International Journal Of Medical Sciences; January 2024;7(1):9-17;
ISSNe:2522-7386; DOI: https:/doi.org/10.32441/ijms.7.1.2

Foeto-maternal Outcome for Pregnant Women with Hemoglobinopathies in Basrah – Southern Iraq

Wassan Mohammed Saed, Mobile: +9647714900384, Email: wassanmohammed 1985@gmail.com, Basrah, Iraq.
Muhsin Al-Sabbak, College of Medicine, University of Basrah, Basrah, Iraq.
Email: muhsin_alsabak@yahoo.com; Mobile: +9647808225008;
ORCID: https://orcid.org/0000-0002-4548-477X.
Mayssara Al-Badran, College of Medicine, University of Basrah, Basrah, Iraq.
Email: mysaram1979@gmail.com; Mobile: +9647712045056.
ORCID: https://orcid.org/0000-0002-5923-8799.

Correspondence author: Wassan Mohammed Saed, Mobile: +9647714900384, Email: wassanmohammed 1985@gmail.com, Basrah, Iraq.

Received: 09/11/2023 Accepted: 20/12/2023 Published: 01/01/2024

To cite the article: Saed, Wasan Mohammed; Al-Sabak, Muhsin; Al-Badran, Maysara. Foeto-maternal Outcome for Pregnant Women with Hemoglobinopathies in Basrah – Southern Iraq. Int J Med Sci 2024;7(1): 9-17. DOI: https://doi.org/10.32441/ijms.7.1.2

Abstract

Background: Anaemia is a significant global health concern. Hereditary haemoglobin abnormalities are one of the most frequent causes of anaemia in pregnant women. Pregnant women with Hemoglobinopathies are at increased risk for adverse pregnancy outcomes, such as preterm birth, intrauterine growth restriction, and low birth weight. The study aimed to determine the fate of pregnancies in women with hemoglobinopathies and to identify the predictors for adverse outcomes among these ladies.

Subjects and Methods: Acase-control study was conducted in Basrah Teaching Hospital for maternity and children from the 1st of September 2022 to the 1st of July 2023. One hundred nine women were included in the study, 33 ladies with sickle cell trait group, 22 ladies with thalassemia minor and 57 ladies as healthy controls. The socio-demographic, pregnancy-related characteristics, maternal morbidity, and maternal and fetal outcomes were assessed in this study.

Results: The current study found thatsickle cell trait has a higher risk of emergency C-section (20%), while Thalassemia minor has a higher risk of elective C-section (22.7%). Sickle cell traits significantly increase the risk of puerperal infection (23.3%), and they also increase the risk of urinary tract infection (20%). Hemoglobinopathies, particularly sickle cell trait, significantly increase the risk of gestational diabetes mellitus (16.7%), but there is no significant increment in the risk of other maternal outcomes. Both sickle cell trait and thalassemia minor are significantly associated with lower BMI, lower Hb, and lower serum ferritin levels (P-value < 0.05).

Conclusion: Sickle cell trait and thalassemia minor increase the risk of poor maternal and fetal outcomes.

Keywords: Pregnancy, anaemia, hemoglobinopathies, Basrah.

Introduction

Anaemia is a significant global health concern. According to the World Health Organisation (WHO), anaemia is characterised by haemoglobin (Hb) levels below 12.0 g/dL in females and 13.0 g/dL in males [1]. While anaemia in pregnancy is defined as having a haemoglobin level below 110 g/L at any point during pregnancy and below 100 g/L postpartum [2]. Up to one-third of the world's population is affected by anaemia, which is a very common disease. This condition is more prevalent in women of reproductive age, expectant women, and the elderly. The World Health Organisation estimates that 37% of expectant women and 30% of women aged 15–49 are anaemic [3].

Anaemia may be caused by acquired causes such as nutrient deficiencies through inadequate diets or inadequate absorption of nutrients, infections (e.g., malaria, parasitic infestations, tuberculosis, HIV), inflammation, chronic diseases, gynaecological and obstetric conditions [4-6], an inherited red blood cell disorders such as sickle-cell anaemia, thalassemia, and hereditary spherocytosis [7]. Anaemia during pregnancy is associated with poor mother and child health and increases the risk of maternal and perinatal death. The mother's poor health outcomes include fatigue, reduced productivity, immune system dysfunction, a greater likelihood of heart disease, and death [8,9].

It is also associated with an increased risk of intrauterine deaths (IUFD), a low APGAR score at 5 minutes, and intrauterine growth restriction (IUGR), which is a risk factor for short stature among children of less than two years [4,10]. According to the WHO, over 5.2% of people worldwide are thought to have a significant variant of a haemoglobin disorder; among pregnant women, the prevalence is even higher than 7% [11].

Sickle cell disease is one of the most prevalent genetic disorders in the world that is characterised by autosomal recessive hemoglobinopathy, which includes sickle cell HbSS disease and various compound heterozygous genotypes (such as sickle cell HbSC disease or sickle cell beta-thalassemia disease [HbSßthal])[12,13].

Thalassemia is an autosomal recessive disorder in which two copies of an abnormal gene must be present for the disease to manifest, whereas carriers or traits who have one abnormal copy have no symptoms but can pass the abnormal gene onto their progeny. According to the number of functioning globin alleles, the severity of thalassemia varies [14]. The main goal of hemoglobinopathies screening in pregnant women is to identify mothers and foetuses at risk for hemolytic anaemia due to sickle cell disease and other abnormal haemoglobin variants, for which early intervention has been shown to significantly reduce morbidity and mortality [15].

Method

This is a case-control study conducted in Basrah Teaching Hospital for maternity and children over a 10-month duration (1st of September 2022 to 1st of July 2023). To determine the fate of the pregnancies in women with hemoglobinopathies and to identify the predictors for adverse outcomes among these ladies. One hundred nine women were included in the study, these women were divided into three groups:

Group 1: contains 30 women with sickle cell trait.
Group 2: contains 22 women with thalassemia minor.
Group 3 contains 57 healthy women without hemoglobinopathies.

All women came to the hospital for delivery, they were sent for a complete blood count to assess the severity of their anaemia, as well as serum ferritin level to screen for the cases who had hemoglobinopathy with iron deficiency anaemia. The data collected from Basrah

Teaching Hospital for Maternity and Children outpatient clinic or labor ward, those who registered at the Centre of Hereditary Blood Diseases in Basra were also included.
A questionnaire was developed for the sake of this study, the questionnaire includes the following:

1. Socio-demographic characteristics of the patient: age, occupation residency, educational level.
2. Pregnancy-related characteristics: gravity, party, any previous abortions, current pregnancy complications, and expected date of delivery.
3. Any maternal morbidity: UTI, preeclampsia, APH, PPH, Gestational diabetes.

The mother's anthropometric measurements were assessed including weight, height, and BMI.
A systemic examination and blood pressure measurement was carried out.
Then for each woman, 4 ml of blood was aspirated.

- Two ml of it was put in an EDTA tube for complete blood count measurement.
- The other 2 ml was put into a plain plastic tube and centrifuged to get the serum which separated and stored at -20 C, then serum ferritin was estimated by a special ELISA kit.

The method of delivery and Neonatal outcomes such as birth weight, Apgar score, and neonatal intensive care unit (NICU) admission were noted. Any abnormalities like neonatal jaundice, malformations, and neonatal death if present were studied also. The patients were followed up till their discharge from the postnatal ward. Data were analysed using Statistical Package for Social Sciences (SPSS) version 26. Quantitative data were presented as (mean ± standard deviation) while qualitative data were presented as frequencies and percentages.The appropriate statistical tests were performed, and the level of significance (p-value) was set at ≤ 0.05.

Results

The study involved 109 pregnant women who were divided into three groups, those with sickle cell trait 30 women, thalassemia trait 22 women, and the control healthy group with 57 women. Their age mean was 30 years. The majority of them were between 20-29 years. Regarding their residency, the majority of participants live in urban areas. the highest percentage of women had primary education and were housewives.

Regarding their parity, 50% of women with sickle cell trait had 1-4 children in comparison to 45.5% of those with thalassemia trait. But still, there are no significant differences between the three groups p-value=0.702. Also, there are no significant differences regarding the gestational age of delivery p-value =0.894. The majority of women in this study delivered at term. All this data is presented in Table 1.

Table 2 shows the mode of delivery among the participants women. The highest percentage of normal vaginal delivery was 70.2% of women in the control group in comparison to around 50% of women in the other groups. The Highest percentage of elective cesarean sections 22.7% was among women in the thalassemia trait group. The emergency cesarean section occurs most commonly among the sickle cell trait group. Even though there are no significant statistical differences regarding the mode of delivery between the three groups since the P value = 0.459.

Table 3 shows the maternal complications among the participant women. There is no significant difference regarding the UTI, preeclampsia, Placenta abruption, APH, and PPH since the p-value >0.05. On the other hand, gestational diabetes and Puerperium infection

were more common among the sickle trait group. There is a significant statistical difference among the three groups p-value < 0.05.

Table 1: The socio-demographic characteristics of the participants

Variables		Sickle cell trait Group	Thalassemia trait Group	Control group	p-value
Age	Mean ±SD	30.6 ±4.9	31.2 ±2.4	32.7 ± 3.4	0.674
	< 20	9 (30.0)	8(36.3)	15 (26.3)	
	20-29	20 (33.3)	10 (45.5)	21 (36.8)	
	30-39	8(26.7)	3 (13.7)	15 (26.3)	
	≥40	3 (10.0)	1 (4.5)	6 (10.6)	
Residency	Rural	12 (40.0)	9 (40.9)	22(38.5)	0.979
	Urban	18 (60.0)	13(59.1)	35 (61.5)	
Social class	Primary	18 (60.0)	14 (63.7)	26 (45.6)	0.561
	Secondary	7 (23.3)	7 (31.8)	22 (38.6)	
	College and higher education	5 (16.7)	1 (4.5)	9 (15.8)	
Employment status	Housewives	25 (56.7)	15(68.2)	36(63.2)	0.894
	Employed	15(43.3)	7 (31.8)	21 (36.8)	
Parity	Primigravida	9 (30.0)	10 (45.5)	22 (38.6)	0.702
	2-4	15 (50.0)	10 (45.5)	28 (49.1)	
	5	6 (20.0)	2 (9.0)	7(12.3)	
Gestational age	Preterm	4 (13.3)	3 (13.6)	6(10.5)	0.894
	Term	26 (86.7)	19 (86.4)	51 (89.5)	
Total		30 (100.0)	22 (100.0)	57 (100.0)	109

Table 2: The mode of delivery among the participant women

Variables	Sickle cell trait Group	Thalassemia trait Group	Control group	p-value
Spontaneous vaginal delivery	17 (56.7)	13 (59.1)	40 (70.2)	0.459
Induced vaginal delivery	3(10.0)	2 (9.1)	7 (12.3)	
Elective cesarian section	4(13.3)	5(22.7)	6 (10.5)	
Emergency cesarian section	6 (20.0)	2 (9.1)	4 (7.0)	

Table 3: The maternal complication among the participant women

Variables	Sickle cell trait	Thalassemia trait	Control group	p-value
UTI	6 (20.0)	3(13.6)	3 (5.3)	0.103
Preeclampsia	2 (6.7)	2(9.1)	3 (5.3)	0.822
Placenta abruption	1 (3.3)	1 (4.5)	3 (5.3)	0.919
APH	1 (3.3)	1 (4.5)	2 (3.5)	0.969
PPH	1(3.3)	1 (4.5)	2(3.5)	0.969
Gestational diabetes	5 (16.7)	1 (4.5)	1(1.8)	0.024
Puerperium infection	7 (23.3)	2 (9.1)	3(5.3)	0.035

Table 4 shows the fetal outcome among the studied women. There is no significant difference regarding abortion, preterm delivery, IUGR, low birth weight, admission to the NICU, and low APGAR score since the p-value > 0.05.On the other hand, neonatal death shows a significant statistical difference between groups p-value=0.001.

Table 4: The fetal outcome among the studied women

Variables	Sickle cell trait Group	Thalassemia trait Group	Control group	p-value
Abortion	3 (10.0)	1(4.5)	2(3.5)	0.440
Preterm delivery	4 (13.3)	3(13.6)	3 (5.3)	0.333
IUGR	2 (6.7)	2 (9.1)	3(5.3)	0.822
Low birth weight	3 (10.0)	3 (13.6)	1 (1.8)	0.099
Admission to the neonatal intensive care unit	4 (13.3)	2 (9.1)	3 (5.3)	0.424
Low Apgar score	2(6.7)	1(4.5)	1 (1.8)	0.493
Neonatal death	1 (3.3)	0 (0.0)	0 (0.0)	0.001

Table 5 shows the clinical profile of the participants, the BMI was higher among the control group and there is a significant statistical difference p-value= 0.035. The postpartum Hb level and serum ferritin level were measured, and it showed lower levels among the sickle cell trait group and the thalassemia trait group in comparison to the control group. P-value <0.05.

Table 5: The clinical profile of the participants

Variables	Sickle cell trait Group	Thalassemia trait Group	Control group	p-value
BMI	**24.6 ±1.4**	**24.3 ±1.3**	**27.3 ±2.1**	**0.035**
Post-partum Hb level	**9.1 ±1.5**	**9.2 ± 2.1**	**10.5±1.8**	**0.045**
Serum ferritin level	**17.3± 1.3**	**16.2± 1.4**	**19.1±2.5**	**0.016**

Discussion

The World Health Organisation (WHO) reports that a minimum of 5.2% of the global population has a significant variant of a haemoglobin disorder; the prevalence is even higher for pregnant women, at over 7%.[16]. The tropics and subtropical areas are recognised as having inherited haemoglobin disorders; Iraq in general and Basrah specifically have a high prevalence of hemoglobinopathies, particularly sickle cell anaemia [17]; therefore, we formulated this study to assess the maternal outcome and complications among pregnant ladies with hemoglobinopathies.Even though anaemia during pregnancy is an important predictor of adverse maternal and neonatal outcomes, previous studies on the impact of a hemoglobinopathy trait on pregnancy have yielded conflicting results and inconsistent conclusions.

Regarding the mode of delivery, the current study found a significant difference neither with sickle cell trait nor with thalassemia minor in comparison with control; however, we found a high occurrence of elective caesarean sections with thalassemia and a high prevalence of emergencycaesarean sections with sickle cell trait. Still, we reported that most of the ladies in both groups had a normal vaginal delivery. Our findings are consistent with the findings of a recent multicentric study from Switzerland by Kasparek et al. (2021), who assessed around 500 pregnant ladies with hemoglobinopathies and found that there was no variation in the mode of delivery or the percentage of having caesarean sections (49.4% vs. 43.6%; $p = 0.227$).[16].

Although there is no significant association between the urinary tract infection and the hemoglobinopathies if compared with control, the study showed a higher risk of UTI among ladies with sickle cell trait. Our results align with the systematic review by Jans et al. (2010)[18] as well as to the study of Kemthong et al. (2016), who found a minimal increase in asymptomaticbacteriuria.[19].

Low renal arterial oxygen tension and abnormal blood flow to the kidneys distinguish SCD patients. This results in unusual urinary acidification and the inability to concentrate urine, which increases the possibility of urinary tract infections.[20]. The current study found no significant association between hemoglobinopathies and increased risk of pre-eclampsia, placental abruption, antepartum, or post-partum haemorrhage. However, it is not in line with Hanprasertpong et al. (2013), who stated that pre-eclampsia should be considered, particularly in nulliparous and high BMI pregnant women with thalassemia trait [21].

The current study found that hemoglobinopathies did not lead to a significantly increased risk of abortion, preterm labour, intrauterine growth restriction (IUGR), or low birth weight; however, there was a higher risk of abortion among sickle cell train (10%) as

well as an equally higher risk of preterm delivery among both sickle cell trait and thalassemia minor in comparison to control.

These findings are consistent with those of Charoenboon et al. (2016), who discovered that the prevalence of small for gestational age and preterm birth tended to be greater in the thalassemia minor group but had not reached statistical significance, whereas the prevalence of low birth weight was significantly higher in the thalassemia minor group [22]. On the other hand, Kasparek et al. (2021) discovered that patients with hemoglobinopathies do not differ substantially in any other adverse neonatal outcome; however, they discovered a significant disparity in the spontaneous abortion rate [16].

Subsequently, the current study did not prove a significant increase in the rate of neonatal admission to intensive care units or a low APGAR score among pregnant women with hemoglobinopathies; however, the rate is higher in comparison with the control. Also, we reported a significant increase in neonatal deaths among ladies with sickle cell trait, but fortunately, there is only one dead newborn, so the statistical analysis will not be as accurate due to the small sample size. Our findings are consistent with Kasparek et al. (2021), who found that hemoglobinopathies will not increase the risk of low APGAR score,NICU admission, neonatal death, or stillbirth; however, they found that those neonates are at higher risk of fatal acidosis when compared to controls [16]. They claimed that a rise in foetal acidosis could be attributable to complications in women with a hemoglobinopathy trait and, consequently, placental insufficiency.

Regarding BMI, we found a significantly lower BMI among sickle and thalassemia patients in comparison with controls, but the mean is within the normal range (around 24). Asare et al. (2017) found that people with sickle disorders have a lower BMI compared to those without sickle disorders due to a higher resting metabolic rate, which may be caused by hypermetabolism, increased hemolysis, red cell turnover, and cardiac demand [23].

This study also reported a significantly lower Hb level in patients with hemoglobinopathies (9.1 g/dl for sickle cell trait and 9.2 g/dl for thalassemia minor) in comparison with healthy controls ($P = 0.045$). We also reported significantly lower serum ferritin in both groups in comparison to controls ($P = 0.016$), but it is within the normal range. These findings are approximately similar to what Kasparek et al. (2021) reported, as they found an Hb level of around 10.6 g/dl, which is slightly higher than what we reported. Furthermore, they reported a higher ferritin level (41 µg/l) which is still within the normal range [21]. Another study by Jans et al. (2010) also reported an increased risk of anaemia among pregnant women with hemoglobinopathies [18].

To sum up, the pregnancy and neonatal outcome is minimally affected by the Hemoglobinopathies trait and most of our findings are in line with the published literature. To the best of our knowledge and according to our revision of the published literature, this is the first study reporting adverse pregnancy and neonatal outcomes among pregnant ladies in Basrah with hemoglobinopathies. However, we faced some limitations, which include the small sample size to gain power in differentiating rates of maternal and neonatal adverse outcomes, a retrospective approach in which several records contained missing or not perfectly reliable data, and some recall bias. Also, we were not surveying for certain complications such as intrahepatic cholestasis, thromboembolism, and foetal acidosis.

Conclusion

Sickle cell trait and thalassemia minor increase the risk of poor maternal and fetal outcomes.Hemoglobinopathies, particularly sickle cell trait, significantly increase the risk of

gestational diabetes mellitus**.** Additionally, both sickle cell trait and thalassemia minor are significantly associated with lower BMI, lower Hb, and lower serum ferritin levels.

ETHICAL APPROVAL

The research protocol was approved by the Ethical Committee of College of Medicine, Basrah University, Basrah, Iraq.

CONSENT TO PARTICIPATE:

Informed consent was taken from each subject before their enrolment in the study.

HUMAN AND ANIMAL RIGHTS

The study conducted in adherence with Helsinki Ethical standards.

FUNDING

No funding

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

Reference

1. Cappellini MD, Motta I. Anemia in Clinical Practice-Definition and Classification: Does Hemoglobin Change With Aging?. SeminHematol. 2015;52(4):261-269.
2. World Health Organization. The global prevalence of anaemia in 2011. Geneva: WHO, 2015 (cited at May 21). Available at www.who.int/nutrition/publications/micronutrients/global_prevalence_anaemia_2011/en
3. Anaemia [Internet]. Who.int. 2023 [cited 2023 May 21]. Available from: https://www.who.int/health-topics/anaemia
4. Msuya SE, Hussein TH, Uriyo J, Sam NE, Stray-Pedersen B. Anaemia among pregnant women in northern Tanzania: prevalence, risk factors and effect on perinatal outcomes. Tanzan J Health Res. 2011;13(1):33-39.
5. Okube O. T., Mirie W., Odhiambo E., Sabina W., Habtu M. Prevalence and Factors Associated with Anaemia among Pregnant Women Attending Antenatal Clinic in the Second and Third Trimesters at Pumwani Maternity Hospital, Kenya. Open Journal of Obstetrics and Gynecology. 2016;06(01):16–27.
6. McClure EM, Meshnick SR, Mungai P, Malhotra I, King CL, Goldenberg RL, Hudgens MG, Siega-Riz AM, Dent AE. The association of parasitic infections in pregnancy and maternal and fetal anemia: a cohort study in coastal Kenya. PLoSNegl Trop Dis. 2014;8(2):e2724.
7. Scott JA, Bass, BF. Hereditary anemia: Types of anemia that can be inherited [Internet]. Everydayhealth.com. 2010 [cited 2023 May 21]. Available from: https://www.everydayhealth.com/anemia/anemia-and-heredity.aspx.
8. Mbule MA, Byaruhanga YB, Kabahenda M, Lubowa A. Determinants of anaemia among pregnant women in rural Uganda. Rural Remote Health. 2013;13(2):2259.
9. Stevens GA, Finucane MM, De-Regil LM, Paciorek CJ, Flaxman SR, Branca F, et al. Nutrition Impact Model Study Group (Anaemia). Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995-2011: a systematic analysis of population-representative data. Lancet Glob Health. 2013 Jul;1(1):e16-25.

10. Gebre A, Mulugeta A. Prevalence of Anemia and Associated Factors among Pregnant Women in North Western Zone of Tigray, Northern Ethiopia: A Cross-Sectional Study. J NutrMetab. 2015;2015:165430.
11. Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. Bull World Health Organ. 2008;86(6):480–487.
12. Piel FB, Steinberg MH, Rees DC. Sickle Cell Disease. N Engl J Med. 2017;376(16):1561-1573.
13. Smith-Whitley K. Complications in pregnant women with sickle cell disease. Hematology Am SocHematolEduc Program. 2019;2019(1):359-366.
14. Harteveld CL, Higgs DR. Alpha-thalassaemia. Orphanet J Rare Dis. 2010;5:13.
15. Balgir RS. Prevalence of Hemolytic Anemia and Hemoglobinopathies among the Pregnant Women Attending a Tertiary Hospital in Central India. Thalassemia Reports. 2015; 5(1):4644.
16. Kasparek J, Burkhardt T, Hoesli I, AmstadBencaiova G. Pregnancy outcomes in women with a hemoglobinopathy trait: a multicenter, retrospective study. Arch Gynecol Obstet. 2021;304(5):1197-1203.
17. Hamamy HA, Al-Allawi NA. Epidemiological profile of common haemoglobinopathies in Arab countries. J Community Genet. 2013 ;4(2):147-67.
18. Jans SM, de Jonge A, Lagro-Janssen AL. Maternal and perinatal outcomes amongst haemoglobinopathy carriers: a systematic review. Int J ClinPract. 2010;64(12):1688-98.
19. Kemthong W, Jatavan P, Traisrisilp K, Tongsong T. Pregnancy outcomes among women with hemoglobin E trait. J Matern Fetal Neonatal Med. 2016;29(7):1146–1148.
20. Nath KA, Hebbel RP. Sickle cell disease: renal manifestations and mechanisms. Nat Rev Nephrol. 2015;11(3):161-71.
21. Hanprasertpong T, Kor-anantakul O, Leetanaporn R, Suntharasaj T, Suwanrath C, Pruksanusak N, Pranpanus S. Pregnancy outcomes amongst thalassemia traits. Arch Gynecol Obstet. 2013;288(5):1051-4.
22. Charoenboon C, Jatavan P, Traisrisilp K, Tongsong T. Pregnancy outcomes among women with beta-thalassemia trait. Arch Gynecol Obstet. 2016;293(4):771-4.
23. Asare EV, Olayemi E, Adomakoh Y, Mensah E, Swarray-Deen A, Ghansah H, et al. Low body mass index in pregnant women with sickle cell disease is associated with premature delivery in sub- Saharan Africa. Blood. 2017; 130:2250.