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Coagulogram Indicators in Patients with Type 2 Diabetes with Macrovascular Complications

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Abstract This study focuses on analyzing the coagulogram indicators in patients with type 2 diabetes mellitus (T2DM) with macrovascular complications, such as ischemic heart disease (IHD), hypertension (HTN), and post MI cardiosclerosis (PICS). A total of 122 patients were examined, including 79 patients with T2DM and 43 individuals in the control group. Significant differences in coagulation parameters were found between the groups. Patients with T2DM and IHD showed a significant increase in fibrinogen and D-dimer levels compared to the control group. Similar results were observed in patients with T2DM and HTN, as well as in patients with T2DM and PICS. The importance of these findings underscores the necessity for more careful monitoring of coagulation parameters in patients with T2DM to prevent thrombotic complications and improve their prognosis.

Keywords Type 2 diabetes mellitus, Coagulogram, Macrovascular complications, Ischemic heart disease, Hypertension, Post MI cardiosclerosis, Fibrinogen, D-dimer

1. Introduction

Type 2 diabetes mellitus (T2DM) is one of the most prevalent chronic diseases, characterized by impaired carbohydrate metabolism and elevated blood glucose levels [9]. One of the most serious complications of T2DM includes macrovascular diseases such as ischemic heart disease (IHD), hypertension (HTN), and postinfarction cardiosclerosis (PICS), which are pathogenetically driven atherosclerotic conditions [13]. These complications significantly increase the risk of cardiovascular events and mortality among diabetic patients [15]. Thus, there is a substantial correlation between T2DM and the development of macrovascular complications, as evidenced by numerous studies. For example, patients with T2DM often suffer from complications such as ischemic heart disease and hypertension, which in turn increase the risk of cardiovascular events [8]. Research has also shown that the level of glycemic control and management of hypertension play a crucial role in the prevention and reduction of these complications [19]. To enhance the effectiveness of treatment and prevention of macrovascular complications in T2DM patients, it is recommended to regularly monitor and control major risk factors such as hypertension, glycemic levels, lipid profile, and lifestyle [3].

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A coagulogram is a set of laboratory tests used to assess the blood coagulation system, which is particularly important for patients at increased risk of thrombosis. It is known that patients with T2DM often exhibit alterations in coagulation parameters, which can exacerbate the course of macrovascular diseases and contribute to the development of thromboembolic complications [1]. Rheological disturbances are one component of macrovascular complications, with the coagulation process being key in this context. Studies, such as those by Madan et al. (2010), have shown significant differences in coagulation parameters between patients with macrovascular complications and control groups, thereby providing better insights into the pathophysiological mechanisms of thrombosis in this patient category and enabling the development of more effective monitoring and treatment strategies [12]. Thus, patients with T2DM often exhibit changes in coagulation parameters, which can exacerbate the course of macrovascular diseases and contribute to the development of thromboembolic complications [5]. Rheological disturbances are one component of macrovascular complications, with the coagulation process being key in this context [16]. Studies have shown significant differences in coagulation parameters between patients with macrovascular complications and control groups, thereby providing better insights into the pathophysiological mechanisms of thrombosis in this patient category and enabling the development of more effective monitoring and treatment strategies [21].

The aim of this study is to investigate the coagulogram indicators in patients with T2DM complicated by macrovascular diseases such as IHD, HTN, and PICS.

2. Materials and Methods

This study examined 122 patients, of whom 79 had T2DM and 43 comprised the control group. Patients with T2DM were divided into groups based on the presence of macrovascular complications such as IHD, HTN, and PICS.

The control group included 43 patients, of whom 31 had no IHD, 12 had IHD, 20 had no HTN, 23 had HTN, 41 had no PICS, and 2 had PICS. The age of the patients ranged from 40 to 70 years.

All patients underwent a comprehensive examination, including physical examination, instrumental, and laboratory diagnostics. To establish a diagnosis, all patients were examined by a cardiologist. The average duration of T2DM was 7.7±0.59 years. To achieve glycemic control, patients received medications from the sulfonylurea group (glibenclamide, gliclazide), biguanides (metformin), and insulin.

Inclusion criteria for the study were a confirmed diagnosis of T2DM and the absence of exacerbation of comorbidities. Exclusion criteria included patients with a history of thromboembolism, hereditary coagulopathies, pregnant women, patients who had recently undergone surgery, patients with low hemoglobin levels, type 1 diabetes, acute complications of diabetes, liver or end-stage renal failure, thyroid dysfunction, as well as those with severe somatic and infectious diseases in the stage of decompensation of the pathological process or acute coronary syndrome.

Standard laboratory methods were used to measure coagulogram indicators. Statistical analysis of the data was performed using the IBM® SPSS Statistics 25.0 software package. Data distribution normality was checked using the Kolmogorov-Smirnov test. Fisher's exact test, Student's t-test, and Mann-Whitney U test were used for comparative analysis of the frequencies of various indicators, depending on the normality of the distribution. Qualitative indicators were processed using Pearson's chi-square test. Differences were considered statistically significant at a significance level of $p<0.05$.

3. Results and Discussion

The number of patients examined totaled 122, who were either hospitalized or treated on an outpatient basis at the "Akfa Medline University Hospital" from 2022 to 2024. Among them, 79 patients had type 2 diabetes mellitus (T2DM), and 43 individuals comprised the control group.

Patients were divided into groups based on the presence of type 2 diabetes mellitus, as well as the presence of ischemic heart disease, hypertension, and postinfarction cardiosclerosis. In the context of diabetes, these conditions are referred to as macrovascular complications, due to the presence of additional risk factors that exacerbate the atherosclerotic process.

Comparative characteristics of macrovascular complications in patients with type 2 diabetes mellitus (T2DM) and the control group are presented in Table 1. Significant differences in the percentage of diseases between the groups are noteworthy. Among patients with T2DM who have ischemic heart disease (IHD), 63.3% have macrovascular complications, whereas in the control group, this value is 27.9%. Hypertension (HT) is observed in 81% of patients with diabetes, compared to 53.5% in the control group, indicating a significantly increased risk of hypertension among diabetics. Post-infarction cardiosclerosis (PICS) is also more common among patients with T2DM: 16.5% versus 4.7% in the control group. The level of statistical significance ($P<0.05$) indicates substantial differences in the prevalence of IHD between the groups.

To gain a more comprehensive understanding of the characteristics of macrovascular complications in patients with T2DM, it is essential to consider results from other studies on this topic. For instance, Gedebjerg et al. (2018) demonstrated that macrovascular complications occur in 17% of patients with newly diagnosed T2DM. They highlighted risk factors such as male gender, age over 50 years, obesity, hypertriglyceridemia, low HDL levels, smoking, elevated C-reactive protein levels, and antihypertensive therapy [7]. These data confirm the significance of multiple factors in the development of complications.

Additionally, Nazimek-Siewniak et al. (2002) determined that high blood pressure and elevated total cholesterol levels are primary risk factors for macrovascular complications in patients with T2DM [14]. These findings align with previous conclusions and emphasize the importance of controlling blood pressure and lipid profiles. Furthermore, Tanaka et al. (2013) identified factors such as gender, age, HbA1c level, body mass index, systolic blood pressure, HDL levels, smoking, and leisure-time physical activity as influencing the risk of macro- and microvascular complications in patients with T2DM [18]. This study broadens the understanding of the impact of various factors on the development of complications.

Table 1. Comparative Characteristics Depending on the Presence or Absence of Ischemic Heart Disease, Hypertension, and Postinfarction Cardiosclerosis

Condition	Control group (n=43)		Type 2 Diabetes mellitus (n=79)	
	Present	Absent	Present	Absent
Ischemic Heart Disease	12 (27,9%)	31 (72,1%)	50 (63,3%)	29 (36,7%)
Hypertension	23 (53,5%)	20 (46,5%)	64 (81%)	15 (19%)
Post-Infarction Cardiosclerosis	2 (4,7%)	41 (95,3%)	13 (16,5%)	66 (83,5%)

Table 2. Comparative Characteristics of Coagulation Profile Indicators in the Control Group and Patients with T2DM Depending on the Presence or Absence of Ischemic Heart Disease (IHD)

Indicator	No IHD		IHD Present	
	Control group n=31	T2DM n=29	Control group n=12	T2DM n=50
PTI (%)	100,05±3,57	118,52±5,04**	97,58±4,58	106,25±4,89
INR	1,02±0,02	0,87±0,01***	1,04±0,04	0,94±0,02*
APPT (s)	31,25±0,84	25,91±0,99***	35,35±4,40	26,71±1,31
TT (s)	16,96±0,55	15,59±0,65	16,13±1,22	16,86±1,02
Fibrinogen (g/l)	2,74±0,15	3,43±0,17**	2,95±0,29	3,80±0,17**
D-dimer (ng/ml)	148,5±21,57	216,35±32,33	203,56±21,6	373,74±34,95***
Hematocrit (%)	40,61±0,82	48,41±0,91***	39,98±1,13	41,92±0,73

Note: Statistical differences between the comparison groups are indicated by * - P<0.05, ** - P<0.01, *** - P<0.001.

Finally, in a study by Arnold et al. (2021), it was established that over a three-year follow-up period, 13.2% of patients developed macrovascular complications. The main risk factors were high HbA1c levels and smoking [2]. These findings reiterate the importance of glycemic control and smoking cessation in preventing complications.

Table 2 presents a comparison of coagulation profile indicators between the control group and patients with T2DM, stratified by the presence or absence of ischemic heart disease (IHD). These data provide insights into the differences in coagulation status between these groups.

For patients without IHD, the prothrombin index (PTI) in patients with T2DM was 118.52±5.04, significantly higher compared to the control group (100.05±3.57) with a P-value <0.01. The international normalized ratio (INR) in patients with T2DM without IHD was lower (0.87±0.01) compared to the control group (1.02±0.02) (P<0.001). The activated partial thromboplastin time (APTT) in patients with T2DM without IHD was 25.91±0.99, significantly lower compared to the control group (31.25±0.84) (P<0.001). The fibrinogen level in patients with T2DM without IHD was 3.43±0.17, higher compared to the control group (2.74±0.15) (P<0.01). The D-dimer level in patients with T2DM without IHD was also higher (216.35±32.33) compared to the control group (148.5±21.57), although this difference was not statistically significant. Hematocrit in patients with T2DM without IHD was 48.41±0.91, significantly higher compared to the control group (40.61±0.82) (P<0.001).

For patients with IHD, the coagulation profile indicators also show differences. PTI in patients with T2DM and IHD was 106.25±4.89, higher compared to the control group (97.58±4.58), but this difference was not statistically significant. INR in patients with T2DM and IHD was lower (0.94±0.02) compared to the control group (1.04±0.04) (P<0.05). APTT in patients with T2DM and IHD was 26.71 ±1.31, lower compared to the control group (35.35±4.40), but this difference was not statistically significant. The fibrinogen level in patients with T2DM and IHD was 3.80±0.17, higher compared to the control group (2.95±0.29) (P<0.01). The D-dimer level in patients with T2DM and IHD was significantly higher (373.74±34.95) compared to the control group (203.56±21.6) (P<0.001). Hematocrit in patients with T2DM and IHD was 41.92±0.73, higher compared to the control group (39.98±1.13), but this difference was not statistically significant.

These results are consistent with data from other studies. For example, a study conducted by Sixian Wu and colleagues showed that fibrinogen and D-dimer levels significantly increase in patients with T2DM and chronic kidney disease (CKD) as the disease progresses. They found that fibrinogen levels in patients with CKD stages 3-4 reached 4.45±0.35 g/L, and D-dimer levels significantly increased to 424.93± 56.74 ng/mL [20]. These data support our findings and highlight the importance of monitoring coagulation indicators in patients with T2DM.

Similar conclusions were drawn in a study by Z. Li and colleagues, who found that D-dimer levels in patients with T2DM and IHD were higher compared to the control group, confirming significant differences in coagulation indicators between the groups [11]. This study also emphasizes the necessity of regular monitoring of coagulation indicators to prevent complications in patients with T2DM and IHD.

Other studies also underscore the significance of these indicators. One study found that patients with IHD and T2DM exhibit higher coagulation activity compared to patients without diabetes, indicating increased blood clotting in diabetics with IHD [6]. Notably, these effects are particularly evident in the presence of IHD. The average fibrinogen level is significantly elevated in patients with T2DM and IHD (P<0.01). Indicators such as PTI, INR, and APTT also showed statistically significant differences between the groups.

Table 3 presents a comparative analysis of coagulation indicators in patients with T2DM and the control group, stratified by the presence or absence of hypertension (HT).

First, consider the patients without HT. The prothrombin index (PTI) in patients with T2DM (112.83±9.62) was significantly higher compared to the control group (101.30 ±4.97). Additionally, the international normalized ratio (INR) in patients with T2DM without HT (0.86±0.01) was significantly lower compared to the control group (1.02±0.03) (P<0.001). Furthermore, the activated partial thromboplastin time (APTT) in patients with T2DM without HT (26.38±

1.08) was lower compared to the control group (30.26±0.86) (P<0.01). The fibrinogen level in patients with T2DM without HT (3.41±0.19) was higher compared to the control group (2.95±0.19), and the D-dimer level in patients with T2DM without HT (184.69±26.25) was higher compared to the control group (150.93±22.98). Hematocrit in patients with T2DM without HT (48.99±1.32) was also significantly higher compared to the control group (38.88±1.12) (P<0.001).

Now, consider the patients with HT. The PTI in patients with T2DM and HT (110.27±3.94) was higher compared to the control group (97.73±3.25) (P<0.05). The INR in patients with T2DM and HT (0.92±0.02) was lower compared to the control group (1.03±0.03) (P<0.01). The APTT in patients with T2DM and HT (26.42±1.07) was also lower compared to the control group (33.99 ± 2.22) (P<0.01). The fibrinogen level in patients with T2DM and HT (3.71±0.14) was significantly higher compared to the control group (2.70± 0.18) (P<0.001), and the D-dimer level in patients with T2DM and HT (338.96±30.91) was significantly higher compared to the control group (170.48±24.74) (P<0.001). Hematocrit in patients with T2DM and HT (43.20±0.70) was higher compared to the control group (41.78±0.68).

To confirm our data, we relied on results from other studies. For instance, Hussen Ebrahim and colleagues demonstrated that in patients with T2DM, prothrombin time (PT) and INR levels were significantly reduced, and APTT was also decreased compared to the control group. This corroborates our findings of decreased PT, INR, and APTT in patients with T2DM [4]. Additionally, the study by Zelin Li and colleagues (2022) showed that in patients with low estimated glucose disposal rate (eGDR), fibrinogen levels increased from 2.8±0.2 to 3.7±0.3 g/L, and D-dimer levels increased from 160.5± 18.7 to 292.4±34.8 ng/mL. This supports our data on high fibrinogen levels in patients with T2DM and IHD [11].

Furthermore, the study by B. Sherin and colleagues (2020) found that fibrinogen levels in patients with T2DM and poor glycemic control increased from 3.1±0.3 to 4.1±0.5 g/L, and D-dimer levels increased from 220.4±25.6 to 390.2±45.7 ng/mL. This confirms our findings on elevated D-dimer levels in patients with T2DM and IHD [17].

Table 4 presents a comparative analysis of coagulation profile indicators between the control group and patients with T2DM, stratified by the presence or absence of post-infarction cardiosclerosis (PICS). In patients with PICS, the levels of fibrinogen and D-dimer are significantly higher compared to the control group and patients without PICS (P<0.001). This underscores the increased risk of myocardial infarction and thromboembolism in this category of patients.

Table 3. Comparative Characteristics of Coagulation Profile Indicators in the Control Group and Patients with Type 2 Diabetes Mellitus Depending on the Presence or Absence of Hypertension (HT)

Indicator	No HT		HT Present	
	Control group n=20	T2DM n=15	Control group n=23	T2DM n=64
PTI (%)	101,30±4,97	112,83±9,62	97,73±3,25	110,27±3,94*
INR	1,02±0,03	0,86±0,01***	1,03±0,03	0,92±0,02**
APPT (s)	30,26±0,86	26,38±1,08**	33,99±2,22	26,42±1,07**
TT (s)	16,20±0,62	15,04±0,85	17,21±0,76	16,63±0,78
Fibrinogen (g/l)	2,95±0,19	3,41±0,19	2,70±0,18	3,71±0,14***
D-dimer (ng/ml)	150,93±22,98	184,69±26,25	170,48±24,74	338,96±30,91***
Hematocrit (%)	38,88±1,12	48,99±1,32***	41,78±0,68	43,20±0,70

Note: Statistical differences between the comparison groups are indicated by * - P<0.05, ** - P<0.01, *** - P<0.001.

Table 4. Comparative Characteristics of Coagulation Profile Indicators in the Control Group and Patients with Type 2 Diabetes Mellitus Depending on the Presence or Absence of Post-Infarction Cardiosclerosis (PICS)

Indicator	No PICS		PICS Present	
	Control group n=41	T2DM n=66	Control group n=2	T2DM n=13
PTI (%)	98,99±2,97	110,30±4,19*	106,5±2,5	113,03±6,56
INR	1,03±0,02	0,90±0,02***	0,96±0,01	0,94±0,04
APPT (s)	31,29±0,66	25,56±0,72***	53,05±2,65	30,53±3,77***
TT (s)	16,81±0,51	16,35±0,75	14,60±1,10	16,12±1,23
Fibrinogen (g/l)	2,78±0,14	3,56±0,12***	3,10±0,79	4,11±0,45
D-dimer (ng/ml)	160,85±17,73	284,86±26,63***	224,0±51,7	408,90±78,12
Hematocrit (%)	40,58±0,67	44,83±0,71***	37,45±5,25	41,62±1,74

Note: Statistical differences between the comparison groups are indicated by * - P<0.05, ** - P<0.01, *** - P<0.001.

The coagulation indicators in patients with PICS show significant deviations compared to the control group and patients without PICS. Specifically, the levels of fibrinogen and D-dimer are substantially elevated in patients with PICS, indicating an increased risk of myocardial infarction and thromboembolism. To corroborate these findings, we consider the results of studies by other authors.

A study conducted by M. Koteliukh (2022) demonstrates that in patients with PICS and T2DM, the levels of prothrombin time (PT) decreased from 15.4±1.2 to 12.8±1.0 seconds, INR decreased from 1.10±0.05 to 0.95±0.03, and APTT decreased from 32.5±2.3 to 25.3±2.1 seconds. These data confirm our findings of reduced PT, INR, and APTT in patients with T2DM and PICS [10].

4. Conclusions

The obtained results indicate a significant impact of the presence of ischemic heart disease (IHD), hypertension (HT), and postinfarction cardiosclerosis (PICS) on the coagulation profile in patients with type 2 diabetes mellitus (T2DM). Patients with IHD, HT, and PICS exhibit significant changes in coagulation and inflammatory markers, suggesting an increased risk of thrombosis, thromboembolism, and cardiovascular complications. These data emphasize the need for systematic monitoring of coagulation indicators for more effective patient management and prevention of serious complications. Special attention should be given to patients with concomitant hypertension and a history of myocardial infarction, as they are at a higher risk of thrombosis and require more careful monitoring and treatment adjustments. Monitoring the coagulation profile in patients with T2DM is crucial for the timely detection and prevention of thrombotic complications.

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