

# Fetomaternal outcome of pregnancy with hemoglobinopathy

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## ABSTRACT

**Objectives:** The objectives of this study are to determine the obstetric and neonatal outcome in pregnancy with hemoglobinopathy. **Methods and materials:** A prospective observational study to evaluate maternal and neonatal outcome in pregnant women with hemoglobinopathy. The medical data of the study group attending antenatal OPD/emergency and delivering at Guwahati medical college and hospital between August 1<sup>st</sup>, 2021 to 31<sup>st</sup> July, 2022 were extracted and recorded in the proforma. **Results:** A total of 200 pregnant women with hemoglobinopathy were included in the study. Among the various types of hemoglobinopathy HbE homozygous constituted the highest with 39% (n=78). Among obstetric outcomes preterm (35.9%, n=14) and caesarean delivery (60%, n=23), maternal complications (87.2%,n=34) were higher in patients with HbE with  $\beta$  Thalassemia trait. Low birth weight (62.1%,n=46), NICU admission (54.1%,n=40) were higher in HbE homozygous group. **Conclusion:** In our study patients with fetomaternal complications were higher in patients having HbE with  $\beta$  thalassemia but there were no maternal mortality or stillbirth in the study population.

**Keywords:** Hemoglobinopathy and pregnancy, maternal outcome, HbE homozygous.

Haemoglobinopathies are disorders affecting the structure, function or production of hemoglobin<sup>1</sup>. It is the most common single gene disorder. They are mostly autosomal recessive disorders and also express co-dominant traits. Over the ages because of human migration, inherited hemoglobinopathy which was once endemic in tropics and sub tropics has become worldwide now. More than 270 million population in the world are heterozygous carriers of hereditary disorders of hemoglobin. About 300,000 homozygotes and compound heterozygotes are born every year<sup>2</sup>. Globally, the population of certain regions are at higher risk of having a hemoglobinopathy<sup>2</sup>.

As per WHO at least 5.2% of the world population, with a prevalence of 7% in pregnant population carries a significant variant of hemoglobin disorder<sup>2</sup>. Among the inherited disorders, hemoglobinopathy forms the major bulk of genetic disease in India. Thalassemia major is most common in India, about 1 to 1.5 lakh of children are affected every year<sup>3</sup>. The prevalence of sickle cell anemia ranges

from 5-40% among the tribal population in India. Hemoglobin variants like HbE range from 3-50% in eastern India<sup>3</sup>. As per ICMR, prevalence of HbE disease is 23% in Assam.

Pregnancy is a state of increase in oxygen consumption, viscosity and physiological anemia is associated with significant morbidity and mortality in women with hemoglobinopathy. Anemia is the most common disease in pregnancy which includes nutritional deficiency and inherited disorders as the major causes. Pregnant women with hemoglobinopathy who are asymptomatic before pregnancy might present with severe anemia in pregnancy due to the physiological changes in pregnancy. In the present study we are going to evaluate the maternal and neonatal outcomes among a cohort of pregnancies with diagnosed hemoglobinopathy attending Guwahati medical college and hospital, a tertiary care center in Assam.

## Materials and methods

Total 200 pregnant women with hemoglobinopathy

**Received:** 12<sup>th</sup> March 2023, **Peer review completed:** 26<sup>th</sup> May 2023, **Accepted:** 31<sup>th</sup> May 2023.

Goswami B, Das P, Monesha K. Fetomaternal outcome of pregnancy with hemoglobinopathy. The New Indian Journal of OBGYN. 2024; 10(2): 388 - 95.

admitted in the department of obstetrics and gynaecology, GMCH were included in the study for a period of 1 year between August 1<sup>st</sup>, 2021 to 31<sup>st</sup> July, 2022.

**Inclusion criteria** - Antenatal patients diagnosed with hemoglobinopathy attending GMCH OPD, emergency and managed in the department of obstetrics and gynaecology, GMCH who are willing to participate in the study were enrolled.

**Exclusion criteria** - Refused participation, Pregnant women with cardiac disease, renal disease, bleeding disorders, gestational hypertension, gestational diabetes mellitus, type 2 diabetes mellitus, hypothyroidism, hyperthyroidism, multifetal pregnancy, ectopic pregnancy.

**Data collection technique** - A prospective observational study to evaluate maternal and neonatal outcome in pregnant women with hemoglobinopathy was approved by the institutional ethics committee of Gauhati Medical College and Hospital, Guwahati.

The medical data of the study group attending antenatal OPD/emergency and delivering at Guwahati medical college and hospital were extracted and recorded in the proforma. Data of the patients were collected in a proforma from time to time from the antenatal period from the time of enrolment till delivery along with neonatal outcome after obtaining a written informed consent from the patient/legal guardian of the patient.

According to current guidelines by the Centre for Disease Control, USA, anemia in pregnancy is defined as hemoglobin less than 11 gm/dl<sup>4</sup>. In our study complete hematogram, serum iron, serum ferritin, TIBC, LFT were done through automated blood count analyzer. Patients with hematogram suggesting microcytic features were further screened for hemoglobinopathy with high performance liquid chromatography in the department of clinical hematology, GMCH. Patients with hemoglobinopathy were further evaluated. Detailed menstrual history, drug history, past surgical history, obstetric history was taken. Presenting complaints and findings of general, systemic and obstetric examinations were documented in the proforma. Other investigations like LFT, RFT, serum TSH, coagulation profile, USG-gravid uterus, urine routine and culture sensitivity, viral markers were done. Partner was also tested for haemoglobinopathy. In case of women and partner having hemoglobinopathy, further genetic counseling was recommended. Patients who developed gestational hypertension, gestational diabetes mellitus, thyroid disorders during the study period were excluded from the study as

these disorders act as a confounding factor for postpartum hemorrhage/ abortion/ stillborn/ congenital anomaly/ IUGR/ preterm birth.

Women with Hb < 8 g/dl along with iron deficiency were treated with injectable iron. Women > 37 weeks with Hb <7 g/dl were given blood transfusion.

Anemia in the postpartum period with hemoglobin levels >7g/dl along with iron deficiency were treated with injectable iron. Women with Hb <7g/dl were given blood transfusion. The following obstetric outcome were examined - abortion, mode of delivery, placenta previa, preterm premature rupture of membrane, premature rupture of membrane, postpartum hemorrhage, puerperal infection including pelvic infections, mastitis, and breast abscesses, urinary infections, postpartum anemia, blood transfusion, hospital stay duration. The following neonatal outcomes were investigated: gestational age at birth, birth weight, preterm delivery (< 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).

**Statistical analysis** - All data were analyzed using Microsoft Excel, Graph Pad Prism, and IBM SPSS V21. All data were analyzed using SPSS version 21. A p-value less than 0.05 is considered statistically significant at a 5% level of significance.

## Results

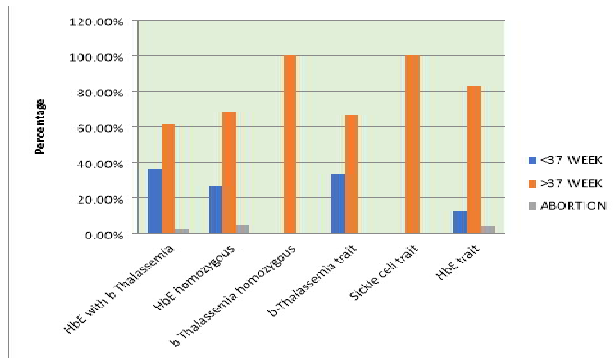
In this study, 82 (41%), 79 (39.5%), 37 (18.5%), 2 (1%) belonged to the age group 19-24 years, 25-29 years, 30-34 years, 35-39 years respectively. The minimum age and maximum age are 19 and 39 years respectively. 79 (39.5%) patients were primigravida. Higher gravida was found in 75 (37.5%) patients due to the increased rate of abortion in patients with hemoglobinopathy. In this study 75 patients had abortions in the previous pregnancy. Spontaneous abortion in 1<sup>st</sup> and 2<sup>nd</sup> trimesters was found in 69 (92%) patients and 6(8%) patients had a medical termination of pregnancy.

The distribution of hemoglobinopathies among the study population of 200 pregnant women is shown in table 1. HbE homozygous were 39% (n=78), HbE heterozygous were 35% (n=70) and HbE with  $\beta$  thalassemia were 19.5% (n=39) and  $\beta$  thalassemia heterozygous were 4.5% (n=9),  $\beta$  thalassemia

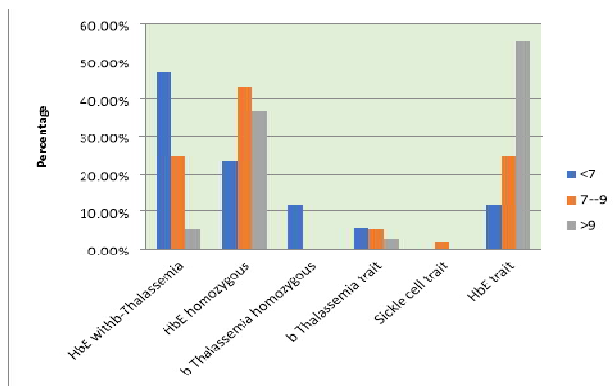
homozygous (n=2) and sickle cell heterozygous (n=2) constituted 1% each.

**Table 1: Distribution of hemoglobinopathies among the study population**

Hemoglobinopathy	Frequency	Percentage
HbE homozygous	78	39%
HbE trait	70	35%
HbE with $\beta$ thalassemia	39	19.50%
$\beta$ thalassemia trait	9	4.50%
$\beta$ thalassemia homozygous	2	1%
Sickle cell trait	2	1%
Total	200	100%



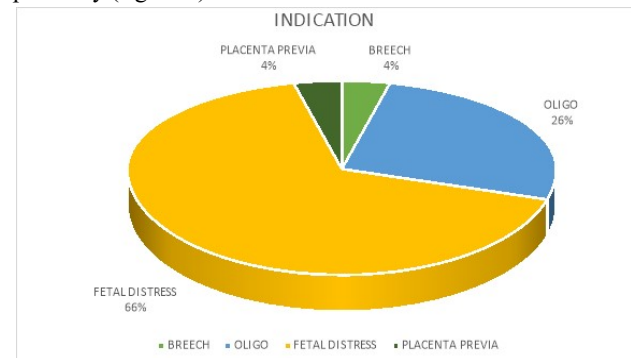
**Figure 1: Gestational age at delivery of the participants.**



**Figure 2: Hb levels at the time of delivery**

In this study out of 200 patients, 192 numbers of women had delivered. 121 (63.02%) patients had a spontaneous vaginal delivery and 71 (36.9%) had lower segment cesarean delivery. 47 patients (23.5%) had a preterm delivery and 145 patients (72.5%) had term delivery. Among hemoglobinopathies preterm delivery was found in 14 (35.9%), 21 (26.9%), 3 (33.3%), and 9 (12.9%) patients with HbE  $\beta$  thalassemia homozygous, HbE homozygous,  $\beta$  thalassemia

trait, and HbE trait respectively. In this study, 8 patients (4%) had abortion, of which 1, 4 and 3 patients belonged to HbE  $\beta$  thalassemia, HbE homozygous and HbE trait respectively (figure 1).



**Figure 3: Indications of cesarean delivery**

Of the 200 patients with hemoglobinopathy, severe anemia was found in 17 (8.5%) patients, 109 (54.5%) had moderate anemia and 74 (37%) patients had mild anemia. In the severe anemia group, 8 (47.1%) patients had HbE with  $\beta$  thalassemia, 4 (23.5%) patients had HbE disease, 2 (11.5%) patients had  $\beta$  Thalassemia homozygous and 2 (11.5%) patients had HbE trait and 1 (5.9%) patient had  $\beta$  thalassemia trait (figure 2). There is a statistically significant association between hemoglobin levels and hemoglobinopathy group with p value <0.001.

In this study out of 121 vaginal delivery, 18 (14.9%) were instrumental vaginal delivery and 103 (85.1%) were non-instrumental vaginal delivery. Out of 71 LSCS procedure, 59 (83.1%) were emergency and 12 (16.9%) were elective surgery. The most common indication of cesarean delivery was fetal distress with 66.1% (n=47) followed by oligohydramnios 25.3% (n=18). Cesarean delivery due to breech presentation was seen in 3 (4.2%) patients. Placenta previa was the indication for cesarean delivery in 3 (4.2%) patients (figure 3). There is a statistically significant association between the mode of delivery and different types of hemoglobinopathies with p value <0.001, cesarean delivery was higher in patients with HbE with  $\beta$  thalassemia with 60% (n=23) and lower in patients with  $\beta$  thalassemia trait with 11.1% (n=1) followed by HbE trait with 11.4% (n=8). Spontaneous vaginal delivery was higher in patients with  $\beta$  thalassemia trait with 88.9% (n=8) followed by HbE trait with 84.3% (n=59) and lower in patient with HbE with  $\beta$  thalassemia with 38% (n=15).

**Table 2: Maternal complications in the patients with hemoglobinopathy**

Maternal complications	Hemoglobinopathy							Total
	HbE with $\beta$ Thalassemia	HbE homozygous	$\beta$ Thalassemia homozygous	$\beta$ -thalassemia trait	Sickle cell trait	HbE trait		
No	Count	5	19	0	3	0	40	67
	% within hemoglobinopathy	12.8%	24.3%	0	33.3%	0	57.1%	33.5%
Yes	Count	34	59	2	6	2	30	133
	% within hemoglobinopathy	87.2%	75.6%	100%	66.7%	100%	42.8%	66.5%
Total	Count	39	78	2	9	2	70	200
	% within hemoglobinopathy	100%	100%	100%	100%	100%	100%	100%

**Table 3: Frequency of various maternal complications in antenatal and postnatal period**

Complications	HbE with $\beta$ Thalassemia	HbE homozygous	$\beta$ Thalassemia homozygous	$\beta$ -thalassemia trait	Sickle cell trait	HbE trait	P value
PROM	4	11	0	1	0	9	<0.001
PPROM	6	12	0	1	0	4	
PPH	11	18	2	0	0	10	
Jaundice	18	14	2	4	2	13	
UTI	9	16	0	3	1	12	
Abortion	1	4	0	0	0	3	
ICP	0	2	0	1	1	2	
None	5	19	0	3	0	40	

PROM – Premature rupture of membrane, PPRM – Preterm premature rupture of membrane, PPH – Postpartum haemorrhage, UTI – Urinary tract infection, ICP – Intrahepatic cholestasis of pregnancy

**Table 4: Birth weight of the baby delivered at term**

Birth weight	Hemoglobinopathy							P value
	HbE with $\beta$ thalassemia	HbE homozygous	$\beta$ thalassemia homozygous	$\beta$ thalassemia trait	Sickle cell trait	HbE trait	Total	
<2.5	8 (33.3%)	25 (47.2%)	2 (100%)	4 (66.7%)	1 (50%)	18 (31%)	58 (40%)	0.1363
$\geq$ 2.5	16 (66.7%)	28 (52.8%)	0 (0%)	2 (33.3%)	1 (50%)	40 (69%)	87 (60%)	
Total	24 (100%)	53 (100%)	2 (100%)	6 (100%)	2 (100%)	58(100%)	145(100%)	

In this study with 200 participants, 100 (50%) patients had hospital stay > 4 days and 100 (50%) patients had hospital stay duration  $\leq$ 4 days. Maximum patients with HbE with  $\beta$  thalassemia 26 (66.6%) had hospital stay > 4 days. Out of 70 patients with HbE trait 27 (38.5%) had hospital stay > 4 days which is lower in comparison with other hemoglobinopathies in this study. There is a statistically significant association between the hospital stay duration and different types of hemoglobinopathy with p value 0.022. Anemia correction and NICU admission was found in 40.59% of the patient being a major reason for hospital stay >4 days.

Among the 200 study population, 133 (66.5%) patients had maternal complications and 67 (33.3%) patients did not have maternal complications (table 2). There is a statistically significant association between maternal complications and different types of hemoglobinopathy with a p value <0.0001, complications were higher in patients with  $\beta$  thalassemia homozygous, sickle cell trait group with 100% (n=2) each followed by HbE  $\beta$  thalassemia with 87.2% (n=34), while 57.1% (n=40) patients with HbE trait had no maternal complications in the antenatal and postnatal period.

In this study out of 200 patients, 133 patients had one or more maternal complications. Of the maternal complications, jaundice (indirect hyperbilirubinemia) was higher and found in 26.50% of the patients followed by PPH and UTI with 20.50% each. Intrahepatic cholestasis of pregnancy was seen in 3% of the patients. Jaundice was higher in patients with HbE with  $\beta$  thalassemia (n=18) followed by HbE homozygous (n=14) and lower in patients with HbE trait (n=13). PPH was higher in patients with HbE homozygous (n=18) followed by HbE with  $\beta$  thalassemia (n=11) and lower in patients with HbE trait (n=10). Abortion was found in 8 (4%) patients with hemoglobinopathy. There is a statistically significant association between the various maternal complication and different types of hemoglobinopathy with a p value < 0.001, complications were higher in patients with HbE with  $\beta$  thalassemia followed by HbE homozygous and lower in patients with HbE trait (table 3).

There is a statistically significant association between blood transfusion in the antenatal period and different types of hemoglobinopathy with p value <0.001, higher in patients with  $\beta$  Thalassemia and sickle cell trait with 100% (n=2)

each followed by  $\beta$  thalassemia trait with 66.7% (n=6) and lower in patients with HbE trait with 77.1% (n=54). There is a statistically significant association between blood transfusion in the postnatal period and different types of hemoglobinopathy with a p value <0.001, higher in patients with  $\beta$  thalassemia and sickle cell trait with 100% (n=2) each followed by  $\beta$  thalassemia trait with 66.7% (n=6) and lower in patients with HbE trait with 77.6% (n=52).

Out of 145 term deliveries, 58 (40%) had fetal growth restriction, higher in patients with  $\beta$  thalassemia homozygous with 100 % (n=2), followed by  $\beta$  thalassemia trait with 66.7% (n=4) and lower in patients having HbE trait with 69% (n=40).

In this study, 2 babies delivered by patients with HbE homozygous had APGAR at 1 minute <7. All the 192 babies had APGAR score >7 at 5 minute

In this study out of 192 babies, 86 (44.7% ) required

**Table 5: APGAR score at 1 minute and 5 minute**

Categories	Time	Hemoglobinopathy						Total
		HbE with $\beta$ thalassemia	HbE homozygous	$\beta$ thalassemia homozygous	$\beta$ thalassemia trait	Sickle cell trait	HbE trait	
APGAR <7	1 MIN	0	2 (2.7%)	0	0	0	0	2 (1%)
	5 MIN	0	0	0	0	0	0	0
APGAR >7	1 MIN	0	0	0	0	0	0	0
	5 MIN	38 (100%)	72 (97.3%)	2 (100%)	9 (100%)	2 (100%)	67(100%)	190 (99%)
Total	Total	38 (100%)	74 (100%)	2 (100%)	9 (100%)	2 (100%)	67(100%)	192(100%)

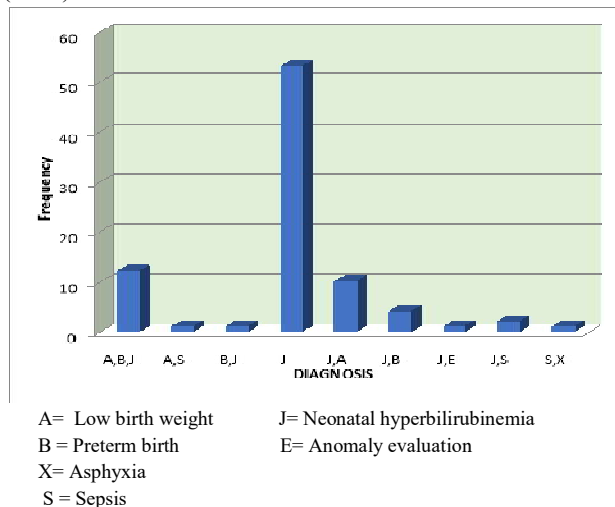
In this study with 200 patients, 192 patients had live birth. Babies with birth weight <2.5kg were 105 (54.6%) and 87 (45.3%) babies were with birth weight >2.5kg. Out of 105 babies with low birth weight, 46 (43.4%), 27 (25.5%), 22 (21.7%), 7 (6.6%), 2 (1.9%), 1 (0.9%) were delivered by patients with HbE homozygous, HbE trait, HbE with  $\beta$  thalassemia,  $\beta$  thalassemia trait,  $\beta$  thalassemia homozygous and sickle cell trait respectively. There is a statistically significant association between birth weight and different types of hemoglobinopathy with P value <0.047, low birth weight was higher in patients with  $\beta$  Thalassemia homozygous 100% (n=2) followed by HbE homozygous 62.1% (n=46) and lower in patients with HbE trait with 40% (n=27).

NICU admission and 106 (55.2%) did not require NICU admission. There is a statistically significant association between NICU admission of the baby and different types of hemoglobinopathy with p value 0.0054. NICU admission was higher in patients with  $\beta$  thalassemia homozygous and sickle cell trait with 100% (n=2) each followed by  $\beta$  thalassemia trait with 66.7% (n=6) and HbE homozygous with 54.1% (n=40) and lower in patients with HbE trait with 28.4% (n=19).In this study, 86 babies delivered by patients with hemoglobinopathy were admitted in NICU. Higher NICU admission was due to neonatal hyperbilirubinemia with 62.4% (figure 4). Congenital anomaly was found in 3 patients. Club foot was in 2 babies and fetal hydrops in 1 fetus.

**Discussion**

In our study out of 200 participants, patients with HbE homozygous were 39% (n=78), HbE trait were 35% (n=70), HbE  $\beta$  thalassemia were 19.50% (n=39),  $\beta$  thalassemia trait were 4.50% (n=9), and there were 2 (1%) patients with sickle cell trait and  $\beta$  thalassemia homozygous each. Kasperek et al<sup>5</sup> observed in a study in 2021, out of 172 women 84 were with HbE  $\beta$  thalassemia which was higher compared to our study due to different geographical locations.

In our study we observed, severe anemia was found in 8 (47.15 %) patients having HbE with  $\beta$  thalassemia trait, 4 (23.5%) patients with HbE disease and 2 (11.5%) patients with HbE trait. There were 2 patients with  $\beta$  thalassemia homozygous, both had severe anemia. The mean hemoglobin of patients with HbE with  $\beta$  thalassemia was 8.24g/dl (SD 0.76) in this study which is comparable to the study



**Figure 4: Reason for NICU admission**

conducted by Luewan et al <sup>6</sup> in 2009 where the mean Hb was 8.12g/dl.

In our study the mean hemoglobin level of HbE homozygous was 8.9g/dl (SD 0.84), whereas in a study conducted by Sirichotiyakul et al <sup>7</sup> in 2016, the mean Hb level was 10.03g/dl (SD 2.10). In a study conducted by Philip et al <sup>8</sup> a high prevalence (15.8%) of hemoglobinopathies was found amongst microcytic hypochromic anemia cases.

In our study, maximum patients had microcytic hypochromic anemia with MCV <76fL found in 101(50.5%) patients, MCH <27pg was found in 180(90%) patients and MCHC <32 g/dl was found in 157(78.5%) patients. Out of 101 (50.5%) patients with microcytosis, higher number of patients belong to HbE trait with 17.8% (n=18) followed by  $\beta$  thalassemia homozygous with 1.9% (n=2). The mean MCV were 62.23 fL (SD 17.3) and 78.2 Fl (SD 4.26) in  $\beta$  thalassemia homozygous and HbE trait respectively. Similarly HbE trait was less microcytic than beta thalassemia traits in a study conducted by Yeo et al <sup>9</sup> their study which is comparable with our study.

In our study out of 200 patients, 79 (39.5%) patients were primigravida. Higher gravida was found in 75 (37.5%) patients due to increased rate of abortion. Out of which 69 patients (92%) had spontaneous abortion in 1<sup>st</sup> and 2<sup>nd</sup> trimesters and 8 (6%) patients had a medical termination of pregnancy. Kasperek et al <sup>5</sup> in 2021 reported, 54 (31.3%) out of 172 patients with hemoglobinopathy had increased gravidity due to previous abortions which is comparable with our study.

Out of 200 patients in the present study, 47 patients (23.5%) had a preterm delivery, 145 patients (72.5%) had a term delivery and 8 (4%) had a spontaneous abortion. Kasperek et al <sup>5</sup> in a study in 2021, observed preterm delivery in 12.8% (n=22) and term delivery in 87.2% (n=152) of the patients with hemoglobinopathy which is comparable to our study. Chauhan et al <sup>10</sup> in 2018, reported, 56 (93%) had term delivery, 2 (2.3%) had preterm delivery and 2 (3.3%) had a spontaneous abortion among 60 patients with hemoglobinopathy. The lower abortion rate and preterm births may be due to the smaller sample size compared to the present study. In this study the preterm delivery rate in patients having HbE trait and HbE with  $\beta$  thalassemia were 12.9% and 35.9% respectively which are comparable to studies of Kemthong et al <sup>11</sup> in 2016 and Luewan et al <sup>6</sup> in 2009. Sirichotiyakul et al <sup>7</sup> reported abortion in 2.5% and preterm delivery in 10.5% in patients having HbE

homozygous. The higher rates in our study may be due poor antenatal visit and follow-up.

In the present study, out of 192 patients, spontaneous vaginal delivery was found in 103 (53.64%) patients, instrumental vaginal delivery in 18 (9.3%) patients and lower segment cesarean delivery in 71 (36.9%). Out of the 71 patients with LSCS, 59 (83.1%) were emergency and 12 (16.9%) were elective surgery. Spontaneous vaginal delivery is higher in patients with  $\beta$  thalassemia trait with 88.9% (n=8) followed by HbE trait with 84.3% (n=59) and lower in patient with HbE with  $\beta$  thalassemia with 38% (n=15) in our study. Chauhan et al <sup>10</sup> reported LSCS in 50%, vaginal delivery in 42%, and instrumental vaginal delivery in 5%. Similarly in a study conducted by Kasperek et al <sup>5</sup>, vaginal delivery was found in 50.6%, cesarean delivery in 49.4%, instrumental delivery in 7.6%, and elective LSCS in 27.3%. The higher rate of vaginal delivery in our study may be due to better intrapartum care. In the present study, cesarean delivery was higher in patients having HbE with  $\beta$  thalassemia with 60% (n=23) and lower in patients having  $\beta$  thalassemia trait with 11.1% (n=1). Cesarean delivery is 50%,11.4% and 11.1% in patients with  $\beta$  Thalassemia homozygous, HbE trait and  $\beta$  Thalassemia trait respectively which is comparable to studies of Al-Riyami et al <sup>12</sup>, Kemthong et al <sup>11</sup> and Charoenboon et al <sup>13</sup>. However, in a study Luewan et al <sup>6</sup> in 2009, reported 27.8% cesarean delivery in patient having HbE with  $\beta$  thalassemia and Sirichotiyakul et al <sup>7</sup>, reported 21.2% cesarean delivery in patients with HbE homozygous. The rate is higher in our study because of increased FGR rate in these hemoglobinopathy group.

The most common indication for cesarean delivery in our study was fetal distress with 66.1% (n=47) followed by oligohydramnios with 25.3% (n=18). Cesarean delivery due to breech presentation and placenta previa was 4.2% (n=3) each. Similarly in a study conducted by Chauhan et al <sup>10</sup>, the most common indication of LSCS was fetal distress (33.3%) which is comparable to our study.

In this study with 200 participants, 100 (50%) patients had prolonged hospital stay >4 days, higher in patients with HbE with  $\beta$  thalassemia (66.6%) and lower in patients with HbE trait where (38.5%). Anemia correction was the reason for prolonged hospital stay in maximum patients (66.33%).

In our study among the 200 study population,133 (66.5%) patients had maternal complications, higher in patients with  $\beta$  thalassemia homozygous, sickle cell trait group with 100% (n=2) each followed by HbE  $\beta$  thalassemia

with 87.2% (n=34), while 57.1% (n=40) patients with HbE trait had no maternal complications in the antenatal and postnatal period. Of the maternal complications, jaundice was most common with 26.5%. It was higher in patients with HbE with  $\beta$  thalassemia with 9% (n=18) followed by HbE homozygous with 7% (n=14) and lower in patients with HbE trait 6.5% (n=13). In a study conducted Natu et al<sup>14</sup>, jaundice was observed in 3.7% of the patients with sickle cell traits. Overall, PPH and UTI were found in 20.50% each in our study. PPH was higher in patients with HbE homozygous 9.3% (n=18) followed by HbE with  $\beta$  thalassemia 5.7% (n=11) and lower in patients with HbE trait 5.2% (n=10) in the present study. Charoenboon et al<sup>13</sup> in 2016, reported PPH in 3.5% and UTI in 2.5% in patients with  $\beta$  thalassemia trait and Luewan et al<sup>6</sup> in 2009, 5.6% with HbE with  $\beta$  thalassemia had PPH which are comparable to our study. However, in a study conducted by Sirichotiyakul et al<sup>7</sup>, PPH was reported in 2.5% in patients with HbE homozygous and Kemthong et al<sup>11</sup>, reported PPH in 3.2% of patients with HbE trait. The higher rate of PPH in our study may be due to poor antenatal visit and anemia correction in the antenatal period.

Intrahepatic cholestasis of pregnancy was reported in 3% of the patients in our study, whereas in a study conducted by Kasperek et al<sup>5</sup>, it was reported in 11.5% patients, the reason is unclear and further studies needed to evaluate the association between hemoglobinopathy and intrahepatic cholestasis of pregnancy. PROM, PPROM, UTI were also higher in patients with HbE homozygous followed by HbE with  $\beta$  thalassemia in our study. Overall, in the present study, higher complications were found in patients with HbE with  $\beta$  thalassemia followed by HbE homozygous and lower in patients with HbE trait. Blood transfusion was higher in this study because of poor antenatal follow up by the patients and failure to correct anemia in the antenatal period leading to increased blood transfusion in the postnatal period.

In this study with 200 patients, 192 patients had live birth. Low birth weight were found in 54.6% (n=105). It was higher in patients with  $\beta$  Thalassemia homozygous with 100% (n=2) followed by HbE homozygous with 62.1% (n=46) and lower in patients having HbE trait with 40% (n=27). Fetal growth restriction was seen in 40% (n=58) of the patients in our study, higher in patients with  $\beta$  thalassemia homozygous with 100% (n=2), followed by  $\beta$  thalassemia trait with 66.7% (n=4) and lower in patients having HbE trait with 69% (n=40). Hanprasertpong et al<sup>15</sup> inferred in a study conducted in 2013, LBW in 6% and FGR

in 1.8% of the patients with hemoglobinopathy. Similarly, in a study conducted by Kasperek et al<sup>5</sup>, low birth weight was found in 12.5% and FGR in 5.1% and Chauhan et al<sup>10</sup>, reported 6.66% had fetal growth restriction. The higher incidence of FGR and LBW in our study may be due to increased preterm births, poor antenatal visits and follow-up and low socio-economic status of the study population.

In our study, out of 192 babies delivered 2 babies had APGAR at 1 minute <7 and they were delivered by patients with HbE homozygous. NICU admission for various reasons seen in 44.7% babies, higher in patients with  $\beta$  thalassemia homozygous and sickle cell trait with 100% (n=2) each followed by  $\beta$  thalassemia trait with 66.7% (n=6) and HbE homozygous with 54.1% (n=40) and lower in patients with HbE trait with 28.4% (n=19). Higher NICU admission is due to neonatal hyperbilirubinemia with 62.4% and lower is due to asphyxia and sepsis with 1% each. However, in a study conducted by Hanprasertpong et al<sup>15</sup>, NICU admission was seen in 1.6% babies and Kasperek et al<sup>5</sup>, reported NICU admission in 10.3%. The higher incidence in our study may be due to increased preterm and FGR rate.

In the present study, 3 (1.5%) patients delivered a baby with congenital anomaly club foot, 1 patient with HbE with  $\beta$  thalassemia delivered a baby with fetal hydrops. However, Luewan et al<sup>6</sup>, reported fetal anomaly is seen in 3.7% in patients with HbE with  $\beta$  thalassemia. No still births were observed in our study due to better intrapartum care.

### Conclusion

Recent advances in the diagnosis and treatment of hemoglobinopathy has made it possible for women to have successful pregnancy. The physiological changes during pregnancy aggravate the effect of hemoglobinopathy which leads to maternal and neonatal complications. Feto-maternal complications were high in patients having HbE with  $\beta$  thalassemia but there was no maternal mortality or still birth of the study population in our study. Thus, with comprehensive obstetric care and multidisciplinary approach better feto-maternal outcome can be achieved.

The strength of this study is patients were recruited from a single center and excluded cases with potential confounders. The limitations of this study are small sample size, shorter period and hemoglobinopathy types were not distributed equally among the study population. So the information retrieved from this study cannot be generalized.

**Conflict of interest:** None. **Disclaimer:** Nil.

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