http:// ijp.mums.ac.ir
Short Communication (Pages: 18163-18171)

An Evaluation of the Relationship between Hemoglobin Level and Blood Transfusion in Pregnant Women with Intermedia Thalassemia: A Case Series Study

Alireza Rezvani [1], Zahra Alizadeh [1], Anahita Bahrampour [1], Nasrin Asadi [1], * Aida Bahrampour [1]

[1] Shiraz University of Medical Science, Shiraz, Iran.

Abstract

Background: Beta thalassemia intermedia is a group of anemias that are in the middle of the symptoms of beta thalassemia minor and major. Disturbance in the balance of alpha and beta chains causes different symptoms in patients. At one end of the spectrum are patients with mild symptoms, and at the other end the patients who may become dependent on blood transfusion, with difficulties deciding which patient needs blood transfusion and when. This challenge is more significant during pregnancy because blood transfusion at the wrong time and not transfusing when needed can cause complications in both mother and fetus.

Methods: In this one-year study, a total of 8 pregnant patients with intermedia thalassemia were studied, and according to the Australian guideline, patients with were not given blood unless they suffered from PHT, massive splenomegaly, IUGR; but patients with were transfused.

Results: Finally, the pregnancy outcome was compared in terms of birth weight and Apgar score; and there was no significant difference.

Conclusion: Hb level 7 during pregnancy can be considered safe for preventing unnecessary blood transfusion and their complications. This study can be the onset of a wider study in this field to help gynecologists for patient management.

Key Words: Blood Transfusion, B Thalassemia Intermedia, Complications, Pregnancy Outcome.

* Please cite this article as: Rezvani A, Alizadeh Z, Bahrampour A, Asadi N, Bahrampour A. An Evaluation of the Relationship between Hemoglobin Level and Blood Transfusion in Pregnant Women with Intermedia Thalassemia: A Case Series Study. Int J Pediatr 2023; 11 (08):18163-18171. DOI: **10.22038/ijp.2023.73456.5312**

****Corresponding Author:***

Aida Bahrampour, Shiraz University of Medical Science, Shiraz, Iran. Email: aydabahrampur@gmail.com

Received date: Jun.30,2023; Accepted date: Aug.13,2023

1- INTRODUCTION

In patients with different types of Thalassemia, as a congenital anemia, the synthesis of one or more globin is less than that in healthy people. Based on the chain whose construction has been damaged, the common types of thalassemia are divided into alpha, beta, gamma, and delta (1). Based on the clinical severity of the disease, beta thalassemia is divided into major, minor, and intermedia types (2); among these three types, intermedia thalassemia is the most challenging one because predicting the disease phenotype from the genotype is difficult. In fact, the severity of beta thalassemia intermedia is not determined based on the lack of beta chain, but based on the degree of imbalance of the chains (3, 4).

Pregnancy is associated with changes in different body systems, which makes the body more sensitive to oxidative stress (5). But the main challenge in pregnant women with thalassemia intermedia is determining whether they need blood transfusion (6). Blood transfusion is a primary treatment for thalassemia, but it has its own risks, such as hemosiderosis, allergic reactions to blood transfusion, alloimmunization, and accumulation of excess iron in organs, severe hyperplasia of the erythroid layer, and massive erythroid hyperplasia (7).

Complications caused by blood transfusions can occur in those who are not dependent on blood transfusions due to the body's attempt to compensate for the loss of red blood cells (RBCs), which itself leads to premature death of the fetus (8, 9). Also, in the case of alloantibody production due to crossing the placenta, hemolytic anemia occurs in the fetus or newborn (10).

Despite all the mentioned challenges, a comprehensive and practical study in the field of blood transfusion in pregnant women with thalassemia intermedia has not yet been conducted, which could be due to the small population of these patients in other countries (11). In general, the annual incidence of people with symptoms of the disease is estimated to be 1 in 100,000 worldwide (12).

Meanwhile, beta thalassemia major is the most common hemoglobinopathy in Iran (13-15). There are about 20,000 involved individuals and about 2-3 million people (4% of the population) carrying the disease in Iran (12, 16-18). As a result, after the completion of this study, it can be possible to design a comprehensive guideline to make decisions about blood transfusion in pregnant women with thalassemia intermedia easier and with scientific support.

Based on all the cases mentioned regarding the prevalence of beta thalassemia disease and the challenges and dangers regarding blood transfusion for pregnant women and the complications caused by blood transfusions in mothers and fetuses, we decided to design this study to determine the limit of hemoglobin for the safe transfusion in these patients. By determining the safe range of hemoglobin, it is possible to prevent inappropriate and unnecessary blood transfusion and the resulting complications for the mother and fetus and reduce the additional burden on the health system.

2- MATERIALS AND METHODS

2-1. Design and population

This project is a case series study conducted in 2019-2020 on patients referred to Hazrat Zainab, Namazi, and Hafez hospitals in Shiraz. The study population consisted of pregnant women with anemia (Hb≤10). The patients who had referred to a gynecologist and met the inclusion criteria were referred to a hematologist to confirm the diagnosis of beta-thalassemia intermedia. After that, they were subjected to periodic and regular follow-up by hematologists and gynecologists until delivery.

Due to the fact that this study is conducted as a pilot and no similar research has been undertaken so far, based on available sampling, all patients who met the inclusion criteria in the period of July 2019-July 2020 were included in the study.

2-2. Inclusion and Exclusion criteria

The target group was selected based on the Australian guideline, which is actually the only source available for making decisions about blood transfusions in pregnant women.

Patients who met at least one of the inclusion criteria, including Splenomegaly, increased RDW or anisopoikilocytosis, and Hb F > 5%, entered the study.

Exclusion criteria were iron deficiency anemia, Sickle cell anemia, other hemoglobinopathy such as HbD and HbS, and underlying diseases including DM and hypercoagulable state.

2-3. Procedure

The patients were divided into two groups:

a) The patients who had anemia and experienced blood injection.

b) The patients who did not experience blood transfusions during pregnancy, unless they had specific complications specified in the transfusion criteria, including PTH, massive splenomegaly, IUGR, and early fatigue that interferes with the patient's daily life.

During the care and follow-ups, the patients were checked for vital signs; and along with general examinations and ultrasound, all of them had to do at least one Transthoracic Echo (TTE) for checking their Pulmonary Hyper-Tension (PHT). They were also examined for splenomegaly and IntraUterine Growth Restriction (IUGR). Also, according to the hematologist's opinion, if necessary, a complete blood count (CBC) test was requested for the patients to determine their anemia status. Finally, the outcome of pregnancy in terms of Apgar score and birth weight of the baby between the two groups was determined according to the Australian guidelines (19).

3- RESULT

During the one-year period of the study, a total of 20 patients referred to the blood clinic; only 8 of them received a definitive diagnosis of beta-thalassemia intermedia by a hematologist, and entered the study. These patients were examined in terms of delivery type, time of delivery, splenomegaly, PHT, and their infants in terms of birth time, weight, and IUGR (**Table 1**).

Table-1: Summary of patients' delivery information

Variable		Value
Patients number		8
Splenomegaly		3
PHT		-
IUGR		1
Delivery Type	Cesarean	6
	Natural	1
Delivery Time	term	6
	preterm	1
	abort	1
Wight	Normal	6
	Less	1

All these patients were divided into two groups according to the implementation method designed in this study. Out of the 8 cases, 3 were included in the first group, who had Hb < 7 and needed blood transfusion; and received blood as a result. Out of these 3 patients, except 1 which led to a miscarriage, 2 other cases succeeded in giving birth to a live baby, one of them was born close to term and had a normal Apgar score, but was underweight due to IUGR. The other one was born during the term and had a normal Apgar score and normal weight.

In the second group of patients, there were 5 cases, all of which had Hb > 8, and since none of them suffered from the complications specified in the transfusion criteria, they were not transfused. All patients gave birth during the term. The Apgar scores of all the newborns were in the normal range and the mean Hb was ≥8. The weight of all newborns was within the normal range, i.e. more than 2500 gr. Most of the patients or their babies had problems during childbirth, but none of them were caused by anemia because at that time they were in a stable condition in terms of anemia. Among the three patients who had splenomegaly, one case was

bulky. The abortion was caused in the first trimester. IUGR resulted in low birth weight babies and all babies had normal Apgar (**Table 2**).

Table-2: The patients' individual and clinical information

Patients	Age	Hb before transfusion	Pack cell transfusion	Hb after transfusion	Spleen Size	pregnancy week	Delivery	birth weight (g)	Apgar first minute	Apgar five minute
1	34	6	Yes	8	202 mm	11	Abortion	-	-	-
2	30	6.6	Yes	8.9	131 mm	38	Cesarean	2940	8	9
3	24	6.7	Yes	8.2	Splenectomy	36	Cesarean	2100	8	9
4	36	10.8	No	-	-	37	Cesarean	3340	8	9
5	27	10	No	-	-	39	Cesarean	2980	9	10
6	30	8.6	No	-	-	Term	Cesarean	2625	9	10
7	29	8.6	No	-	-	39	Cesarean	3040	9	10
8	31	8.7	No	-	160 mm	39	Cesarean	3990	9	10

4- DISCUSSION

Beta thalassemia intermedia is a disease with intermediate symptoms of thalassemia major and minor and is very challenging in terms of the need for blood transfusion (20, 21). Based on the investigations, there is a possibility of a safe and successful pregnancy in these patients with the supervision and care of a specialist physician (22). This disease has a relatively high prevalence in Iran; however, there is no unified guideline for the management of blood transfusion in these patients (23-25). The purpose of this study was to determine a safe level of hemoglobin in pregnant women with thalassemia intermedia, which will help in making decisions about blood transfusion.

In almost all the developing countries of the world, anemia during pregnancy is considered as one of the most important causes of maternal and fetus complications, and also child death (26). To manage this problem in pregnant

women with thalassemia, blood transfusion is usually used (27), but determining the time of injection and managing it is very important (28). According to most studies conducted on pregnancy in women with thalassemia intermedia, 60-80% of patients require blood transfusion during pregnancy, although 30% of them have never had blood transfusion before (29). The treatment protocol in these studies considers the mother's hemoglobin to be above 8 gr/dl for optimal fetal growth. But this approach is not useful for the mother and the fetus, because it can lead to hemolysis, aggravate anemia, and other complications; and it is also difficult to find compatible blood (30, 31).

The results of other studies contrary to these results, showed that a high percentage of these pregnant patients can spend their pregnancy well without receiving blood (32). For example, in the study of LEE Bee Sun and her colleagues, 41.6% of thalassemia patients were not dependent on blood transfusion (hemoglobin range of 6.7-9.7 gr/ dl) and had a good pregnancy without blood transfusion (33). Therefore, it is very important to find a comprehensive protocol that has the least complications for the mother and the fetus. The outcome of pregnancy, which was actually based on the Apgar score and the birth weight of the baby, was not significantly different in pregnant mothers with Hb > 7 compared to mothers with Hb < 7. According to the Australian guideline, which was the reference of this study, hemoglobin 7 gr/ dl was the appropriate level of hemoglobin in pregnant women with thalassemia intermedia; not performing blood transfusion at this level and above, does not make the mother and the fetus suffer from complications caused by anemia, and they do not become anemic. If blood transfusion is performed at levels below 7 gr/ dl, the mother and the fetus benefit from the correction of anemia.

No similar study has been conducted in the field, but other studies on thalassemia intermedia clearly state the challenging nature of this disease and the difficulty of deciding on the time of blood transfusion, especially during pregnancy (8). Because blood transfusion at the wrong time and also lack of it at the necessary time can cause side effects, which affect both mother and fetus during pregnancy (34). Some medical centers keep the mother's hemoglobin level above 10g/dL in pre-pregnancy examinations to ensure the proper development of the fetus (35), but this approach can cause serious complications for the mother and fetus. Because blood transfusion can increase the amount of alloantibody production in the mother's body and cause hemolytic anemia in the fetus (36, 37).

In the largest investigated case series of pregnant women with thalassemia intermedia, the incidence rate of IUGR was reported to be 20-30% (31), while the incidence rate of this complication was much higher in Ersi's study (29). Also, several studies have observed a high percentage of IUGR in pregnant mothers who kept Hb<10 (31, 38). This is despite the fact that in the present study, only one case of IUGR was observed in cases with Hb>7 gr/ dl; and she reached hemoglobin 8.2 by blood transfusion. Similarly, in a study in Malaysia examining pregnancy complications in all thalassemia patients who were not dependent on blood transfusion, no cases of IUGR were observed (33). Therefore, it can be concluded that the occurrence of IUGR is not solely dependent on the hemoglobin level and mother anemia and several factors can be effective in causing this complication.

In most studies, more than half of patients with thalassemia intermedia had a normal pregnancy (39), while cesarean section

was mainly performed due to the lack of proper growth of the fetus with low hemoglobin levels (40-42). This is despite the fact that in our study, except for one case that had a normal delivery, all other pregnant mothers underwent cesarean section due to clinical conditions.

4-1. Limitations of the study

Among the limitations that existed in the process of this plan was that due to the spread of Corona, the number of referrals decreased, and on the other hand, some patients did not cooperate to carry out follow-ups. They did not have regular check-ups, and some patients came after delivery for follow-up and determination of thalassemia type. As a result, there was no possibility of intervention in terms of follow-up and determining the appropriate time for blood sampling. In the process of information collection, some cases had not given birth in the hospitals under investigation, so it was not possible to access their information. These limitations caused the final number of the study population to be eight.

This study was done in a limited time and with a limited number of cases, but it can be done more widely in future, both in terms of time and number of patients, and other variables, including the underlying diseases of the mother. Moreover, considering the effect of alloimmunization on the fetus can give more accuracy and comprehensivity to the results.

Finally, the sample size examined in this study was small. And, blood transfusion was not compared with other treatments, especially drug treatments.

As predicted by the hypothesis of the study there was no difference between the two groups, and this method and hemoglobin level can be used to make decisions about blood transfusions in pregnant women with intermedia thalassemia, as defined by the Australian guidelines; and its effectiveness was confirmed by this study.

5- CONCLUSION

A successful pregnancy and the birth of a baby with normal conditions is possible in patients with intermedia thalassemia, but it requires simultaneous care of the mother and the fetus by a specialist physician. It is suggested that these patients regularly be examined during pregnancy in terms of the condition of the mother and the fetus. Hemoglobin level can be used to make decisions about blood transfusions in pregnant women with intermedia thalassemia, as defined by the Australian guidelines; and its effectiveness was confirmed by this study. In many of these patients, safe pregnancy is possible without any need for blood transfusion.

This pilot study was a preliminary investigation of the effectiveness of this method, which can be a reference for similar decisions about patients with similar disorders. Applying the findings of the present study can help prevent blood transfusions in unnecessary cases and the resulting complications in mother and fetus. So, the burden on patients and the treatment system will be reduced. This research is not solely enough and more extensive and detailed studies are needed.

6- ETHICAL CONSIDERATIONS

All the procedures performed in the studies involving human participants were in accordance with the ethical standards of the local ethics committee of Shiraz University of Medical Sciences (IR.SUMS.MED.REC.1400.191), as well as the 1964 Helsinki declaration. Written informed consent was obtained from all patients and healthy subjects.

7- REFERENCES

1. Greer JP, Arber DA, Glader BE, List AF, Means RM, Rodgers GM. Wintrobe's clinical hematology: Lippincott Williams & Wilkins; 2018.

2. Weatherall DJ, Clegg JB. The thalassaemia syndromes: John Wiley & Sons; 2008.

3. No G-tG. Management of beta thalassaemia in pregnancy. 2014.

4. Abdolalian M, Ebrahimi M, Aghamirzadeh M, Eshraghi N, Moghaddasi M, Eslamnik P. The role of leukemia inhibitory factor in pathogenesis of pre-eclampsia: molecular and cell signaling approach. Journal of Molecular Histology. 2021; 52(4):635-42.

5. Abdallah AM. Thalassemia and pregnancy complications. World Journal of Advanced Research and Reviews. 2022; 14(1):363-7.

6. Virot E, Thuret I, Jardel S, Herbrecht R, Lachenal F, Lionnet F, Lucchini MJ, Machin J, Nimubona S, Ribeil JA, Galacteros F, Cannas G, Hot A. Pregnancy outcome in women with transfused beta-thalassemia in France. Annals of Hematology. 2022; 101(2):289-96.

7. Halim-Fikri BH, Lederer CW, Baig AA, Assyuhada Mat-Ghani NS, Rahayu-Karmilla Syed-Hassan SN, Yusof W, Rashid DA, Azman NF, Fucharoen S, Panigoro R, Silao CLT, Viprakasit V, Jalil N, Yasin NM, Bahar R, Selvaratnam V, Mohamad N, Nik Hassan NN, Esa E, Krause A, Robinson H, Hasler J, Stephanou C, Raja-Sabudin RZA, Elion J, El-Kamah G, Coviello D, Yusoff N, Latiff ZA, Arnold C, Burn J, Kountouris P, Kleanthous M, Ramesar R, Zilfalil BA, On Behalf Of The Global Globin Network Ggn. Global Globin Network Consensus Paper: Classification and Stratified Roadmaps for Improved Thalassaemia Care and Prevention in 32 Countries. Journal of personalized medicine. 2022; 12(4):552.

8. Petrakos G, Andriopoulos P, Tsironi M. Pregnancy in women with thalassemia: challenges and solutions. International journal of women's health. 2016; 8:441.

9. Rajagopalan KS, Kazeminia S, Glasstetter LM, Farahani RA, Zhu X-Y, Tang H, Jordan KL, Chade AR, Lerman A, Lerman LO, Eirin A. Metabolic Syndrome Induces Epigenetic Alterations in Mitochondria-Related Genes in Swine Mesenchymal Stem Cells. Cells. 2023; 12(9):1274.

10. Shahverdi E, Moghaddam M, Gorzin F. Maternal red blood cell alloantibodies identified in blood samples obtained from Iranian pregnant women: the first population study in Iran. Transfusion. 2017; 57(1):97-101.

11. Zdanowicz JA, Surbek D. Patient blood management in obstetrics–Review. Transfusion and apheresis science. 2019; 58(4):412-5.

12. Hosseini H, Far MJ, Saki N, Galehdari H, Saki A. Study of beta-globin chain mutations in patients with beta thalassemia trait among different racial groups in Khouzestan Province. Genetics in the 3rd millennium. 2013; 10(4):2868-73.

13. Al-Gazali L, Hamamy H, Al-Arrayad S. Genetic disorders in the Arab world. Bmj. 2006; 333(7573):831-4.

14. Tadmouri GO, Al Ali MT, Al-Haj Ali S, Al Khaja N. CTGA: the database for genetic disorders in Arab populations. Nucleic Acids Res. 2006; 34(Database issue):D602-6.

15. Genetic services in Europe. A comparative study of 31 countries by the Concerted Action on Genetic Services in Europe. Eur J Hum Genet. 1997; 5 Suppl 2:1-220.

16. Pouranfard J, Vafaei F, Afrouz S, Rezaeian M. Thalassemia gene mutations in Kohgiluyeh and Boyer-Ahmad province. Iranian Journal of Blood and Cancer. 2020; 12(1):18-23.

17. Farashi S, Bayat N, Faramarzi Garous N, Ashki M, Montajabi Niat M, Vakili S, Imanian H, Zeinali S, Najmabadi H,

Azarkeivan A. Interaction of an α-globin gene triplication with β-globin gene mutations in Iranian patients with β-thalassemia intermedia. Hemoglobin. 2015; 39(3):201-6.

18. Akbari E, Sarbazi F, Karimi A, Nouri B, Ardebili SN. Comparison of Laparoscopic Myomectomy Outcomes Based on Myoma Weight: A Cross-sectional Study. International Journal of Women's Health & Reproduction Sciences. 2022; 10(1).

19. Ho P, Tay L, Lindeman R, Catley L, Bowden D. Australian guidelines for the assessment of iron overload and iron chelation in transfusion-dependent thalassaemia major, sickle cell disease and other congenital anaemias. Internal medicine journal. 2011; 41(7):516-24.

20. Singh A, Sharma K, Venkateswaran V, Trikha A. Pregnancy in thalassemia, anesthetic implication and perioperative management-A narrative review. Journal of Obstetric Anaesthesia and Critical Care. 2021; 11(2):81.

21. Origa R, Comitini F. Pregnancy in thalassemia. Mediterranean journal of hematology and infectious diseases. 2019; 11(1).

22. Sharma A, Uppal N, Kukreja S, Kaur M, Kaur S. Screening of thalassemia in pregnant females visiting tertiary hospital in Amritsar. Int J Clin Biochem Res. 2020; 7:226-31.

23. Abbasinejad F, Shashshahani HJ, Ghalibaf MA. A Comparative Study of Transfusion Reactions in the Thalassemia Patients before and after Implementation of the Hemovigilance System in Yazd Province, Iran. Iranian Journal of Pediatric Hematology & Oncology. 2020; 10(4).

24. Rezabeigi Davarani E, Mohseni Takaloo F, Vahidnia A, Daneshi S, Rezabeigi Davarani M, Khanjani N, Hushmandi K, Raei M. Epidemiological Investigation of a Twenty-Year Major β-Thalassemia Surveillance in Kerman, Iran. Archives of Hygiene Sciences. 2020; 9(4):265-74.

25. Yaghobi M, Miri-Moghaddam E, Majid N, Bazi A, Navidian A, Kalkali A. Complications of transfusion-dependent β-thalassemia patients in Sistan and Baluchistan, south-east of Iran. International journal of hematology-oncology and stem cell research. 2017; 11(4):268.

26. 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.

27. Susheela A, Mondal N, Gupta R, Ganesh K, Brahmankar S, Bhasin S, Gupta G. Effective interventional approach to control anemia in pregnant women. Current Science. 2010:1320-30.

28. Charoenboon C, Jatavan P, Traisrisilp K, Tongsong T. Pregnancy outcomes among women with beta-thalassemia trait. Archives of gynecology and obstetrics. 2016; 293(4):771-4.

29. Voskaridou E, Balassopoulou A, Boutou E, Komninaka V, Christoulas D, Dimopoulou M, Delaki EE, Loukopoulos D, Terpos E. Pregnancy in beta-thalassemia intermedia: 20-year experience of a Greek thalassemia center. Eur J Haematol. 2014; 93(6):492-9.

30. Levy A, Fraser D, Katz M, Mazor M, Sheiner E. Maternal anemia during pregnancy is an independent risk factor for low birthweight and preterm delivery. European journal of obstetrics & gynecology and reproductive biology. 2005; 122(2):182-6.

31. Nassar AH, Naja M, Cesaretti C, Eprassi B, Cappellini MD, Taher A. Pregnancy outcome in patients with β-thalassemia intermedia at two tertiary care centers, in Beirut and Milan. Haematologica. 2008; 93(10):1586-7.

32. Zhou Y, Ding Y-L, Zhang L-J, Peng M, Huang J. Direct antiglobulin test-negative autoimmune hemolytic anemia in a patient with β-thalassemia minor during pregnancy: A case report. World Journal of Clinical Cases. 2022; 10(4):1388.

33. Lee BS, Sathar J, Sivapatham L, Lee LI. Pregnancy outcomes in women with non-transfusion dependent thalassaemia (NTDT): A haematology center experience. Malays J Pathol. 2018; 40(2):149-52.

34. Taher A, Radwan A, Viprakasit V. When to consider transfusion therapy for patients with non-transfusion-dependent thalassaemia. Vox sanguinis. 2015; 108(1):1-10.

35. Origa R, Piga A, Quarta G, Forni GL, Longo F, Melpignano A, Galanello R. Pregnancy and β-thalassemia: an Italian multicenter experience. haematologica. 2010; 95(3):376-81.

36. Nassar AH, Usta IM, Rechdan JB, Koussa S, Inati A, Taher AT. Pregnancy in patients with β-thalassemia intermedia: Outcome of mothers and newborns. American journal of hematology. 2006; 81(7):499-502.

37. Al-Joudi F, Ali AB, Ramli MBH, Ahmed S, Ismail M. Prevalence and specificities of red cell alloantibodies among blood recipients in the Malaysian state of Kelantan. Asian journal of transfusion science. 2011; 5(1):42.

38. Nassar AH, Usta IM, Taher AM. Beta-thalassemia intermedia and pregnancy: should we anticoagulate? J Thromb Haemost. 2006; 4(6):1413-4.

39. Verma A, Jamal S. Thalassemia and Pregnancy: An Update. Jaypee Brothers Medical Publishers (P) Ltd.35.

40. Sun LB, Sathar J, Sivapatham L, Ing LL. Pregnancy outcomes in women with non-transfusion dependent thalassaemia (NTDT): A hematology center experience. The Malaysian Journal of Pathology. 2018; 40(2):149-52.

41. Sorrentino F, Maffei L, Caprari P, Cassetta R, Dell'Anna D, Materazzi S, Risoluti R. Pregnancy in thalassemia and sickle cell disease: the experience of an Italian thalassemia center. Frontiers in Molecular Biosciences. 2020; 7:16.

42. Sookaromdee P, Wiwanitkit V. Pregnancy in thalassemia: Correspondence. Journal of Obstetric Anaesthesia and Critical Care. 2022; 12(1):78-.