EFFECT OF CHOLESTEROL LEVEL ON PLATELET AGGREGABILITY IN NORMAL INDIVIDUALS

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ABSTRACT

Objective: *The aim of present study was to find the effect of cholesterol level on platelet aggregability in normal individuals.*

Methodology: *This study was conducted in Cardiology department, Lady Reading Hospital, Peshawar in September- October 2007. Normal individuals aged 18 years or above were randomly included. Patients who were suffering from any cardiovascular or other diseases were excluded. Those who were taking ante-platelets, anti coagulants and lipid lowering drugs were also excluded. Thus a total of 101 individuals were examined, after taking informed written consent. Fasting blood samples were taken from each patient. Total cholesterol was measured in hospital laboratory, while platelet aggregation was measured with chronolog whole-blood platelet aggregometer (WBA).*

Results: *A total of 101 patients were examined. Their mean age was 51.24 ± 8.23 years. Male were 60(59.41%) and female were 41(40.59%). Mean platelet aggregability of these individuals was 7.87 ± 4.40 ohms. Mean cholesterol was 163.47 ± 20.75 mg/dl. When age was correlated with aggregability, both had a weak negative correlation. Pearson correlation coefficient was -.018 (p=0.855). When age was correlated with cholesterol, again both have a weak negative correlation. Pearson correlation coefficient was -.152 (p=0.129). When aggregability was correlated with cholesterol, both have a significant positive correlation. Pearson correlation coefficient was +0.269 (p=0.006)*

Conclusion: *Platelet aggregability is increased in patients with high cholesterol. These patients may need higher doses of anti platelets and more aggressive treatment of lipids to avoid vascular events.*

Key Words: *Serum cholesterol, Platelet aggregability, Whole-blood platelet aggregometer (WBA)*

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INTRODUCTION

Coronary artery disease has become a global problem and the largest cause of death worldwide. In Pakistan it is estimated that one in five middle-aged adults may have underlying coronary artery disease (CAD)[1]. Hypercholesterolemia is one of the major modifiable risk factors for CAD. Deranged lipid levels can cause CAD including myocardial infarction by different mechanisms, like development of atherosclerotic plaques, disruption of protective endothelial surface and disturbance of haemostatic system, of which platelets are an important component.

Key events in the pathogenesis of myocardial infarction are the rupture of a coronary atherosclerotic plaque and subsequent thrombosis[2]. The initial step in this process is the adhesion of platelets to the disrupted endothelium[3-5] followed by platelet activation and aggregation which results in plug formation[6,7]. Platelet adherence and aggregation are augmented in hypercholesterolemic animals and humans[8,9]. Platelets derived from individuals with type IIa hyperlipidemia manifest enhanced sensitivity to agonists of aggregation in vivo[9]. Cholesterol sulfate is now recognized as an important component of lipid family and is constituent of red blood cells

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and platelets[10,11]. In platelets, cholesterol sulfate has been shown to support platelet adhesion[10,11]. Plasma levels of cholesterol sulfate are elevated in hypercholesterolemia[12]. Blache et al[13] also showed that the exposure of platelets to cholesterol sulfate enhanced aggregation responses to ADP and thrombin. Hypercholesterolemia may also exert its effects by altering the activity of endogenous regulators of platelet reactivity such as prostacyclin and nitric oxide. Endothelium-derived nitric oxide and prostacyclin act synergistically to inhibit platelet adherence and aggregation[14,15]. In the normal healthy microcirculation, endothelium-derived nitric oxide acts on circulating platelets to reduce their tendency to aggregate[16,17]. In hypercholesterolemic animals and humans, vascular nitric oxide activity is reduced[18,19].

Like western countries CVD risk factors including hypercholesterolemia is also common in our nation[20,21]. To our knowledge till date no one has studied the effect of cholesterol on platelet aggregabilty in Pakistani population. The aim of present study was to find the effect of cholesterol on platelet aggregabilty in normal local population.

METHODOLOGY

This study, after approval by the hospital ethical committee, was conducted in Cardiology department, Lady Reading Hospital Peshawar in September- October 2007. Normal individuals aged 18 years or above were randomly included from patient's attendants and ward staff. Patients who were suffering from any cardiovascular or other diseases were excluded. Those who were taking lipid lowering drugs or ante-platelets like aspirin or clopidogrel and anti coagulants like warfarin or heparin were also excluded from the study. Thus after taking informed written consent, a total of 101 individuals were examined.

Fasting blood Samples were taken from each patient. Total cholesterol was measured in hospital laboratory, while platelet aggregation was measured with chronolog whole-blood platelet aggregometer (WBA). Other supplies needed for performing whole-blood aggregation were reagents, curettes, stir bars, micropipettes, tips etc.

Whole blood (0.5 ml) was diluted with an equivalent volume of isotonic saline and incubated for 5 minutes. The impedance of each sample was monitored at sequential 1-minute intervals until a stable baseline established. The agonist ADP (20 µmol/L) was then added to the sample and aggregation was monitored for 6 minutes. With time platelets aggregates over electrodes and impedance increases. The final increase in impedance (in ohms) over this period was displayed as a numeric readout. Result of each individual along with age and gender was noted.

All the information collected was analyzed using SPSS version 11. Categorical variables were presented as frequencies and percentages. Continuous variables were presented as mean and standard deviation. Bivariate correlations were used for measuring correlation between age, aggregability and cholesterol. The coefficient used was Pearson's correlation coefficient for continuous data and the test of significance was two-tailed. Correlation was taken as significant at 0.01 levels.

RESULTS

A total of 101 patients were examined. Their mean age was 51.24 ± 8.23 years (range; 30-70). There were 60(59.41%) males and 41 (40.59%) females. Mean platelet aggregability of these individuals was 7.87 ± 4.40 ohms (Figure 1). Mean choles terol of the sample was 163.47 ±20.75 (108-252) mg/dl (Figure 2).

When age was correlated with aggregability, it had a weak negative correlation with a Pearson correlation coefficient = -.018 (p=0.855) (Figure 3).

When age was correlated with cholesterol, it also had a weak negative correlation with a Pearson correlation coefficient = -.152 (p=0.129) (Figure 4).

When platelet aggregability was correlated with cholesterol, it had a significant positive correlation at the 0.01 level (2-tailed) with a Pearson correlation coefficient = +.269 (p=0.006) (Figure 5).

DISCUSSION

The coagulation system has been proposed as a possible mechanism of thrombogenesis and atherosclerosis in patients with hyperlipidemia. Some studies have demonstrated increased coagulation activity and platelet function in patients with hyperlipidemia[22,23] but others have produced conflicting results[24-27]. Thus, the role of coagulation factors and platelets in hyperlipidemia remain to be clarified.

In our study cholesterol level and platelet aggregability showed a strong positive correlation. This is in accordance with other studies[11,22,23]. Friend et al[28] also showed significant positive correlation of platelet aggregability with cholesterol as well as triglyceride. They suggested that these patients may need higher doses of anti platelets and more aggressive treatment of lipids to avoid vascular events.

Figure 1: Distribution of different levels of platelet aggregability (x-axis) among normal individuals

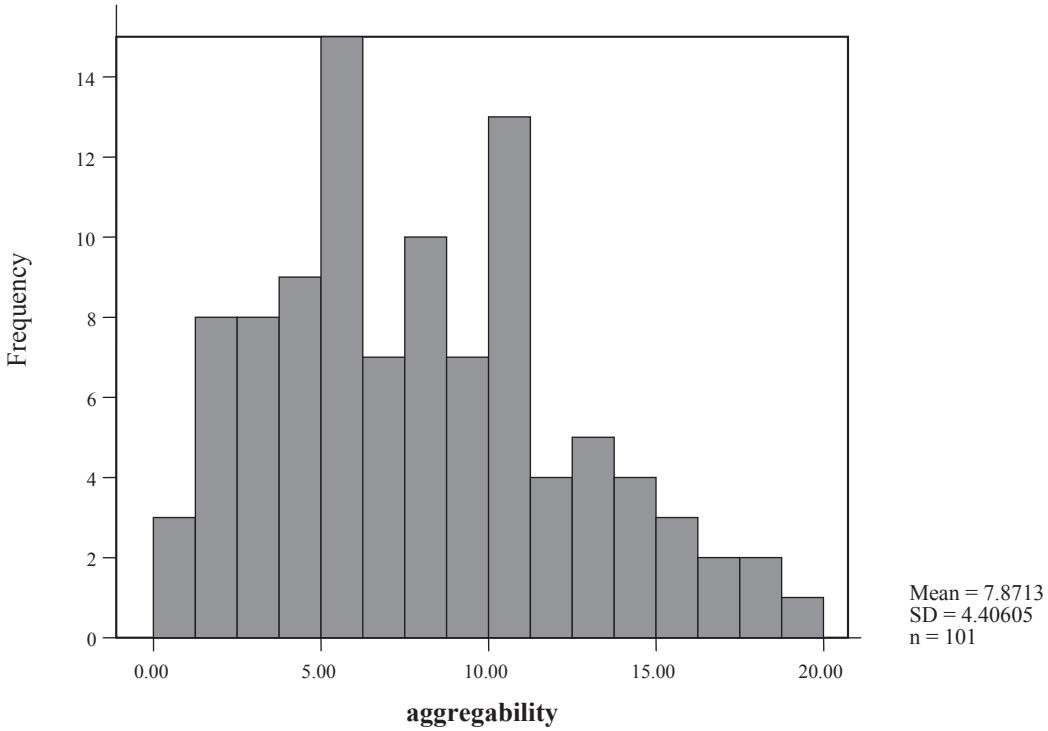


Figure 2: Distribution of different levels of cholesterol (x-axis) among normal individuals

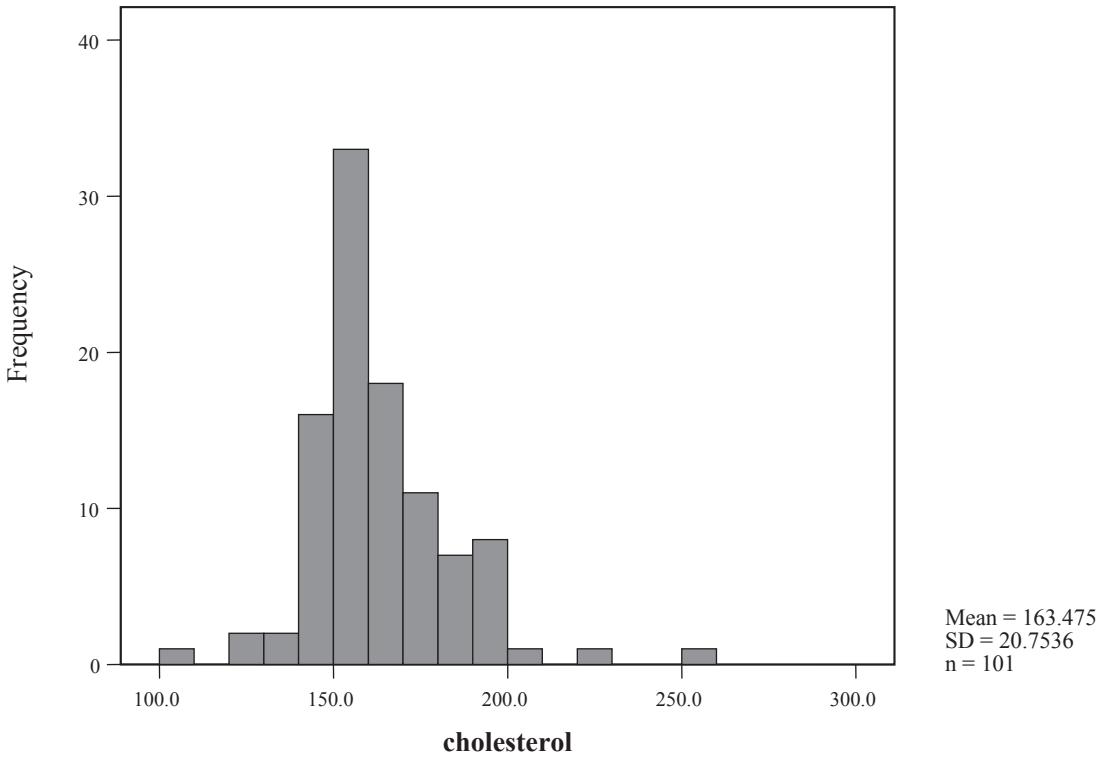


Figure 3: Correlation of age with platelet aggregability

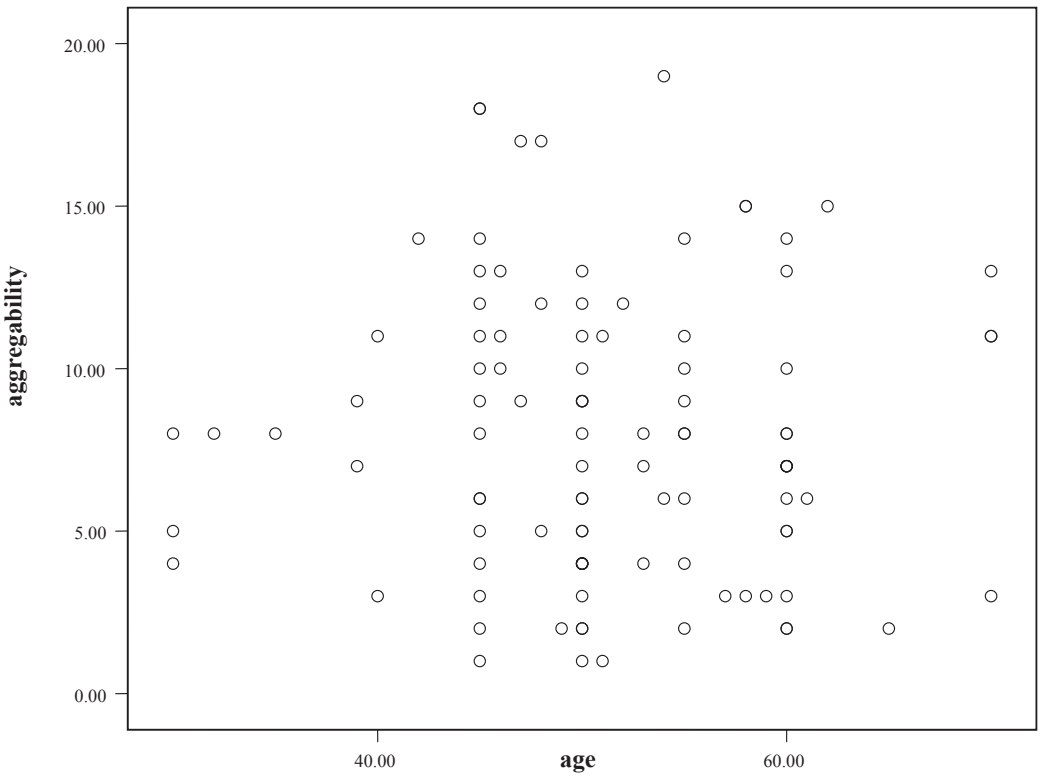


Figure 4: Correlation of age with cholesterol

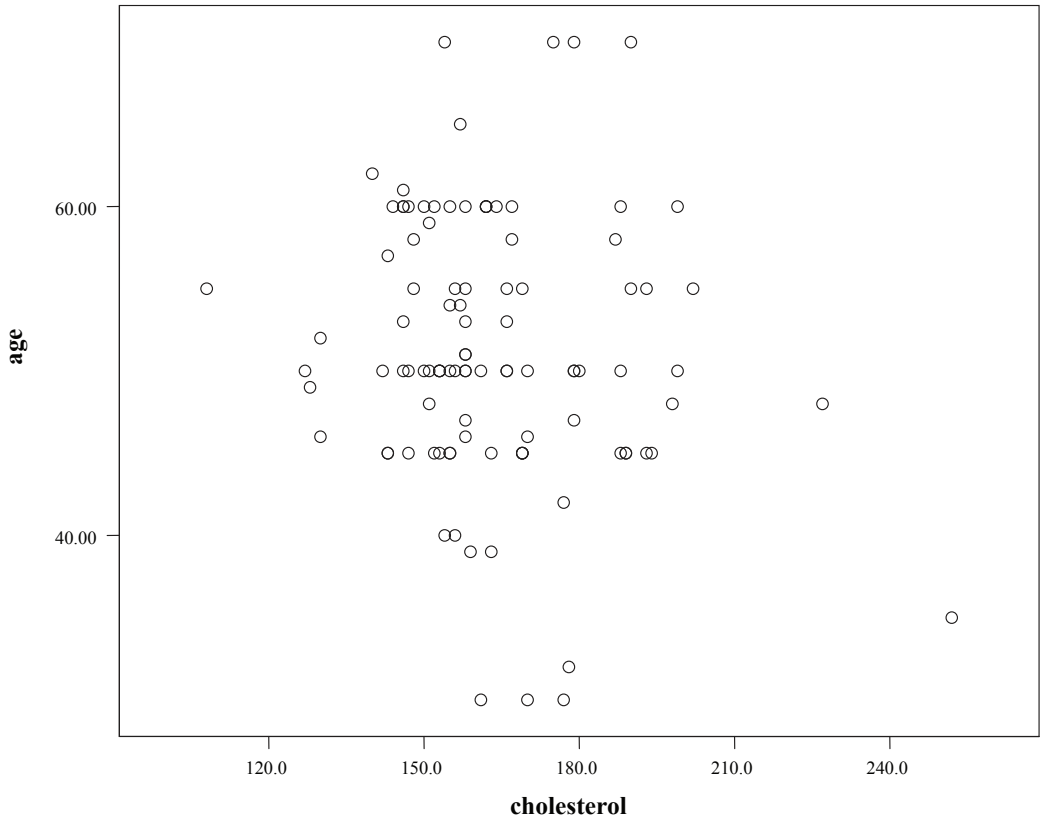
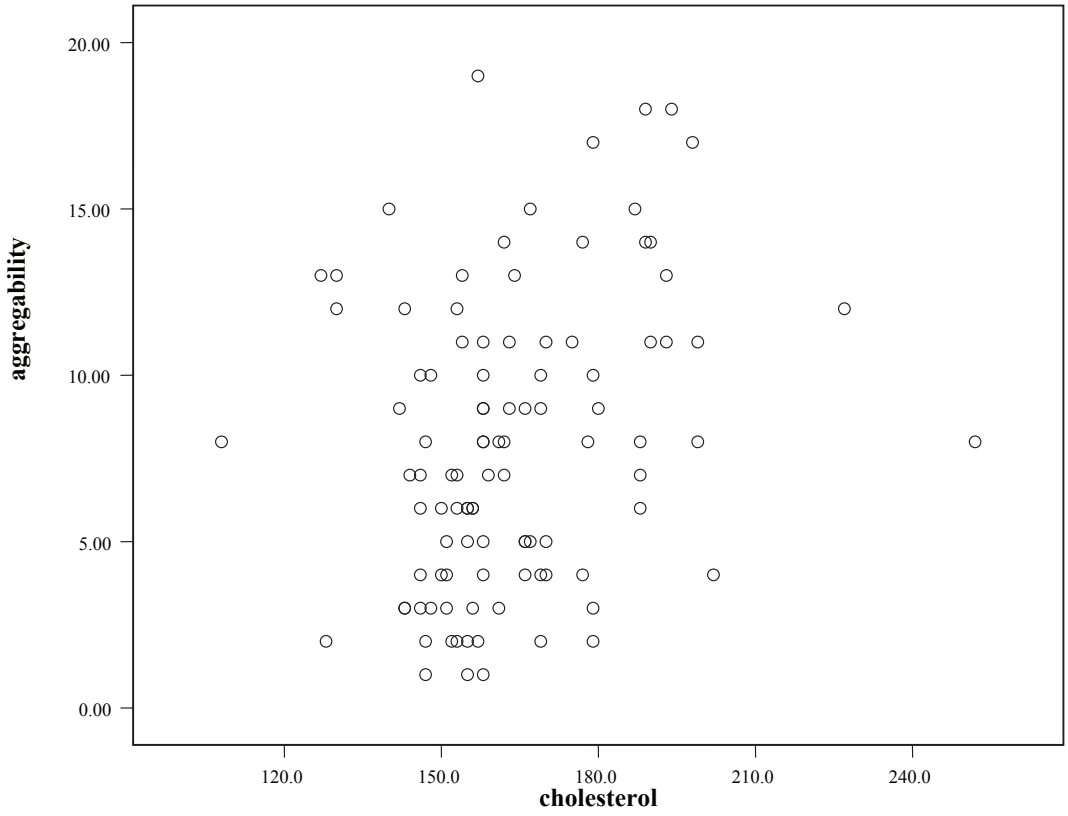


Figure 5: Correlation of cholesterol with platelet aggregability



Kameda et al found that lipid levels significantly influence platelet aggregability in Japanese general population as well as in cardiovascular patients. Their study also revealed association of gender and age with platelet aggregability as well as platelet count[29]. Fusman et al also reported a significant correlation between the state of adhesiveness/aggregation of erythrocytes, leukocytes and platelets in the peripheral blood and total and LDL cholesterol[30].

In our study there is a trend towards lower platelet aggregability as the age increases, but this negative correlation is weak (r = -.018) and insignificant (p= 0.855). Previous studies reported contradicting results about the association of age and platelet aggregability. Ivandic et al showed that age has no association with platelet aggregability[31].

Light transmission aggregometry is considered the historical gold standard for testing platelet function[32]. Its use is very time consuming and its standardization is often poor, limiting its use to dedicated laboratories[32,33]. We used whole blood aggregometry (WBA) using chronolog aggregometer , because it is easy to use, gives faster results, does not require centrifugation and evaluates platelets in a physiologic milieu in presence of red and white blood cells, which are known to modulate platelet functions[34]. WBA measures the electrical impedance, in ohms, between two electrodes immersed in whole blood as the platelets are aggregated on them[35].

LIMITATIONS

Our study has certain limitations. It was a single centre study. Instead of clinical events, effect of cholesterol on platelet aggregation was measured only in vitro. Normal individuals were tested upon and cardiovascular patients were excluded.

CONCLUSION

Patients with high cholesterol show increased platelet aggregability. Further prospective study is needed to follow up these patients for clinical events.

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CONTRIBUTORS

MF conceived the idea, planned and wrote the manuscript of the study. IS, LN, MA & H helped in the write-up of the manuscript. MH supervised the study. All the authors contributed significantly to the research that resulted in the submitted manuscript.