Prevalence of splenomegaly in Sickle cell anemia patients in relation to Hemoglobin F

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ABSTRACT

Background: The sickle cell disease (SCD) is a very common single gene disorder; 50% of world population affected by SCD resides in India. The average frequency of SCD gene ranges between 22-44%. High prevalence of sickle gene has been demonstrated in various tribal communities of Gujarat, India. Hematological profile of SCD is extremely variable.

Aim: To determine fetal Hb value, other major Hb fractions in sickle cell disease patients and assess the significance of high fetal hemoglobin level on persistence of splenomegaly.

Methods: Patients with sickle cell disease showing positive sickling test attending V.S.S Medical College Hospital, Burla, during Nov’2003 - 2005, total number of cases 95, were selected for study. Detail history was taken in a proforma and Hemoglobin electrophoresis was done for the detection of most common clinical important hemoglobin variants. Foetal hemoglobin was estimated by Betke’s method.

Results: Splenomegaly was found in 50 cases (52.63%). In cases with splenomegaly the mean level of fetal hemoglobin in males was 23.1% and in females was 21.9% while in cases without splenomegaly the mean level was 21.5% in males and 20.6% in females. The mean Hb F level was between 1 – 20% in 35 cases (36.84%) out of which 26 were males and 9 were females. 60 cases (63.16%) had Hb F level greater than 20% out of which 46 were males and 14 were females.

Conclusion: Splenomegaly was found in more than 50% of cases of sickle cell disease signifying the persistence of it even in adult age. High fetal hemoglobin level found in these cases suggests Hb F as one of the important etiological cause of persistence of splenomegaly.

Keywords: sickle cell disease, splenomegaly, hemoglobin F

INTRODUCTION

The sickle cell disease (SCD) is a very common single gene disorder; 50% of world population affected by SCD resides in India. The average frequency of SCD gene ranges between 22-44%. High prevalence of sickle gene has been demonstrated in various tribal communities of Gujarat, India.

The sickle haemoglobinopathies are heterozygous (sickle cell trait), homozygous (SS disease) states for Haemoglobin S and conditions in which HbS is combined with other hemoglobin structural variants or thalassaemia. The amount of haemoglobin varies considerably in the various forms of sickle cell disorders. In sickle cell anaemia, Hbs ranges from 75-95% and Hb F ranges from 1-20%, and in sickle cell thalassaemia the amount Hbs is above 60% and HbF ranges from 2-30%. Similarly in sickle cell trait HbS 38-45% and HbF is normal. Homozygous sickle cell disease in parts of Saudi Arabia and India is associated with elevated HbF and is typically a very mild disorder.1

Splenomegaly usually is evident at six month of age and remains enlarged throughout early childhood. Repeated infraction eventually leads to atrophy and autosplenectomy by 8 yrs of age and the spleen is no longer palpable and its function impaired.2

In the present study, Hb F and Hb S concentration has been estimated in different types of sickle cell disorders and attempt has been made to find out the pattern of quantitative distribution of HbS and correlate the HbF concentration to the severity of clinical symptoms.

MATERIALS AND METHODS

Patients with sickle cell disorders attending V.S.S Medical College Hospital, Burla, during the period November’2003 -2005, were included for study. The cases showing positive sickling test were selected for the study. Their parents and other
siblings were also studied when available. Detailed history, clinical findings along with laboratory investigations findings were recorded in the proforma.

Sickling test was performed with 2% sodium metabisulphite. Hemoglobin electrophoresis at Alkaline pH was done using cellulose acetate membrane. Foetal hemoglobin was estimated by Betke’s method (Dacie & Lewis, 2001).

Test – 0.25 ml of haemolysate (10 gm%) was added to 4.75 ml of Drabkin’s solution. 0.2 ml of 1.2 NaOH is added to 5.0 ml of resultant HiCN solution and the mixture was gently agitated for 2 minutes. 2 ml of saturated Ammonium Sulphate was added and after shaking, the mixture is allowed to stand for at least 5 minutes. It was then filtered through a double layer of Whatman no.1 filter paper.

Standard – As a standard, 0.4 ml of HiCN solution, 13.9 ml of water was mixed together. The absorbance of both the test and standard are read using 420 nm filters against water blank. The percentage of HbF was calculated as follows:

\[
\%\text{HbF} = \frac{\text{Test (Abs)} \times 100}{\text{Std. (Abs)} \times 20}
\]

RESULTS

The value of hemoglobin above 13 gm% in case of male and above 11.5 gm% in case of female was considered as normal for this study. Out of 95 persons with sickle cell disease hemoglobin level is between 6 -10 gm% in 59 cases (62.10%), below 6 gm% in 25 cases (26.33%) and 11 cases (11.57%) had Hb more than 10 gm%.

The highest incidence of Sickle cell disease 45.26 was seen in 21 – 31 yrs of age group, followed by 26.31% in 11 – 20 yrs and least, 1.05% was found in 0 – 10yrs and 61 – 70 yrs decade of life.

Out of 95 cases splenomegaly was found in 50 cases (52.63%) of which 42 cases (44.21%) were males while only 8 cases (8.42%) were females. In cases with splenomegaly the mean level of fetal haemoglobin in males was 23.1% and in females it was 21.9%. In cases without splenomegaly the mean level was 21.5% in males and 20.6% in females.

In patients with crisis the mean fetal Hb level in males was 22.01% and in females was 22.47%, where as in patients without crisis the mean fetal Hb level was 23.82% in males and 23.21% in females. The mean Hb S level in patients with crisis was 74.28% in males & 75.5% in females, whereas in patients without crisis the mean Hb S level was 70.35% in males & 73.88% in females.

In patients with crisis the total hemoglobin level in males was 7.28 gm% & in females was 6.53 gm%, whereas in patients without crisis the total haemoglobin level was 7.92 gm% in males & 7.05 gm% in females. The mean Hb S level is found to be less than 75% in 53 cases (55.78%) out of which 41 were males & 12 were females. The mean Hb S level was between 75 – 95% in 42 cases (44.22%) out of which 31 were males & 11 were females.

The mean Hb F level was between 1 – 20% in 35 cases (36.84%) out of which 26 were males & 9 were females 60 cases (63.16%) had Hb F level greater than 20% out of which 46 were males & 14 were females. The mean Hb A2 level is found to be less than 2% in 27 cases (28.42%), between 2 – 5% in 66 cases (69.47%) and only 2 cases (2.11%) had HbA2 greater than 5%. The common symptomology observed is tabulated in Table 2.

<table>
<thead>
<tr>
<th>Signs &amp; Symptoms associated with Disease</th>
<th>No. of cases presented</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>42</td>
</tr>
<tr>
<td>Jaundice</td>
<td>18</td>
</tr>
<tr>
<td>Pain including limb, joint, chest, abdominal &amp; Body</td>
<td>42</td>
</tr>
<tr>
<td>Generalized weakness</td>
<td>12</td>
</tr>
<tr>
<td>Others</td>
<td>37</td>
</tr>
</tbody>
</table>
**DISCUSSION**

In present study 50 cases (52.63%) had splenomegaly and the mean HbF in cases with splenomegaly was 23.1% in males and 21.9% in females. Patients who had no splenic enlargement had a mean HbF of 21.5% in males and 20.6% in females. Thus our result relates with the findings of another study with higher mean HbF in patients with splenomegaly.\(^5\)

Our study included 95 patients of age group 2 to 65 yrs with 72 males and 23 females. The mean Hb level in patients with crisis was 7.28gm% in males and 6.5% in females. The mean Hb level in patients without crisis was slightly higher (Males 7.92gm% and Females 7.05gm %) and it is comparable with the study by Shrikhande.\(^6\)

Sanjay et al in his study on 155 sickling positive patients of tribal of Rajasthan, found the homozygous state SS in 14 patients. M:F ratio was 3.6.\(^7\) The common presentations were anemia, pain, recurrent infection and splenomegaly.

Sanjeev in 2012 in South Gujarat studied 33 sickle cell disease patients of age range 5 to 15 years and found the M:F ratio of 2.6, Hb in g/dl was 7.73±1.86 (male 7.86±1.87 female 7.41±1.92), mean HbF was 12.3% (male 12.5±7.6% female 11.97±6.68%). Mean HbF level was high and no sex related difference in HbF values was observed in their study (P>0.05).\(^8\) In our study difference in mean HbF level was 23.1% in males and 21.9% in females in patients with splenomegaly while in cases without splenomegaly had mean HbF level 21.5% in males and 20.6% in females.

Mpalampa et al in 2012 on 216 children with sickle cell disease aged 1 to 18 yrs in Uganda found 115 (53.2%) were female and 101 (46.8%) male.\(^7\) The mean HbF level was 9.0% (SD 5.58) and the median was 7.9%. High levels of Hb F ≥10% were found in 80 (37.0%) out of which 24 (30%) had palpable spleen. Low levels of Hb F<10% was found in 136 (63%) out of which 20 (20.6%) had palpable spleen. Our study had 60 cases with HbF >20%, 35 cases had HbF between 1-20%. Thus the mean HbF level in most of our cases was significantly higher thus relating with the higher mean HbF found in homozygous SCD patients of Saudi Arabia and India who have typically a milder form of this disorder.

**CONCLUSION**

Splenomegaly was found in more than 50% of cases of sickle cell disease signifying the persistence of it even in adult age. High fetal hemoglobin level found in these cases suggests Hb F as one of the important etiological cause of persistence of splenomegaly. Also the high Hb F level has an ameliorating effect on the clinical severity of the disease, mainly the occurrence of sickle cell crisis and late onset of symptoms.

**AUTHOR NOTE**

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**REFERENCES**