

**SERUM COMPLEMENT HS-CRP, C3D, AND MBL LEVELS IN MICROVASCULAR COMPLICATIONS OF TYPE 2 DIABETES****SERUMSKI NIVOI KOMPONENTI KOMPLEMENTA HS-CRP, C3D I MBL KOD MIKROVASKULARNIH KOMPLIKACIJA DIJABETESA TIP 2**Ping Huang<sup>1</sup>, Zixuan Tang<sup>2</sup>, Yanyan Liu<sup>3</sup>, Jieru Huang<sup>4</sup><sup>1</sup>Department of Endocrinology and Metabolism, Affiliated Hospital of Nantong University, No. 20, Xi-Si Street, Nantong 226000, China<sup>2</sup>Department of Endocrinology and Metabolism, Huai'an Hospital Affiliated to Yangzhou University, No. 1, Huaihe East Road, Huai'an 223300, China<sup>3</sup>Endocrinology Department, Peking University First Hospital, No. 8, Xishiku Street, Xicheng District, Beijing 100034, China<sup>4</sup>Department of Endocrinology and Metabolism, Nantong Tongzhou People's Hospital, No. 999 Jianshe Street, Jinsha Subdistrict, Tongzhou 226300, China**Summary**

**Background:** To investigate the connections between microvascular complications (DMCs) and serum complement hs-CRP, C3d, and MBL levels in individuals with type 2 diabetes mellitus (T2DM).

**Methods:** From January 2023 to January 2025, 100 patients with simple T2DM admitted to our hospital were selected as the T2DM group, 100 patients with T2DM combined with DMC were selected as the DMC group, and 100 healthy individuals who underwent physical examinations during the same period were selected as the control group. The serum levels of complement hs-CRP, C3d, and MBL were compared among the three groups. The relationships between complement hs-CRP, C3d, and MBL and the blood glucose and lipid markers of DMC patients were examined using Pearson correlation analysis. Binary logistic regression analysis was used to investigate the risk factors for DMC in patients with type 2 diabetes. The diagnostic value of blood complement hs-CRP, C3d, and MBL for DMC in T2DM patients was evaluated using the receiver operating characteristic curve (ROC) and the area under the curve (AUC).

**Results:** Comparison of serum complement hs-CRP, C3d, and MBL levels revealed the following trend: DMC group

**Kratak sadržaj**

**Uvod:** Cilj je bio da se ispita povezanost mikrovaskularnih komplikacija dijabetesa (DMC) sa serumskim nivoima hs-CRP, C3d i MBL kod osoba sa dijabetesom melitusom tip 2 (T2DM).

**Metode:** U periodu od januara 2023. do januara 2025. godine u istraživanje je uključeno 100 pacijenata sa T2DM bez mikrovaskularnih komplikacija, hospitalizovanih u našoj ustanovi, koji su činili T2DM grupu, 100 pacijenata sa T2DM i pridruženim DMC, koji su činili DMC grupu, kao i 100 zdravih osoba koje su u istom periodu obavile sistematski pregled i činile kontrolnu grupu. Između ove tri grupe su upoređeni serumski nivoi hs-CRP, C3d i MBL. Povezanost hs-CRP, C3d i MBL sa pokazateljima glikemije i lipidnog statusa kod pacijenata sa DMC je ispitana Pirsonovom korelacionom analizom. Faktori rizika za razvoj DMC kod pacijenata sa T2DM su ispitani binarnom logističkom regresionom analizom. Dijagnostička vrednost serumskih nivoa hs-CRP, C3d i MBL za otkrivanje DMC kod pacijenata sa T2DM je procenjena pomoću ROC krive i površine ispod krive (AUC).

**Rezultati:** Poređenjem serumskih nivoa hs-CRP, C3d i MBL utvrđen je sledeći trend: DMC grupa > T2DM grupa > kontrolna grupa, pri čemu su razlike bile statistički

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> T2DM group > control group, with statistically significant differences ( $P < 0.05$ ). Body mass index (BMI), length of illness, fasting blood glucose (FPG), glycosylated haemoglobin (HbA1c), lipid markers (triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), insulin resistance index (HOMA-IR), blood uric acid (UA), and creatinine (Scr) were significantly different between the DMC and T2DM groups. In T2DM patients who developed DMC, blood complement hs-CRP, C3d, and MBL levels were favourably correlated with FPG, HbA1c, TG, TC, and LDL-C levels and negatively correlated with HDL-C levels ( $P < 0.05$ ), according to the Pearson correlation analysis. Binary logistic regression analysis revealed that disease duration and FPG, HbA1c, hs-CRP, C3d, and MBL levels were factors associated with DMCs in patients with T2DM ( $P < 0.05$ ). ROC curve analysis showed that the optimal hs-CRP cut-off value for detecting DMCs in patients with T2DM was 293.68 mg/L, with an AUC of 0.834 (95% CI 0.754–0.914), a sensitivity of 0.844, and a specificity of 0.803. The optimal C3d cut-off value was 394.25 mg/L, with an AUC of 0.835 (95% CI 0.741–0.919), a sensitivity of 0.830, and a specificity of 0.805. The optimal MBL cut-off value was 330.32 mg/L, with an AUC of 0.827 (95% CI 0.739–0.915), a sensitivity of 0.823, and a specificity of 0.776.

**Conclusion:** The pathogenic progression of DMC in T2DM is significantly influenced by serum complement activation. Elevated levels of serum complement components hs-CRP, C3d, and MBL can increase the risk of DMC in T2DM patients. In patients with type 2 diabetes, these three markers can be used as trustworthy predictors of the development of DMC.

**Keywords:** type 2 diabetes, diabetic microvascular complications, complement factor hs-CRP, complement factor C3d, complement factor MBL

## Introduction

Diabetic microvascular complications (DMCs) are specific complications of diabetes. DMC has become a major public health issue that poses a substantial threat to people's health due to its relatively high mortality and disability rates (1). Multiple studies have confirmed (2–4) that the inflammatory response mediated by the complement activation pathway plays an important role in the occurrence and development of DMC. Abnormalisation of mitochondria in podocytes of the complement C3 system is the molecular basis of the immune-metabolic pathway in diabetic nephropathy (5). The positive rate of complement MBL detection in the kidneys of patients with diabetic nephropathy is relatively high, and it is consistent with changes in the urine microalbumin-to-creatinine ratio of patients (6).

The microvascular complications of type 2 diabetes, as the main cause of disability and death for patients, involve long-term chronic low-level inflammation and immune disorders. Traditional high-sensitivity C-reactive protein has limitations in

značajne ( $P < 0.05$ ). Između DMC i T2DM grupe utvrđene su značajne razlike u indeksu telesne mase (BMI), trajanju bolesti, koncentraciji glukoze u krvi natašte (FPG), glikozilovanom hemoglobinu (HbA1c), pokazateljima lipidnog statusa – trigliceridima (TG), ukupnom holesterolu (TC), holesterolu lipoproteina male gustine (LDL-C) i holesterolu lipoproteina velike gustine (HDL-C) – kao i indeksu insulinske rezistencije (HOMA-IR), mokraćnoj kiselini (UA) i serumskom kreatininu (Scr). Prema rezultatima Pearsonove korelacione analize, kod pacijenata sa T2DM kod kojih su se razvile DMC, serumski nivoi hs-CRP, C3d i MBL bili su pozitivno povezani sa nivoima FPG, HbA1c, TG, TC i LDL-C, a negativno povezani sa nivoima HDL-C ( $P < 0.05$ ). Rezultati binarne logističke regresione analize pokazali su da su trajanje bolesti i nivoi FPG, HbA1c, hs-CRP, C3d i MBL faktori koji utiču na razvoj DMC kod pacijenata sa T2DM ( $P < 0.05$ ). Analiza ROC krive je pokazala da je granična vrednost hs-CRP za dijagnostikovanje DMC kod pacijenata sa T2DM iznosila 293,68 mg/L, uz AUC od 0,834 (95% CI: 0,754–0,914), osetljivost od 0,844 i specifičnost od 0,803. Granična vrednost C3d za dijagnostikovanje DMC kod pacijenata sa T2DM je iznosila 394,25 mg/L, uz osetljivost od 0,830, specifičnost od 0,805 i AUC od 0,835 (95% CI: 0,741–0,919). Granična vrednost MBL za otkrivanje DMC kod pacijenata sa T2DM je iznosila 330,32 mg/L, uz AUC od 0,827 (95% CI: 0,739–0,915), osetljivost od 0,823 i specifičnost od 0,776.

**Zaključak:** Aktivacija sistema komplementa značajno utiče na patogenetsko napredovanje DMC kod pacijenata sa T2DM. Povišeni serumski nivoi hs-CRP, C3d i MBL mogu povećati rizik od razvoja DMC kod ovih pacijenata. Ova tri pokazatelja mogu se koristiti kao pouzdani prediktori razvoja DMC kod pacijenata sa dijabetesom tip 2.

**Ključne reči:** dijabetes tip 2, mikrovaskularne komplikacije dijabetesa, hs-CRP, faktor komplementa C3d, lektin koji vezuje manozu (MBL)

representing the particular activation of the complement system and endothelial damage, despite being considered a diagnostic for assessing systemic inflammation (7–9). The complement system serves as a key bridge connecting metabolic abnormalities and vascular damage, and the cascade reactions of its classical, alternative, and lectin pathways play a central role in microvascular lesions. This study innovatively combines the detection of hs-CRP with the complement activation terminal product C3d and the lectin pathway-initiating molecule mannan-binding lectin (MBL), aiming to overcome the limitations of a single inflammatory indicator and reveal the specific role of the complement system in the occurrence and development of diabetic retinopathy and nephropathy from multiple dimensions (10).

This research not only helps clarify the deep immunological mechanism of microvascular damage but also has significant clinical translational value. It can provide precise biomarker evidence for the early identification of high-risk populations, monitoring of disease progression, and the develop-

ment of novel therapeutic strategies targeting the complement pathway, thereby filling the knowledge gap in the current field of diabetes immune micro-environment regulation.

## Materials and Methods

### *General information*

From January 2023 to January 2025, 100 patients with simple type 2 diabetes mellitus (T2DM) admitted to our hospital were selected as the T2DM group. Another 100 patients with T2DM combined with DMC were selected as the DMC group (including 44 cases of diabetic retinopathy and 56 cases of diabetic nephropathy).

Another 100 healthy individuals undergoing physical examinations were selected as the control group, including 54 males and 46 females, aged 18 to 78 years, with an average age of  $(55.28 \pm 3.70)$  years and a body mass index (BMI) ranging from 23.99 to 24.51 kg/m<sup>2</sup>, with an average of  $(24.24 \pm 1.95)$  kg/m<sup>2</sup>. There was no statistically significant difference in gender and age among the groups ( $P > 0.05$ ).

This study was approved by the hospital's medical ethics committee (NO. ZN-2023-058). All the research subjects gave their consent, and all signed the informed consent form voluntarily.

### *Inclusion and exclusion criteria*

Inclusion criteria: ① All patients met the diagnostic criteria for T2DM; ② Patients with DMC were clearly diagnosed according to relevant diagnostic criteria; ③ All were newly diagnosed with no previous history of diabetes; ④ Age ranged from 18 to 80 years old.

Exclusion criteria: ① Those with other types of diabetes; ② Those with severe organ dysfunction such as liver or kidney diseases, autoimmune diseases, tumours, infections, blood diseases, immune abnormalities, etc.; ③ Those with cognitive or mental disorders and unable to cooperate with the researchers; ④ Those who have received recent treatment with hypoglycaemic or lipid-lowering drugs that may affect the results of this study.

### *Blood sample collection and processing*

All research subjects collected their elbow venous blood in the early morning on the day of admission or during the physical examination, after fasting for at least 8 to 12 hours, in a quiet state.

Serum separation: 5 mL of whole blood was collected into a dry vacuum blood collection tube

without anticoagulant. It was left at room temperature to stand for 30 minutes. After the blood fully coagulated, it was centrifuged at 3000 r/min for 15 minutes (centrifugal radius 10 cm), and the upper layer of serum was carefully aspirated and aliquoted into EP tubes. These tubes were stored at -80°C for testing. Avoid repeated freezing and thawing.

### *Laboratory index testing procedure*

For all the research subjects, 10 mL of fasting venous blood was collected upon admission. Using an AU-2700 (a fully automatic biochemical analyser produced by Olympus Optical Industry Co., Ltd., Japan) and enzymatic methods, fasting plasma glucose (FPG), triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), blood uric acid (UA), serum creatinine (Scr), and fasting insulin (FINS) levels were detected. The insulin resistance index (homeostasis model assessment-insulin resistance, HOMA-IR) was calculated as  $FPG \times FINS / 22.5$ . Glycated haemoglobin (HbA1c) levels were detected by high-performance liquid chromatography, and serum complement hs-CRP, C3d, and MBL levels were detected by immunoradiometric scattering turbidimetry. The reagents were provided by Mike Biotechnology Co., Ltd.

### *Statistical analysis*

Data analysis was conducted using SPSS 24.0 statistical software, and measurement data are expressed as  $\bar{x} \pm s$ . Pairwise comparisons were performed using t tests, comparisons among multiple groups were conducted using F tests, and pairwise comparisons within groups were carried out using t tests. Count data are presented as n (%), and pairwise comparisons were performed using  $\chi^2$  tests. Pearson correlation analysis was used to investigate the correlations between serum hs-CRP, C3d, and MBL levels and blood glucose and lipid levels in DMC patients. Logistic regression analysis was employed to analyse the factors influencing the development of T2DM into DMC. The receiver operating characteristic curve (ROC) and the area under the curve (AUC) were used to assess the diagnostic value of serum hs-CRP, C3d, and MBL for T2DM progression to DMC. A P value < 0.05 was considered to indicate statistical significance.

## Results

### *Comparison of serum complement hs-CRP, C3d, and MBL levels*

Comparisons of serum complement hs-CRP, C3d, and MBL levels revealed the following trend:

**Table I** Comparison of serum complement levels (hs-CRP, C3d, MBL) among three groups ( $\bar{x} \pm s$ ).

| Group         | n   | hs-CRP (mg/L)      | C3d (mg/L)         | MBL (mg/L)         |
|---------------|-----|--------------------|--------------------|--------------------|
| Control group | 100 | 170.56 $\pm$ 13.20 | 192.26 $\pm$ 15.11 | 221.29 $\pm$ 20.74 |
| T2DM group    | 100 | 222.17 $\pm$ 21.61 | 281.42 $\pm$ 26.73 | 282.86 $\pm$ 22.67 |
| DMC group     | 100 | 285.81 $\pm$ 23.58 | 385.27 $\pm$ 32.54 | 321.84 $\pm$ 20.92 |
| F value       |     | 23.057             | 31.662             | 16.414             |
| P value       |     | <0.001             | <0.001             | <0.001             |

**Table II** Data comparison between the DMC and non-DMC groups [n (%), ( $\bar{x} \pm s$ )].

| Item                              | T2DM group (n=100) | DMC group (n=100)  | T or $\chi^2$ value | P value |
|-----------------------------------|--------------------|--------------------|---------------------|---------|
| Gender                            |                    |                    | 0.164               | 0.685   |
| Male                              | 56 (56.00)         | 60 (60.00)         |                     |         |
| Female                            | 44 (44.00)         | 40 (40.00)         |                     |         |
| Age (years)                       | 55.46 $\pm$ 3.68   | 56.15 $\pm$ 3.93   | 1.036               | 0.307   |
| BMI (kg/m <sup>2</sup> )          | 24.28 $\pm$ 2.00   | 25.56 $\pm$ 2.24   | 2.932               | 0.004   |
| Disease duration (years)          | 5.39 $\pm$ 1.05    | 9.25 $\pm$ 1.55    | 14.914              | <0.001  |
| History of hypertension           |                    |                    | 0.171               | 0.676   |
| Yes                               | 32 (32.00)         | 36 (36.00)         |                     |         |
| No                                | 68 (68.00)         | 64 (64.00)         |                     |         |
| History of hyperlipidaemia        |                    |                    | 0.056               | 0.810   |
| Yes                               | 24 (24.00)         | 26 (26.00)         |                     |         |
| No                                | 76 (76.00)         | 74 (74.00)         |                     |         |
| History of coronary heart disease |                    |                    | 0.212               | 0.643   |
| Yes                               | 26 (26.00)         | 22 (22.00)         |                     |         |
| No                                | 74 (74.00)         | 78 (78.00)         |                     |         |
| FPG (mmol/L)                      | 8.88 $\pm$ 1.19    | 12.14 $\pm$ 2.04   | 9.936               | <0.001  |
| HbA1c (%)                         | 7.26 $\pm$ 1.27    | 9.26 $\pm$ 1.32    | 7.955               | <0.001  |
| TG (mmol/L)                       | 1.82 $\pm$ 0.15    | 2.38 $\pm$ 0.11    | 15.039              | <0.001  |
| TC (mmol/L)                       | 4.61 $\pm$ 0.29    | 4.96 $\pm$ 0.23    | 5.382               | <0.001  |
| HDL-C (mmol/L)                    | 1.11 $\pm$ 0.13    | 1.06 $\pm$ 0.13    | 7.503               | <0.001  |
| LDL-C (mmol/L)                    | 2.89 $\pm$ 0.12    | 3.18 $\pm$ 0.17    | 8.682               | <0.001  |
| HOMA-IR                           | 1.96 $\pm$ 0.26    | 3.48 $\pm$ 0.33    | 28.435              | <0.001  |
| UA ( $\mu$ mol/L)                 | 272.70 $\pm$ 22.47 | 298.18 $\pm$ 19.64 | 6.025               | <0.001  |
| Scr ( $\mu$ mol/L)                | 55.56 $\pm$ 3.77   | 61.01 $\pm$ 4.22   | 6.898               | <0.001  |

**Table III** Analysis of correlations between blood glucose and lipid markers and serum complement hs-CRP, C3d, and MBL.

| Indicator | hs-CRP  |         | C3d     |         | MBL     |         |
|-----------|---------|---------|---------|---------|---------|---------|
|           | R value | P value | R value | P value | R value | P value |
| FPG       | 0.461   | <0.001  | 0.470   | <0.001  | 0.435   | <0.001  |
| HbA1c     | 0.414   | <0.001  | 0.427   | <0.001  | 0.429   | <0.001  |
| TG        | 0.299   | <0.001  | 0.365   | <0.001  | 0.310   | <0.001  |
| TC        | 0.316   | <0.001  | 0.337   | <0.001  | 0.308   | <0.001  |
| HDL-C     | -0.358  | <0.001  | -0.344  | <0.001  | -0.332  | <0.001  |
| LDL-C     | 0.323   | <0.001  | 0.350   | <0.001  | 0.318   | <0.001  |

**Table IV** Binary logistic regression analysis of DMC occurrence in T2DM patients.

| Factor            | value | SE value | Wlad value | OR (95%CI) value    | P value |
|-------------------|-------|----------|------------|---------------------|---------|
| Course of disease | 0.344 | 0.031    | 79.458     | 1.409 (1.307~1.518) | <0.001  |
| FPG               | 0.039 | 0.019    | 5.484      | 1.030 (1.009~1.062) | 0.019   |
| HbA1c             | 0.560 | 0.234    | 6.028      | 1.766 (1.124~2.775) | 0.014   |
| hs-CRP            | 1.040 | 0.274    | 14.928     | 2.842 (1.678~4.849) | <0.001  |
| C3d               | 1.029 | 0.175    | 35.586     | 2.793 (1.994~3.901) | <0.001  |
| MBL               | 1.078 | 0.338    | 10.200     | 2.933 (1.523~5.653) | <0.001  |

DMC group > T2DM group > control group, with statistically significant differences ( $P<0.05$ ), see Table I.

#### *Clinical data comparison between the DMC and non-DMC groups*

BMI, disease duration, and blood FPG, HbA1c, TG, TC, LDL-C, HOMA-IR, UA, and Scr levels were higher in the DMC group than in the T2DM group; in contrast, the former group's HDL-C level was lower. There was a statistically significant difference ( $P<0.05$ ) between the two groups. The two groups did not differ substantially in age, sex, or medical history (history of coronary heart disease, hypertension, or hyperlipidaemia) ( $P>0.05$ ), see Table II.

#### *Correlation analysis of serum complement hs-CRP, C3d, and MBL levels with blood glucose and lipid indicators in patients with T2DM and DMC*

The results of the Pearson correlation analysis revealed that in patients with T2DM and DMC, serum complement hs-CRP, C3d, and MBL levels were

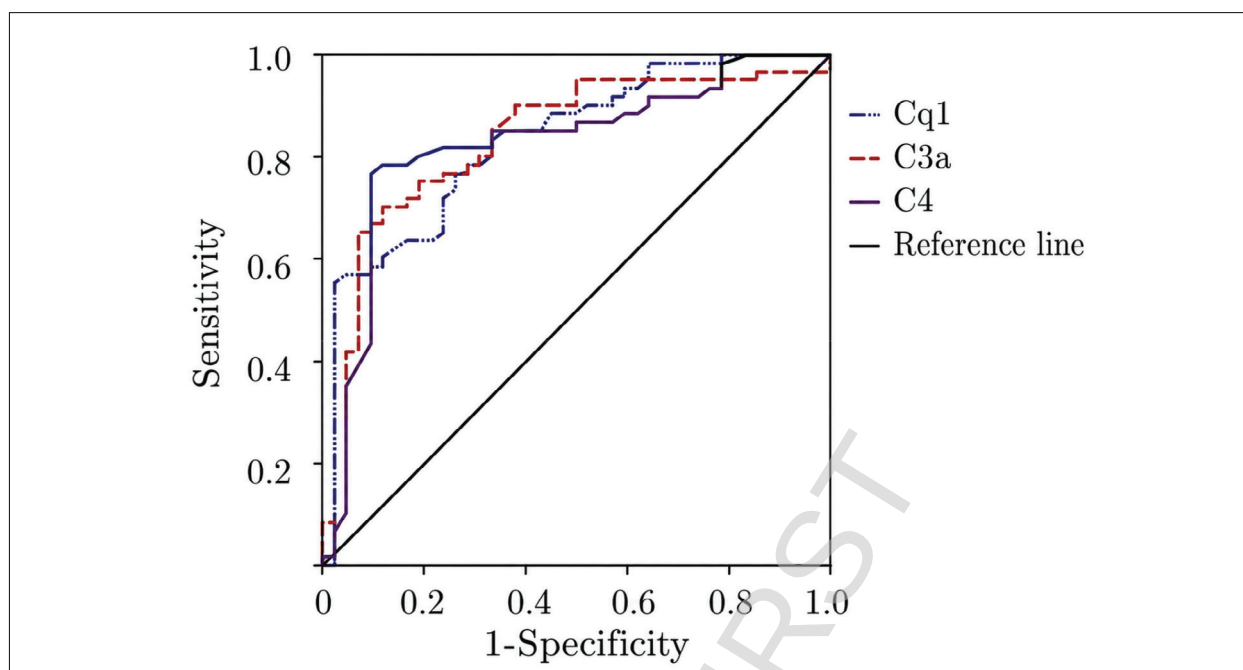
positively correlated with FPG, HbA1c, TG, TC, and LDL-C levels and negatively correlated with HDL-C levels ( $P<0.05$ ), see Table III.

#### *Risk factors for DMC in T2DM patients: a binary logistic regression analysis*

The occurrence of DMC in T2DM patients was taken as the dependent variable (no DMC = 0, occurrence of DMC = 1), and the differences in clinical data indicators were used as the dependent variable (BMI, disease duration, FPG, HbA1c, TG, TC, LDL-C, HDL-C, HOMA-IR, UA, and Scr were used as continuous variables; the original values were input) for binary logistic regression analysis. FPG, HbA1c, hs-CRP, C3d, and MBL were the variables that affected the incidence of DMC in T2DM patients ( $P<0.05$ ); refer to Table IV.

#### *ROC curve for diagnosing DMC in T2DM patients*

With an AUC of 0.831 (95% CI 0.751–0.911), a sensitivity of 0.841, and a specificity of 0.800, the ROC curve results showed that the threshold value



**Figure 1** ROC curve for the diagnosis of DMC in patients with T2DM.

of hs-CRP for the diagnosis of DMC in T2DM patients was 293.65 mg/L. C3d was utilised to identify DMC in T2DM patients with a cutoff value of 394.22 mg/L, a sensitivity of 0.837, a specificity of 0.802, and an AUC of 0.832 (95% CI 0.748–0.916). With an AUC of 0.824 (95% CI 0.736–0.912), specificity of 0.773, sensitivity of 0.8208, and threshold value of 330.39 mg/L, MBL was used to diagnose DMC in T2DM patients (Figure 1).

## Discussion

Because DMC often shows no typical symptoms in its early stage, patients tend to ignore their condition (11–13). By the time obvious symptoms appear, the disease has usually progressed to the middle or advanced stage, making treatment more difficult and limiting its effectiveness. Therefore, early diagnosis of DMC in patients with T2DM is highly clinically important. The complement system is a monitoring system that maintains immune homeostasis (14). If it undergoes pathological activation, it can trigger a complement cascade reaction, leading to the release of a large number of cytokines and causing vascular and tissue damage. As the initiating molecule of the classical complement activation pathway, hs-CRP can activate macrophages and aggravate inflammatory infiltration and tissue damage around microvessels (15–17). By attaching to its receptor C3dR, C3d contributes to the onset and progression of diabetes and other vascular disorders. Hyperglycaemia can promote

the cleavage and activation of MBL, resulting in the formation of MBLa and MBLb, which further aggravates DMC (18). In this study, the serum levels of complement hs-CRP, C3d, and MBL in the DMC group were significantly greater than those in T2DM patients without DMC and healthy individuals who underwent physical examinations, suggesting that the complement system is activated in patients with T2DM who develop DMC and that the serum levels of complement hs-CRP, C3d, and MBL gradually increase, promoting disease progression (19).

Excessive activation of the complement system in DMC is not only associated with direct inflammation and cell damage but also closely related to metabolic disorders and immune regulation imbalance (20–22). According to the study's logistic regression analysis, disease duration, FPG level, and the levels of HbA1c, hs-CRP, C3d, and MBL were factors impacting the occurrence of DMC in T2DM patients. The levels of complement factors hs-CRP, C3d, and MBL in T2DM patients are correlated with blood glucose and lipid indicators, reflecting the close connection between metabolic disorders and immune inflammatory responses (23). Additionally, a high-glucose environment can promote the formation of advanced glycation end products (AGEs), which can bind to hs-CRP and trigger the complement cascade, increasing the synthesis of effector molecules like C3d and MBL. Impairment of the insulin signalling pathway in DMC patients can increase fat tissue breakdown, resulting in the release of large amounts of adipokines (24). These

molecules not only exacerbate metabolic disorders but also directly stimulate the production of complement proteins. Several pathogenic processes, including the inflammatory response, endothelial damage, oxidative stress, and fibrosis, are involved in the development of microvascular problems in type 2 diabetes, which are largely caused by aberrant activation of complement components (25). The AUCs of complement hs-CRP, C3d, and MBL for diagnosing the occurrence of DMC in T2DM patients were 0.831, 0.832, and 0.824, respectively, according to the ROC curve results. This implies that complement hs-CRP, C3d, and MBL are sensitive early markers for identifying DMC in patients with type 2 diabetes.

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## Conclusion

The pathogenic progression of DMC in T2DM is significantly influenced by serum complement activation. Elevated levels of serum complement components hs-CRP, C3d, and MBL can increase the risk of DMC in T2DM patients. In patients with type 2 diabetes, these three markers can be used as trustworthy predictors of the development of DMC.

## Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

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