

ORIGINAL ARTICLE

Re-evaluating the need for universal iron supplementation in pregnant Indian women in the light of gestational age specific low hemoglobin prevalence

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Abstract

Background: Anemia prevalence among Indian pregnant women in 2015-16 was 50.4% and has not declined from 49.7% in 1998-99 despite the national policies on iron-folic acid supplementation. New gestational age-specific cut-offs (INTERGROWTH cut-off) for risk of low Hemoglobin (Hb) have been identified. **Aims and objectives:** Compare prevalences of low Hb based on WHO and INTERGROWTH cut-offs **Methods:** The prevalence of anemia/low Hb among pregnant women in trimesters 2 and 3 from NFHS-4 data were estimated using the current WHO recommendations and the INTERGROWTH cut-offs. **Results:** Prevalence of low Hb by the INTERGROWTH cut-off was 28.1%(95% CI:26.9-29.4) and 21.7%(95% CI:20.6-22.9) in trimesters 2 and 3. Anemia prevalence by WHO cut-off was much higher at 41.2%(95% CI:39.8-42.5) and 54.8%(95% CI:53.2-56.3) in trimesters 2 and 3. The prevalence of low-Hb was similar between ANC and no-ANC reported groups in both trimesters (26.1% and 28.9% in trimester-2; 20.1% and 22.4% in trimester-3). **Conclusion:** The prevalence of low-Hb with gestational age specific cut-offs is much lower compared to earlier estimates using WHO cut-off. The universal iron supplementation program for pregnant women in India need to be re-examined in this light and a tragetter Hb testing based supplementation may be more beneficial in reducing anemia prevalence.

Keywords

Anemia; Dietary Supplements; Health Surveys; Program Evaluation

Introduction

Anemia in pregnancy is considered a public health nutrition problem in India as the prevalence of anemia is 50.4% according to the National Family Health Survey-4 (2015-16)(1) and has not declined from 49.7% in 1998-99(2) despite the national policies of iron-folic acid (IFA) supplementation in pregnant women. More recently in NFHS-5(2019-20), 40% of the 18 states for which reports have been released, have anemia prevalence exceeding 50% and no substantial reduction in prevalence in the others (3).

Among several reasons for the failure to reduce anemia prevalence, the primary one could be the current cut-offs for anemia. Instead of WHO-recommended cutoffs of hemoglobin(Hb) (4), robust gestational age-specific cut-

offs for low Hb in pregnant women were derived recently using good quality multi-country data (5). The universal supplementation of IFA in pregnant women in India is based on WHO classification of the country as having a severe problem of anemia in pregnancy due to its very high prevalence(6). In this study we re-estimate the prevalence of anemia based on the new cut-off for low Hb in pregnant women(5). Thus there is a need to re-examine the prevalence base on gestational age specific cut-off in Indian pregnant women.

Aim & Objective

To estimate the prevalence of anemia in NFHS-4 using the new method and examine the intended effect of universal iron supplementation on anemia prevalence

Material & Methods

Data sources: The nationally representative data from NFHS-4 (2015-16) was considered for this study. The survey employed a stratified (rural, urban strata) 2 stage sampling with 2011 census as the base sampling frame. Selection of primary sampling units which were villages in rural areas and Census Enumeration Blocks in urban areas contributed to first stage. Villages or Census Enumeration Blocks were sampled with the probability of selection being proportional to population size. 22 households were randomly sampled from each primary sampling unit at the second stage of sampling. All women aged 20–49 years in the selected households were invited to participate in the survey. Person level data on household and individual socio-demographic characteristics, and blood biochemistry including Hb from 28241 pregnant women residing in 27851 households, across 640 districts covering 29 states and 6 union territories of India(1) was used. Women in second or third trimester of pregnancy (14-40 weeks of gestation) were considered for the analysis. Data on month of pregnancy, receipt antenatal care services (ANC) were self-reported. Data on IFA supplementation was not available for pregnant women. Hemoglobin was measured from capillary blood samples (by finger pick) by trained surveyors using HemoCue Hb 201+ analyser(7). Values less than 30 g/L or above 170 g/L were excluded as extreme values(8). Finally, 19964 valid values of pregnant women with gestational age between 14 and 40 weeks were considered for the analysis.

We also used individual level data of NFHS-3 (2005-2006) to aid a comparison of prevalence between rounds. The data included valid Hb values of 3170 pregnant women in second or third trimesters of pregnancy, residing 3138 households across India. The households were sampled by a 2 stage sampling method similar to NFHS-4, to obtain precise national and state level estimates.

Anemia cut-off: The NFHS-4 reports used WHO recommended cut-off Hb<105 g/L in second trimester (13-24 weeks) and <110 g/L in third trimester of pregnancy, after adjustment for cigarette smoking and altitude >1000 metres(4). Recently the WHO recommendation of anemia cut-off in pregnancy was re-examined in the data from the INTERGROWTH-21st Project (2009-2016) which consisted of women from eight geographically diverse urban areas including Nagpur in India. The areas selected had to be located at altitude <1600 m above sea level and the pregnant women had to be with a low risk of fetal and infant growth and developmental disturbances, as well as an absence or low levels of major, known, non-microbiological contamination and should have registered with an antenatal care centre before 14 weeks of gestation (by last menstrual period). The women were well nourished with body mass index between 18 and 25 kg/m². Hb tests were taken as part of routine antenatal care, and Hb concentration was assessed from venous

blood samples using commercially available methods (automatised colorimetry, automatised turbidimetry, high efficiency liquid chromatography, sysmex autoanalyser, automated flow fluorescent analyser, photometric method using automated cell counter, high efficiency liquid chromatography and cyanide-free sodium lauryl sulphate). From smoothed centiles for maternal hemoglobin(g/L) according to exact gestational week starting from 14 weeks of gestation to 40 weeks of gestation, the new recommended cut-off for Hb are as follows: Normal Hb corresponding to ≥ 10th centile and Hb<3rd centile as Low Hb concentration, 3rd to <5th centile as High risk of low Hb concentration, 5th to <10th centile as Moderate risk of low Hb concentration(5). Median of four weekly cut-offs was considered as cut-off for gestational age in month. The various cut-offs are provided in (Table 1).

Statistical methods: Pregnant women were classified based on WHO and INTERGROWTH cut-off and appropriate survey sampling weighted national anemia prevalence and different grades of Low Hb concentration with 95% confidence interval were estimated. The prevalence was compared between women who received ANC and did not by the overlap in 95% confidence interval of the prevalence estimate. All weighted prevalence estimated using the sampling weights provided in the NFHS-3 and NFHS-4 data sets and the Survey package of R statistical software version 4.02 (R core Team, 2020) was used to arrive at the weighted estimates.

Results

The overall prevalence of anemia among pregnant women in trimester 2 (Table 2) by the WHO cut-off (41.18%; 95% CI 39.8,42.5) was higher than the prevalence of Low Hb which is the percentage of women with Hb value <3rd percentile in the INTERGROWTH Hb distribution for trimester 2 (28.1%; 95% CI 26.9,29.4). In trimester 3 as well, the overall prevalence of anemia was higher at 54.8% (95% CI 53.2,56.3) compared to prevalence of Low Hb (21.7%; 95% CI 20.6,22.9) by INTERGROWTH cut-off. In trimester 2, 5.4% and 10.3% of women were classified as being at high and moderate risk of low Hb and in trimester 3, 4.3% and 8.2% were identified to be at high and moderate risk of low Hb (Table 2). The prevalence of Low Hb in NFHS-3 by the INTERGROWTH cut-off was 33.2% (95% CI:30.1,36.3) in trimester 2 and 29.2% (95% CI:26.4, 32.2) in trimester 3 while the corresponding anemia prevalence by WHO cut off was 65.4% and 54.8% respectively.

About 28% women in second trimester and 32% in the third trimester received ANC. The prevalence of anemia in trimester 2 by WHO cut-off was 38.6% (95% CI:36.1,42.1) in the ANC group and 42.1% (95% CI:40.5,43.7) in the no ANC groups. By the INTERGROWTH cut-off, the prevalence of Low Hb (<3rd percentile) was 26.1% in the ANC group and 28.9% in the no ANC group. In the third

trimester also, the prevalence was comparable between the ANC and no-ANC group by both methods (Table 3). The Hb distribution overlapped between the ANC and no ANC groups in both trimesters (Figures 1) & (Figure 2). Therefore, receiving ANC and possibly IFA did not alter the distribution of Hb in both trimesters.

Discussion

The national prevalence of low Hb in pregnant women in India according to the carefully collected data from the INTERGROWTH study is lower than anemia prevalence according to WHO cut-off, in both second and third trimesters of pregnancy. This reduced prevalence is due to the lower cut-off for Low Hb. The INTERGROWTH study introduced a classification of moderate and high risk of Low Hb rather than classifying pregnant women to classes of anemia. The prevalence of anemia/Low Hb was comparable between those receiving and those not receiving ANC during pregnancy, when computed by WHO and INTERGROWTH cut-off. The relative decline in the prevalence of anemia/Low-Hb from NFHS-3 to NFHS-4 was comparable by both cut-offs.

The WHO cut-off for anemia in pregnancy was drawn as an action point for guidance in antenatal care for positive outcomes in pregnancy based on low certainty evidence(4). A blanket cut-off of <110g/L is also used across trimesters of pregnancy to estimate prevalence in surveys and this cut-off is based on the distribution of Hb in six studies(9) but not selectively in healthy populations which should have been criteria for selecting studies to identify Hb cut-off. Two studies in India were also considered representing urban and rural populations and the average Hb in these two studies were only around 100 g/L, lower than the cut-off proposed by WHO. An exploration of Hb distributions of healthy White, Black, Mexican and Hispanic and Asian non-pregnant women obtained from nine rounds of the National Health and Nutrition Examination Survey in the United States and two rounds of National Diet and Nutrition Survey in United Kingdom showed that the mean Hb of Asians residing in these countries were lower than Whites, and the value corresponding to the 4.95th percentile of Hb distribution in healthy women was 112.2 g/L, which is lower than the WHO cut-off of 120 g/L for anemia(10). Thus, the INTERGROWTH cut-off developed in carefully sampled healthy pregnant women prompted us to re-examine the prevalence of anemia/Low Hb in the NFHS-4 survey as the INTERGROWTH study included an Indian sample as well(5).

With the reduced estimates of prevalence, WHO consideration of countries that require universal supplementation in pregnancy need to be revisited(6). The lack of association with universal iron folic acid supplementation has been reported earlier(11) and there has been a recommendation for testing and supplementing(12). While there are several reasons for

the failure of the universal IFA supplementation program to reduce anemia prevalence in the country such as compliance and supply side challenges(13), one of the main reasons would be the cause of anemia. It has been documented that less than 50% of anemia would be iron deficiency anemia in countries with prevalence greater than 40% and in countries with high levels of inflammation(14). It may be noted that the risk of inadequacy of iron intake is only 33% in Indian women according to the NSSO consumer expenditure survey(15) considering recently published dietary requirements for Indians(16) as the reference for requirement. Thus, there is a reason to do targeted tested supplementation. Excess iron in pregnancy has been associated with higher prevalence of low birthweight babies(17) and higher oxidative stress markers(18).

This study is a preliminary exploration of the likely true prevalence of low Hb in pregnant women in India using data available in NFHS-4 which could have errors in the measurement of Hb. The comparison of low Hb with respect to IFA supplementation has not been performed on observed data on supplementation and could be subject to reporting error. However, in the absence of reported data the predicted IFA supplementation has been used for the comparison. It is important to have future studies that examine the distribution of iron status in the new cut-off groups namely moderate risk of low Hb, high risk of low Hb and Low Hb and identify the group that can benefit from iron supplementation.

Conclusion

The true prevalence of low Hb in India among pregnant women is likely to be much lower than the currently reported prevalence of 50% and close to 28% and 21% in second and third trimesters as estimated by the new INTERGROWTH cut-off. In this context the need for universal IFA supplementation program in India could be evaluated and a targeted supplementation followed by Hb testing be recommended.

Recommendation

The need for the current universal IFA supplementation program for pregnant women in India could be evaluated and a targeted supplementation followed by Hb testing be recommended.

Limitation of the study

The study utilizes secondary data for the analysis.

Relevance of the study

The study re-examines the prevalence of low Hb in pregnant women in India in the light of the newly derived standard Hb distribution and gestational age specific cut-off for low Hb.

Authors Contribution

Concepts: AS, JB, AK,TT; Literature research: AS, JB; Statistical analysis: AS, JB; Manuscript preparation: AS, JB,

TT; Manuscript editing and reviewing: AS, JB, AK, TT; Guarantor: TT.

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Tables

TABLE 1 GESTATIONAL AGE SPECIFIC CUT-OFF FOR HB (G/L) IN PREGNANT WOMEN

Gestational age (months)	WHO cut-off of Hb (g/L)				Low Hb	High risk of low Hb	Moderate risk of low Hb	Normal Hb
	Severe	Moderate	Mild	Normal				
4	<105			≥105	<102	102-104	104-108	≥108
5	<105			≥105	<100	100-102	102-106	≥106
6	<105			≥105	<98	98-100	100-104	≥104
7	<70	70-99	100-109	≥ 110	<96	96-98	98-102	≥103
8	<70	70-99	100-109	≥ 110	<94	94-97	97-101	≥102
9	<70	70-99	100-109	≥ 110	<94	94-97	97-101	≥102
10	<70	70-99	100-109	≥ 110	<97	97-99	99-103	≥104

TABLE 2 NATIONAL PREVALENCE OF HB CATEGORIES BASED ON WHO CUT-OFF AND INTERGROWTH CUT-OFF AMONG PREGNANT WOMEN IN NFHS-4

Trimester	Method	Category	Prevalence% (95% CI)
2 (n=11344)	WHO	Anemia	41.2 (39.8,42.5)
		Low Hb	28.1 (26.9,29.4)
	INTERGROWTH	High risk of low Hb	5.4 (4.7,6.0)
		Moderate risk of low Hb	10.3 (9.5,11.1)
3 (n=8620)	WHO	Severe Anemia	1.7 (1.3,2.0)
		Moderate Anemia	29.6 (28.3,31.0)
		Mild Anemia	23.5 (22.3,24.8)
	INTERGROWTH	Low Hb	21.7 (20.6,22.9)
		High risk of low Hb	4.3 (3.8,4.9)
		Moderate risk of low Hb	8.2 (7.3,9.2)

Values are prevalence % (95% Confidence Interval)

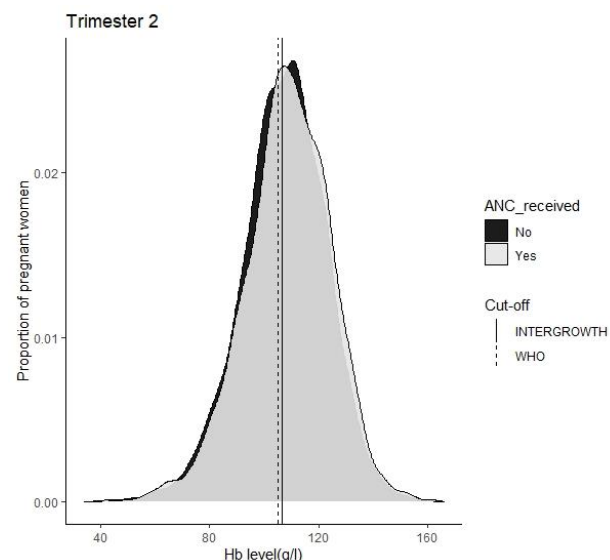
TABLE 3 NATIONAL PREVALENCE OF HB CATEGORIES BASED ON WHO CUT-OFF AND INTERGROWTH CUT-OFF AMONG PREGNANT WOMEN BY REPORTED RECEIPT OF ANTENATAL CARE (ANC) IN NFHS-4

Trimester	Method	Category	ANC (95% CI)	No ANC (95% CI)
2	WHO	Anemia	38.6 (36.1,42.1)	42.1 (40.5,43.7)
		Low Hb	26.1 (23.9,28.5)	28.9 (27.5,30.3)
	INTERGROWTH	High risk of low Hb	4.6 (3.6,5.8)	5.6 (4.9,6.4)
		Moderate risk of low Hb	10.5 (9.1,1.2)	10.2 (9.3,11.2)
3	WHO	Severe	1.8 (1.1,2.5)	1.6 (1.3,2)
		Moderate	27.8 (25.4,30.3)	30.4 (28.8,32)
		Mild	24.1(21.8,26.4)	23.3 (21.8,24.8)
	INTERGROWTH	Low Hb	20.1(18.1,22,3)	22.4 (21,23.8)
		High risk of low Hb	4.2 (3.2,5,6)	4.4 (3.7,5.2)
		Moderate risk of low Hb	7.9 (6.6,9.5)	8.4 (7.2,9.6)

Values are prevalence % (95% Confidence Interval)

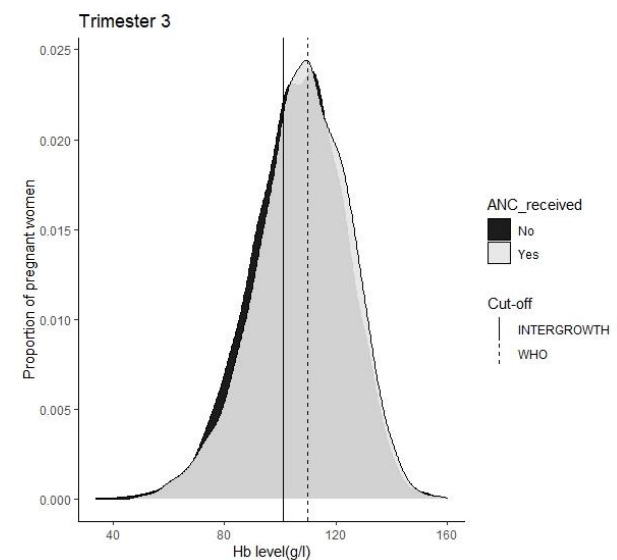
Figures

FIGURE 1 DISTRIBUTION OF HEMOGLOBIN AMONG PREGNANT WOMEN IN TRIMESTER 2 BY ANC VISITS.



Dotted line: WHO method of cut-off of anemia (105 g/l) ; Solid line : INTERGROWTH cut-off for moderate risk of low hemoglobin (106.5 g/l);prevalence of anemia among pregnant women receiving ANC is 38.6% and for not receiving ANC visit is 42.1%: prevalence of low Hb/risk of low Hb among who are receiving ANC is 41.2% and for not receiving ANC visits is 44.8%. Mean (SD) of Hb level in ANC group is 108.3(15.8) g/L and non-ANC group is 107(15) g/L.

FIGURE 2 DISTRIBUTION OF HEMOGLOBIN AMONG PREGNANT WOMEN IN TRIMESTER 3 BY ANC VISITS



Dotted line: WHO method of cut-off of anemia (100 g/l) ; Solid line : INTERGROWTH cut-off for moderate risk of low hemoglobin (97 g/l);prevalence of anemia among pregnant women receiving ANC is 53.7% and for not receiving ANC visit is 55.3%: prevalence of low Hb/risk of low Hb among who are receiving ANC is 32.2% and for not receiving ANC visits is 35.2%. Mean (SD) of Hb level in ANC group is 107.5(16.4) g/L and non-ANC group is 106.3(16.3) g/L