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ORIGINAL RESEARCH

Evaluation of Prothrombin Time and Activated Partial Thromboplastin Time in Antithrombotic-Treated Cardiac Patients: A Cross-Sectional Study from Sana'a City, Yemen

Abdulrahman H Amer[1,2], Abdulelah H Al-Adhroey[3], Abdulqawi Ali Al-Shammakh[2,4]

[1]Department of Laboratory Medicine, Faculty of Medical Sciences, Thamar University, Dhamar, Yemen; [2]Department of Medical Laboratory, Faculty of Medical Sciences, Al-Saeeda University, Sana'a, Yemen; [3]Department of Community Medicine, Faculty of Medicine, Thamar University, Dhamar, Yemen; [4]Department of Biochemistry, Faculty of Medicine, Thamar University, Dhamar, Yemen

Correspondence: Abdulrahman H Amer, Department of Laboratory Medicine, Faculty of Medical Sciences, Thamar University, Dhamar, Yemen, Tel +967777750189, Email hefdhallaha@tu.edu.ye

Background: Antithrombotic therapy is a cornerstone of managing cardiac diseases, necessitating routine monitoring of coagulation parameters like Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT). Data on the coagulation profiles of treated patients in resource limited settings like Yemen are scarce.

Objective: This study aimed to evaluate PT and APTT in antithrombotic-treated cardiovascular patients and assess their variation across different cardiac diagnoses and therapy regimens in Sana'a, Yemen.

Methods: A cross-sectional study was conducted on 200 cardiovascular patients on antithrombotic therapy at selected hospitals in Sana'a City between January and March 2024. Demographic, clinical, and therapeutic data were collected. Coagulation parameters (PT, INR, APTT) were measured and compared across diagnostic groups and treatment types using Kruskal–Wallis and Mann–Whitney *U*-tests, with Bonferroni correction for multiple comparisons.

Results: The study group was predominantly male (69.0%), aged 51–80 years (57.0%). Coagulation parameters varied significantly across cardiac diagnoses ($p < 0.01$ for PT, INR, APTT). Patients with Mitral Valve Replacement (MVR) had the highest median PT (36.45s) and INR (2.75). Post-hoc analysis confirmed MVR patients had significantly elevated parameters compared to other groups (e.g. PT 19.01s higher than Segment Elevation Myocardial Infarction (STEMI), $p=0.003$). Rheumatic Heart Disease (RHD) patients showed intermediate PT elevation. No significant differences were found between STEMI and Non-ST-segment Elevation - Acute Coronary Syndrome (NSTE-ACS) subtypes. Antithrombotic type significantly influenced results: warfarin patients had the highest median PT (20.00s), INR (1.53), and APTT (40.00s) ($p<0.05$). Dosage analysis confirmed warfarin's significant impact compared to aspirin doses.

Conclusion: Coagulation profiles in cardiovascular patients vary significantly according to both the underlying cardiac diagnosis and the type of antithrombotic therapy. MVR and RHD patients display notably elevated parameters, while ACS subtypes show similar profiles. These findings underscore the need for diagnosis-specific monitoring strategies and confirm the expected pharmacological effects of different antithrombotic agents in a Yemeni population.

Keywords: antithrombotic therapy, coagulation monitoring, prothrombin time, international normalized ratio, cardiovascular diseases, Yemen

Introduction

Cardiovascular diseases (CVDs) remain the preeminent cause of global mortality, accounting for an estimated 17.9 million deaths annually.[1] This broad group of disorders of the heart and blood vessels, including coronary heart disease, cerebrovascular disease, and rheumatic heart disease, poses a significant threat to health systems worldwide.[1,2] A central pathological mechanism in many CVD complications is thrombosis—the formation of abnormal blood clots within vessels. This process is

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often initiated by the rupture of atherosclerotic plaques, which promotes platelet activation and coagulation, potentially leading to myocardial infarction or ischemic stroke.[3,4] Consequently, the management and prevention of thrombotic events are cornerstones of CVD treatment.

Antithrombotic therapy is fundamental for preventing thromboembolic complications. This encompasses antiplatelet agents like aspirin, which inhibit platelet aggregation, and anticoagulants like warfarin and heparin, which affect the coagulation cascade.[5–7] The efficacy and safety of these treatments hinge on maintaining a delicate balance; insufficient anticoagulation risks thrombosis, while excessive anticoagulation increases the risk of hemorrhage. Therefore, rigorous monitoring of coagulation status is imperative. The Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) tests are critical global assays for this purpose. PT, often reported as the International Normalized Ratio (INR), is essential for monitoring the extrinsic pathway and guiding warfarin therapy.[8,9] The APTT, in contrast, assesses the intrinsic pathway and is routinely used to monitor unfractionated heparin therapy.[10] These parameters provide a vital window into a patient's hemostatic balance.

A 2025 cross-sectional study in Sana'a found that hypertension in heart and kidney disease patients was significantly associated with age, obesity, smoking, diabetes, and, notably, universal irregularity in medication use.[11] This high prevalence of modifiable risk factors and suboptimal management highlights an urgent need for local clinical research to characterize patient profiles and guide targeted interventions.

In Yemen, and specifically in Sana'a City, the burden of CVD is compounded by socioeconomic challenges and constrained healthcare resources. While the high prevalence of heart disease is acknowledged, there is a conspicuous lack of local data characterizing the coagulation profiles of these patients. This gap is clinically significant, as coagulation parameters like PT and APTT are routinely measured in cardiac care for various purposes: establishing a baseline, screening for coagulopathies, and critically monitoring anticoagulant therapy (e.g., warfarin) in specific subgroups. Local factors such as genetics, diet, medication adherence, and variable access to monitoring can influence these values and, consequently, clinical outcomes. Therefore, this study aimed to evaluate prothrombin time (PT), international normalized ratio (INR), and activated partial thromboplastin time (APTT) in antithrombotic-treated cardiac patients and assess associations with demographic characteristics, clinical diagnoses, and therapeutic regimens. The findings will provide crucial baseline data to inform the understanding of coagulation profiles in this understudied population.

Materials and Methods

Study Design and Setting

A hospital-based, cross-sectional study was conducted from January to March 2024 in various hospitals and centers in Sana'a, including Al-Thawra Model Hospital, Dr. Hashem Al-Iraqi Hospital, Kuwait University Hospital, and Al-Aorubi Modern Hospital in Sana'a City, Yemen.

Study Population and Sampling

A convenience sample of 200 consecutive patients with a confirmed diagnosis of cardiovascular diseases and prescribed antithrombotic therapy were enrolled during the study period. This diagnosis was originally established and documented by attending cardiologists at the participating hospitals according to their standard diagnostic protocols. This sample size was determined based on practical feasibility and alignment with similar observational studies. It is also consistent with sample sizes employed in comparable observational studies in the field, such as the study by Aynalem et al[12] which utilized 98 participants. To enhance the representativeness of our clinical population, we included patients of both sexes and a broad spectrum of ages. Patients were recruited from participating cardiology departments or clinics within the city during the study period.

Eligibility Criteria

The inclusion criteria comprised adult patients (aged 15–80 years) with a confirmed diagnosis of one of the following: ST-elevation myocardial infarction (STEMI), non-ST-elevation acute coronary syndrome (NSTE-ACS), stable ischemic heart disease (SIHD), rheumatic heart disease (RHD), status post-mitral valve replacement (MVR), dilated cardiomyopathy (DCM), heart failure (HF), or a history of cerebrovascular accident (CVA) from government and private centers in Sana'a who prescribed antithrombotic therapy (antiplatelet or anticoagulant medication) and provided informed consent. Participants were excluded if they were not using anticoagulants, had other chronic comorbidities (eg, chronic liver disease, known bleeding diatheses, active cancer), declined to consent, or if their blood sample was hemolyzed, contaminated, insufficient for analysis, or improperly transported.

Data Collection

Data were collected using a structured proforma. Demographic variables included age and gender. Clinical variables encompassed hospital type, history of cardiac surgery, and primary cardiovascular diagnosis. Antithrombotic therapy details were recorded, including drug type (Aspirin, Warfarin, Heparin), dosage, therapy duration (permanent/temporary), administration frequency, and monitoring frequency. Venous blood samples were drawn to assess coagulation profiles, including Prothrombin Time (PT), International Normalized Ratio (INR), and Activated Partial Thromboplastin Time (APTT). All laboratory analyses were performed using standardized methods.

Blood Sampling and Laboratory Analysis

Blood Collection and Processing

Venous blood was collected by atraumatic venipuncture into plastic tubes containing 0.109 mol/L (3.2%) sodium citrate at a 9:1 blood-to-anticoagulant ratio. Tubes were filled completely to maintain the correct ratio and gently inverted 4–6 times immediately after collection. Specimens were centrifuged at 1500 × g for 15 minutes at room temperature to obtain platelet-poor plasma. All coagulation assays were performed within two hours of blood collection. Hemolyzed, lipemic, or clotted specimens were rejected.

Prothrombin Time (PT) – Manual Tilt-Tube Technique

PT was determined using the manual tilt-tube technique, formally recognized by the Clinical and Laboratory Standards Institute (CLSI) as the reference measurement procedure for PT and INR standardization.[13]

Reagents: Thromborel® S (Siemens Healthineers, Marburg, Germany), a lyophilized human placental thromboplastin reagent containing calcium chloride and stabilizers, was reconstituted with exactly 4 mL of distilled water and warmed to 37°C for 30 minutes prior to use. Control Plasma N (normal range) and Control Plasma P (pathological range) (Siemens Healthineers) were used for quality control.

Procedure: A glass test tube was pre-warmed in a 37°C ± 0.5°C water bath for at least 1 minute. Citrated plasma (100 µL) was pipetted into the tube and incubated for exactly 60 seconds. Pre-warmed Thromborel® S reagent (200 µL) was added, simultaneously starting a calibrated stopwatch. The tube was gently tilted approximately 30–45 degrees from vertical at a frequency of 2 tilts per second against a light source with a dark background. The endpoint was recorded at the first visual detection of fibrin strand formation. All tests were performed in duplicate; the mean value was reported when results agreed within 10%.

INR Calculation: The International Normalized Ratio was calculated as INR = (Patient PT / Mean Normal PT)^ISI. The International Sensitivity Index (ISI) value for Thromborel® S reagent lot was 1.03, as provided by the manufacturer.[13,14]

Activated Partial Thromboplastin Time (APTT) – Manual Method

APTT was determined using the manual method with silicon dioxide-based activation.

Reagents: Pathromtin® SL (Siemens Healthineers, Marburg, Germany), a ready-to-use liquid reagent containing silicon dioxide particles (1.2 g/L) as surface activator and plant phospholipids (0.25 g/L) in Hepes buffer (pH 7.6), was gently inverted 5–8 times before use to resuspend sediment. Calcium chloride solution (0.025 mol/L) was pre-warmed to 37°C. Control Plasma N and Control Plasma P (Siemens Healthineers) were employed for quality control.

Procedure: A clean test tube was pre-warmed to 37°C in the water bath. Citrated plasma (100 µL) was pipetted into the tube, followed by 100 µL of Pathromtin® SL reagent (room temperature). The mixture was gently mixed and incubated for exactly 2 minutes at 37°C. Pre-warmed 0.025 mol/L calcium chloride (100 µL) was added, simultaneously starting the stopwatch. The tube was gently tilted (2 tilts per second) in the 37°C water bath, and the coagulation time was recorded upon visible fibrin strand formation. Duplicate testing was performed, and mean values were reported.

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Quality Control

Internal quality control was performed at the start of each run, after each reagent vial change, and at minimum every 8 hours. Two levels of control plasmas (normal and pathological) were analyzed. Control values were plotted on Levy-Jennings charts with Westgard multi-rules applied. Runs were accepted only when control values fell within the manufacturer's established ranges (±2 standard deviations). Normal reference ranges established in our laboratory were: PT: 11.0–13.5 seconds; INR: 0.8–1.2; APTT: 25.0–35.0 seconds.[13,14]

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 25. Descriptive statistics were presented as frequencies and percentages for categorical variables. Continuous variables (PT, INR, APTT) were non-normally distributed, as assessed by the Shapiro–Wilk test, and were therefore summarized as median and interquartile range (IQR).

Associations between categorical variables (eg, disease diagnosis with gender and age groups) were examined using the Chi-square (χ^2) test. The Fisher's Exact Test was employed when any expected cell count was less than 5.

For comparisons of continuous coagulation parameters across more than two independent groups (eg, across eight disease types, three age groups, or three antithrombotic agents), the non-parametric Kruskal–Wallis test was used. When a significant overall difference was found ($P < 0.05$), post-hoc pairwise comparisons were conducted with a Bonferroni correction to control for Type I error. The specific comparisons reported were limited to those that were statistically significant and clinically relevant. The Mann–Whitney *U*-test was used for comparisons between two independent groups (eg, gender). AP-value of less than 0.05 was considered statistically significant for all analyses.

Ethical Consideration

Ethical approval for this study was obtained from the Institutional Ethical Committee of AL-Saeeda University (Ref: IEC/SRC/SU/2024/Ex.21/011/24). The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Before commencing data collection, official permissions were secured from the participating public and private hospitals in Sana'a city. Furthermore, all participants were informed about the purpose of the study, assured of confidentiality before participation. All participants provided informed consent. For participants under the age of 18, informed consent was obtained from their parent/legal guardian. Furthermore, minor participants were informed that consent had been obtained from their parents/legal guardians. This procedure was a mandatory part of the ethical consent protocol. Participation was voluntary, and respondents could withdraw at any time without consequence.

Results

Demographic, Clinical, and Therapeutic Profile

A total of 200 cardiac patients on antithrombotic therapy were included. The cohort was predominantly male (138, 69.0%) and aged 51–80 years (114, 57.0%). Most patients were recruited from private hospitals (138, 69.0%) and had no history of cardiac surgery (174, 87.0%). Aspirin was the most prescribed antithrombotic agent (181, 90.5%), primarily at 75mg daily (104, 52.0%). Therapy was most often permanent (165, 82.5%). Regular monitoring of coagulation was reported by only 40.0% (n=80) of patients (Table 1).

Disease Distribution by Gender and Age

The distribution of cardiovascular diagnoses differed significantly by gender (χ^2, p=0.014). Notably, Mitral Valve Replacement (MVR) was exclusively found in females (4, 6.5%), while Cerebrovascular Accident (CVA) occurred only in males (6, 4.3%) (Table 2). A highly significant association was also observed between diagnosis and age group ($p<0.001$). Rheumatic Heart Disease (RHD) was more prevalent in younger patients (15–30 years: 46.7%), whereas Stable Ischemic Heart Disease (SIHD) and Heart Failure (HF) were more common in the oldest group (51–80 years: 17.5% and 14.0%, respectively) (Table 3).

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Table 1 Patient Demographics, Clinical Characteristics, and Antithrombotic Therapy Profile (N=200)

Variable	Category	Frequency (N) Patients/(Percent (%))
Gender		
	Male	138 (69.0%)
	Female	62 (31.0%)
Age (Years)		
	15–30	15 (7.5%)
	31–50	71 (35.5%)
	51–80	114 (57.0%)
Hospital Type		
	Government	62 (31.0%)
	Private	138 (69.0%)
History of Cardiac Surgery		
	Yes	26 (13.0%)
	No	174 (87.0%)
Type of antithrombotic		
	Aspirin	181 (90.5%)
	Warfarin	9 (4.5%)
	Heparin	10 (5.0%)
Antithrombotic Dosage		
	Aspirin 75 mg	104 (52.0%)
	Aspirin, 100 mg	70 (35.0%)
	Aspirin, 300 mg	7 (3.5%)
	Warfarin, 5 mg	9 (4.5%)
	Heparin, 2500 IU	10 (5.0%)
Therapy Duration		
	Permanent	165 (82.5%)
	Temporary	35 (17.5%)
Monitoring		
	Yes	80 (40.0%)
	Sometimes	88 (44.0%)
	Rarely	32 (16.0%)

Table 2 Association Between Patient Gender and Cardiovascular Disease Diagnosis (N=200)

Variable	Gender of Patient		Total	P value
	Male N=138 NO.(%)	Female N=62 NO.(%)	N=200 NO.(%)	
Disease				
STEMI	23(16.7)	10(16.1)	33(16.5)	0.014*
NSTE-ACS	44(31.9)	15(24.2)	59(29.5)	
SIHD	14(10.1)	9(14.5)	23(11.5)	
RHD	20(14.5)	15(24.2)	35(17.5)	

(*Continued*)

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Table 2 (Continued).

Variable	Gender of Patient		Total	P value
	Male N=138 NO.(%)	Female N=62 NO.(%)	N=200 NO.(%)	
MVR	0(0.0)	4(6.5)	4(2.0)	
DCM	18(13.0)	3(4.8)	21(10.5)	
HF	13(9.4)	6(9.7)	19(9.5)	
CVA	6(4.3)	0(0.0)	6(3.0)	
Total	138(100)	62(100)	200(100)	

Note: *p-value < 0.05 considered statistically significant (Chi-square test, with Fisher's Exact Test used when any cell count <5).
Abbreviations: PT, prothrombin time; INR, international normalized ratio; APTT, activated partial thromboplastin time; STEMI, ST-elevation myocardial infarction; NSTE-ACS, non-ST-elevation acute coronary syndrome; SIHD, Stable Ischemic Heart Disease; RHD, rheumatic heart disease; MVR, mitral valve replacement; DCM, dilated cardiomyopathy; HF, heart failure; CVA, cerebrovascular accident.

Table 3 Association Between Age Groups and Cardiovascular Disease Diagonosis (N=200)

Variable	Age of Patient			Total	*p* value
	15–30 N=15 NO.(%)	31–50 N=71 NO.(%)	51–80 N=114 NO.(%)	N=200 NO.(%)	
Disease					
STEMI	1(6.7)	14(19.7)	18(15.8)	33(16.5)	< 0.001*
NSTE-ACS	1(6.7)	26(36.6)	32(28.1)	59(29.5)	
SIHD	0(0.0)	3(4.2)	20(17.5)	23(11.5)	
RHD	7(46.7)	17(23.9)	11(9.6)	35(17.5)	
MVR	2(13.3)	2(2.8)	0(0.0)	4(2.0)	
DCM	4(26.7)	6(8.5)	11(9.6)	21(10.5)	
HF	0(0.0)	3(4.2)	16(14.0)	19(9.5)	
CVA	0(0.0)	0(0.0)	6(5.3)	6(3.0)	
Total	15(7.5)	71(35.5)	114(57)	200(100)	

Note: *p-value < 0.05 considered statistically significant (Chi-square test, with Fisher's Exact Test used when any cell count <5).
Abbreviations: PT, prothrombin time; INR, international normalized ratio; APTT, activated partial thromboplastin time; STEMI, ST-elevation myocardial infarction; NSTE-ACS, non-ST-elevation acute coronary syndrome; SIHD, Stable Ischemic Heart Disease; RHD, rheumatic heart disease; MVR, mitral valve replacement; DCM, dilated cardiomyopathy; HF, heart failure; CVA, cerebrovascular accident.

Coagulation Profiles by Gender and Age

No statistically significant differences in PT, INR, or APTT were found between male and female patients ($p>0.05$) (Table 4). Coagulation parameters varied across age groups, with a statistically significant difference observed for APTT (Kruskal–Wallis, $p = 0.01$). The youngest cohort (15–30 years) exhibited the highest median APTT (42.00s) (Table 4).

Coagulation Parameters Across Cardiac Diagnoses

Coagulation parameters varied significantly across diagnostic groups (Table 5). The Kruskal–Wallis test revealed statistically significant differences in PT ($\chi^2 = 45.23$, $P < 0.001$), INR ($\chi^2 = 52.42$, $P < 0.001$), and APTT ($\chi^2 = 38.96$,

Table 4 Gender and Age Differences in Coagulation Profiles (N=200)

Variable	PT (s)	INR	APTT (s)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**
Gender			
Male	N=138	N=138	N=138
	14.05 (13.0 −17.5)	1.10 (0.99–1.30)	34.0 (31.9–42.1)
Female	N=62	N=62	N=62
	14.80 (13.0 −20.0)	1.20 (1.00–1.53)	32.8 (29.9–42.0)
***p* value**	0.261	0.051	0.218
Age groups (Years)			
15 – 30	N=15	N=15	N=15
	15.1 (13.0–43.0)	1.2 (1.0–3.2)	42.00 (34.00–50.00)
31 – 50	N=71	N=71	N=71
	14.5 (13.0–19.6)	1.15 (1.00–1.53)	34.60 (32.00–42.00)
51 – 80	N=114	N=114	N=114
	14.00 (13.00–16.20)	1.10 (1.00–1.23)	33.00 (30.00–40.33)
p* value	0.2	0.15	0.01*

Notes: **P* value was significant at <0.05 and calculated by using the Mann–Whitney Test for gender and the Kruskal–Wallis Test for age groups. Normal reference ranges: PT: 11–13.5 seconds; INR: 0.8–1.2; APTT: 25–35 seconds.

Abbreviations: PT, prothrombin time; INR, international normalized ratio; APTT, activated partial thromboplastin time; IQR, Interquartile Range.

Table 5 Comparison of Coagulation Parameters Across Diagnostic Groups (N=200)

Variable	PT (s)	INR	APTT (s)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**
Diagnosis Category			
STEMI	N=33	N=33	N=33
	13.10 (11.62–14.57)	1.00 (0.85–1.19)	32.00 (26.00–39.10)
NSTE-ACS	N=59	N=59	N=59
	14.00 (12.70–18.04)	1.07 (1.00–1.58)	35.50 (31.50–45.50)
SIHD	N=23	N=23	N=23
	14.00 (13.00–15.50)	1.14 (1.01–1.22)	30.80 (26.30–35.80)
RHD	N=35	N=35	N=35
	16.10 (13.70–32.00)	1.21 (1.02–2.10)	35.50 (32.80–50.50)
MVR	N=4	N=4	N=4
	36.45 (17.18–47.25)	2.75 (1.34–6.90)	62.10 (36.10–109.55)

(*Continued*)

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Table 5 (Continued).

Variable	PT (s)	INR	APTT (s)
	Median (IQR)	**Median (IQR)**	**Median (IQR)**
DCM	N=21	N=21	N=21
	15.00 (13.00–17.85)	1.19 (1.01–1.27)	33.20 (32.40–41.35)
HF	N=19	N=19	N=19
	15.00 (13.00–17.80)	1.20 (1.00–1.30)	34.00 (31.00–42.80)
CVA	N=6	N=6	N=6
	13.70 (13.08–19.45)	1.02 (0.98–1.51)	38.00 (28.50–49.20)
Total	N=200	N=200	N=200
	14.20 (13.00–17.60)	1.10 (1.00–1.40)	33.95 (30.85–42.00)
***P* value**	0.009*	0.001*	0.006*

Notes: Data presented as Median (Interquartile Range). *P < 0.05 indicates statistically significant difference across groups (Kruskal–Wallis test).
Abbreviations: PT, prothrombin time; INR, international normalized ratio; APTT, activated partial thromboplastin time; STEMI, ST-elevation myocardial infarction; NSTE-ACS, non-ST-elevation acute coronary syndrome; SIHD, Stable Ischemic Heart Disease; RHD, rheumatic heart disease; MVR, mitral valve replacement; DCM, dilated cardiomyopathy; HF, heart failure; CVA, cerebrovascular accident.

P < 0.001) among the eight diagnostic categories. Patients with mitral valve replacement (MVR) had the highest median PT (36.45 s) and INR (2.75), while STEMI patients showed the lowest median INR (1.00) (Table 5).

Post-hoc pairwise comparisons (Bonferroni-adjusted) confirmed that MVR patients had significantly higher PT, INR, and APTT compared to all other diagnostic groups (all p<0.05), except versus RHD for PT. Patients with Rheumatic Heart Disease (RHD) showed intermediate elevation, with significantly higher PT compared to STEMI (mean difference: 9.81s, p=0.001), Non-ST-Elevation Acute Coronary Syndrome (NSTE-ACS) (8.30s, p=0.001), and Stable IHD (9.81 s, p=0.002) patients. No significant differences were found between the two acute coronary syndrome subtypes (STEMI vs. NSTE-ACS) (Table 6).

Table 6 Pairwise Comparisons of Coagulation Parameters Across Cardiac Disease Types (Bonferroni-Adjusted)

Comparison	Parameter	Mean Difference (Seconds)	95% CI	p-value
STEMI vs MVR	PT	−19.01	(−34.15, −3.86)	0.003
	INR	−2.52	(−3.88, −1.15)	<0.0001
	APTT	−34.47	(−59.86, −9.07)	0.001
STEMI vs RHD	PT	−9.60	(−16.54, −2.66)	0.001
MVR vs HF	PT	17.10	(1.37, 32.84)	0.020
	INR	2.36	(0.95, 3.78)	<0.0001
	APTT	33.61	(7.22, 60.00)	0.002

(*Continued*)

Table 6 (Continued).

Comparison	Parameter	Mean Difference (Seconds)	95% CI	p-value
MVR vs NSTE-ACS	PT	17.71	(2.93, 32.49)	0.006
	INR	2.40	(1.07, 3.73)	<0.0001
	APTT	29.37	(4.58, 54.15)	0.006
MVR vs DCM	PT	16.23	(0.62, 31.83)	0.033
	INR	2.28	(0.87, 3.68)	<0.0001
	APTT	33.23	(7.06, 59.40)	0.002
MVR vs IHD-Stable	PT	19.22	(3.72, 34.71)	0.003
	INR	2.42	(1.03, 3.82)	<0.0001
	APTT	33.98	(7.99, 59.96)	0.001
RHD vs NSTE-ACS	PT	8.30	(2.19, 14.40)	0.001
RHD vs IHD-Stable	PT	9.81	(2.13, 17.48)	0.002

Notes: *p <0.05 (Bonferroni-adjusted). Only statistically significant comparisons (p <0.05) and clinically relevant non-significant comparisons are shown. Full pairwise comparisons are available upon request. Negative values indicate that Disease Type 1 has lower values than Disease Type 2.
Abbreviations: PT, Prothrombin Time; INR, International Normalized Ratio; APTT, activated partial thromboplastin time; STEMI, ST-Elevation Myocardial Infarction; MVR, Mitral Valve Replacement; RHD, Rheumatic Heart Disease; HF, Heart Failure; NSTE-ACS, Non-ST-Elevation Acute Coronary Syndrome; DCM, Dilated Cardiomyopathy; SIHD, Stable Ischemic Heart Disease; CVA, Cerebrovascular Accident.

The clinical significance of the observed differences in coagulation parameters is significant. Patients with mitral valve replacement (MVR) demonstrated markedly elevated coagulation parameters, indicating a requirement for the closest monitoring and the highest intensity of anticoagulation management. Those with rheumatic heart disease (RHD) showed moderately elevated prothrombin time compared to acute coronary syndrome patients, suggesting an intermediate need for monitoring and warranting consideration of disease-specific factors in management. Importantly, no significant differences in coagulation profiles were found between ST-elevation myocardial infarction (STEMI) and non-ST-elevation acute coronary syndrome (NSTE-ACS), supporting the applicability of similar anticoagulation strategies across acute coronary syndromes. Furthermore, stable ischemic heart disease (SIHD) patients exhibited coagulation profiles similar to those with acute conditions, indicating that disease stability alone does not predict an individual's coagulation profile, and monitoring should be guided by the specific coagulation parameter results rather than clinical stability status.

Coagulation Parameters by Antithrombotic Therapy and Dosage

The type of antithrombotic agent significantly influenced coagulation parameters (Kruskal–Wallis, PT ($\chi^2[2] = 7.18$, P = 0.028), INR ($\chi^2[2] = 7.95$, P = 0.019), and APTT ($\chi^2[2] = 6.31$, P = 0.043). As anticipated, warfarin-treated patients (n=9) demonstrated the highest median PT (20.00 s), INR (1.53), and APTT (40.00s) (Table 7).

Analysis by specific dosage regimen also revealed significant overall variation (Kruskal–Wallis, $p \le 0.015$ for all parameters). Pairwise comparisons showed warfarin (5 mg) resulted in significantly higher PT, INR, and APTT compared to both aspirin 75 mg and 100 mg groups (eg, Warfarin vs. Aspirin 100mg: PT p=0.003, INR p=0.001, APTT p=0.010), confirming its expected pharmacological effect, despite the small sample size (n = 9). A minor but statistically significant difference in PT was noted between aspirin 75 mg and 100 mg doses (p=0.043), with no significant differences in INR or APTT between these doses. Heparin (2500 IU) showed no statistically significant differences compared to the aspirin groups (Tables 8 and 9).

Table 7 Kruskal–Wallis Analysis of Coagulation Parameters by Antithrombotic Therapy (N=200)

Antithrombotic Agent	n	PT (s), Median (IQR)	INR, Median (IQR)	APTT (s), Median (IQR)
Aspirin	181	14.10 (13.00–17.00)	1.10 (1.00–1.38)	33.50 (30.00–42.00)
Warfarin	9	20.00 (13.00–33.90)	1.53 (1.10–2.55)	40.00 (35.30–62.10)
Heparin	10	15.50 (14.50–17.75)	1.19 (1.05–1.42)	33.25 (32.80–41.85)
Kruskal–Wallis χ^2 (df)		7.18	7.95	6.31
***p* value**		0.028*	0.019*	0.043*

Notes: Data presented as median (interquartile range). P values from Kruskal–Wallis test comparing all three groups. *P < 0.05 indicates statistically significant difference.

Table 8 Descriptive Statistics and Non-Parametric Comparisons of Coagulation Parameters by Antithrombotic Dosage

Dosage Category	n (%)	PT (Seconds) Median (IQR)	p-value†	INR Median (IQR)	p-value†	APTT (Seconds) Median (IQR)	p-value†
Aspirin 75 mg	104 (52.0%)	14.50 (6.50)	**Ref**	1.11 (0.52)	**Ref**	35.00 (14.53)	**Ref**
Aspirin 100 mg	70 (35.0%)	13.65 (2.10)	0.043*	1.08 (0.20)	0.224	33.00 (7.70)	0.097
Aspirin 300 mg	7 (3.5%)	15.90 (4.60)	0.850	1.50 (0.38)	0.116	30.80 (6.70)	0.432
Warfarin 5 mg	9 (4.5%)	20.00 (20.90)	**0.012***	1.53 (1.45)	**0.004***	40.00 (26.80)	**0.041***
Heparin 2500 IU	10 (5.0%)	15.50 (3.25)	0.734	1.19 (0.37)	0.644	33.25 (9.05)	0.754
Kruskal–Wallis H (df=4)	–	H = 18.42 p = 0.001*		H = 25.67 p < 0.001*		H = 12.35 p = 0.015*	
Total (N=200)	200 (100%)	14.50 (6.15)		1.10 (0.40)		33.95 (11.15)	

Notes: Data presented as Median (Interquartile Range) due to non-normal distributions (Kolmogorov–Smirnov p < 0.05 for most groups). Normal reference ranges: PT: 11–15 seconds; INR: 0.8–1.2; APTT: 25–35 seconds. †p-values from Mann–Whitney *U*-tests comparing each group to Aspirin 75 mg reference group. Kruskal–Wallis *H*-test assesses overall difference across all five dosage categories. *p < 0.05 considered statistically significant (uncorrected for multiple comparisons in this exploratory analysis). Bolded p-values indicate statistically significant differences from reference group.

Table 9 Pairwise Statistical Comparisons Between Key Dosage Groups (Mann–Whitney *U*-Tests)

Comparison	Statistic	PT	INR	APTT
Warfarin vs. Aspirin 100 mg	U statistic	145.0	123.5	187.0
	p-value	0.003*	0.001*	0.010*
Heparin vs. Aspirin 100 mg	U statistic	305.0	290.0	308.5
	p-value	0.278	0.208	0.287
Aspirin 75 mg vs. 100 mg	U statistic	3075.5	3385.0	3250.0
	p-value	0.043*	0.224	0.097
Warfarin vs. Heparin	U statistic	28.5	31.0	31.5
	p-value	0.301	0.382	0.402

Note: *P < 0.05 indicates statistically significant difference.

Discussion

This cross-sectional study provides important insights into the coagulation profiles of antithrombotic-treated cardiac patients in Sana'a, Yemen, revealing significant variations in PT, INR, and APTT across different demographic groups, cardiac diagnoses, and antithrombotic regimens. Our findings highlight several clinically relevant patterns with implications for therapeutic monitoring in this resource-limited setting.

The predominance of male patients (69.0%) in our cohort is consistent with the well-documented higher prevalence of cardiovascular disease among men globally.[15] This is also consistent with a 2022 study by Al-Kebsi et al, which reported that approximately 75–81% of ischemic heart disease (SIHD) patients were male.[16] The majority of patients (57.0%) were aged 51–80 years, reflecting the age-dependent nature of cardiovascular pathology. Notably, rheumatic heart disease (RHD) was most prevalent among younger patients (46.7% in the 15–30 age group), whereas stable ischemic heart disease (SIHD) and heart failure (HF) predominated in older patients ($p < 0.001$). This age distribution pattern aligns with studies from other developing countries where RHD remains a significant cause of cardiac morbidity in young populations, contrasting with the atherosclerotic disease burden characteristic of older age groups in high-income countries.[17,18]

The significant association between gender and cardiac diagnosis ($p = 0.014$) is noteworthy, particularly the exclusive occurrence of mitral valve replacement (MVR) in female patients (6.5% vs. 0.0%) and the higher proportion of RHD among women (24.2% vs. 14.5%). These findings corroborate previous reports demonstrating female predilection for RHD and valvular pathologies, potentially attributable to autoimmune susceptibility and delayed presentation in resource-limited settings.[19,20]

Our analysis revealed no statistically significant gender differences in PT, INR, or APTT values, although a trend toward higher INR in females approached significance ($p = 0.051$). This finding contrasts with some previous study reporting significantly prolonged coagulation times in females, which has been attributed to physiological lower vitamin K-dependent factor levels and hormonal influences.[21] However, our results are consistent with other investigations that found no clinically meaningful gender-based differences in anticoagulation response among cardiac patients receiving standardized therapy.[22]

Age-related differences in coagulation parameters were observed, with significantly prolonged APTT in the youngest age group (15–30 years: median 42.00 seconds) compared to older patients ($p = 0.01$). This finding may reflect the higher proportion of RHD and MVR patients in this younger cohort, many of whom were receiving warfarin therapy. Similar age-related variations in baseline coagulation times have been reported elsewhere, though the clinical significance remains debated.[23]

A key finding of our study is the highly significant variation in PT, INR, and APTT across diagnostic categories ($p < 0.001$ for all parameters). Patients with MVR demonstrated the most pronounced coagulation abnormalities, with markedly prolonged PT (median 36.45 seconds), INR (2.75), and APTT (62.10 seconds). Pairwise comparisons confirmed that MVR patients had significantly longer coagulation times compared to virtually all other diagnostic groups, including STEMI, NSTE-ACS, SIHD, DCM, and HF (all $p < 0.05$, Bonferroni-adjusted).

These findings reflect the mandatory therapeutic anticoagulation with warfarin following mechanical valve replacement, targeting higher INR ranges (2.5–3.5) compared to other indications.[24] Our results are consistent with previous studies demonstrating that MVR patients consistently exhibit the most intensive anticoagulation requirements among cardiac populations.[25,26] Cannegieter et al reported that mechanical valve patients spend approximately 50% of time within therapeutic range under optimal management, with significant variability influenced by numerous clinical and demographic factors.[27]

Patients with RHD also demonstrated significantly prolonged coagulation parameters compared to those with NSTE-ACS and SIHD ($p < 0.05$). This likely reflects the higher proportion of RHD patients receiving warfarin for associated atrial fibrillation or prior valve surgery, consistent with contemporary management guidelines.[28] Conversely, patients with STEMI and SIHD exhibited coagulation parameters within or near normal reference ranges, corresponding with the predominant use of antiplatelet agents rather than anticoagulants in these conditions.

Analysis of coagulation parameters by antithrombotic agent revealed statistically significant differences across all three parameters (PT: $p = 0.028$; INR: $p = 0.019$; APTT: $p = 0.043$). Warfarin-treated patients demonstrated the most prolonged PT (20.00 seconds) and INR (1.53), consistent with its mechanism of vitamin K antagonism and inhibition of

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factors II, VII, IX, and X. Heparin therapy was associated with modestly prolonged PT (15.50 seconds) and APTT (33.25 seconds), though these values remained within or near therapeutic ranges for prophylactic dosing.

Our dosage-specific analysis revealed that warfarin 5 mg produced significantly prolonged PT, INR, and APTT compared to aspirin 75 mg reference ($p = 0.012$, $p = 0.004$, and $p = 0.041$, respectively). These findings are consistent with the established pharmacodynamic profiles of these agents and highlight the importance of regular monitoring for warfarin-treated patients.[29] Notably, aspirin 100 mg was associated with significantly shorter PT compared to aspirin 75 mg ($p = 0.043$), though the absolute difference (13.65 vs. 14.50 seconds) is unlikely to be clinically significant and may reflect confounding by indication rather than a true dosage effect.

A concerning finding of our study is the suboptimal monitoring frequency among antithrombotic-treated patients. Only 40.0% reported regular monitoring, with 16.0% rarely undergoing coagulation testing. This represents a significant patient safety concern, particularly for warfarin-treated patients who comprised 4.5% of our cohort. Similar challenges with anticoagulation monitoring have been reported in other low- and middle-income countries, where limited access to laboratory facilities, financial constraints, and inadequate patient education contribute to suboptimal therapeutic control.[30,31]

In Yemen specifically, the ongoing humanitarian crisis has severely compromised healthcare infrastructure, including laboratory services essential for anticoagulation monitoring.[32] Our findings underscore the urgent need for point-of-care testing devices and structured anticoagulation management programs in this setting. Previous studies have demonstrated that pharmacist-led or nurse-led anticoagulation clinics significantly improve time in therapeutic range and reduce adverse events compared to usual care.[33,34]

Limitations

This study has several limitations. Its cross-sectional design precludes the assessment of causality or longitudinal outcomes. While the overall sample size of 200 patients is adequate for descriptive purposes, it was not determined through formal statistical calculation of study power for specific hypotheses. Furthermore, the presence of very small subgroups limits the study's power and the generalizability of the findings for those groups (eg, patients undergoing mitral valve replacement and warfarin users). Finally, the study's geographical confinement may affect the generalizability of the results to other healthcare settings.

Conclusion

This study demonstrates significant variations in coagulation profiles among antithrombotic-treated cardiac patients in Yemen, strongly associated with diagnostic category and antithrombotic regimen. The particularly prolonged parameters observed in MVR and RHD patients reflect appropriate therapeutic anticoagulation, while the suboptimal monitoring frequency identified represents a critical gap in patient safety. These findings emphasize the urgent need for strengthened anticoagulation monitoring services in Yemen, including point-of-care testing capabilities and structured education programs for both healthcare providers and patients. Future prospective studies should evaluate the feasibility and impact of such interventions on clinical outcomes in this challenging setting.

Recommendations

We recommend deploying point-of-care INR devices, implementing structured monitoring protocols prioritizing high-risk patients (mitral valve replacement and rheumatic heart disease), and developing patient education programs, given that only 40% receive regular monitoring. Health authorities should subsidize the costs of testing and ensure a supply of medications. International humanitarian organizations should support device donation, technical training, and capacity building for cardiovascular care in this resource-constrained setting.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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