INTRODUCTION

Megakaryocyte a well known bone marrow giant cell, produces platelets, playing a key role in hemostasis. The main function of platelet is the formation of mechanical plug during the normal hemostatic response to vascular injury. The platelets before reaching the general circulation appear to be sequestrated in the spleen for 24-48 hours. About 10-20% of the total number of platelet count in the peripheral blood is maintained at a fairly constant level which ranges between 150—400x10^9/L in normal subjects. When circulating they are membrane bound smooth discs expressing a number of glycoprotein receptors of integrin family on their surface. Platelets contain two specific types of granules. Alpha granules express the adhesion molecule P-selectin on their membranes and contain fibrinogen, fibronectin, factor V, factor V, platelets factor EV, platelets derived growth factor and transforming growth factor-B. The other granules are dense bodies which contain adenine nucleotides, adenosine triphosphate, ionized calcium, histamine, serotonin and epinephrine.

After vascular injury, platelets encounter extracellular matrix. These include collagen, proteoglycans, fibronectin and other adhesive glycoproteins. On contact with these extracellular matrices, platelets undergo three general reactions: adhesion, secretion and aggregation.

Liver is very important viscera in the body. Its functions are numerous and multi-faceted. It plays very essential and central role in hemostasis.

Liver disorders are common health problems in Pakistan. Increased platelets associated IgG is found in all forms of chronic liver diseases suggesting possible role of an autoimmune mechanism for thrombocytopenia in liver diseases.

Normal spleen contains a sizable fraction of the total platelet mass in the form of an exchangeable pool. This sequestration may be further increased in cirrhotic patient with enlarged spleen leading to thrombocytopenia.

Multiple factors can contribute to the development of thrombocytopenia including splenic platelets sequestration, bone marrow suppression by chronic hepatitis, antiviral treatment with interferon and reduction in level or activity of thrombopoietin. Patients with advanced cirrhosis have a complex hemostatic disturbances and
thrombocytopenia is a common feature of this derangement.\textsuperscript{12-15}

Bleeding Time is a procedure in which a standard incision is made on the volar surface of forearm and the time the incision bleed is measured. Cessation of bleeding indicates the formation of hemostatic plugs which are in turn dependent on an adequate number of platelets to adhere to the subendothelium to form aggregates. A prolonged bleeding time may be due to: Thrombocytopenia, disorders of platelets function, von Willebrand disease, vascular abnormalities and occasionally severe deficiency of Factor V and XI.\textsuperscript{16}

Cirrhosis is among the top 10 causes of the death in Western World. The chief worldwide contributors are alcohol abuse and viral hepatitis. Other causes include biliary diseases and iron overload. Cirrhosis is defined by three characteristics:

1. Bridging fibrous septae in the form of delicate band or broad scars linking portal tracts with terminal hepatic veins
2. Parenchymal nodules containing proliferating hepatocytes encircled by fibrosis with diameter varying from very small (<3mm micronodules) to loose (several cm macronodules)
3. Distruption of the architecture of entire liver\textsuperscript{16}

The central pathogenetic process in cirrhosis is progressive fibrosis and reorganization of the vascular micro architecture of the liver.\textsuperscript{17}

Long standing congestion may cause congestive splenomegaly. The degree of enlargement varies widely up to 1000 gm. Massive splenomegaly may secondarily induce a variety of hematological abnormalities attributed to hypersplenism.\textsuperscript{16}

Objective of this study was to correlate thrombocytopenia with the bleeding tendency in known cirrhotic patients.

MATERIAL AND METHODS

This retrospective study was done in Department of Pathology Gomal Medical College Dera Ismail Khan from January 2006 to December 2008. It encompassed the correlation of platelets count with the bleeding time in 100 patients of hepatic cirrhosis. Fifty normal controls were also included in the study. The patients with a history of recent blood/platelets transfusion were excluded from the study. Blood samples were collected in EDTA tubes for platelet count. Platelet count was analyzed on automated hematologiy analyzer (Nihon). The count was also verified by making a thin film stained with Giemsa and examined under the microscope.

Bleeding time was performed by standard Ivy's Method.

The Data was analyzed by Student ‘t’ test.

RESULTS

In 100 cirrhotic patients the commonest affected age was 40-80 years. The most common physical signs were splenomegaly, and ascites. Among these patients 92 had thrombocytopenia (p<0.01) and 44 had prolonged bleeding time (p<0.001). (Table-1 & 2)

In 8 patients (8%) the platelets count was normal (150-350x10\(^9\)/l), while in 92 patients (92%), it was decreased (<150x10\(^9\)/l).

Out of 92 patients thrombocytopenia was mild (100-149 x10\(^9\)/l) in 69 cases (75%) while moderate (50-100 x10\(^9\)/l) in 21 cases (22.8%) and severe (<50 x10\(^9\)/l) in 2 cases (2.2%).

<table>
<thead>
<tr>
<th>Patient</th>
<th>Normal Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean + SD</td>
<td>Mean + SD</td>
</tr>
<tr>
<td>116 ±24.6 x10(^9)/l</td>
<td>266 ± 22.8</td>
</tr>
</tbody>
</table>

\(<0.01\)

| Table-1: Comparison of platelet count of cirrhotic patients (n= 92) having thrombocytopenia with normal control (n= 50). |

<table>
<thead>
<tr>
<th>Patient (minutes) Mean ± SD</th>
<th>Normal control (minutes) Mean ± SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.7 ± 3.0</td>
<td>3.5 ± 0.9</td>
<td>&lt;0.001</td>
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DISCUSSION

Thrombocytopenia is a common complication in patients with chronic liver disease. In our study 92% of the patients were thrombocytopenic, while one of the previous workers have reported 76%\textsuperscript{13} and others have also reported thrombocytopenia in cirrhotic patients.\textsuperscript{1-3,18-21} Thrombocytopenia in this study was mild in 75% of the cases; Moderate in 21% and severe in 2.2% of the cases. Moderate thrombocytopenia is reported to be 13% by one previous study\textsuperscript{13} and also by others study.\textsuperscript{18}

In the present study the platelets count in patients with cirrhosis was significantly decreased as compared to control subject which is an agreement with Ratanoff and Sherlock.\textsuperscript{21,22}
Weiss also described thrombocytopenia as common cause of bleeding in patients with cirrhosis. In our study bleeding time was prolonged in 44% of patients while Hellen and Nelson studied 20 patients with cirrhosis of which had low platelets count but non had prolonged Duke bleeding time.

Our findings are not correlating with finding of Hellen and Nelson, the reason of difference might be the technique and number of patients.

CONCLUSION

Thrombocytopenia and prolonged bleeding time are significant and common findings in cirrhosis of liver.

It is suggested that platelet count and bleeding time may be performed on all cirrhotic patients undergoing invasive procedures.

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