Original Research Article

Studies on the hepatic and renal status of patients with sickle cell disease from western zone of Maharashtra, India

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ABSTRACT

Background: Sickle cell disease (SCD) is the most common inherited monogenic genetic disorder in Indian tribal and non-tribal population. This condition is caused by mutations in the hemoglobin gene and inherited in an autosomal recessive pattern. Pathogenesis in SCD varies widely from patient to patient. Most of the infections affect SCD pathogenesis, so early diagnosis of the same is important.

Methods: The present study was designed to evaluate the biochemical parameters to assess the hepatic and renal status in SCD subjects from west zone of Maharashtra, India. Patients with sickle cell disease (n=50) from primary health centres of Palghar were included in this study and age and sex matched healthy persons (n=50) were controls. Informed written consent was obtained from all the study subjects.

Results: Our findings showed that Aspartate transaminase (AST), Alanine transaminase (ALT), bilirubin and creatinine increased significantly above normal level in SCD subjects. Albumin and urea levels in SCD were found to have decreased in the SCD subjects. There is a slight increase in uric acid and creatinine levels; this indicates an adverse effect on hepatic function and moderate effect on renal function in sickle cell anemia patients. Most common events of SCD pathogenesis, can be categorized into hemolytic events and vaso-occlusive crisis-based events. Adverse effect on hepatic function can lead to further hemolytic events.

Conclusions: Although specific biomarkers related to these different events needs to understand for assessment of pathogenesis, the ones we have studied can be useful to assess the status of hepatic and renal function to follow the effectiveness of therapeutic interventions.

Keywords: Hemolytic events, Liver function, Pathogenesis, Renal function, Sickle cell disease

INTRODUCTION

Sickle cell disease (SCD) is a genetic disorder of great epidemiological and clinical importance. Its hallmark is the inheritance of the S beta-globin gene (gene βs). This gene causes the S variant of hemoglobin to be produced in red blood cells.1 Vaso-occlusive phenomena and chronic hemolysis are the main causes of the clinical manifestations of SCD and, while the primary abnormalities are restricted to erythrocytes, the result is a systemic disease that can affect any organ.2 Clinical severity varies widely from sickle cell trait (heterozygous) to sickle cell anemia (homozygous). SCD patients suffer with varied clinical and physical problems including urinary tract infection, gross hematuria, exertional heat illness and idiopathic sudden death.3,4 In Maharashtra, sickle gene is widespread in all the eastern districts, also known as the Vidarbha region, in the
Satpura ranges in the north and in some parts of Marathawada. The prevalence of sickle cell carriers in different tribes varies from 0 to 35%. The tribal groups with a high prevalence of HbS (20-35 %) include the Bhils, Madias, Pawaras, Pardhans and Otkars. It has also been reported that Gadchiroli, Chandrapur, Nagpur, Bhandara, Yoetmal and Nandurbar districts have more than 5000 cases of sickle cell anaemia. However relatively few studies describe the prevalence and demographic patterns of SCD in western zone of Maharashtra. Progression of SCD pathogenesis starts once a homozygous SS kids complete their first six months after birth. Most of the paediatric population suffers with hemolytic events and most of the blood transfusions are reported in early age, below 5 and remaining in the range of 5 to 15 years of age, where as arthropathies develops at a later age and in adult population. Since most of the infections aggravate SCD pathogenesis, early diagnosis and vaccine regimen is strictly advised. Our study intended to find out renal function and liver function status in SCD population in tribal western Maharashtra region.

METHODS

This study comprises of 50 SCD patients and 50 healthy, age and sex matched controls. All the patients included were in the steady state of the disease and persons with bone diseases, diabetes, malignancies, pregnancy, alcoholics, renal failure, myocardial infarction and who were on medication were excluded from the study. The ethical guideline of 1975 declaration of Helsinki was followed and informed consent was taken from adult population. Intravenous blood was collected and centrifuged at 3000 rpm for separation of serum to perform biochemical parameters. Urea (Berthelot method), Creatinine (Alkaline picrate method), Uric acid (uricase method), Aspartate transaminase, Alanine transaminase (Kings method), Alkaline phosphatise, Lactate dehydrogenase, Albumin (Bromocresol green method) and Bilirubin (Jendrassik and Grof's method) were carried out by using commercially available kits.5,12

Statistical analysis

All values are reported as Mean ± SE. The unpaired two tailed Student's t-test was used to assess the significance of the difference in the values in the sickle cell disease subjects and in healthy controls.

RESULTS

Table 1 presents the results of serum biochemical parameters related to liver function. There is extremely significant increase in levels of total, direct and indirect bilirubin and significant increase in the activities of transaminases in SCD subjects as compared to controls. A highly significant decrease in levels of albumin was observed in the SCD cases as compared to the controls.

No significant difference was observed in serum LDH and ALP levels between the cases and controls.

Table 1: Biochemical liver function parameters in SCD and controls.

<table>
<thead>
<tr>
<th>Parameters(Unit)</th>
<th>Control</th>
<th>SCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALP (IU/L)</td>
<td>69.53±3.44</td>
<td>63.86±2.94NS</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>23.37±1.30</td>
<td>47.24±1.28*</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>20.79±1.17</td>
<td>46.05±1.34*</td>
</tr>
<tr>
<td>LDH (U/L)</td>
<td>302.07±5.94</td>
<td>295.77±6.79NS</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>3.52±0.058</td>
<td>3.21±0.072**</td>
</tr>
<tr>
<td><strong>Bilirubin (mg/dl)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>0.56±0.02</td>
<td>1.6±0.02***</td>
</tr>
<tr>
<td>Direct</td>
<td>0.06±0.0030</td>
<td>0.088±0.0054***</td>
</tr>
<tr>
<td>Indirect</td>
<td>0.48±0.018</td>
<td>1.51±0.031***</td>
</tr>
</tbody>
</table>

Values are expressed as Mean ±SE and significance is at *P <0.05, **P < 0.005, *** P < 0.001

Table 2 represents the comparison of the different renal function tests conducted in the SCD and controls. Kidney function tests were altered in the SCD cases but it was found to be non significant when compared to that of controls.

Table 2: Renal function parameters in SCD and controls.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>SCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea (mg/dl)</td>
<td>26.58±1.04</td>
<td>24.71±0.87NS</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.26±0.13</td>
<td>1.64±0.23NS</td>
</tr>
<tr>
<td>Uric acid (mg/dl)</td>
<td>4.27±0.11</td>
<td>4.56±0.15NS</td>
</tr>
</tbody>
</table>

Values are expressed as Mean ±SE and significance NS

DISCUSSION

India has the largest concentration of tribal populations globally. They are believed to be the early settlers in the country and are considered to be the original inhabitants. Present study included 50 SCD patients and 50 age and sex matched controls. None of the patients had a history of drug or alcohol abuse. Age wise these patients were further subdivided into 3 groups (Figure 1 and 2) in which number of patients in group I (0-15 yrs) was more as compare to other two groups (group II, 16-30 yrs and group III, 31-50 yrs).

Results show that 78% subjects had increased alanine transaminase (ALT) activities in comparison to control group. Majority of this patients are heterozygous or SCD trait in nature and they were fall in group I and II. The activity of aspartate transaminase (AST) in 74% subjects was found above normal level and 26% subjects were found within reference range. Majority of patients were from group I and II, heterozygous and asymptomatic. Possible reason for elevated transaminases (ALT, AST) levels may be acute intra hepatic cholestasis or due to massive accumulation of sickle cells in hepatic sinusoids and stasis causing serious damage to hepatocytes and Kupffer cells. SCD patients may have increased risk of
cholelithiasis which could also be a possible reason for hepatic dysfunction in these patients. The liver frequently enlarges and become sensitive, which cause frequent rise in liver enzymes level in blood.\textsuperscript{11} Serum bilirubin was above control range in 86\% subjects while only 14\% subjects had their serum bilirubin within normal range. Extremely significant increase in bilirubin may be due to combination of on-going haemolysis, intra hepatic cholestasis and renal impairment encountered in sickle cell hepatopathy in comparison with remaining disease groups as reported by Stephan \textit{et al.}\textsuperscript{14} Another study by Gurkan \textit{et al}, also reported hyperbilirubinemia in 13\% of patients and elevated trasaminins in 15\% of patients.\textsuperscript{15}

renal condition.\textsuperscript{17} We also found elevated levels of uric acid and creatinine in SCD subjects than control. Creatinine is the end product of creatine metabolism. Creatine found in muscle, in free form as well as in the form of creatinine phosphate.\textsuperscript{18} Increase in serum creatinine is seen in any renal impairment when its clearance is significantly reduced. This may be due to intrinsic renal lesion, decreased perfusion of kidney or by obstruction of the lower urinary tract. Since majority of the subjects are heterozygous and mostly asymtomatic the altered LFT and RFT have to take in to consideration while treating these patients to prevent further damage to these vital organs.

CONCLUSION

In our study we found an adverse effect on hepatic function and moderate effect on renal function in SCD patients from Western Indian population. Most common events of SCD pathogenesis can be categorized into hemolytic events and vaso-occlusive crisis. Serum enzymes (AST, ALT) and serum bilirubin were significantly increased as compared with control which indicates likelihood of continuous ongoing hemolysis in sickle cell population. Renal function tests are not altered significantly which suggest that renal metabolism still healthy, but this will help to understand future clinical manifestation of patients. The finding of our study suggests that the biochemical profile can play an important role in assessing the sickle cell patient’s physiopathology and can be used for effective management of the disease.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES


Figure 1: Age wise distribution of SCD patients.

Figure 2: Age wise distribution of control.

Thus, the hepatic dysfunction in sickle cell disease patients could be of multi-factorial origin. We can consider liver function test as an important parameter to understand severity and complications arising due to sickling. There was significantly decrease in levels of albumin, may be due to proteinuria or decrease in albumin synthesis because of liver dysfunction. The mild but non significant decrease in urea can also be attributed to compromised liver function.\textsuperscript{16} Decreased levels of urea are generally observed in pre renal, renal and post

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