Pregnancy and Its Outcome in Sickle Cell Hemoglobinopathies: A Study of Central India

Abstract

Sickle cell hemoglobinopathies are the most important disorders of hemoglobin structure associated with pregnancy. The effect of pregnancy on patients with sickle cell disease and the effects of maternal sickle cell disease on the outcome of pregnancy have been the subject of many discussions.

Objective:
1. To study the effect of sickle cell hemoglobinopathies over the course of pregnancy.
2. To study the complications occurring in patients of sickle cell hemoglobinopathies during antepartum, intrapartum, and postpartum period.
3. To study the effect of maternal sickle cell hemoglobinopathies on the fetus and its outcome.
4. To compare pregnancy, including maternal and fetal outcome, in sickle cell hemoglobinopathy patients with that of controls having normal HbAA pattern.

Materials and methods: This study was carried out from December 15, 2010 to September 15, 2012 in the Department of Obstetrics and Gynaecology.

Study design: A hospital-based prospective study, the subjects consisted of 54 pregnant women with sickle cell hemoglobinopathy, of which 12 had homozygous sickle cell disease or sickle cell anemia (HbSS) and 42 had sickle trait (HbAS); 54 pregnant women with normal Hb pattern, i.e., HbAA pattern, were chosen as control and their maternal and fetal outcome were noted and compared with that of pregnant women with normal HbAA pattern.

Results: The most common complication in the present study was anemia and was seen in 85.19% of subjects and 66.67% of controls. Sickle cell anemia is a significant cause of spontaneous abortions. Thus, past pregnancy wastage was seen in 24.07% of subjects and 14.81% of control.

Conclusion: Pregnancy in sickle cell hemoglobinopathies mandates vigilant multidisciplinary management so as to reduce maternal and fetal morbidity and mortality

Keywords: Complications during pregnancy, Hemoglobinopathies, Pregnancy outcome, Sickle cell.

Introduction

Pregnancy is a blessing to every woman, a sign of womanhood. But it may be a burden to the life in many women, and causes are innumerable. One such cause is “sickle cell hemoglobinopathies,” which pose a threat to the lives of both the pregnant woman and her baby.

Sickle cell disorders account for about 70% of the worldwide hemoglobin disorders. As per the World Health Organization (WHO) report, 60 million carriers of sickle cell and 1,20,000 sickle cell homozygotes are added every year in the world.

Inherited in an autosomal recessive manner, it is characterized primarily by chronic anemia and periodic episodes of pain.

During pregnancy, patients with major sickle hemoglobinopathies are susceptible to exacerbations of their disease, probably as a result of increased metabolic demands, hypercoagulable state, and increased vascular stasis. Vasoocclusive crisis is more common in the later half of pregnancy. There is an increased incidence of pycnephritis, pulmonary infarction, pneumonia, acute chest syndrome, prematurity of infants, low birth weight, and fetal death in pregnant women having sickle cell anemia. The birth weight of infants is below average and fetal wastage is high, the cause of which is obscure, but may sometimes result from vasooclusion of placenta. The maternal mortality in sickle cell disease was formerly prohibitively high, rates averaging 33%, but is now much lower.

India

With a population of 1,000 million at the new millennium (2000) year and a birth rate of 25 per 1,000 live...
births, there would be about 45 million carriers and about 15,000 infants born each year with hemoglobinopathies in India. However, the exact share of sickle cell disease is still unknown in India. The sickle cell hemoglobinopathy has remained a neglected field of research in India and the magnitude of the problem has never been properly appreciated.\(^1\)

Considering the above said facts, the following study was undertaken to know the course of pregnancy in patients with sickle cell hemoglobinopathies, and its effect on maternal and fetal outcome.

**MATERIALS AND METHODS**

This study was carried out from December 15, 2010 to September 15, 2012 in the Department of Obstetrics and Gynaecology of Shri Vasantrao Naik Government Medical College of Yavatmal.

**Study Design**

A hospital-based prospective study, where pregnant women having sickle cell hemoglobinopathies were studied and their maternal and fetal outcome were noted and compared with that of pregnant women with normal HbAA pattern.

**Study Setting**

This study was conducted in the Department of Obstetrics and Gynaecology at a government medical college of Central India.

**Study Duration**

The study was carried out from December 15, 2010 to September 15, 2012, total duration of the study being 21 months.

Data collection was done from December 15, 2010 to June 15, 2012.

Data entry and data analysis were done from June 16, 2012 to September 15, 2012.

**Sampling**

The study population consisted of pregnant women attending antenatal outpatient department (OPD) services or admitted in the antenatal wards in the Department of Obstetrics and Gynaecology during the period from December 15, 2010 to June 15, 2012.

**Sample Size**

The total number of pregnant women studied during the study period was 108, of whom 54 women had sickle cell hemoglobinopathies (12 had homozygous sickle cell disease of HbSS and 42 had sickle cell trait of HbAS), taken as study subject and remaining 54 women had normal hemoglobin HbAA pattern, taken as controls.

**Selection Criteria**

**Inclusion Criteria**

- Pregnant women attending antenatal OPD having sickle cell hemoglobinopathies as diagnosed by Hb electrophoresis, who were willing to participate in the study.
- Pregnant women having sickle cell hemoglobinopathies, as diagnosed by Hb electrophoresis, who were admitted in ward and were willing to participate in the study.

**Exclusion Criteria**

- Women not willing to participate in the study or not providing written informed consent.
- Pregnancies which terminated in abortion in the study were excluded.

**Data Analysis**

All cases and controls were followed through pregnancy, labor, and puerperium. The statistical difference of complications between the two groups of patients was calculated by Fisher extract test; p value <0.05 was considered significant.

**RESULTS**

The study subjects consisted of 54 pregnant women with sickle cell hemoglobinopathy. Of them 12 had homozygous sickle cell disease or sickle cell anemia (HbSS) and 42 had sickle trait (HbAS); 54 pregnant women with normal Hb pattern, i.e. HbAA pattern, were chosen as control (Table 1).

Table 2 shows that previous spontaneous abortions were seen in 14.81% of subjects and 9.26% of controls;

<table>
<thead>
<tr>
<th>Group</th>
<th>Severe anemia, Hb &lt;7 gm%</th>
<th>Moderate anemia, Hb 7–9.9 gm%</th>
<th>Mild anemia, Hb 10–&lt;11 gm%</th>
<th>No anemia (WHO) Hb&gt;11 gm%(^5)</th>
<th>No anemia (developing countries) Hb&gt; 10 gm%(^6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SS (n = 12)</td>
<td>4</td>
<td>33.33</td>
<td>8</td>
<td>66.67</td>
<td>0</td>
</tr>
<tr>
<td>AS (n = 42)</td>
<td>3</td>
<td>7.14</td>
<td>31</td>
<td>73.81</td>
<td>7</td>
</tr>
<tr>
<td>AA (n = 54)</td>
<td>1</td>
<td>1.85</td>
<td>35</td>
<td>64.81</td>
<td>13</td>
</tr>
</tbody>
</table>
In SS group—100% (p = 0.0271)
In AS group—80.95% (p = 0.1650)

Thus, anemia (Hb < 10 gm%) was statistically significant in SS patients (p < 0.05) when compared with controls, but was not significant in AS patients.

Severe anemia (Hb < 7 gm%) was seen in 33.33% of SS patients (p = 0.0031), 17.14% of AS patients (p = 0.3155), and 1.85% of controls. Thus, severe anemia was statistically significant in SS patients (p < 0.05) when compared with controls.

Blood transfusion was given at some stage in the study to 100% of SS patients (p = 0.0001), 38.09% of AS patients (p = 0.0209), and 16.67% of controls. Thus, blood transfusion was statistically significant in both SS and AS patients (p < 0.05) when compared with controls.

### DISCUSSION

Mean Hb% in controls (AA) was 9.289 ± 1.217 gm%. The mean Hb% in subjects was 8.357 ± 1.371 gm%, 0.932 gm% less than that of controls. Among the subjects, mean Hb% in SS group was 7.083 ± 1.0 gm% and in AS group, 8.721 ± 1.246 gm%.

Anemia (Table 1) was seen in 85.19% of subjects and 66.67% of controls. Anemia was significant in SS patients compared with controls (100 vs 66.67%, p = 0.0271). Severe anemia was also significant in SS patients when compared with controls (33.33 vs 1.85%, p = 0.0031). In sickle cell anemia (HbSS) patients, incidence of anemia was reported to be 93% by Hendrickse et al., 65% by Tuck et al., 95.25% by Omo-Aghoja and Okonofua, and 84.3% (p < 0.0001) by Al Jama et al.

### Table 2: Maternal complications during pregnancy, labor, and puerperium

<table>
<thead>
<tr>
<th>Maternal complications</th>
<th>SS (n = 12)</th>
<th>AS (n = 42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>16.67%</td>
<td>100%</td>
</tr>
<tr>
<td>UTI</td>
<td>41.67%</td>
<td>26.2%</td>
</tr>
<tr>
<td>HDP</td>
<td>33.33%</td>
<td>21.42%</td>
</tr>
<tr>
<td>Jaundice</td>
<td>25%</td>
<td>2.38%</td>
</tr>
<tr>
<td>Crisis</td>
<td>58.33%</td>
<td>0%</td>
</tr>
<tr>
<td>Postpartum hemorrhage</td>
<td>25%</td>
<td>7.14%</td>
</tr>
<tr>
<td>Puerperal complications</td>
<td>25%</td>
<td>2.38%</td>
</tr>
<tr>
<td>Maternal mortality</td>
<td>8.33%</td>
<td>0%</td>
</tr>
</tbody>
</table>

### Table 3: Past pregnancy wastage in subjects and controls

<table>
<thead>
<tr>
<th>Group</th>
<th>Previous spontaneous abortions</th>
<th>Previous perinatal loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>SS</td>
<td>33.33%</td>
<td>16.67%</td>
</tr>
<tr>
<td>AS</td>
<td>9.52%</td>
<td>7.14%</td>
</tr>
<tr>
<td>AA</td>
<td>9.26%</td>
<td>5.56%</td>
</tr>
</tbody>
</table>

*Calculated by Fisher’s exact test; p < 0.05 is taken as significant value. Calculated in comparison to AA controls; HDP: Hypertensive disorders of pregnancy; UTI: Urinary tract infections

### Table 4: Summary of pregnancy outcome in subjects and controls

<table>
<thead>
<tr>
<th>Pregnancy outcome</th>
<th>SS (n = 12)</th>
<th>AS (n = 42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous spontaneous abortions</td>
<td>9.26%</td>
<td>9.52%</td>
</tr>
<tr>
<td>Previous pregnancy wastage</td>
<td>14.81%</td>
<td>16.67%</td>
</tr>
<tr>
<td>Preterm deliveries</td>
<td>9.26%</td>
<td>9.52%</td>
</tr>
<tr>
<td>Cesarean sections</td>
<td>18.52%</td>
<td>26.19%</td>
</tr>
</tbody>
</table>

*Calculated by Fisher’s exact test; p < 0.05 is taken as significant value. Calculated in comparison with AA controls
About 80.95% of AS patients had anemia. It was not statistically significant (p = 0.1650) when compared with controls.

Among the other complications (Table 2), urinary tract infections (UTIs) were significant in SS patients when compared with controls (41.67 vs 11.11%, p = 0.0220). The UTI during pregnancy in sickle cell anemia is noted to be 33% by Freeman and Ruth,10 16.7% by Rahimy Mohamed et al,11 37.5% by Rathod et al, 12 17.3% (p < 0.0003) by Al Jama et al.9

Jaundice was seen in 25% of SS patients (p = 0.0308 when compared with AS patients and p = 0.0048 when compared with controls) and 2.38% of AS patients (p = 0.4375) had jaundice. Jaundice was not seen in any of the control subjects. Thus, jaundice was a statistically significant complication in SS patients (p < 0.05) when compared with AS patients and controls.

Crisis was significant in SS patients when compared with AS patients (58.33 vs 0%, p < 0.05). About 33.33% patients had painful crisis and 25% had hemolytic crisis. Crisis in SS patients was noted to be 48.6% by Dare et al,13 56% by El-Shafei et al,14 and 40% by Sonwane and Zodpey.15 Painful crisis was reported to be 50% by Seoud et al,16 57% by Rahimy Mohamed et al,11 41.4% by Odum et al,17 23.81% by Omo Aghoja and Okonofua,8 26.6% by Al Jama et al.9 Hemolytic crisis was 34.4% by Odum et al12 and 17.7% by Al Jama et al.9

There was one maternal death in SS group, on the 7th day of postcesarean section (indicated for prolonged second stage of labur), due to pneumococcal pneumonia and septicemia.

As seen in Tables 3 and 4, past pregnancy wastage was significant in SS group when compared with control group (50 vs 14.81%, p = 0.0144). Previous spontaneous abortions were also significant in SS patients (33.33 vs 9.26%, p = 0.0497). Freeman and Ruth10 reported pregnancy wastage of 36.4% in SS patients in their study. In the study by Rahimy Mohamed et al,11 previous unsuccessful pregnancies were reported to be 21.43% in SS patients.

Table 5 shows the distribution of birth weight of infants. The mean birth weight of infants born to SS mothers was 2413.64 ± 412.50 gm, and of those born to controls was 2543.64 ± 438.96 gm.

When compared with the control group, there was significantly higher risk of adverse fetal outcome in the SS group. As shown in Table 6, low birth weight of infants was statistically significant in SS group compared with controls (84.62 vs 23.64%, p = 0.0001; Table 6). One infant in SS group had extremely low birth weight (<1,000 gm).

Low birth weight reported by different studies are 31% by Poddar et al,18 42% by Serjeant et al,19 77.78% by Sonwane and Zodpey.15 In studies by Kale et al 20 (56%, p < 0.05) and Al Jama et al 9 (16.5% p < 0.05), low birth weight in SS group was significant.

In AS subjects, 36.36% infants had low birth weight, which, though higher than in controls, was not significant (p = 0.1881).

Intrauterine growth retardation was statistically very significant (p < 0.01) in SS patients compared with controls (50 vs 11.11%, p = 0.0054). Al Jama et al9 reported 20.8% intrauterine growth retardation (IUGR) in SS patients, which was statistically significant (p < 0.0001) when compared with controls in their study.

The significant antenatal complications seen in SS subjects in the study were anemia, UTI, sickling crisis, and jaundice. In AS subjects, though the complications were high, they were not significant. Anemia was the most common complication, with most of the patients having either moderate or severe anemia. In SS group, anemia was seen in all the patients and was either of moderate

**Table 5:** Distribution of birth weights in subjects and controls

<table>
<thead>
<tr>
<th>Group</th>
<th>&lt;1,000 gm</th>
<th>1,000–1,500 gm</th>
<th>1,500–2,000 gm</th>
<th>2,000–2,500 gm</th>
<th>≥2,500 gm</th>
</tr>
</thead>
<tbody>
<tr>
<td>SS (n = 13)</td>
<td>1</td>
<td>7.69</td>
<td>1</td>
<td>7.69</td>
<td>3</td>
</tr>
<tr>
<td>AS (n = 44)</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2.27</td>
<td>5</td>
</tr>
<tr>
<td>AA (n = 55)</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3.64</td>
<td>5</td>
</tr>
</tbody>
</table>

**Table 6:** Summary of fetal complications and perinatal outcome

<table>
<thead>
<tr>
<th>Fetal complications and perinatal outcome</th>
<th>SS</th>
<th>AS</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA%</td>
<td>%</td>
<td>Statistical significance*</td>
</tr>
<tr>
<td>Low birth weight</td>
<td>23.64</td>
<td>84.62</td>
</tr>
<tr>
<td>IUGR</td>
<td>11.11</td>
<td>50</td>
</tr>
<tr>
<td>Still births</td>
<td>1.85</td>
<td>8.33</td>
</tr>
<tr>
<td>END</td>
<td>3.70</td>
<td>8.33</td>
</tr>
<tr>
<td>Perinatal mortality</td>
<td>55.56/1,000</td>
<td>1671,000</td>
</tr>
</tbody>
</table>

END: Early neonatal death; IUGR: Intrauterine growth retardation; *Calculated by fisher’s exact test; p < 0.05 is taken as significant value; Calculated in comparison to AA control
or of severe grades. Puerperal complications were also significantly high in SS patients than AA and AS patients. Maternal mortality was not significant in either group.

Past pregnancy wastage and spontaneous abortions were also significant in SS subjects. Among the fetal complications, low birth weight and IUGR were significant in SS group.

Though the rate of preterm deliveries in SS mothers was more than in AA mothers, it was not significantly high. In AS patients, preterm delivery rate was similar to that of women having normal HbAA (Table 7). Perinatal loss in SS group was more than that of AS and AA groups, but was not statistically significant.

**CONCLUSION**

Thus, sickle cell hemoglobinopathies put pregnant woman and her fetus into several complications, and the pregnancy outcome may not be fruitful always. Women with sickle cell trait have a near-normal pregnancy with a good maternal and fetal outcome, almost comparable to that of women with normal HbAA pattern.

But, in sickle cell anemia patients, pregnancy is a burden which puts the woman into a high-risk group with high rates of antenatal and postnatal complications. The course of pregnancy and its outcome is also gloomy, with high rates of pregnancy wastage and preterm deliveries. The fetus of a sickle cell anemia mother also suffers the brunt of the disease by having higher rates of low birth weight and IUGR.

So pregnancy in sickle cell hemoglobinopathies mandates vigilant multidisciplinary management, so as to reduce maternal and fetal morbidity and mortality.

**REFERENCES**