

Prevalence of latent iron deficiency in early pregnancy in a tertiary care hospital in Sri Lanka: A cross-sectional study

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Abstract

Objectives To estimate the prevalence of latent iron deficiency (LID) among pregnant women, assess LID in relation to parity, age, education, and household income, and to determine correlations between LID and red cell indices, red cell distribution width (RDW), and red cell morphology. **Design** Cross-sectional design **Setting** North Colombo Teaching Hospital, Sri Lanka. **Sample** Participants comprised 355 pregnant women with normal haemoglobin levels seeking antenatal care within < 20 weeks of gestation. **Method** Data were obtained from interviews and antenatal records. Participant full blood count (FBC), serum ferritin levels, and blood films were analysed. **Main Outcome Measures** Prevalence of LID, demographic data (age, parity, period of gestation, gap between pregnancies, income, and education), and blood film morphology. **Results** LID prevalence was 54%. Statistical significance for the gap between pregnancies being < 2 years was observed but not for participant's age, parity, income, and education. Blood film morphology depicted statistically significant presence of hypochromic microcytic red cells and pencil cells. RDW was significant in indicating the presence of LID. Among those with LID, 25% had ferritin level in the iron deficiency range. **Conclusions** LID is highly prevalent in early pregnancy and 25% of participants had ferritin levels in the iron deficiency range. Presence of raised RDW, hypochromic microcytic red cells, pencil cells, and <2 years' gap between pregnancies were indicators of LID. To identify pregnant women with LID, blood film, haemoglobin, and RDW could be recommended as basic tests, and ferritin test as an affirmative one.

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Prevalence of LID, demographic data (age, parity, period of gestation, gap between pregnancies, income, and education), and blood film morphology.

Results

LID prevalence was 54%. Statistical significance for the gap between pregnancies being < 2 years was observed but not for participant's age, parity, income, and education. Blood film morphology depicted statistically significant presence of hypochromic microcytic red cells and pencil cells. RDW was significant in indicating the presence of LID. Among those with LID, 25% had ferritin level in iron deficiency range.

Conclusions

LID is highly prevalent in early pregnancy and 25% of participants had ferritin levels in the iron deficiency range. Presence of raised RDW, hypochromic microcytic red cells, pencil cells, and <2 years' gap between pregnancies were indicators of LID. To identify pregnant women with LID, blood film, haemoglobin, and RDW could be recommended as basic tests, and ferritin test as an affirmative one.

Keywords : Latent iron deficiency, iron deficiency anaemia, pregnancy, red cell distribution width, full blood count, serum ferritin

Tweetable Abstract:

Latent iron deficiency is prevalent in pregnant women and can be identified through blood film, haemoglobin, serum ferritin, and red cell distribution width tests

Introduction

Worldwide, iron deficiency is the most common nutritional deficiency^(1,2). Approximately 20% of pregnant women worldwide suffer from anaemia due to this⁽³⁾.

During pregnancy, iron deficiency risk increases due to the requirement of additional iron to sustain the expansion of red cell mass, and the growth of the fetus and placenta⁽¹⁾. Iron deficiency contributes to adverse pregnancy outcomes such as intrauterine growth retardation and perinatal death^(4,2). Some studies have shown maternal iron deficiency at delivery to be associated with lower serum ferritin levels in the cord blood of neonates, especially when the mother's serum ferritin level was below 13 $\mu\text{g/l}$ ^(5,6,7). This perhaps explains why iron deficiency impacts fetal and infant well-being by affecting brain development, auditory neural maturation, and increasing the risk of poorer cognitive, motor, social-emotional, and neurophysiologic development^(4,8,9).

Iron deficiency is progressive: iron stores in the body gradually diminish, resulting in iron deficiency anaemia (IDA)^(5,10). Latent iron deficiency (LID) occurs when iron stores are exhausted but the blood haemoglobin (Hb) levels are within normal limits⁽¹¹⁾. Hence women with LID are at a higher risk of developing IDA – associated with pregnancy complications, if not for early detection and treatment.

Assessment of Hb level alone, however, is not adequate to identify LID⁽¹²⁾. Estimation of serum ferritin is the more pertinent method to detect body iron stores^(5,13),⁽⁵⁾. A serum ferritin level of $<30 \text{ ug/l}$ in pregnancy is considered as LID⁽⁵⁾. Even though serum ferritin is currently available in most general hospitals in Sri Lanka, it is an expensive test and is not performed routinely. Therefore, surrogate screening tests are needed to identify women with LID.

In LID, the mean corpuscular volume (MCV) usually remains within normal limits, but a few microcytes may be detected on a blood smear⁽¹⁴⁾. Therefore, increased red cell distribution width (RDW) may be an early indicator for LID^(15,16). Red cell indices and RDW are low-cost investigations included in the full blood count (FBC), which can be undertaken in hospitals in Sri Lanka and other developing countries.

The prevalence of LID among pregnant women in Sri Lanka is currently not well known. Better awareness would enable clinicians to act within the routine antenatal care plan. Thus, the primary objective of this study was to assess the prevalence of LID in early pregnancy. Furthermore, the secondary objective was to identify LID using red cell indices, RDW, and blood films as surrogate screening tools.

Methods

This cross sectional study was conducted in the obstetrics and gynaecology units of North Colombo Teaching Hospital, Sri Lanka from December 2014 to January 2017. All pregnant women with normal Hb levels ($[?]110 \text{ g/l}$ in <12 weeks, $>105 \text{ g/l}$ in 13-20 weeks of gestation), booked for antenatal care within <20 weeks of gestation, were the potential study subjects⁽⁵⁾. Among them, those with haematological diseases, active infections, liver disease, chronic connective tissue disorders, malignancies, and haemoglobinopathies were excluded⁽⁴⁾. Written informed consent was obtained from the selected subjects. Data were gathered from interviews and antenatal records. The study was approved by the Ethics Review Committee, Faculty of Medicine, University of Kelaniya, Sri Lanka.

Blood samples were collected for FBC, blood film, and serum ferritin level. Any further treatment or follow-up was in accordance with routine clinical practice. Full blood count was analysed by a five-part Beckman Coulter analyser, while serum ferritin was estimated by a two-step immune metric technique. Blood film morphology was reported by three independent observers. If a blood film showed features of the exclusion criteria listed above, the subject's data were excluded. Existing data from a similar Sri Lankan population at the booking visit estimated the LID to be 18%^(10,17).

The sample size of the cross-sectional study was 355, calculated on the basis of 4% acceptable difference at a 95% confidence interval. The preliminary statistical analysis was limited to descriptive statistics. IBM SPSS (version 16) was used for socio-demographic, FBC, and morphology data analysis. Pearson's chi squared test

was applied to determine statistical significance. The independent t-test analysed the effect of prophylactic use of haematinics. Receiver Operating Characteristic (ROC) curves were constructed to identify optimal cut off values for red cell indices (4,12). Statistically significant P value was taken as <0.05.

Results

The total number of pregnant women under 20 weeks of gestation was 355. While 192 women were in the LID group (54%), 163 women were a part of the normal group (46%).

Majority (56%) were between 21–30 years. Primi gravida pregnancies were noted among 43.2% in LID group, while it varied in the normal group. Majority were with a period of gestation of 13 to 20 weeks (56.2% in the LID group, 46.6% in the normal group). Gap of less than 2 years between pregnancies was 60.4% in LID and 44.2% in normal group. Most of the subjects (72%) were well educated to GCE Ordinary level or above, yet 89.6% of them were unemployed. Approximately, 68% of spouses were skilled workers. Nearly half of the sample belonged to low-income families with monthly earnings <LKR 50,000 (USD 278). Of the demographic data, statistical significance (P=0.006) was noted only for the gap between pregnancies being <2 years, but not for participants' age, parity, period of gestation, income, or education.

The values for Hb, RBC, Red cell indices, and RDW, according to the iron status, are shown in Table 1, along with descriptive statistics. Considering the FBC parameters, the RDW values for participants in the LID vs. normal group were significant (P=0.001). No significant differences for Hb, RBC, MCV, mean corpuscular hemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC) values were found between the groups.

Blood film morphology depicted a statistically significant presence of hypochromic microcytic red cells (P=0.001) and pencil cells (P=0.007) between groups. Morphology findings according to iron status are shown in Table 2.

Among the LID group, 25% participants had ferritin levels in the iron deficiency range (<15 µg/l). Although 43% of participants in the cohort were on iron supplements, there was no statistical difference for haematinics between the two groups. The ROC was constructed for red cell indices to identify predictive values. Significant area under the curve (AUC) and P values (P=0.0001) were noted only for RDW.

Discussion

Main findings

In the study group, 54% of the participants had LID, that is, they had depleted iron stores from the start of pregnancy. Therefore, they would be at high risk for IDA. Notably, one fourth of the participants in the LID group had serum ferritin at a severe iron deficiency level (<15ug/L). They had normal Hb levels, hence their deficiency would not have been identified by routine tests done in the antenatal clinics. They, thus, would not have received appropriate care to prevent anaemia with the progression of pregnancy. Their new-born would also have been at the risk of developing cognitive impairment associated with IDA.

Strengths and limitations

Though socio-demographic factors could influence iron deficiency status, the reduced gap between pregnancies was the only significant risk factor identified. The finding of this study was compatible with other studies such as the one by Lazović and Pocekovac⁽¹⁸⁾.

Haemoglobin on its own is a poor indicator of iron deficiency, and previous studies have emphasised its poor sensitivity for identifying iron deficiency^(19,20). Since the number of women with LID was high, reflecting an overall high incidence in the population, it is important to have easily assessable and affordable tests to screen for iron deficiency. Due to the high cost and low availability of the serum ferritin estimation method, the red cell indices, RDW, and blood film were considered as substitute screening tests. However, the correlation of red cell indices with LID did not show any statistical significance. This may be due to the

counter effects of pregnancy induced changes, especially the MCV, as it increases by 4 fl with progression of pregnancy⁽²¹⁾. A study by Tiwari et al. among 100 pregnant women in India supported these findings⁽²¹⁾.

It is known that few microcytes can be seen in the blood film in LID⁽²²⁾. This could contribute to the increase in RDW^(16,23). Though the study by Tiwari et al.⁽²¹⁾ had shown no significant indicators to detect LID, our data showed a significant increase of RDW in the LID group. Blood film morphology observed by three haematologists revealed that hypochromic microcytic red cells and pencil cells were present in a significant number of participants with LID. These two tests (blood film and RDW) can be used independently or in combination as routine tests to screen for LID. The use of ROC cut off values for red cell indices to detect LID has been shown by Rabindrakumar et al.⁽⁴⁾, with a smaller number (70) of participants. However, such results were not reflected in the analysis of the present study, even with a larger sample size of 194.

Due to logistical constraints, the study has one limitation: subjects could not be followed-up with to monitor their pregnancy outcome.

Conclusion

Study results revealed a high prevalence of LID in early pregnancy with one fourth of the sample having ferritin levels in the iron deficiency region. The presence of raised RDW, hypochromic microcytic red cells, and pencil cells acted as indicators of LID. It is recommended that to identify pregnant women with LID, blood film, Hb level, and RDW could be measured as basic screening tests. Serum ferritin test could be recommended as an affirmative follow-up. The step-wise testing suggested in this study is a cost-effective procedure, especially suitable for resource-strapped obstetrics and gynaecology clinics in developing countries.

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Disclosure of interests

There are no competing interests to be disclosed.

Contribution to authorship

HND is the main and corresponding author. She contributed to the study by writing the proposal and collecting the clinical data from the pregnant women. She was the first observer for the blood film. The abstract and final research paper was written by her under the guidance of co-authors.

SW was the main supervisor for the study. She provided guidance on conducting the haematology procedures and acted as an independent observer for the blood films. Furthermore, she contributed to the writing of the abstract and the main research paper.

DM contributed to the research by being the second independent observer for blood films. She provided guidance on forming information leaflets on the research. Furthermore, she contributed to the writing of the abstract and the main research paper.

IS was the primary statistician for the study.

AM and AP were contributors to different parts of the statistical analyses, and they rechecked statistic results for coherence.

TP was the main author who provided the guidance for the concept of the research. He was involved in writing up the research proposal for the ethical clearance.

CM provided guidance on obstetrics concept of the research. She was initially involved in developing the concept and for writing up the research proposal for the ethical clearance.

Details of ethics approval

The study was approved by the Ethical Review Committee of the Faculty of Medicine, University of Kelaniya, Ragama, in November 2014.

(ref. P/228/11/2014).

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Tables/Figures caption list

Table 01: Data from FBC test from LID and normal group

Table 02: Morphology data from blood film analysis

Table 1 Data from Full Blood Count (FBC) test from Latent Iron Deficiency (LID) and Normal group

	LID	LID	LID	LID	Normal	Normal	Normal	Normal
	Mean	Median	Mode	Standard Deviation	Mean	Median	Mode	Standard Deviation
Hb	11.9	11.7	11.2	0.9	12.3	12.2	11.9	0.9
RBC	4.36	4.34	4.13	0.44	4.43	4.43	4.43	0.42
MCV	86	86	83	5	87	88	85	4
MCH	27.4	27.2	28	2	27.8	27.7	27.3	1.7
MCHC	31.7	31.5	31.8	1.6	31.8	31.6	31.6	1.3
RDW	15	14	13	1	14	14	14	1

Hb: Haemoglobin, RBC: Red cell count, MCV: Mean corpuscular volume, MCH: Mean corpuscular haemoglobin, MCHC: Mean corpuscular haemoglobin concentrate, RDW: Red cell distribution width.

Table 2 Morphology data from blood film analysis

Morphology	Status	LID	LID	Normal	Normal	Significance (Pearson Chi Square Test)
Normal red cells	0	1	0.50%	1	0.60%	-
	1	191	99.50%	162	99.40%	0.907
Hypochromic microcytic red cells	0	101	52.60%	117	71.80%	-
	1	91	47.40%	46	28.20%	0.00
Acanthocytes	0	169	88.00%	148	90.80%	-
	1	23	12.00%	15	9.20%	0.399
Pencil cells	0	82	42.70%	93	57.10%	-
	1	110	57.30%	70	42.90%	0.007

Note: 0- Absent, 1- Present on the blood film