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Clinical observation and analysis of thyroid hormone levels in patients with idiopathic membranous nephropathy

Yu Huang, MM[c], Luhuai Feng, MM[a], Xian Li, MM[b], Shanshan Huang, MM[b], Ying Deng, MM[b], Zhong-e Liang, MM[b], Ning Xia, MD[d], Zhenhua Yang, MD[c,*]

Abstract

We sought to investigate the effect of total triiodothyronine (TT$_3$) reduction in the follow-up of patients with idiopathic membranous nephropathy (IMN). A total of 121 patients were enrolled and classified into a low TT$_3$ group or a normal group. Clinical indicators were compared between the groups, and changes in estimated glomerular filtration rate (eGFR), albumin (ALB), thyroid-stimulating hormone, serum creatinine, total protein, total cholesterol (TC), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C) during follow-up were analysed. In the analysis by TT$_3$ level, ALB was significantly lower in the low TT$_3$ group ($P < .05$), while TC, TG, LDL-C, fibrinogen, and renal pathological staging were significantly higher in the low TT$_3$ group ($P < .05$). Analysis of variance for repeated measurement during follow-up showed that there were no significant differences in eGFR and ALB between the groups. TC, TG, and LDL-C levels were significantly higher in the low TT$_3$ group ($P < .05$). Approximately 37% of patients with IMN showed a decrease in TT$_3$, which was accompanied by significantly decreased ALB level, higher pathological stage, and increased serum lipid level compared with patients having a normal TT$_3$ level. The management of TT$_3$, and appropriate intervention, may therefore help to prevent the kidney damage progress in patients with IMN.

Abbreviations: ALB = albumin, eGFR = estimated glomerular filtration rate, IMN = idiopathic membranous nephropathy, LDL-C = low-density lipoprotein cholesterol, MN = membranous nephropathy, SCr = serum creatinine, TBG = thyroid hormone-binding globulin, TC = total cholesterol, TG = triglyceride, TP = total protein, TSH = thyroid-stimulating hormone, TT$_3$ = total triiodothyronine.

Keywords: clinical indicators, follow-up, idiopathic membranous nephropathy, metabolism, triiodothyronine

1. Introduction

Membranous nephropathy (MN) is a common pathological condition of the glomeruli, and characteristic pathological changes include diffuse thickening of the glomerular basement membrane (GBM) and subepithelial deposits. MN is divided into 2 categories: idiopathic membranous nephropathy (IMN), also known as primary MN; and secondary MN. IMN accounts for about 13.28% of primary glomerular disease in China,[1] and has a male-to-female predominance of approximately 1.2:1. IMN is a common glomerular disease that causes nephrotic syndrome in middle-aged and older adults, and accounts for more than half of all cases of nephrotic syndrome in older adults. The clinical manifestations of IMN in most patients are mass proteinuria of non-selective and nephrotic syndrome, although some patients may have microscopic haematuria or hypertension. The natural course of IMN can differ widely among patients, and the condition can resolve spontaneously in approximately 25% of patients while 30% to 40% will progress to end-stage renal disease within 5 to 10 years. IMN can take a considerable length of time to treat, and can result in variable outcomes, multiple side effects, and ineffective corticosteroid monotherapy.[2,3]

The active thyroid hormones are thyroxine (T$_4$) and triiodothyronine (T$_3$), which are primarily found in combination with proteins such as thyroid hormone-binding globulin (TBG), and infrequently in the free form. Thyroid hormones can change from 1 form to the other to maintain a dynamic equilibrium. The state of binding to proteins is a store of thyroid hormones that prevent T$_3$ and T$_4$ from filtering through the glomerulus. The mechanical barrier and charge barrier of GBM are damaged in IMN, especially when nephrotic syndrome is present, leading to the generation of large quantities of negatively charged proteins with high molecular weight (including TBG) that are leached from the glomerulus in large quantities, resulting in a reduction in T$_3$ and T$_4$ levels in circulation, despite normal thyroid function.[4] Patients with nephrotic syndrome frequently have reduced levels of thyroid hormones, primarily T$_3$, which manifests as lower triiodothyronine syndrome, and these factors should be considered during patient treatment. There have been many reports on

the relationship between nephrotic syndrome and thyroid hormone levels, most of which support the process describe above. However, a decrease in thyroid hormone level can also occur in patients with ongoing severe disease, which is considered by most researchers as an adaptive response to the state of illness and thus part of the self-protection regulation mechanism.[5,6] Multiple recent studies have examined the relationship between nephrotic syndrome and thyroid hormone levels, although few have examined the effects of decreased thyroid hormone levels, particularly total triiodothyronine (TT_3), on the onset and follow-up of IMN patients.[4,7,8] Here, we analysed the influence of TT_3 level on clinical indicators of patients with IMN as well as the effect of TT_3 reduction on the main clinical indicators during follow-up to investigate the clinical implications of TT_3 reduction in IMN patients.

2. Materials and methods

2.1. Case selection

The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (Approval Number: 2019KY-E-067), and all patients or patients' authorized persons signed the informed consent form. Data from 121 patients with MN were included in this retrospective analysis. All patients were admitted to the Department of Nephrology at the First Affiliated Hospital of Guangxi Medical University from June 2013 to April 2018, and their diagnosis was confirmed by renal biopsy. Patients with secondary MN; primary hypothyroidism; with confirmed or suspected acute kidney injury; or those not treated according to the 2012 Kidney Disease Improving Global Outcomes[9] guidelines during follow-up were excluded. No patients received thyroid hormone replacement therapy.

2.2. Clinical data

We used data from the patient's first hospitalisation as baseline data and data from each subsequent outpatient or inpatient visit as follow-up data. The baseline clinical data of each patient were obtained from the inpatient medical record system, and follow-up data were obtained from the inpatient and outpatient medical records system. Clinical data included age, sex, routine biochemistry tests, renal function, plasma total protein (TP), serum albumin (ALB), thyroid function, blood lipids, and 24-hours urinary protein (24 hours UP). The estimated glomerular filtration rate (eGFR) was calculated for each patient using sex, age, and serum creatinine (SCr) level. Renal pathology data were also collected (all pathological tissues were examined by light microscopy, electron microscopy, and immunofluorescence, and renal pathological changes were classified into 1 of 4 stages [I–IV]; if 2 or more stages were identified simultaneously, the highest stage was recorded). The end point of follow-up was loss to follow-up, renal replacement therapy, or the cut-off date of April 31, 2017. Data on routine biochemistry testing, renal function, blood lipids, TP, ALB, and 24 hours UP were collected during follow-up.

On the basis of TT_3 level, 121 patients were classified into a low-TT_3 group (n=45, 37.19%) or a normal TT_3 group (normal group) (n=76, 62.81%). Differences in sex, age, blood lipids, renal function, 24 hours UP, ALB, total protein, and renal pathological stage were compared between the 2 groups. During follow-up, changes in eGFR, ALB, total cholesterol (TC),

triglycerides (TG), and low-density lipoprotein-cholesterol (LDL-C) were compared between the groups.

2.3. Diagnostic criteria

Nephrotic syndrome was evaluated according to the following criteria:

(1) hyperproteinuria (>3.5 g/24 hours),
(2) hypoalbuminemia (plasma ALB <30 g/L),
(3) oedema, and
(4) hyperlipidaemia

Among these, (1) and (2) were considered necessary conditions, and nephrotic syndrome was diagnosed when both (1) and (2) were present.

Based on the reference ranges of the clinical laboratory at our centre, the TT_3 range was 1.34 to 2.75 nmol/L, the TT_4 range was 78.38 to 157.4 nmol/L, and the TSH range was 0.34–5.65 mIU/L. TT_3 and TT_4 levels outside of these ranges were considered to be decreased or increased, as applicable.

2.4. Statistical analysis

The SPSS 20.0 statistical software package was used for all statistical analysis. Normality testing was carried out for measurement data, and normal distribution was expressed as $\overline{x} \pm s$ while a t test was used for comparisons between groups. The mean value of non-normal distribution data was represented by the median [M (P25, P75)], and a rank-sum test was used for comparisons between groups. Frequency data were expressed as a percentage, and between-group comparisons were performed using the chi-square test. Spearman correlation analysis was used for correlation analysis of rank variables, while Pearson correlation analysis was used for continuous variables. Follow-up data were analysed by analysis of variance (ANOVA) with repeated measurement data. Values of $P < .05$ were considered statistically significant.

3. Results

3.1. Patient information

Data from 121 patients, including 71 males and 50 females (1.42:1) with an average age of 46 [32, 54] years (range: 15–75 years), were evaluated. The average course from onset to renal biopsy was 2 [1,6] months (range: 0.13–84 months). There were 57 cases (47.11%) with a diagnosis of nephrotic syndrome at the time of renal biopsy, and 44 cases with hypertension at the time of admission (36.36%). The mean follow-up time after renal biopsy was 16.97 [12.65, 24.03] months (range: 6.33–49.43 months).

3.2. Analysis by serum TT_3 level
3.2.1. Comparison of clinical indicators in patients with IMN.
There were no significant differences between the low TT_3 group and the normal group in sex ratio, age, proportion of patients with high blood pressure, treatment course before renal biopsy, proportion of patients with nephrotic syndrome, thyroid-stimulating hormone (TSH), FT_4, haemoglobin, SCr, eGFR, PT, 24 hours UP, and proportion of patients with 24 hours UP >3.5 g ($P>.05$). However, the levels of TT_4, FT_3, and ALB were significantly lower in the low TT_3 group than in the normal group ($P<.05$), while the levels of TC, TG, LDL-C, and FIB were

Table 1

Comparison of patient characteristics by TT_3 level grouping.

Indicators	Normal group (n = 76)	Low TT_3 group (n = 45)	Statistic	P
Male (%)	41 (53.95)	30 (66.67)	$X^2 = 1.886$	.170
Age, yr	46.5[35.25,53.75]	45[25.50,54.00]	$Z = -0.853$	.394
Patients with high blood pressure (%)	31 (40.79)	13 (28.89)	$X^2 = 1.730$	.188
Course before renal biopsy, mo	3.00[1.00,6.00]	2.00[0.67,6.00]	$Z = -0.768$	.442
Patients with NS (%)	32 (42.11)	24 (53.33)	$X^2 = 1.433$	.231
Level of TSH (mIU/L)	3.00[2.00,4.00]	3.00[1.93,3.05]	$Z = -0.240$	.811
Level of TT_4 (nmol/L)	90.37[80.25,108.49]	67.00[56.0,76.00]	$Z = -6.205$	.000
Level of FT_3 (pmol/L)	4.36[4.00,5.00]	4.00[3.49,4.31]	$Z = -3.624$	.000
Level of FT_4 (mol/L)	10.04[8.99,12.84]	10.00[7.93,12.00]	$Z = -1.696$	.090
Haemoglobin (g/L)	125.22 ± 16.51	128.90 ± 17.64	$t = 1.154$	.251
ALB (g/L)	26.00[21.87,30.00]	20.00[17.00,25.00]	$Z = -4.553$	.000
Scr (umol/L)	74.50[62.25,85.00]	86.00[64.00,95.00]	$Z = -1.674$	.094
eGFR (ml/min/1.73m^2)	100.51 ± 25.28	98.37 ± 25.32	$t = -0.112$	.911
eGFR<90ml/min/1.73m^2 (%)	33 (43.42)	24 (53.33)	$X^2 = 1.115$	.291
TC (mmol/L)	7.00[5.82,8.00]	8.61[6.06,12.00]	$Z = -3.369$	.001
TG (mmol/L)	1.56[1.00,2.72]	2.00[1.11,3.00]	$Z = -1.967$	.049
LDL-C (mmol/L)	4.22[3.25,6.00]	6.00[4.39,8.54]	$Z = -3.440$	.001
APTT (S)	30.35[28.70,33.47]	31.40[29.50,33.60]	$Z = -1.065$	.287
PT (S)	10.00[9.63,10.60]	10.20[9.70,10.70]	$Z = -0.757$	.449
FIB (g/L)	4.78[3.99,5.60]	5.76[4.55,6.46]	$Z = -2.727$	.006
24 h UP (g/24 h)	3.44[1.77,5.98]	4.54[2.32,7.00]	$Z = -1.140$	.254
24 h UP>3.5 g/24 h (%)	36 (47.37)	26 (57.78)	$X^2 = 1.226$	.268
Renal pathological stage(n,%)				
I	31 (40.79)	8 (17.78)	$X^2 = 7.353$	.025
II	43 (56.58)	34 (75.56)		
III	2 (2.63)	3 (6.67)		

ALB = albumin, APTT = activated partial thromboplastin time, eGFR = estimated glomerular filtration rate, FIB = fibrinogen, FT_3 = free T_3, FT_4 = free T_4, LDL-C = low-density lipoprotein cholesterol, PT = prothrombin time, SCr = serum creatinine, TC = total cholesterol, TG = triglycerides, TSH = thyroid-stimulating hormone, TT_3 = total triiodothyronine, TT_4 = total thyroxine, UP = urinary protein.

significantly higher in the low TT_3 group than in the normal group ($P < .05$). In patients with renal pathological staging, the proportion of patients with stage II and III disease was significantly higher in the low TT_3 group than in the normal group ($P = .025$) (Table 1).

3.2.2. Repeated ANOVA for the effect of follow-up time and TT_3 grouping on change in eGFR and ALB

3.2.2.1. Change in eGFR. During follow-up, eGFR levels generally followed a downward trend. eGFR levels in the low TT_3 group tended to initially increase slowly, followed by a continuous decline, with a maximum value of 90.310 mL/min/1.73 m^2. EGFR in the normal group decreased continuously before stabilising at 80 to 90 mL/min/1.73 m^2. However, no

significant difference in eGFR was observed between the 2 groups ($F = 0.097$, $P = .785$). There was a significant difference in eGFR between different time points in the follow-up period ($F = 4.085$, $P = .004$) as well as in the normal group ($F = 4.932$, $P = .004$). However, there was no significant difference in eGFR at different time points in the low TT_3 group ($F = 1.727$, $P = .165$), or between the 2 groups at each time point ($P > .05$). Finally, there was no interaction effect observed between follow-up time and grouping ($F = 1.614$, $P = .176$) (Table 2, Fig. 1).

3.2.2.2. Change in ALB. During follow-up, ALB levels generally followed an upward trend. ALB levels gradually increased before stabilising at 35 to 40 g/L in both groups. ALB levels were lower in the low TT_3 group than in the normal group, but the difference

Table 2

Repeated ANOVA for the effect of follow-up time and TT_3 grouping on change in eGFR.

Group		Follow-up time (mo)							
		0	6	12	18	24	Sum	F	P
Low TT_3 group	x	88.730	90.310	87.057	83.163	77.586	85.369	1.727	.165
	s	27.316	24.398	20.631	20.164	25.100	22.923		
Normal group	x	97.430	86.591	84.531	84.966	85.028	87.710	4.932	.004
	s	24.142	17.848	24.784	18.699	19.037	21.151		
Sum	x	94.532	87.830	85.370	84.365	82.547	86.929	4.085[*]	.004[*]
	s	25.116	19.915	23.152	18.868	21.111	21.786		
t		−8.942	0.476	0.277	−0.243	−0.907	0.097[*]	($F = 1.614$, $P = .176$)[**]	
P		.380	.638	.784	.810	.372	.785[*]		

ANOVA = analysed by analysis of variance, TT_3 = total triiodothyronine.

[*] F statistic and P value of main effect.

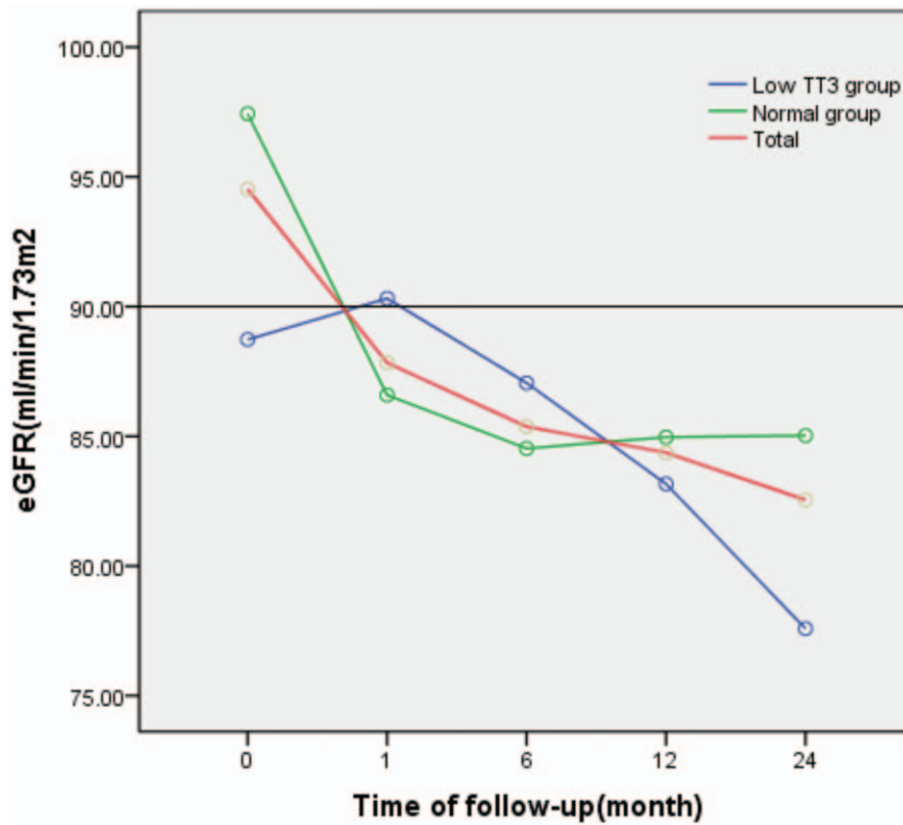[**] F statistic and P value of interaction effect.

Figure 1. Change in eGFR during follow-up. eGFR = estimated glomerular filtration rate.

was not statistically significant ($F=1.426$, $P=.241$). A significant difference in ALB was observed between the different time points in the follow-up period ($F=38.561$, $P=.000$), both in the low TT$_3$ group and the normal group, with F values of 11.590 and 33.863, respectively, and $P=.000$. There was no significant difference in ALB between the 2 groups at each time point ($P>.05$), and no interaction effect was observed between follow-up time and grouping ($F=0.388$, $P=.817$) (Table 3, Fig. 2).

3.3. Repeated ANOVA for the effect of follow-up time and TT$_3$ grouping on change in TC, TG, and LDL-C

TC levels generally decreased during follow-up, but were significantly higher in the low TT$_3$ group than in the normal

group ($F=7.116$, $P=.014$). There was also a significant difference in TC between different time points during follow-up ($F=7.034$, $P=.002$), as well as in the normal group ($F=4.566$, $P=.032$). However, there was no significant difference in TC between different time points during follow-up in the low TT$_3$ group ($F=2.447$, $P=.138$). Except for a significant difference in TC between the 2 groups at 12 months ($t=2.594$, $P=.025$), there was no significant difference observed between the 2 groups at any time point ($P>.05$), and there was no interaction effect between follow-up time and grouping ($F=1.030$, $P=.367$) (Table 4, Fig. 3).

TG levels generally decreased during follow-up in both groups. TG levels showed an initial trend to increase and subsequently

Table 3

Repeated ANOVA for the effect of follow-up time and TT$_3$ grouping on change in ALB.

Group		Follow-up time (mo)					Sum	F	P
		0	6	12	18	24			
Low TT$_3$ group	x	21.415	32.690	37.690	38.540	37.150	33.482	11.590	.000
	s	6.098	10.242	7.687	7.457	7.526	9.897		
Normal group	x	25.185	35.400	39.150	38.900	38.650	35.469	33.863	.000
	s	5.955	6.549	6.218	6.198	6.907	8.158		
Sum	x	23.700	34.330	38.580	38.760	38.060	34.686	38.561[*]	.000[*]
	s	6.205	8.161	6.713	6.610	7.080	8.937		
t		−1.760	−0.929	−0.603	−0.151	−0.587	1.426[*]	($F=0.388$, $P=.817$)[**]	
P		.088	.360	.551	.881	.561	.241[*]		

ALB = albumin, ANOVA = analysed by analysis of variance, TT$_3$ = total triiodothyronine.

[*] F statistic and P value of main effect.

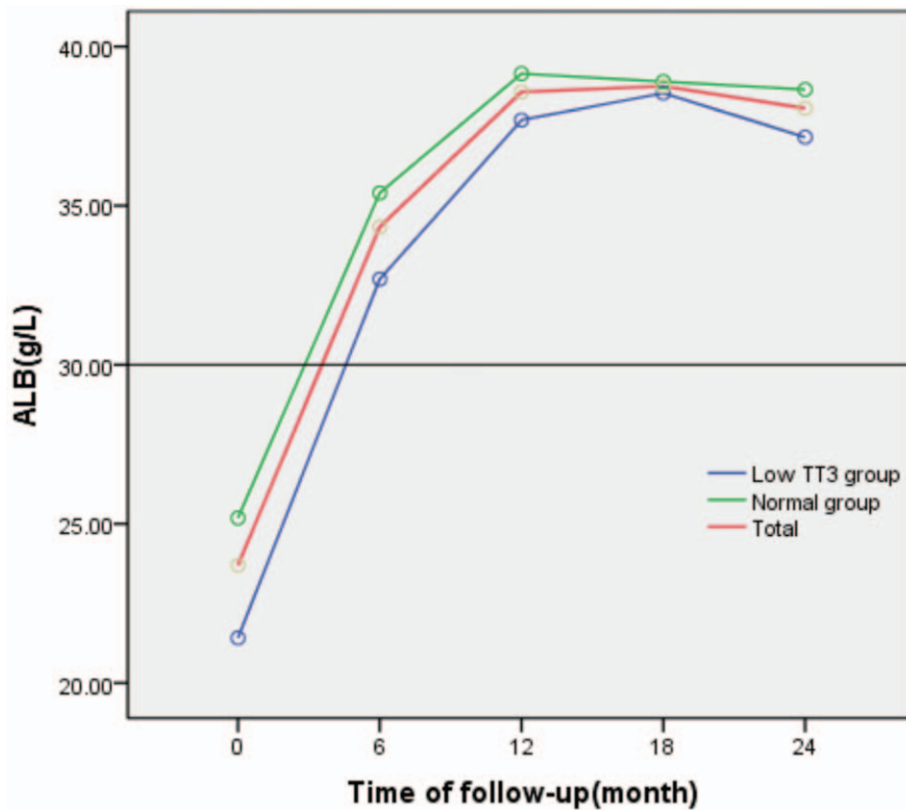[**] F statistic and P value of interaction effect.

Figure 2. Change in ALB during follow-up. ALB = albumin.

decreased in the low TT_3 group, with a maximum value of 2.71 mmol/L. However, a steady decline in TG level was observed in the normal group. TG levels in the low TT_3 group were significantly higher than in the normal group ($F=8.496$, $P=.009$). A significant difference in TG was observed at different time points during follow-up ($F=3.513$, $P=.020$), as well as in normal group ($F=3.024$, $P=.040$). However, there was no significant difference in TG observed between different time points during follow-up in the low TT_3 group ($F=1.398$, $P=.336$). With the exception of a significant difference in TG between the 2 groups at 6 months ($t=2.461$, $P=.042$), there was no significant difference between the 2 groups at any time point ($P>.05$). Furthermore, there was no interaction effect observed

between follow-up time and grouping ($F=1.124$, $P=.346$) (Table 5, Fig. 4).

LDL-C levels generally decreased during follow-up, but were significantly higher in the low TT_3 group than in the normal group ($F=18.664$, $P=.000$). There was a significant difference in LDL-C observed between different time points during follow-up ($F=11.361$, $P=.000$), both in the low TT_3 group and the normal group, with F values of 4.186 and 6.421 and P values of .046 and .007, respectively. There was a significant difference in LDL-C observed between the 2 groups at each time point during follow-up ($P<.05$). There was no interaction effect observed between the follow-up time and grouping ($F=1.237$, $P=.301$) (Table 6, Fig. 5).

Table 4

Repeated ANOVA for the effect of follow-up time and TT_3 grouping on changes in TC.

Group		Follow-up time (mo)				Sum	F	P
		0	6	12	18			
Low TT_3 group	$\bar{x}$	9.378	8.750	7.250	5.500	7.771	2.477	.138
	s	2.964	5.726	1.581	1.414	3.453		
Normal group	$\bar{x}$	7.063	6.070	5.800	5.000	5.989	4.566	.032
	s	2.652	1.580	1.082	1.069	1.816		
Sum	$\bar{x}$	7.868	7.000	6.300	5.170	6.608	7.034*	.002*
	s	2.922	3.705	1.428	1.193	2.649		
t		1.916	1.357	2.594	0.978	7.116*	($F=1.030$, $P=.367$)**	
P		.069	.214	.025	.339	.014*		

ANOVA = analysed by analysis of variance, TC = total cholesterol, TT_3 = total triiodothyronine.
* F statistic and P value of main effect.
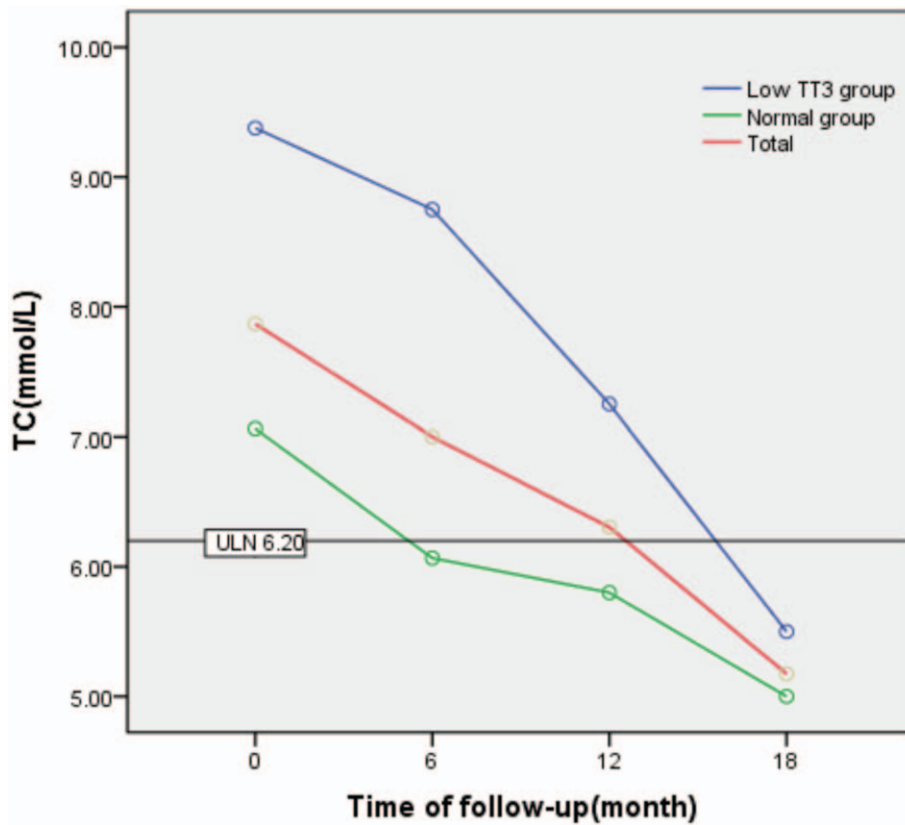** F statistic and P value of interaction effect.

Figure 3. Change in TC during follow-up. TC = total cholesterol.

4. Discussion

The incidence of IMN has increased in recent years, from 8.89% of primary glomerular disease in 2005 to 2009 to 19.11% in 2010 to 2014.[1] A close relationship exists between the thyroid, an important endocrine organ, and the kidneys, which can produce, secrete, and regulate hormones. Kidney growth is affected by thyroid hormone, which also influences the haemodynamics, glomerular filtration rate, and regulation of sodium and water in the kidney by direct or indirect action.[10–12] Thyroid hormone is partially metabolised and removed by the kidneys, meaning that kidney disease can effect a significant change in thyroid hormone levels.[13–15] Hypothyroidism, even in

a subclinical form, can lead to decreased GFR level and increased incidence of chronic kidney disease (CKD).[16] Previous studies have shown that more than 55% of patients with hypothyroidism may experience a decline in GFR to some extent.[17] Hypothyroidism can also lead to pathological changes in glomerular structure, which may further reduce renal blood flow.[13] In the present study, we showed that the average eGFR level among the 121 patients with IMN was 93.79 ml/min/1.73 m^2 and that 53.33% of patients in the low TT$_3$ group had an eGFR level < 90 ml/min/1.73 m^2, a similar finding to that reported previously.[9] Furthermore, approximately 63.64% of patients were renal pathological stage II, while stages I and III accounted for 32.23%

Table 5

Repeated ANOVA for the effect of follow-up time and TT$_3$ grouping on the changes of TG.

Group		0	6	12	18	Sum	F	P
		Follow-up time (mo)						
Low TT$_3$ group	x	2.197	2.570	2.710	1.710	2.239	1.398	.336
	s	0.671	1.134	1.704	0.951	1.191		
Normal group	x	1.685	1.470	1.600	1.200	1.446	3.024	.040
	s	0.877	0.516	0.828	0.414	0.714		
Sum	x	1.848	1.820	1.950	1.360	1.698	3.513*	.020*
	s	0.838	0.907	1.253	0.658	1.919		
t		1.362	2.461	1.642	1.371	8.496*	(F=1.124, P=.346)**	
P		.188	.042	.143	.212	.009*		

ANOVA = analysed by analysis of variance, TG = triglyceride, TT$_3$ = total triiodothyronine.

* F statistic and P value of main effect.
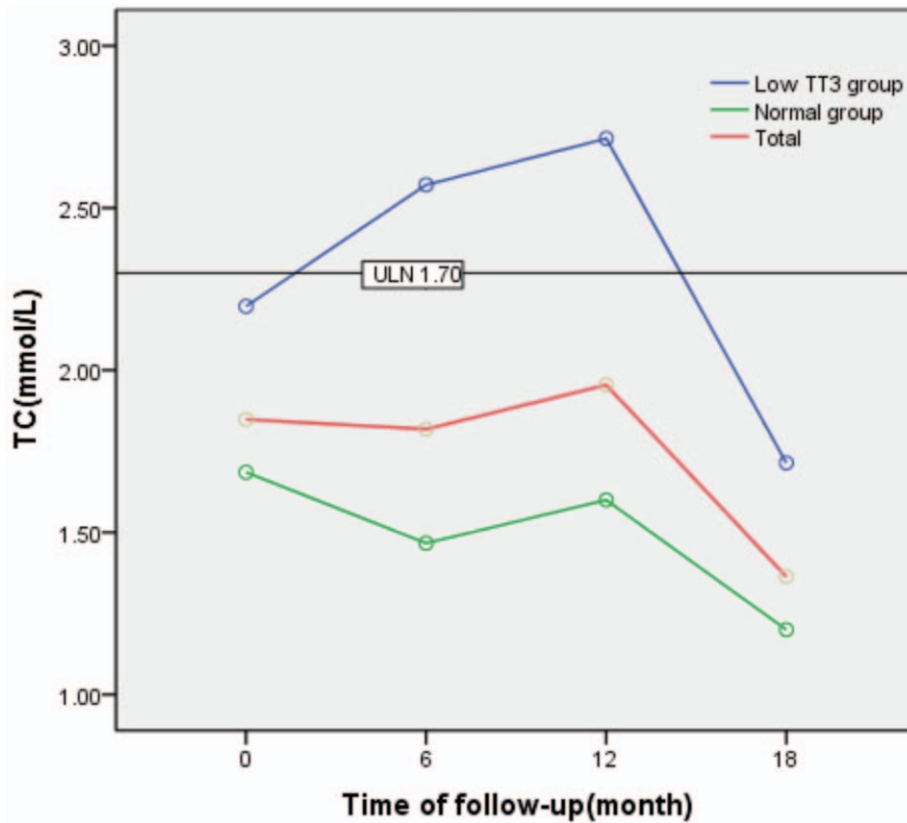
** F statistic and P value of interaction effect.

Figure 4. Change in TG during follow-up. TG = triglycerides.

and 4.13% of patients, respectively. After grouping by TT_3 level, eGFR level in the low TT_3 group was found to be lower than that in the normal group, the difference was not statistically significant ($P > .05$),. However, pathological staging in the low TT_3 group was significantly higher than that in the normal group ($P = .025$), potentially indicating that a reduction in TT_3 may raise SCr levels over time. Decrease in eGFR was greater in the low TT_3 group than in the normal group, but there was no significant difference between the 2 groups ($P > .05$). This finding may be explained by the observation that the average course of disease onset among patients with IMN in our study was relatively short (2 months), although a decrease in TT_3 can affect pathological staging, it

cannot alter the glomerular filtration rate significantly. Furthermore, the follow-up period in the present study was too short to observe a significant effect of the reduction of TT_3 level on eGFR.

Most T_3 and T_4 in the circulation is bound to proteins, while the remainder is in the free form. Each form can transform into the other to maintain a dynamic balance. T_4 metabolism is the main source of T_3 in the body, accounting for about 80% of T_3. T_3 and T_4 cannot readily cross the GBM when combined with protein, owing to a large molecular weight under physiological conditions. However, in nephrotic syndrome, the permeability of the GBM is altered, resulting in the leakage of a large amount of protein from the kidney, including TBG. TBG is the most

Table 6

Repeated ANOVA for the effect of follow-up time and TT_3 grouping on change in LDL-C.

Group		Follow-up time (mo)				Sum	F	P
		0	6	12	18			
Low TT_3 group	x	7.569	6.130	4.880	3.630	5.488	4.186	.046
	s	2.596	4.224	1.126	1.061	2.798		
Normal group	x	4.703	3.500	3.060	2.630	3.493	6.421	.007
	s	2.297	1.366	0.772	0.719	1.491		
Sum	x	5.658	4.370	3.670	2.960	4.158	11.361[*]	.000[*]
	s	2.720	2.871	1.239	0.955	2.231		
t		2.762	2.300	4.652	2.740	18.664[*]	(F=1.237, P=.301)[**]	
P		.011	.031	.000	.012	.000[*]		

ANOVA = analysed by analysis of variance, LDL-C = low-density lipoprotein cholesterol, TT_3 = total triiodothyronine.
[*] F statistic and P value of main effect.
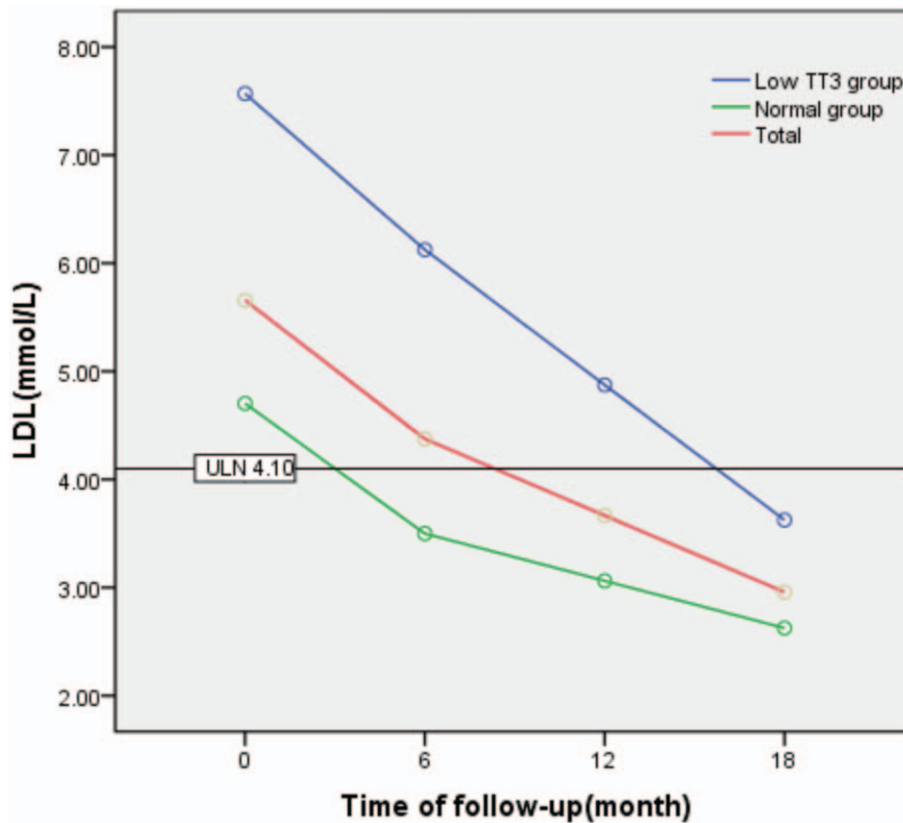[**] F statistic and P value of interaction effect.

Figure 5. Change in LDL during follow-up. LDL = low-density lipoprotein.

important thyroid hormone-binding protein, and the loss of large quantities in the urine is 1 contributing factor to a decrease in serum T_3 and T_4.[18,19] In patients with nephrotic syndrome, hypothyroidism is secondary to the loss of large amounts of protein from the urine rather than the result of a defect in the thyroid itself.[20] In the present study, we found that ALB levels in the low TT_3 group were significantly lower than in the normal group (20 g/L vs 26 g/L) ($P < .01$), while there was no difference in 24 hours UP or in the proportion of patients with 24 hours UP > 3.5 g/d between the 2 groups ($P > .05$). This finding indicates that the loss of proteins bound to thyroid hormones in the urine is not the only contributing factor in the decrease in T_3 observed in patients with IMN. For example, ALB may act as a buffer protein for thyroid hormone in the blood, and when its level is critically low, thyroid hormone transport may be reduced and be unable to dissociate from the protein-hormone complex in sufficient quantities, resulting in low levels of T_3, T_4, FT_3, and FT_4. Another factor is a reduction in thyroid hormone synthesis resulting from a reduction in iodine and protein absorption during digestive tract oedema in hypoproteinaemia. Furthermore, no significant correlation was observed between hypothyroidism and urinary protein quantification, partly because hypothyroidism is an adaptive response to IMN and is involved in the self-protection regulation mechanism.

Hyperlipidaemia is 1 of 4 clinical symptoms of nephrotic syndrome, and is characterised by elevated serum TC, TG, and LDL-C.[21] Thyroid hormones play an important role in the metabolism of blood lipids, and are implicated in the synthesis, transport, and degradation of blood lipids.[22] For example, Cooper and Biondi[23] found that TSH >10 mIU/L was related to

an increase in serum cholesterol, while Bindels et al[24] found that for each 1 mIU/L increase in TSH, the plasma cholesterol level increased by 0.09 mmol/L (females) or 16 mmol/L (males). In the present study, we found that TC, TG, and LDL-C in the low TT_3 group were significantly higher than in the normal group ($P < 0.05$). By analysing TC, TG, and LDL-C levels during follow-up using repeated ANOVA, we observed an overall decrease in these parameters, although TC, TG, and LDL-C levels were higher in the low TT_3 group than in the normal group. However, there was no interaction effect between follow-up time and group ($P > .05$), that is, there was no significant difference in TC, TG, and LDL-C observed between the 2 groups during follow-up.

In conclusion, the onset age of patients with IMN can vary widely, but is the condition most prevalent in middle-aged and older individuals. The main clinical manifestations of IMN are hypoalbuminemia, massive proteinuria, and hyperlipidaemia, and hypertension and renal insufficiency may also be present. A decrease in TT_3 is also common in IMN, affecting approximately 37% of patients, The present study had some limitations; for example, a reduction in TT_3 was associated with higher renal pathological staging and higher blood lipid levels compared with normal TT_3, although there was no significant difference between the groups regarding change in eGFR. This observation may be explained by a relatively short follow-up time in most patients, as there was insufficient time to observe a significant effect of the reduction of TT_3 level on eGFR. In addition, only a few patients underwent regular 24 hours UP testing during the follow-up period, resulting in a significant amount of missing data and an inability to further analyse the correlation between change in TT_3 level and remission of proteinuria in patients with IMN.

5. Conclusion

Approximately 37% of patients with IMN showed a decrease in TT_3 level, which was accompanied by significantly decreased ALB level, higher pathological stage, and increased serum lipid level compared with patients with a normal TT_3 level. The management of TT_3, and appropriate intervention, may therefore help to prevent the kidney damage progress in patients with IMN.

Author contributions

Conceptualization: Zhenhua Yang.
Data curation: Zhenhua Yang, Luhuai Feng.
Formal analysis: Zhenhua Yang.
Funding acquisition: Zhenhua Yang.
Investigation: Yu Huang.
Methodology: Yu Huang.
Software: Zhenhua Yang, Luhuai Feng.
Supervision: Ning Xia.
Validation: Yu Huang.
Writing – original draft: Yu Huang.
Writing – review and editing: Zhenhua Yang.
Ning Xia orcid: 0000-0003-2812-1202

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