopsy.

Using the Ehrenreich–Churg staging system, patients with IMN were categorized into stages I–IV. The degree of tubulointerstitial lesions was evaluated by a semi-quantitative scoring method, including indicators such as tubular atrophy, interstitial fibrosis, and inflammatory cell infiltration. Each indicator was scored with 0 to 3 points according to the degree of the lesion. Immunofluorescence was performed using a fluorescence microscope to assess the deposition intensity of immunoglobulin G (IgG) in the glomeruli.

After fasting, 2 mL of peripheral venous blood was collected from each patient. The white blood cell counts were measured using an automatic blood cell analyzer. The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR) were calculated. SII was calculated as $SII = \frac{\text{platelet count}\times\text{neutrophil count}}{\text{lymphocyte count}}$.

The systemic inflammation response index (SIRI) was calculated as $SIRI = \frac{\text{neutrophil count} \times \text{monocyte count}}{\text{lymphocyte count}}$. PIV was calculated as $PIV = \frac{\text{neutrophil count} \times \text{platelet count} \times \text{monocyte count}}{\text{lymphocyte count}}$. The types, doses, and treatment duration of medications such as glucocorticoids and immunosuppressants, were recorded. The use of special treatments, such as plasma exchange and immunoadsorption, including the number of sessions and treatment duration, was also documented.

Statistical Analysis

All analyses were performed using SPSS version 26.0. Normally distributed continuous data are presented as mean±standard deviation (SD) and were compared using the independent-samples t-test. Enumeration data were expressed as the number of cases or rates, and the χ^2 test was used for comparison between groups. When the theoretical frequency was less than 5, Fisher's exact probability method was used. Spearman correlation analysis was used to explore the correlations between differential indicators and nonremission after treatment.

Variables with statistical significance (p<0.05) in the univariate analysis were included in a multivariate logistic regression analysis using the forward stepwise regression method to identify independent risk factors associated with non-remission. The odds ratio (OR) and 95% confidence interval (CI) for each risk factor were reported. Receiver operating characteristic (ROC) curves were plotted, and the area under the curve (AUC) was calculated to evaluate the efficacy of peripheral blood inflammatory indicators and other influencing factors in independently and jointly predicting the risk of non-remission after treatment. The range of AUC is 0.5–1.0, and the closer it is to 1.0, the better the predictive efficacy is. An AUC of 0.5 indicates no predictive value. The optimal cutoff values of each indicator were determined, and their sensitivity, specificity, positive predictive value, and negative predictive value were calculated. DeLong's test was used to compare AUC differences between SII, SIRI, and PIV. p<0.05 was considered statistically significant.

RESULTS

General Clinical Data

There were no significant differences between the two groups in terms of age, gender, body mass index (BMI), disease duration, diabetes, cardiovascular diseases, smoking history, and drinking history (p>0.05). The proportion of patients with hypertension in the non-remission group was higher than in the clinical remission group (p<0.05). Details are shown in Table 1.

Clinicopathological Features

Compared to the clinical remission group, the non-remission group had higher 24-hour urinary protein, serum creatinine level, proportion of patients in stages III–IV, and semi-quantitative score of tubulointerstitial lesions (p<0.05). The eGFR in the non-remission group was lower than that in the clinical remission group (p<0.05). The results of immunofluorescence and electron microscopy showed that the IgG deposition intensity in the non-remission group was mainly strongly positive, with a higher proportion than that in the clinical remission group (p<0.05).

In electron microscope examinations, the non-remission group showed extensive foot process fusion, obvious basement-membrane thickening, and more electron-dense deposits. The foot process fusion in the clinical remission group was relatively mild, the basement-membrane thickening was not obvious, and there were fewer electron-dense deposits. Details are shown in Table 2.

Inflammatory Indicators and Treatment Characteristics

The NLR, PLR, SII, SIRI, and PIV in the non-remission group were higher than those in the clinical remission group, while the LMR was lower (p<0.05), as shown in Table 3.

Table 1. Comparison of general clinical data between the non-remission group and the clinical remission group [($\bar{x} \pm SD$), n (%)]

Clinical data	Clinical remission group (n=69)	Non-remission group (n=118)	t/χ^2 value	p
Age, y	47.20 ± 9.56	46.15 ± 9.67	0.720	0.473
Gender			0.013	0.909
Male	38 (55.1)	66 (55.9)		
Female	31 (44.9)	52 (44.1)		
BMI, kg/m^2	23.05 ± 1.52	23.29 ± 1.69	-0.823	0.411
Disease duration, mo	12.01 ± 2.87	12.08 ± 3.29	-0.147	0.883
Hypertension			4.259	0.039
No	48 (69.6)	54 (45.8)		
Yes	21 (30.4)	64 (54.2)		
Diabetes			3.065	0.080
No	56 (81.2)	82 (69.5)		
Yes	13 (18.8)	36 (30.5)		
Cardiovascular diseases			1.930	0.165
No	59 (85.5)	91 (77.1)		
Yes	10 (14.5)	27 (22.9)		
Smoking history			0.798	0.372
No	38 (55.1)	57 (48.3)		
Yes	31 (44.9)	61 (51.7)		
Drinking history			1.242	0.265
No	51 (73.9)	78 (66.1)		
Yes	18 (26.1)	40 (33.9)		

BMI: body mass index.

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Table 2. Comparison of clinicopathological features between the non-remission group and the clinical remission group ($\bar{x} \pm SD$)

Clinicopathological features	Clinical remission group (n=69)	Non-remission group (n=118)	t/χ^2 value	*p*
24-hour urinary protein quantification, g	3.67 ± 0.97	4.40 ± 1.73	-3.208	0.002
Serum creatinine, μmol/L	100.72 ± 22.55	109.35 ± 29.52	-2.097	0.037
eGFR, mL/min/1.73m^2	82.06 ± 9.97	76.57 ± 12.37	3.137	0.002
Glomerular lesions			4.259	0.039
Stages I-II	48 (69.6)	64 (54.2)		
Stages III-IV	21 (30.4)	54 (45.8)		
Tubulointerstitial lesions, score	1.71 ± 0.38	1.90 ± 0.52	-2.614	0.01
Immunofluorescent IgG deposition intensity			4.391	0.036
Non-strongly positive	57 (82.6)	81 (68.6)		
Strongly positive	12 (17.4)	37 (31.4)		

Egfr: estimated glomerular filtration rate; IgG: immunoglobulin G.

Table 3. Comparison of peripheral blood-related inflammatory indicators between the non-remission group and the clinical remission group ($\bar{x} \pm SD$)

Peripheral blood-related inflammatory indicators	Clinical remission group (n=69)	Non-remission group (n=118)	t value	*p*
NLR	2.57 ± 0.43	2.81 ± 0.68	-2.540	0.012
PLR	190.86 ± 58.67	211.16 ± 42.91	-2.718	0.007
LMR	1.80 ± 0.38	1.68 ± 0.37	2.195	0.029
SII	586.81 ± 125.18	735.50 ± 196.55	-5.647	<0.001
SIRI	41.81 ± 13.10	52.08 ± 16.75	-4.367	<0.001
PIV	265.75 ± 67.14	323.18 ± 68.27	-5.585	<0.001

LMR, lymphocyte-to-monocyte ratio; NLR: neutrophil-to-lymphocyte ratio; PIV: pan-immune inflammation value; PLR: platelet-to-lymphocyte ratio; SII: systemic immune inflammation index; SIRI: systemic inflammation response index.

In the clinical remission group, 73.9% (n=51) of patients achieved complete or partial remission. In the non-remission group, 0% achieved complete remission, and 100% (n=118) of patients did not achieve remission after treatment. There was no significant difference in the choice of treatment regimens between the two groups (χ^2=3.627, p=0.057). The average treatment cycle in the clinical remission group was 8.99 ± 1.17 months, but there was no statistical difference from that in the non-remission group (9.05 ± 1.14 months, t=-0.375, p=0.708).

Correlation Analysis

The treatment remission status was assigned values of 1 for non-remission after treatment and 0 for remission after treatment. The Spearman correlation analysis showed that hypertension, 24-hour urinary protein, serum creatinine, eGFR, glomerular lesions, tubulointerstitial lesions, immunofluorescent IgG deposition intensity, NLR, PLR, SII, SIRI, and PIV were all positively correlated with non-remission after treatment, while eGFR and LMR were negatively correlated (p<0.05). Details are shown in Table 4.

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Influential Factors for Non-remission

The indicators with $p<0.05$ in the univariate analysis were used as independent variables for assignment. A value of 0 was assigned for no hypertension, glomerular lesions in stages I–II, and non-strongly positive immunofluorescent IgG deposition. A value of 1 was assigned for hypertension, glomerular lesions in stages III–IV, and strongly positive immunofluorescent IgG deposition. The original values of 24-hour urinary protein, serum creatinine, eGFR, tubulointerstitial lesions, NLR, PLR, LMR, SII, SIRI, and PIV were used.

The multivariate logistic regression analysis, adjusted for treatment regimen, showed that hypertension, high 24-hour urinary protein, SII, SIRI, and PIV were independent risk factors for non-remission after treatment, and eGFR was an independent protective factor ($p<0.05$). The treatment regimen was not an independent factor ($p<0.05$). Details are shown in Table 5.

Predictive Efficacy for Non-remission

Using the independent risk factors (hypertension, high 24-hour urinary protein quantification, SII, SIRI, PIV) and protective factor (eGFR) from the multivariate logistic regression analysis, ROC curves were plotted to verify the efficacy of predicting non-remission after treatment. The results showed that the predictive AUCs of each influencing factor were 0.577, 0.647, 0.743, 0.690, 0.759, and 0.631, respectively. In particular, SII and PIV had high accuracy in predicting non-remission after treatment (AUC>0.70). DeLong's test revealed PIV had superior AUC vs SII ($Z=2.17$, $p=0.03$) and SIRI ($Z=3.01$, $p=0.003$). Details are shown in Figure 1 and Table 6.

Table 4. Correlation analysis between differential indicators among groups and non-remission of IMN patients after treatment

Correlation analysis parameters	r value	*p* value
Hypertension	0.151	0.039
24-hour urinary protein quantification	0.246	0.001
Serum creatinine	0.153	0.036
eGFR	-0.219	0.003
Glomerular lesions	0.151	0.039
Tubulointerstitial lesions	0.195	0.008
Immunofluorescent IgG deposition intensity	0.153	0.036
NLR	0.215	0.003
PLR	0.268	<0.001
LMR	-0.16	0.028
SII	0.406	<0.001
SIRI	0.317	<0.001
PIV	0.433	<0.001

eGFR: estimated glomerular filtration rate; IgG: immunoglobulin G; IMN: idiopathic membranous nephropathy; LMR: lymphocyte-to-monocyte ratio; NLR: neutrophil-to-lymphocyte ratio; PIV: pan-immune inflammation value; PLR: platelet-to-lymphocyte ratio; SII: systemic immune inflammation index; SIRI: systemic inflammation response index.

Table 5. Logistic regression analysis of factors affecting non-remission of IMN patients after treatment

Factors	β	S.E.	Wald χ^2	*p*	OR	95% CI lower limit	95% CI upper limit
Hypertension	1.404	0.513	7.482	0.006	4.073	1.489	11.142
24-hour urinary protein	0.445	0.182	5.987	0.014	1.560	1.092	2.227
Serum creatinine	0.014	0.009	2.379	0.123	1.014	0.996	1.032
eGFR	-0.049	0.022	5.128	0.024	0.952	0.912	0.993
Glomerular lesions	0.204	0.466	0.193	0.661	1.227	0.492	3.057
Tubulointerstitial lesions	0.34	0.535	0.404	0.525	1.404	0.493	4.004
Immunofluorescent IgG deposition intensity	1.099	0.617	3.173	0.075	3.002	0.896	10.063
NLR	0.63	0.38	2.751	0.097	1.877	0.892	3.951
PLR	0.007	0.004	2.87	0.090	1.007	0.999	1.016
LMR	-0.77	0.591	1.695	0.193	0.463	0.145	1.476
SII	0.006	0.002	16.232	<0.001	1.006	1.003	1.009
SIRI	0.055	0.017	10.759	0.001	1.057	1.022	1.092
PIV	0.016	0.004	16.907	<0.001	1.017	1.009	1.025
Constant	-13.357	3.466	14.855	<0.001			

CI: confidence interval; eGFR: estimated glomerular filtration rate; IgG: immunoglobulin G; IMN: idiopathic membranous nephropathy; LMR: lymphocyte-to-monocyte ratio; NLR: neutrophil-to-lymphocyte ratio; OR: odds ratio; PIV: pan-immune inflammation value; PLR: platelet-to-lymphocyte ratio; S.E.: standard error; SII: systemic immune inflammation index; SIRI: systemic inflammation response index.

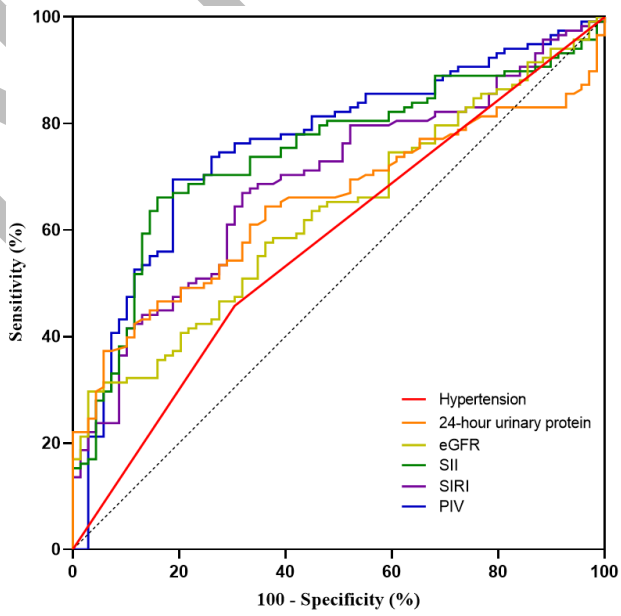

Figure 1. ROC Curve of the Prediction Model for Non-remission of IMN Patients after Treatment

Table 6. Analysis of the predictive efficacy of each factor for non-remission of IMN patients after treatment

Factors	AUC	95% CI lower limit	95% CI upper limit	Sensitivity, %	Specificity, %	Youden index
Hypertension	0.577	0.493	0.661	45.76	69.57	0.153
24-hour urinary protein	0.647	0.57	0.725	61.02	66.67	0.277
SII	0.743	0.671	0.815	74.56	71.41	0.46
SIRI	0.69	0.614	0.765	71.22	64.78	0.36
PIV	0.759	0.687	0.831	80.24	75.78	0.56
eGFR	0.631	0.552	0.71	65.37	NA	NA

AUC: area under the curve; CI: confidence interval; eGFR: estimated glomerular filtration rate; IMN: idiopathic membranous nephropathy; NA: not applicable; PIV: pan-immune inflammation value; ROC: receiver operating characteristic; SII: systemic immune inflammation index; SIRI: systemic inflammation response index.

DISCUSSION

In this research, the proportion of hypertension patients in the non-remission group was distinctly higher than that in the clinical remission group. This finding is in line with those of Lu et al[12] and suggests that hypertension has a substantial impact on disease progression and poor prognosis. As a systemic disorder, hypertension can bring about structural and functional alterations in renal blood vessels.[13] Persistent hypertension raises the pressure within the glomeruli, leading to a state of high perfusion and high filtration. Such a situation can damage the glomerular basement membrane and podocytes, thereby enhancing the excretion of proteinuria.[14]

Moreover, hypertension can induce renal arteriosclerosis, which reduces renal blood flow, causes renal ischemia and hypoxia, and further aggravates kidney damage.[15] Long-term hypertensive status can expedite the progression of kidney diseases and make it more difficult to achieve treatment remission.[16] The multivariate logistic regression analysis indicated that hypertension is one of the risk factors for non-remission. These results imply that blood pressure should be closely monitored for patients with IMN in clinical practice, and active regulation of hypertension is required to lower the risk of kidney damage.

Clinicopathological features have a significant impact on the prognosis assessment of IMN. There were remarkable disparities in indicators as such 24-hour urinary protein, serum creatinine, eGFR, glomerular lesions, and tubulointerstitial lesions between the clinical remission group and the non-remission group. Twenty-four-hour massive proteinuria is one of the significant clinical manifestations of IMN and a key element influencing prognosis. Prolonged massive proteinuria can give rise to high filtration and high perfusion in the glomeruli, cause damage to the glomerular basement membrane, and result in the detachment of podocytes, thereby accelerating the processes of glomerulosclerosis and tubulointerstitial fibrosis.[17,18] Some investigations have demonstrated that for every 1-g increment in 24-hour urinary protein, the risk of progression from IMN to end-stage renal disease escalates by 20%–30%.[19] Proteinuria can also harm the renal tubular epithelial cells, leading to disorders in renal tubular reabsorption and excretion functions, as well as greater kidney damage.[20]

LMR was lowered in the non-remission group, although indicators such as NLR, PLR, SII, SIRI, and PIV were noticeably higher. Furthermore, PIV, SIRI, and SII each acted as a separate risk factor for non-remission. These markers are very important for determining the prognosis of diseases and can reflect the body's immune-inflammatory state. The body is in a highly inflammatory state, as indicated by the rise of SII and SIRI, which are comprehensive inflammatory signs.[21] SII, SIRI, and PIV provide a more thorough representation of the body's inflammatory state by accounting for the quantitative changes of platelets, neutrophils, lymphocytes, and monocytes.[22,23]

In the inflammatory response, the activation of platelets and neutrophils leads to an increase in the release of inflammatory mediators, and the function of

lymphocytes is inhibited, resulting in elevation of SII, SIRI, and PIV. Research has demonstrated that SII, SIRI, and PIV are closely associated with the prognosis of diverse inflammation-related diseases, such as sepsis and rheumatoid arthritis.[24,25] In IMN, the elevation of SII and SIRI might indicate disease activity and progression, which is highly valuable for the assessment of prognosis. Furthermore, elevation of these inflammatory indicators may reflect abnormal activation of the immune response and the persistent presence of inflammatory damage, which would make it difficult for renal tissue to repair and recover.

Compared to conventional pathological and clinical factors, these peripheral blood inflammatory indicators have certain advantages as biomarkers. They can be obtained through simple blood tests that are convenient to perform and cost-effective, which facilitates their application in clinical practice. These indicators can reflect the immune-inflammatory state of the body in real time. Thus, they provide timely information for early disease diagnosis and prognosis assessment.

This study has certain limitations. Regarding the sample size, only 187 patients were included in this study, which is rather small and might not capture all possible traits and circumstances. A small sample size could result in insufficient representativeness of the research findings and an inability to precisely reflect the characteristics of the overall population. In subsequent investigations, the sample size should be increased and cover more diverse regions and ethnic groups to enhance the universality and reliability of the research results.

Furthermore, the follow-up duration was only 1 year, which is relatively brief. IMN is a chronic illness, and its progression and prognosis may require longer observations. A short follow-up time may not accurately reflect the long-term prognosis of patients and cannot capture the long-term complications and recurrence of the disease. For instance, the development of end-stage renal disease or the long-term impact of treatment on renal function could not be fully assessed. Thus, future research should use longer follow-up times and observation periods to address these concerns.

This study primarily concentrated on the associations among clinicopathological features, peripheral blood inflammatory indicators, and treatment-related characteristics. Nevertheless, other factors that impact the prognosis, such as gene polymorphisms, lifestyle, and psychological factors. Gene polymorphisms may influence patients' responses to treatment and disease susceptibility. Lifestyle factors like diet and exercise may also influence the disease development and prognosis. Psychological factors such as anxiety and depression may affect treatment compliance and quality of life and thereby impact the prognosis. Future research should take these factors into account to further explore the prognostic mechanisms of IMN.

In conclusion, this research showed that hypertension, elevated 24-hour urinary protein, SII, SIRI, and PIV were independent risk factors for non-remission of IMN, while eGFR was an independent protective factor. Notably, SII and PIV provided the strongest predictive efficiency for non-remission, highlighting their potential utility in guiding clinical decision-making." These findings provide a reference framework for assessing disease severity and prognosis and offer a solid foundation for the formulation of personalized treatment plans. Implementing a structured framework that utilizes these biomarkers, in conjunction with clinicopathological parameters, has the potential to improve early risk stratification, guide treatment decisions, and ultimately enhance patient outcomes in IMN.

STATEMENT OF ETHICS

This experiment was approved by North China University of science and technology affiliated Hospital Ethics Committee (No.SQ2024018).

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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Not applicable.

DATA AVAILABILITY

The data supporting the findings of this study on the association of the systemic immune inflammation index

(SII) and pan-immune inflammation value (PIV) with the prognosis in idiopathic membranous nephropathy (IMN) can be accessed as follows:

The datasets generated and analyzed during the current study are not publicly available due to patient privacy and confidentiality concerns. However, the relevant data may be made available upon reasonable request. Interested researchers can contact the corresponding author, Jingyuan Gao, via email at gaojingyuan2009@126.com, to discuss data access and any potential collaboration opportunities.

Additionally, any further inquiries regarding specific methodologies or statistical analyses can also be directed to the corresponding author at the same contact.

We appreciate your understanding regarding the limitations on data sharing and are committed to promoting scientific collaboration while adhering to ethical research practices. Thank you.

AI ASSISTANCE DISCLOSURE

This study did not involve the assistance of AI.

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