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Research Article

**INTERLEUKIN-6 LEVELS IN CASES OF ANGINA PECTORIS**<sup>1</sup>Qurat Ul Ain, <sup>2</sup>Muhammad Asadullah, <sup>3</sup>Amina Abdullah

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**Abstract:**

Chest pain is well reported in emergency settings and angina pectoris reveals sever underlying cardiovascular disease. The search for various inflammatory markers including interleukin 6 (IL-6) to label it is under investigation. **Objective:** To determine the frequency of raised Interleukin-6 levels in patients with angina pectoris. **Methods;** This cross sectional study was conducted during July to December 2018 at Benazir Bhutto Hospital, Rawalpindi; where 100 cases of angina pectoris with normal ECG and cardiac enzymes were included and their detailed sociodemographic and clinical history was taken. Three ml of venous blood was collected in a sterilized disposable syringe and assessed for IL-6 level. The values more than 5 ng/ml were considered as raised.

**Results:** In this study there were total 100 cases out of which 66 (66%) were males and 34 (34%) females. The mean age was 54.19±6.72 years. There were 70 (70%) cases that had age more than 50 years. There were 18 (18%) cases with DM, 28 (28%) had HTN and 42 (42%) had smoking history positive. Raised IL-6 was seen in 72 (72%) of cases. Raised IL-6 were almost equal in both genders ( $p= 0.89$ ) while it affected more with age group of more than 50 years comprising 80% of its respective group with  $p= 0.07$ . IL-6 levels were significantly higher in cases with DM and HTN with  $p$  values of 0.04 and 0.02 respectively while this difference was not significant in smokers and non smokers.

**Conclusion;** Angina pectoris is a first step towards to ischemic cardiac diseases. Raised IL-6 levels are almost seen in every 3 out of 4 (72%) cases. These levels are significantly raised in cases with DM and HTN.

**Key words:** Angina Pectoris, DM, HTN, IL-6.

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**INTRODUCTION:**

Angina pectoris (AP) is a symptom complex of Coronary heart disease (CHD). CHD is a major cause of morbidity and mortality in the South-Asia despite the use of new lipid-lowering drugs, aggressive anti-hypertensive therapy, and changes in lifestyle. CHD is responsible for 20% of all medical emergency admissions with the highest risk for complications and death. [1]

Angina pectoris is characterized by paroxysmal and recurrent attacks of chest pain / discomfort caused by transient myocardial ischemia.[2-3] AP and CHD are major consequence of atherosclerosis of coronary arteries. Recent researches have shown that inflammation plays a key role in atherosclerosis. Inflammatory mechanisms mediate initiation, progression and complications of atherosclerotic lesions.[4]

Increasing age, male sex, cigarette smoking, hypertension, hyperglycemia, atherogenic lipoproteins and genetic predisposition are well-established risk factors causing chronic endothelial injury/ dysfunction. Recently, various inflammatory and haemostatic factors have been identified which may cause endothelial dysfunction. Fibrinogen, plasminogen activator inhibitor-1, von Willebrand factor, factor VII, C-reactive protein, pro-inflammatory cytokines and interleukins are among these factors. [5-6]

IL-6, an intercellular mediator, belongs to hematopoietin family of cytokines. It is produced by a variety of cells in the body including T and B-lymphocytes, monocytes/macrophages, fibroblasts, endothelial cells and adipose tissue.[6] IL-6 then stimulates the liver to produce acute-phase reactants and coagulation factors, leading to a prothrombotic state. IL-6 also stimulates macrophages to produce tissue factor and proteolytic enzymes, adhesion molecules and TNF. IL-6 causes platelet aggregation and vascular smooth muscle cell proliferation. [7]

**Objectives:**

To determine the frequency of raised Interleukin-6 levels in patients with angina pectoris.

**Sample selection:****Inclusion Criteria:**

1. Age 45-65 years.
2. Patients of either sex.
3. Patients who present with typical chest pain but with normal ECG and cardiac enzymes.

**Exclusion Criteria:**

1. Patients with acute myocardial infarction.
2. Patients with valvular or congenital heart disease.
3. Pregnancy, renal and hepatic failure (because these conditions may affect haemostatic variables).
4. Patients with deep vein thrombosis and acute pulmonary embolism.
5. Patients with chronic inflammatory conditions like rheumatoid arthritis, systemic lupus erythematosus etc.
6. Patients having a history of acute infection within last 2 weeks.

**Data collection procedure;**

This cross sectional study was conducted during July to December 2018 at Benazir Bhutto Hospital, Rawalpindi.; where the cases as per inclusion criteria were included and their detailed sociodemographic and clinical history was taken. Then these cases underwent ECG to excluded MI and also the cardiac enzymes. The cases with normal ECG and cardiac enzymes then assessed for IL-6 level. Three ml of venous blood was collected in a sterilized disposable syringe and assessed for IL-6 level. The values more than 5 ng/ml were considered as raised.

**Statistical Analysis:**

The data was entered and processed through computer software "SPSS" version 19.0 " and analyzed by applying chi square test. The variables were presented as means with standard deviation (SD) or as percentages. The categorical/ qualitative variables were compared using a Chi square test / fisher's exact test. The values less than 0.05 was considered as significant.

**RESULTS:**

In this study there were total 100 cases out of which 66 (66%) were males and 34 (34%) females. The mean age was  $54.19 \pm 6.72$  years. There were 70 (70%) cases that had age more than 50 years. There were 18 (18%) cases with DM, 28 (28%) had HTN and 42 (42%) had smoking history positive. Raised IL-6 was seen in 72 (72%) of cases. Raised IL-6 were almost equal in both genders ( $p= 0.89$ ) while it affected more with age group of more than 50 years comprising 80% of its respective group with  $p= 0.07$  (table 1). IL-6 levels were significantly higher in cases with DM and HTN with  $p$  values of 0.04 and 0.02 respectively while this difference was not significant in smokers and non smokers as in table 2.

**TABLE 01**  
**RAISED IL-6 LEVEL WITH RESPECT TO DEMOGRAPHICS**  
**n= 100**

DEMOGRAPHICS		Raised IL-6		Significance
		Yes	No	
Gender	Male	48 (72.73%)	18 (27.27%)	P= 0.89
	Female	24 (70.59%)	10 (29.41%)	
Age groups	> 50	56 (80%)	14 (20%)	p= 0.07
	< 50	16 (50%)	16 (50%)	

**TABLE 02: RAISED IL-6 LEVEL WITH RESPECT TO STUDY VARIABLES**  
**n= 100**

		Raised IL-6		Significance
		Yes	No	
DM	Yes	15	3	p= 0.04
	No	57	25	
HTN	Yes	20	8	p= 0.02
	No	52	20	
Smoking	Yes	24	18	P= 0.29
	No	48	10	

### DISCUSSION:

Cardiovascular disease is a life threatening entity and a very common encountered emergency issue. Lots of people daily report to emergencies and clinics with different variety of symptoms, which are hallmark of CAD and pose a great burden to quickly sort out the nature and severity of the disease. The ones with normal ECG and cardiac enzymes are hard to label as normal or suffering from angina pectoris. Here are the investigations required to add a bit surety regarding the further management. Different biomarkers have been used in the past to label Angina Pectoris or to send the patient home by labeling a non-cardiac patient. These include CRP, D

dimers, IL-6, TLC, Monocytes, Polymorph nuclear cells, ICAM-1, VCAM-1 and so on.

In the present study IL-6 levels were high in number in cases of angina pectoris and were observed in 72% of cases. This is also proved by other studies in the past that IL-6 is highly raised in the cases of AP. Studies done by Yamashita et al [8] and Lee et al [9] has shown that IL-6 is not only associated with coronary atherosclerosis and CHD but it is also used as an marker for risk stratification in patients with CHD. [10] In a another study, IL-6 is proved to be the marker to display plaque vulnerability to rupture. Elevation of circulating IL-6 is a strong and

independent marker of increased mortality in acute coronary events. [11]

In a study Lai S et al in 2009, they compared IL-6 and CRP and it was seen that the association of IL-6 was significantly better ( $p=0.02$ ) for IL-6 levels while levels of CRP measured were not significantly elevated ( $p=0.92$ ).<sup>12</sup> In contrast to all above studies in a study conducted by Kosmala W et al found no significant association of IL-6 and angina pectoris. ( $p=0.23$ ). [13]

In our study DM and Hypertension were significantly associated with raised levels of IL-6. This was consistent with the study conducted by Orak et al and Mahemuti A et al, that also had significant high results. [14-15] The reason of higher number of IL-6 in cases with DM and HTN can be explained by the factor that these both conditions are pre atherosclerotic and also a risk factor for vascular injury. So, they predispose the injury and starting the cascade of reaction leading to raise IL-6 levels.

There were few limitations of this study. As we did not use the other inflammatory markers of the angina pectoris and we also did not categorize the patients into groups of stable and unstable angina.

### CONCLUSION:

Angina pectoris is a first step towards to ischemic cardiac diseases. Raised IL-6 levels are almost seen in every 3 out of 4 (72%) cases. These levels are significantly raised in cases with DM and HTN.

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