

Magnitude of Coagulation Abnormalities and Associated Factors Among Patients with Heart Diseases at the University of Gondar Comprehensive Specialized Hospital

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Background: Heart disease is a leading cause of hospitalization, death, and poor physical function due to comorbid conditions such as atrial fibrillation and stroke. It affects the blood hemostatic system, vasculature, and flow dynamics, causing both arterial and venous thrombosis. Thus, this study aimed to determine the magnitude of coagulation abnormalities among patients with heart disease attending the University of Gondar Comprehensive Specialized hospital.

Methods: A cross-sectional study was conducted on a total of 98 patients with heart disease. Pretested structured questionnaires were used to collect data on socio-demographic and clinical variables. About 6 mL of venous blood was collected with the vacutainer method and analyzed using Huma cue-due plus and Sysmex KX-21N hematology analyzers for assessing coagulation abnormalities. Stool samples were processed via a direct wet mount. Thin and thick blood films were examined to assess malaria parasites. Data was entered into EPI-Info version 3.5.3 and then transported to SPSS version 20 for analysis. Descriptive statistics were summarized using frequency and percentage. Univariate and multivariate logistic regression models were fitted to identify factors associated with coagulopathy. P-value <0.05 was considered to be statistically significant.

Results: The overall magnitude of coagulation abnormalities (thrombocytopenia, prolonged prothrombin time, and activated partial thromboplastin time) in patients with heart diseases was 85.7% (95% CI: 81.96, 89.45). Besides, prolonged prothrombin time, prolonged activated partial thromboplastin time, and thrombocytopenia were detected in 83.7%, 33.7%, and 12.2% of the study participants, respectively. Participants who are taking medications for chronic disease (AOR = 0.17; 95% CI: 0.04, 0.69), participants with stroke (AOR = 20; 95% CI: 14.7, 35), and participants taking antibiotics (AOR = 8.17; 95% CI: 1.66, 40.27) were significantly associated with prolonged coagulation time.

Conclusion: This study showed that patients with heart disease had prolonged prothrombin time, activated partial thromboplastin time, and thrombocytopenia. Therefore, coagulation parameters are required to be checked regularly to monitor coagulation disorders and their complications in heart disease patients.

Keywords: heart diseases, coagulation abnormalities, cardiovascular diseases, Gondar, Ethiopia

Introduction

Cardiovascular disease (CVD) is the leading cause of mortality globally, taking estimated 17.9 million lives each year.¹ It is a group of disorders of the heart and blood vessels and includes heart attacks, strokes, coronary heart disease, cerebrovascular disease, rheumatic heart disease and others.^{1,2} It can cause abnormal clotting as a result of heart attacks or stroke. Blood vessels damaged by smoking, cholesterol, and high blood pressure form cholesterol-rich plaques that line the blood vessel, which can rupture and cause platelets to form a clot.³ Thrombosis is the main cause of death and complication in CVD.⁴ Thrombin, fibrin,

and platelets are the prominent components of the thrombi that occlude arteries and participate in the initiation and progression of the atherosclerosis.^{5,6}

The World Health Organization estimates that heart diseases cause 12 million deaths worldwide each year.⁷ It has an effect on blood hemostatic system, vasculature, and flow dynamics, which predisposes to both arterial and venous thrombosis. Platelet activation and aggregation is the leading cause of heart disease predisposes to the formation of arterial thrombi and venous thromboembolism which contributes to an increased risk of cardioembolic stroke and death.⁸

Previous study has shown that heart failure leads to activation of coagulation, with increased levels of thrombin formation as well as activation of fibrinolysis.⁹ Higher level of hemostatic markers including von Willebrand factor and fibrinogen; platelet and endothelial adhesion molecules; tissue-type plasminogen activator, D-dimer; vascular cell adhesion molecules; cytokines, and thromboxane reductase is reported in patients with congestive heart diseases.^{10,11} Platelets and a coagulation cascade are involved in the pathogenesis of ischemic heart disease. Following injury, platelets adhere to collagen and von Willebrand factor in subendothelial tissue, where they are activated and release stored granules such as adenosine diphosphate and thromboxane A₂, stimulating platelet aggregation.¹²

Prolonged values of prothrombin time (PT), and activated partial thromboplastin time (aPTT) were seen frequently in congenital heart disease¹³ and coronary artery disease.¹⁴ Increased international normalized ratio (INR) is associated with poor clinical outcomes in acute decompensated heart failure (ADHF) patients.⁹ High platelet count was associated with an increased risk of heart disease.^{15,16} Platelet activation has been described in patients with heart failure as increased whole blood aggregation, higher mean platelet volume and higher expression of platelet bound and soluble P-selectin.¹⁷ A study by Mehta et al reported that patients with heart failure had significantly more circulating platelet aggregates than controls.¹⁸ However, studies confirm that platelet count is reduced in patients with CVD due to decreased production, increased destruction of platelets and platelet sequestration.^{19,20}

Heart disease is a major cause of hospitalization, death, poor physical function, and impaired quality of life due to comorbid conditions such as atrial fibrillation and stroke.^{21,22} Coagulation abnormalities are at risk for developing myocardial infarction, stroke, and atherothrombotic events in the vascular beds.²³ In the Ethiopian health care system, testing of those coagulation parameters is not routinely performed in heart disease patients, unless the patients experience complications such as arterial thrombi and venous thromboembolisms. Besides, the previous study by Aynalem et al, which was primarily aimed to assess coagulopathy among all bleeding diathesis patients, found that cardiac patients were significantly associated with coagulopathy.²⁴ However, they did not specify which coagulation abnormalities were prevalent among cardiac patients, which inspired us to conduct this study. As a result, the current study sought to determine the magnitude of coagulation abnormalities in patients with heart disease. The study provides evidence for policymakers and clinicians to consider assessing such coagulation parameters when managing patients with heart disease.

Methods and Materials

Study Setting and Period

A facility-based cross-sectional study was conducted from January to May 2020 at the University of Gondar comprehensive specialized hospital. The hospital is located in Gondar town. According to the central and statistical agency of Ethiopia's report, the town has a total projected population of 323,900.²⁵ The University of Gondar comprehensive specialized hospital is a teaching hospital, and it is the oldest academic institution in Ethiopia that provides different medical services to more than 7 million people in the region and people of the neighboring region.²⁶

Study Population

This study includes all individuals who have been diagnosed with any type of heart disease. All participants who had heart disease and who fulfilled the inclusion criteria during the study period were considered as the study population. Study participants who had a history of snakebite within one-week, active bleeding due to trauma, or were critically ill and unable to give informed consent were excluded from the study. A total of 98 heart disease patients aged 18 years and older were included. The study participants were selected by using a simple random sampling technique within the specified study period.

Study Variables

The dependent variables for this study were blood coagulation abnormalities, such as prolonged PT, aPTT, and thrombocytopenia. Socio-demographic characteristics (age, gender, residence, educational status, occupation, and marital status), clinical characteristics (family history of bleeding disorder, presence of chronic disease, hypertension, malaria infection, intestinal parasitic infection, and drug intake), having a habit of alcohol consumption, and physical exercise were considered as independent variables.

Operational Definitions

Thrombocytopenia was defined as a platelet count of less than 150,000 cells/mm³.²⁷ Besides, prolonged PT time was defined as PT > 16 seconds and prolonged was defined as INR > 1.2.²⁸ Moreover, prolonged aPTT was defined as aPTT > 36 seconds.²⁸

Data Collection Procedures

Socio-Demographic and Clinical Data Collection

A pre-tested structured questionnaire was used to collect the socio-demographic variables via face-to-face interview. The questionnaire includes variables for the assessment of the socio-demographic characteristics, mainly gender, age, residence, educational status, religion, marital status, and occupation. Similarly, the clinical data was collected by using a data collection sheet. Clinical characteristics like a family history of bleeding, history of drug intake within two weeks, physical exercise, smoking habits, and taking any traditional medicine were collected by physicians.

Blood Sample Collection and Laboratory Analysis

Blood Sample Collection

Under aseptic conditions, a total of 6 mL of venous blood was collected by using a standardized vacutainer collection system. The collected blood samples were mixed with 1 to 9 sodium citrate anticoagulants to blood proportion and 1.5 mg to 1mL for the ethylene diamine tetra acetic acid test tube.

Platelet Count

The platelet count was done by using Sysmex KX-21. The machine is an automatic multi-parameter blood cell counter for in vitro diagnostic use in clinical laboratories. The principle is based on the impedance principle, in which a constant electric current is passed through a solution. Counting the cells measures the changes in electrical resistance that occur when blood cells pass through the detection aperture.²⁹

Blood Coagulation Tests

Blood coagulation profile tests (PT/INR, and aPTT) were analyzed by the Huma cue-due plus semi-automated machine, which uses the turbidity meter principle.³⁰ The PT and aPTT were analyzed by a laboratory technician on an automated instrument at 37°C. The venous blood was mixed with liquid sodium citrate anticoagulant and centrifuged to separate the platelet poor plasma (PPP) from the whole blood. The PPP is placed into a measuring test tube and incubated for 3 minutes. Then, the PPP was mixed with thromboplastin reagent. The time taken from the addition of thromboplastin reagent to the formation of the fibrin clot was measured by the automated system as the PT/INR. Similarly, the aPTT time test requires two types of reagents. Initially, the PPP was mixed and incubated with reagent one for 3 minutes. Then, reagent two was added to the mixture of PPP and reagent one to activate the intrinsic pathway of coagulation. The time from the addition of reagent two to the formation of the fibrin clot was measured optically.³⁰

Mixing Test

Mixing tests were performed on citrated PPP, which were used to distinguish factor deficiencies from factor inhibitors. Mixing studies work as a fact that factor levels up to 50% lower than the normal value can give a normal PT or aPTT. Hence, the patient plasma was mixed 1:1 with normal pooled plasma that contained 100% of the normal factor level. Then, the coagulation test was repeated again. If the abnormal result is corrected by the addition of NPP, a factor

deficiency is indicated. However, when there was no correction of the abnormal result, it indicates the presence of a circulating inhibitor. This mixing test can be done immediately or after incubation of NPP with the PPP to detect inhibitors that act on body temperature.³¹

Stool Examination

A pea-sized stool was collected from all study participants using a standardized, clean, leak-proof, and wide mouth trap. Then, a wet mount was prepared by mixing the stool sample with normal saline. Then, the smear was directly observed microscopically by laboratory professionals.

Blood Film Examination

A blood film examination was conducted to assess malaria parasites. The malaria parasite was detected by using light microscopic examination. A thin and thick peripheral blood smear was prepared on a clean microscope slide. Then, the slide was allowed to air dry and fixed with absolute methanol, stained with 10% Giemsa, and examined by a professional laboratory technician.

Data Quality Control

To maintain socio-demographic and clinical data quality control, the questionnaire was prepared in English and translated to Amharic, then returned to English to check for consistency. The questionnaire was pre-tested among 10% of the sample size. All study participants were informed about the aim and importance of the study before data collection to make them fully concerned about their response. The collected data were checked daily for completeness and accuracy. Data collection was closely supervised by investigators. The blood sample's quality was maintained by ensuring that it met acceptable criteria such as hemolysis, clotting, volume, and collection time. To avoid hemolysis, blood collection and blood handling were conducted by following all protocols. All manufacturer's procedures and standard operational procedures (SOP) were strictly followed. Background checks were used to control the machine data quality for complete blood counts. For coagulation tests, similarly normal and abnormal lyophilized samples were used daily before the sample was run. Maintenance for the machines was done daily, and the machines were filled and prepared as per the clinical laboratory institute for standardization standards.³⁰

Data Entry and Analysis

Data was entered into EPI-Info version 3.5.3 and then transported to SPSS version 20 for analysis. First, skewness and kurtosis were used to check the data distribution. Then, descriptive statistics were summarized as percentages, means, and standard deviations for the normally distributed data and presented in figures and tables. Each of the independent variables was computed with the outcome variables. The association of the independent variable with the categorical outcome variable was measured by calculating the odds ratio with a 95% confidence interval (CI) using bi-variable and multi-variable logistic regression analysis. Variables having a p-value of less than 0.2 in the bi-variable logistic regression analysis were selected for multivariate logistic regression analysis. P-value <0.05 was considered to be statistically significant.

Ethical Considerations

This study was conducted based on the Declaration of Helsinki. The ethical clearance was obtained from the School of Biomedical and Laboratory Sciences ethical review committee, College of Medicine and Health Sciences, University of Gondar. Moreover, written informed consent was obtained from each study participant. Confidentiality of data was secured using codes for each specimen, and results were used only for this research without using any personal identifier. All abnormal results were reported to their medical doctors to seek medical follow-up and to get medication.

Results

Socio-Demographic Characteristics of Study Participants

A total of 98 adults with heart disease were included. Among them, 63/98 (64.3%) were females, and 61/98 (62.2%) lived in cities. The median age of the study participants was 55 (IQR = 19) years old, ranging from 18 to 87 years (Table 1).

Clinical Characteristics of Study Participants

From the total study participants, 21.4% (21/98) and 14.3% (14/98) of them had hypertension and stroke as comorbidities, respectively. About 90.8% (89/98) were taking different types of drugs. Of these drugs, 18.4%, 7.1%, and 6.1% were taking antibiotics, drugs for stomach ulcers, and pain killers, respectively (Table 2).

Magnitude of Coagulation Abnormalities

The overall magnitude of blood coagulation disorders (thrombocytopenia, prolonged PT, and aPTT) in heart disease patients was 84/98 (85.7%; 95% CI: 81.96, 89.45). Of the participants, prolonged PT, prolonged aPTT, and thrombocytopenia were detected in 83.7%, 33.7%, and 12.2% of the participants, respectively (Figure 1).

Table 1 Socio-Demographic Characteristics of Patients with Heart Disease at the University of Gondar Comprehensive Specialized Hospital Northwest Ethiopia in 2020

Variables	Categories	Frequency	Percentages
Sex	Male	35	35.7
	Female	63	64.3
Age in years	18–45	39	39.8
	46–65	24	24.5
	>65	35	35.7
Residence	Urban	61	62.2
	Rural	37	37.8
Educational level	Unable to read and write	64	65.3
	Attend primary school	17	17.3
	Attend secondary school	6	6.1
	Attend higher education	11	11.2
Religion	Orthodox	77	78.6
	Muslim	16	16.3
	Other	5	5.1
Occupational status	Employed	14	14.3
	Student	5	5.1
	House wife	45	45.9
	Farmer	18	18.4
	Private work	5	5.1
	Merchant	6	6.1
	Daily laborer	5	5.1
Marital status	Single	16	16.3
	Married	63	64.3
	Divorced	5	5.1
	Widowed	14	14.3

Table 2 Clinical Characteristics of Patients with Heart Disease at the University of Gondar Comprehensive Specialized Hospital Northwest Ethiopia in 2020

Variables	Categories	Frequency	Percentages
Family bleeding history	Yes	10	10.2
	No	88	89.8
Nasal bleeding	Yes	4	4.1
	No	94	95.9
Hypertension	Yes	21	21.4
	No	77	78.6
Diabetes mellitus	Yes	2	2.0
	No	96	98.0
Stroke	Yes	14	14.3
	No	84	85.7
Renal disease	Yes	2	2.0
	No	96	98.0
Anemia	Yes	3	3.1
	No	95	96.9
Drug taking during sample collection	Yes	89	90.8
	No	9	9.2
Pain killer taking during sample collection	Yes	7	7.1
	No	91	92.9
Antibiotics taking during sample collection	Yes	18	18.4
	No	80	81.6
Drugs for stomach ulcer	Yes	6	6.1
	No	92	93.9
High protein and vitamin food intake	Yes	85	86.7
	No	13	13.3
Physical exercise habit	Yes	16	16.3
	No	82	83.7
Smoking habit	Yes	0	0
	No	98	100
Alcohol drinking	Yes	9	9.2
	No	89	90.8
Traditional medicine (within 2 weeks)	Yes	18	18.4
	No	80	79.6
Malaria infection	Yes	2	2.0
	No	96	98.0
Intestinal parasite infection	Yes	13	13.3
	No	85	86.7

Prevalence of Factor Deficiency

The magnitude of the prolonged aPTT/PT test was 83.67% (82/98). Of them, factor deficiency and inhibitors were detected in 7.3% (6/82) and 92.7% (76/82) of the participants, respectively (Figure 2).

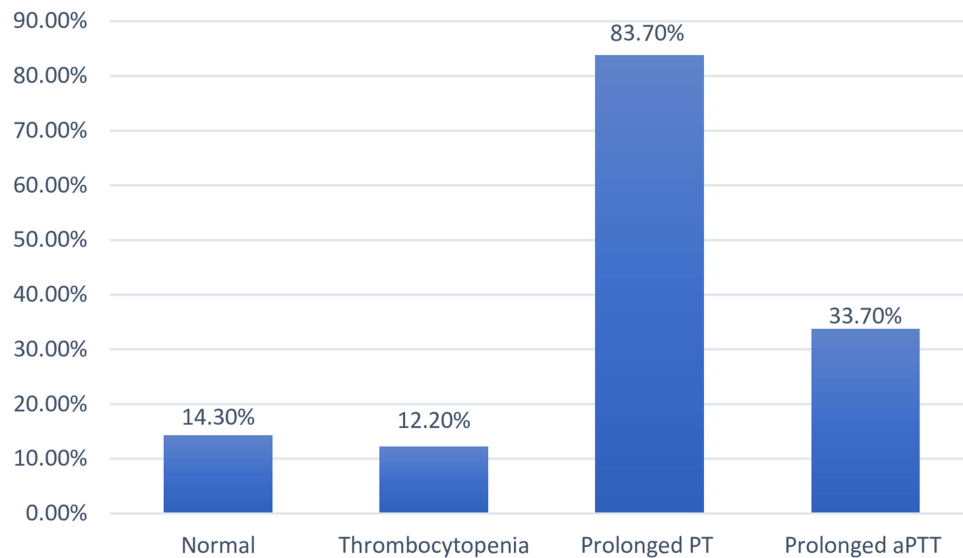


Figure 1 Magnitude of coagulation abnormalities among patients with heart disease at the University of Gondar comprehensive specialized hospital.

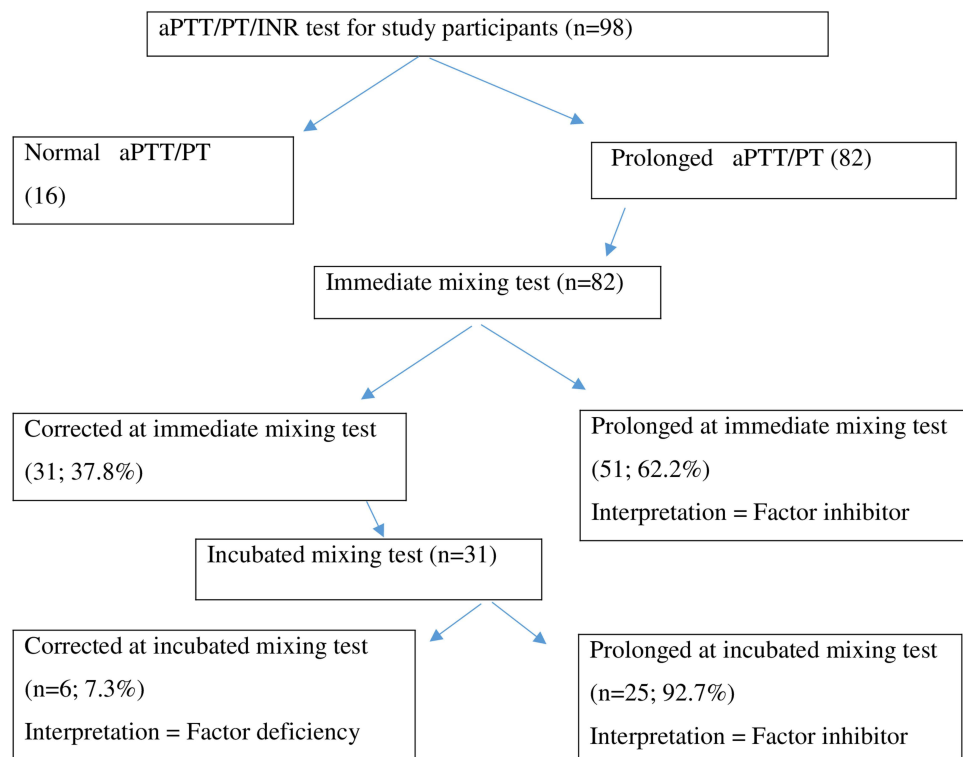


Figure 2 Mixing test algorithm for the determination of factor deficiency and inhibitory among patients with heart disease at the University of Gondar comprehensive specialized hospital.

Factors Associated with Prolonged Coagulation Time

To determine associated factors, a binary logistic regression was done on the independent variables (gender, age in years, residence, drugs for chronic disease, stroke, hypertension, participants taking antibiotics, and traditional medicine) with the prolonged coagulation time as the dependent variable. Based on these variables, univariate logistic regression analysis revealed that gender, age, residence, drugs for chronic disease, stroke, hypertension, participants taking antibiotics, and traditional medicine use showed an association with prolonged coagulation time. In multivariate analysis, however, participants taking

Table 3 Factors Associated with Prolonged Coagulation Time of Patients with Heart Disease at the University of Gondar Comprehensive Specialized Hospital Northwest Ethiopia in 2020

Characteristics		Prolonged Coagulation Time		COR (95% CI)	AOR (95% CI)
		Yes	No		
Gender	Male	27(77.1%)	8(22.9%)	1	1
	Female	55(87.3%)	8(12.7%)	0.49 (0.16, 1.45)	2.89 (0.64, 13.18)
Age in year	<65	57(90.5%)	6(9.5%)	1	1
	≥65	25(71.4%)	10(28.6%)	3.8 (1.25, 11.6)	0.29(0.06, 1.48)
Residence	Urban	49(81.7%)	11(18.3%)	0.67(0.21, 2.12)	–
	Rural	33(86.8%)	5(13.2%)	1	
Drugs for chronic disease	Yes	67(91.8%)	6(8.2%)	0.62(0.21, 1.88)	0.17(0.040, 0.69) *
	No	15(60%)	10(40%)	1	1
Stroke	Yes	8(57.1%)	6(42.9%)	5.55 (1.59, 19.32)	20 (14.7, 35) *
	No	74(88.1%)	10(11.9%)	1	1
Hypertension	Yes	14(66.7%)	7(33.3%)	3.77 (1.2, 11.85)	0.58(0.11, 3.14)
	No	68(88.3%)	9(11.7%)	1	1
Antibiotics	Yes	9(50.0%)	9(50.0%)	10.42 (3.12, 34.84)	8.17 (1.66, 40.27) *
	No	73(91.3%)	7(8.8%)	1	1
Traditional medicine	Yes	5(27.8%)	13(72.2%)	2.41 (0.72, 8.1)	0.29(0.06, 1.48)
	No	11(13.8%)	69(86.2)	1	1

Note: * Indicates significant association.

Abbreviations: AOR, Adjusted Odds Ratio; CI, Confidence Interval; OR, Odds Ratio.

chronic disease medications (AOR = 0.17; 95% CI: 0.04, 0.69), stroke patients (AOR = 20; 95% CI: 14.7, 35), and antibiotics (AOR = 8.17; 95% CI: 1.66, 40.27) were significantly associated with prolonged coagulation time (Table 3).

Discussion

Hemostatic function has been linked to the pathogenesis of the complications of CVD like coronary artery disease.³² Standard coagulation screening tests such as aPTT and PT are important constituents of basic examinations in the clinical laboratories.¹⁴ This study comprised a total of 98 patients to determine the magnitude of coagulation abnormalities in patients with heart disease. Accordingly, the overall magnitude of coagulation abnormalities (thrombocytopenia, prolonged PT, and aPTT) was 85.7% (95% CI: 81.96, 89.45). Of the total participants, 83.67% showed prolonged coagulation time (both prolonged PT and aPTT) and 12.2% had thrombocytopenia. Besides, 33.7% and 83.7% of the participants developed prolonged PT and aPTT, respectively. The findings of this study are consistent with previous studies. A study conducted by Akhan et al showed that there were significant increases in PT levels in patients as compared to the control groups.³³ Another study by Colon-Otero et al reported that 10% of patients experienced a prolonged PT.¹³ Similarly, a study by Okada et al showed that acute decompensated heart failure patients had an elevated PT/INR value. The study also declared that increased INR was independently associated with increased all-cause mortality in those patients (HR = 1.89) (95% CI: 1.14–3.13).⁹ In contrast to the findings of this study, Anvari et al¹⁴ and Abdullah et al³⁴ reported that a shortened aPTT was correlated with acute arterial thrombosis in patients presenting with acute coronary syndrome.

PT and aPTT measure the extrinsic and intrinsic pathways of the coagulation system, respectively, and are used to determine the bleeding or clotting tendency of blood.³³ PT is regulated by multiple coagulation factors synthesized in the liver and is widely used to monitor anticoagulation, to assess liver function, and to evaluate coagulation abnormalities.⁹ Previously, aPTT has been regarded as a one-tailed test; that is, only prolonged aPTT has clinical relevance as an indication of factor deficiency or the presence of inhibitors. However, the clinical association of shortened PTTs with hypercoagulability has recently suggested a new

use of PTT for assessing the risk of occurrence or recurrence of venous thrombosis.³⁵ Coagulation mechanisms are known to be affected by CVD, as evidenced by prolonged aPTT and PT.³⁶ Several mechanisms can be considered for the prolonged PT/INR and aPTT in CVD patients. Initial stage, hemostasis is closely related to inflammation. Inflammation-induced during infection generally diverts the hemostatic mechanism toward thrombosis by upregulation of procoagulant factors, down-regulation of anticoagulants, and inhibition of the fibrinolytic system. Activation of the coagulation system may result in the consumption of coagulation factors.^{36,37} Dysfunction of the damaged liver might be responsible for the decreased synthesis of specific factors in the intrinsic pathway. Decreased concentrations of plasma coagulation factors have been previously reported in patients with severe chronic heart failure.³⁶ Hemodilution has also been reported as a cause of increased INR.³⁸ Increased INR could reflect hemostatic derangement, possibly through systemic inflammation, neurohormonal activation and venous congestion, thereby making INR a stronger prognostic predictor.³⁹

Thrombocytopenia was detected in 12.2% of the study participants. This magnitude is higher than the study by Colon-Otero et al, reporting that 4% of the patients developed thrombocytopenia.¹³ In cardiology, the most frequent cause of thrombocytopenia is an abnormal immune response caused by drug therapy, particularly with heparin (heparin-induced thrombocytopenia), diuretics, antidiabetic medications, or antiplatelet drugs.³ On the contrary, reports suggest that patients with higher levels of platelets are found to have an increased risk of CVD. PAI-1 is directly proportional to the platelet mass. Since PAI-1 is an inhibitor of fibrinolysis, the high platelet count may indirectly reflect the tendency for thromboresistance.⁴⁰

Our study showed that participants having a stroke were at higher risk of prolonged coagulation time. This might be related to chronic heart failure, which is associated with endothelial abnormalities that may lead to an increased risk of stroke and venous thromboembolism.^{41,42} In stroke, coagulopathies are characterized by a condition in which blood is too quick to clot.⁴³ Deficiency of plasminogen, plasminogen activator, dysfibrinogenemia, and factor XII has been linked to thrombosis in stroke patients.⁴⁴ Low circulating fibrinogen levels have been associated with post-thrombolysis hemorrhage in ischemic stroke patients.⁴⁵

Our findings showed that participants taking antibiotics (AOR = 8.17; 95% CI: 1.66, 40.27) were significantly associated with prolonged coagulation time. Macrolide antibiotics are commonly used in the treatment of upper and lower respiratory infections and other sexually transmitted diseases.⁴⁶ Although considered generally free of adverse effects, including cardiovascular toxicity, several of the macrolide agents were recently reported to have arrhythmia-related cardiac effects.⁴⁷ A recent observational study showed that use of azithromycin was associated with a risk of death from cardiovascular causes that was 2 to 3 times higher than the risk associated with no use of antibiotics.⁴⁸ The cardiovascular risk associated with macrolides, however, was not significantly linked to other investigations.⁴⁹ Increased cardiovascular risk then delays the formation of blood clot contributing to prolonged PT and aPTT.

The results of the present study showed that patients taking medications for treatment of chronic diseases were not at risk of developing prolonged PT and aPTT. Drugs that interfere with blood coagulation (anticoagulants) are a mainstay of cardiovascular therapy.⁵⁰ Current anticoagulation practice involves the use of drugs that inhibit thrombin directly or indirectly by interacting with other clotting factors. Anticoagulants in the current use can be divided into heparins (unfractionated and low molecular weight), vitamin K antagonists, and new agents, such as factor Xa inhibitors and thrombin inhibitors. Vitamin K antagonists, most notably warfarin, have represented the mainstay of anticoagulation for the last 50 years.⁵¹ Treatment of arterial clots may include aspirin and clopidogrel, intravenous anti-platelet agents, and clot busters (thrombolytic agents).⁵² Aspirin is effective in the prevention of cardiovascular events in high-risk patients. The primary established effect of aspirin on hemostasis is to impair platelet aggregation via inhibition of platelet thromboxane A₂ synthesis, thus reducing thrombus formation on the surface of the damaged arterial wall.⁵³

The study has its limitations: The study did not take into account the investigation of specific factor assays because of resource scarcity. Since the study was cross-sectional, it does not show the connection between prolonged test results and cardiovascular morbidity and mortality. Besides, the study does not assess the effect of various cardiovascular medications on the patients' coagulation parameters. Moreover, the inadequate sample size may limit the generalizability of the findings of the study.

Conclusion

The results of this study showed that patients with heart disease had prolonged PT and aPTT, indicating the potential of these tests as hemostatic markers for patients with heart disease. However, other studies showed that shortened PT and

aPTT levels are evidenced in patients with heart diseases. Thus, further investigation is needed to elucidate the association between hemostatic markers and heart disease.

Abbreviations

aPTT, Activated Partial Thromboplastin Time; INR, International Normal Ratio; NPP, Normal Pooled Plasma; PPP, Platelet Poor Plasma; PT, Prothrombin Time; AOR, Adjusted Odd Ratio; CI, Confidence Interval; COR, Crude Odd Ratio; CVD, Cardiovascular Disease.

Data Sharing Statement

The data sets used and/or analyzed during this study are available from the corresponding authors on reasonable request.

Ethical Approval

Ethical approval was obtained from the School of Biomedical and Laboratory Sciences ethical review committee, College of Medicine and Health Sciences, University of Gondar (Ref. No. SBLS/2445/2020). Written informed consent was obtained from each study participant. Confidentiality of the data was secured using codes.

Author Contributions

All authors made substantial contributions to conceptualization and design, data acquisition, analysis and interpretation, took part in drafting of the initial manuscript and revising it critically, gave approval for the final version to be published, agreed to submit to the current journal, and agreed to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in relation to this work.

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