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ORIGINAL ARTICLE

Outcome of Pregnancy with Hemoglobinopathy in a Tertiary Care Center

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Abstract

Purpose The objective was to observe the characteristics among pregnant patients with a diagnosed hemoglobinopathy and to study the obstetric and medical morbidity patterns during the antenatal and the perinatal periods in this group of patients.

Methods A prospective observational study was conducted in a tertiary care center.

Results Sixty patients were studied in 11 months. Primigravidae (43.3%) formed the highest percentage of patients. β Thalassemia trait was the most common hemoglobinopathy, seen in 81.66% of study subjects. The hemoglobin value ranged from 5.7 to 13.0, with an average of 9.2 g/dl. Thyroid problems were the most common associated medical disorder. Though IUGR and placenta previa were common, there were no major obstetric problems. There were 57 live births and 1 fresh stillbirth. Two patients had spontaneous abortion for which uterine

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curettage was done. LSCS was the most common obstetric outcome. Patients with sickle-cell disease required more blood transfusion than those with beta-thalassemia trait. There were 2 maternal mortalities, and both the patients were the diagnosed cases of sickle-cell disease.

Conclusions While the perinatal outcomes among women with sickle-cell disease are poor, the outcomes in pregnant patients with beta-thalassemia trait were not a cause of major concern.

Keywords Hemoglobinopathy · Beta-thalassemia · Pregnancy outcomes · Perinatal outcomes

Introduction

Hemoglobinopathies are a group of disorders which affect the hemoglobin molecule in its structure, function or production. The morbidity among females with hemoglobinopathies during pregnancy can range from asymptomatic investigational abnormality to mortality. Recent advances in the treatment of these disorders have increased the life expectancy and quality of life of affected patients. It is increasingly being recognized first time during pregnancy. It is more common than ever before for women with hemoglobinopathies to reach childbearing age and to undergo pregnancy. While a lot of emphasis has been put on the prevention, the focus of this study was to observe the maternal and neonatal outcomes among a cohort of pregnancies with an already-diagnosed hemoglobinopathy. This has previously not been studied or reported in much detail.

In this context, the study was undertaken with the objectives as follows.

- To observe the demographic characteristics among pregnant patients with a diagnosed hemoglobinopathy.
- To study the obstetric and medical morbidity patterns during the antenatal period in this group of patients.
- To study the neonatal outcomes among this group of patients.

Materials and Methods

A prospective observational study was conducted in the department of gynecology and obstetrics in a tertiary care referral hospital after institutional ethics approval. Pregnant women attending the department for antenatal follow-up and delivery were checked for an abnormal hemoglobin electrophoresis report. Those with a diagnosed hemoglobinopathy were identified and included in the study. All hemoglobinopathies were included, including 'traits.' Only those women who delivered or underwent completion of pregnancy at the institute were included. Patients were included irrespective of parity status and registration status. Medical termination of pregnancy on request was excluded from the study. It is to be emphasized that hemoglobin electrophoresis was not advised for the purpose of this study.

The sample size was calculated with the formula, $n = t^2 \times p(1\text{-}p)\ m^2$, where N = required sample size, t = confidence level at 95% (standard value of 1.96) p = estimated prevalence of the problem in the area = 4.0% [1], M = margin of error (standard value of 0.05%). The value worked out to be 59. For mathematical convenience, the chosen sample size was 60.

At the time of admission for delivery, physical examination and relevant investigations were all documented. The patients were followed up till their discharge from the postnatal ward. The parameters which were studied are as follows. Details regarding whether antenatal genetic counseling and invasive attempts (chorionic villus sampling (CVS)) to diagnose problems in the fetus was done, were noted. All complications during the antenatal–perinatal–postnatal periods were noted. Requirement of transfusion of blood or blood products in the antenatal–perinatal periods was noted. Obstetric outcomes such as length of pregnancy, mode of delivery, details regarding any abnormal course in the labor were noted. Neonatal outcomes such as birth weight, Apgar score, neonatal intensive care unit (NICU) admission were noted. Any abnormalities like neonatal jaundice, malformations, hydrops fetalis and neonatal death, if present were noted. The details were compiled and statistical methods performed. During the hospital stay, the patients were explained in detail about the nature of their condition and counseled regarding further follow-up.

Statistical Calculations: Being an observational study, simple statistical calculations using mean and percentages were performed.

Results

Sixty patients with hemoglobinopathies were included in the study, and they were identified in duration of 11 months. During this study period, there were 6972 deliveries in the hospital. As shown in Fig. 1, β thalassemia trait was the most common hemoglobinopathy identified, which was seen in 49 patients (81.66%). Sickle-cell disease formed the second most common hemoglobinopathy, found in 8 patients (13.3%), while 3 patients had other types (one each of HbD, HbE and Hb beta thal/HbF combination).

The highest number of patients belonged to the age group of 26–30 (36.6%), followed closely by the age group

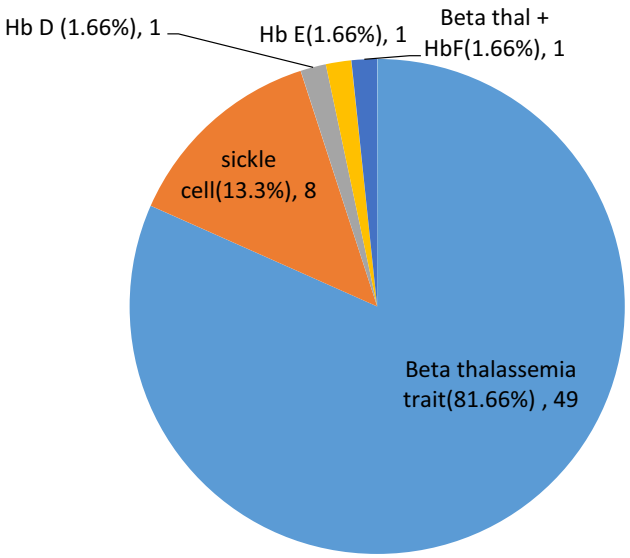

Fig. 1 Distribution of hemoglobinopathies

of 21–25 (35%). Only one patient was above 36. Only one patient in the study group was unmarried, and two couples had second-degree consanguinity. Rest all were nonconsanguineous marriages. Primigravidae (43.3%) formed the highest percentage of patients. Multigravidae with previous vaginal delivery were more common than multigravidae with previous cesarean section. A smaller percentage had previous abortion(s) (16.6%).

63.3% of the patients had registered with the hospital on outpatient basis, while the rest of the patients were referred at the time of delivery to the hospital. Thirty-three out of the 60 patients (55.55%) had at least 3 antenatal outpatient department (OPD) visits, suggesting less-than-optimal compliance to regular antenatal follow-up. A majority of the patients (30%) were referred to the institution at the time of delivery, after 30 weeks of gestation. This was closely followed by 28.33% of patients having registered in the OPD between 21 and 30 weeks of gestation. A majority of the patients (70%) delivered between 37 and 40 weeks of gestation. Fifteen percent of the patients were delivered postdated, while 11% were preterm deliveries. A total of 9 patients required induction of labor. With respect to the time of detection of hemoglobinopathy, 60% of the patients were detected to have a hemoglobinopathy during the current pregnancy.

The hemoglobin value ranged from 5.7 g/dl to 13.0 g/dl, with an average of 9.2 g/dl and a standard deviation of 1.33. With respect to the husband's electrophoresis report, 40% of the husbands did not have an electrophoresis report. Out of the remaining 60% who got the report done, a small number 5 (8.33%) had an abnormal report. All the 5 had β thalassemia trait in the hemoglobinopathy detected. In other words, 13% of husbands who underwent testing had an abnormal hemoglobin electrophoresis report. Among those patients whose husbands who had an electrophoresis report, 80% were following up in the antenatal OPD.

While analyzing the number of previous child affected by hemoglobinopathies, only 2 patients (3.33%) had a previous child diagnosed with a hemoglobinopathy.

11.66% (7 out of 60) of patients had undergone an invasive test for prenatal diagnosis of fetal affliction. Among these, 2 patients had a history of a previous child being affected by the disease. All the 7 tests were CVS done in late first trimester–early second trimester; and in all of these, the fetus was not affected by the disease and pregnancy was continued successfully.

Requirement of blood transfusion: Among those with beta-thalassemia trait, 8 patients required blood transfusion in the antepartum period, while 11 patients required transfusion in the peripartum period. Two patients required blood transfusion both antepartum and peripartum periods. Out of 8 patients with sickle-cell disease, 2 required blood transfusion in the antenatal period and 3 required in the peripartum period. One patient required blood transfusion in both antenatal and peripartum periods.

Associated medical high risks: As shown in the Table 1, thyroid problems were the most common associated medical disorder.

Surgical problems: One patient (with HIV positive status) developed a gluteal abscess which required incision and drainage. One patient had nephrolithiasis which worsened and required percutaneous nephrolithotomy. Six patients had prior history of appendicectomy. Three patients with sickle-cell disease had avascular necrosis of the hip and were yet to undergo any surgical management.

Antenatal obstetric problems: As shown in Table 2, there were no major obstetric problems. Intrauterine growth restriction and placenta previa were common.

Obstetric outcomes: As shown in Fig. 2, there were 57 live births and 1 fresh stillbirth. Two patients had spontaneous abortion for which uterine curettage was done. As shown in Fig. 1, lower segment cesarean section (LSCS) was the most common obstetric outcome, which

Table 1 Medical high risk factors

Medical high risk	Number	Percentage (%)
Hypothyroidism	7	11.66
Hyperthyroidism	2	3.33
HIV	1	1.67
HBsAg	1	1.67
ANA positive	1	1.67
Hyperbilirubinemia	2	3.33
Chronic hypertension	1	1.67
Depression	1	1.67

Table 2 Distribution of obstetric problems

Obstetric problem	Number	Percentage (%)
GDM	1	1.66
Polyhydramnios	2	3.33
Oligohydramnios	2	3.33
Uterine septum	1	1.66
Fibroid uterus	1	1.66
Preterm labor	1	1.66
Placenta previa	4	6.66
PIH	3	5
IUGR	4	6.66
Fetal renal pelvis dilatation	1	1.66
Fetal ovarian cyst/mesenteric cyst	1	1.66

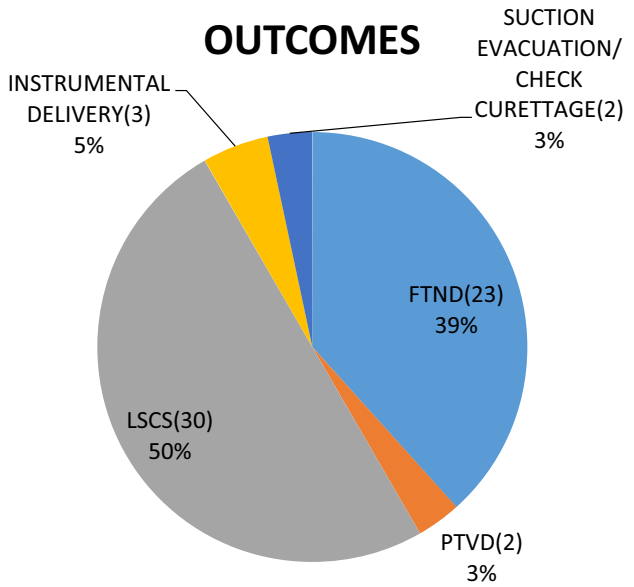

Fig. 2 Distribution of delivery outcomes

constituted 50% of all the patients studied. Thirty-nine percent of the patients delivered by full-term vaginal deliveries, while 2 were preterm vaginal deliveries. The most common indication of LSCS in the present study was fetal distress (33.3%). One patient required B-lynch suturing in view of atonic postpartum hemorrhage.

Maternal mortality: Among the 60 patients studied, there were 2 maternal mortalities. Both the patients were diagnosed cases of sickle-cell disease.

The first was a 32-year-old G4A3 referred at 32 weeks of gestation with bad obstetric history with sickle-cell anemia with IUGR with previous 1 LSCS, with hypothyroidism, severe anemia and severe preeclampsia. Two units of blood was given for the correction of anemia. Evaluation of IUGR revealed severe changes in Doppler flow; as patient refused consent for vaginal birth, LSCS was performed. However, there was sudden fetal distress just prior to LSCS and she delivered a fresh stillbirth of 1.365 kg. Patient was stable during initial postoperative period, but developed fever, urinary tract infection and surgical site infection on day 7 of LSCS, after which she showed signs of sepsis and multiorgan failure. She deteriorated progressively despite intensive unit care and expired on day 14 of LSCS due to sepsis with acute respiratory distress syndrome.

The second patient, a 22-year-old primigravida with 38 weeks of gestation, was referred for acute onset of breathlessness. Prior to this episode, pregnancy had been uneventful. Patient was admitted in active labor and delivered a healthy male child of 2.1 kg, following which she was transferred to the intensive care unit for further care. The patient developed severe breathlessness, which did not improve despite medications, and required intubation. She succumbed on day 2 of delivery.

Neonatal outcomes: There were 51.5% females and 48.5% males. 57 were live births, while only one was a fresh stillbirth. There were no early neonatal deaths. The birth weights ranged between 1.365 kg and 3.7 kg, with an average weight of 2.79 kg and a standard deviation of 0.488. One baby had persistent hyperbilirubinemia needing phototherapy, one was transferred to NICU for transient tachypnea and one had large mesenteric cyst managed conservatively. One baby was transferred for adoption.

Discussion

Survival in hemoglobinopathies has improved, is becoming increasingly safe and forms the basis of this study [2]. The prevalence of abnormal hemoglobin in the West Bengal state of India is approximately 12% as reported in the large prospective study over 10 years by Mondal et al. [3]. The most common abnormality was beta-thalassemia trait which was found in 4.6%. This was followed by HbE trait, beta-thalassemia major and other abnormal hemoglobin types. A single-center study in central India which undertook population screening estimated the prevalence of beta-thalassemia carrier state to be around 2.78% [4]. A slightly higher prevalence of abnormal hemoglobin types may be found in rural areas [5]. The prevalence reported by Colah et al. in western India where this study was conducted is 4.0% [1]. In our study, only those with an already-available abnormal hemoglobin electrophoresis report were included, and no hemoglobin electrophoresis was advised for this study purpose. We identified 60 patients in around 11 months when the corresponding deliveries were 6972, which gives a rate of 0.86%. This is not comparable with population statistics because a heterogeneous population is referred to the hospital for management of various

problems. The mean hemoglobin in the study was 9.2 g/dl. In a 20-year experience with pregnancies with beta-thalassemia intermediate in a Greek cohort of patients, Voskaridou et al. estimated the average hemoglobin was 8.4 g/dl [6]. The lowest hemoglobin recorded in the present study was 5.5 g/dl. This is similar to the findings of a study conducted by Nassar et al. who studied beta-thalassemia intermedia at two tertiary care centers in Europe, and the lowest hemoglobin of 5.2 g/dl [7]. Vuthiwong et al. studied the attitudes of husbands of patients with abnormal screening in Thailand and demonstrated that when the female has an abnormal test, the husbands have a favorable attitude toward self-testing. Similarly, 63% husbands of the mothers in this group of patients underwent testing to look for a carrier status [8]. Patients who were antenatal registered and had regular follow-up, along with their spouses, were more likely to have undergone screening for hemoglobinopathies. This is in agreement with the study conducted by El-Beshlawy et al. In their study conducted regarding attitudes toward prenatal diagnosis of hemoglobinopathies, it was demonstrated that appropriate counseling improves acceptance for screening methods among at-risk patients and their relatives [9].

Chorionic villus sampling (CVS) is a safe procedure for prenatal diagnosis of hemoglobinopathies. Asnafi et al. have described a large series of patients undergoing CVS and confirmed the same [10]. Seven patients in our study underwent CVS, and there were no procedure-related complications; pregnancy continued successfully. 19.5% of patients were not transfused at all or they had been transfused only once during pregnancy. Similar results, i.e., 26.5% of patients not transfused at all or had been transfused only once during gestation, were reported by Voskaridou et al. [6]. However, Nassar et al. reported that 79.5% of pregnancies with β thalassemia intermedia required blood transfusion [7]. Most patients with sickle-cell disease required blood transfusion, and it was more when compared to the beta-thalassemia trait. This higher requirement of blood transfusion among sickle-cell disease is supported by the study by Daigavne et al. also [11].

Thyroid abnormalities were the most common associated medical condition in our patients. Other major medical complications were not observed. This is supported by a study by Tsatsalas, who has described the pregnancies with beta-thalassemia carriers as 'an uneventful journey' [12]. Similar results have been described by Charoenboon et al. [13]. In the present study, the prevalence of preeclampsia was 5% while that of GDM was 1.66%. This is in agreement with the studies conducted by Yordanova et al. and Hanprasertpong et al. Both had concluded that the rate of these obstetric conditions in patients with hemoglobinopathies is comparable to that of the normal population [14, 15]. Most of the patients in our study carried on till full-term pregnancy. Our group of patients had very small rate of preterm labor and small-for-gestational age. In their respective studies, Voskaridou et al., Yordanova et al. and Kemthong et al. have all reported that the rate of obstetric complications in hemoglobinopathies is of negligible concern [6, 14, 16].

LSCS was the most common mode of delivery. Yordanova et al. have also recently reported that cases with β thalassemia minor have significantly higher prevalence of cesarean section delivery [14]. There were two maternal mortalities in our group of 60 patients, of which both were sickle-cell disease. In other developing countries also, sickle-cell disease causes significant morbidity and mortality [17, 18].

Higher risk of adverse pregnancy outcomes and need for specialized care in those with sickle-cell disease has been emphasized in community studies also [19].

To conclude, beta-thalassemia trait was the most common hemoglobinopathy affecting pregnancy. The obstetric outcomes in the group of patients with beta-thalassemia trait were not a cause of major concern. Sickle-cell anemia though lower in incidence causes significant maternal morbidity. There were no major neonatal problems.

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Compliance with Ethical Standards

Conflict of interest Anahita Chauhan and Madhva Prasad declare that they have no conflict of interest.

Ethical Statements All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 1975 Declaration of Helsinki, as revised in 2008.

Ethical Approval Institutional ethics committee approval was obtained. Informed consents were obtained from the patients in the study.

Human and Animal Rights This article does not contain any study involving animal subjects.

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