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Determinants of Hematological Abnormalities in Patients with Type 2 Diabetes Mellitus: a Cross Sectional Study

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ABSTRACT

Hematological abnormalities are commonly observed in patients with type 2 diabetes mellitus (T2DM) and may serve as markers of complication risk, thereby playing an important role in T2DM management; however, the determinants and regional variations remain incompletely understood, particularly in Lampung. This cross-sectional observational study was conducted among patients with T2DM attending the Internal Medicine Outpatient Clinic of RSUD Dadi Tjokrodipo, Bandar Lampung, from April to September 2024, enrolling 80 participants who met the inclusion and exclusion criteria. Data were obtained from complete blood count testing, medical records, and structured interviews with direct observation, and were analyzed using bivariable and multivariable logistic regression. The most frequently identified hematological abnormalities were anemia (45%), leukocytosis (32%), and an elevated neutrophil-to-lymphocyte ratio (NLR) (46%). In multivariable analysis, anemia was independently associated with uncontrolled glycemic status (adjusted OR = 15.914; p = 0.001), not following a recommended dietary pattern (adjusted OR = 7.402; p = 0.003), smoking (adjusted OR = 7.920; p = 0.015), and age ≥61 years (adjusted OR = 29.643; p = 0.004), whereas leukocytosis was independently associated only with uncontrolled glycemic status (adjusted OR = 4.310; p = 0.020). High NLR was independently associated with uncontrolled glycemic status (adjusted OR = 18.811; p = 0.001), employment status (adjusted OR = 8.630; p = 0.003), and not following a recommended dietary pattern (adjusted OR = 5.287; p = 0.015). Overall, uncontrolled glycemic status was the most dominant and consistent factor associated with hematological abnormalities among patients with T2DM.

ABSTRAK

Abnormalitas hematologi merupakan suatu kondisi yang sering ditemukan pada DM tipe 2. Abnormalitas hematologi berperan sebagai marker risiko komplikasi dan memiliki peranan penting dalam penatalaksanaan DM tipe 2. Namun demikian, faktor penyebabnya belum sepenuhnya diketahui, terutama di Provinsi Lampung. Penelitian ini bertujuan untuk mengidentifikasi faktor-faktor sosiodemografi, klinis dan antropometri yang berhubungan dengan abnormalitas hematologi pada penderita DM tipe 2. Penelitian ini merupakan penelitian observasional dengan desain cross sectional yang dilakukan pada pasien DM tipe 2 di Poli Penyakit Dalam RSUD Dadi Tjokrodipo Bandar Lampung pada April – September 2024. Sebanyak 80 subjek yang memenuhi kriteria inklusi dan eksklusi terlibat dalam penelitian ini. Data diperoleh melalui pemeriksaan laboratorium darah lengkap, rekam medis, serta wawancara dan observasi langsung pada subjek. Data selanjutnya dianalisis

menggunakan uji regresi logistic bivariat dan multivariat. Hasil penelitian menunjukkan bahwa abnormalitas hematologi yang paling sering ditemukan adalah anemia (45%), leukositosis (32%), dan NLR tinggi (46%). Pada analisis multivariat, anemia berhubungan secara independen dengan status glikemik tidak terkontrol (adjusted OR=15.914; p=0.001), tidak mengikuti pola diet (adjusted OR=7.402; p=0.003), merokok (adjusted OR=7.920; p=0.015), dan usia ≥61 tahun (adjusted OR=29.643; p=0.004). Leukositosis hanya berhubungan secara independen dengan status glikemik tidak terkontrol (adjusted OR=4.310; p=0.020). NLR tinggi berhubungan secara independen dengan status glikemik tidak terkontrol (adjusted OR=18.811; p=0.001), status pekerjaan (adjusted OR=8.630; p=0.003), dan tidak mengikuti pola diet (adjusted OR=5.287; p=0.015). Simpulan: Status glikemik yang tidak terkontrol merupakan faktor paling dominan dan konsisten dengan abnormalitas hematologi pada penderita DM tipe 2.

A. BACKGROUND

Type 2 diabetes mellitus (T2DM) is a serious public health challenge and has been classified as a global epidemic (Herman & Zimmet, 2012; Singer et al., 2021). In recent decades, a substantial increase in the prevalence and mortality of patients with T2DM has been observed, especially among individuals aged 55 and older (Yu et al., 2025; Zhu et al., 2022). This trend is expected to continue in the upcoming years, with a higher increase projected for men compared to women (Ye et al., 2023).

Type 2 diabetes mellitus is a chronic metabolic disease characterized by persistent hyperglycemia, insulin resistance, and the presence of low-grade chronic inflammation (ADA, 2025; IDF, 2025; Okdahl et al., 2022). It has been recognized that low-grade chronic inflammation is the root cause of various long-term complications associated with T2DM (Nedosugova et al., 2022; Ramesh et al., 2022; Stoian et al., 2024). Consequently, persistent low-grade inflammation in T2DM contributes to progressive dysfunction across multiple organ systems (Kacem et al., 2025; Oda et al., 2023; Ramesh et al., 2022; Zhang et al., 2024).

The hematological system is among the organ systems significantly affected by low-grade inflammation in T2DM (Bashir et al., 2020). Accumulating evidence indicates that T2DM is frequently accompanied by hematological abnormalities, including anemia, leukocytosis, elevated neutrophil-to-lymphocyte ratio (NLR), and increased platelet count and mean platelet volume (MPV) (Arkew et al., 2021; Bryk-Wiązania & Undas, 2021; Cardoso et al., 2021; Ebrahim et al., 2022). Importantly, these hematological abnormalities are not merely indicators of inflammation but also have broader clinical consequences.

Previous studies have reported that anemia in T2DM may exacerbate tissue hypoxia and impair cardiovascular function (Qian, 2023), increase the risk of cognitive decline (Choi et al., 2020), accelerate the development of chronic kidney disease (Al-Dwairi et al., 2024a; Xie et al., 2023), and increase the risk of diabetes-related complications (Cao et al., 2024). Elevated leukocyte and neutrophil counts have been closely linked to insulin resistance (Rodríguez-Rodríguez et al., 2022), may promote atherosclerosis leading to cardiovascular disease and stroke (Chang et al., 2023; Jagadish et al., 2018; Madaudo et al., 2024; Mauersberger et al., 2022), and are associated with an increased risk of diabetic kidney disease (Fang et al., 2024; Li et al., 2024). In addition, increased platelet count and mean platelet volume (MPV) in T2DM suggest platelet hyperreactivity, which may raise thrombosis risk, correlate with arterial stiffness and myocardial damage, and also contribute to accelerated atherosclerosis (Agarwal et al., 2024; Di Marco et al., 2022; Kakouros et al., 2011; Rodriguez & Johnson, 2020). Therefore,

abnormalities in these hematological parameters should not be regarded as secondary phenomena but rather as integral to understanding the clinical status and complication risk among patients with T2DM.

Hematological abnormalities in T2DM have been frequently described in many studies. However, the determinants contributing to the development of these abnormalities has not been comprehensively studied. Previous studies have primarily focused on the effects of inflammation and its related complications, with less research on how sociodemographic factors, lifestyle, and clinical status contribute to the emergence of these hematological abnormalities. A better understanding of these factors can enrich our knowledge on the pathogenesis of T2DM and strengthen strategies for early complication prevention. Additionally, identifying relevant risk factors may help clinicians to manage a highly susceptible to complications patients more effectively and support more targeted and personalized treatment strategies. In Indonesia, social determinants of health, like dietary habits, physical activity, and smoking behavior, may vary across regions and may substantially affect glycemic control and inflammatory status. As a referral hospital in Bandar Lampung City, Dadi Tjokrodipo General Hospital serving a diverse population, and also represents a unique demographic profile. It makes this study relevant for generating locally applicable evidence to improve early detection and management of hematological complications in patients with T2DM. Therefore, this study was conducted to identify the sociodemographic, clinical, and anthropometric factors associated with abnormal hematological parameters in patients with type 2 DM.

B. METHODS

Study Design

This study employed an observational cross-sectional design. It was conducted among patients with type 2 diabetes mellitus (T2DM) receiving care at the Internal Medicine Outpatient Clinic of RSUD Dadi Tjokrodipo, Bandar Lampung, from April to September 2024. A total sampling method was applied in this study. All patients with T2DM who met the inclusion criteria and attended the study site during the study period were included. A total of 80 patients with a confirmed diagnosis of T2DM who were undergoing treatment at RSUD Dadi Tjokrodipo were enrolled. Patients were excluded if they had a malignancy, a primary hematological disorder, were pregnant, or had received a blood transfusion within the preceding three months. All participants received a full explanation of the study and provided written informed consent. Ethical approval was obtained from the Health Research Ethics Committee of Politeknik Kesehatan Tanjungkarang (No. 465/KEPK-TJK/VI/2024).

Data Collection

The data were obtained from laboratory examinations, structured interviews, direct patient observations, and medical record review. Hematological abnormalities were assessed using complete blood count (CBC) testing. Approximately 2 mL of venous blood was collected using a vacutainer and transferred into a K3EDTA tube for analysis with a hematology analyzer (Sysmex XN-550). The measured parameters included erythrocyte, leukocyte, and platelet counts, along with related hematological indices. Anemia was defined based on Hb levels, with cut-off values of < 13g/dL for men and < 12 g/dL for women, in accordance with World Health Organization criteria. Leukocytosis was defined as a total leukocyte cell count greater than 10,000 cells/μL. The NLR ratio was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. An NLR value greater than 3.5 was considered elevated. Sociodemographic variables (sex, age, occupational status, dietary pattern, physical activity, and smoking habit) and anthropometric data (body mass index [BMI]) were collected through

structured interviews and direct observation. The questionnaire used in the interviews was developed by the researchers. The questionnaire had undergone validity and reliability testing prior to its use and was deemed appropriate for data collection in this study. Clinical characteristics (blood glucose level, HbA1c, and glycemic control status) were extracted from patients' medical records.

Statistical Analysis

The proportions of abnormalities were calculated for erythrocyte, leukocyte, and platelet related parameters. Binary and Multiple logistic regression analysis was performed to identify the sociodemographic, anthropometric, and clinical factors most strongly associated with hematological abnormalities among patients with T2DM. Variables with a p-value <0.25 in the univariate analysis were subsequently included in the multivariate logistic regression model to identify independent factors associated with hematological abnormalities. Statistical significance was determined using a p-value <0.05. All statistical analyses were conducted using SPSS software version 23.0.

C. RESULTS AND DISCUSSION

1. Results

a. Sociodemographic, Anthropometric, and Clinical Characteristics of the Study Participants

Most participants were female (62.5%), with a mean age of 56.43 ± 9.83 years. More than half were not employed (52.5%), did not engage in regular physical activity (63.7%), did not follow a recommended dietary pattern (52.5%), and were non-smokers (78.7%). The median fasting blood glucose level was 226 mg/dL, and the median HbA1c was 8.6%. Most participants had uncontrolled glycemic status (61.3%). The mean body mass index (BMI) was 25.6 ± 3.8 kg/m^2 (Table 1).

Table 1. Sociodemographic, Anthropometric, and Clinical Characteristics of the Study Participants

Characteristics of the Respondents	N (%)	Mean±SD / Median (Min-Max)
Gender		
Male	30 (37.5%)	
Female	50 (62.5%)	
Ages (Years)	80	56.43±9.83
Occupational Status		
Not Employed	42 (52.5%)	
Employed	38 (47.5%)	
Physical Activity		
Not Regular	51 (63.7%)	
Regular	29 (36.3%)	
Dietary Pattern		
Not Following Recommended Diet	42 (52.5%)	
Following Recommended Diet	38 (47.5%)	
Smoking Habbit		
Yes	17 (21.3%)	
No	63 (78.7%)	
BMI (kg/m^2)	80	25.6±3.8
FBG (mg/dL)	80	226 (49 – 949)
HbA1c (%)	80	8.6 (4.0 – 15.0)
Glycemic Status		
Uncontrolled	49 (61.3%)	
Controlled	31 (38.7%)	

b. Hematological Abnormalities

In this study, the most frequently observed hematological abnormalities among patients with T2DM were anemia (45%), leukocytosis (32%), and an elevated neutrophil-to-lymphocyte ratio (NLR) (46%) (Table 2).

Table 2. Hematological Abnormalities Among Patients with T2DM

Type of Hematological Abnormalities	N (%)
Anemia	
No	44 (55%)
Yes	36 (45%)
Leukocytosis	
No	54 (68%)
Yes	26 (32%)
High NLR	
No	43 (54%)
Yes	37 (46%)

c. Association Between Anemia and Sociodemographic, Anthropometric, and Clinical Factors

The study found that anemia among patients with T2DM was significantly associated with age ≥61 years (p = 0.009; OR = 9.50), occupational status (p = 0.023; OR = 0.346), not following a recommended dietary pattern (p < 0.001; OR = 5.80), smoking (p = 0.025; OR = 5.993), and uncontrolled glycemic status (p < 0.001; OR = 8.956). In the multivariable logistic regression analysis, uncontrolled glycemic status (adjusted OR = 15.914; p = 0.001), smoking (adjusted OR = 7.920; p = 0.015), not following a recommended dietary pattern (adjusted OR = 7.402; p = 0.003), and age ≥61 years (adjusted OR = 29.643; p = 0.004) remained independently associated with anemia among patients with T2DM (Table 3).

Table 3. Univariate and Multivariate Analysis of Factors Associated with Anemia

Parameter	**Univariat**		**Multivariat**	
	Crude OR (95% CI)	***P***	**Adjusted OR (95% CI)**	***p***
Gender				
Male	Ref	0.816		
Female	0.898 (0.362–2.229)			
Age				
≤ 45 years	Ref			
46-60 years	3.125 (0.600–16.265)	0.176	6.424 (1.096–81.005)	0.041*
≥ 61 years	9.50 (1.735–52.021)	0.009*	29.643 (2.963–296.537)	0.004*
Occupational Status				
Not employed	Ref			
Employed	0.346 (0.138–0.866)	0.023*	0.423 (0.078–2.310)	0.321
Physical Activity				
Regular	Ref			
Not Regular	2.50 (0.957–6.528)	0.061	0.410 (0.076–2.206)	0.299
Dietary Pattern				
Following Recommended Diet	Ref			
Not Following Recommended Diet	5.80 (2.180–15.432)	0.000*	7.402 (1.931–28.366)	0.003*
Smoking Habits				
No	Ref			

Yes	5.652 (1.648–19.385)	0.001*	7.920 (1.501–41.806)	0.015*
Glycemic Status				
Controlled	Ref			
Uncontrolled	8.956 (2.923–27.435)	0.000*	15.914 (3.039–83.344)	0.001*
BMI				
Normal	Ref			
Overweight	1.369 (0.565–3.315)	0.486		

Note: *Statistically significant association ($p < 0.05$). Model fit: Omnibus test, $p < 0.001$; Hosmer–Lemeshow test, $p = 0.057$; Nagelkerke $R^2 = 0.590$; AUC = 0.906.

d. Association Between Leukocytosis and Sociodemographic, Anthropometric, and Clinical Factors

The study found that leukocytosis among patients with T2DM was significantly associated with lack of regular physical activity ($p = 0.015$; OR = 3.686), not following a recommended dietary pattern ($p = 0.032$; OR = 2.80), and uncontrolled glycemic status ($p = 0.002$; OR = 5.878). In the multivariable logistic regression analysis, uncontrolled glycemic status remained the strongest independent factor associated with leukocytosis (adjusted OR = 4.310; $p = 0.020$). In contrast, physical activity (adjusted OR = 1.557; $p = 0.485$) and dietary pattern (adjusted OR = 2.088; $p = 0.159$) were not independently associated with leukocytosis (Table 4).

Table 4. Univariate and Multivariate Analysis of Factors Associated with Leukocytosis

Parameter	**Univariat**		**Multivariat**	
	Crude OR (95% CI)	***P***	**Adjusted OR (95% CI)**	***p***
Gender				
Male	Ref			
Female	1.448 (0.563–3.723)	0.442		
Age				
≤ 45 years	Ref			
46-60 years	1.357 (0.342–5.393)	0.664		
≥ 61 years	1.322 (0.488–3.581)	0.583		
Occupational Status				
Not employed	Ref			
Employed	1.309 (0.531–3.225)	0.558		
Physical Activity				
Regular	Ref			
Not Regular	3.686 (1.286–10.564)	0.015*	1.557 (0.450–5.393)	0.485
Dietary Pattern				
Following Recommended Diet	Ref			
Not Following Recommended Diet	2.800 (1.092–7.182)	0.032*	2.088 (0.750–5.814)	0.159
Smoking Habits				
No	Ref			
Yes	1.546 (0.524–4.560)	0.430		
Glycemic Status				
Controlled	Ref			
Uncontrolled	5.878 (1.938–7.826)	0.002*	4.310 (1.259–14.761)	0.020*
BMI				
Normal	Ref			
Overweight	1.024 (0.416–2.519)	0.959		

Note: *Statistically significant association ($p < 0.05$). Model fit: Omnibus test, $p = 0.002$; Hosmer–Lemeshow test, $p = 0.799$; Nagelkerke $R^2 = 0.228$; AUC = 0.742.

e. Association Between High NLR and Sociodemographic, Anthropometric, and Clinical Factors

In this study, NLR was considered abnormal when the value exceeded 3.5. High NLR was significantly associated with employment status ($p = 0.016$; OR = 3.067), lack of regular physical activity ($p = 0.001$; OR = 5.942), not following a recommended dietary pattern ($p = 0.004$; OR = 3.989), and uncontrolled glycemic status ($p < 0.001$; OR = 13.922). Multivariable logistic regression showed that uncontrolled glycemic status was the strongest independent factor associated with high NLR (adjusted OR = 18.811; $p = 0.001$), followed by employment status (adjusted OR = 8.630; $p = 0.003$) and not following a recommended dietary pattern (adjusted OR = 5.287; $p = 0.015$). In contrast, physical activity and smoking were not independently associated with high NLR among patients with T2DM (Table 5).

Table 5. Univariate and Multivariate Analysis of Factors Associated with High NLR

Parameter	Univariat		Multivariat	
	Crude OR (95% CI)	***P***	**Adjusted OR (95% CI)**	***p***
Gender				
Male	Ref			
Female	1.207 (0.486–3.001)	0.658		
Age				
≤ 45 years	Ref			
46-60 years	2.833 (0.692–11.599)	0.148		
≥ 61 years	1.095 (0.414–2.896)	0.855		
Occupational Status				
Not employed	Ref			
Employed	3.067 (1.230–7.646)	0.016*	8.630 (2.080–35.813)	0.003*
Physical Activity				
Regular	Ref			
Not Regular	5.942 (2.059–17.147)	0.001*	1.775 (0.439–7.176)	0.421
Dietary Pattern				
Following Recommended Diet	Ref			
Not Following Recommended Diet	3.989 (1.562–10.188)	0.004*	5.287 (1.389–20.128)	0.015*
Smoking Habits				
No	Ref			
Yes	2.609 (0.856–7.948)	0.092	1.286 (0.307–5.388)	0.731
Glycemic Status				
Controlled	Ref			
Uncontrolled	13.922 (4.160–46.591)	0.000*	18.811 (3.443–102.762)	0.001*
BMI				
Normal	Ref			
Overweight	0.824 (0.342–1.986)	0.666		

Note: *Statistically significant association ($p < 0.05$). Model fit: Omnibus test, $p < 0.001$; Hosmer–Lemeshow test, $p = 0.768$; Nagelkerke $R^2 = 0.552$; AUC = 0.870.

2. Discussion

This study examined hematological abnormalities in patients with T2DM and identified sociodemographic, anthropometric, and clinical factors associated with these abnormalities.

The findings showed that the most frequently observed hematological abnormalities were anemia, leukocytosis, and a high NLR. These results are consistent with previous studies reporting similar patterns of hematological abnormalities among patients with T2DM (Aslam et al., 2022; Duman et al., 2019; Ozdin et al., 2022; Tadasa & Kemal, 2025). Collectively, these findings support the notion that hematological abnormalities in T2DM reflect broader underlying pathophysiological processes and may be linked to an increased risk of complications.

In this study, several factors were independently associated with anemia, leukocytosis, and high NLR. Among all variables analyzed, uncontrolled glycemic status was the most dominant and consistent factor associated with all three abnormalities. Uncontrolled glycemia reflects persistent chronic hyperglycemia, which may impair erythropoiesis through reduced erythropoietin production, increased hepatic hepcidin synthesis, and shortened erythrocyte lifespan, ultimately leading to anemia (Al-Dwairi et al., 2024; Wang et al., 2025; Williams et al., 2023). In addition, uncontrolled glycemic status can promote the release of pro-inflammatory cytokines such as IL-6 and TNF, which enhance leukocyte activation and stimulate the bone marrow to produce more neutrophils (De Vries et al., 2015; Nagareddy et al., 2013). Concurrently, the systemic stress response accompanying heightened inflammation may increase endogenous cortisol levels, thereby suppressing lymphocyte counts (Dong et al., 2016; Reiske et al., 2019). This combination of neutrophilia and lymphopenia is reflected in an high NLR among patients with T2DM (Carollo et al., 2025; Shiny et al., 2014).

Beyond glycemic status, another factor identified as contributing to hematological abnormalities was a dietary pattern that did not align with recommended guidelines. Several studies have reported that diets high in sugar and low in fiber are associated with poorer glycemic control among patients with T2DM (Antonio et al., 2019; Rahman et al., 2025). As noted above, poor glycemic control was the dominant factor related to anemia, leukocytosis, and high NLR in this study. An unhealthy diet may also contribute to deficiencies in key micronutrients, such as iron, vitamin B12, and folate, which are essential for erythropoiesis (Alzahrani et al., 2025). Dietary patterns high in fat and sugar and low in antioxidants may also increase the generation of reactive oxygen species (ROS), thereby exacerbating oxidative stress and sustaining chronic inflammation, which in turn may contribute to anemia, leukocytosis, and high NLR (Shafras et al., 2024). Notably, dietary pattern remained significantly associated with hematological abnormalities even after adjustment for glycemic control (HbA1c) in the multivariate analysis. This finding suggests that the effect of diet may not be mediated solely through glycemic control, but may also involve independent biological pathways. Poor dietary quality may directly contribute to hematological abnormalities through deficiencies of essential micronutrients, such as iron, vitamin B12, and folate, which are crucial for hematopoiesis. In addition, inadequate intake of anti-inflammatory nutrients may exacerbate systemic inflammation, thereby influencing hematological parameters independently of glycemic status.

Smoking was also a factor with a strong influence on hematological abnormalities, particularly anemia. Cigarette smoke is a source of free radicals that can increase oxidative stress, damage erythrocyte membranes, and promote erythrocyte death (Attanzio et al., 2019; Kamceva et al., 2016). These adverse effects may be further amplified by the chronic inflammatory state in T2DM, thereby increasing susceptibility to anemia. In addition to smoking, older age was also strongly associated with anemia in T2DM. Aging is linked to a reduced regenerative capacity of the bone marrow, heightened baseline inflammation, and a diminished physiological response to erythropoietin (Wacka et al., 2024; Yun, 2015). Moreover, older patients are more likely to have a longer duration of T2DM, which may result in stronger cumulative effects of diabetes-related complications on overall physiological function (Taderegew et al., 2020; Trevest et al., 2014).

In this study, several other factors, such as BMI, physical activity, and sex, were not independently associated with hematological abnormalities in the multivariable analysis. This suggests that, in this study population, metabolic inflammation related to T2DM may have a stronger influence on hematological abnormalities than certain lifestyle factors. Therefore, primary interventions in T2DM management should continue to prioritize optimizing glycemic control and dietary patterns, although lifestyle factors remain important for achieving glycemic targets and preventing long-term complications (Amsalu et al., 2024; David, 2023).

This study has several limitations. First, its cross-sectional design, in which exposures and outcomes were measured at the same time, does not allow determination of temporal sequence and therefore precludes causal inference. Second, the sample was drawn from a single center and was relatively small, limiting the generalizability of the findings to broader populations of patients with T2DM. Finally, lifestyle variables were assessed through patient interviews, which may be subject to respondent-related bias. Therefore, further studies with larger sample sizes and multicenter designs are needed to confirm these findings and to elucidate the underlying mechanisms.

D. CONCLUSION AND SUGGESTIONS

The study found that the most frequently observed hematological abnormalities among patients with T2DM were anemia, leukocytosis, and high NLR. Uncontrolled glycemic status was the most dominant and consistent factor associated with all three abnormalities. In addition, not following a recommended dietary pattern was closely associated with anemia and high NLR, whereas smoking and older age were associated with anemia. These findings underscore the importance of optimizing glycemic control and addressing modifiable lifestyle factors—particularly improving dietary practices and promoting smoking cessation—as strategies to prevent complications, including hematological abnormalities, in patients with T2DM.

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