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Original Research Article

Altered Coagulation Parameters in Type 2 Diabetes Mellitus and Their Association with Diabetic Complications: A Cross-Sectional Study

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Abstract:

Background: Type 2 diabetes mellitus (T_2DM) is associated with hemostatic abnormalities that may contribute to microvascular and macrovascular complications. This study evaluated coagulation parameters in T_2DM patients and investigated their association with diabetic complications.

Methods: This prospective, cross-sectional study included 130 adult T_2DM patients attending a tertiary hospital. Patients were divided into those with complications (n=69) and without complications (n=61). Prothrombin time (PT) activated partial thromboplastin time (aPTT), international normalized ratio (INR), bleeding time (BT), and clotting time (CT) were measured. Statistical analysis included Student's t-test and Pearson correlation.

Results: A significant majority of T_2DM patients exhibited low PT and INR values. All patients with diabetic complications had low PT and INR compared to only a portion of those without complications ($p<0.001$). Mean PT and INR were significantly lower in patients with complications versus those without ($p<0.001$). For aPTT, a substantial proportion of patients with complications had low values compared to none without complications ($p<0.001$), with lower mean aPTT in the complications group ($p<0.001$). All patients had normal BT and CT, but mean BT was significantly shorter in patients with complications ($p<0.001$).

Conclusions: T_2DM patients, especially those with complications, demonstrate a hypercoagulable state characterized by shortened PT, aPTT, and BT. The strong correlation between HbA1c and coagulation parameters suggests that poor glycemic control contributes to coagulation abnormalities. These findings highlight the importance of monitoring coagulation parameters in T_2DM patients for early identification of thrombotic risk.

Keywords: Type 2 Diabetes Mellitus, Coagulation Profile, Diabetic Complications, Glycemic Control, Hypercoagulable State.

Introduction

Diabetes mellitus, particularly Type 2 Diabetes Mellitus (T_2DM), has emerged as a global health epidemic affecting millions worldwide, with a prevalence of 10.5% among adults aged 20-79 years [1]. Beyond its well-established metabolic dysregulation, recent research has unveiled intricate connections between diabetes and hemostatic abnormalities, particularly alterations in coagulation profiles.

The chronic hyperglycemic state in diabetes promotes a pattern of coagulation factors that favors thrombosis or impedes thrombolysis, affecting various stages of coagulation including platelet activation and endothelial cell function [2]. This hypercoagulable state is increasingly recognized as a significant contributor to both microvascular and macrovascular complications, which are major causes of morbidity and mortality in diabetic patients [3].

Clinical observations have consistently demonstrated shortened coagulation times in diabetic patients. Reduced Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT) have been documented in T_2DM patients compared to non-diabetics [4,5]. Suggesting an activation of both intrinsic and extrinsic coagulation pathways in diabetes. The relationship between glycemic control and coagulation abnormalities is also noteworthy. Reduced aPTT appears to be associated with high HbA1c levels [6]. Indicating that poor glycemic control may exacerbate coagulation disturbances.

Despite these findings, diabetic patients are not routinely screened for thrombotic status. Consequently, individuals often present to

clinicians only when complications have manifested, at which point organ damage may be irreversible. This study aims to comprehensively assess coagulation parameters in T_2DM patients and investigate their association with diabetic complications, potentially informing preventive strategies and targeted interventions to mitigate thrombotic risk in this vulnerable population.

Methodology

The present study employed a prospective, observational, cross-sectional design conducted at the Department of Pathology, Fakhruddin Ali Ahmed Medical College, and Hospital, Barpeta, Assam over a period of one year and two months. Ethical clearance was obtained from the Institutional Ethics Committee (FAAMC&H/IEC_PG/498/2020/4970), and written informed consent was secured from each participant after explaining the study procedure.

A total of 130 patients diagnosed with Type 2 Diabetes Mellitus (T_2DM) as per standard diagnostic criteria were enrolled. Participants were divided into two groups: Group A comprising T_2DM patients with complications and Group B including T_2DM patients without complications, as assessed by the Department of Medicine. The study excluded patients on drugs affecting coagulation profiles, those with history of coagulation disorders, hypertension, chronic liver disease, malignancy, and pregnant or lactating women.

Under aseptic precautions, 5 milliliters of fasting and postprandial venous blood samples were collected in appropriate vacutainers (EDTA, sodium fluoride, and citrate) for analysis. Samples were processed within two hours of collection following National Committee for Clinical Laboratory Standards guidelines.

Coagulation parameters assessed included Prothrombin Time (PT) and International Normalized Ratio (INR) using automated Coagulation Analyzer ECL 760, Activated Partial Thromboplastin Time (aPTT) using ERBA Actime and Calcium chloride reagents, Bleeding Time (BT) via the Duke Method, and Clotting Time (CT) using Wright's method. The normal reference ranges for these parameters were as follows: PT (11-13 seconds), INR (0.8-1.2), aPTT (21-35 seconds), BT (1-6 minutes), and CT (2-8 minutes). Additionally, complete hemogram, glycosylated hemoglobin (HbA1c), fasting and postprandial blood glucose were measured using standard laboratory protocols.

Statistical Analysis

Data was compiled using MS Excel and analyzed with SPSS software (version 21.0). Categorical data was expressed as frequency and percentage, while continuous data was presented as mean and standard deviation. Student's t-test was used for comparing means between groups, and Pearson correlation coefficient assessed relationships between variables. A p-value less than 0.05 was considered statistically significant.

Results and Discussion

The present study enrolled 130 patients with Type 2 Diabetes Mellitus (T_2DM). The age distribution showed that the majority of participants (39.2%) were between 51-60 years, followed by those under 50 years (27.7%), 61-70 years (26.9%), and only 6.2% were above 70 years. The minimum reported age was 45 years, while the maximum was 72 years. This age distribution is consistent with Cigolle et al., 2022 [7], who reported a similar age pattern among diabetic patients, with significant proportions diagnosed between 50-69 years. However, Yan et al., 2023 [8] found a trend toward earlier onset of T_2DM in their population study, reflecting the growing prevalence of diabetes in younger adults due to changing lifestyle factors.

Gender distribution revealed a slight male predominance, with 53.8% male and 46.2% female participants. This finding aligns with Jiskani and Singh, 2021 [9], who reported comparable gender distribution in their diabetic cohort. The male predominance may be attributed to hormonal differences, variations in visceral fat distribution, and gender-specific lifestyle factors affecting insulin sensitivity.

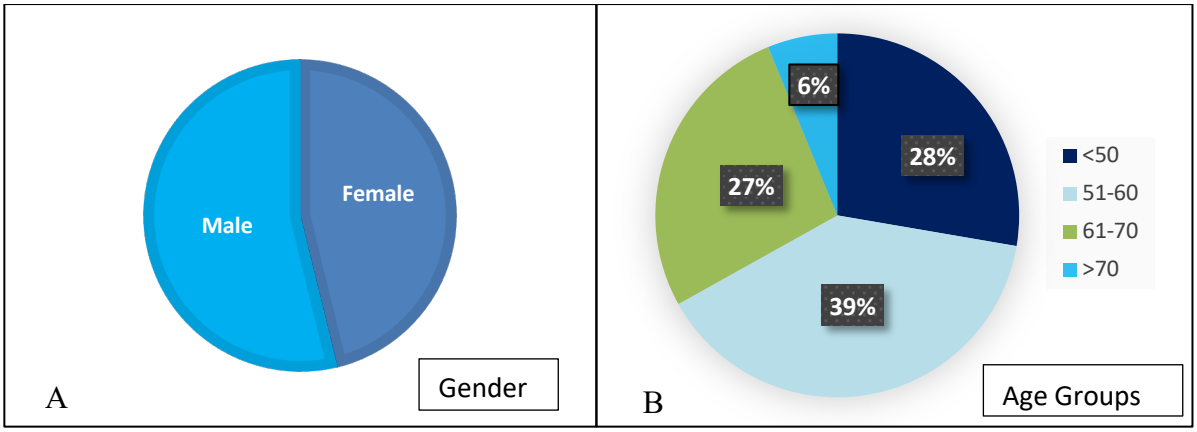

Figure 1: Distribution of patients of T₂DM according to A. gender and B. different age groups

Analysis of body mass index (BMI) showed that a significant majority of participants (69.2%) were overweight (BMI 25-29.9 kg/m²), while 23.1% were obese (BMI >30 kg/m²), and only 7.7% had normal weight. These findings demonstrate a strong association between elevated BMI and T₂DM, as also reported by Pujani et al., 2018 [10] and Akinsegun et al., 2014 [11]. The high prevalence of overweight and obesity in diabetic patients reflects insulin resistance patterns associated with excess adiposity, particularly visceral fat, which increases inflammatory cytokines that impair insulin signaling pathways.

Among the study participants, 53.1% presented with at least one diabetic complication, while 46.9% had no complications. This prevalence of complications is consistent with Taderegew et al., 2021 [12], who reported that 33.2% of participants in their study suffered from at least one microvascular complication. The higher percentage in the present study may be attributed to the inclusion of both microvascular and macrovascular complications, providing a more comprehensive assessment of diabetic complications.

Coagulation Parameters

The present study revealed that a substantial majority (84.6%) of T₂DM patients exhibited low PT values, and 66.2% had low INR values. These findings align with Ephraim et al., 2017 [4], who reported significantly shorter PT in T₂DM patients compared to non-diabetics, and lower INR values. Similarly, Kadiyala et al., 2017 [13] found lower mean PT in diabetics. The probable reason for this observation is glycation of coagulation factors in chronic hyperglycemia, which can alter their structure and enhance their activity, leading to faster coagulation. Additionally, elevated levels of procoagulant factors commonly found in diabetic patients contribute to shortened PT and reduced INR [2].

Interestingly, Thukral et al., 2018 [5] reported contradictory findings with higher PT in diabetic patients (17.48 seconds compared to 14.52 seconds in controls). This discrepancy might be explained by differences in study populations, diabetes duration, glycemic control status, or concurrent medications affecting coagulation.

For aPTT, 37.7% of patients demonstrated low values, consistent with Ephraim et al., 2017 [4], who found significantly shorter aPTT in T₂DM patients.

The shortened aPTT likely results from increased levels of intrinsic pathway factors (particularly Factor VIII) in diabetes, possibly due to endothelial dysfunction and chronic inflammation. However, Abdulla et al., 2017 [14] found no significant difference in aPTT between diabetic patients and controls, suggesting that the relationship between diabetes and intrinsic pathway activation may be influenced by factors like disease severity, concurrent vascular complications, or patient selection criteria.

All patients showed BT and CT within normal ranges, consistent with Kaur et al., 2018 [15], who reported no significant difference in BT and CT between diabetic patients and healthy controls. The maintenance of normal BT and CT despite altered PT and aPTT suggests that primary hemostasis may be preserved in T₂DM, with more prominent alterations occurring in the coagulation cascade.

This could be explained by compensatory mechanisms in platelet function and vascular response that maintain effective hemostasis despite alterations in coagulation factor activities.

Table 1: Distribution of Coagulation Parameters in T_2DM Patients with and without Complications

Parameter	Complications Status	Normal Values	Low Values	P-value
PT (11-13 seconds)	Present	0 (0.0%)	69 (100.0%)	<0.001*
	Absent	20 (32.8%)	41 (67.2%)	
INR (0.8-1.2)	Present	0 (0.0%)	69 (100.0%)	<0.001*
	Absent	44 (72.2%)	17 (27.8%)	
aPTT (21-35 seconds)	Present	20 (29.0%)	49 (71.0%)	<0.001*
	Absent	61 (100.0%)	0 (0.0%)	
BT (1-6 minutes)	Present	69 (100.0%)	0 (0.0%)	-
	Absent	61 (100.0%)	0 (0.0%)	
CT (2-8 minutes)	Present	69 (100.0%)	0 (0.0%)	-
	Absent	61 (100.0%)	0 (0.0%)	

[*Statistically significant]

The most striking finding was the strong association between diabetic complications and altered coagulation parameters. All patients (100%) with diabetic complications had low PT and INR values, compared to 67.2% (PT) and 27.8% (INR) of those without complications ($p<0.001$) (Table-1). Mean PT was significantly lower in patients with complications (9.52±0.21 seconds) versus those without (10.77±0.72 seconds, $p<0.001$) (Table-2). Similarly, mean INR was lower in the complications group (0.73±0.015 vs. 0.84±0.053, $p<0.001$). These findings suggest that the hypercoagulable state is more pronounced in patients with diabetic complications, potentially due to more severe endothelial dysfunction, increased inflammation, and more pronounced alterations in coagulation factor levels associated with diabetic vasculopathy [3].

For aPTT, 71% of patients with complications had low values compared to none without complications ($p<0.001$) (Table-1), with lower mean aPTT in the complications group (20.42±0.76 seconds vs. 23.79±0.89 seconds, $p<0.001$) (Table-2). This pattern is supported by Agarwal et al., 2019[3] and Acang and Jalil, 1993 [16], who reported significantly lower aPTT values in T_2DM patients with complications. The probable reason is increased activation of the intrinsic pathway in diabetic vasculopathy, possibly due to exposure of subendothelial collagen and tissue factor from damaged vessels, promoting activation of the coagulation cascade.

While all patients had normal BT, the mean value was significantly shorter in patients with complications (2.89±0.45 minutes vs. 3.68±0.23 minutes, $p<0.001$) (Table-2). This subtle reduction, though still within normal range, suggests enhanced primary hemostasis, potentially due to increased platelet reactivity and adhesiveness in patients with diabetic complications [17]. However, no significant difference was observed in CT between groups, suggesting that the final stage of clot formation may not be significantly altered in relation to diabetic complications. This could indicate that alterations in the initial activation of coagulation and thrombin generation are more prominent than changes in fibrin polymerization in diabetic patients.

Table 2: Mean Values of Coagulation Parameters in T2DM Patients with and without Complications

Parameter	Complications		T-statistic	P-value
	Present (Mean ± SD)	Absent (Mean ± SD)		
PT (seconds)	9.52 ± 0.21	10.77 ± 0.72	-13.79	<0.001*
INR	0.73 ± 0.015	0.84 ± 0.053	-13.827	<0.001*
aPTT (seconds)	20.42 ± 0.76	23.79 ± 0.89	-23.206	<0.001*
BT (minutes)	2.89 ± 0.45	3.68 ± 0.23	-12.351	<0.001*
CT (minutes)	4.79 ± 0.56	4.79 ± 0.55	0.034	0.973

[*Statistically significant]

Correlation analysis demonstrated strong negative associations between HbA1c and coagulation parameters (PT: $r=-0.824$, $p<0.001$; aPTT: $r=-0.923$, $p<0.001$; BT: $r=-0.622$, $p<0.001$), indicating that poor glycemic control is associated with a more pronounced hypercoagulable state. These findings align with Zhao et al., 2011 [6], who reported that reduced aPTT was associated with high HbA1c levels. The probable mechanism involves glycation of coagulation proteins proportional to glycemic control, with higher HbA1c reflecting more extensive glycation and consequently greater alteration of coagulation factor function.

Limitations

This single-center, cross-sectional study cannot establish causality between coagulation abnormalities and diabetic complications. The absence of a healthy control group, limited sample

size, and lack of adjustment for potentially confounding factors such as diet, physical activity, and specific medications may affect the generalizability of our findings and warrant larger, longitudinal studies to confirm these results.

Conclusion

Present cross-sectional study demonstrates that Type 2 diabetes mellitus patients exhibit a distinct hypercoagulable state characterized by shortened Prothrombin Time, reduced International Normalized Ratio, and decreased Activated Partial Thromboplastin Time, with these alterations being significantly more pronounced in patients with diabetic complications. While Bleeding Time and Clotting Time remained within normal ranges, the subtle but significant reduction in mean Bleeding Time in patients with complications suggests enhanced primary hemostasis. The strong negative correlations between glycemic control markers (HbA1c) and coagulation parameters indicate that poor glycemic control likely contributes to coagulation abnormalities through mechanisms including glycation of coagulation proteins, endothelial dysfunction, and chronic inflammation. These findings highlight the clinical importance of routinely monitoring coagulation parameters in diabetic patients, particularly those with poor glycemic control, as they may serve as early indicators of thrombotic risk and guide timely preventive interventions, potentially reducing the burden of vascular complications in this vulnerable population.

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