Case Report
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Role of Reticulocyte Hemoglobin to Detect Functional Iron Deficiency in a Parturient with β-thalassemia Trait Undergoing Cesarean Delivery Under Spinal Anaesthesia: A Case Report

Berrin Günaydın[1], Nuray Bozkurt[2], Pelin Sim Küçük Ellialtıoğlu[2], Ekin Deniz Kutlu[1], Ayça Özcan[1], Beyza Büyükgebiz Yeşil[3]

[1]Gazi University Faculty of Medicine, Department of Anaesthesiology and Reanimation, Ankara, Türkiye
[2]Gazi University Faculty of Medicine, Department of Obstetrics and Gynecology, Ankara, Türkiye
[3]Kahramanmaraş State Hospital, Clinic of Anaesthesiology, Kahramanmaraş, Türkiye

Abstract

We aimed to report the case of a 29-year-old primiparous woman at 38 weeks' gestation with β-thalassemia trait who was scheduled for elective cesarean delivery under spinal anaesthesia. She had hypochromic microcytic anemia with normal serum ferritin and iron levels, but low transferrin saturation and reticulocyte hemoglobin (Ret-Hb). These findings support iron-restricted erythropoiesis despite normal ferritin levels. Ret-Hb and Ret-Hb factor, considered together with conventional iron indices, helped contextualize the interpretation of anemia, rather than directly determine treatment. This case highlights the perioperative interpretation of discordant iron indices in a pregnant patient with β-thalassemia trait. Multidisciplinary perioperative planning may help avoid unnecessary transfusions or iron supplementation while ensuring preparedness for obstetric blood loss in pregnant patients with thalassemia trait and anemia.

Keywords: Beta-thalassemia, iron-deficiency anemia, pregnancy, cesarean section, spinal anaesthesia, reticulocytes

Main Points

- Thalassemia minor, caused by reduced β-globin synthesis, generally results in mild anemia with microcytosis; pregnancy exacerbates this by causing hemodilution and increased iron demand for the fetus, placenta, and maternal red blood cells.
- In pregnant patients with β-thalassemia trait, normal ferritin levels do not always exclude iron-restricted erythropoiesis, especially when transferrin saturation is low and total iron binding capacity is elevated.
- Reticulocyte hemoglobin reflects iron available for erythropoiesis and may be interpreted together with conventional iron indices, which can be integrated into routine peripartum anemia screening tests using the same autoanalyzer for complete blood count measurement.
- In obstetric anaesthesia, such interpretation may support perioperative planning, transfusion preparedness, and avoidance of unnecessary treatment.

Introduction

Thalassemia minor is a disease characterized by reduced β-globin synthesis and generally results in mild anemia with microcytosis. Pregnancy adds hemodilution and increased iron demand by the fetus, placenta, and red blood cells (RBCs).[1] The incidence of iron deficiencey anemia (IDA) in pregnant women with common various genotypes of β-thalassemia minor was less than 10.85%.[2] Distinguishing isolated thalassemia trait from concomitant iron-restricted erythropoiesis is clinically relevant

Corresponding author: Beyza Büyükgebiz Yeşil MD, **E-mail:** beyza.bgz@gmail.com
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for preventing both undertreatment and unnecessary iron overload. Conventional markers such as hemoglobin (Hb), mean corpuscular volume (MCV), and mean corpuscular HB (MCH) are useful for describing anemia but may not reliably helpful in the differential diagnosis between genetic microcytosis and iron-restricted erythropoiesis.[3] Although determination of ferritin has been commonly used to estimate iron store levels, it may be influenced by inflammation, and its interpretation in pregnancy can be challenging due to varying thresholds across trimesters and physiological changes. Reticulocyte HB (Ret-Hb) has been an early marker of iron available for erythropoiesis and showed high diagnostic performance for iron-deficiency patterns in pregnancy.[4] In this case report, we aimed to highlight the supportive perioperative interpretation of Ret-Hb in a term parturient with β-thalassemia trait, microcytosis, normal ferritin, and discordant iron indices undergoing elective cesarean delivery with spinal anaesthesia by presenting Ret-Hb as an exploratory adjunct in multidisciplinary peripartum decision-making, rather than as a stand-alone diagnostic tool.

Case Presentation

A 29-year-old primiparous ASA II parturient (body mass index: 31.9 kg/m^2) at 38 weeks' gestation was scheduled for elective cesarean delivery after in vitro fertilization. Written informed consent was obtained from the patient. She had previously been diagnosed with a unicornuate uterus. She had β-thalassemia trait (HbA_2 5% on Hb electrophoresis), hypothyroidism, and a heterozygous Factor V Leiden mutation. Her medications included oral levothyroxine 25 µg day, iron (ferrous preparation 100 mg day), and enoxaparin 6000 anti-Xa IU subcutaneously once daily. Her history included laparoscopic ovarian cyst excision, hysterosalpingography, and oocyte retrieval under general anaesthesia without any complications.

Preoperative laboratory values showed hypochromic microcytic anemia (Hb 8.9 g dL^{-1}, Hct 27.3%, MCV 67.7 fL, MCH 22.1 pg) with a normal platelet count (263,000/µL), normal serum ferritin (35.7 µg L^{-1}), and normal serum iron (78 µg dL^{-1}). However, serum iron-binding capacity (IBC) was elevated to 460 µg dL^{-1} and transferrin saturation (TSAT) decreased to 16%. In the reticulocyte (RET) panel, the RET percentage increased to 2.5%, the immature RET fraction increased to 25.3%, and the Ret-Hb decreased to 22.6 pg (Table 1). Thyroid, renal, and liver function tests, electrolytes, and coagulation profile were unremarkable. Given the presence of maternal anemia and the possibility of obstetric blood loss, and based on the multidisciplinary consultation with hematology, anaesthesia, and obstetrics, 2 units of packed RBCs were cross-matched and kept ready before the operation.

The last dose of enoxaparin was administered 24 hours before the operation. After standard monitoring, spinal anaesthesia was administered using 0.5% hyperbaric bupivacaine (10 mg), fentanyl (10 µg), and morphine (100 µg), along with careful colloid coloading. Onset of surgery was allowed after achieving a sensory block level at T4. A male newborn (3140 g) was born, and his Apgar scores were 9 and 10 at 1 and 5 minutes, respectively. After umbilical cord clamping, uterotonic management included the administration of intravenous (IV) carbetocin 50 µg and intramuscular methylergometrine 0.2 mg. The estimated blood loss was acceptable (approximately 500 mL), and a total of 1000 mL crystalloid and 500 mL colloid were administered intraoperatively. No vasopressor support was required, as hypotension did not occur. The intraoperative hemodynamic course remained stable throughout the procedure. No transfusion was required. On the postoperative 2nd day, she was discharged from the hospital with stable vital signs and no complications.

Table 1. Reticulocyte and Hemogram (Complete Blood Count) Indices with Iron Panel

Parameter	Result	Reference values
Reticulocyte panel		
RET percent	2.5%	0.86-1.36
RET count (#)	0.1008	0.039-0.057
IRF percent	25.3%	9.3-17.4
Ret-Hb	22.6 pg	30.2-36.2
Hemogram (CBC)		
Hb	8.9 g/dL	≥ 11 g/dL
Htc	27.3%	≥ 33%
MCV	67.7 fL	82.9-98 fL
MCH	22.1 pg	27-32.3 pg
RDW	15	11.5-14.5%
RDW-SD	34.9	38.2-49.2 fL
Iron panel		
Serum ferritin	35.7 ug/L	13-150
Serum iron	78 ug/dL	33-93
TIBC	460 ug/dL	135-392
TSAT	16%	≥ 20%

RET, reticulocyte; IRF, immature reticulocyte fraction; Ret-Hb, reticulocyte hemoglobin; CBC, complete blood count; Hb, hemoglobin; Htc, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; RDW, red cell distribution width; RDW-SD, red cell distribution width-standard deviation; TSAT, transferrin saturation; TIBC, total iron binding capacity

Discussion

In the present case report, low Ret-Hb with microcytosis and low TSAT with elevated total iron binding capacity (TIBC), despite a normal ferritin level, supported iron-restricted erythropoiesis in a patient with thalassemia trait who underwent an uneventful elective cesarean delivery under spinal anaesthesia. Ret-Hb did not directly determine treatment or alter the anesthetic technique. Rather, it served as an adjunctive parameter that helped contextualize the patient's anemia and supported multidisciplinary perioperative planning. Although the case was completed uneventfully without IV iron treatment or transfusion, the diagnostic value of Ret-Hb in a pregnant woman with β-thalassemia trait and a normal serum ferritin level, where ferritin interpretation can be uncertain, was not overlooked. Ret-Hb, reflecting iron incorporation into newly produced erythrocytes over the preceding few days, can identify iron-restricted erythropoiesis earlier than a decline in Hb.

In pregnancy, anemia is generally defined as Hb <11 g dL^{-1}. By contrast, ferritin thresholds used to define iron deficiency are less uniform across guidelines, although a value <30 μg L^{-1} is commonly used in contemporary obstetric anaesthesia and hematology practice.[3] In the present case, ferritin was not below this threshold; therefore, our interpretation did not rely on ferritin alone. Instead, low TSAT, elevated total IBC, microcytosis, and low Ret-Hb were interpreted together as suggestive of iron-restricted erythropoiesis in the setting of β-thalassemia trait. In preoperative settings, this distinction is clinically relevant because antenatal anemia may reduce maternal tolerance to obstetric blood loss.

In a first-trimester pregnancy cohort, Ret-Hb at a cut-off around 27.8 pg showed high sensitivity (93%) and specificity (83%) for microcytic/hypochromic patterns, outperforming ferritin at low cut-off.[4] Mehta et al.[5] demonstrated that Ret-Hb levels in 102 patients with iron depletion were differentiated from those with functional iron deficiency. Ret-Hb also correlated strongly and positively with serum ferritin, suggesting that it may reflect bone marrow iron availability and serve as a practical marker for diagnosing iron deficiency. In our patient, Ret-Hb was 22.6 pg, which was below the lower reference limit despite a ferritin value within the laboratory reference interval. However, decreased TSAT and elevated TIBC were consistent with iron-restricted erythropoiesis. This presentation is known as functional iron deficiency. Aedh et al.[6] emphasized that Ret-Hb content could effectively flag latent iron deficiency earlier than conventional markers, thereby serving as a vital tool in peripartum assessments. Importantly, women with β-thalassemia minor can develop IDA during pregnancy, although the incidence may vary according to population and/or genotype.[2] Therefore, Ret-Hb served as a practical adjunct for multidisciplinary decision-making and peripartum planning, supporting a conservative transfusion strategy to maintain readiness for hemorrhage. Additionally, a new formula Ret-Hb factor (RHF) has been proposed by Jamnok et al.[7] in thalassemia-prevalent settings. This parameter, calculated using the formula [Ret-Hb/ red cell distribution width-standard deviation (RDW-SD)] ×10, may provide complementary information to Ret-Hb, particularly in patients with microcytosis undergoing thalassemia screening. In this framework, Ret-Hb reflects the Hb content of newly produced RETs and may indicate reduced iron availability, whereas RHF incorporates RDW-SD to account for anisocytosis in interpreting microcytic anemia. Jamnok et al.[7] suggested that women with thalassemia and RHF values below 6.1 may be considered for iron supplementation. In our case, Ret-Hb (22.6 pg)/ RDW-SD (34.9 fL) ×10 yielded an RHF value of 6.47, which was slightly above this proposed cut-off. Thus, while low Ret-Hb supported iron-restricted erythropoiesis, RHF did not independently support iron supplementation. Both parameters were therefore interpreted cautiously, in the context of the overall laboratory profile, including low TSAT, elevated TIBC, normal ferritin, and microcytosis. Given the limited validation of RHF, especially in pregnancy, it was considered a supportive exploratory parameter rather than a stand-alone basis for treatment decisions.

In addition, multidisciplinary assessment was particularly important in such complex clinical scenarios. Involving hematology, obstetrics, and anaesthesia specialists helps optimize patient care and ensures that patient safety remains the primary concern while addressing the unique needs of parturients with thalassemia trait. For instance, including cross-matched blood in multidisciplinary planning, as in our case, illustrates preparedness for potential transfusion needs without prematurely subjecting the patient to iron loading, which could exacerbate iron overload conditions.[8]

From an anaesthesiology perspective, the main relevance of this interpretation is its contribution to perioperative risk assessment and patient blood management. In anemic parturients with β-thalassemia trait, reliance on Hb, MCV, or ferritin alone may lead either to under-recognition of iron-restricted erythropoiesis or to unnecessary iron treatment. Interpreting Ret-Hb and RHF together with TSAT, TIBC, ferritin, and red cell indices may help the anaesthesiology team assess the patient's tolerance to potential obstetric blood loss, plan blood availability, and avoid prophylactic transfusion in the absence of clinical instability or active bleeding. In this case, the approach did not alter the choice of spinal anaesthesia but supported multidisciplinary preparation for cesarean delivery within a patient blood management framework.

Although anemia during pregnancy is commonly defined using trimester-specific Hb thresholds (<11, 10.5, and 11g dL^{-1} in the 1st, 2nd, and 3rd trimester, respectively), we did

not target a specific Hb value because current national PBM guidelines for obstetrics and maternity emphasize optimization of antenatal anemia rather than a single universal pre-cesarean Hb threshold.[9]

Since the role of Ret-Hb in the assessment of iron deficiency has already been described, we have revisited the educational value of Ret-Hb/RHF in the peripartum period as complementary parameters, emphasizing a multidisciplinary approach to clinical decision-making rather than claiming diagnostic superiority over conventional iron studies. Therefore, the novelty of the present case report lies not in the introduction of Ret-Hb itself but in its interpretation in the perioperative obstetric anaesthesia setting of a term parturient with β-thalassemia trait, microcytosis, normal ferritin, and discordant iron indices.

However, this report has several limitations. First, it describes a single patient and therefore cannot establish the diagnostic superiority of Ret-Hb versus RHF. Secondly, inflammatory markers, including C-reactive protein, were not assessed. Because ferritin is an acute-phase reactant, occult inflammation could have influenced the interpretation of the apparently normal ferritin level. Therefore, the absence of inflammatory markers limits the certainty with which ferritin status can be interpreted in this case.

Conclusion

Functional iron deficiency may coexist with β-thalassemia trait and can be challenging to recognize during pregnancy because Hb indices and ferritin thresholds may be misleading. This case emphasizes the importance of interpreting discordant iron indices together, rather than relying on ferritin or Hb indices alone. Ret-Hb reflects iron immediately available for new RBC production (erythropoiesis) and may complement conventional iron studies in selected pregnant patients with β-thalassemia trait who have discordant indices of iron status, thereby aiding peripartum planning to avoid unnecessary transfusion and/or iron loading. However, broader clinical use requires validation in larger studies.

Ethics

Informed Consent: Written informed consent was obtained from the patient.

Footnotes

Authorship Contributions: Surgical and Medical Practices - B.G., N.B., P.S.K.E., E.D.K., A.Ö.; Concept - B.G., N.B.; Design - B.G., N.B.; Data Collection and/or Processing - P.S.K.E., E.D.K., A.Ö., B.B.Y.; Analysis and/or Interpretation - B.G., N.B., B.B.Y.; Literature Search - P.S.K.E., E.D.K., A.Ö., B.B.Y.; Writing - B.G., E.D.K., B.B.Y.

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