ORIGINAL RESEARCH

Assessing Feto-Maternal Outcomes In Pregnancies With Hemoglobinopathies

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Received: 20 July, 2018 Accepted: 24 August, 2018

ABSTRACT

Background: Anemia is one of the most common diseases of pregnancy that includes inherited disorders and nutritional deficiency as the major causes of anemia. Pregnant females who have hemoglobinopathies and are asymptomatic before pregnancy can present with severe anemia in pregnancy owing to the physiological changes.

Aim: The present study aimed to assess the feto-maternal outcomes along with neonatal and obstetric outcomes in pregnancies with hemoglobinopathy.

Methods: The present study assessed 400 pregnant females with hemoglobinopathies where neonatal and maternal outcomes were assessed for the subjects that presented to the Institute within the defined study period. In all the included subjects, medical data were assessed and recorded followed by statistical analysis for formulation of the results.

Results: Among 400 pregnant females with hemoglobinopathies, in different types of hemoglobinopathies, HbE homozygous has shown the highest presence with 39% (n=78) subjects. In obstetrics outcomes preterm were seen in 35.9% (n=28) subjects and cesarean deliveries in 60% (n=46) subjects, the highest maternal complications were seen in subjects with HbE with β Thalassemia trait with 87.2% (n=68) subjects. In the HbE homozygous group, NICU admissions and low birth weight were higher and seen in 54.1% (n=80) and 62.1% (n=92) study subjects respectively.

Conclusion: The present study concludes that in subjects with feto-maternal complications, they are higher in subjects with HbE along with β Thalassemia trait, however, there is no associated neonatal stillbirth or maternal mortality in these subjects.

Keywords: Hemoglobinopathy, HbE homozygous,maternal outcome, pregnancy,β Thalassemia

INTRODUCTION

Hemoglobinopathies signify the disorders that affect the production, function, or structure of the hemoglobin. It is the most common disorder affecting the single gene. These are mostly the autosomal recessive disorders that present co-dominant traits. Since ages, owing to human migration, inherited hemoglobinopathy which was once endemic in the tropics and subtropics has become global. More than 270 million subjects globally are heterozygous carriers of hereditary disorders of hemoglobin and nearly 300,000 homozygotes and compound heterozygotes are born every year. Across the world, subjects residing in certain regions are at higher risk of encountering hemoglobinopathy.[1]

Following the data by WHO, a minimum of 5.2% of the global population with a 7% prevalence in pregnant females have a significant variant of hemoglobin disorder. In all the inherited disorders, hemoglobinopathy forms the major bulk of genetic diseases in India.Thalassemia major is most common in India, nearly 1-1.5 lakh child subjects are affected every year. The prevalence of sickle cell anemia is in the range of 3-50 in eastern India. Following ICMR data, the prevalence of HbE disease is high in India.[2]

Pregnancy is a state depicting the increase in consumption of oxygen, viscosity, and physiological anemia linked to significant mortality and morbidity in females with hemoglobinopathy. Anemia is the most common disorder seen in pregnant females including inherited disorders and nutritional deficiency as the major causes.[3]

Pregnant females who have hemoglobinopathies and are asymptomatic before pregnancy can present with severe pregnancy anemia owing to physiological changes in pregnancy.[4] The present study aimed to

assess the feto-maternal outcomes along with neonatal and obstetric outcomes in pregnancies with hemoglobinopathy.

MATERIALS AND METHODS

The present prospective clinical study was aimed to assess the feto-maternal outcomes along with neonatal and obstetric outcomes in pregnancies with hemoglobinopathy. The study subjects were from the Department of Obstetrics and Gynaecology of the Institute. Verbal and written informed consent were taken from all the subjects before participation.

The study assessed 400 pregnant females with hemoglobinopathies who presented to the Institute within the defined study period. Inclusion criteria for the study were subjects that were managed with emergency, antenatal subjects with hemoglobinopathies reporting to the institute, and subjects willing to participate in the study. The exclusion criteria for the study were ectopic pregnancy, multifetal pregnancy, hyperthyroidism, hypothyroidism, type 2 diabetes mellitus, gestational diabetes mellitus, gestational hypertension, bleeding disorders, renal disease, cardiac diseases, and reduced participation.

The females attending antenatal OPD and delivered at the Institute were considered for data collection which was done on preformed structured proforma from time to time from participation to delivery along with neonatal outcomes. Following current guidelines by the CDC (Centre for Disease Control), USA, anemia in pregnancy is considered for 11gm/dl.[5] In all the subjects, an automated blood count analyzer was used to assess LFT, TIBC, serum ferritin, serum iron, and complete hematogram. Subjects with hemograms suggesting microcytic features were further assessed for hemoglobinopathy using high-performance liquid chromatography at the Institute.

Subjects with hemoglobinopathy were further assessed for detailed obstetric history, past surgical history, drug history, and menstrual history. Presenting complaints and findings of obstetrics, systemic, and general examination were reported on the proforma. Other investigations done were viral markers, culture sensitivity, urine routine assessment, USG-gravid uterus, coagulation profile, serum TSH, RFT, and LFT. On assessing hemoglobinopathies, females/partners with prior hemoglobinopathy history, further genetic counseling was advised. Subjects with thyroid disorders, gestational diabetes mellitus, and gestational hypertension were excluded as these diseases act as confounding factors for postpartum hemorrhage, preterm birth, IUGR, congenital anomaly, stillborn, and/or abortion.

Subjects with <8g/dl hemoglobin with iron deficiency were treated with injectable iron. Females >37 weeks with Hb 7g/dl with iron deficiency were managed with injectable iron. Females with Hb <37 weeks of gestation, birth weight – macrosomia, intrauterine growth restriction defined as birth weight below 3rd percentile, low birth weight defined as a birth weight below 2500 g, Apgar score at 1 minute and 5-minute, stillbirth and neonatal death defined according to UNICEF and WHO, and admissions to the neonatal unit care (NICU).

The data gathered were analyzedstatistically using SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk. NY, USA) for assessment of descriptive measures, Student t-test, ANOVA (analysis of variance), and Chi-square test. Pearson correlation coefficient was used to assess correlation in various parameters. The results were expressed as mean and standard deviation and frequency and percentages. The p-value of <0.05 was considered.

RESULTS

The present prospective clinical study was aimed to assess the feto-maternal outcomes along with neonatal and obstetric outcomes in pregnancies with hemoglobinopathy. The present study assessed 400 pregnant females with hemoglobinopathies where neonatal and maternal outcomes were assessed for the subjects that presented to the Institute within the defined study period. For distribution of hemoglobinopathies in study subjects, HbE homozygous was seen in 39% (n=156) subjects, HbE trait in 35% (n=140) study subjects, HbE with β thalassemia in 19.50% (n=78) subjects, β thalassemia trait in 4.50% (n=18) subjects, and β thalassemia homozygous and sickle cell trait in 1% (n=4) study subjects each (Table 1).

It was seen that for maternalcomplications in subjects with hemoglobinopathies, no maternal complications were seen in 12.8% (n=10), 24.3% (n=38), 0, 33.3% (n=6), 0, and 57.1% (n=80) subjects with HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively. Maternal complications were seen in 87.2% (n=68), 75.6% (n=156), 100% (n=4), 66.7% (n=12), 100% (n=4), and 42.8% (n=60) subjects respectively with HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait. In total, with HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait were seen in 78, 156, 4, 18, 4, and 140 subjects respectively (Table 2).

The study results showed that for various maternal complications in postnatal and antenatal period in study subjects, ICP was seen in 0, 4, 0, 2, 2, and 4 subjects with HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively, abortion was positive in 2, 8, 0, 0, 0, and 6 subjects with withHbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively, UTI in 18, 32, 0, 6, 2, and 24 subjects with HbE with β thalassemia, HbE homozygous, β

thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively, jaundice in 36, 28, 4, 8, 4, and 26 subjects withwithHbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively, and PPH in 22, 36, 4, 0, 0, and 20 subjects with withHbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively.PPROM was seen in 12, 24, 0, 2, 0, and 8 subjects with HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively and PROM in 8, 22, 0, 2, 0, and 10 subjects with HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively. No complication was seen in 10, 38, 0, 6, 0, and 80 subjects withHbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively which was statistically significant with p<0.001 (Table 3).

For assessment of birth weight of neonates delivered at birth, for birth weight of <2.5kg, HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait was seen in 33.3% (n=16), 47.2% (n=50), 100% (n=4), 66.7% (n=8), 50% (n=2), and 40% (n=116) subjects respectively. For the birth weight of ≥2.5 kg, HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait was seen in 66.7% (n=32), 52.8% (n=56), 0, 33.3% (n=4), 50% (n=2), and 60% (n=174) subjects respectively. The difference was statistically non-significant with p=0.1361 (Table 4).

It was also seen that for APGAR scores in neonates at 1 and 5 minutes, APGAR score <7 at 1 min was 0, 4, 0, 0, 0, and 0 and was 0, 0, 0, 0, 0, 0, and 0 at 5 minutes. APGAR score >7 was 0, 0, 0, 0, 0, 0, and 0 at 1 minute and was seen in 100% (n=76), 97.3% (n=144), 100% (n=4), 100% (n=18), 100% (n=4), and 100% (n=134) subjects respectively (Table 5).

Hemoglobinopathy	Number (n)	Percentage (%)
Sickle cell trait	4	1
β thalassemia homozygous	4	1
β thalassemia trait	18	4.50
HbE with β thalassemia	78	19.50
HbE trait	140	35
HbE homozygous	156	39
Total	400	100

Table 1: Distribution of hemoglobinopathies in study subjects

Maternal complications	HbE with β thalassemia	HbE homozygous	β thalassemia homozygous	β thalassemia trait	Sickle cell trait	HbE trait	total
No (n)	10	38	0	6	0	80	134
%	12.8	24.3	0	33.3	0	57.1	33.5
Yes (n)	68	118	4	12	4	60	266
%	87.2	75.6	100	66.7	100	42.8	66.5
Total (n)	78	156	4	18	4	140	400
%	100	100	100	100	100	100	100

Table 2: Maternal complications in subjects with hemoglobinopathies

Complications	HbE with β thalassemia	HbE homozygous	β thalassemia homozygous	β thalassemia trait	Sickle cell trait	HbE trait	p-value
ICP	0	4	0	2	2	4	**<0.001**
Abortion	2	8	0	0	0	6	
UTI	18	32	0	6	2	24	
Jaundice	36	28	4	8	4	26	
PPH	22	36	4	0	0	20	
PPROM	12	24	0	2	0	8	
PROM	8	22	0	2	0	10	
None	10	38	0	6	0	80	

Table 3: Various maternal complications in the postnatal and antenatal period in study subjects

Birth weight	HbE with β thalassemia	HbE homozygous	β thalassemia homozygous	β thalassemia trait	Sickle cell trait	HbE trait	p-value
<2.5	16 (33.3)	50 (47.2)	4 (100)	8 (66.7)	2 (50)	116 (40)	0.1361
≥2.5	32 (66.7)	56 (52.8)	0	4 (33.3)	2 (50)	174 (60)	
Total	48 (100)	106 (100)	4 (100)	12 (100)	4 (100)	290 (100)	

Table 4: Birth weight of neonates delivered at birth

Categories	HbE with β thalassemia	HbE homozygous	β thalassemia homozygous	β thalassemia trait	Sickle cell trait	HbE trait	Total
APGAR <7							
1 min	0	4 (2.7)	0	0	0	0	4 (1)
5 min	0	0	0	0	0	0	0
APGAR >7							
1 min	0	0	0	0	0	0	0
5 min	76 (100)	144 (97.3)	4 (100)	18 (100)	4 (100)	134 (100)	380 (99)
Total	76 (100)	148 (100)	4 (100)	18 (100)	4 (100)	134 (100)	384 (100)

Table 5: APGAR scores in neonates at 1 and 5 minutes

DISCUSSION

The present study assessed 400 pregnant females with hemoglobinopathies where neonatal and maternal outcomes were assessed for the subjects that presented to the Institute within the defined study period. For distribution of hemoglobinopathies in study subjects, HbE homozygous was seen in 39% (n=156) subjects, HbE trait in 35% (n=140) study subjects, HbE with β thalassemia in 19.50% (n=78) subjects, β thalassemia trait in 4.50% (n=18) subjects, and β thalassemia homozygous and sickle cell trait in 1% (n=4) study subjects each. These data were comparable to the previous studies ofHanprasertpong T et al[6] in 2013 and Natu N et al[7] in 2014 where authors assessed subjects with demographic and disease data comparable to the present study in their respective studies.

The study results showed that for maternal complications in subjects with hemoglobinopathies, no maternal complications were seen in 12.8% (n=10), 24.3% (n=38), 0, 33.3% (n=6), 0, and 57.1% (n=80) subjects with HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively. Maternal complications were seen in 87.2% (n=68), 75.6% (n=156), 100% (n=4), 66.7% (n=12), 100% (n=4), and 42.8% (n=60) subjects respectively with HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait. In total, with HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait were seen in 78, 156, 4, 18, 4, and 140 subjects respectively. These results were consistent with the findings of Charoenboon C et al[8] in 2015 and Al-Riyami N et al[9] in 2014 where maternal complications in subjects with hemoglobinopathies reported by the authors in their studies were comparable to the results of the present study.

It was seen that for various maternal complications in postnatal and antenatal period in study subjects, ICP was seen in 0, 4, 0, 2, 2, and 4 subjects with HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively, abortion was positive in 2, 8, 0, 0, 0, and 6 subjects with withHbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively, UTI in 18, 32, 0, 6, 2, and 24 subjects with HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively, jaundice in 36, 28, 4, 8, 4, and 26 subjects withwithHbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively, and PPH in 22, 36, 4, 0, 0, and 20 subjects with withHbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait respectively which was statistically significant with $p<0.001$. These findings were in agreement with the results of Kemthong W et al[10] in 2015 and Chauhan A[11] in 2015 where maternal complications in the postnatal and antenatal period in study subjects

similar to the present study were reported by the authors in their respective studies.

On assessing the birth weight of neonates delivered at birth, for birth weight of <2.5kg, HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait was seen in 33.3% (n=16), 47.2% (n=50), 100% (n=4), 66.7% (n=8), 50% (n=2), and 40% (n=116) subjects respectively. For the birth weight of ≥2.5 kg, HbE with β thalassemia, HbE homozygous, β thalassemia homozygous, β thalassemia trait, sickle cell trait, and HbE trait was seen in 66.7% (n=32), 52.8% (n=56), 0, 33.3% (n=4), 50% (n=2), and 60% (n=174) subjects respectively. The difference was statistically non-significant with p=0.1361. These results were in line with the findings of theKasparek J et al[12] in 2015 and AngastiniotisM et al[13] in 1998 where the birth weight of neonates delivered at birth and hemoglobinopathies reported by the authors in their studies were comparable to the results of the present study.

The study results also showed that for APGAR scores in neonates at 1 and 5 minutes, APGAR score <7 at 1 min was 0, 4, 0, 0, 0, and 0 and was 0, 0, 0, 0, 0, 0, and 0 at 5 minutes. APGAR score >7 was 0, 0, 0, 0, 0, 0, and 0 at 1 minute and was seen in 100% (n=76), 97.3% (n=144), 100% (n=4), 100% (n=18), 100% (n=4), and 100% (n=134) subjects respectively. These findings correlated with the results ofSirichotiyakulS et al[14] in 2015 and LuewanS et al[15] in 2009 where APGAR scores in neonates at 1 and 5 minutes similar to the present study were also reported by the authors in their respective studies.

CONCLUSIONS

The present study, within its limitations, concludes that in subjects with feto-maternal complications, they are higher in subjects with HbE along with β Thalassemia trait, however, there is no associated neonatal stillbirth or maternal mortality in these subjects.

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