ORIGINAL ARTICLE

Effect of Hemoglobinopathy on Maternal and Fetal Outcome: Single Center Study

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Abstract

Background and aim: Hemoglobinopathies pose to be a major risk factor for pregnancy leading to potentially fatal maternal and neonatal complications. The aim of our study was to compare maternal and neonatal outcomes of pregnancy in women with a hemoglobinopathy and without a hemoglobinopathy.

Materials and methods: The present study is a comparative retrospective analysis of 153 pregnant women with hemoglobinopathies and 153 pregnant women without hemoglobinopathies who were treated between June 2020 and May 2023, in Dhiraj Hospital,Vadodara. We analyzed various data regarding maternal as well as neonatal outcomes and complications in hemoglobinopathies.

Results: Among the maternal outcomes, the rate of previous miscarriage, intrauterine growth restriction (IUGR), postpartum hemorrhage (PPH), and anemia were significantly increased in women with hemoglobinopathies. Among the neonatal outcomes, the rate of anemia and low birth weight were significantly increased in all type of hemoglobinopathic pregnancies. Hepatic encephalopathy, septicemia, jaundice, perinatal death, and fetal acidosis were also increased in sickle cell disease (SCD) pregnancies.

Conclusion: It is pivotal to supervise pregnancies with hemoglobinopathies for minimal morbidity and mortality in mother as well as fetus. Timely multispecialty intervention can help in improving the fetomaternal outcomes.

Keywords: Hemoglobinopathic pregnancies, Maternal outcomes, Neonatal outcomes.

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Introduction

The most common disease in pregnancy and postpartum period is anemia. The most common causes of anemia among pregnant women are iron deficiency and inherited hemoglobin (HB) disorders. While anemia has been proven to be a significant risk factor leading to adverse fetomaternal outcomes, effect of a hemoglobinopathy on fetomaternal outcomes has been sparsely studied. Hemoglobinopathies are a group of disorders which affect the hemoglobin molecule in its structure, function, or production. According to World Health Organization (WHO), overall at least 5.2% of the world population carry a significant variant of a hemoglobin disorder while among pregnant women the prevalence is even higher with over 7%.[1] During pregnancy, females with hemoglobinopathies can face morbidity ranging from asymptomatic investigational abnormality to death. It is very common for women with hemoglobinopathies to reach childbearing age and undergo pregnancy with the hemoglobinopathy being first time diagnosed in pregnancy.[2] 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 pregnancies with an already diagnosed hemoglobinopathy, mainly sickle cell disease (SCD), trait, and other heterozygous hemoglobinopathies (HHs).

Sickle cell disease is a genetically inherited group of conditions with an abnormal hemoglobin (HbS) due to its genetic alteration. Sickle cell disease comprises homozygous – HbSS or heterozygous – HbSß thal, HbSC, HbSD Punjab, and HbSE – genotypes. India ranks second when it comes to SCD burden globally. The highest prevalence of SCD is in India among all south Asian countries, where over 20 million people live with SCD.[1] India holds for 14.5% of total SCD newborns. Pregnancy in women with SCD and its complications are included in this study.[3]

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In Gujarat, SCD is common in the tribal belts of Chhotaudepur, Panchmahal, Dahod, Godhra, Narmada, and our center receives many referrals from there.[4] Thalassemia is an autosomal recessive disorder which affects the hemoglobin synthesis process. The genes that encode for globin proteins are located on beta and alpha globin gene clusters of chromosomes 11 and 16, respectively.[5] It is the most common single gene disorder in the world causing significant morbidity and mortality in India and abroad. Approximately 5% of the world population are carrier of hemoglobinopathies and about 2.9% are of thalassemia. Carriers are healthy individuals with mild anemia.[6] Identification of these disorders is immensely important epidemiologically and they can be detected by population screening.[7] Proper identification of hemoglobin variants during pregnancy can help in planning and timely intervention during pregnancy for optimization of fetomaternal outcome.

The aim of our study was to compare maternal and neonatal outcomes of pregnancy in women with a hemoglobinopathy

Table 1: Characteristics of the study and control group

Sr. No.	*Variable*	*Sickle cell disease*	*Relative risk*	*Sickle cell trait*	*Relative risk*	*Heterogeneous hemoglobinopathy*	*Relative risk*	*Control*
1	Gravidity	9	2.08	22	1.42	4	1.73	22
2	Gestational age at delivery <37 weeks	13	1.78	19	0.73	2	0.51	37
3	Gestational age at delivery >37 weeks	17	0.73	88	1.08	14	1.31	116
4	Total	30		107		16		153

Table 2: Relation of hemoglobin concentration with SCD, SCT, and other HHs

Sr. No.	*Hemoglobin concentration*	*Sickle cell disease*	*Sickle cell trait*	*Heterogeneous hemoglobinopathy*	*Control*
1	≤6	15	6	0	4
2	6.1–9	9	46	6	48
3	9.1–11	6	50	6	89
4	>11	0	5	4	12
5	Total	30	107	16	153

(*n* = 153), and without a hemoglobinopathy (*n* = 153). Our study aims at finding associations and comparing various characteristics between both the populations.

Materials and Methods

This retrospective cohort study was conducted at Dhiraj Hospital, Vadodara between July 2020 and May 2023. In our institute, approximately 10,000 deliveries were done in 3 years. Complete medical data were extracted from the patient's clinical records. Out of them, approximately 238 deliveries were of pregnancies with a hemoglobinopathy. The ones matching our inclusion and exclusion criteria were accepted for the study

Inclusion Criteria

Inclusion criteria for the study group were healthy women with a hemoglobinopathy without other comorbidities and age ≥18 years (*n* = 153). The control group included pregnant women without a hemoglobinopathy and comorbidities (*n* = 153).

Exclusion Criteria

The following criteria were excluded from the study:

- Pregnant women with other established medical disorders like renal disease, cardiac disease, diabetes, hypertensive disorder, asthma, or any chronic medical condition before pregnancy.
- Previous history of coagulopathy, bad obstetric history, and sepsis.
- Women gave birth outside the center.
- Women not willing to provide written and informed consent.

Statistical analysis was conducted. Data were analyzed using SPSS software. The Chi-square test was used for the comparison of the two groups. The *p*-value of the probability was considered significant for a value < 0.05. Relative risks were also calculated.

Results

It is well known that pregnancy and sickle cell disease have a reciprocal influence on each other and their alliance is a risk situation. Out of the approx 10,000 deliveries in our institute in 3 years, about 238 deliveries were of pregnancies with a hemoglobinopathy. Out of them, 153 deliveries met our inclusion criteria which have included in our study. Out of 153 deliveries, 30 were SCD pregnancies, 107 were sickle cell trait (SCT) pregnancy, and 16 were HHs including heterozygous b thalassemia, delta thalassemia, hemoglobinopathy C, D, and E.

Table 3: Relation of route of delivery with hemoglobinopathies

Sr. No.	*Route of delivery*	*Hemoglobinopathy*	*Relative risk*	*Control*
1	Vaginal	81	0.87	93
2	Instrumental	3	0.25	12
3	Elective C-section	69	1.43	48

In our study increased gravidity was found in pregnancies with SCD, SCT, and HHs with a relative risk of 2.08, 1.42, and 1.73, respectively, as shown in Table 1. The mean age of the study group and control group was derived to be 25.9 and 24.5 years, respectively, and no significant association was found between them. As depicted in Table 1, greater chance of preterm deliveries was found in SCD pregnancies (gestational age at delivery <37 weeks) with RR value of 1.78 while no such association with SCT or heterozygous pregnancies is found.

In our study, Hb concentration levels were markedly decreased in SCD pregnancies, less so in SCT and heterogeneous hemoglobinopathies when compared with control group as shown in Table 2. The mean hemoglobin levels in case of SCD pregnancies, SCT pregnancies and other HHs were found to be 6.38, 8.25, and 9.29 gm%, respectively, while it was found to be 10.1 gm% in the control group.

Increased elective C-section deliveries are associated with SCD and SCT pregnancies as compared with control group, most likely due to increase in fetal distress and fetal acidosis and in order to prevent the complications which can be induced by vaginal delivery (Table 3).

As seen in Table 4, in SCD pregnancies, obstetric complications like previous miscarriage, preeclampsia, intrauterine growth restriction (IUGR), PPH, and mortality are found to have a positive association along with relative risks of 2.07, 2.42,3.5, 2.8, and 9.9, respectively, while gestational diabetes mellitus (GDM) does not a significant association (*p*-value > 0.05). Previous miscarriage and IUGR have a significant association with SCT pregnancies

Table 4: Relation of various maternal complications with SCD, SCT, and other heterogeneous hemoglobinopathies

Sr. No.	*Obstetric complications*	*Sickle cell disease*	*p-value (<0.05-significant)*	*Sickle cell trait*	*p-value (<0.05-significant)*	*Heterogeneous hemoglobinopathy*	*p-value (<0.05-significant)*	*Control*
1	Previous miscarriage	13	0.0175	38	0.0135	8	0.0349	32
2	Preeclampsia	10	0.0186	6	0.056	1	0.6490	21
3	Gestational diabetes mellitus	3	0.5453	13	0.4455	1	0.4837	25
4	IUGR	9	0.0062	19	0.0405	3	0.3765	13
5	Postpartum hemorrhage	8	0.0168	8	0.8019	1	0.9411	14
6	Mortality	4	0.0047	1	0.7541	0	0	2
	Nonobstetric complications							
7	Anemia	27	0.0085	78	0.0002	7	0.86	76
8	Blood transfusion	6	0.0268	5	0.75	0	0	9
9	Crisis	8	<0.00001	1	0.0027	0	0	2
10	Urinary tract infection	9	0.9025	29	0.6230	1	0.8037	18
11	Intrahepatic cholestasis	1	0.56	4	0.51	0	0	9

Table 5: Relation of neonatal complications with SCD, SCT, and other heterogeneous hemoglobinopathies

Sr. No.	*Neonatal complications*	*Sickle cell disease*	*p-value (<0.05-significant)*	*Sickle cell trait*	*p-value (<0.05-significant)*	*Heterogeneous hemoglobinopathy*	*p-value (<0.05-significant)*	*Control*
1	Hepatic encephalopathy	5	0.0234	1	0.2823	0	0	6
2	Septicemia	13	<0.000001	6	0.387	0	0	9
3	Anemia	15	0.0008	31	0.00253	7	0.0124	20
4	Jaundice	10	0.0094	10	0.425	1	0.748	19
5	Low birth weight	19	0.00003	39	0.0336	3	0.489	36
6	Perinatal death	8	0.0168	3	0.0746	1	0.941	14
7	Fetal acidosis	7	0.0032	6	0.8839	1	0.6163	8

with relative risks of 1.6 and 2.08, respectively, and also with other heterogeneous pregnancies with relative risk of 2.09 and 2.20, respectively, as depicted in Table 4. Whereas preeclampsia, GDM, PPH, and maternal mortality do not have positive association with HH including SCT. As seen in Table 4, non-obstetric complications like anemia, blood transfusion, crisis, and urinary tract infections have a positive association with SCD pregnancies with relative risk of 1.8, 3.4, 19.8, and 2.5, respectively, while intrahepatic cholestasis does not have a significant association.

As shown in Table 5, in SCD pregnancies, neonatal complications like hepatic encephalopathy, septicemia, anemia, jaundice, low birth weight, perinatal death, and fetal acidosis have a significant association with relative risk values of 4.08, 7.36, 3.82, 2.6, 2.6, 2.8, and 1.85, respectively, while only anemia and low birth weight have a significant association with SCT pregnancy and heterogeneous hemoglobinopathy with relative risk of 2.21 and 1.91, respectively.

Discussion

Hemoglobinopathic pregnancies are considered high risk for both mothers and fetus. Favorable outcomes can be obtained by continuous preconceptional, antenatal, and postpartum assessment. Premarriage counseling and prenatal screening of partners of these women should be done to decrease the burden of the society. In the present study in women with sickle cell disease, significant increase in gravidity is seen along with slight increase in gravidity in women with HHs. The reason for this being a higher abortion rate in such women, likewise corresponding with previous findings by Charoenboon et al.[8] The mean age of study group and control group in our study were 25.9 and 24.5 years, respectively, which corresponds well with the study by Anderson et al.[9]

The mean HB concentration in SCD, SCT, HH, and control group were 6.38, 8.25, 9.29, and 10.1%, respectively, in our study which corresponds well with similar study by Tuck et al. which concluded that 65% of SCD mother in UK had hemoglobin concentration of less than 10 gm%.[10] Another study by Sonwane et al. also found mean hemoglobin as –7.65 gm% in SCD mothers, 8.77 gm% in SCT mothers.[11] The reasons for lower HB in these women are sequestration crisis, iron and folate deficiency and continued hemolysis owing to qualitative defect in HB. This further increases incidence of blood transfusion and iron overload. Prophylactic blood transfusion during pregnancy is not advised by Children's Oncology Group (COG). In the present study, SCD requires blood transfusion during pregnancy which is significantly high (20%) compared with SCT group and Control group. Similar findings were also found in a study by Daigavane et al. and Resende et al.[12,13]

There is significant increase in incidence of urinary tract infection observed in SCD women, little bit increase in SCT women as compared with control group presumably due to decreased resistance due to low immunity and severe anemia. These findings are in accordance with study by Curdy and Tuck.[10,14] Increased incidence of crisis in SCD due to hemolytic crisis and anemia is also observed by Oteng-Ntim et al., Mayur M.,Daigavane et al., Al Kahtani, and Alayed et al.[12,15–17] Maternal death is significantly high in case of SCD mother when compared due to disseminated intravascular coagulation (DIC), severe anemia and atonic uterus in our study. This was in concordance with other studies by Daigavane et al. (10%) and Resende et al. (29.6%).[12,13]

In our study, incidence of PPH in SCD women is significantly higher compared with control group, similar results are reported in a study by Kobak et al.[18] More PPH is due to anemia and toxemia of pregnancy.

Conclusion

Our study has identified significantly increased morbidity among pregnant women with sickle cell disease and slightly increased in morbidity in heterogeneous hemoglobinopathies associated pregnancies. Perinatal outcome was also found to be adverse in SCD pregnancies more than SCT pregnancies. A close supervision of these pregnancies with a multidisciplinary approach by hematologist, obstetrician, and pediatrician is essential for early identification, prompt and better antenatal care and effective treatment of complications. Information, education, and communication session for sickle cell women are essential to minimize these risks.

Clinical Significance

This study would help in determining the effect of various hemoglobinopathies, with focus on SCD and SCT, on pregnancy with relation to mother's and baby's health which in essential for counselling the couple for prevention. The associations established by this study would further help in minimizing and possibly preventing the adverse fetomaternal outcomes.

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