IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 20, Issue 3 Ser.8 (March. 2021), PP 42-45
www.iosrjournals.org

Is routine iron supplementation during pregnancy justified? A two years study from a tertiary care hospital serving large tribal population

Sunita Bagdi[1], Himel Bera[2], Saptarshi Chatterjee[3], Tapan Kumar Ghosh[4], Ritam Sengupta[5], Sanjay Sengupta[6]

[1](Demonstrator, Department of Pathology, B.S. Medical College, Bankura WB)
[2](Assistant Professor, Department of Pathology, B.S. Medical College, Bankura WB)
[3](Associate Professor, Department of Forensic medicine & Toxicology, B.S. Medical College, Bankura WB)
[4](Demonstrator, Department of Pathology, B.S. Medical College, Bankura WB)
[5](Final year MBBS student, MGM Medical College, Kishanganj, Bihar)
[6](Professor, Department of Pathology, B.S. Medical College, Bankura, WB)
Corresponding author- *Himel Bera, Address- 234/1/11 Mahendra Bhattacharya Road, P.O.- Santragachi, Dist. Howrah, WB, PIN-711104.*

Abstract:
Total numbers of 1017 healthy primigravida were screened for Hb-varinats (HPLC) and body iron status (serum ferritin assay). 10.13% of screened women (103 out of 1017) presented with globin gene mutations. High iron status was found in 3.5% all cases. All these cases were related to globin gene disorders.
High proportion of iron overload denies the justification of universal iron supplementation during pregnancy. Iron status should be assessed before therapy particularly for cases with Hb-variants. Further detailed studies should be undertaken for verification of findings of this pioneering work.
Key words: *Iron supplementation during pregnancy, Iron overload, Hb-variant analysis.*

Date of Submission: 02-03-2021 Date of Acceptance: 16-03-2021

I. Introduction

Iron deficiency anaemia is a major public health problem in India. It will lead to increased rate of maternal mortality, preterm delivery, and low birth weight of new born and other complications. So, universal iron folic acid supplementation (IFA), for all pregnant women was recommended by Indian National Nutritional Prophylaxis programme. This routine iron prophylaxis is also endorsed by World health Organisation (WHO) and is currently an accepted policy all over India.[1,2,3]

Iron is a double edged sword. Low level will lead to anaemia but excess level can cause serious and irreversible organic damage. Over accumulation of this toxic metal for a prolonged period may lead to dilated cardiomyopathy, cirrhosis of liver, hypogonadism, hypothyroidism, diabetes mellitus and other endocrine abnormalities.[4,5]

Iron overload is often a troublesome complication of various heamoglobinopathies and thalassaemias. Homozygous cases commonly suffer from ill-effects of the molecule with enhanced morbidity and mortality. But various studies have clearly shown that even heterozygous cases like ß-thalassaemia trait can develop iron overload with clinical manifestations.[6,7,8]

Globin gene disorders are the commonest single gene abnormalities and according to WHO approximately 5% of world's population are carriers of this type of defect.[9]

In India, common haemoglobin disorders are ß-thalassaemia, sickle cell anaemia, haemoglobin E and Haemoglobin D. Different studies have shown variable prevalence of these disorders in different geographic areas of this country with an average of 3%-9%.[10,11,12.] Mutation of globin genes is much more frequently reported from tribal population. A trait frequently rate of 10%-40% is documented in literatures.[13] This high incidence of genetic disorder both among general and tribal population of India is surely to be reflected among pregnant population/ mothers.

Present study was done/ conducted at Bankura Sammilani Medical College and Hospital, studied in a semi-urban set up. Tribal population in West Bengal (5.1%) is lower than that of national average (approximately 8.5%). But BSMC serves population of Bankura and other neighbouring districts like Purulia and Midnapur (East and West), having significantly higher proportion of tribal population. So, it is expected that

globin gene disorders are much more common among population including pregnant women served by this institute. [14,15,16]

With this background, we planned to conduct our study to assess the incidence of different Hb-variants and iron status among pregnant women.

High prevalence of iron overload would question justification of universal iron supplementation during pregnancy.and establish necessity of assessment of ironstatus prior to therapy.

Objectives of our study were:

1. To ascertain the incidence of different abnormal haemoglobin variants among pregnant women of both tribal and non-tribal population.
2. To detect the iron status of all among pregnant women including those with haemoglobin disorders (diseased or trait).
3. To find out the proportion of women with high iron stores among all screened for justification of universal iron therapy.

II. Material and methods:

The study was done at BSMC, Bankura for a period of 2 years (1st January 2017 to 31st December, 2018). During this period after obtaining permission from institutional Ethics Committee and written consent from participants, blood samples were collected from all healthy primigravida attending antenatal clinic during first trimester. Routine haematological investigations were done over all samples. In addition, Hb-variant analysis was done by high performance liquid chromatography (HPLC).

For assessment of iron status serum ferritin level (Normal value among healthy adult females: 15-200 mcg/L) was measured. Serum ferritin level almost accurately reflects body stores and high and low values indicate iron overload and deficiency, respectively. But, inflammation can raise serum ferritin level and for that is the reason only healthy mothers were included in our study.[17]

III. Results:

Results of different tests were analyzed and tabulated. Below the important findings of our study are shown: diseased were not included.

ßTC: ß-Thalassaemia carrier
HbEC: Haemoglobin E- carrier
HbSC: Haemoglobin S- carrier
HbDC: Haemoglobin D-carrier
EßT: Double heterozygous E/ß-Thal

Out of 1017 pregnant women undergoing evaluation, 103 cases (10.13%) presented with globin chain disorders. ß-thalassaemia trait was the most common abnormality. Only a single case of E-ß thalassaemia was detected (Table no.1).

TABLE NO. 1

Total No. of cases screened	No. of cases with Hb-variant	% of cases with Hb- variant	Different types of Haemoglobino pathies with number & %		
			Variants	No	%
1017	103	10.13	BTC	74	71.9
			HbEC	21	20.5
			HbSC	05	4.8
			HbDC	02	1.9
			EBT	01	0.9

TABLE NO. 2

Table no.2 shows that out of 1017 women screened, the proportion of cases with low normal and high body iron stores (as reflected by low, normal or high serum ferritin level, respectively) were 21.2% (216 cases), 75.3% (766 cases) and 3.5% (35 cases) respectively. 34% women carrying any globin gene disorder (35 cases) showed high serum ferritin level in comparison to none of the normal Hb cases.

TOTAL NUMBER OF CASES SCREENED	CATEGORY OF CASES		CATEGORIZATION ACCORDING TO SERUM FERRITIN ASSAY		
			LOW < 15 mcg/dl	NORMAL 15- 200 mcg/dl	HIGH >200 mcg/dl
1017	NORMAL Hb	914 (100 %)	209 (22.9 %)	705 (77.1 %)	NIL
	Hb- VARIANT	103 (100 %)	7 (6.8 %)	61 (59.2 %)	35 (34 %)
TOTAL		1017 (100 %)	216 (21.2 %)	766 (75.3 %)	35 (3.5 %)

TABLE NO. 3

Table no.3 shows that majority of the cases presented with normal serum ferritin as reflected by MSF 80.6 mcg/L with SD 40.4 mcg/L. Very high (264 mcg/L) and very low values (8 mcg/L) were reported. But, there was significant difference in MSF between normal and cases with globin chain disorders.

Total Cases	Mean Serum Ferritin (MSF)	SD	Maximum Serum Ferritin	Minimum Serum Ferritin	Serum Ferritin values in different categories			
					Categories	No.	MSF	SD
1017	80.6	40.4	264	8	Normal Hb	914	66.8	9.3
					Hb- Variant	103	186.9	40.5

IV. Discussion:

At BSMC, thalassaemia screening of mothers is mandatory for last five years. So, only primigravida cases were chosen in our study assuming that multigravida cases were already screened.

Table no.1 showed that 10.13% of screened mothers were suffering from globin gene disorders and almost 72% of them were ß-thalassaemia carriers. Similar high incidence among pregnant women was reported by other workers. [18, 19]

We have already mentioned the reliability of serum ferritin value for assessment of body iron stores in absence of inflammation. Table no.2 showed that 3.5% of screened women (35 out of 1017) presented with serum ferritin value >200 mcg/dL. All of them were carriers of various globin gene mutations. According to Camaschella C and Yen et al. serum ferritin level >200 mcg/L must be investigated to establish causes of iron overload.[20] High serum ferritin level with or without significant clinical and laboratory signs of overload were repeatedly reported from ß-thalassaemia trait or E-ß thalassaemia double heterozygous cases 7, 8. On the other hand iron deficiency, as evidenced by < 15 mcg/L serum ferritin, was also observed among ß-thalassaemia trait cases, similar to our study. [21]

Table no.3 has compared the mean serum ferritin (MSF) level of both categories of pregnant women- normal as well as with Hb-variants. Statistical analysis proved that the difference between MSF of normal and variant cases (66.8±9.3 mcg/dL vs 186.9±40.5 mcg/dL) was significant (p= <0.001). similar finding were aalso reported by previous researchers7,17.

So, the important findings of present study are:

- Incidence of different haemoglobin variants among screened pregnant women is 10.13%.
- ß-thalassaemia trait is the commonest globin chain disorder in our set up.
- Approximately 3.5% of screened women have >200 mcg/dL serum ferritin level indicating iron overload.
- Iron overload is solely reported from Hb-variant cases.

These findings definitely question the justification of universal iron therapy during pregnancy. At least prior assessment of iron status of carriers of ß-globin gene mutation should be done before administering iron to avoid potential toxicity of overload.

V. Conclusion:

IFA supplementation is a routine therapy of all pregnant and lactating women in our country. This supplementation is beneficial for both mother and child. Iron overload is also a common troublesome complication of different haemoglobinopathies in both homozygous as well as hetrerozygous or double heterozygous cases. The incidence of globin gene mutation carriers is quite high in India. In our present study, we have estimated the incidence of iron overload among pregnant women. High iron status is shown to be related to Hb-variants. Our finding of high prevalence of iron overload (3.5%) speaks against universal iron supplementation. It also advocates that iron status must be assessed before supplementation particularly in cases with Hb-variants.

We should admit that our study population and duration are far from adequate. Large multi-institutional studies and following should be planned for longer period in order to reach unequivocal conclusion. Ill effects of iron therapy during pregnancy over cases with high iron store must also be assessed. Another potential angle of evaluation is 'cost-effect' assessment of universal screening of pregnant ladies by HPLC with estimation of iron status of all with Hb-varinats.

We hope that our pioneering work will pave the steps of further research works. In near future there can be necessary adjustments of universal IFA therapy during pregnancy to prevent therapy induced organ damage.

Conflict of interest: None.

Author's contribution: Dr. Sunita Bagdi & Dr. Tapan K. Ghosh conducted the study. Prof. Sanjay Sengupta & Dr. Himel Bera drafted the manuscript & revised it critically for intellectual content. Dr. Saptarshi Chatterjee also helped in the study. Ritam Sengupta helped in typographical jobs.

Dr. Himel Bera acted as the **corresponding author** and performed the jobs related to sending the manuscript.

References

[1]. Allen LH. Anemia and iron deficiency: effects on pregnancy outcome. Am J Clin Nutr. 2000 May;71(5 Suppl):1280S-4S. doi: 10.1093/ajcn/71.5.1280s. PMID: 10799402.

[2]. Ministry of Health and Family Welfare.Review of the policy regarding micronutrients- Iron Folic Acid(IFA)2007[Internet].New Delhi: Ministry of Health and Family Welfare, April 2007[cited 2021 Feb22].Available from:https://nhm.gov.in/images/pdf/programmes/child-health/guidelines/goi_ifa.pdf

[3]. Pasricha, SR., Biggs, BA., Prashanth, N. et al. Factors Influencing Receipt of Iron Supplementation by Young Children and their Mothers in Rural India: Local and National Cross-Sectional Studies. BMC Public Health 11, 617 (2011). https://doi.org/10.1186/1471-2458-11-617.

[4]. Galanello, R., Origa, R. Beta-thalassemia. Orphanet J Rare Dis 5, 11 (2010). https://doi.org/10.1186/1750-1172-5-11.

[5]. Byatnal A, Byatnal AA, Parvathi Devi MK, Badriramkrishna B. β-Thalassemia hijacking ineffective erythropoietin and iron overload: Two case reports and a review of literature. J Nat Sci Biol Med. 2014 Jul;5(2):456-9. doi: 10.4103/0976-9668.136245. PMID: 25097435; PMCID: PMC4121935.

[6]. Qureshi TZ, Anwar M, Ahmed S, Ahmed Khan D, Saleem M. Serum ferritin levels in carriers of beta-thalassaemia trait. Acta Haematol. 1995;94(1):7-9. doi: 10.1159/000203963. PMID: 7653214.

[7]. Edwards CQ, Griffen LM, Dadone MM, Skolnick MH, Kushner JP. Mapping the locus for hereditary hemochromatosis: localization between HLA-B and HLA-A. Am J Hum Genet. 1986 Jun;38(6):805-11. PMID: 3460331; PMCID: PMC1684861.

[8]. Fargion S, Taddei MT, Cappellini MD, Piperno A, Fiorelli G. The iron status of Italian subjects with beta-thalassemia trait. Acta Haematologica. 1982 ;68(2):109-114. DOI: 10.1159/000206961.

[9]. World Health Organization:Thalassaemia and other haemoglobinopathies: WHO report 2006. Available :https://apps.who.int/gb/archive/pdf_files/EB118/B118_5-en.pdf. Accessed 22 February,2021.

[10]. Varawalla NY, Old JM, Sarkar R, Venkatesan R, Weatherall DJ. The spectrum of beta-thalassaemia mutations on the Indian subcontinent: the basis for prenatal diagnosis. Br J Haematol. 1991 Jun;78(2):242-7. doi: 10.1111/j.1365-2141.1991.tb04423.x. PMID: 2064964.

[11]. Balgir, R. S. "The Burden of Haemoglobinopathies in India and the Challenges Ahead." Current Science, vol. 79, no. 11, 2000, pp. 1536–1547. JSTOR, www.jstor.org/stable/24104846. Accessed 12 Feb. 2021.

[12]. De M, Das SK, Bhattacharya DK, Talukder G. The occurrence of beta-thalassemia mutation and its interaction with hemoglobin E in the eastern India. Int J Hematol. 1997 Jul;66(1):31-4. doi: 10.1016/s0925-5710(97)00585-9. PMID: 9220658.

[13]. Ghosh K, Colah RB, Mukherjee MB. Haemoglobinopathies in tribal populations of India. Indian J Med Res [serial online] 2015 [cited 2021 Feb 12];141:505-8. Available from: https://www.ijmr.org.in/text.asp?2015/141/5/505/159488

[14]. Statistical Profile of Scheduled Tribes in India 2013.[Internet]2013.[cited 22 January 2021].Available from:https://ruralindiaonline.org/en/library/resource/statistical-profile-of-scheduled-tribes-in-india-2013/

[15]. https://censusindia.gov.in/2011-common/censusdata2011.html

[16]. https://censusindia.gov.in/2011-Common/Latest_Releases.html

[17]. Bain BJ, Bates I, Laffan MA, Lewis MS. Dacie and Lewis practical haematology. 11th ed.: Elsevier Churchill Livingstone; 2011.

[18]. Gupta V, Sharma P, Jora R, Amandeep M, Kumar A. Screening for Thalassemia Carrier Status in Pregnancy and Pre-Natal Diagnosis. Indian Pediatr. 2015 Sep;52(9):808-9. PMID: 26519723.

[19]. Bain BJ. Screening of antenatal patients in a multiethnic community for beta thalassaemia trait. J Clin Pathol. 1988 May;41(5):481-5. doi: 10.1136/jcp.41.5.481. PMID: 3384979; PMCID: PMC1141496.

[20]. Understanding iron homeostasis through genetic analysis of hemochromatosis and related disorders. Camaschella C. Blood. 2005 December;106(12):3710-7.

[21]. Hussein S, Hoffbrand AV, Laulicht M, Attock B, Letsky E. Serum ferritin levels in beta-thalassaemia trait. Br Med J. 1976 Oct 16;2(6041):920. doi: 10.1136/bmj.2.6041.920. PMID: 974665; PMCID: PMC1688477.