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Research Article

The Role of Hematological Parameters in Atrial Fibrillation Risk Assessment

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Abstract: Atrial fibrillation (AF) is an irregular and rapid heartbeat in the heart's atrial chambers. Conversely, haematological parameters are commonly utilized in clinical settings to evaluate overall health and disease. Our research explored the potential role of haematological parameters in atrial fibrillation within the Pakistani population. In this case-control a total of 400 participants were enrolled from the Punjab Institute of Cardiology, Lahore, Pakistan. The participants were divided into two groups: a control group comprising 200 healthy individuals, and an AF group consisting of 200 individuals diagnosed with atrial fibrillation. Haematological parameters were assessed using an automated hematology analyzer. The AF group had higher levels of white blood cells, red blood cells, and mean corpuscular volume as compared to control group. Conversely, lower levels of haemoglobin, hematocrit, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration and platelets were observed in AF group compared to control group. In conclusion, our research established a significant relationship between haematological parameters and atrial fibrillation in the Pakistani population.

Keywords: Atrial Fibrillation, Haematological Parameters, Relationship, Blood Count, Risk Assessment, Pakistani Population.

1. INTRODUCTION

The common heart arrhythmia in the general population known atrial fibrillation (AF) which is linked to an higher danger of several health problems. These complications encompass thromboembolism, stroke, neurological damage, major and minor organ dysfunction or failure, as well as hospital readmissions, leading to significantly increased medical expenses [1-3]. In 2021, Lippi *et al*. [4] reported 3.046 million additional cases of AF were reported globally by the record. With 403 instances per million people, the predicted incidence rate for that year was 31% higher than the incidence rate for 1997. Atrial fibrillation is present in 37.574 million people worldwide, or 0.51% of the world's population. Over the past two decades, the incidence of AF has risen by 33%. High socio-demographic index countries bear the greatest burden of atrial fibrillation, although there has been a significant increase in middle socio-demographic

index countries as well. By 2050, atrial fibrillation may cause an absolute rise in cases of nearly 60%, according to future predictions [4].

In clinical practice, reference ranges for haematological and immunological parameters are commonly employed to assess the health status and disease conditions of individuals. These reference ranges play a vital role as biomarkers in evaluating how patients respond to treatment or the progression of their disease. Notably, these reference ranges can change based on racial, gender, age, genetic, and environmental variables [5, 6].

The predictive role of haematological factors in the onset and recurrence of atrial fibrillation has been established. One of the most frequently advised blood tests by physicians is the complete blood count (CBC) which counts different kinds of blood components including platelets, red blood cells (RBCs), and white blood cells (WBCs). The

complete blood count includes the following tests: The three main tests are the (1) WBC total and differential count; (2) erythrogram (RBC count, hemoglobin (Hb) and hematocrit determination; and (3) platelet count indices calculation, which includes mean platelet volume (MPV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW). The diagnostic process for cardiovascular disease usually includes the CBC, one of the most significant blood tests in clinical practice. Given the possible predictive significance of haematological markers for both new-onset and recurrent AF, a CBC test has been recommended as a component of the diagnostic procedure for AF in clinical practice [7]. Previous investigations have explored the association between haematological factors and AF, but the results have been inconclusive. Despite the extensive research on AF diagnosis and treatment in recent years, the precise mechanism of this complex condition remains incompletely understood [2]. The ongoing controversy and discussions surrounding AF diagnosis and treatment are justified due to the involvement of numerous intricate mechanisms in its development [2, 3]. In the current study, we designed to examine the relationship between haematological parameters and atrial fibrillation in Pakistani population.

2. MATERIALS AND METHODS

This study, which was a case-control investigation, was conducted at the Punjab Institute of Cardiology (PIC), Lahore and the Department of Zoology at Lahore College for Women University. The selection of participants involved a non-probability purposive sampling approach during July 2021 to December 2022. Individuals suffering from atrial fibrillation were identified by physicians at the PIC on the basis of electrocardiogram (ECG). The ECG showed aberrant impulse conduction to the ventricles, uneven R-R intervals, and a lack of P waves. The subjects were not suffering from any other illness.

The Rao program was used to calculate the sample size for this investigation, accounting for a 5% margin of error and the disease's prevalence. A total of 400 participants were recruited, with 200 individuals assigned to the control group, who were in good health and had no family history of

atrial fibrillation, diabetes, or hypertension. The remaining 200 participants were included in AF group. Prior to enrollment, each participant gave their permission and answered a series of questions about age, gender, job history, marital status, educational attainment, and renal disease history. The haematological parameters were analyzed using an automated Hematology Analyzer (DC 2400 PLUS, Pakistan) at the research laboratory of Lahore College for Women University. The examined haematological parameters consisted of white blood cell count, total red blood cell count, haemoglobin level, hematocrit, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, and platelet count. Reference ranges were applied as follows: WBC count (4-11 x 10^9/L), total RBC count (4.5 - 6.5 million/cm), Hb level (130-180 g/L), HCT (38-58%), MCV (76-96 fl), MCH (27-33 pg), MCHC (30-37%), and platelet count (150-400 x 10^9/L).

Utilizing the Statistical Package for the Social Sciences (SPSS, IBM statistics, version 22.0, NY) software, the statistical analysis was performed. The standard error of the mean (SEM) and mean were used to portray the continuous data, while percentages and frequencies were used to present the categorical data. The T-test is utilized to ascertain whether there is a significant difference between the means of AF sufferers and the control group. A P-value of less than 0.001 was considered very significant, while a P-value of less than 0.05 was considered statistically significant.

2.1 Ethical Approval Statement

The institutional review of PIC (Ref. no: RTPGME-Research-179) and ethical review committee of Zoology Department, LCWU (REF/NO/LCWU/ ZOO/690; Dated: 01-01-2021) approved the study. Enrolled subjects also gave their approval to take part in the research.

3. RESULTS AND DISCUSSION

The case-control study involved a total of 400 participants, with males accounting for 51.5% and females comprising 48.5% in a control group, whereas in AF group, males were 60% and females were 40%. The electrophysiologic characteristics change according to gender. In comparison to men, women often have a QT interval that is 10–20 ms

longer [8]. During adolescence, this differential in ventricular repolarization manifests itself as a persistent shortening of the QT interval in males. The alteration is thought to be connected to androgen hormones, while the underlying mechanism for this difference is not fully known. Sex hormones may have an impact on the density of potassium channels and the transmural dispersion of calcium channels in the ventricular myocardium, according to animal studies [9]. The electrophysiologic characteristics of the atria differ throughout genders, but these differences have not been as well investigated as those in ventricular repolarization. There is a dearth of published research on the sex variations in atrial electrical remodelling between men and women [10]. The baseline demographic characteristics of the participants are shown in Table 1.

Table 2 shows the mean values for the following parameters: age, total red blood cells (RBCs), white blood cell count, hemoglobin (Hb),

Table 1. Baseline demographic characteristics of studied groups.

Variables [n (%)]	Control Group (n=200)	AF Group (n=200)
Gender		
Male	103 (51.5)	120(60)
Female	97 (48.5)	80(40)
Education status		
No	14 (7)	155 (77.5)
Yes	186 (93)	29 (14.5)
Marital status		
No	08 (4)	22 (11)
Yes	192 (96)	133 (66.5)
Employment status		
No	06 (3)	139 (69.5)
Yes	194 (97)	16 (08)

hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and platelet count. Age, total RBCs, and MCV of the research groups did not differ statistically, according to the analysis. WBC, Hb, HCT, MCH, MCHC, and platelet counts, however, showed statistically significant variations across the groups. While the mean values for hemoglobin, hematocrit, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and platelet count were lower in the atrial fibrillation group when compared to the control group, the AF group showed greater mean values for white blood cell count, red blood cell count, and MCV.

This study's goal was to examine the possible significance of haematological markers in atrial fibrillation patients, which was carried out at the PIC in Lahore, Pakistan. The study's findings showed a significant association between AF and a number of haematological measures, such as platelet count, mean corpuscular hemoglobin concentration, hematocrit, white blood cell count, and hemoglobin level. Regarding mean corpuscular volume and total red blood cell count, however, no meaningful correlations were found.

Our investigation revealed that the AF group had a higher white blood cell (WBC) count than the control group; moreover, very significant differences were discovered, as shown in Table 2. Inflammation markers have been consistently associated with atrial fibrillation in various studies. WBC count is a commonly used and easily accessible indicator of systemic inflammation. Evidence suggests that a greater WBC count was linked with occurrence of atrial fibrillation during a 5-year follow-up [11]. WBCs may contribute to atrial remodelling

Table 2. Biochemical analysis of control and AF groups.

Variables	Control group (n=200)	AF group (n=200)	P-value
Age (years)	52.07 ± 15.91	54.31 ± 15.82	0.158
White blood cell count ($\times 10^9$/L)	8.27 ± 2.06	12.28 ± 10.10	0.001
Total red blood cells (Million/cm)	5.04 ± 0.75	6.04 ± 7.91	0.074
Haemoglobin (g/L)	138.43 ± 20.84	127.41 ± 21.47	0.001
Hematocrit (PCV) (%)	54.12 ± 43.18	38.90 ± 7.08	0.001
Mean corpuscular volume	79.06 ± 8.83	80.46 ± 8.81	0.112
Mean corpuscular haemoglobin (pg)	32.29 ± 8.64	26.35 ± 3.26	0.001
Mean corpuscular haemoglobin concentration (%)	34.18 ± 1.89	32.76 ± 1.71	0.001
Platelets ($\times 10^9$/L)	306.54 ± 80.15	230.55 ± 122.91	0.001

at multiple levels, including electrical and structural changes. Numerous cytokines released by activated WBCs cause intrinsic inflammatory cascades in fibroblasts that cardiomyocytes, and even leukocytes. Consequently, biopsies taken from AF patients have demonstrated a connection between inflammation and the development of atrial fibrosis [12-14]. Atrial fibrillation is growing in both prevalence and frequency. One indicator of systemic inflammation and a danger cause for cardiovascular disease is the white blood cell count. Across the Japanese population as a whole, higher WBC counts were significantly linked to a higher prevalence of AF, particularly in smoker women [15].

While the overall red blood cell count did not differ significantly across the groups under investigation in our study, Table 2 shows that the atrial fibrillation group had more mean RBCs as compare to the healthy group. However, the heterogeneity of red blood cell size and volume was reflected by the red blood cell distribution width (RDW). RDW is an cheap and simply measurable index that has been associated with various cardiovascular diseases. Growing evidence recommends that RDW can serve as a prognostic indicator for atrial fibrillation in different therapeutic contexts [16]. A distinct risk factor for stroke and mortality in patients with atrial fibrillation is left ventricular hypertrophy (LVH). In AF patients, Yao *et al.* [17] show a connection between LVH and RDW. Those with AF and LVH showed considerably higher RDW than those in the non-LVH group. RDW has also been connected to a number of other illnesses. A number of cardiovascular disorders have been related to the relationship between RBC distribution width, a measurement of erythrocyte volume change and AF. RBC distribution width was related with the occurrence of AF which included middle-aged individuals from the general public, independent of other nutritional, medical, and cardiovascular factors. Although several hypotheses have been put up, the processes underlying these correlations are still unknown. Elevated RDW was linked to a considerable reduction in heart rate variability in a current study of individuals suffering from systolic left heart failure [18].

The atrial fibrillation group in this research had lower mean corpuscular hemoglobin and hemoglobin levels than the control group. Table 2 shows that there were noteworthy alterations in both hemoglobin and mean corpuscular hemoglobin between the analyzed groups. The red blood cells that contain the protein called hemoglobin are responsible for transporting oxygen from the lungs to the body's tissues and releasing carbon dioxide when exhaled. Chronic or acute blood loss can lead to reduced haemoglobin levels. In the context of AF, individuals might be at an higher danger of bleeding, especially if they were taking anticoagulant medications to prevent blood clots. A reduction in the mean corpuscular haemoglobin levels in individuals with atrial fibrillation may be indicative of anaemia or other underlying health issues. An indicator of the usual quantity of Hb in each RBC is the MCH. This discovery was even with the findings of a research study by Lim *et al.* [19], which showed that, after controlling for other cardiovascular and demographic risk variables, there was a U-shaped relationship between hemoglobin concentrations and the chance of atrial fibrillation. The study showed that having high or low Hb levels presented the largest risk of AF, while keeping levels within the normal range was linked to the lowest risk. Additionally, Katayama *et al.* [20] observed that in individuals with normal left ventricular (LV) systolic function, there was an independent relationship between left atrial (LA) enlargement and both a lower Hb concentration and a higher LV mass index. This shows that hemodynamic abnormalities associated with Hb levels may have a role in LA remodelling and the start of AF prior to the manifestation of other abnormalities such systolic dysfunction or LV hypertrophy .

In comparison to the control group, the atrial fibrillation group exhibited lower hematocrit levels, according to our study's findings. Additionally, a very significant difference was found between the groups that were investigated, as revealed in Table 2. The percentage of cellular blood in total blood volume is known as the hematocrit, and it is a measure of this proportion. It is commonly used to diagnose and monitor various medical conditions. Chronic blood loss, whether due to gastrointestinal bleeding, genitourinary bleeding, or other sources, can lead to a decrease in hematocrit levels. This may be relevant in AF patients if they have an underlying condition causing bleeding. It was found that the rate of hematocrit change from sinus rhythm to atrial fibrillation varied among paroxysms in patients with multiple episodes. A 5-point increase in hematocrit leads to hemoconcentration,

which results in an approximately 10% increase in the plasma concentration of macromolecular compounds, including hemostatic agents. This hemoconcentration typically occurs within hours or less after the onset of the paroxysm. Given the observation of localized blood stasis in the left atrial appendage during AF, the abrupt development of specific hemoconcentration may promote the formation of an intracardiac thrombus. According to this, when AF first develops, platelet initiation and coagulation happen in a time-dependent way [21-23].

In the present study, we found that the AF group had higher mean corpuscular volume levels and lower mean corpuscular hemoglobin concentrations as compared to a control group. According to Table 2, there were significant variations in the study groups' mean corpuscular haemoglobin concentration but not in their mean corpuscular volume. Similarly, Takahashi *et al*. [24] previously reported that atrial fibrillation patients exhibited higher mean corpuscular volumes. Another study found that patients with lower mean corpuscular volumes had more dilated left ventricles, which has been linked to iron deficiency. It was noted that women typically had smaller mean corpuscular volumes compared to men, and the authors suggested that iron deficiency may contribute to the association between the female gender and a higher risk of thromboembolism in AF, along with other hormonal factors [25, 26].

As demonstrated in Table 2, platelets in the investigated groups likewise revealed extremely significant differences. The mean value of platelets in the AF group was found to be lower than in the control group, according to research results. Similarly, thrombocytopenia, characterized by a platelet count below $100×10^9/L$, was estimated to affect approximately 6% to 24% of patients with AF [27, 28]. Although there were no obvious abnormalities in platelet aggregation among atrial fibrillation patients, fluctuations in plasma indicators of platelet function were observed. However, despite the decreased thrombogenesis associated with warfarin use, treatment with either aspirin or warfarin did not demonstrate important benefits in terms of platelet activation (fibrin D-dimer). This suggests that platelet initiation may not significantly influence the aetiology of thromboembolism in AF [29].

Furthermore, Liu *et al*. [30] revealed that active platelets release significant amounts of Transforming growth factor β 1 (TGF-β1) into the bloodstream after stimulation by angiotensin II (Ang II). Concurrently, initiated platelets enter the atria and discharge TGF-β1 at the local level. The presence of TGF-β1, in conjunction with angiotensin II infusion, promotes atrial fibrosis and increases atrial fibrillation inducibility by enhancing the activity of atrial fibroblasts both locally and systemically. It is worth noting that platelet-fibroblast interaction, along with other factors released by platelets, also contribute to atrial fibrosis. Since platelets play a role in atrial thrombosis, antiplatelet treatment may be beneficial in preventing both thrombosis and fibrosis . Haematological parameters can serve as valuable indicators for assessing the danger of problems and associated comorbidities in atrial fibrillation patients. An increased danger of stroke, thromboembolism, and other cardiovascular events might be linked to abnormalities in haematological parameters. The evolution of atrial fibrillation and the problems that accompany it can be understood by looking at changes in haematological markers over time. Frequent monitoring of these measures can be used to track the effectiveness of therapeutic interventions and detect any deterioration in the patient's health. Patients with atrial fibrillation may use haematological measures as biomarkers to assess how well their medication is working. It is possible to assess if the treatment strategy is working or whether changes need to be made by keeping an eye on changes in these parameters. It might be useful in identifying possible links between haematological anomalies and the onset or development of atrial fibrillation.

4. CONCLUSIONS

Overall, this research indicated that there was a significant alteration in platelet levels, MCH, MCHC, Hb, HCT, WBC count, and HCT among the control and atrial fibrillation groups. Nevertheless, among the populace we analyzed, there were no discernible variations in total RBCs or MCV. However, this study did not clarify the exact mechanism by which these haematological characteristics lead to the development of AF. In common, examining haematological markers in individuals with atrial fibrillation can help with risk assessment, diagnosis, monitoring, and therapy evaluation. It can also shed light on the underlying causes of the disorder.

6. CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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