How to Cite:
Hadi, N., Asfandiyar, Khan, M. Q., Suhanuddin, Jehandad, Raza, S., & Faizullah. (2021). Inflammatory and hemostatic abnormality in atrial fibrillation patients at tertiary care hospital, Mardan: A descriptive cross sectional study. *International Journal of Health Sciences*, *5*(S1), 862–868. https://doi.org/10.53730/ijhs.v5nS1.14698

Inflammatory and hemostatic abnormality in atrial fibrillation patients at tertiary care hospital, Mardan: A descriptive cross sectional study

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Abstract---Objective: To determine the levels of C-reactive protein (CRP) and D-dimers in patients presenting with atrial fibrillation. Study design: Descriptive Cross sectional/Observational. Place and duration of study: From Januarty 2019 to June 2020, the study was carried out in the cardiology and pathology departments of Mardan Medical Complex and Bacha Khan Medical College Mardan. Material and Methods: This study included a total of 100 patients with atrial fibrillation, with 50 people serving as the control group. The levels of CRP and D-dimers were determined in all cases. Results: 35% of the individuals in this study had increased CRP levels. The average CRP level was 2.99 +/- 0.652mg, which was substantially higher than in

the control group. Similarly, 45% of patients had an increased D-dimer level. Among these individuals, 30% had D-dimer levels between 250 and 500mg, and 50% had levels between 500 and 1000 ng/ml, which were considerably higher than the control group. Conclusion: According to the findings of the study, atrial fibrillation is related with both inflammatory and coagulation abnormalities, as seen by higher CRP and D-dimer levels. Both these indicators are thromboembolic risk factors. As a result, every patient should be closely followed in order to decrease morbidity and death from atrial fibrillation.

Keywords---atrial fibrillation, CRP, D – dimers, inflammatory marker, coagulation activation marker.

Introduction

Atrial fibrillation is the abnormality of heart rate and is defined as irregularly irregular heart rate which is prevalent in general population. (1) In clinical practice, atrial fibrillation is perhaps the most prevalent heart arrhythmia in the population at large. (2) If not treated effectively, this condition has been linked with severe morbidity and mortality, and leads to various cardiac and extra cardiac complications like stroke, myocardial infarction, heart failure and renal functional impairment. It is one of the strongest risk factors for stroke, due to cerebral embolization. (3)

Atrial fibrillation is a hypercoagulable state and associated with hemostatic abnormality as evidenced by thromboembolic complication and elevated D-dimer level. (4) Atrial fibrillation (AF) is also related to inflammation, and multiple histological studies have revealed inflammation in biopsies from individuals suffering from atrial fibrillation. (5) Inflammation in atrial fibrillation is best detected by measurement of CRP levels, which is associated with atrial fibrillation and its recurrences. (6) Inflammatory infiltrates and oxidative damage have been reported in AF and subclinical inflammation and atrial strain play major role in the onset of atrial fibrillation. (7,8)

The study's goal is to assess CRP, D-dimer, PT, and APTT levels in patients with atrial fibrillation. Due to the fact that AF goes hand in hand with the inflammatory and hemostatic abnormalities, combined inflammatory and hemostatic irregularities encompass a prothrombotic state and are capable of causing major complications. As a result, measuring CRP and D-dimer levels provides significant information to physicians. CRP levels reflect the recurrence of atrial fibrillation, and elevated D-dimer levels reflect the patient's thromboembolic status, therefore raised CRP and the level of D-dimers are key risk factors in patients with atrial fibrillation, and have diagnostic and prognostic value.

Materials and Methods

From Januarty 2019 to June 2020, the study was carried out in the cardiology and pathology departments of Mardan Medical Complex and Bacha Khan Medical College Mardan. This study included a total of 100 patients with atrial fibrillation,

with 50 people serving as the control group. The levels of CRP and D-dimers were determined in all cases. Patients with illness, septicemia, diabetes mellitus, a history of DVT and malignancy, pregnancy, chronic inflammatory ailments (such as SLE, Rheumatoid arthritis, osteoarthritis), consumers of alcohol, and steroid drug users were all excluded from the study.

D-dimer is a plasma fragment that mediates the proteolytic destruction of fibrin clots. Its level rises in every state where clot formation and subsequent disintegration rises, and its detection can identify thromboembolic conditions in patients. CRP levels were assessed from serum samples utilizing a computerized immunoassay machine (CLIA system). The CRP testing relies on the interaction that occurs among C- reactive protein and antibodies within the reagent reacting with CRP in the sample, and the result is automatically represented on the machine. All data was analyzed statistically using a Chi-square test and the t-test. The probability of significance was established at less than.0005 for P-valve.

Results

An aggregate of 100 patients with AF were included in this study. ECG was used to diagnose all atrial fibrillation patients. Adult males and ladies were among the patients. In the current study, 35% of participants had increased CRP levels. The mean C-reactive protein level was 2.96 +/- 0.652. Which were substantially higher than in the control group (P.00325). Similarly, D-dimer levels were elevated in 45% of patients with AF. 30 out of 100 patients had D-dimer levels between 250 and 500ng/dl, and 50 out of 100 patients had D-dimer levels between 500 and 1000ng/dl, which is considerably higher than the control group (P less than 0.00256).

Table 1
Frequency of elevated c-reactive protein and D-dimer level in atrial fibrillation

S.No.	Inflammatory and hemostatic markers	Percentages of patients
1.	CRP level (C- reactive protein)	35%
2.	D-dimer level	45%

Table 2
Mean value of CRP and D- Dimer level in atrial fibrillation

S.No.	Inflammatory and hemostatic markers	Mean value	Mean value (control group)
1.	CRP	2.99 +/- 0.652	Less than 0.9 mg/dl
2.	a) D-dimer Number of patients = 30	250 -- 500ng/dl	Less than 0.250ng/dl
	b) Number of patients = 50	500----1000 ng/dl	

Prevalence of CRP P < 0.00362
Prevalence of D-dimers P < 0.00265

Discussion

Atrial fibrillation is the sustained cardiac arrythmia commonly reported in general population and clinical practice. Despite prophylaxis and advancement in treatment, Atrial fibrillation comes with significant morbidity and hospitalization. Atrial fibrillation has been increasing prevalence in clinical practice and is associated with both inflammatory and hemostatic abnormalities which lead to complications like stroke and other systemic embolization. The inflammation and homeostatic abnormalities are best detected by measurements of C- reactive protein (CRP) and D- Dimer levels which provide immediate and useful information to the clinicians.

The current investigation found that 35% of patients with AF had high C- reactive protein concentrations. The average CRP level was 2.56 +/- 0.652 mg/dl. Many investigations have been undertaken, and they have all reported higher CRP levels in patients with atrial fibrillation. In their investigation, Nortamo et al. discovered that the condition is related with considerably higher CRP levels. (9) Several authors conducted investigations and found that atrial fibrillation is associated with higher CRP levels. (10, 11, 12).

The frequent link between heart rate variability and inflammatory disorders such as myocarditis or pancreatitis and atrial fibrillation supports the association. (13) In atrial biopsies, there was an increase in frequency following heart surgery, as well as the detection of infiltrates of inflammatory cells and oxidative damage. (14) Interleukin-6 has also been significantly associated with atrial fibrillation (15) and a high CRP level is a risk factor for atrial fibrillation on its own. All these biomarkers suggest association of chronic inflammation with atrial fibrillation. (16)

Atrial fibrillation is linked to both an inflammatory and thrombotic condition. (17) In the current study, 45% of atrial fibrillation patients had increased D-dimer levels. Various authors studied D-dimer levels in atrial fibrillation as reported by Mahe et al that D-dimer is highly associated with atrial fibrillation and cardiovascular events. (18) Several publications have found similar findings that AF is associated with higher D-dimer levels. (19-20) An important complication is the development of one or more thrombi in the left atrium and their successive embolization to cerebral and peripheral parts, and all these thromboembolic complications are due to hypercoagulable state present in the atrial fibrillation which is evidenced by increased levels of D-dimer and elevated levels of CRP. (20,21) D-dimer bits are produced when clot formation and subsequent degradation are increased, but their amount additionally rises in non-thrombotic conditions such as inflammatory disease, liver disease, eclampsia, and so on, and their increased level represents a hypercoagulable occasion in the body. (22) However, its negative levels safely exclude a thromboembolic condition and allow patient safely for early cardioversion of atrial fibrillation.

(23.24) Consequences in atrial fibrillation are caused primarily by a prothrombotic and hypercoagulable situation. However, the pathogenesis and mechanism of prothrombotic and hypercoagulable states in atrial fibrillation are multifactorial, yet one evidence is the presence of the Virchow triad, which refers

to abnormalities in blood flow, blood constituents, and vessel walls that correspond to the underlying mechanism for prothrombotic state. (25) Inflammation, growth factors, structural remodeling of atria, platelet activation, gene influencing and activation of hemostasis all contribute to thrombotic tendency in atrial fibrillation. (26)

Inflammation induces endothelial dysfunction; angiotensin interaction and TNF contribute to hypercoagulable and prothrombotic state and hence to Atrial fibrillation. (27,28) Atrial fibrillation is the underlying cause of 30000 to 40000 embolic strokes per year in United state and strokes increase with age by 1.5% percent in patients aged between 50 to 59 years to 23.5% in patients aged 80 to 89 years. (29)

Conclusions

The investigation came to the conclusion that atrial fibrillation is related to both proinflammatory and hemostatic abnormalities, as demonstrated by considerably higher CRP and D—Dimer levels. So, cardiologists and physicians should equally monitor such patients to avoid any thromboembolic phenomenon as this would bolster its life-threatening consequences. Thus, good management and observation mitigate both morbidity and mortality.

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