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Alterations in Coagulation and Hematological Parameters in Coronary Artery Disease: A Case–Control Study in Owerri, Nigeria

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ABSTRACT

Background: Coronary artery disease (CAD) is a leading cause of major cardiovascular illness globally. CAD has been linked to various coagulation and inflammatory disorder pathways. This research is on activated partial thromboplastin time (APTT) and blood cell components of CAD patients in Owerri, Nigeria.

Methods: This hospital-based unmatched case-control study was conducted among 100 persons (50 CAD and 50 apparently healthy persons serving as the controls). They were all recruited from the Federal University Teaching Hospital, Owerri. APTT, RBC and WBC counts were determined using routine laboratory techniques from the analysis of venous blood samples. Data was analysed data with the IBM SPSS Statistics software (version 26.0). The independent samples t-test was used to compare means of different parameters. The correlation between two variables was determined with the Pearson correlation coefficient. A 95% confidence limit was the cut-off point for statistical significance.

Results: APTT was significantly prolonged in CAD patients compared with controls. RBC count was significantly reduced, while WBC count was significantly elevated. A modest inverse correlation was observed between RBC and WBC, while the association between APTT and WBC did not reach statistical significance. Sex-based analysis revealed a significant difference in RBC count, but not in APTT or WBC.

Conclusion: These findings suggest that CAD is associated with concurrent alterations in coagulation and hematological parameters, reflecting a possible thrombo-inflammatory profile. APTT, RBC count, and WBC count may serve as accessible adjunct markers in CAD assessment, although their clinical utility should be interpreted cautiously.

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Keywords: *Coronary artery disease; Activated partial thromboplastin time; Red blood cell count; White blood cell count; Coagulation; Inflammation; Nigeria*

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INTRODUCTION

Coronary artery disease (CAD) continues to be the major cause of morbidity and mortality globally and a significant and increasing burden on the population health especially in low- and middle-income nations that are in the rapid epidemiological transition phase[1]. Recent concepts of CAD have developed further than a lipid-based paradigm to that of a complex, chronic inflammatory and thrombotic disease due to endothelial dysfunction, immune activation, and progressive atherosclerotic plaque development[2]. Thrombus formation after rupture of the plaque is critically involved in the process of transition of stable atherosclerotic lesions into acute coronary events, which explains the primary role of the interaction between inflammation and coagulation in the pathogenesis of the disease[1-3]. Nigeria and sub-Saharan Africa exemplify the increasing prevalence and complex origins of many lifestyle and age-related conditions culminating in mortality and morbidity of a more developed nation, like coronary artery disease[1]. Rapid urbanization, a changing diet, a more sedentary lifestyle, an aging population, and the increasing prevalence of hypertension, type 2 diabetes, overweight and obesity, and dyslipidemias have a considerable negative impact[2]. Injuries and infectious diseases remain dominant public health problems, but the increasing recognition of CAD in tertiary health-care services indicates the importance for Nigeria and the need for more specific and contextual approaches to cardiovascular risk assessment.

The coagulation cascade is a key factor in this mechanism, and changes in clotting dynamics are a risk factor of thrombosis and poor cardiovascular outcomes. Activated partial thromboplastin time (APTT), which is a readily available laboratory value, gives a functional evaluation of the intrinsic and common coagulation pathways, which represents the activity of clotting factors VIII, IX, XI and XII. Dysregulation of coagulation parameters such as a long clotting time have been observed in cardiovascular disease and can be indicative of a dysregulated hemostatic condition[4,5]. In addition to their diagnostic value, coagulation indices are also becoming a significant adjunct in the risk stratification of coronary syndromes, which supports the idea that thrombosis is not only a result but also is believed to be a significant factor of disease progression[1].

Simultaneously, hematological parameters obtained based on routine blood counts have been proposed as useful and inexpensive biomarkers of the inflammatory milieu of CAD. The number of red blood cells (RBCs) is critical in blood viscosity, oxygen supply, which are key factors that determine myocardial perfusion, and its change has been shown to contribute to cardiovascular dysfunction and atherogenesis. Likewise, the count of white blood cell (WBC) is a strong predictor of systemic inflammation and the high count of the latter is always linked with the progression of atherosclerosis, unstable plaque, and poor clinical outcomes[3,6,7]. A leukocytosis has also been found as an independent mortality and complication predictor of acute coronary syndromes[1,6,7]. Notably, interdependence of inflammation, hematological changes and coagulation mal-function reflects a single thrombo-inflammatory axis in CAD. The inflammatory mediators not only hasten atherogenesis, but also regulates the coagulation pathways, supporting a hypercoagulable state, which predisposes to thrombotic events. This two-way communication highlights the clinical importance of considering hematological and coagulation data in the process of cardiovascular risk evaluation, in particular, because such commonly used indices as APTT, RBC count, and WBC count are cheap, and their presence is ubiquitous, as well as informative clinically[8-10].

Despite the increasing evidence associating CAD with various hematological disorders and abnormalities in the coagulation cascade, the majority of the studies have analyzed composite hematological parameters, differential cell count ratios, or other advanced biomarkers. Little research has focused on the combined analysis of coagulation parameters, RBC, and WBC, which are readily available in most clinical laboratories. This is particularly true in sub-Saharan Africa, where the interplay of environmental, genetic, and healthcare factors may impact the expression and interpretation of biomarkers. Furthermore, in Nigeria, studies that investigate the combined effect of hematological and coagulation abnormalities on CAD, are almost nonexistent. This may impact the ability to evaluate cardiovascular risk with low-cost, accessible laboratory assessments in low-resource areas.

Consequently, this study assessed the coagulation and hematological profiles of coronary artery disease patients in Owerri, Nigeria, focusing on APTT, RBC, and WBC counts. The study aimed to provide local evidence and context to improve the assessment of cardiovascular risk and associated clinical decision-making, using laboratory tests that are straightforward and readily available. It was hypothesized that among

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this population, APTT would be longer, RBC counts would be lower, and WBC counts would be elevated when compared to healthy controls.

METHODOLOGY

Study Design and Setting: This hospital-based unmatched case-control study was conducted at the Federal University Teaching Hospital, Owerri (FUTH Owerri), a tertiary healthcare institution located in Owerri, Imo State, Nigeria. This study took place from April through June of 2024. Participants in the study were drawn from attendees at the hospital's Cardiology Clinic, while controls were drawn from the healthy external adult community. The report of the study was done in accordance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines of observational studies [11].

Study population: Adults aged 18 years and above constituted the study group. Patients with clinically confirmed coronary artery disease (CAD) formed the case group. The control group consisted of healthy individuals with no documented case of cardiovascular disease. The clinical diagnosis of CAD was supplemented by the findings of the electrocardiogram and/or the doctor's diagnosis as recorded in the patient's file.

Patients were recruited on a consecutive basis from the Cardiology Clinic and related wards of the Federal University Teaching Hospital, Owerri. The control group consisted of healthy adults from the hospital. Potential control group members were screened using their medical history and the study eligibility criteria. Individuals with documented cardiovascular disease and/or other conditions that could affect coagulation and hematological parameters were excluded. Recruitment continued until the target sample sizes for both groups were met.

Sample size determination and sampling technique: For participant recruitment, a convenience sampling technique was utilized. Eligible patients with coronary artery disease (CAD) were identified in the Federal University Teaching Hospital at the Cardiology Clinic and associated medical units in Owerri. During their clinic visit, patients that had a physician diagnosis of coronary artery disease and met the study inclusion criteria were identified and invited to participate. Recruitment was sustained until a total sample of fifty (50) CAD patients was realized. The control group population was constituted of healthy adults that were within the hospital environment. These were predominantly hospital staff and patient relatives; as well as volunteers. Using a structured questionnaire and a review of medical histories, potential controls were examined to identify and exclude individuals with a history of coronary artery disease, other cardiovascular disorders, diseases related to blood and its constituents, acute infectious diseases, chronic inflammation, and other diseases that may affect blood and hematological parameters. Individuals who fit the inclusion criteria and provided written informed consent were enrolled until a total of 50 controls were obtained. Sample size was estimated using the formula for evaluating the difference between two independent means, as study variables (activated partial thromboplastin time, red blood cell, and white blood cell counts) were continuous laboratory parameters[12].

The sample size estimation was based on WBC values from a comparable case–control study, which reported mean WBC counts of $7.49 \pm 2.46 \times 10^9$/L in cases and $6.25 \pm 1.54 \times 10^9$/L in controls[13].

$$n = \frac{[2(Z\alpha/2 + Z\beta)^2\ \sigma^2}{\mu_1 - \mu_2{}^2}$$

Where: n = minimum required sample size per group; $Z\alpha/2 = 1.96$; $Z\beta = 0.84$; $\mu_1 - \mu_2$ = difference between group means; σ = pooled standard deviation.

$$\sigma = \sqrt{\frac{(2.46^2 + 1.54^2}{2}}$$

$\mu_1 - \mu_2 = 7.49 - 6.25 = 1.24$

$n = 42.86 \approx 43$ per group

After adjusting for a 10% non-response rate, the sample size was increased to 50 participants per group, yielding a total of 100 participants (50 cases and 50 controls).

Inclusion criteria: Participants were included if they were 18 years older and if signed written consent was provided. Cases included if CAD was diagnosed by a physician through a clinical evaluation and associated diagnostic records. Controls included individuals who were healthy, had no CAD and no history of major cardiovascular diseases, and had no medical condition that would alter the coagulation or hematological parameters and who were stable in the medical history screening.

Exclusion criteria: Participants were excluded if they had conditions that could independently affect coagulation or hematological parameters. These included bleeding disorders, chronic liver disease, renal failure, malignancy, hematological diseases, acute infections, or inflammatory conditions. Individuals

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receiving anticoagulant therapy and pregnant women were also excluded.

Data and specimen collection: Demographic and clinical data were collected using a structured pro forma and participants' medical records. Venous blood samples were obtained aseptically under standard phlebotomy procedures.

For APTT analysis, 2.7 mL of venous blood was collected into a 3.2% sodium citrate tube and centrifuged to obtain platelet-poor plasma[14].

For RBC and WBC analysis, approximately 2 mL of venous blood was collected into an EDTA anticoagulant tube[15].

Laboratory analysis: APTT was measured using a standard phospholipid-based coagulation method on an automated coagulation analyzer, following the manufacturer's instructions.

RBC and WBC counts were determined using an automated hematology analyzer, with EDTA-anticoagulated blood samples processed according to standard laboratory procedures[16, 17].

Quality control: Internal quality control procedures were maintained throughout the study. Commercial control materials were analyzed prior to sample testing. Proper specimen handling and timely processing were ensured to minimize pre-analytical errors[18].

Statistical analysis: The IBM SPSS Statistics software (version 26.0) was used for all statistical analyses (IBM Corp., Armonk, NY, USA). Prior to statistical analyses, the characteristics of the distribution of continuous variables were subjected to the Shapiro-Wilk test of normality. Variables which did not significantly deviate from normality ($p > 0.05$) were reported as mean ± standard deviation (SD) and analyzed with parametric statistical methods. The normality of the distribution of scores justified the application of independent samples t-tests, as well as Pearson's correlation analysis. The distribution of categorical variables was reported as frequencies and percentages. Frequency distribution of baseline characteristics of CAD patients and controls were compared using the Chi-square test. Independent Samples t-test was used to compare APTT levels and RBC and WBC counts of CAD patients and controls and of male and female CAD patients. Mean differences with 95% confidence intervals were reported. Because of nearly normal distribution, associations between APTT, RBC count, and WBC count were assessed using Pearson's correlation coefficient. Correlation coefficients (r) were evaluated as negligible (<0.10), weak (0.10–0.39), moderate (0.40–0.69), strong (0.70–0.89), and very strong (≥0.90). To augment statistical significance testing for measuring the size of the differences among groups, the effect sizes calculated as Cohen's d. Cohen's d is calculated as the difference between the means of the compared groups divided by the pooled standard deviation. Effect size is categorized as small (0.20–0.49), medium (0.50–0.79), large (0.80–1.19), and very large (≥1.20), as per Cohen's guidelines[20]. The sign of Cohen's d indicates the direction of the effect and the size is given by the absolute value.

Ethical considerations: Ethical approval was obtained from the Health Research Ethics Committee of the Federal University Teaching Hospital Owerri (Approval No.: FUTH/REC/ECC/2024/537 approved on 12th March). Written informed consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki [19].

RESULTS

Baseline Demographic and Clinical Characteristics of Study Participants

Socio-demographic and clinical participant data can be found in Table 1. Patient cohorts for CAD and controls were well-matched based on multiple relevant demographic variables. Age, gender, marital status, education, occupation, and residence were statistically analyzed and determined to be non-significant. (age – $\chi^2 = 2.11$; $p = 0.55$; gender - $\chi^2 = 0.00$; $p = 1.00$; marital status - $\chi^2 = 0.74$; $p = 0.69$; education - $\chi^2 = 1.26$; $p = 0.53$; occupation - $\chi^2 = 1.14$; $p = 0.77$; residence - $\chi^2 = 0.16$; $p = 0.69$). Therefore, the study groups were balanced for these baseline characteristics. However, smoking, hypertension and diabetes, CAD patient histories were more notable when compared to control groups for smoking ($\chi^2 = 8.46$; $p = 0.015$), hypertension ($\chi^2 = 16.98$; $p < 0.001$), and diabetes mellitus ($\chi^2 = 9.14$; $p = 0.003$). There was no statistical significant difference detected for alcohol consumption in both groups ($\chi^2 = 5.32$; $p = 0.070$).

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Table 1. Baseline Demographic and Clinical Characteristics of Study Participants

Variable	CAD Patients(n=50)	Controls (n=50)	Test Statistic	p-value
Age group (years) n (%)			χ^2 = 2.11	0.55
40-49	7 (14)	10(20)		
50-59	14(28)	16(32)		
60-69	17(34)	14(28)		
≥70	12(24)	10(20)		
Sex, n (%)				
Male	31 (62.0)	31 (62.0)	χ^2 = 0.00	p = 1.00
Female	19 (38.0)	19 (38.0)		
Marital Status, n (%)			χ^2 = 0.74	p = 0.69
Married	35 (70.0)	33 (66.0)		
Single	5 (10.0)	7 (14.0)		
Widowed	8 (16.0)	8 (16.0)		
Divorced/Separated	2 (4.0)	2 (4.0)		
Educational Level, n (%)			χ^2 = 1.26	p=0.53
Primary	10 (20.0)	8 (16.0)		
Secondary	18 (36.0)	16 (32.0)		
Tertiary	22 (44.0)	26 (52.0)		
Occupation, n (%)			χ^2 = 1.14	p=0.77
Civil Servant	11(22.0)	13(26.0)		
Trader	17(34.0)	16(32.0)		
Farmer/Artisan	7(14.0)	8(16.0)		
Retired	15(30.0)	13(26.0)		
Residence, n (%)			χ^2 = 0.16	p=0.69
Urban	38 (76.0)	40 (80.0)		
Rural	12 (24.0)	10 (20.0)		
Smoking Status, n (%)			χ^2 = 8.46	p=0.015
Current Smoker	16 (32.0)	8 (16.0)		
Former Smoker	12 (24.0)	10 (20.0)		
Never Smoked	22 (44.0)	32 (64.0)		
Alcohol Consumption, n (%)			χ^2 = 5.32	p=0.070
Current Drinker	18 (36.0)	11 (22.0)		
Occasional Drinker	15 (30.0)	18 (36.0)		
Non-drinker	17 (34.0)	21 (42.0)		
Hypertension History, n (%)			χ^2 = 16.98	p=<0.001
Yes	33 (66.0)	14 (28.0)		
No	17 (34.0)	36 (72.0)		
Diabetes Mellitus History, n (%)			χ^2 = 9.14	p=0.003
Yes	20 (40.0)	7 (14.0)		
No	30 (60.0)	43 (86.0)		

Coagulation and Hematological Profiles Visualization

In order to further depict the distribution and interrelationships of the coagulation and hematological parameters, a multi-panel figure was created (Figure 1). There are evident distributional differences between the CAD patients and controls in Panels A- C (Figure 1A-C) whereby the APTT and WBC values are high and the number of RBCs are low in CAD patients. The relationships between the variables in CAD group are illustrated in panels D–F (Figure 1D-F). APTT had a positive correlation with WBC count, whereas, there were negative correlations between RBC and WBC, and APTT and RBC. These trends offer the visual aid in the interaction between the abnormalities of coagulation and the inflammatory processes in CAD..

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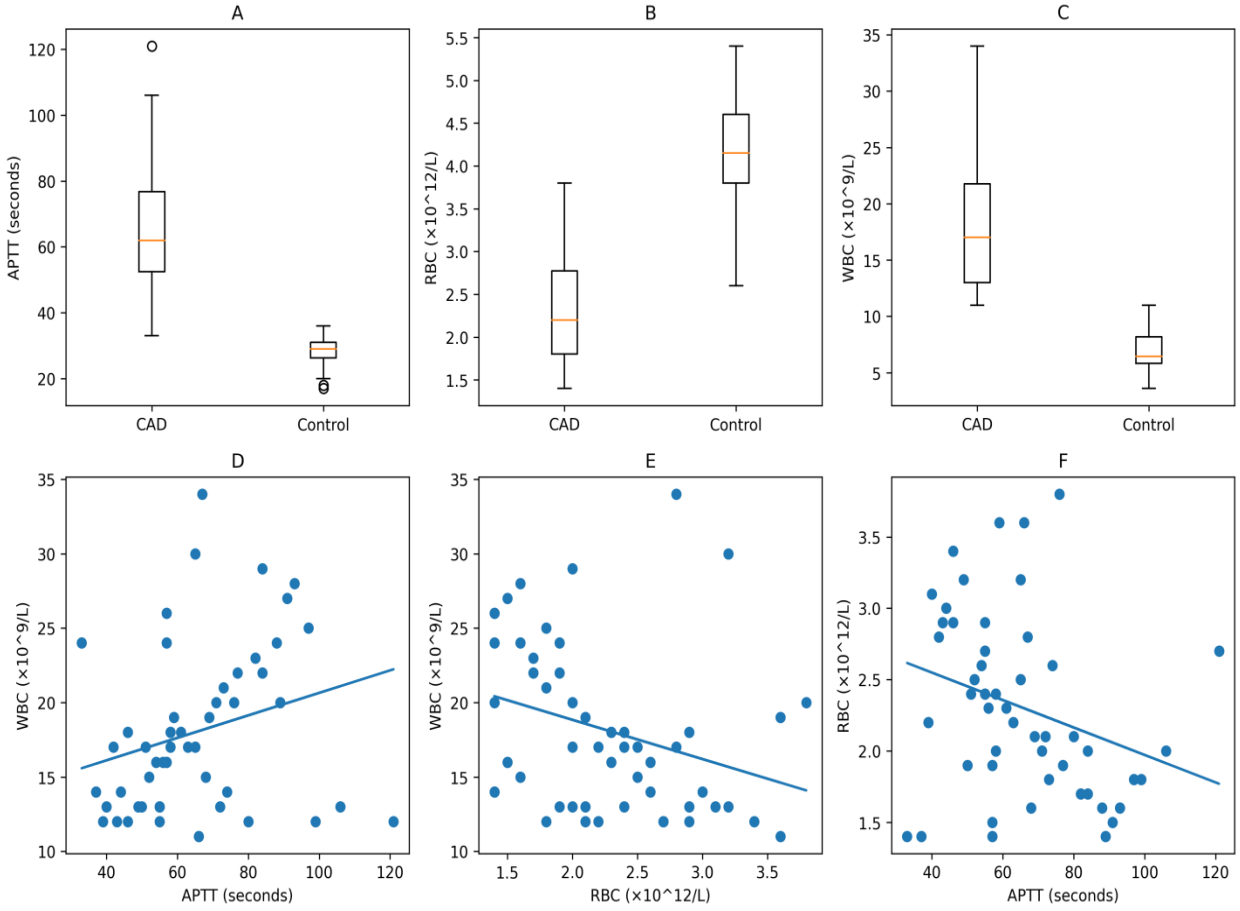

Figure 1. Distribution and relationships of coagulation and hematological parameters among study participants
(A) Boxplot of APTT with extremely high values in CAD patients as compared to controls.
(B) Boxplot of RBC count showing lower counts in CAD patients.
(C) Boxplot of the WBC count with high levels in CAD patients.
(D) Scatter plot to show that there is a positive correlation between APTT and WBC in CAD patients.
(E) Scatter plot of the inverse relationship between the RBC and WBC.
(F) Scatter plot that shows the correlation between APTT and RBC in patients with CAD.

Comparison of Coagulation and Hematological Parameters: Coagulation and Hematological parameters were compared in CAD patients and Controls.
The Shapiro – Wilk test was used to assess score distribution. In both CAD patients and controls, APTT, RBC count, and WBC count were approximately normally distributed in both CAD patients and control ($p > 0.05$). They were computed as mean ± standard deviation. The independent samples t-test was applied for the difference of means.
Significant differences were observed in all measured hematology and coagulation parameters between CAD patients and controls (Table 2). In CAD patients APTT was significantly prolonged (compared to the control mean, APTT was 37.16 seconds longer, 95% CI: 31.31–43.01, $p < 0.001$), RBC count was significantly lower (compared to the control mean, CAD patients' RBC count was lower by 1.84 $\times 10^{12}$/L, 95% CI: −2.08 to −1.60, $p < 0.001$), and WBC count was significantly higher (compared to the control mean, CAD patients' WBC count was higher by 11.15 $\times 10^{9}$/L, 95% CI: 9.44–12.86, $p < 0.001$). APTT and the WBC count were measured in units of seconds and $\times 10^{9}$

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Table 2. Comparison of APTT, RBC count, and WBC count between CAD Patients and Controls

Parameter	CAD Patients (n = 50)	Control (n = 50)	Mean difference (95%CI)	t-value	p-value
APTT (seconds)	65.48 ± 19.32	28.32 ± 4.41	37.16 (31.31–43.01)	13.26	1.37×10^{-23}
RBC($\times10^{12}$/L)	2.30 ± 0.64	4.14 ± 0.62	-1.84(-2.08 to -1.60)	-14.52	3.72×10^{-26}
WBC($\times10^{9}$/L)	18.04 ± 5.65	6.89 ± 1.71	11.15(9.44–12.86)	13.37	8.19×10^{-24}

Comparison of Sex based among CAD patients.

Table 3 shows the sex-based analysis of CAD patients. There was no statistically significant difference between APTT of male and female subjects (p = 0.388). Also, RBCs in males was significantly higher than that of females (p = 0.003). There was no significant difference in the count of WBC according to sex (p = 0.162).

Table 3. Comparison of APTT, RBC count, and WBC count between Male and Female CAD Patients

Parameter	Male (n = 31)	Female (n = 19)	t-value	p-value
APTT (seconds)	66.94 ± 19.84	63.05 ± 18.44	-0.87	0.388
RBC($\times10^{12}$/L)	2.50 ± 0.63	1.98 ± 0.52	3.41	0.003
WBC($\times10^{9}$/L)	18.62 ± 5.72	17.05 ± 5.49	-1.42	0.162

Effect Size of differences between CAD patients and Controls

The analysis of effect size demonstrated very large differences between the CAD patients and controls for all evaluated parameters.

Table 4. Effect Size of Differences in APTT, RBC, and WBC

Parameter	Cohen's d	Interpretation
APTT	2.33	Very Large
RBC	-2.91	Very Large
WBC	2.34	Very Large

APTT, RBC and WBC correlations in CAD Patients

Table 5 shows weak correlation of each of the studied parameters in CAD patients. APTT and RBC count exhibited a weak negative correlation (r = -0.29, p = 0.041). WBC's and APTT's correlation was weak and not statistically significant (r = 0.26, p = 0.070). RBC and WBC count's negative correlation was also weak, but statistically significant (r = -0.30, p = 0.034).

Table 5. Correlation between APTT, RBC Count, and WBC Count in CAD Patients

Variable	APTT	RBC	WBC
APTT	1	r= -0.29, p = 0.041	r= 0.26, p = 0.070
RBC	r= -0.29, p = 0.041	1	r= -0.30, p = 0.034
WBC	r= 0.26, p = 0.070	r= -0.30, p = 0.034	1

DISCUSSION

This research assessed the amounts of activated partial thromboplastin time (APTT), red blood cell (RBC) count, and white blood cell (WBC) count of patients with coronary artery disease (CAD) in Owerri, Nigeria, and compared them to seemingly healthy controls. The results repeatedly indicated a significant extension of the APTT, decrease in the number of RBCs and increase in the number of WBCs with large effect sizes. Taken together, these findings indicate that CAD is not a purely lipid-based disease but could be a multifactorial relationship of coagulation changes, hematological changes, and systemic inflammation.

The measured increase in the APTT of CAD patients could be due to interference of the intrinsic and common coagulation pathways. Despite the traditional belief that CAD is a condition that is hypercoagulable,

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long clotting times can be a sign of coagulation factors, endothelial dysfunction, or dysregulation of hemostasis caused by inflammatory factors. Interleukin-6 and tumor necrosis factor-α cytokines have been known to regulate coagulation factor production and activity and could play a role in the changes in clotting tests during chronic inflammatory diseases. This explanation is in line with the results of Tripodi [21] and Esmon [22], who have shown that systemic inflammation has the potential to dysfunction the global coagulation pathways. Moreover, endothelial dysfunction, which is one of the characteristics of atherosclerosis, could contribute to the expression of tissue factor and endogenous anticoagulant pathways, and thus, lead to hemostatic imbalance [23].

These results however contrast with those that have found a shortening or normalization of APTT in acute coronary syndrome that are usually proposed to be due to increased thrombin generation and hypercoagulability[24]. These differences could be associated with differences in clinical presentation, exposure to treatment, and population-specific differences, highlighting that the dynamics of coagulation in CAD are multifaceted and context-specific, as opposed to homogeneous.

The decrease in the number of RBCs in CAD patients is in line with the trend in chronic inflammatory conditions, whereby, a defective erythropoiesis and iron metabolic abnormalities are prevalent. The inflammatory mediators have the ability to boost the expression of hepcidin, thus decreasing the iron supply and inhibiting hemoglobin production. This could lead to decreased RBC numbers and has clinical implications, since decreased oxygen-carrying capacity may result in worsening myocardial ischemia and increased cardiac workload. The same associations have been described by Fang et al. [25] and Anand et al.[26] who associated anemia in cardiovascular disease with high morbidity and mortality. In addition, lower levels of RBC can affect the viscosity of blood and shear stress of the endothelium, which further leads to the vascular dysfunction [27].

On the other hand, there have been studies which have identified normal or increased RBC parameters in CAD populations, which is usually because of hemoconcentration, compensatory erythropoiesis, or environmental influences like altitude and hydration status [28]. These differing results emphasize the significance of specific context interpretation and support the importance of population-based data like those obtained in the current study.

The high level of WBC that was found in this study is probably an indication of an underlying inflammatory reaction. Endothelial injury, plaque formation and destabilization are actively mediated by leukocytes via the release of cytokines, proteolytic enzymes, and reactive oxygen species. The processes can enhance thrombosis and cause adverse cardiovascular events. This observation has been observed to be consistent with the study of Libby [29] and Hansson [30] who determined inflammation as a major cause of atherosclerosis. Increased WBC counts are also found to be independent predictors of cardiovascular events and mortality [31-32].

Conversely, other studies have indicated that there are only small or insignificant increases in WBC counts, especially in stable CAD groups, which indicates that inflammatory processes can be different according to clinical manifestations and the properties of underlying diseases [33]. The comparatively high WBC of the current research could suggest the presence of an inflammatory milieu in the study group, but the lack of particular biomarkers of inflammation does not allow further characterization of it.

The correlation analysis helps to further understand the relationships between these parameters. There was a weak negative correlation between RBC and WBC counts, which indicates that there could be an inflammatory mechanism and inhibition of erythropoiesis. It was also found that there was a weak negative correlation between APTT and RBC count which could indicate that there are some underlying interactions between hematological status and coagulation function. Though there was a positive correlation between APTT and WBC count, this was not statistically significant, which suggested that the effect of inflammation on the parameters of coagulation might be exhibited in this dataset, but not so strongly. These results are generally consistent with the idea of immunothrombosis, where the two processes of coagulation and inflammation are not independent mechanisms but instead, they are biological systems [34].

Sex analysis showed that there were significant differences in the number of RBCs of patients with CAD of both sexes, with more males having higher values. On the contrary, APTT or WBC count did not show any statistically significant differences. This trend indicates that the majority of the changes that are

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observed are probably disease-associated, but some hematological parameters can also be indicative of biological differences between sexes. Sex-related differences in hematological indices have been reported to be variable in previous studies suggesting that physiological and disease-related factors might be involved in causing the same[35].

Notably, the effect sizes are large in all the parameters, which means that the differences between the CAD patients and controls are statistically significant, but may be of clinical importance. Since APTT, RBC count, and WBC count are regularly accessible and relatively cheap, they could be considered as supportive parameters in the evaluation of CAD, especially in low resource environments. Their use however should be viewed with caution and they should be used alongside the proven diagnostic methods.

STRENGTHS AND LIMITATIONS OF THE STUDY

The integrated assessment of thrombo-inflammatory processes in patients with coronary artery disease (CAD) due to the combined evaluation of coagulation and several hematologic parameters is the main strength of this study. Although temporal evaluation was not possible, inclusion of a healthy control group, addition of a healthy control group, and standardized laboratory methods increased the level of evidence of the study. The study, based on the combined evaluation of activated partial thromboplastin time (APTT), red blood cells (RBC), and white blood cells (WBC) in patients with CAD, is the first of its kind to provide context-related data from Nigeria.

There are a number of limitations pertaining to the findings of this particular study that must be taken into consideration. First, the use of a hospital-based case-control study design negatively impacts the ability to generalize the findings to a larger population. The method of convenience sampling has a greater potential for selection bias, and therefore must be taken into account. Additionally, the rigor put into the assessment of other clinical variables such as disease severity and other clinical variables was lacking in this study. Furthermore, the rigor put into the assessment of other cardiovascular drugs and their potential impact on the results of the study, and the results with respect to APTT and other studies on APTT, was also lacking. The modest size of the study population and the single-center design also has a negative impact on the external validity of the study. Larger, more robust, multicenter, and longer duration studies, with the listed design improvements, will be needed to assess the potential for other findings.

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IMPLICATIONS OF THE FINDINGS

These findings hold value for clinical practice and public health research based on the responses. Clinically, the changes in APTT, RBC, and WBC counts suggest that some standard laboratory parameters could be assistive indicators for CAD, especially in developing nations where there is limited access to sophisticated laboratory testing for advanced cardiovascular biomarkers. APTT working in conjunction with an inflammatory marker is CAD supportive given the increased WBC counts and the observed delay in APTT.

From the perspective of research, these findings provide a basis for the need of a larger scale of prospective studies. In particular, the study of the coagulation pathway, the integrative study of the hematological changes coupled with an assessment of the cardiovascular risk and the adverse events that could be associated with this would be of value. The studies of the aggravating factors would also be of particular interest to research: the severity of the condition, the type of medical treatment, and the inflammatory biomarker.

From the perspective of public policy, the affordability of laboratory testing would facilitate the integration of standard laboratory hematological and coagulation testing to monitoring and evaluating cardiovascular care in resource-limited settings. While these parameters and testing would be an adjunct to established CAD testing and would be a cost-effective measure for determining clinical decision-making and CAD related issues.

CONCLUSION

In this experiment, the patients of coronary artery disease at Owerri had a much longer activated partial thromboplastin time (APTT), low count of red blood cell (RBC) and high count of white blood cell (WBC) than seemingly healthy controls. The results indicate the existence of a thrombo-inflammatory profile, which indicates a possible interplay between the changes in coagulation, defective erythropoiesis, and widespread inflammation in CAD. Although there was no significant sex-based difference in most of the parameters, there was a significant difference in the number of RBCs between the male and female patients, which implies that not only disease-related but also biological factors can be

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responsible of the hematological alterations in this group.

The size of the differences observed highlights the clinical potential of these parameters which are routinely available. APTT, RBC count and WBC count can be used as convenient and inexpensive supplemental markers in the diagnosis of CAD especially in resource constrained environments. Nonetheless, their use must be viewed with caution and be used in combination with the existing diagnostic and prognostic instruments.

Declarations

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Conflict of Interest: The authors declare that they do not have any conflict of interest in this study.

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Ethical approval and consent to participate: This study was carried out as per the ethical guidelines in the world medical association declaration of Helsinki. The Health Research Ethics Committee of the Federal University Teaching Hospital, Owerri, Nigeria gave the ethical approval (Approval No.: FUTH/REC/ECC/2024/537 approved on 12th March).

Abbreviations: CAD: coronary artery disease; APTT: activated partial thromboplastin time; RBC: red blood cell; WBC: white blood cell; CI: confidence interval; SD: standard deviation; IQR: interquartile range; EDTA: ethylenediaminetetraacetic acid; STROBE: strengthening the reporting of observational studies in epidemiology

Declarations

Authors' contribution: Melford Uche Elendu and Chigaemezu Remmy-Martin Akubuo conceived and designed the study, Chigaemezu Remmy-Martin Akubuo carried out the manuscript preparation. Eustace Mary Nzube Nwosu, Feziechi Benigna Egwurugwu, and Paschaline Odichimma Egwurugwu contributed in data acquisition and supervision of the study. Chinedu Barry Iheukwumere and Ernest Emeka Ngwu provided the manuscript critical review and editing. Chigaemezu Remmy-Martin Akubuo carried out the analysis and result interpretation. All the authors approve the final version of the manuscript.

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