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Assessment of Basic coagulation Profile and platelet parameters Among Type 2 Diabetes Mellitus Patients attending at Durame General Hospital, Durame, Southeast Ethiopia: Comparative cross-sectional study.

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This is to certify that the thesis prepared by; Yazal Abay, entitled: **Assessment of Basic Coagulation Profiles and platelet parameters Among Type2 Diabetes Mellitus Patients Attending at Durame General Hospital, Southeast Ethiopia** and submitted in partial fulfillment of the requirements for Master of Science Degree in Clinical Laboratory Sciences (Hematology and Immunohematology) complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

Signed by Examining committee:

Examiner_____Signature_____Date_____

Examiner_____Signature_____Date_____

Advisor_____Signature_____Date_____

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Abbreviation

APTT	Activated partial thromboplastin time
BMI	Body mass index
CVD	Cardiovascular disease
DM	Diabetes mellitus
FDP	Fibrin degradation products
INR	International normalized ratio
MPV	Mean platelet volume
PDW	Platelet Distribution Width
PAI	Plasminogen activator inhibitor
PT	Prothrombin time
TF	Tissue factor
TPA	Tissue plasminogen activator
VTE	Venous thrombotic embolism
vWF	Von Willebrand factor

Abstract

Back ground: Diabetes mellitus is related with disturbances of hemostasis that could subsidize the occurrence of thrombogenic complications. Diabetic patients are exposed to thrombosis abundantly, followed by cardiovascular events, the rest from cerebrovascular events along with peripheral vascular complications, and these is accounted for most of diabetes morbidity, and mortality. The current study was carried out to determine the coagulation profiles of type 2 diabetes mellitus patients in comparison with apparently healthy controls.

Objective: To determine basic coagulation profiles and platelet parameters.

Methods: A comparative cross-sectional study was carried out at Durame General Hospital from June 2023 to January 2024. Socio-demographic and clinical data were collected using questionnaires and checklist. Platelet parameters were determined from EDTA anticoagulated venous blood using ADVIA 560 hematological analyzer, whereas coagulation analysis was done by using ARES LiNEAR coagulation analyzer fom citrated plasma. The data was analyzed using SPSS version 26 statistical software. Kolmogorov-Smirnov test was used to check the data distribution. Independent t-test was used to compare mean between groups, whereas the Kruskal Wallis test was used for comparison of different category in groups. Statistical significance was set at $P< 0.05$.

Result: There was significant shortening of prothrombin time (PT) (12.9±1.5, vs 13.5±1.3), ($p=0.02$), and International normalized ratio (INR) (1.08±0.16, vs 1.13±0.17), ($p= 0.04$) and significant increased of platelet count, MPV (12.1±1.9, vs 10.9±1.5, $p<0.001$), PDW (16.7±2.1, vs 15.5±1.8, $p<0.001$) cases compared to controls respectively. Platelet count showed a weak positive correlation with fasting blood glucose level ($r=0.26$, $p=0.02$).

Conclusion: The present study revealed reduced value of PT, and INR, and increased values of Platelet count, Mean platelet volume and Platelet distribution width among type 2 diabetic patients compared to apparently healthy controls. Thus, the finding is suggestive of hypercoagulable tendencies of diabetic patients compared to controls

Key words: T2DM, coagulation profiles, platelet indices

1. Introduction

1.1 Background

Diabetes mellitus is group of genetically heterogenous metabolic disorders that causes for glucose intolerance, connected with impaired insulin secretion and action. The diseases affects how the body uses blood sugar (glucose), which is induced by both genetic, and environmental factors[1]. Diabetes mellitus is grouped to depends on its origin and clinical manifestation. Type one diabetes, type two diabetes, pregnancy induced(gestational), and variants of other specialized classes of diabetes mellitus[2].

Type two diabetes, is also called non-insulin dependent diabetes, is supposed to be more common form of the illness, comprises approximately 90% of all cases of diabetes, and its onset is a long-term process with a latent stage that lasts for around decades before the disease clinical presentation[3, 4]. Diabetes can be diagnosed by using laboratory test if the following criteria meet, fasting plasma glucose level greater than 126 mg/dl(≥7.0 mmol/l) or two-hour plasma glucose level greater than 200 mg/dl (≥11.1 mmol/l) following a 75g oral glucose load or a random glucose level > 11.1 mmol/l (200 mg/dl) or HbA1c ≥ 48 mmol/l [5].

The concept of blood coagulation dates back “Ratnoff and Macfarlane” explains that waterfall and cascade theories sketch the basic principle for pathway of pro-enzymes tends to activation of moving in the direction toward lower a stream of enzymes[6]. Coagulation is dynamic process, and comprehending of the coagulation system has derived over the recent years in in versatile health conditions. In spite of the fact that, the classical division of the system into intrinsic, and extrinsic path is up-to-now valid, the newer insights into coagulation layout more authentic elucidation[7].

Coagulation encompasses both cellular mainly platelet and soluble protein components. The platelets are activated by vascular injury and aggregate at the injured site. Whereas the soluble proteins are activated by a series of proteolytic reactions of coagulation pathway, resulting in a fibrin clot[8]. The prothrombin time (PT), activated partial thromboplastin time (APTT) tests are commonly used to identify defects of the extrinsic, intrinsic, and terminal common pathway of the coagulation process[9].

Diabetes is characterized by a series of alterations unequivocally results in a thrombophilic state in patients with this disease. This is indicated by many epidemiological studies which indicate that diabetic patients more rapidly develop a thromboembolic events[10]. Hyperglycemia and insulin insensitivity cause changing in number of platelets and activation, as well qualitative and quantitative alteration of coagulatory and fibrinolytic factors, leading to fibrinolysis-resistant clots in patients with diabetes[11].

Persistent hyperglycemia in diabetics exposes red blood cells(RBC) to elevated amount of glucose, resulting in glycation of clotting factors, and it affects the hematological/hemostatic status[12]. Moreover, patients with diabetes could show thrombophilia and high levels of coagulation factors, including both type one and type two, which is due to upregulation of coagulation factors and prolongation of clot lysis, and rising of concentration of clotting factors is pronouncedly reported in type 2 diabetics[13, 14].

The thrombotic propensities occurred, because of platelet reactivity and an enhanced activation of prothrombotic clotting factors, such as VII, VIII,X, XI, and XII, simultaneously with declined of anticoagulant protein C level and the deterioration of the fibrinolysis process[15]. The Anomalies observed involves in all stages of coagulation, affecting both generation of thrombus and its hindrance, fibrinolysis, platelet and endothelial function. Hyperglycemia probably determine the these abnormalities through process of non-enzymatic glycation[16].

1.2 Statement of problem

Type two diabetes mellitus (T2DM) is suddenly raising important global health trouble, closely associated with the epidemics of overweight, and which is high risk for both micro, and macrovascular complications, owing to hyperglycemia, and individuals insulin resistance (metabolic) disorder [17]. It is presumed that changes in human behavior, and environment are favoring rapid increment in the number of obese diabetic individuals[3]. Type two diabetes should be inspected, and treated as a heterogeneous disorder with multiple pathophysiological abnormalities, varying susceptibility to complications and diverse clinical response to therapeutic intervention. Ultimately, to cure for T2DM will require corroborate of its molecular etiology and effective intercessions to combat the obesity epidemic[18]. Diabetic patients around 80% die as a result of thrombosis, with 75% of the deaths results from cardiovascular effects, the rest come up from peripheral vascular complications events as well as cerebrovascular. These complications related with diabetes are responsible for most of its morbidity, and mortality[19].

Worldwide rise of incidence and prevalence of type 2 diabetes has raised suddenly as a result of urbanization and changes in life style. As global burden increment of diabetes is appraised to 9.3% (463 million people) in 2019 and rising to 10.9% (700 million) by 2045[20]. In marvelous 79% deaths due to diabetes in Africa occurred among people below the age of 60. International Diabetes Federation (IDF) estimated that large number of diabetic people in Africa going to raise from 14.2 million in 2015 to 34.2 million in 2040, and More than half of the adults in Africa live in some of the regions of densely populated countries, South Africa, Democratic Republic of Congo, Nigeria and Ethiopia [21].

For sub-Saharan Africa, type two diabetes prevalence is predicted to elevate from 1.1% in 1995 to 1.3% in 2025, from an estimation of 3 million subjects to 8 million[22]. The increased disease burden is a challenge to the healthcare systems of poor countries lacking of sufficient resources as they demand to invest in systems, train healthcare workers who will be in a position of personnel of chronic diseases[23].

As being said type two diabetes mellitus is a threatening metabolic disorder that is usually related with various vascular abnormalities, there are 1.9 million people alive with diabetes in Ethiopia; which is found to be the ninth foremost cause of mortality linked to its complications.[24]. Diabetes mellitus is currently emerging as an important public health problem in Ethiopia, a systematic review study in (2021) revealed that compiled prevalence of DM in Ethiopia was resulting to 6.5% (95% CI (5.8, 7.3)[25].

The colossal death and ailment occurred with patients of diabetes mellitus specially in type 2(non-insulin dependent) diabetes is the result of both micro and macro-vascular occlusive disorder in which thrombosis play vital role an important part of complication[26].

Many studies have shown a variety of diabetes mellitus is associated with aberrations in hemostasis and thrombosis. Venous thrombosis has been found to be happen more often in diabetic patients. Coagulation begins almost instantly after an injury to blood vessel has damaged the endothelium. Lying open of the blood proteins such as tissue factor initiates changes to blood platelets, a clotting factor and the plasma protein fibrinogen[27].

Diabetes mellitus is accompanied by principal modification in all aspect of hemostasis. Vascular endothelium, platelet, co-factors and coagulation factors, the natural anticoagulant as well as fibrinolytic pathway are unfavourably affected. The levels of coagulation factors elevated in diabetes, whereas levels of naturally occurring anticoagulants such as antithrombin, protein C and S are reduced and rising level of plasminogen activator inhibitor type-1 which decreases fibrinolysis; thus conducive of diabetes results for prothrombotic state[19].

There is paucity of data on coagulation profile among diabetic patients in Ethiopia. Moreover, studies reported contradictory results on coagulation profiles in diabetes mellitus patients; some imply hypercoagulable state while others revealed normal coagulation status. Thus, the current study aimed to assess the basic coagulation profiles and platelet parameters among type 2 diabetes mellitus patients in comparison with apparently healthy individuals in southeast Ethiopia [28, 29].

1.3 Significance of the study

The paramount importance of study is to indicate the clinical significance of basic coagulation tests in diabetes management and its ability to predict the development of complications, it helps to active preventive measures can be introduced. The observations made in our study can contribute in better understanding of relationship between type 2 diabetes, and coagulation profile.

Hence, data from this study could be helpful in order to predict the complications as early as possible to prevent other fatal outcomes and improve the life style of those patients before getting 5worse management with diabetes. The current study can be serve as an input for further studies that will be conduct for the future investigators and it supports to provide a source of updated information.

1.4 Conceptual frame work

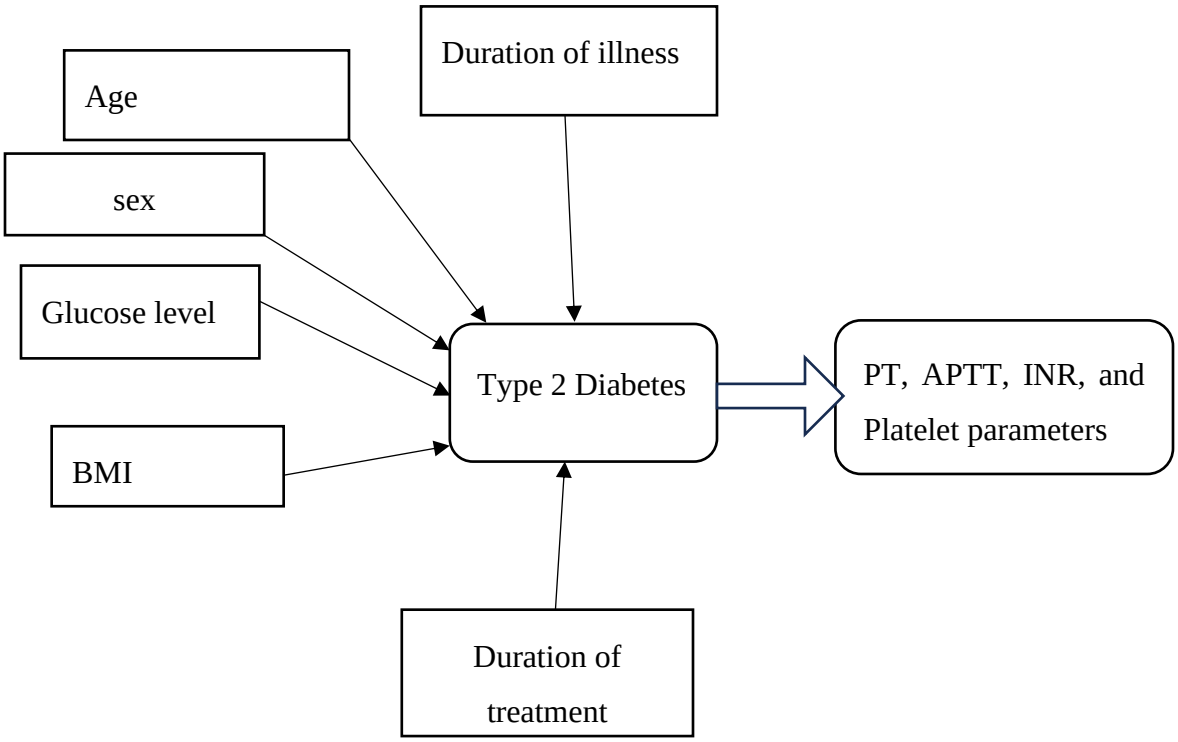

Figure 1. Conceptual framework to determine basic coagulation profiles and platelet parameters in type 2 diabetic patients and controls.

2. Literature review

2.1 Type 2 Diabetes and basic coagulation profiles

Diabetes considered as a global health concerned disease, it was committed by the World Health Organization (WHO) and patients with diabetes might have a hypercoagulable state, and retarded fibrinolysis state. There is plenty of studies about heart, and vascular effects on diabetic patients, but limited about the clotting system[30]. Diabetes come to have epidemic character due to large increase in number of individuals affected, over recent decades and related mortality is linked with thrombotic events peculiarly cardiovascular[31]. Areas particularly affected by this disease China and India, where the prevalence of T2DM has increased dramatically, despite the relatively reduce their obesity and Asians inclined to have a higher percentage of body fat mass, greater abdominal obesity and low muscle mass[32].

Based on the comparative study in panata, the finding of activated partial thromboplastin time (APTT) and prothrombin time (PT) in patients with type two diabetics as compared to the control group. Accordingly prothrombin time in type two diabetes mellitus was shortened as compared to non- diabetic Population, whereas APTT is slightly prolonged in type 2 diabetes mellitus[33]. A cross-sectional study in Odisha, India (2024), underlines the association between diabetes mellitus and altered coagulation profiles, emphasizing importance of routine PT and APTT assessments. Effective glycemic control is not only pivotal in managing diabetes but also plays a crucial role in mitigating prothrombic states [34].

To compare the haemostatic profile of T2DM patients and control participants of diabetic patients attending at S.S.G. hospital diabetic clinic in India (2020), revealed that mean prothrombin time for diabetic patients was significantly lower than mean of control participants. While mean of activated partial thromboplastin time for diabetic patients was significantly decreased than mean of control participants[35]. Likewise, study in Lahore Pakistan (2021) as reported to measure of variations in PT, APTT and Platelet count and their correlation with glycated hemoglobin in type 2 diabetes mellitus. Activated partial thromboplastin times (APTT), and Prothrombin time (PT) were significantly lower in type two DM patients, and platelet count was slightly higher in T2DM than the control group [36].

Patients with T2DM and healthy controls of hemostatic parameter was studied in Iraq(2022), and the finding showed that, when cases compared to controls, patients with type 2 diabetes had significantly shorter activated partial thromboplastin times (APTT), lower platelet counts, higher levels of fibrinogen, and D-dimer(D-D)[37]. As stated the study in Bangladesh (2015) coagulation impairment in type two diabetes mellitus activated partial thromboplastin time (APTT), and prothrombin time (PT) were illustrated shortened values in diabetes mellitus in contrast to control group, and there was strongly statistical significant difference[38].

According to the study conducted in Nepal (2013) a comparative study of diabetic patients have relatively reduced APTT as compared to healthy controls, so this result might reflect prothrombic state, which is linked with elevated thrombotic risk and adverse heart and blood vessel events.[39]. While the study at Gulf of Sidra University in Libya (2022) divulged that diabetes mellitus had no effects on PT, APTT, and platelet count compared to the control group [40]. Based on comparative method of study which was done at university of Ilorin in Nigeria(2021), the mean prothrombin time was greater in the cases than the controls, and it was significant, whereas, Platelet count, INR, and activated partial thromboplastin times (APTT) did not revealed significant differences observed [41].

Similarly, a case control study indicated, prothrombin time (PT), international normalized ratio (INR), and activated partial thromboplastin time (APTT) were significantly reduced results among patients of type two DM compared to those of controls. On the other hand, there was insignificant difference found in platelet counts of cases and controls [42].

The study conducted in Khartoum state Sudan (2015) revealed that insignificant prolongation of PT and APTT was observed in patients compared to control but within normal range. So, PT and APTT was increased in control than diabetic patients[43]. However, investigations illustrate in Atbara Eastern Sudan (2021) significantly shorter means of PT, APTT, and INR among type two diabetics in contrast to controls[44].

Descriptive analytical cross-sectional study was employed to recruit participants study in Kenya (2021) the mean PT for the diabetics was (12.726±1.3070 seconds), while the PT of normal group was (12.487±1.0157 seconds) but there was no statistically significant difference; low degree of correlation between patient's INR and normal group INR. The mean INR for the diabetics was greater than normal group, and not showed statistically significant difference. Similarly the mean APTT for the diabetics was lower than that of normal group but having no statistically significant difference[45].

As a report of a comparative study denotes that prothrombin time (PT), and international normalized ratio (INR) indicated to significantly decreased in type two DM contrast to type one DM, and apparently healthy controls. However, mean platelet volume (MPV), and Platelet distribution width (PDW) were significantly higher in both type one and type two DM compared to apparently healthy individuals. Besides, fasting blood glucose (FBG) negatively correlated with PT and INR in type one DM. Whereas APTT, PT, and INR were negatively correlated with fasting glucose in type two diabetics[29].

In accordance to the report in Ethiopia, a comparative cross-sectional study exhibits the hemostatic alterations in diabetic patients was found to be high. The APTT and platelet count were lower in diabetic patients whilst the fibrinogen level was higher, and prothrombin time (PT) did not demonstrate significant difference between comparison of diabetics to controls [46].

2.2 Type 2 diabetes mellitus, and platelet parameters

Platelets play vital role for synthesis of thrombosis, various studies that had been carried out in order to associate clotting abnormalities were related to platelet functions, which could change platelet metabolism, and platelet signaling path finally causes to impaired of many metabolic process[47]. Based on case-control study report by Waghale R. et al (2020). MPV, PDW, P-LCR increased in diabetic subjects, and these were found significantly elevated in diabetic patients compared to controls, that can be used as signpost of subclinical atherosclerosis, and predictor of future cardiovascular events in T2DM [48].

According to a prospective case control study in India (2018) platelet parameters PDW, P-LCR, and MPV were done on 280 cases of diagnosed with type two diabetes mellitus, and 280 healthy controls with euglycemic blood glucose levels. PDW, P-LCR, and MPV were greater, and significant in diabetics as opposed to controls[49].

A case-control study was carried out in northern India (2021) platelet indices mean platelet volume, plateletcrit, platelet large cell ratio (P-LCR), and platelet distribution width (PDW) were increased with significant variation in diabetic individuals compared to healthy control. Study in Saud Arabia (2023) Platelet count and plateletcrit (PCT) were comparable in patients and controls without significant difference. Conversely, Mean platelet volume (MPV), and platelet distribution width (PDW) were significantly lower in patients compared to controls, whereas platelet large cell ratio increased significantly in comparison of type two DM over those of healthy controls[50].

A Comparative study of the apparently healthy age, and gender-matched controls was conducted in Nigeria(2022) to evaluate selected platelet parameters in type two diabetics (T2DM) patients in contrast to healthy individuals, the values of the platelet indices revealed significant increase in platelet distribution width (PDW), mean platelet volume (MPV), and the plateletcrit (PCT) in the type two DM compared with corresponding controls, and these finding could supports platelet activation in type two DM patients[51].

A cross-sectional study was carried out in Ethiopia (2021) among 352 type two diabetes patients PDW, MPV, and P-LCR were larger and significant in type two diabetes with microvascular complications to those of non-complicates[52].

From the overall literatures included in this study many studies of coagulation profile disclose statistically significant lower/shortened values of coagulation parameters in diabetic patients than the corresponding controls. Whereas the rest of studies show statistically insignificant differences. Studies of platelet parameters among type two DM patients demonstrated that significantly higher value than controls, while few studies display significantly lower and remained closely related result in diabetics than controls.

3. Objective

3.1 General objective

- To determine basic coagulation profiles and platelet parameters between type two diabetic patients and apparently healthy controls at Durame General Hospital Southeastern Ethiopian from June 2023 to January 2024.

3.2 Specific objective

- To compare basic coagulation parameters (PT, INR, and APTT) of type two diabetes patients and controls.
- To compare platelet parameters of type two diabetic patients and controls.
- To investigate the relationship between coagulation profiles, and fasting blood glucose level

4. Hypothesis: Ho: There is no significant difference of coagulation profiles between type two diabetes, and healthy individuals of control group.

5. Method and materials

5.1 Study area

The study was conducted at Durame General Hospital, Durame is a town in Southeastern Ethiopia, located in the region of southern nations, nationality and people. The town is located 343 kilometers south of Addis Ababa and 139 kilometers far from Hawassa. Durame general Hospital (DGH) is established in 1998, and provides service for approximately 1.5 million people in its catchment area. The Hospital is found at Durame town the capital of Kembata zone and it serves as referral hospital for all seven woredas. The hospital has four wards (surgical, obstetrics and gynaecology, pediatrics and medical) it gives service for outpatient, and inpatients.

5.2 Study Design, and Period

A Comparative cross-sectional study was conducted from June 2023 to January 2024 at Durame General Hospital, Durame southeastern Ethiopia

5.3 Population

5.3.1 Source population

- For case group: All type two diabetic patient attends at Durame General Hospital.
- For control group: All apparently healthy clients who visited to Durame General Hospital for medical and master health check-ups.

5.3.2 Study population

- Case-group: Type two diabetic patient who attended the hospital during study period, and willing to take part in the study.
- Control-group: Apparently healthy clients visit hospital during study period who were willing to take part in the study. Those were medical, and master health check-ups.

5.4 Eligibility criteria

5.4.1 Inclusion criteria

- Case group: Type two diabetic subjects of adult age groups giving consent, since one-year undertreatment.
- Control group: Apparently healthy subjects of adult who are matched to case groups and giving consent.

5.4.2 Exclusion criteria

For both cases and control group:

- Patients who take oral anti-coagulant, anti-platelet and fibrinolytic drug therapy
- Pregnant women.
- Women use oral contraceptives
- Patients who had recent history of surgery
- Patients had history of chronic illness (malignancy, hypertension, chronic kidney disease, Liver disorder).
- Alcoholism
- smoking
- Immobility problem

5.5 Study variables

5.5.1 Dependent variable

- Prothrombin time (PT),
- International normalized ratio (INR)
- Activated partial thromboplastin time (APTT)
- selected platelet parameters.

5.5.2 Independent variable

- Age
- Gender
- Marital state
- Residence

- Occupational status
- Educational level
- Duration of illness
- Blood glucose level
- BMI

5.6 Measurement and Data collection

5.6.1 Sample size determination

Sample size calculations was done by using sample size determination formula for comparison of mean between two groups when the endpoint is quantitative. APTT value is taken from a similar study conducted in Felege Hiwot Hospital, northwest Ethiopia [28].

$$\frac{2(SD)^2(Z\alpha/2 + Z_b)^2}{(d)^2}$$

$Z_{\alpha/2} = Z_{0.05/2} = Z_{0.025} = 1.96$

$Z\beta = Z0.20 = 0.84$ at 80% power

Where, n= desired sample size, Sd= Standard deviation, d= mean difference

$$n= \frac{2(4.12)^2.(1.96 + 0.84)^2}{(1.61)^2}$$

n= 102 per group

Therefore, the size of sample of this study calculated value is 204 (102 case group versus 102 for controls).

5.6.2 Sampling technique

Non-probability convenient sampling technique was used to recruit study participants.

5.6.3 Data collection procedure

The data was collected after informed consent obtained from participants for procedure. Then clinical history was collected without breaching the confidentiality of the patient and information was attained from chronic outpatient department. Socio-demographic data was collected through self-administered questionnaire for those who can read and face to face interview for who cannot read. The respondent reads the questions and filled answers by him/herself in the presence of an interviewer to give assistance.

Measurements of anthropometrics was done for every study participant and the assessment was performed by a calibrated instrument.

Body mass Index: It is measured by the ratio of weight to height square. The measurement tool used was standardized and calibrated IDA balance. The height measurement used calibrated and have good standard meter measurement. Body mass index (BMI) was calculated by the WHO recommended formula; BMI equal to weight per height square

Blood pressure: Blood pressure was measured by instrument sphygmomanometer (riester). These was well standardized, it meets to the Association for the Advancement of Medical Instrumentation (AAMI) standard protocol, and large adult cuff used.

5.6.4 Principle and measurement of Laboratory Analysis

The sample was venous blood taken from the study participants, using EDTA tube for platelet parameters test, citrated plasma was used in coagulation analysis, and using serum separator tube (SST) for glucose measurement. Hematological analyzer was Siemens ADVIA 560 and it can perform 26 parameters including 5-part differential with histogram, and scattergrams for RBC and PLT. Working principle of Siemens hematological analyzer is Laser light scatter technology for 5-part WBC differential, and impedance method of complete blood count (CBC) Light absorbance for Hb measurement.

Coagulation analyzer (ARES LiNEAR) was used, and its measurement principle is photo-optical. Fibrinogen converts into fibrin and form clotting; changes of the turbidity during the formation of fibrin clot is measured as an increase in scattered light intensity when exposed to light at a wavelength (470nm). and the analyzer can detect the coagulation end-point in seconds. Blood is drawn into a test tube containing sodium citrate, which acts as an anticoagulant through binding to calcium blood[53].

Glucose measurement principle: chemistry analyzer is semiens X200 dimension, The accurate measure of glucose is required for the diagnosis and management of hyperglycemia. Working principle is through enzyme hexokinase (HK) which catalyze the reaction between adenosine triphosphate (ATP), and glucose to form glucose-6- phosphate, and adenosine diphosphate (ADP). In the presence of NAD, the enzyme glucose-6-phosphate dehydrogenase (G6P-DH), oxidizes glucose-6-phosphate to 6-phosphogluconate. Increased NADH concentration is directly proportional to the glucose concentration, and can be measured at 340 nm spectrophotometrically [54].

5.7 Data Quality assurance

The data for the purpose of this research was collect by the principal investigator, and with assistance of staffs in working area. Laboratory tests for complete blood count (CBC), and coagulation profile test were performed in hematology department and glucose test analysis was done in chemistry department.

In the pre analytical phase: The occurrence of errors is mainly happened in pre analytical phase and it is crucial steps to assure quality. Patients sample collected by experienced phlebotomist, and transported to analysis section, and Samples were properly labelled with corresponding patients ID number. Adequate sample volume for analysis, preventing hemolysis, sample shipment time to be processed was monitored. Main issues in coagulation, Platelet poor plasma and impact of anticoagulant proportionality was considered.

Analytical phase; to enhance accuracy of result quality control of sample was run and checked; tests were performed by trained laboratory technologist. Siemens recommends that ADVIA 560 Hematology System should be monitored using the ADVIA 560 Controls (Low, Normal, and High). Control materials was assayed at the beginning of each shift or at some other interval chosen by the laboratory, after a reagent lot number change, and after replacement of any part or component of the analytical module that may affect analytical performance.

Coagulation controls.

Following manufacturer's instructions for reconstitution and stability of coagulation analysis, and controls are run at the beginning of shift. If quality control is out, repeat the test.

Post analytical phase; proper recording, result interpretation using their reference range and cross check the result with its correspondent labeling was performed. Data was checked before results recorded. All laboratory procedures were performed through strictly following standard operating procedures (SOP). Remark flagging values.

5.8 Data analysis and interpretation

The Data were coded, entered, and cleaned via Microsoft Excel and transferred to SPSS version 26 for analysis. Basic descriptive analysis means, standard deviation as appropriate was done. Distribution was tested analytically, and graphically. The most common analytical tests to check data for normal distribution, Kolmogorov-Smirnov tests was used. Data was checked for completeness, discerned, and entered in to SPSS version 26. In order to compare means between group, independent t-test was used, and Kruskal-Wallis was used for comparison of different category in groups. Statistical significance of results was designed at ($P< 0.05$).

5.9 Ethical consideration

All the study procedures, and issues were reviewed, and approved by the Ethics Committee of Addis Ababa University College of Health Science, Department of Medical Laboratory Sciences, Department of Research, and Ethics Committee (DRERC/728/23). Support letter was written to Durame General Hospital to get permission to start study. Informed, and written consent was attained from each of the participants at the time of enrollment for study, and risk of harm, confidentiality, anonymity, and conflict of interest was considered and kept. Hence, all these ethical issues were managed.

5.10 Dissemination of result

Result will be distributed to Addis Ababa Univrsity college of health science on its research depository catalogue, and hard copy shelving; then, serious attempts will be made to publish paper in peered review of good repute journals. The responsible, and concerned government bodies could use this material in the advancement of community health as part of utilization plan.

5.11 Operational definition

Apparently healthy controls: an individual with physical well-being, and physiological status, without detectable diseases or infirmities.

Coagulation profile: A coagulation profile(coags) includes, PT, INR, APTT, platelets, and fibrinogen. It is a screening test for abnormal blood clotting.

6. Results

6.1 Sociodemographic characteristics of participants

A total number of 204 adults with T2DM and healthy individual controls met inclusion criteria were selected. Among participant of this study with 102 cases and 102 controls. Determination of basic coagulation profile and platelet parameters were carried out on all type two diabetic patients, and healthy controls included in the study. Thus, based on gender frequency, females constituted 45.6%, and males about 54.4% from overall. There was no statistically significant difference among gender, residence, educational level, and marital status of diabetic patients and control groups. Mean age of the case groups was 48.4±8.7 and controls was 46.8±8 years, respectively, revealing insignificant disparity between the cases and controls. The majority of participants belongs to 41-50 years age category (41.2% among cases and 45.1% among controls), followed by 31-40 years (19.6% among cases and 24.5% among controls). Residence distribution of our study participants in urban were 75.5% of case group and 70.6% in control, while in rural 24.5% in case group and 29.4% in control groups. (Table 1).

Table 1. Sociodemographic characteristics of the study participants at Durame General Hospital, Southeast Ethiopia, 2024 (N=204)

Variables	Case group		Control group		
	Frequency(N)	Percentage	Frequency(N)	Percentage	P value
Gender					
Male	54	52.9%	57	55.9%	0.78
Female	48	47.1%	45	44.1%	
Age group					
18-30	3	2.9%	4	3.9%	0.19
31-40	20	19.6%	25	24.5%	
41-50	42	41.2%	46	45.1%	
51-60	25	24.5%	20	19.6%	
>=61	12	11.8%	7	6.9	
Marital status					0.39
Married	92	90.2%	84	82.4	
Unmarried	6	5.9%	15	14.7	
Divorced/widowed	4	3.9%	3	2.9%	
Residence					
Urban	77	75.5%	72	70.6%	0.53
Rural	25	24.5%	30	29.4%	
Occupation					
Employed	23	22.5	16	15.7	0.132
Self employed	46	45.1	44	43.1	

Others	33	32.4	42	41.2	
Educational status					
No formal education	31	30.4%	38	37.3	0.33
Primary school	33	32.4%	32	31.4	
Secondary school	21	20.6%	19	18.6	
Tertiary education	17	16.7%	13	12.7	

6.2 Clinical information of study participants

The study revealed that 54.9% diabetic patients had history of diabetes of 1–5 years and 57.8% diabetic patients were taking antidiabetic medications during this year. The most frequent duration of illness and treatments were belonged to less than five years, which is followed by 6-10, and the least frequent was greater than 10 years. Body Mass Index (BMI), diastolic blood pressures (DBP), and systolic blood pressures (SBP) showed significant difference between the case and control group((P<0.001) (Table 2)

Table 2. Clinical information of type 2 diabetes and control at Durame General Hospital, Southeast Ethiopia, 2024 (N=204)

Variables	Frequency	Percentage	P -value
Duration of illness			
<5	56	54.9%	
6-10	35	34.3%	
>10	11	10.8%	
Treatment duration			
<5	59	57.8%	
6-10	35	34.3%	
>10	8	7.8%	
	Mean±SD (cases)	Mean±SD (controls)	
BMI	24.4±3.1	21.9±1.9	<0.001
SBP	123.7±9.2	116.3±9	<0.001
DBP	81.5±6.1	78.1±6.5	<0.001

Independent t-test was used

6.3 Comparison of basic coagulation and platelet parameters of type 2 DM and control groups.

The mean prothrombin time (PT), (12.9±1.5 vs 13.5±1.3) and international normalized ratio (INR) (1.08±0.16, vs 1.13±0.17) were significantly reduced among diabetics compared to control. Whereas, the platelet counts (238.4±54.2 vs 216.9±41.8) mean platelet volume (12.1±1.9 vs 10.9±1.5), and platelet distribution width (16.7±2.1 vs 15.5±1.8) were significantly larger in T2DM compared to controls. Activated partial thromboplastin time (37.2±5.7 vs 35.8±4.8) showed no significant difference among cases and controls(P=0.072) (Table 3)

Table 3. Comparison of basic coagulation and platelet parameters between cases and controls of study participants at Durame General Hospital, Southeast Ethiopia, 2024 (N=204).

Parameters	Case-Group (M±SD)	Control-Group (M±SD)	P value
FBS	145.9±34.2	87.7±10.9	<0.001
PT (sec)	12.9±1.5	13.5±1.3	0.02
INR (sec)	1.08±0.16	1.13±0.17	0.04
APTT (sec)	37.2±5.7	35.8±4.8	0.072
Platelet count 10^3/ul	238.4±54.2	216.9±41.8	0.03
MPV fl	12.1±1.9	10.9±1.5	<0.001
PDW fl	16.7±2.1	15.5±1.8	<0.001

Independent t-test was used for comparison.

Significance level at P<0.05

6.4 Gender based distribution of basic coagulation profile and platelet parameters

In this study, the basic coagulation profiles and MPV did not demonstrate significant difference between male and female participants of the case and controls groups. On the other hand, statistically significant variation of platelet distribution width (15±1.4, P=0.02) and platelet count (209.8±36.8, P=0.04) were observed between genders in the control group (Table 4).

Table 4. Basic coagulation profile and platelet parameters on the basis of gender difference of type 2 diabetes and controls at Durame General Hospital, Southeast Ethiopia, 2024 (N=204).

Parameters	Diabetics group			Controls		
	Male (Mean±SD	Female (Mean±SD)	P value	Male (Mean±SD)	Female (Mean±SD)	P value
PT, sec	12.8±1.5	13.1+1.4	0.3	13.6±1.3	13.5±1.3	0.78
INR	1.07±0.16	1.08±0.17	0.86	1.15±0.16	1.14±0.15	0.82
APTT, sec	37.5±5.5	37±6.1	0.68	35.9±5.1	35.9±4.5	0.99
Platelet count 10^3/ul	234±57.4	235.5±50.8	0.88	227.7+47.6	209.8+36.8	0.04
MPV, fl	12.2±1.8	11.8±2	0.36	11.1+1.7	10.7+1.3	0.2
PDW, fl	16.8+2.1	16.4+2.2	0.36	15.9+1.9	15+1.4	0.02

Independent t-test was used

Significance level at P<0.05

FBS, Fasting Blood Sugar, PT, Prothrombin Time, APTT, Activated Partial Thromboplastin Time, INR, International Normalized Ratio, plt count, platelet count, MPV, mean platelet volume; PDW, platelet distribution width, fl, femto litre

6.5 Correlation of blood glucose level with coagulation profiles, and platelet parameters

Correlational analysis gives out that no significant relationship of fasting blood glucose (FBS) with basic hemostatic variables PT, INR, and APTT. Similarly, platelet parameters mean platelet volume, and platelet distribution width did not indicate significant differences with exception of weak positive correlation between glucose level, and platelet count (r= 0.26, p=0.02) in case groups, and PT value in control groups (r=0.22, p=0.03) (**Error! Reference source not found.**).

Table 5. Correlation of blood glucose level with basic coagulation profiles, platelet parameters, BMI, and blood pressure of type 2 diabetes and controls at Durame General Hospital, Southeast Ethiopia, 2024 (N=204).

Variables	FBS			
	Case group		Controls	
	r	P value	r	P value
PT (sec)	-0.053	0.6	0.22	0.03
INR (sec)	0.004	0.96	0.1	0.31
APTT (sec)	-0.12	0.23	-0.06	0.58
PLT count $10^3/\mu L$	0.26	0.007	0.04	0.6
MPV fl	0.036	0.72	-0.07	0.5
PDW fl	0.11	0.29	-0.006	0.96
BMI	0.09	0.34	-0.82	0.41
SBP	-0.004	0.96	-0.79	0.43
DBP	0.12	0.22	0.75	0.45

r = Pearson correlation coefficient

P value level of significance is at $p<0.05$

6.6 Basic coagulation profile and platelet parameters according to glycemic level

On the basis of glycemic controls of less than and greater or equal to 130 mg/dl glucose level comparison of basic coagulation tests and platelet parameters was done. Among platelet parameters, platelet count results illustrated that statistically significant difference (U = 1002. P= 0.001). However, basic coagulation profiles PT, INR and APTT, mean platelet volume and platelet distribution width did not show statistically significant difference.

Table 6 Comparison of basic coagulation profile and platelet parameters according to glycemic level at Durame General Hospital, Southeast Ethiopia, 2024 (N=102).

Parameters	Median +IQR	P value
PT	12.7±1.6	0.14
INR	1.1±0.24	0.77
APTT	36.7±9.7	0.32
PLT count	223±76	0.001
MPV	12.3±2.9	0.33
PDW	16.6±2.9	0.23

Mann Whitney U-test was used

Significance level is $p< 0.05$

6.6 Relationship between basic coagulation profiles and platelet parameters with duration of illness.

The coagulation profiles across the different durations of diabetic illness was evaluated using Kruskal Wallis test. Accordingly, the PT value showed significant difference among patients with diabetes for less than 5 years, between five and ten years, and above ten years (H=8.5, df=2, p=0.014). Pairwise comparison result revealed significant difference among those with diabetes for less than five years and more than ten years as well as between six to ten years and above ten years. (<5->10, p=0.011, 6 to10->10, P=0.04) (Table 7).

Table 7. Relationship between basic coagulation profiles and platelet parameters with duration of illness among type 2 diabetes at Durame General Hospital, Southeast Ethiopia, 2024 (N=204).

Variables	Duration in year	Mean rank	P value
PT, sec	<5	52.5	0.014
	6-10	57.3	
	>10	27.6	
INR, sec	<5	50.2	0.33
	6-10	56.5	
	>10	42.1	
APTT, sec	<5	52.2	0.11
	6-10	55.6	
	>10	34.5	
Platelet cout/ 10^3	<5	52.9	0.3
	6-10	45.5	
	>10	62.0	
MPV fl	<5	47	0.22
	6-10	58	
	>10	52.8	
PDW fl	<5	52.3	0.78
	6-10	52	
	>10	45.6	

Kruskal Wallis test was used.

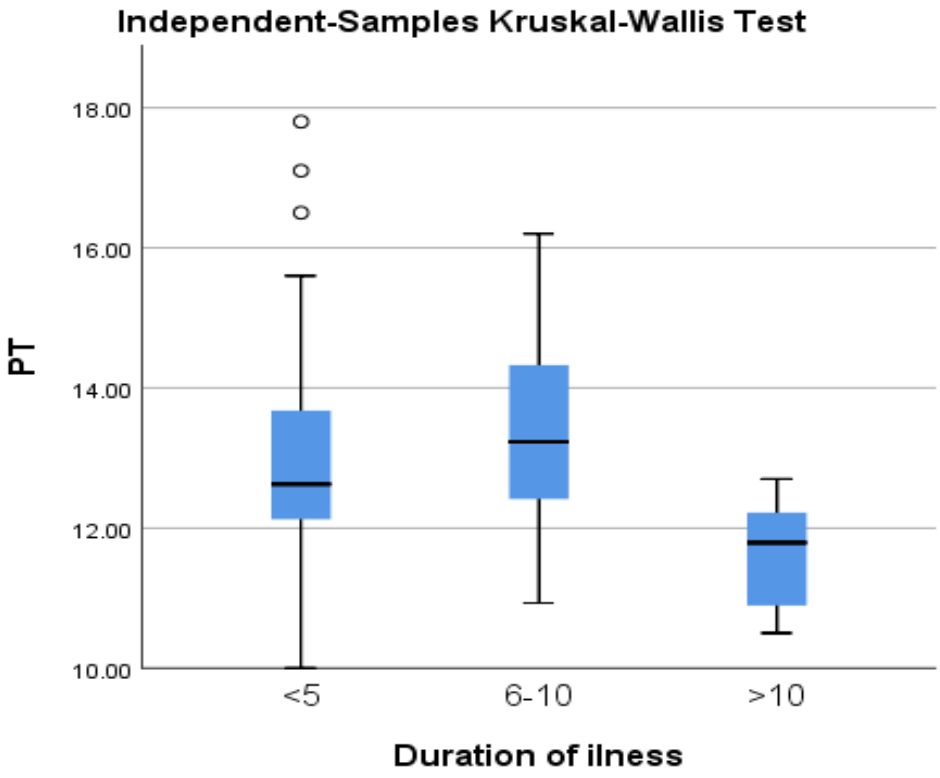

Figure 2. Independent samples Kruskal wallis test of PT with duration of illness

Table 8: Relationship between basic coagulation profiles and platelet parameters with duration of treatment among type 2 diabetes at Durame General Hospital, Southeast Ethiopia, 2024 (N=102).

The coagulation profiles across the durations of diabetic treatment was evaluated using Kruskal Wallis test. Accordingly, the PT value showed significant difference among patients with diabetes (H=7.5, df=2, p=0.024). Pairwise comparison result revealed significant difference among those between less than five and greater than ten, as well six to ten years and above ten years. (<5 and >10, 6 to 10 and >10 years, P=0.024)

Variables	Duration in year	Mean rank	P value
PT, sec	<5	53.11	0.024
	6-10	55.01	
	>10	24.25	
INR, sec	<5	49.75	0.17
	6-10	57.69	
	>10	37.38	
APTT, sec	<5	52.16	0.8
	6-10	51.91	
	>10	44.81	
Platelet cout/ 10^3	<5	53.17	0.44
	6-10	46.86	
	>10	59.50	
MPV fl	<5	46.86	0.18
	6-10	58.21	
	>10	56.31	
PDW fl	<5	52.59	0.74
	6-10	51.40	
	>10	43.88	

Kruskal Wallis test was used.

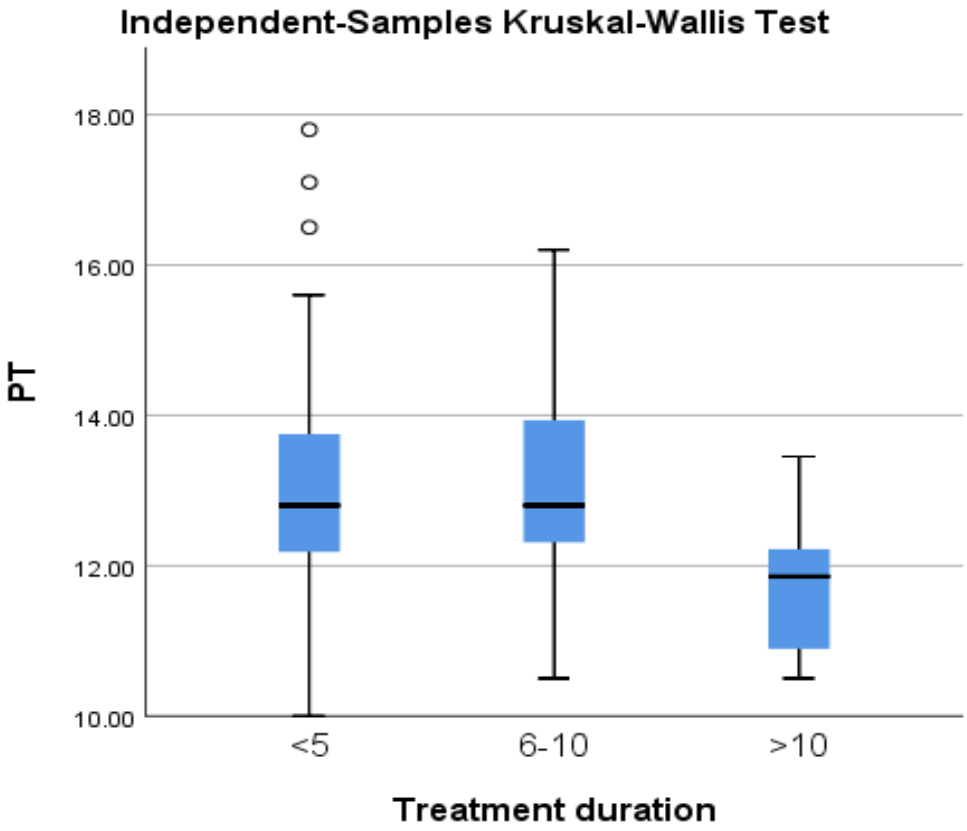

Figure 3 Independent samples Kruskal wallis test of PT with duration of treatment

7. Discussion

Diabetes mellitus affects numerous biological systems such as fibrinolytic, and coagulation system that are linked with changes of blood coagulability, including remodeling of clot structure, kinetics of clot formation and lysis[55]. People with the metabolic syndrome, as in type 2 diabetes, shows model of coagulation factors enhance of thrombosis or hinder thrombolysis, and it is attributed by heavy risk of atherothrombotic complications affecting the peripheral arterial trees, cerebral, and coronary[42].

The goal of the current study was to compare the coagulation tests in patients with type two diabetes, and healthy individuals. In diabetic patients of non-insulin dependence, there is structural damage and functional detriment of the endothelium, which has proven to be required for stimulating different clotting factors. It is presumed that high levels of von Willebrand factor (vWF) in DM indicate excessive activation of coagulation factors, which may results in shorter PT and APTT in diabetic patients than healthy control[36]. Many studies have shown that coagulation abnormality appeared in the course of diabetes mellitus, resulting in prothrombic condition, and this observation is believed that emanated by the hyperglycemia[56].The present study showed that significantly shortened PT, and INR values, while APTT showed insignificant variation between T2DM compared to controls.

On the other hand, significantly higher value of platelet count, mean platelet volume (MPV), and platelet distribution width (PDW) in type two diabetes compared to the non-diabetics. These findings could exhibit an increased predisposition to thrombotic events in type 2 diabetes patients over healthy controls. Our study finding was consistent with comparative study conducted in India, prothrombin time in diabetic patients is shortened as compared to non- diabetic controls with significant difference, whereas APTT did not show significant difference between type two DM and controls[33]. Similarly, Pandaya et al. reported decreased PT and INR among type 2 diabetics compared to non-diabetics [35].

Neverthless, the present study revealed the APTT value of Type two diabetes did not significantly differ from apparently healthy controls. This finding agreed with a similar study in Khartoum. [43]. The correlational analysis of the current study divulged to no significant difference in contrast, a comparative cross-sectional study in Ethiopia (2021) revealed a statistically significant negative correlation on fasting blood sugar with PT, INR, and APTT [29].

Von Willebrand's factor(vWF) is predisposing factor of thrombotic development in T2DM patients as endothelial dysfunction occurring as a result of hyperglycemia in T2DM patients lead to the disturbances in blood flow and the accumulation of vWF plasma concentration leads to increase the concentration of factor VIII and increased adherence of platelets to the sub-endothelial layer and hence promoting hypercoagulability[57]

The protraction of APTT might be as a result of in-vitro interference of fibrin clump generation through inhibitors, and it could be also occurred as a consequence of damage to the liver where majority of the clotting factors are synthesized. Thus, increased levels of APTT, and PT are consistent with aberrated coagulation mechanisms and can be interpreted as a propensity for bleeding [58]. A case control study in Terhan Iran hypothesized that decreased mean activity of Factor V and Factor VIII is cause for prolonged APTT in Non-Insulin Dependent Diabetic patients (NIDD), and also observed insignificant change in prothrombin levels of type 2 diabetics (12.48) and control (12.39)[59].

Unlike to the current study finding, the results of previous reports indicated that the levels of PT and INR did not show statistically significant difference between cases and healthy controls, whereas APTT was significantly shortened among cases compared to controls [60, 61]. Similarly, a comparative cross-sectional study in Libya reported no significant differences of PT value, and platelet count among diabetics compared to healthy controls[40]. Moreover, a case-control study in Kenya showed that, insignificant difference in PT and INR values among type 2 diabetics and healthy controls.[45].

The reasons for these contradictory results have not been satisfactorily explained and justified that need for additional studies. Balance of thrombosis and haemostasis in diabetes also depend on the effects of antidiabetic drugs varied effects on the process. Hence it is possible to said a combination of drugs in diabetes favorably affect thrombohaemorrhagic balance[62].

The present study showed significantly high value of mean platelet volume, platelet count, and platelet distribution width in type two diabetes contrasted to non-diabetic controls. Similarly, comparative study report, signified that platelet distribution width, and mean platelet volume in case group were significantly increased compared to the controls[63].

Additionally studies in consonance with our finding of MPV was larger in cases of diabetes as opposed to, prediabetics and diabetes free controls[64, 65]. Despite our study results of PDW, and Platelet count were significantly increased in cases compared to controls, in contrariwise comparative cross-sectional study revealed PDW and platelet count did not display significant variation in group of diabetes, and healthy control[66].

A case-control investigation in Ghana, in contrast to present study, notes insignificant difference of platelet count in type two diabetes and matched apparently healthy controls[42]. Moreover, antithetical to our study, Essawi K. et al. observed that Mean platelet volume, and platelet distribution width were low, and significant in type two diabetes compared to controls[50]. Previous report states in concordance with current study of correlation between fasting blood glucose with platelet indices, mean platelet volume, and platelet distribution width of diabetic patient revealed no significant difference[67].

The platelet volume indices, mean platelet volume is an indicator of average size, and activity of the platelets; it is reported to larger in diabetes and take it as a risk agent for heart disease. Similarly, PDW is an index of variation in platelet size which may be reflects a sign of active platelet release[68]. Platelet parameters in patients with T2DM point out significant differences, suggests to the presence of more aggregable, and reactive platelets in this set of individuals. Thus, platelet parameters assessment may be essential in the early detection of long-dawn complications in diabetic individuals, taking into considering that it is a simple and low-cost accessible diagnostic tool[69].

In general, variation of the coagulation test results (Platelet Count, MPV. PDW, PT, aPTT) observed among various studies could be owing to differences in size of sample, race, geographical region, and measuring instruments. The exact reason for the contradiction among different studies is not known explicitly yet.

8. Strength, and limitation

8.1 Strength

- This study determined platelet parameters alongside with basic coagulation profiles.
- Comparative study was employed, which is important for valid conclusion
- The current study used relatively adequate sample size.

8.2 Limitation

In present study, we found changes among type two diabetes patients and controls with some coagulation abnormality indicators, the clear mechanism of this relationship still needs to be explored. The current study was conducted by using screening methods of coagulation profiles only, and to evaluate specific factor assays, fibrinolytic tests, D-dimer, and fibrinogen were not integrated. The cross-sectional nature of study design, and coexisting factors of type 2 diabetes was not assessed in current study. Moreover, the study was limited to a single hospital; these sample might not be representative for the whole case to generalize the findings of the study.

9. Conclusion, and recommendation

9.1 Conclusion

This study demonstrated that PT and INR were both significantly shortened among diabetic patients compared to controls. Whereas platelet count, PDW, and MPV were significantly greater in diabetic patients compared to controls. These findings might suggest to hypercoagulable tendencies of diabetic patients compared to controls.

9.2 Recommendation

Our study disclosed that patients with diabetes have the tendency to manifest hypercoagulation state, despite the fact that mean results were under normal reference range. Global tests used to evaluate hemostatic system in clinical setting, examination of PT, APTT. and platelet parameters should be integral part to coagulation alterations weigh up in diabetic patients to keep thromboembolic event. As a result, additional biomarkers influencing hemostasis study is needed. Current study was limited to diabetic patients under treatment. However, there is a need to conduct studies on both newly diagnosed diabetics and those undergoing treatment independently.

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Annex

Annex I : Standard Operating Procedure

Standard operating procedure of blood collection (phlebotomy).

Equipment:

- Needle for each participant with closed vacutainer system
- Blood collection tubes for each participant
- Tourniquet
- Box of nitrile /vinyl gloves
- 70% Alcohol wipes
- Cotton balls/swabs
- Seat with comfortable elevation
- Disposable, single use materials or equipment are to be used whenever possible
- Any reusable materials or equipment must be cleaned and disinfected with Alcohol-based sanitizers before use with another participant Safeguards /safety procedures

Standard Operating Procedure Procedure for drawing blood

- Assemble equipment Collect all the equipment needed for the procedure and place it within safe pack which is simple for transport to collection site and place easy reach on a flat surface table ensuring that all the items are clearly visible.
- Identify and prepare the participants and allow to sit comfortably preferably be stretching his/her arm
- Perform hand hygiene and put on gloves
- Select the site of injection
- apply the tourniquet, and prepare the arm by swabbing the antecubital fossa with a gauze pad or cotton moistened with 70% alcohol.
- insert the needle properly into the vein
- draw the required amount of blood
- mix the sample properly
- Draw samples in the correct order and label the sample using unique code of participants
- Prepare samples for transportation

Standard Operating Procedure Glucose measurement analysis

Principle: chemistry analyzer is semiens X200 dimension, The accurate estimation of glucose is important in the diagnosis and management of hyperglycemia. working principle is via enzymatic hexokinase (HK) catalyzes the reaction between glucose and adenosine triphosphate (ATP) to form glucose-6- phosphate and adenosine diphosphate (ADP). In the presence of NAD, the enzymeglucose-6-phosphate dehydrogenase(G6P-DH), oxidizes glucose-6-phosphate to 6-phosphogluconate. The increase in NADH concentration is directly proportional to the glucose concentration and can be measured at 340 nm spectrophotometrically**.**

Sample Dilution Automatic dilution: 1:1.5 up to 1:200 vary to analytes

Sample volume: 10 ul serum/plasam sample

EXL 200 uses automated wash protocols, single-use cuvettes and it helps to minimize carryover

Reagent Compartment: 44 positions, refrigerated between 2–8°C (36–47°F)

Assay time from aspiration to result for glucose is 4 minutes

Validate sample types: Serum, plasma, urine, cerebrospinal fluid, whole blood (varies by assay)

Reference range: 0-500mg/dl

Interpretation: based on WHO guideline the expected values for normal fasting blood glucose concentration between 70 mg/dL (3.9 mmol/L) and 100 mg/dL (5.6 mmol/L). When fasting blood glucose is between 100 to 125 mg/dL (5.6 to 6.9 mmol/L) changes in lifestyle and monitoring glycemia are recommended. If fasting blood glucose is 126 mg/dL (7 mmol/L) or higher on two separate tests, diabetes is diagnosed.

Standard Operating Procedure Hematological analyzer

Principle: Hematological analyzer is Siemens ADVIA 560 and it can perform 26 parameters including 5-part Differential with histogram, and scattergrams For RBC and PLT. Working principle of Siemens hematological analyzer is Laser light scatter technology for 5-part WBC differential Impedance method for complete blood count, and Light absorbance for HGB measurement.

Procedure

- venous blood was collected from each subject.
- Three milliliters of blood dispense into K2EDTA anticoagulant tubes.
- The specimens were labeled with subject's age, sex and identification number.
- Confirm that the Siemens Advia 560 is ready.
- Sample Processing Whole Blood (WB) Mode:
- press (Sample ID).
- Enter the number using the panel keyboard, or the handheld barcode reader.
- Use the (C) key to clear incorrect entries. Press Enter (ENT.).
- Mix the sample by gentle end to end inversion.
- Remove the cap and set uncapped specimen to sample probe and press the Start Switch.
- After the screen displays Analyzing and two audible beeps sound, remove the sample tube.
- After the completion of process result is print out and record it.
- Results interpreted high, low and normal based on reference range

Standard Operating Procedure coagulation analysis

Principle: Coagulation analyzer (Ares linear) was used and its measurement principle is photo-optical. Fibrinogen converts into fibrin and form clotting; changes of the turbidity during the formation of fibrin clot is measured as an increase in scattered light intensity when exposed to light at a wavelength. and the analyzer can detect the coagulation end-point in seconds. Blood is drawn into a test tube containing liquid sodium citrate, which acts as an anticoagulant through binding to calcium blood.

Coagulation analysis procedure

A venous collected of 2.7ml blood dispense into 5 ml sterile vacutainer bottle containing 0.3ml of 3.2% tri- sodium citrate solution in a ratio of blood- citrate, 9:1 (v/v) as an anticoagulant and gently mixed by inverting the container several times for the determination of PT and aPTT. Plasma will be separated from the blood after centrifuging at 2000g/m for 10minutes in standard bench centrifuge to obtain platelet poor plasma is required for these coagulation assay

PT/INR Procedure

- Prepare reagents and controls.
- Place reagents and control into analyzer.
- repeat controls if necessary and document any abnormal controls.
- Load centrifuged specimen onto instrument with cap removed.
- place 50 μL of the patient's plasma into a cuvette
- Incubates the sample for 3 minutes, and 100 μL of thromboplastin is added
- Result is displayed, and interpreted in second.
- Normal range: 12-14.7

APTT Procedure

- It Follow similar steps of PT procedure.
- Place 50 μL of the patient's plasma into a cuvette for 5 minutes.
- Then 50 micro litre aPTT reagent was added to the warmed plasma and mixed and again incubated at 37°C for 3 minutes
- finally adds 50 μL of calcium chloride.
- The clotting time displayed, and results interpreted in seconds.
- Normal range: 30-44

Annex II Questionnaire

Please respond to all the questions in the questionnaire appropriately and honestly. The information given will be treated highly confident and will only be used for research purpose only.

Socio demographic information

1. Age in year----------
2. Sex: A). Male B). Female
3. Residence? A) Urban B) rural
4. Marital status A) married B) not-married C) divorced
5. Educational background? A) Illiterate B) primary C) secondary School D) Higher ducation (University or College)
6. Occupational status A) Employed B) Self employed C) Others

Part 2 Clinical history of patient's data

7. Have you had liver disease? A) Yes B) No
8. Have you had chronic kidney disease? A) Yes B) No
9. Are you pregnant (female)? A) Yes B) No
10. Have you taken any anticoagulant drug? A) Yes B) No
11. Have you had cancer case? A) Yes B) No
12. Have you recent history of surgery? A) Yes B) No
13. have you immobility problem A) Yes B) No
14. have you had history of hypertension? A) Yes B) No
15. Do you have you smoking habit? A) Yes B). No
16. Do you have alcohol drinking Habit? A). Yes B). No

17. If yes, A, monthly or less B, 2-4 times per month C, 2-3 times per week D, 4 times or more per week

18. how long have you had diabetes? -------- year

19. For how long you have had taken hypoglycemic drug? _____

20. Blood presssure 1, Systolic blood pressure (SBP)_____

2, Diastolic blood pressure (DBP)_____

21. BMI? (Kg/m2) _____

Laboratory results data

22. Glucose level mg/dl _____

23. Platelet parametres

A) Platelet count_____

B) MPV fl_____

C) PDW fl_____

24. PT value in seconds_____

25. INR In seconds_____

26. APTT value in second_____

Data collector……sign……date……

Annex II : questionnaire amharic version

መጠይቆች

ለስኳር ህመምተኛ እና ለስኳር ህመምተኛ ጤናማ ቁጥጥሮች መጠይቆች

ዕድሜ----------

ጾታ፡ ሀ) ወንድ ለ) ሴት

1. መኖሪያዎ የት ነው? ሀ) ከተማ ለ) ገጠር

2. የጋብቻ ሁኔታ ሀ) ያገባ ለ) ያላገባ መ) የተፋታ

3. የትምህርት ዳራህ/ሽ ስንት ነው? ሀ) ያልተማረ ለ) አንደኛ ደረጃ ሐ) ሁለተኛ ደረጃ ትምህርት ቤት መ) ከፍተኛ ትምህርት (ዩኒቨርሲቲ ወይም ኮሌጅ)

4. ሙያ ሀ) ተቀጥሮ ለ) በራስ ተቀጣሪ ሐ) ሌሎች

5 ሥር የሰደደ የኩላሊት በሽታ ነበረብወ? ሀ) አዎ ለ) የለም

6. የጉበት በሽታ ነበረብወ? ሀ) አዎ ለ) የለም

7. እርግዝና አለወት? ሀ) አዎ ለ) የለም

8. የካንሰር በሽታ ኢጋጥሞዎታል ያውቃል? ሀ) አዎ ለ) የለም

9. ማንኛውንም የደም መርጋት መድሃኒት ወስደዋል? ሀ) አዎ ለ) የለም

10. የቀዶ ጥገና የቅርብ ጊዜ ታሪክ አለዎት? ሀ) አዎ ለ) የለም

11. የማጨስ ልማድ አለህ/ሽ? ሀ) አዎ ለ) የለም

12. አልኮል የመጠጣት ልማድ አለወት? ሀ) አዎ ለ) የለም

13. አዎ ከሆነ ሀ), ወርሃዊ ወይም ያነሰ ለ, በወር 2-4 ጊዜ በወር ሐ, 2-3 ጊዜ በሳምንት መ, 4 ጊዜ ወይም ከዚያ በላይ በሳምንት

14. ስኩር የሚቀንስ መድሃኒት ለምን ያህል ጊዜ ወስደዋል? .....

መረጃ ሰብሳቢ ፊርማ…….

የተሳታፊዉ ፊርማ ……

Annex III: Information sheet

Title of the Research Project: Assessment of coagulation profile Among Type 2 Diabetes Mellitus at Durame General Hospital, South East Ethiopia.

Principal investigator

Phone no: +251 943483632

Department: hematology and immunohematology

Address: AAU

Email: yazalabay12@gmail.com

Purpose of the Research Project We are asking you to take part in this study to assess the the relationships of coagulation profile in type 2 diabetic patients.

Potential risks and Discomforts During collection of blood sample from you, appropriate precaution will be taken and all samples will be collected by trained health professionals. If anything happened, appropriate medical care will be provided to you.

Potential benefits to subjects or to the society: There is the benefits anticipation achieved from this research. Include benefits to participants, or the body of knowledge. If there is no direct benefit of your participation in this study. However, we hope that the information obtained from this study may provide information to relationship of coagulation status of diabetic patients and it will be essential for assessments of complication and treatment monitoring.

Confidentiality: Any information that I am going to collect about you during this research will be kept confidential. Your name and identity on the information paper will be changed to anonymous code for the purpose of this study.

Withdrawal from the study: Your participation in this study is by your willingnes, and you may drop the participation at any time or you may refuse to answer some of the questions if you feel discomfort.

Contact information: If you have any questions about this study, you can contact the following principal investigators and advisors for further information.

Principal Investigator: Mobile no: +251943483632

Email: yazalabay12@gmail.com

Advisor: zemenu Tamir (MSc, PhD candidate)

Mobile Phone: Tel: +251915992362

E-mail: zemenut266@gmail.com

Advisor: Melatwork Tibebu (MSc, PhD candidate)

Mobile Phone: Tel: +251931566437

melatwork.tibebu@aau.edu.et

Annex Iv: Informed consent

Hello! My name is Yazal Abay from Addis Ababa university collage of health science. I invite you to take part in a research study about assessment of coagulation profile Among type 2 Diabetic patients at Durame general Hospital, which seeks to identify a more effective means of treating (illness, complications). The purpose of this study is to evaluate PT, INR, aPTT and platelet count. I am requesting your permission to give your blood specimen for analysis purpose. This study will help you to know the status of your PT, aPTT and platelet count and I also assure you that laboratory result will not bring any harm and I will inform to you taking part in this study is entirely voluntary. We urge you to discuss any questions about this study. Talk to your family and friends about it and take your time to make your decision. If you decide to participate you must sign this form to show that you want to take part

Your responses to this study will be anonymous. For the purposes of this research study, your comments will not be anonymous. Every effort will be made by the researcher to preserve your confidentiality including the following:

- ✓ Assigning code names/numbers for participants that will be used on all research notes and document
- ✓ Keeping notes, interview transcriptions, and any other identifying participant information in a locked in personal possession of the researcher

If you are interested in participation, please sign and give me the consent form. Thank you for your time and for agreeing to participate in this study. I (The participant) have read and understand the information above, and any questions I have asked have been answered to my satisfaction. I understand that my participation is voluntary and I agree to participate in this research, knowing that I can withdraw at any time.

Participant’s signature: _____ Date: _____

Investigator's signature _____ Date _____

Annex Iv : Informed consent: amharic version

በመረጃ የተደገፈ ስምምነት

ሰላም! ያዛል እባላለሁ ከአዲስ አበባ ዩኒቨርሲቲ የጤና ሳይንስ ኮሌጅ ። በዱራሜ አጠቃላይ ሆስፒታል ውስጥ ዓይነት 2 የስኳር ህመምተኞች መካከል መሰረታዊ የደም መርጋት መገለጫን በሚመለከት በምርምር ጥናት ላይ እንድትሳተፉ እጋብዛችኋለሁ ፣ ይህም የበለጠ ውጤታማ የሕክምና ዘዴዎችን መለየት ይፈልጋል ። የዚህ ጥናት ዓላማ PT፣ INR፣ aPTT (ደም መርጋትና ተያያዥ ነገሮችን መለያ ዘዴዎች ናቸው) ።እና ፕሌትሌት ቆጠራን መገምገም ነው። ለትንተና ዓላማ የደም ናሙና እንድትሰጥ ፍቃድ እጠይቃለሁ። ይህ ጥናት የ PT፣ aPTT እና ፕሌትሌት ቆጠራን ሁኔታ ለማወቅ ይረዳችኋል እና የላብራቶሪ ውጤቱ ምንም አይነት ጉዳት እንደሌለው አረጋግጣለሁ እና አሳውቃችኋለሁ በዚህ ጥናት ውስጥ መሳተፍ ሙሉ በሙሉ በፈቃደኝነት ነው። ስለዚህ ጥናት ማንኛውንም ጥያቄ እንድትወያዩ እናሳስባለን። ለመሳተፍ ከወሰኑ መሳተፍ እንደሚፈልጉ ለማሳየት ይህንን ቅጽ መፈረም አለብዎት

ለዚህ ጥናት የሰጡት ምላሾች ስም-አልባ ይሆናሉ። ለዚህ የምርምር ጥናት ዓላማ፣ አስተያየቶችዎ የማይታወቁ ይሆናሉ። የሚከተሉትን ጨምሮ ምስጢራዊነትዎን ለመጠበቅ መረጃ ሰብሳቢው የተቻለውን ሁሉ ጥረት ያደርጋል፡- በሁሉም የምርምር ማስታወሻዎች እና ሰነዶች ላይ ጥቅም ላይ የሚውሉ የተሳታፊዎች ኮድ ስሞች/ቁጥሮች መደብ ማስታወሻዎችን መያዝ፣ የቃለ መጠይቅ ግልባጮችን እና ማንኛውንም ሌሎች የተሳታፊዎችን መለያ በተመራማሪው የግል ይዞታ በተቆለፈ የፋይል ካቢኔት ውስጥ ይቀመጣል ለመሳተፍ ፍላጎት ካለህ/ሽ፣ እባክህወትን ፈርመው የስምምነት ቅጹን ይስቱኝ። በዚህ ጥናት ውስጥ ለመሳተፍ ስለተስማሙ እና ስለ ጊዜዎ እናመሰግናለን።

እኔ (ተሳታፊው) ከላይ ያለውን መረጃ አንብቤ ተረድቻለሁ፣ እና ማንኛውም የጠየኳቸው ጥያቄዎች እርካታ አግኝተውኛል። የእኔ ተሳትፎ በፈቃደኝነት እንደሆነ ተረድቻለሁ እናም በማንኛውም ጊዜ ማቋረጥ እንደምችል አውቄ በዚህ ጥናት ላይ ለመሳተፍ ተስማምቻለሁ።

የተሳታፊው ፊርማ፡_____ ቀን: ---------

መረጃ ሰብሳቢ ፊርማ……

Declaration

I, the undersigned, declare that this M.Sc. research is my original work, has not been presented fora degree in this or any other university and that all sources of materials used for this thesis have been duly acknowledged.

M.Sc. candidate: Yazal Abay (B.Sc.)

Signature: _____

Date of submission: _____

This thesis work has been submitted with our approval as advisors.

Advisor: Zemenu Tamir (MSc, PhD candidate)

Signature: _____

Date: _____

Place: Addis Ababa, Ethiopia.

Advisor: Melatwork Tibebu (MSc, PhD Candidate)

Signature: _____

Date: _____

Place: Addis Ababa, Ethiopia.