IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 2 Ser.8 (February. 2020), PP 46-52
www.iosrjournals.org

Concomitant Beta Thalassmia Trait and Iron Deficiency Anemia in Pregnancy.

Dr. Michelle Siew[1]
[1]*(Junior Resident, RGSSH,India)*

***Abstract**: Thalassemia syndromes and iron deficiency anemia (IDA) are the two most common etiologies of microcytic hypochromic anemia in children and adults. It has long been considered that iron deficiency does not exist in thalassemia syndromes, including thalassemia major as well as trait. However, studies have shown the occurrence of iron deficiency in patients with beta thalassemia trait (BTT). Earlier authors have demonstrated lower initial hemoglobin levels in patients with coexisting IDA and BTT . This has been explained by the lack of hemopoietic nutrients due to iron deficiency superimposing on the imbalance in globin chain synthesis.This case report showed that the concomitant existence of beta thalassemia minor and iron deficiency anemia in pregnancy. The evaluation of anemia in pregnancy is a tricky subject and is essential to treat. This case showed a normal HbA2(<3.5%) finding in a patient with beta thalassemia minor with concomitant iron deficiency anemia leading to difficulty in diagnosing beta thalassemia in patients. The combination of these two anemias along with anemia of pregnancy can justify the severe anemia seen in this patient.*

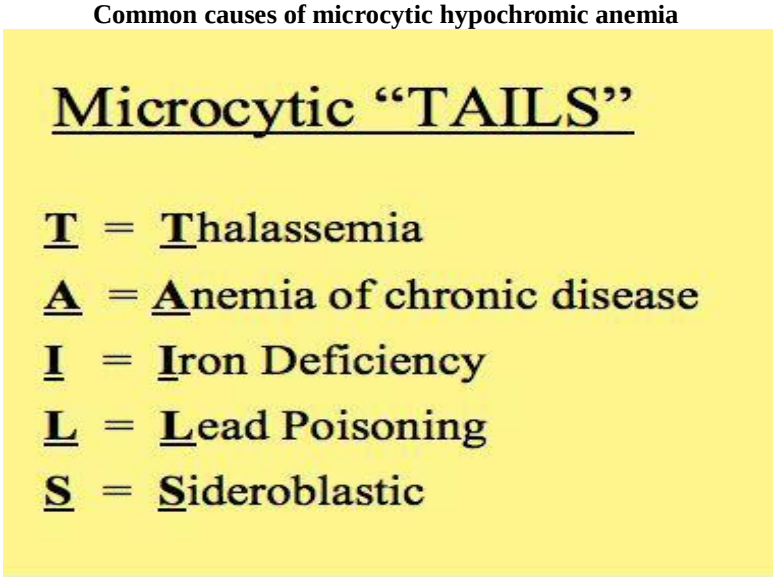
***Keywords:** Microcytic hHypochromic Anemia, Beta Thalassemia Trait (BTT), Hemopoietic.*

Date of Submission: 30-01-2020 Date of Acceptance: 15-02-2020

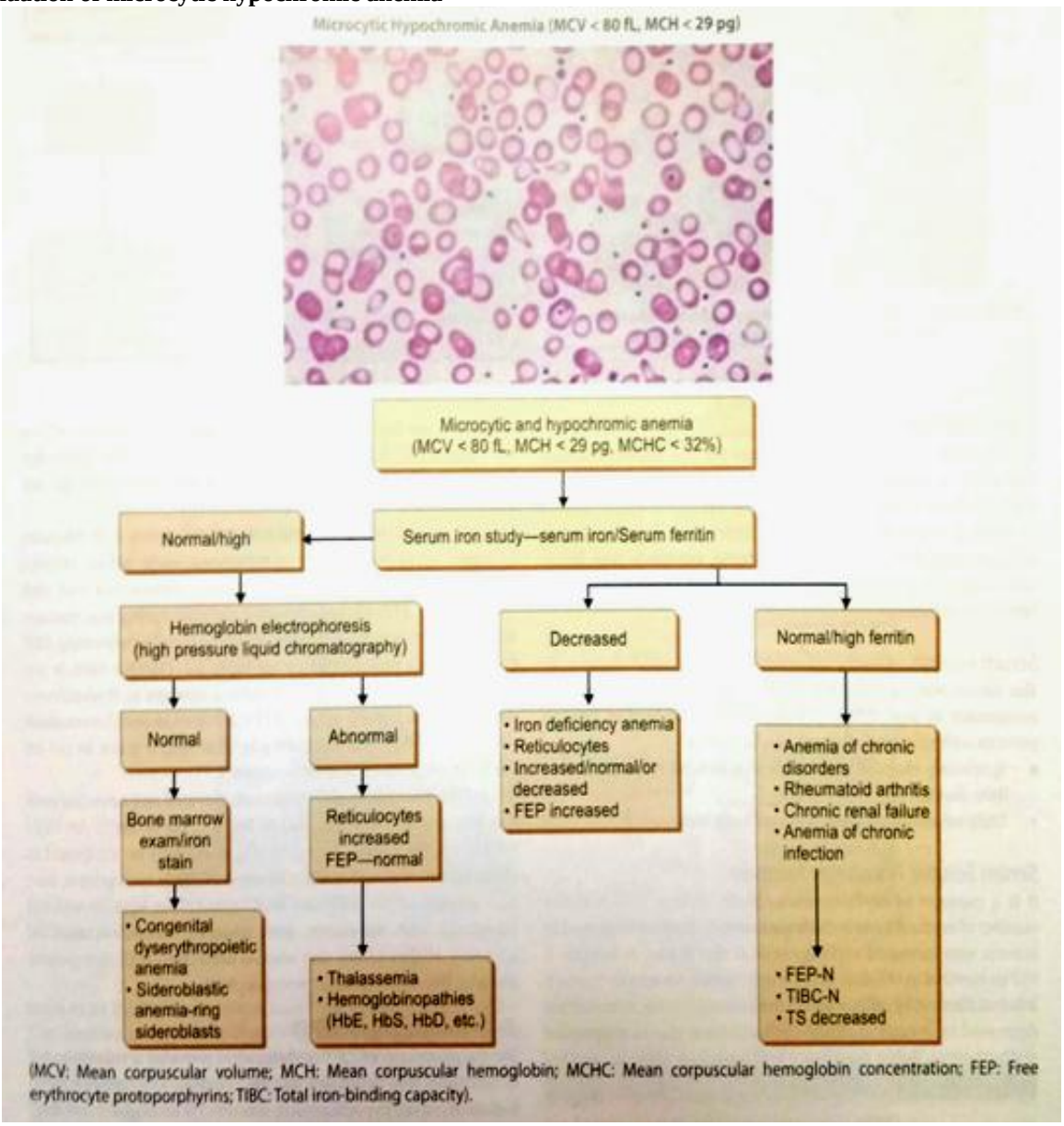
I. Background

The beta-thalassemia trait (BTT) is a heterozygous condition in which only a single beta-globin gene is affected. The estimated prevalence of BTT in different regions of India is reported to vary between 2.7% and 14.9% (mean: 4.5%) [1,2]. Most individuals with BTT are asymptomatic and are identified incidentally when their complete blood count (CBC) shows microcytosis [3]. Red blood cells are considered to be microcytic when the mean corpuscular volume (MCV) is <80 fL [4].

Common causes of microcytic hypochromic anemia



valuation of microcytic hypochromic anemia



The hemoglobinopathies should be evaluated further with hemoglobin electrophoresis. High Performance Liquid Chromatography which is also known as High Pressure Liquid Chromatography. It is a popular analytical technique used for the separation, identification and quantification of each constituent of mixture. HPLC is an advanced technique of column liquid chromatography. The solvent usually flows through column with the help of gravity but in HPLC technique the solvent will be forced under high pressures upto 400 atmospheres so that sample can be separated into different constituents with the help of difference in relative affinities[5-11].

Syndrome	*β-globin gene affected*	*Clinical presentation*	*Hemoglobin pattern*
Silent carrier	Heterozygous state	Asymptomatic persons without anemia	Normal with normal HPLC
Thalassemia trait/carrier	Heterozygous state	Mild anemia↑ RBC count ↓ MCV and MCH	HbA_2> 3.5%
Thalassemia intermedia (NTDT)	Homozygous/ heterozygous state	Moderate anemia not dependent on blood transfusion, hepatosplenomegaly Growth retardation Bone abnormalities May require blood transfusion occasionally	Raised HbF or HbA_2level
Thalassemia major	Homozygous state	Develops severe anemia below 2 years, hepatosplenomegaly, blood transfusions dependent	Markedly raised HbF level

In a study conducted by Rachna Khera et.el used High-performance liquid chromatography (HPLC) is a technique introduced for the accurate diagnosis of hemoglobinopathies and thalassemias. The advantage of the HPLC system is the excellent resolution, reproducibility & quantification of several normal & abnormal hemoglobin resulting in accurate diagnosis of thalassemia syndromes.The study evaluated the use of HPLC technique in diagnosis of thalassemia syndromes and also correlate it with clinicohematological profile in these cases.The results of the study are shown in the table [12].

Hemoglobin profile in each case obtained on HPLC (mean ± SD, range)

Presumptive HPLC diagnosis (no. of cases)	**Hb A (%) (range)**	**Hb F (%)**	**HbA_2 (%)**	**Variant Hb (%)**
β-Thal trait (62)	83.6 ± 2.7 (71.7–89.1)	1.5 ± 1.2 (0.2–4.9)	5.7 ± 0.9 (4.0–8.2)	
β-Thal major (6)	25.0 ± 22.7 (4.6–60.5)	65.8 ± 29.8 (30.6–91)	2.8 ± 1.5 (0–4.5)	
β-Thal Intermedia (5)	30.4 ± 31.6 (0.5–65.9)	62.0 ± 37 (22–98)	5.5 ± 2.6 (2.1–8.2)	
HbS/β-thal (2)	1.6 ± 2.8 (1.4–1.8)	19.3 ± 9.4 (14.2–24.3)	5.0 ± 0.6 (4.9–5.1)	74.4 ± 7.8 (69.2–79.5)
HbE/β-thal (8)	24.4 ± 18.1 (6.5–47.2)	18.7 ± 22.2 (4.4–33.2)	–	52.8 ± 17.9 (34.2–60.9)
HbH disease (4)	88.1 ± 4.9 (81.5–93.3)	0.8 ± 0.6 (0.2–1.8)	2.6 ± 0.6 (2–3.4)	
Sickle cell trait (1)	46.3	1.2	6.9	33.8
Homozygous Sickle cell ds (1)	0	9.8	3.1	85.7
HbE-trait (7)	62.3 ± 2.7 (59.8–67.7)	0.96 ± 0.7 (0.4–2.3)	0	28.2 ± 5.0 (17–31.2)
Homozygous HbE ds (1)	4.0	0.7	0	93.7
HbD-Punjab trait (8)	54.5 ± 8.5 (50.7–77)	0.6 ± 0.4 (0.2–1.2)	1.4 ± 0.4 (0.7–1.8)	34.8 ± 8.0 (13.4–38.5)
Homozygous HbD ds (1)	5.0	1.2	2.1	86.5
Double hetero HbSE ds (1)	1.4	0.4	61(E)	30.7
HbD-Iran trait (1)	45.1	0.8	0	43.3
Hb J Oxford (2)	72.5 ± 8.3 (66.4–78.6)	2.3 ± 2 (0.8–3.7)	1.9 ± 0 (1.9)	18.2 ± 4 (15.3–21)

β-thalassemia minor represents the heterozygous state. In general, a heterozygote for thalassemia is diagnosed with a mild anemia (hemoglobin A level 1 or 2 g below normal range), low mean cell volume, low mean corpuscular hemoglobin, elevated hemoglobin A2, and normal or elevated hemoglobin F.

During pregnancy, women with thalassemia minor will often show more significant anemia, which is often most prominent during the latter half of the second trimester and early third trimester [13-16]. In a study

conducted by Amooee S et.el showed that β-thalassemia minor does not significantly influence the pregnancy outcome in the negative way in terms of Cesarean delivery, hypertensive disorders, gestational diabetes mellitus, premature rupture of membranes and preterm labor.

Globally, the commonest cause for anemia in pregnancy is IDA. The Nutrition Impact Model Study, a systematic analysis of 257 population-representative data sources from 107 countries, estimated the global prevalence of anemia in pregnancy as 43% in 1995 and 38% in 2011 with the range varying from 17% in developed and 56.4% in developing countries.

Antepartum complications	**Intrapartum complications**	**Postpartum complications**	**Fetal outcome**
Increased risk of preterm delivery	Prolonged labor	Postpartum hemorrhage	Low birth weight
Premature rupture of membranes	Increased rates of operative delivery and induced labor	Purperal sepsis	Prematurity
Preecclampsia	Fetal distress	Lactation failure	Infections
Intrauterine Death	Abruption	Pulmonary thromboembolism	Congenital malformation
Intercurrent infection		Subinvolution of uterus	Neonatal Anemia
Antepartum hemorrhage		Postpartum depression	Abnormal cognitive development
Congestive Heart Failure			Increased risk of Schizophrenia

During pregnancy, the total blood volume increases by about 1.5 liters, mainly to supply the demands of the new vascular bed and to compensate for blood loss occurring at delivery [17].

Red cell mass (driven by an increase in maternal erythropoietin production) also increases, but relatively less, compared with the increase in plasma volume, the net result being a dip in hemoglobin concentration. The drop in hemoglobin is typically by 1–2 g/dL by the late second trimester and stabilizes thereafter in the third trimester.

White blood cell count is increased in pregnancy with the lower limit of the reference range being typically 6,000/cumm. Leucocytosis, occurring during pregnancy is due to the physiologic stress induced by the pregnant state [18].

Large cross-sectional studies done in pregnancy of healthy women (specifically excluding any with hypertension) have shown that the platelet count does decrease during pregnancy, particularly in the third trimester. This is termed as "gestational thrombocytopenia." It is partly due to hemodilution and partly due to increased platelet activation and accelerated clearance [19].

CASE PRESENTATION

A 26 year old female with 32weeks pregnancy presented to outpatient department with complaints of shortness of breath and fatigue for past two weeks. The shortness of breath was gradual in onset, present at rest, increased on exertion. It was not associated with chest pain, cough, orthopnea, paroxysmal nocturnal dyspnea, fever. She developed fatigue gradually. No decrease in appetite, no weight loss, no bleeding episodes.

Past history- No significant past history.

Personal history- Normal bladder and bowel.
Non- vegetarian diet.
No smoking, alcohol or illicit drug use.

Menstrual history- Amenorrhea for past 8 months, menarche at 14 years age, regular, soaks 2-3 pads per day, last for 3-5 days.

Family history- Thalassemia minor in father.

EXAMINATION- Patient lying comfortably in bed.

Patient conscious, Oriented to time/place and person.

Pallor present/ no icterus/ no cyanosis/no clubbing/no lymphadenopathy.

Vitals: BP- 110/70 mmhg
PR- 98/min
RR-22/min
SpO2-98%

Systemic: CVS- S1/S2 normal, no additional heart sound.
RESPIRATORY- Bilateral air entry clear, no additional sound.
CNS- Within normal limit .
Abdominal- Soft, 32 weeks gestation, FHS 140/min.

INVESTIGATION:

Parameters	Pre-pregnancy	pregnancy
Hb	11.6	4.6
MCV	80	76
RDW	14	16
Mentzer Index	19	34
TLC	4400	4000
RBC	4.1	2.2
S. Ferritin	113	35
S. Iron	160	56
TIBC	323	486
Platelet	2.8	1.98
Reticulocyte count	1.2	0.4

HPLC FINDNGS

Hb F	2.8%
Hb A	92%
Hb A2	3.3%

Bone marrow biopsy- Normal
Peripheral smear- Hypochromic microcytic anemia

II. Conclusion

Thalassemia syndromes and iron deficiency anemia (IDA) are the two most common etiologies of microcytic hypochromic anemia in children and adults. It has long been considered that iron deficiency does not exist in thalassemia syndromes, including thalassemia major as well as trait. However, studies have shown the occurrence of iron deficiency in patients with beta thalassemia trait (BTT). Earlier authors have demonstrated lower initial hemoglobin levels in patients with coexisting IDA and BTT [20-22]. This has been explained by the lack of hemopoietic nutrients due to iron deficiency superimposing on the imbalance in globin chain synthesis [23]. Similar changes have also been shown in other red cell parameters, serum iron, ferritin, and total iron binding capacity. These changes have also been demonstrated to improve after adequate iron replacement therapy [21, 22, 24].

HbA_2 levels have been reported to be lower in patients with coexisting IDA and BTT, with improvement in levels after iron therapy [20, 25]. However, other studies have shown no significant difference in HbA_2 levels in such patients [26, 27]. The reduction in HbA_2 levels in patients with concomitant BTT and IDA has been suggested to interfere in the diagnosis of the former. A recent study has hypothesized that such an occurrence can lead to these patients with BTT marrying another person with BTT with attendant risk of birth of thalassemia major child [28].

An extensive search of the available indexed English literature yielded only few Indian reports of concomitant BTT and iron deficiency [23, 29-31].

This case report showed that the concomitant existence of beta thalassemia minor and iron deficiency anemia in pregnancy. The evaluation of anemia in pregnancy is a tricky subject and is essential to treat. This case showed a normal HbA2(<3.5%) finding in a patient with beta thalassemia minor with concomitant iron deficiency anemia leading to difficulty in diagnosing beta thalassemia in patients. The combination of these two anemias along with anemia of pregnancy can justify the severe anemia seen in this patient.

In a study conducted by Sarika Verma et.el showed the changes in blood parameters in patients with concomitant beta thalassmia minor and iron deficiency anemia. In the study the mean hemoglobin level rose to g/dL and this difference was statistically significant (P<0.001). Similarly, serum iron levels rose to a mean of μg/dL with statistically significant difference (P<0.001). Serum ferritin also showed a significant increase after therapy, while TIBC reduced.

HbF levels remained largely unchanged after iron therapy while HbA_2 values showed significant rise after therapy (P=0.04).

References

[1]. Madan N, Sikka M, Sharma S, Rusia U. Frequency of coincident iron deficiency and beta-thalssemia trait. J Clin Pathol. 1996;49:1021–1022. [PMC free article][PubMed] [Google Scholar].

[2]. Sachdev R, Dam AR, Tyagi G. Detection of Hb variants and hemoglobinopathies in Indian population using HPLC: Report of 2600 cases. Indian J Pathol Microbiol. 2010;53:57–62. [PubMed] [Google Scholar].

[3]. Muncie LH, Campbell JS. Alpha and Beta Thalassemia. American Family Physician. 2009;80:339–344. [PubMed] [Google Scholar].

[4]. Tiwari AK, Chandola I. Comparing prevalence of Iron Deficiency Anemia and Beta Thalassemia Trait in microcytic and non-microcytic blood donors: Suggested algorithm for donor screening. Asian J Transfus Sci. 2009;3:99–102.[PMC free article] [PubMed] [Google Scholar]

[5]. Rogatsky E. Modern high performance liquid chromatography and HPLC 2016 International Symposium. J Chromatogr Sep Tech. 2016;7:e135.

[6]. Mulubwa M, et al. Development and validation of high performance liquid chromatography tandem mass spectrometry (HPLC-MS/MS) method for determination of tenofovir in small volumes of human plasma. J Chromatogr Sep Tech. 2015;6:300.

[7]. Santini DA, et al. Development of a high performance liquid chromatography method for the determination of tedizolid in human plasma, human serum, saline and mouse plasma. J Chromatogr Sep Tech. 2015;6:270.

[8]. Lin G, et al. Determination of sodium tanshinone iia sulfonate in rat plasma by high performance liquid chromatography and its application to pharmacokinetics studies. Pharm Anal Acta. 2015;6:383.

[9]. AL-Jammal MKH, et al. Development and validation of micro emulsion high performance liquid chromatography(MELC) method for the determination of nifedipine in pharmaceutical preparation. Pharm Anal Acta. 2015;6:347.

[10]. Myron P, et al. Tributylamine facilitated separations of fucosylated chondroitin sulfate (fucs) by high performance liquid chromatography (HPLC) into its component using 1-phenyl- 3-methyl-5-pyrazolone (pmp) derivatization. J Chromatogr Sep Tech. 2015;6:256.

[11]. Tang M, et al. HPLC analysis of monomer release from conventionally and high temperature high-pressure polymerised urethane dimethacrylate intended for biomedical applications. J Chromatograph Separat Techniq. 2014;5:227.

[12]. Khera R, Singh T, Khuana N, Gupta N, Dubey AP. Indian J Hematol Blood Transfus. 2015 Mar;31(1):110-5. doi: 10.1007/s12288-014-0409-x. Epub 2014 Jun 5.

[13]. 4. Hillman R, Ault K. Hematology in Clinical Practice. 3rd ed. New York: McGraw-Hill; 2002. [Google Scholar]

[14]. Savona-Ventura C, Bonello F. Beta-thalassemia syndromes and pregnancy. Gynecol Surv. 1994;49:129–137. [PubMed] [Google Scholar]

[15]. Abolghasemi H, Amid A, Zeinali S, Radfar MH, Eshghi P, Rahiminejad MS, et al. Thalassemia in Iran: Epidemiology, Prevention, and Management. J Ped Hematol Oncol. 2007;29:333–338. [Google Scholar]

[16]. Najmabadi H, Karimi-Nejad R, Sahebjam S, Pourfarzad F, Teimourian S, Sahebjam F. The beta-thalassemia mutation spectrum in the Iranian population. Hemoglobin. 2001;25:285–296. [PubMed] [Google Scholar]

[17]. Ramsay Margaret. Normal hematological changes during pregnancy and the puerperium. In: Pavord S, Hunt B, editors. The obstetric hematology manual. Cambridge: Cambridge University Press; 2010. pp. 1–11. [Google Scholar]

[18]. Fleming AF. Hematological changes in pregnancy. Clin Obstet Gynecol. 1975;2:269. [Google Scholar]

[19]. Shehlata N, Burrows RF, Kelton JG. Gestational thrombocytopenia. Clin Obstet Gynecol. 1999;42:327–334. doi: 10.1097/00003081-199906000-00017. [PubMed] [CrossRef] [Google Scholar]

[20]. J. B. Alperin, P. A. Dow, and M. B. Petteway, "Hemoglobin A_2 levels in health and various hematologic disorders," American Journal of Clinical Pathology, vol. 67, no. 3, pp. 219–226, 1977.View at: Google Scholar

[21]. T. Z. Qureshi, M. Anwar, S. Ahmed, D. A. Khan, and M. Saleem, "Serum ferritin levels in carriers of β-thalassaemia trait," Acta Haematologica, vol. 94, no. 1, pp. 7–9, 1995.View at: Google Scholar

[22]. T. K. Dolai, K. S. Nataraj, N. Sinha, S. Mishra, M. Bhattacharya, and M. K. Ghosh, "Prevalance of iron deficiency in thalassemia minor: a study from tertiary hospital," Indian Journal of Hematology and Blood Transfusion, vol. 28, no. 1, pp. 7–9, 2012.View at: Publisher Site | Google Scholar

[23]. A. K. Saraya, R. Kumar, S. Kailash, and A. K. Sehgal, "Iron deficiency in beta-heterozygous thalassaemia," The Indian Journal of Medical Research, vol. 79, pp. 68–75, 1984.View at: Google Scholar

[24]. El-Agouza, A. Abu Shahla, and M. Sirdah, "The effect of iron deficiency anaemia on the levels of haemoglobin subtypes: possible consequences for clinical diagnosis," Clinical and Laboratory Haematology, vol. 24, no. 5, pp. 285–289, 2002.View at: Publisher Site | Google Scholar

[25]. P. Wasi, P. Disthasongchan, and S. Na-Nakorn, "The effect of iron deficiency on the levels of hemoglobins A_2 and E," The Journal of Laboratory and Clinical Medicine, vol. 71, no. 1, pp. 85–91, 1968.View at: Google Scholar

[26]. N. Kurlekar and B. C. Mehta, "Haemoglobin A_2 levels in iron deficiency anaemia," Indian Journal of Medical Research, vol. 73, no. 1, pp. 77–81, 1981.View at: Google Scholar

[27]. C. Passarello, A. Giambona, M. Cannata, M. Vinciguerra, D. Renda, and A. Maggio, "Iron deficiency does not compromise the diagnosis of high HbA_2 β thalassemia trait," Haematologica, vol. 97, no. 3, pp. 472–473, 2012.View at: Publisher Site | Google Scholar
[28]. M. Usman, M. Moinuddin, and S. A. Ahmed, "Role of iron deficiency anemia in the propagation of beta thalssemia gene," Korean Journal of Hematology, vol. 46, no. 1, pp. 41–44, 2011.View at: Publisher Site | Google Scholar
[29]. M. R. Keramati and N. T. Maybodi, "The effect of Iron Deficiency Anemia (IDA) on the HbA_2 level and comparison of hematologic values between IDA and thalassemia minor," International Journal of Hematology and Oncology, vol. 17, no. 3, pp. 151–156, 2007.View at: Google Scholar
[30]. N. Madan, M. Sikka, S. Sharma, and U. Rusia, "Phenotypic expression of hemoglobin A_2 in beta-thalassemia trait with iron deficiency," Annals of Hematology, vol. 77, no. 3, pp. 93–96, 1998.View at: Publisher Site | Google Scholar
[31]. B. C. Mehta, P. D. Iyer, and S. G. Gandhi, "Diagnosis of heterozygous beta thalassemia in a population with high prevalence of iron deficiency," Indian Journal of Medical Sciences, vol. 27, no. 11, pp. 832–835, 1973.View at: Google Scholar

Dr. Michelle Siew. "Concomitant Beta Thalassmia Trait and Iron Deficiency Anemia in Pregnancy.." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(2), 2020, pp. 46-52.