RELATIONSHIP OF WHITE BLOOD CELL COUNTS, HAEMOGLOBIN AND ESR WITH IHD
Farhana Shahzad, Shahzad Tawwab*, Afia Abbas
Department of Immunology, University of Health Sciences, *Punjab Institute of Cardiology, Lahore, Pakistan

Objectives: To find any association of white blood cells, haemoglobin and ESR with ischemic heart disease in high risk native population. Methodology: The study included 93 male patients with ischemic heart disease, between 40 and 60 years of age; 96 age and gender matched subjects. All study participants were non-diabetics. Complete blood cells count, haemoglobin and ESR levels were compared between the patient and control groups. Results: Total leukocyte counts along with neutrophils were significantly higher in the test group compared to the control population ($p<0.001$) and lymphocytes were significantly lower ($p<0.001$) in the patient group as compared to the control group. Haemoglobin levels were significantly lower ($p<0.001$) and ESR was higher ($p=0.030$) in the patient group as compared to the control group. Conclusion: Although, our findings of the study variables extend previous reports, the prevalence and prognostic importance of these variables in IHD should be assessed in future experimental studies. These parameters could be important in public health because they are routinely measured by clinicians and may be helpful to predict the risk of future and secondary ischemic events in a high risk population.

Keywords: TLC, DLC, Haemoglobin, ESR, Ischemic Heart Disease

INTRODUCTION
Cardiovascular disease is the leading cause of death all over the world.$^1$ Recent researches have shown that inflammation plays a key role in ischemic heart disease (IHD) and leukocyte count is a marker of inflammation. Leukocytes are involved in the pathogenesis of atherosclerosis due to proteolytic and oxidative vascular damage, abnormal leukocyte aggregation and adhesion, release of cytokines and chemokines.$^2,3$ Correlation of leukocyte counts with coronary artery disease has been consistently shown to be an independent risk factor and prognostic indicator.$^3$ An increase of 1 SD in leukocyte counts was associated with a 65% increase in the risk of death from IHD.$^4$ Various types of blood born inflammatory and immune cells including neutrophils, lymphocytes, monocytes and eosinophils have been implicated in IHD.$^5,6$ Very few studies are available on the role of individual types of leukocytes in IHD$^1$ so, it is important to consider the role of various cell types in cardiovascular diseases.

Decreased haemoglobin levels are known to be associated with an increased risk of coronary atherosclerosis due to increase in blood flow and shear stress resulting in endothelial damage and vessel wall thickness. Studies have shown that 1 g/dl decrease in haemoglobin level is an independent, statistically significant risk factor for the development of cardiac morbidity and mortality especially in patients with chronic renal failure.$^7$ Anaemia is an independent risk factor for cardiovascular disease outcomes in the general population.$^8$ Recent researches suggested that decrease haemoglobin is an independent predictor of increased morbidity and mortality in patients presenting with acute myocardial infarction.$^9$ However, previous studies are for the Caucasian population and the values may vary with ethnicity. There is a need for studies to establish the association of haemoglobin with cardiovascular diseases in native population.

The notion that rheologic characteristics of blood contribute to the pathogenesis of IHD by influencing blood flow, is gaining growing support.$^{10,11}$ With regard to erythrocyte sedimentation rate (ESR) it is associated with an increased risk of coronary heart disease events. An elevated ESR is a fast and inexpensive valuable marker for the extent and intensity of atherosclerosis and increased risk of IHD.$^{12}$ Few studies are available to show any association of ESR and IHD.

MATERIAL AND METHODS
The study population was divided in to two groups. The test group consisted of male patients, between forty and sixty years of age, with angiographically proven ischemic heart disease. Second group consisted of the subjects of same age and gender with no known history of ischemic heart disease. All participants were asked to fill a questionnaire to obtain information on history of hypertension, diabetes mellitus, ischemic heart diseases, smoking and other major diseases (immunosuppressive, immuno-proliferative, and autoimmune diseases). This questionnaire also required the information on history of acute infections. Subjects with diabetes mellitus, immunodeficiency and immunoproliferative disorders, acute or recent infections, cardiogenic shock, history of immunosuppressive treatment, and taking statins (lipid lowering drugs) were excluded from the study.

After drawing 5 ml of venous blood from the subject, it was poured into a purple top (with EDTA) vacutainer tube. Samples were analyzed for complete blood counts and haemoglobin by using haematology auto-analyzer (Sysmex XS-1000i, Kobe, Japan). ESR was determined by conventional Westergren method.

Statistical analysis was done using SPSS version 12. Categorical data is presented as percentages (frequencies), and quantitative data as medians and IQR values. For categorical data, Pearson chi-square test was used to determine any significant association between the groups for different variables. For quantitative data, Mann Whitney rank sum test was used to determine any significant differences between the study groups. The \( p \)-value \(<0.05\) was considered statistically significant.

**RESULTS**

The baseline clinical characteristics of study subjects are summarized in Table-1.

A significant difference in the frequency of smoking between control and test groups was observed. The fasting blood sugar levels were also significantly higher in the test group as compared to the control group, although they remain within the expected normal range.

Table-2 shows that total leukocyte counts were significantly higher in test group compared to control group population (\( p<0.001\)). The median values of control and patient groups were 6.88 with inter-quartile range value (IQR) of 1.74 and 9.40 (IQR 3.95) respectively. Percentage of polymorphonuclear cells was significantly higher in the patient group as compared to the control group (\( p<0.001\)). The patient group has median value of 68.00 (IQR 14.50) and the control group has 57.00 (IQR 13.0). The percentage of lymphocytes was significantly lower in the patient group as compared to the control group (\( p<0.001\)). The median values of control and patient groups were 35.00 (IQR 10.00) and 28.00 (IQR 15.00) respectively. Percentage of monocytes in total leukocytes showed no difference between the patient and control groups. The median values being 2.00 in both groups. The IQR values of control and patient groups were 2.00 and 1.00. No significant difference was seen in eosinophils between the control and patient groups. The median value was 2.00 in both groups and IQR values were 3.00 and 2.00 respectively.

Table-3 shows that haemoglobin levels were significantly lower in the patient group as compared to the control group (\( p<0.001\)). The median value of control group was 15.00 and patient group was 13.70 and IQR values of these two groups were 8.00 and 21.00 respectively.

The overall ESR levels were significantly higher in the patient group as compared to the control group (\( p=0.030\)). The median values of control and patient groups were 10.00 (IQR 2.00) and 12.00 (IQR 1.95).

**Table-1: Base line Clinical Characteristics of the study groups**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control (Number)</th>
<th>Patient (Number)</th>
<th>( p )-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>101</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>101</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family H/O IHD</td>
<td>101</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting Blood Sugar</td>
<td>101</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholesterol</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglyceride</td>
<td>100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**p-value was determined by Pearson chi-Square test and for Fasting blood sugar by Mann Whitney rank sum test. Smoking= considered as smoker if the individual is currently smoking or has quit smoking within the last six months. Family H/O IHD= Positive if first degree relatives have ischemic heart disease. Fasting Blood Sugar= reference values by Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Median values. Inter-quartile range value (IQR)**

**Table-2: Comparison of total leukocyte counts and differential leukocyte counts between patients with atherosclerosis and control group**

<table>
<thead>
<tr>
<th>TLC/mm(^3)</th>
<th>Polys%</th>
<th>Lymphocyte%</th>
<th>Monocytes%</th>
<th>Eosinophils %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Number)</td>
<td>96</td>
<td>31</td>
<td>15.5</td>
<td>99</td>
</tr>
<tr>
<td>Patient (Number)</td>
<td>93</td>
<td>99</td>
<td>14.5</td>
<td>99</td>
</tr>
<tr>
<td>( p )-value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Table-3: Comparison of fasting blood sugar, erythrocyte sedimentation rate (ESR), and haemoglobin levels between patients with atherosclerosis and control group**

<table>
<thead>
<tr>
<th>ESR mm Hr</th>
<th>Hgb g/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Patient</td>
</tr>
<tr>
<td>Control</td>
<td>96</td>
</tr>
<tr>
<td>Patient</td>
<td>10.00</td>
</tr>
<tr>
<td>( p )-value</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**IQR= Inter-quartile range. \( p \)-Value= determined by Mann Whitney rank sum test**

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DISCUSSION
Numerous epidemiological and clinical studies have shown leukocyte counts as an independent risk factor of IHD and a strong predictor of future cardiovascular events. In our study TLC is significantly higher in the patient group as compared to the control group. These results are supported by various prospective and retrospective studies that have showed a positive correlation between the leukocyte counts and risk of IHD. The mechanisms linking leukocyte counts to cardiovascular risk are not well understood. However, increased number and activation of circulating leukocytes could contribute to atherogenesis by increased adhesion to and damage of the endothelium, and by disturbance of micro-vascular flow. According to a study in age, gender and risk matched subjects, mean TLC was higher in patients of IHD than in control subjects. A study by Jia et al reported a strong association of TLC especially neutrophils in patients with angiographically established atherosclerosis. Inflammation not only plays an important role in initiation and progression of atherosclerosis but also cause acute rupture of plaques with superimposed thrombus formation. In a one-year follow-up study of patients with UA, patients who had the highest leukocyte counts were roughly eight times more likely to have a major cardiovascular event than patients with the lowest counts. So, leukocytes and differential counts may predict future and recurrent events.

In our study, differential cell counts shows that neutrophils are significantly higher and lymphocyte counts re significantly lower in the test group as compared to the control group. For neutrophils, our findings are consistent with the previous data that neutrophil counts have an independent association with coronary atherosclerosis. According to a meta-analysis by Wheeler et al neutrophil counts are much stronger predictors of IHD than other components. Similarly, a retrospective study of patients with IHD showed that five year survival was significantly better in the patient group as compared to the control group supporting the previous data. Dijk et al showed that in patients with manifest arterial disease, increasing haemoglobin levels were associated with reduced severity of atherosclerosis. Another study by Sarnak et al showed that decreased haemoglobin level is an independent risk factor for IHD in general population. In a study by Zeidman et al anaemia was significantly correlate with advanced IHD, congestive heart failure, arrhythmias and higher mortality rates. Lower haemoglobin is also associated with adverse cardiovascular outcome in patients with ischemic symptoms as it is indicated in a study by Arant et al. ESR is a measure of the tendency of red blood cells to aggregate and it is a time dependent analysis of infection and inflammation. Accelerated erythrocyte aggregation is caused by large, asymmetrical plasma proteins inhibiting the negative electrical forces that normally keep the erythrocytes apart. Atherosclerosis is an inflammatory disease and may result in higher levels of ESR. According to a study by Natale et al. ESR was progressively higher in the presence of angiographically documented major narrowing of 0, 1, 2, 3-vessel disease in patients indicating that ESR is an independent correlate of coronary atherosclerosis. Significantly higher ESR level in the patient group as compared to the control group in the present study was consistent with the previous findings. In a study by Erikson et al. ESR was emerged as a strong long and
short term predictor of coronary heart disease mortality and prognostic information among healthy men, men with a positive exercise ECG test and men with angina pectoris. However, this should be studied further and measurement of this variable in some large studies might substantially further strengthen the present overall results and their interpretation.

CONCLUSION

Although, our data for these measured variables is consistent with the previous studies but still, there is a need for sufficiently powered studies to help assess the separate and combined impact of inflammatory cells on IHD in the native population. This is a low cost, good reproducibility test routinely measured by clinicians and may be helpful to predict the future risk of ischemic events in a high risk population and also, the risk of secondary events in patients with previous ischemic diseases. According to the results of our study the prevalence and prognostic importance of haemoglobin and ESR levels in this population also necessitate further confirmation and investigation.

REFERENCES


Address for Correspondence:
Dr. Farhana Shahzad, House No. 97/8, Nisar Colony, Shami Road, Lahore Cantt, Pakistan. Cell: +92-321-4240200, 6667488
Email: shahzadtaawab@hotmail.com