A Prospective Study of Variation in Haematological Parameters in Chronic Liver Disease

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Abstract
Introduction: The liver is the largest organ in the body and one of the most complex functioning organs with a wide array of functions. It plays a major role in carbohydrate, protein, lipid metabolism; inactivation of various toxins, metabolism of drugs, hormones, synthesis of plasma proteins & maintenance of immunity (Kupffer cells).
Materials and Methods: This descriptive comparative study was undertaken in tertiary care centre in Chennai. A total of 100 chronic liver disease patients were studied from January 2017 to December 2019 and was compared with 100 normal control. In all the cases age, gender and relevant clinical history were obtained. Sample size was taken based on the convenience of the study. Patient’s demographic data and history were recorded, complete physical examination was conducted, and haematological parameters were measured for all subjects in this study.
Results: A total of 100 chronic liver disease patients were studied who had abnormalities in liver function test with elevated total bilirubin, direct bilirubin, serum globulin, aspartate amino transferase (AST), alanine amino transferase (ALP). Total protein and albumin were decreased in these patients. The patient’s age was ranging from 18-71 yrs. with predominance of male. There was decrease in complete blood parameters (Hb%, Mean RBC count, mean MCH, MCHC and platelets), except MCV and MCH was increased. The deranged liver function test showed total protein and albumin levels lower in these and renal function parameters especially serum urea and creatinine not significantly altered.
Conclusion: Chronic liver disease patients are frequently associated with haematological and biochemical abnormalities showing anaemia, leucopenia and thrombocytopenia along with derangement in liver enzymes and decrease in renal function test. Prolonged prothrombin time and abnormal peripheral smear are also seen in these patients. It is associated with increased morbidity and mortality. In our study, haematological parameters (Hb, RBC, PCV MCHC, platelet, PT) all were decreased except MCV and MCH which were increased. However, MCH was statistically not increased. MCV was reduced significantly and biochemical parameters like deranged liver function test were all increased except total protein, albumin and renal function test. S. Urea and Creatinine were reduced. Thus, the complete blood count picture had shown the picture of anaemia, leucopenia and thrombocytopenia. Highly significant p values <0.001 were seen.
Key Words: ASP,ALP, MCV, MCH, RBC

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I. Introduction
The liver is the largest organ in the body and one of the most complex functioning organs with a wide array of functions. It plays a major role in carbohydrate, protein, lipid metabolism; inactivation of various toxins, metabolism of drugs, hormones, synthesis of plasma proteins & maintenance of immunity (Kupffer cells).¹ Right from being a primary site of haematopoiesis in fetal life to maintenance of hematological parameters in postnatal life; the liver has an extremely important role in maintenance of blood homeostasis.² It acts as a storage depot for Iron, Folic acid & Vitamin B12, secretes clotting factors and inhibitors. Hence it’s not surprising to see a wide range of hematological abnormalities in liver diseases.² In chronic liver disease the presence of jaundice, liver cell failure, portal hypertension and hypersplenism, reduced red cell half-life all influence peripheral blood picture.³ Both Liver cell failure & cholestasis can derange the coagulation system. Dietary deficiencies, bleeding, alcoholism and abnormalities in hepatic synthesis of proteins used for blood formation or coagulation add to the problem liver disease. This study was undertaken to describe the coagulation abnormalities in chronic liver disease so that measures could be taken to correct them and reduce morbidity.³
II. Materials And Methods

This descriptive comparative study was undertaken in tertiary care centre in Chennai. A total of 100 chronic liver disease patients were studied from January 2017 to December 2019 and was compared with 100 normal control. In all the cases age, gender and relevant clinical history were obtained. Sample size was taken based on the convenience of the study.

Patient’s demographic data and history were recorded, complete physical examination was conducted, and haematological parameters were measured for all subjects in this study.

Complete Blood Count (By Automated Counter)
1. Haemoglobin in gm%.
2. RBC count in million/cmm.
3. Total WBC count in cells/cmm.
4. MCV in fl.
5. MCHC in pg.
6. Platelet count in lakhs/cmm.
7. Microscopic peripheral smear study.
8. Prothrombin time in seconds.
9. Liver function study- Total bilirubin, Direct and Indirect fraction, SGOT, SGPT, Total protein, Albumin, Alkaline phosphatase.

Inclusion Criteria
1. Chronic liver disease patients with abnormalities in liver function test with elevated total bilirubin, direct bilirubin, serum globulin, aspartate amino transferase (AST), alanine amino transferase (ALP).
2. Age group 18-75 yrs.

Exclusion Criteria
1. Haematological malignancies
2. Infants and children
3. Patients with pre-existing anaemia
4. Patients suffering from end stage medical disease like COPD, coronary artery disease, ca.

Haematological Analysis
All EDTA-anticoagulated blood samples were obtained to perform complete haemogram analysis using Automated Haematology analyser (Sysmex XN 1000) and liver and renal function test by using Architect Abbott c1 4100.

The normal range of complete hemogram parameters are Hb- 10-12 gm/dl, RBC- 4-5.5 million/cmm, PCV- 35-45%, MCV- 76-100 fl, MCH- 27-32 pg, MCHC- 32-35%, Platelet- 150-450 lakhs/cmm, Prothrombin time- 12-14/second, ESR- 0-10 mm/hr.

Liver Function Test
Total bilirubin- <1.2 mg/dl, Bilirubin direct- <0.4 mg/dl, Total protein- 6.2-8 gm/dl, Serum albumin- 3.4-5.5 g/dl, Serum. Globulin- 2.3-3.5 g/dl, AST- 5-46 U/L, ALP- 5-49 U/L.

Renal Function Test
Serum Urea- 15-45 mg/dl, Serum Creatinine- 0.7-1.4 mg/dl.

Statistical Analysis
All the haematological and biochemical parameters were expressed by mean and Interquartile range (IQR). A p-value was calculated by Mann Whitney test. Further test like standard deviation and median was calculated as the data was not correlating with normality. A p-value of <0.001 was considered significant.

III. Results
A total of 100 chronic liver disease patients were studied who had abnormalities in liver function test with elevated total bilirubin, direct bilirubin, serum globulin, aspartate amino transferase (AST), alanine amino transferase (ALP). Total protein and albumin were decreased in these patients.

The patient’s age was ranging from 18-71 yrs. with predominance of male. There was decrease in complete blood parameters (Hb%, Mean RBC count, mean MCH, MCHC and platelets), except MCV and MCH was increased. The deranged liver function test showed total protein and albumin levels lower in these and renal function parameters especially serum urea and creatinine not significantly altered.
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Table 1: Haematological Parameters in Chronic Liver Disease Patients

<table>
<thead>
<tr>
<th>Group</th>
<th>SD</th>
<th>Mean</th>
<th>Mann Whitney Test p value</th>
<th>25th Percentile</th>
<th>Median</th>
<th>75th Percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>9.71</td>
<td>2.92</td>
<td>&lt;0.001</td>
<td>8.23</td>
<td>9.60</td>
<td>11.38</td>
</tr>
<tr>
<td>RBC</td>
<td>2.95</td>
<td>0.69</td>
<td>&lt;0.001</td>
<td>2.44</td>
<td>2.90</td>
<td>3.54</td>
</tr>
<tr>
<td>PCV</td>
<td>27.52</td>
<td>10.37</td>
<td>&lt;0.001</td>
<td>22.43</td>
<td>26.55</td>
<td>31.43</td>
</tr>
<tr>
<td>MCV</td>
<td>89.62</td>
<td>11.55</td>
<td>0.141</td>
<td>84.75</td>
<td>90.85</td>
<td>95.73</td>
</tr>
<tr>
<td>MCH</td>
<td>31.56</td>
<td>5.40</td>
<td>&lt;0.001</td>
<td>31.05</td>
<td>31.55</td>
<td>34.55</td>
</tr>
<tr>
<td>MCHC</td>
<td>30.68</td>
<td>4.77</td>
<td>&lt;0.001</td>
<td>33.20</td>
<td>33.20</td>
<td>33.75</td>
</tr>
<tr>
<td>Platelet</td>
<td>132.22</td>
<td>90.98</td>
<td>&lt;0.001</td>
<td>82.00</td>
<td>116.00</td>
<td>151.50</td>
</tr>
<tr>
<td>PT</td>
<td>28.46</td>
<td>32.47</td>
<td>0.001</td>
<td>18.70</td>
<td>21.85</td>
<td>28.15</td>
</tr>
<tr>
<td>S.Urea</td>
<td>35.12</td>
<td>26.51</td>
<td>0.786</td>
<td>17.00</td>
<td>28.00</td>
<td>47.00</td>
</tr>
<tr>
<td>S.Creatinine</td>
<td>1.30</td>
<td>0.99</td>
<td>0.600</td>
<td>0.80</td>
<td>0.90</td>
<td>1.53</td>
</tr>
<tr>
<td>ESR</td>
<td>44.88</td>
<td>34.09</td>
<td>&lt;0.001</td>
<td>13.50</td>
<td>39.00</td>
<td>76.50</td>
</tr>
</tbody>
</table>

Figure 1: Gender Distribution in Chronic Liver Disease Patients

Figure 2: Age Distribution in Chronic Liver Disease Patients
IV. Discussion

Chronic Liver Disease (CLD) refers to disease of the liver, which last for more than six months and involves progressive destruction and regeneration of liver parenchyma leading to fibrosis and cirrhosis. The most common cause of CLD is alcoholism. Alcohol abuse is a one of the most common problem encountered in India, especially among men and among young adults. Therefore, patients who have varying degrees of compensated liver function and clinicians need to differentiate between those who have stable, compensated cirrhosis and those who have decompensated cirrhosis.

Various studies have shown that haematological and biochemical parameters are altered in these patients. In this study 7 patients were female, and 93 patients were male which was comparable to study done by Suresh et al in which 85% were males and 15% were females. Mean age of study population in this study was 49.3 with 40% patients belonging to 41-50 years of age. 27% patients were more than 51 years of age and 16% less than 40 years of age. In this study 72% patients were anaemic. Mean Hb in males were lower than females. A study by Rosario Gonzalez-Casas et al showed that anaemia due to various aetiologies occur in 75% cases of CLD patients which was comparable in this study. Most of cases in this study group were alcoholics and all were men and so low mean Hb were observed in men than in females and alcoholics are at more risk of anaemia by various mechanisms and comparable results were seen in study done by Suresh et al also. Most common anaemia observed in this study was normocytic normochromic anaemia (25.8%), 22.5% had macrocytic anaemia and 16.1% had microcytic hypochromic anaemia and 12.9% dimorphic blood picture was observed. This was comparable to a study done by Suresh et al in which most common anaemia observed was normocytic normochromic (40.9%), macrocytic anaemia in 28.8%, microcytic anaemia in 22.7% and 4% in dimorphic anaemia.

In this low Hb values goes in parallel with low PCV and RBC value in most of the cases and mean PCV value is 27.5%, mean RBC count was 2.9 million/cmm which was comparable to study done by Suresh et al. Thrombocytopenia was seen in 59.8% of cases and abnormal prothrombin time was seen in 95.8% cases and was comparable with study done by Rajkumar et al. Mean corpuscular volume(MCV) and Mean corpuscular haemoglobin (MCH) were the parameters which were increased in this study which was comparable with study done by Esmeralda et al and Maruyama et al where MCV was significantly increased. Deranged liver function test was seen in which all parameters were elevated except total protein and albumin was decreased in our study which was comparable to study done by Elanchezhian et al. Renal function test were not altered.

V. Conclusion

Chronic liver disease patients are frequently associated with haematological and biochemical abnormalities showing anaemia, leucopenia and thrombocytopenia along with derangement in liver enzymes and decrease in renal function test. Prolonged prothrombin time and abnormal peripheral smear are also seen in these patients. It is associated with increased morbidity and mortality. In our study, haematological parameters (Hb, RBC, PCV MCHC, platelet, PT) all were decreased except MCV and MCH which were increased. However, MCH was statistically not increased. MCV was reduced significantly and biochemical parameters like deranged liver function test were all increased except total protein, albumin and renal function test. S. Urea and
Creatinine were reduced. Thus, the complete blood count picture had shown the picture of anaemia, leucopenia and thrombocytopenia. Highly significant p values <0.001 were seen.

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