# Anaemia and iron deficiency in pregnant women attending an antenatal clinic in a Teaching Hospital in Southern Sri Lanka

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## Abstract

*Introduction* In Sri Lanka the current prevalence of anaemia during pregnancy is estimated to be less than 20%.

*Objectives* To determine the rate of anaemia defined as hemoglobin concentration < 11 g/dl, and the rate of iron deficiency using the best cut off level of serum ferritin, in women presenting for antenatal care.

*Methods* Three hundred and fifty consecutive pregnant women with gestations between 12 to 20 weeks, presenting to the Academic Obstetric Unit at the Teaching Hospital Mahamodera, Galle, Sri Lanka from 10.11.2014 to 13.01.2015 had their heamoglobin and hematocrit measured by flow-cytometry and hydro-dynamic focusing methods using a Sysmex- XS-500i System and serum ferritin measured by electro-chemiluminescence method using a Cobas-e411 Analyzer. The rate of anaemia was calculated. The best cut off level of serum ferritin for the detection of anaemia was obtained using a Receiver Operator Characteristics (ROC) curve, and using this cut off, the rate of iron deficiency was calculated.

*Results* The rate of anaemia was 16.6%. The best cut off level of serum ferritin for the detection of anaemia was < 30 µg/L (the area under the ROC curve was 0.77; 95% CI -0.72 to0.81), with a sensitivity of 78.3% (95% CI 65.8 - 87.9) and a specificity of 74% (95% CI 68.6 -79.0) in detecting anaemia. Using this cut off, 36.9% of the pregnant women had iron deficiency.

*Conclusion* Rates of anaemia (16.6%) and iron deficiency (36.9%) in pregnancy are at levels of mild to moderate public health significance respectively.


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## Introduction

In 2011 the World Health Organization (WHO) estimated that the prevalence of anaemia during pregnancy in Sri Lanka was approximately 29% [1]. The Sri Lanka Demographic and Health Survey in 2007 found an estimated overall prevalence of anaemia of 34%, with 20.7% mild anaemia and 13.3% moderate to severe anaemia [2]. However, a study carried out in 2009, using a small sample of 228 pregnant women, estimated the prevalence of anaemia during pregnancy to be approximately 17% in Sri Lanka, ranging from approximately 7% in Kurunegala to 29% in the Colombo Municipality. In this study the estimates of anaemia in non pregnant women were as high as 35% in some regions [3]. Regional studies on the prevalence of anaemia in pregnant women have reported a prevalence of 14.4% in Dankotuwa in the Puttalam district in 1999, 8.2% in northern Sri Lanka in 2009 and 14.1% in the Anuradhapura district in 2012 [4-6]. Although demonstrating a wide variation in the rates reported, all these regional studies suggest that the national prevalence could be less than the available estimates.

The current antenatal supplementation program in Sri Lanka consists of daily administration of 60mg of oral iron with 1mg of folic acid to all pregnant women. However, it is now recommended by the WHO that even if daily antenatal oral iron supplements are administered, the dose of elemental iron should be reduced to 30mg per day in communities which have a prevalence of anaemia in pregnancy of < 20% [7]. Furthermore, for non-anaemic pregnant women, weekly antenatal oral iron supplements are recommended as they are considered adequate and as effective as daily supplements [8, 9]. If this latter recommendation of weekly supplementation is to be adopted, there are

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two pre-requisites. Firstly, prevalence of anaemia in pregnancy in the community should be < 20%. Secondly there should be a strong health care system which can confirm the non-anaemic status of the pregnant women at the booking visit and also monitor their hematological status during the pregnancy, to enable appropriate interventions if a pregnant woman becomes anaemic while on weekly supplements. As Sri Lanka has the second requirement, it is essential to establish the first requirement of a low prevalence of anaemia in pregnancy of < 20% at national as well as regional level, if any modifications to the current routine daily antenatal oral iron and folate supplementation program are to be considered.

A healthy, iron replete, non-anaemic person can develop mild-to-moderate iron deficiency without becoming anaemic and progress to developing anaemia only if there is further iron depletion. Therefore, although the hemoglobin concentration<11g/dl is considered as the diagnostic level for anaemia, it is a poor indicator of iron deficiency [10-15]. When the prevalence of iron deficiency anaemia is ≤ 40% the prevalence of iron deficiency is always higher and could even be 2.5 times more. With higher rates of iron deficiency anaemia the prevalence of iron deficiency would be virtually 100% [10,11,15]. Although serum ferritin is commonly used to detect iron deficiency, its usefulness as an indicator of iron deficiency may be limited to early pregnancy, because serum ferritin concentrations decrease during late pregnancy, mainly due to hemo-dilution. This occurs even with high daily oral iron supplements and when bone marrow iron is present [11,12]. As serum ferritin is also elevated in the presence of infection and inflammation, it has been suggested that the cut-off points should be adjusted by considering additional assessments of C- reactive protein to address the issue of background infections and inflammation [16-17]. An alternative method would be to use higher cut off levels to address this issue, but these levels have still not been properly defined [15, 18-21]. Although the additional measurement of serum transferrin receptor (sTfr) levels, a classification using serum ferritin and sTfr, the calculation of sTfr –Sf Index , and assessment of serum hepcidin are also described for the diagnosis of iron deficiency, they are available only in well resourced settings [12, 15, 22 - 24].

A study conducted in 1995 in the Academic Obstetrics and Gynaecology unit at Teaching Hospital Mahamodera Galle, Sri Lanka, reported that the rate of anaemia, (defined as Hb < 11g/dl) was 56% and iron deficiency (serum ferritin < 12 µg /L) was 69% in women presenting for antenatal care [10]. Therefore, the objective of this study was to assess the current anaemia and iron deficiency rates in pregnant women presenting for antenatal care to the the Academic Obstetrics and Gynaecology unit at Teaching Hospital Mahamodera Galle, Sri Lanka.

## Method

Consecutive pregnant women, with gestations between 12 to 20 weeks, presenting to the antenatal clinic of the Academic Obstetrics and Gynaecology unit at the Teaching Hospital Mahamodera Galle, Sri Lanka from 10.11.2014 to 13.01.2015 were recruited for the study. Assuming that the rate of anaemia in women presenting for antenatal care in the Academic Obstetric Unit of the hospital would be a maximum of 30%, the minimum sample size required with a precision of 5%, was 323 [25]. However, as the current study was the precursor to a randomized controlled trial, recruitment was continued up to 350 subjects, until the 292 women who were included in the randomized controlled trial were identified. When venous blood was drawn for routine antenatal investigations an additional 5 ml of blood was obtained for the current study. As facilities for assessment of serum ferritin were not available in the hospital laboratory, this second sample of blood was sent to Durdan's Hospital Laboratory, Galle, where the hematological indices were measured by flow-cytometry and hydro-dynamic focusing methods using a Sysmex-XS-500i System, (Diamond Diagnostics, Holliston, USA) and serum ferritin was measured by electro-chemiluminescence method using a Cobas-e411 Analyzer, (Roche Diagnostics, Indianapolis, USA). At this laboratory internal quality control of the serum ferritin assays were carried out twice a day using BIORAD Internal Quality Control materials and monthly external quality control was carried by BIORAD External Quality Assurance System (BIORAD Laboratories Inc, California, USA). Details of previous iron supplementation were documented.

Anaemia was defined as Hb< 11 g/dl. As the definition iron deficiency vary from serum ferritin < 12 µg/l to as high as serum ferritin < 60µg/l it was decided to identify the best cut-off level of serum ferritin for the detection of anaemia by using a Receiver Operator Characteristics (ROC) curve [11-21]. The rate of iron deficiency was calculated using this best cut-off value for serum ferritin. Continuous variables with normal distributions were presented as means with standard deviations and 95% confidence intervals. Means were compared using t-test. Discrete numeric variables and ordinal variables were presented as medians with inter-quartile ranges. Nominal and categorical variables were presented as

percentages. The Statistical Package for Social Sciences (SPSS version 20) was used for data analysis.

Approval for the study was obtained from the Ethical Review Committee, Faculty of Medicine, University of Ruhuna and the Director of the Teaching Hospital Mahamodera, Galle. Written informed consent was obtained from all the participants.

## Results

A total of 350 women were recruited for the study. Their characteristics are shown in Table 1. The mean Hb was 11.6g/dl (95% CI 11.4-11.7) and the mean hematocrit was 33.8% (95% CI 33.3-34) (Table 2). A serum ferritin of 29.3µg/L was the best cut off value for the detection of anaemia according to the coordinates of the ROC curve. This value was rounded off to 30 µg/L to obtain a clinically acceptable value. The area under the curve was 0.77 (95% CI - 0.72 to 0.81). In detecting anaemia, a serum ferritin of < 30 µg/L had a sensitivity of 78.3% (95% CI 65.8 - 87.9) and specificity of 74% (95% CI 68.6 -79.0) (Supplementary Figure 1 and Table 3). The positive correlation of serum ferritin with the Hb is shown in Supplementary Figure 2 ($r = 0.21$, $p< 0.001$). Of the 350 subjects, 58 (16.6 %) were anaemic and 129 (36.9%) had iron deficiency with serum ferritin < 30µg/L. There were 81 (28%) non anaemic subjects who had serum ferritin < 30µg/L.

The rates of iron deficiency increased from 3.7% to 15% and to 36.9% when the cut off level of serum ferritin for the diagnosis of iron deficiency was increased from < 12 µg/l to < 20 µg/l and to < 30 µg/l respectively (Table 4). There was no association between the parity of the women and their hematological indices (Table 5). Although 23 women presenting between 12-16 weeks gestation and 34 presenting between 17-20 weeks gestation had received some form of oral iron supplementation prior to the booking visit, there were no significant differences in the mean Hb, hematocrit and serum ferritin between those who had received prior oral iron supplementation and those who had not (Table 6).

## Discussion

The rate of anaemia in pregnancy (16.6%) reported in the current study supports the suggestion that in Sri Lanka the prevalence of anaemia during pregnancy is < 20%. Using a cut-off level of serum ferritin < 30 µg/l, which appears to be the most appropriate for the diagnosis of iron deficiency in this population, iron deficiency in these pregnant women was 36.9%. This indicates that anaemia and iron deficiency of pregnancy are probably of mild to moderate public health significance in these women [11]. In the Academic Obstetrics and Gynaecology unit at Teaching Hospital Mahamodera, the rate of anaemia and iron deficiency (defined as a serum ferritin< 12 µg/l) in women presenting for antenatal care has markedly reduced from 56% and 69% in 1995 to the current 16.6% and 3.7% respectively [10].

Of 292 non anaemic women in the current study, 81(28%) had serum ferritin < 30 µg/l. This is important because previous studies have shown that intermittent oral iron supplementation (twice or thrice a week) can increase the risk of pregnant women becoming anaemic and developing iron deficiency at term. This is so especially if they had iron deficiency during early pregnancy, which need not necessarily have made them anaemic during early pregnancy [26 - 28]. Furthermore, the latest Cochrane Review shows that the risk of mild anaemia is increased at term with daily as well as weekly oral iron supplementation programs [9]. Therefore, further evidence is needed not only to establish the prevalence of anaemia and the underlying iron deficiency, but also to study the effectiveness of weekly antenatal oral supplementation in non-anaemic pregnant women, at national and regional level, before changing the current practice of routine daily antenatal oral supplementation with 60mg of elemental iron to all pregnant women.

The strength of this study is that the serum ferritin was assessed in all 350 women. In many studies in Sri Lanka, serum ferritin is not assessed and only Hb is measured, because serum ferritin assays are expensive and are not available in the state health sector. The limitation of this study is that it is a state hospital based study. Although 99.9% of women deliver in hospitals and only approximately 10% of deliveries in Galle occur in private hospitals, the results may not accurately reflect the actual prevalence of anaemia and iron deficiency in the Galle district.

In conclusion, for the diagnosis of iron deficiency, a cut off level of serum ferritin < 30 µg/L appears to be appropriate for women presenting for antenatal care to the Academic Obstetrics Unit of Teaching Hospital Mahamodara. Rates of anaemia (16.6%) and iron deficiency (36.9%) in pregnancy are at levels of mild to moderate public health significance respectively in the population they represent.

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## Conflicts of Interest

The authors have no conflicts of interest

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Table 1. **Characteristics of the study population**

| | **Mean (SD) (n=350)** |
|---|---|
| Age in years | 27.4 (6.1) (Range 13 – 42) |
| Gestational age | 15.9 (2.6) (Range 12 – 20) |
| Parity | |
| Median (IQR) | 1 (1 – 2) |
| Range | (Range 1 – 6) |
| | **Number (%)** |
| Education | |
| Grade 1-5 | 18 (5%) |
| Grade 6-10 | 57 (16%) |
| O/L qualified | 114 (33%) |
| Up to A/L | 89 (25%) |
| A/L qualified | 44 (12%) |
| Diploma or Degree | 25 (7%) |
| Occupation | |
| Housewife | 265(76%) |
| Professional | 22 (6%) |
| Skilled worker | 15 (4%) |
| Others | 48(14%) |
| Monthly family income in thousand rupees | |
| Median (IQR) | 25 – 30 (20 – 40) |
| Gestational age at registration 12-16 weeks | 213 (60.9%) |
| Received iron supplements before registration between 12-16 weeks | 23(6.5%) |
| Gestational age at registration 17-20 weeks | 137 (39.1%) |
| Received iron supplements before registration between 17-20 wks | 34 (9.7%) |

Table 2. **Hematological indices of the study population (n=350)**

| | **Mean (95% CI)**<br>**Range** |
|---|---|
| **Hemoglobin g/dl** | 11.6 (11.4-11.7)<br>8.7-13.9 |
| **Hematocrit %** | 33.8 (33.3-34.2)<br>29.4-43.2 |
| **Serum Ferritin µg/l** | 47.7 (42.3-53.1)<br>9.1-154.9 |

Table 3. **Validity of a serum ferritin value of < 30 µg/l to detect anaemia**

| | | 95% CI |
|---|---|---|
| **Sensitivity** | 78.3% | 65.8 - 87.9 |
| **Specificity** | 74.0% | 68.6 - 79.0 |
| **Positive predictive value** | 61.9% | 53.8 - 69.6 |
| **Negative predictive value** | 86.4% | 80.8 - 90.9 |
| **Likelihood ratio of a positive test** | 3.02 | 2.4 - 3.8 |
| **Likelihood ratio of a negative test** | 0.29 | 0.2 - 0.5 |

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Table 4. **Prevalence of anaemia and iron deficiency**

| Serum ferritin (µg/l) | Hb<11g/dl Prevalence (95% CI) n=60 | Hb≥ 11g/dl Prevalence (95% CI) n=290 |
|---|---|---|
| <12 | 16.7% (9.3-28.0) | 1.0% (0.4-3.0) |
| 12-19.9 | 26.7% (17.1-39.0) | 7.2% (4.8-10.8) |
| 20-29.9 | 35% (24.2-47.6) | 1. (15.5-24.6) |
| ≥30 | 21.7% (13.1-33.6) | 72.0% (66.6-76.9) |

Table 5. **Hematological indices according to the parity of the subjects**

| | **Parity=1 (n=193) Number (%)** | **Parity= 2 (n=96) Number (%)** | **Parity=3 (n=44) Number (%)** | **Parity>4 (n=17) Number (%)** |
|---|---|---|---|---|
| Hb g/dl ≥11 | 163 (84.46) | 78 (81.25) | 33 (75) | 16 (94.11) |
| Hb g/dl <11 | 30 (15.54) | 18 (18.75) | 11 (25) | 1 (5.88) |
| Relative risk of anaemia ( 95% CI) | 1.0 | 1.21 (0.71-2.05) | 1.61 (0.86-3.0) | 0.38 (0.05-2.60) |
| P value | | .505 | .182 | 0.478 |
| Hematocrit % >33 | 134 (69.43) | 72 (75) | 33 (75) | 12 (70.59) |
| Hematocrit % <33 | 59 (30.57) | 24 (25) | 11 (25) | 5 (29.41) |
| Relative risk ( 95% CI) | 1.0 | 0.82 (0.54-1.23) | 0.82 (0.47-1.42) | 0.96 (0.45-2.07) |
| P value | | .338 | .583 | 1.0 |
| Serum ferritin µg/l ≥30 | 122 (63.21) | 60 (62.5) | 28 (63.64) | 12 (70.59) |
| Serum ferritin µg/l <30 | 71 (36.79) | 36 (37.5) | 16 (36.36) | 5 (29.41) |
| Relative risk ( 95% CI) | 1.0 | 1.02 (0.74-1.40) | 0.99 (0.64-1.52) | 0.80 (0.37-1.71) |
| P value | | 1.0 | 1.0 | 0.609 |

Table 6. **Effect of previous iron supplementation on hematological indices according to the gestational age of the pregnancies at presentation**

| | **Gestational age 12-16 weeks (n = 213)** | | **P value** | **Gestational age 17-20 weeks (n = 137)** | | **P value** |
|---|---|---|---|---|---|---|
| | **Previous supplementation Yes (n = 23) Mean (95% CI)** | **Previous supplementation No (n = 190) Mean (95% CI)** | | **Supplementation Yes (n =34) Mean (95% CI)** | **Supplementation No (n = 103) Mean (95% CI)** | |
| Hb g/dl | 11.6 (11.5-11.7) | 11.6 (11.4-11.6) | 0.399 | 11.6 (11.4-11.7) | 11.5 (11.4-11.7) | 0.219 |
| Haematocrit % | 34.0 (33.7-34.5) | 33.8 (33.2-34.2) | 0.449 | 34.0 (33.6-34.5) | 33.6 (33.6-34.4) | 0.081 |
| Serum ferritin | 45.0 (41.2-48.7) | 47.9 (42.3-47.6) | 0.295 | 44.3 (36.5-46.3) | 45.4 (37.1-44.6) | 0.455 |