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Prevalence of anaemia and iron deficiency in pregnant women and the effect of different iron supplements on third trimester maternal iron status: A prospective cohort study in Bope – Poddala Health Division in Galle District

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Abstract. Iron deficiency (ID) is still a significant health problem in Sri Lankan pregnant women. Recent national data showed that the prevalence of anaemia during pregnancy is about 30%. Usage of iron supplements to prevent ID in pregnancy is part of the routine antenatal care programmes in Sri Lanka. This study aimed to assess the prevalence of anaemia and the effect of different iron supplements on maternal iron status at the end of the third trimester (T3). In this prospective cohort study, 425 pregnant women attending antenatal clinics in Bope-Poddala health division in Galle were enrolled during the booking visit. Anaemia and ID were determined by haemoglobin (Hb <11.0g/dL) and serum ferritin (SF <15.0ng/mL) levels respectively at the study entry and the end of T3. Details of iron supplements were also obtained. In this sample 20 (4.8%) women were anaemic in the first trimester (T1) and the number increased to 49 (13.8%) at the end of the T3 ($p<0.001$). The mean Hb level at the study entry was 12.4 ± 0.92 g/dL and it dropped to 12.1 ± 1.1 g/dL by T3 (z test =4.47; $p<0.001$). In contrast, 178 (42.1%) pregnant women were iron deficient (SF <15.0 ng/mL) in T1, but iron deficiency has been significantly ($p<0.001$) reduced as only 64 (17.5 %) subjects having SF <15.0 ng/mL at T3. The median SF level was 17.5 ng/mL (IQR 9.2; 30.0 µg/L) at the study entry and it improved to 30.3 ng/mL (17.4; 50.8 µg/L) at the T3 (z test = 9.2; $p<0.001$). Total iron intake during pregnancy was adequate and there was no significant difference ($p=0.92$) in the iron status (by both Hb and SF levels) of pregnant women depending on the type of iron supplements obtained. Although the prevalence of anaemia was low in T1, it was increased significantly with the advancement of the pregnancy and comparable with many of the regional studies. However, iron deficiency was high in early pregnancy according to SF and it was significantly decreased at T3. Generic and commercial iron preparations did not show any significant difference in effect on the iron status at the end of T3 and the generated results did not prove any benefit over the generic preparations given from the government clinics.

Keywords. Anaemia, Iron deficiency, Iron preparations, Pregnancy, Serum ferritin

INTRODUCTION

Iron deficiency is one of the most common nutritional deficiencies affecting more than two billion people globally and represents significant public health challenges. Iron deficiency represents a spectrum ranging from iron depletion to iron deficiency anaemia (1). Globally, iron deficiency anaemia has medical and social impacts, accounting for impairment of cognitive performance in young children, adverse outcomes of pregnancy for both mothers and newborns, decreased physical and working capacities in adults, and cognitive decline in the elderly (2).

Pregnant women and children are the most vulnerable groups in the population for iron deficiency. During pregnancy, there is a significant increase in the amount of iron required to increase the red cell mass, expand the plasma volume and to allow for the growth of the foetal-placental unit and iron deficiency is the most common nutritional problem encountered during pregnancy (3,4). Iron deficiency during pregnancy causes anaemia and it contributes to 20% of all maternal deaths worldwide. Anaemia in pregnancy also leads to premature births, low birth weight, foetal impairment and infant deaths (5). A pregnant

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woman is considered to be anaemic if her haemoglobin concentration during the first and third trimester of gestation is lower than 110 g/L, at sea level according to the criteria of World Health Organization (WHO) (6).

Iron deficiency is considered the leading cause of anaemia in Sri Lanka (7) and WHO estimates showed that the prevalence of anaemia during pregnancy in Sri Lanka as 29.3%. According to the Sri Lanka Demographic and Health Survey (DHS) data in 2007, the overall prevalence of anaemia was 34%, with 20.7% mild anaemia and 13.3% moderate to severe anaemia (8).

However, these data indicated that iron deficiency and anaemia are still significant health problems in Sri Lankan pregnant women. Most of the time screening was done using the haemoglobin level as the tool which was shown as a poor indicator of iron deficiency and it may not reveal the exact situation of iron status in pregnant women (9). When considering vitamin-mineral supplementation during pregnancy, two sub-groups of pregnant women exist in Sri Lanka. One group of women are getting the recommended iron, folate, calcium and vitamin C tablets through the Government ante-natal clinics whereas, others depend on commercial preparations prescribed by the medical practitioners. There is a common belief that the commercial preparations are better than the supplements provided by the government in generic form, which is costly and there may be a difference in post-supplemental iron status in two groups when compared to the baseline level, at the end of the pregnancy.

With this background, a study was planned to assess the prevalence of anaemia with haemoglobin concentration and the actual iron status of pregnant women by means of serum ferritin levels. Furthermore, this study evaluates the effectiveness of different iron supplements (government or commercial preparations) on the iron status of pregnant women at the end of the pregnancy.

METHODS

This prospective cohort study was conducted in Bope-Poddala Health Division of the Galle District in the Southern Province and ethical approval for the study was obtained from the Ethical Review Committee of the Faculty of Medicine University of Ruhuna. All pregnant mothers visiting antenatal field clinics during the study period were considered as the study population and pregnant mothers who were in the 1st trimester [period of amenorrhoea (POA) ≤ 12weeks - as judged by the date of last menstrual period] were selected consecutively. Those who were willing to participate in the study were recruited after obtaining their written informed consent and 425 subjects were enrolled in the study via a convenient sampling method. At the study entry selected pregnant mothers were interviewed to obtain data on basic information, socio economic status and educational qualifications, details on past and present pregnancies and intake of iron supplements if any. Blood samples were collected to assess the serum ferritin and haemoglobin levels separately. The subjects were met in their second trimester (at or around 24th week of gestation) and details about iron supplementation were obtained. In this visit, exact date of starting of iron supplements and type of iron supplements were noted from the antenatal clinic records and prescriptions. Whether the subjects are taking the supplements daily and side effects if any were also noted. At the third trimester (at or around 36th week of gestation) they were visited again and further details about iron supplementation were obtained. Pregnant mothers who obtained both commercial iron preparations and iron tablets prescribed by the government clinics in mixed manner were not included in the study. Blood samples were collected to assess the serum ferritin and haemoglobin levels separately as did in the study entry.

To determine the iron status, serum ferritin assay was done at the Nuclear Medicine Unit, Faculty of Medicine Galle by using Ferritin Enzyme Immunoassay Test Kits (MP Biomedicals, Diagnostic Division, USA) and haemoglobin estimation was done on the same day of collection by using Sysmex automated haematology analyzer. The results were verified with the manufacturer certified Quality Control (QC) material. To determine the status of anaemia and iron deficiency in the pregnant women, haemoglobin level of <11g/dL and ferritin level of <15ng/mL were taken as the cut off points.

Statistical analysis was done using the Statistical Package for Social Sciences (SPSS) software (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics were

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presented as mean ± standard deviation for continuous measures while absolute values and percentages were given for categorical variables. A $p<0.05$ was considered to be statistically significant throughout the analysis.

RESULTS

Altogether 425 pregnant women were recruited for the study but only 416 and 423 samples were available for the analysis of haemoglobin (Hb) and serum ferritin (SF) levels respectively. Available serum was insufficient for repeat analysis among two women for initial SF analysis. The reason for missing samples for Hb in nine pregnant women was sample clotting. At the third trimester, Hb and SF were estimated on 354 and 366 mothers and some were missing due to dropout or moving to other areas. Table 1 describes the socio-demographic characteristics of the study sample. The mean age of the study subjects was 28.4 (±5.6) years and the majority of the sample was Sinhalese (71%) whereas 27.8% of the subjects were Muslims. Of the pregnant women, 58.1% studied up to GCE Ordinary Level and the remainder had the education up to GCE Advanced Level or higher education. Hundred and sixty-six (39.1%) pregnant mothers in the sample were in their first pregnancy (P1) while 234 (55.1%) were in P2 / P3 and 24 (5.6%) were in ≥P4 respectively.

The mean Hb level at the study entry was 12.4 ± 0.92 g/dL and it dropped to 12.1 ± 1.1 g/dL by the third trimester (z test =4.47; $p<0.001$). The median SF level was 17.5 ng/mL (IQR 9.2; 30.0 µg/L) at the study entry and it improved to 30.3 ng/mL (17.4; 50.8 µg/L) at the third trimester (z test = 9.2; $p<0.001$).

The frequency distribution of Hb and SF levels is given in Table 2. It was noted that only 20 (4.8%) women were anaemic (Hb<11.0 g/dL) in the first trimester. However, the number of anaemic subjects increased to 49 (13.8%) at the end of the third trimester ($p<0.001$). In contrast, 178 (42.1%) pregnant women were iron deficient (SF <15.0 ng/mL) in the first trimester, but iron deficiency has decreased significantly ($p<0.001$) as only 64 (17.5 %) pregnant women were having SF <15.0 ng/mL at third trimester (Table 5.1).

Pregnant women received mandatory iron and calcium supplements from antenatal clinics of the Ministry of Health. Yet, some of them opted to purchase multiple micronutrient supplements from the private sector upon the recommendation of medical practitioners. In this sample, a group of 181 mothers (51.1%) obtained iron tablets ($FeSO_4$) from antenatal clinics and the remainder (n=171, 48.3%) consumed commercial preparations of iron tablet/capsules (Ferrous fumarate, gluconate, etc.) purchased from the private sector. Two (0.6%) pregnant women were non-responders. Out of the 49 pregnant women who were anaemic at the third trimester 25 (51.0%) received iron supplements from the Government antenatal clinics and the rest (n=24; 49.0%) obtained them from the private sector. Similarly, of the non-anaemic women in the third trimester, about 51% received iron supplements from the antenatal clinics (Table 3). Findings on the Hb level reveal that the effect had been the same whether supplements were obtained from the antenatal clinics or as commercial preparations.

Of the 64 pregnant women who were iron deficient (SF<15.0 g/dL) in the third trimester, 31 (48.4%) obtained iron supplements from Government antenatal clinics and the rest (n=33; 51.6 %) from the private sector. It appears that almost half the pregnant women in the sample obtained supplements from the private sector (Table 4). No significant difference in the number (%) of subjects with iron deficiency was observed in the two categories.

The total content of iron consumed by each woman was calculated during pregnancy by the amount of elemental iron in each preparation and the number of dates consumed. The pregnant women who received iron supplements from government clinics had a median intake of 10,080.0 mg (IQR 8,820.0; 10,500.0 mg) of iron whereas those who obtained from the private sector had a median intake of 8,400.0 mg (IQR 7,896.0; 8,750.0 mg) of iron during pregnancy. A statistically significant

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difference is seen in the two intakes (z test 1.94; p = 0.05).

Table 1. Frequency distribution of socio-demographic characteristics in the study sample

Characteristics	Frequency	%
Age group in years		
16 – 20	37	8.7
21 – 25	101	23.8
26 – 30	139	32.8
31 – 35	103	24.3
36 – 40	34	8.0
≥ 41	10	2.4
Total*	**424**	**100.0**
Mean ±SD, Min/Max	28.4±5.6, 16/44 years	
Ethnicity		
Sinhalese	301	71.0
Muslim	118	27.8
Tamil	5	1.2
Total*	**424**	**100.0**
Level of education		
Primary	9	2.1
Secondary	91	21.6
Passed GCE O/L	145	34.4
Passed GCE A/L	140	33.2
Technical education	6	1.4
Higher education (Graduate & Postgraduate)	31	7.3
Total*	**422**	**100.0**
Parity		
1	166	39.1
2-3	234	55.1
≥4	24	5.6
No response	1	0.2

The associations between Hb level and serum ferritin levels in the first and third trimesters are shown in Table 5. In the first trimester, out of the 20 subjects who were anaemic, 13 (65%) had low serum ferritin levels. Of those who had normal Hb, 158 (40.1%) had low ferritin levels (p=0.03). However, in the third trimester, there were 49 anaemic women and 17 (34.7%) had low ferritin levels. Furthermore, of the 297 pregnant women who had sufficient Hb levels only 47(15.8%) had low ferritin values. This indicated that the iron status of the study sample was significantly improved towards the end of the pregnancy compared with the status in the first trimester (p=0.001).

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Table 2. Frequency distribution of Hb level and serum ferritin Level

Characteristics	Trimester				Significance
	1st		3rd		
	n	%	n	%	
Haemoglobin Level (g/dL)					
Low (<11.0)	20	4.8	49	13.8	χ^2 = 19.13
Normal (≥11.01)	396	95.2	305	86.2	df=1, p<0.001
Total number of pregnant women	416		354		
Serum Ferritin Level (ng/mL)					
Low (<15.0)	178	42.1	64	17.5	χ^2 = 55.82
Normal (≥15.01	245	57.9	302	82.5	df=1, p<0.001
Total number of pregnant women	423		366		

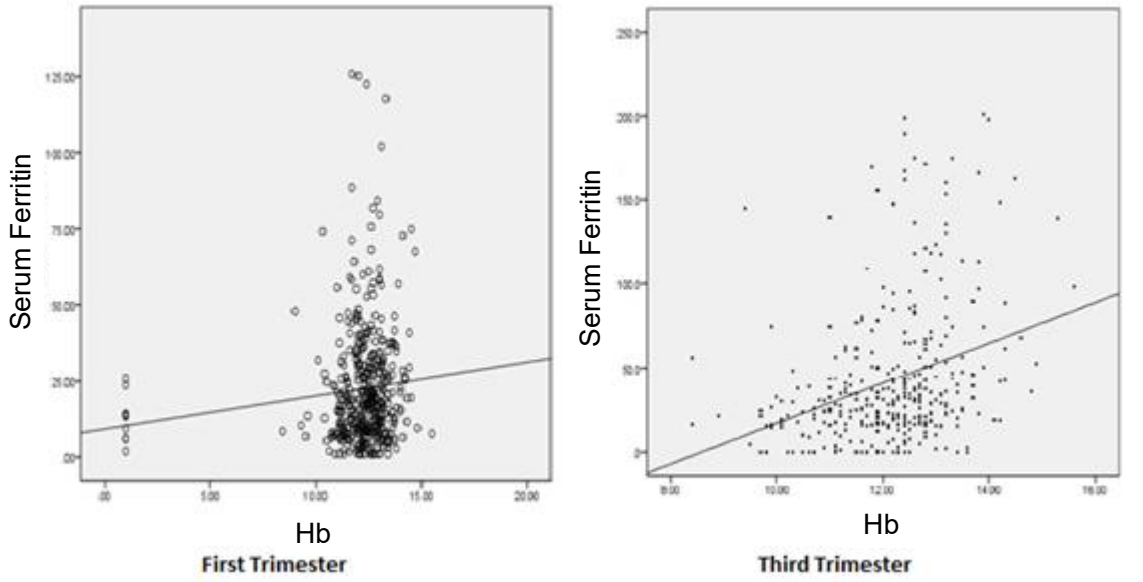

Figure 1. describes that there is a significant positive correlation between Hb and SF levels in the first trimester (r=0.11; p=0.03) as well as in the third trimester (r= 0.32; p<0.001).

Table 3. Haemoglobin levels in the 3rd trimester by the Source of iron/mineral supplements during pregnancy

Sources	Hb level (g/dL)				Total		Significance*
	Low (<11.0)		Normal (≥11.01)				
	n	%	n	%	n	%	
Government	25	51.0	156	51.1	181	51.1	
Private	24	49.0	147	48.2	171	48.3	χ^2 =0.01;
Not responded	0	0.0	2	0.7	2	0.6	p=0.92
Total	49	100	305	100	354	100	

Excluded not responded category for statistical test * Yates corrected test was applied

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Table 4. Sources of iron/mineral supplements during pregnancy by serum ferritin level at 3rd trimester

Sources	Serum Ferritin Level (ng/mL)				Total		Significance
	Low (<15.0)		Normal (≥15.01)				
	n	%	n	%	n	%	*
Government	31	48.4	153	50.7	184	50.3	χ^2 =0.01;
Private	33	51.6	146	48.3	179	48.9	p=0.92
Not responded	0	0.0	3	1.0	3	0.8	
Total	64	100	302	100	366	100	

Table 5. Association between haemoglobin and serum ferritin concentrations

Haemoglobin Level (g/dL)	Serum Ferritin Concentration (ng/mL)				Significance
	Iron deficiency (<15.0)		Normal (≥15.01)		
	n	%	n	%	
1st trimester					
Anaemia (<11.0 g/dL)	13	65.0	7	35.0	χ^2 = 4.87
Normal (≥11.0 g/dL)	158	40.1	236	59.9	df=1, p=0.03
3rd trimester					
Anaemia (<11.0 g/dL)	17	34.7	32	65.3	χ^2 = 11.09
Normal (≥11.01 g/dL)	47	15.8	250	84.2	df=1, p=0.001

DISCUSSION

Iron deficiency is one of the most recognized nutritional deficiencies in the world (3). The available data illustrate that anaemia is a significant health problem in Sri Lanka and iron deficiency has been described as the leading cause of anaemia. Higher prevalence rates have been indicated in some studies done among pregnant women (10, 11, 12)), but relatively low prevalence rates also have been shown in studies done in several areas (7, 13, 14).

The serum ferritin level is the most specific biochemical test that correlates with total body iron stores (1). Even though it has some limitations during pregnancy, it is the best test that can be used (15). A low serum ferritin level reflects depleted iron stores and hence is a predictor for iron deficiency in the absence of infection (16). The other tests for assessing iron status such as erythrocyte protoporphyrin, serum iron, transferrin, transferrin saturation and serum transferrin receptors, also have various limitations (16). Therefore, measurement of serum ferritin was used as the preferred method for detecting depleted iron stores in the present study. The assessment of iron status by serum ferritin and anaemia by Hb concentration gives a better picture of the iron status of pregnant women. The most common strategy used to combat iron deficiency during pregnancy at present is iron supplementation, especially in developing

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countries (16). In the present study, we studied the effect of iron supplementation on maternal iron status prospectively concerning the baseline iron status.

The prevalence of anaemia among pregnant women in the first trimester in this sample was only 4.8%. This finding was relatively low when compared with the other studies done in Sri Lanka. Recently it has been published that the prevalence rate of anaemia was 23% among pregnant women in the first trimester in the Bope-Poddala health division (17). However, data on Hb were obtained from available records in that study and the haemoglobin estimation had been done at various outside laboratories by the mothers themselves and as such, there may not be a uniformity of the assay method and the quality of the data. In the Anuradhapura District, the prevalence of anaemia had been reported as 7.6% in the 1st trimester and 19.7% and 19.3% in the other trimesters respectively with an overall prevalence of 14.1% (95% CI = 12.0-16.4%) (7). Although it was not a prospective study, a closer low prevalence rate of anaemia was shown. The reported prevalence of anaemia among pregnant women in the Gampaha District was 7.1% (13) and in the Vavuniya District, it was 8.2% (14). In the western province, it was as high as 18% (18). A prospective study done in 2010 of two Medical Officers of Health areas in Sri Lanka revealed that the prevalence of anaemia was 7.1% (19). The Medical Research Institute (MRI) has reported a 16.7% prevalence of anaemia among Sri Lankan pregnant women (20).

Studies done to assess the iron status using serum ferritin (SF) as the marker were few in Sri Lanka. In 1995, one study showed that 57% of pregnant women had SF <10.0 ng/mL indicating complete depletion of iron stores (21). It has been reported in India that iron deficiency was 64% when a cut-off value of ≤12 ng/mL was used for ferritin in pregnancy (22). In Saudi Arabia, 62% of the pregnant women during the third trimester of pregnancy were iron deficient (23). A recent study in Switzerland revealed that the prevalence of anaemia was 18.3% and the depleted iron stores were 32.2% of the study population (24), indicating that anaemia and iron deficiency are still significant health problems in pregnancy even in a developed country. In agreement with these findings, 42.1% of the pregnant women in the present study sample also had depleted iron stores in the first trimester despite a low prevalence (4.8%) of anaemia.

Regarding iron status during pregnancy, dietary measures alone have been shown ineffective in obtaining a good iron status in the majority of pregnant women. A safe way suggested for securing an adequate iron status in the mother and the child was to give iron supplements during pregnancy. Evidence-based data were available that oral iron supplements in appropriate doses were very effective in the prevention of iron deficiency and iron deficiency anaemia (25,26,27). According to Peña-Rosas & Viteri in 2006, women who received daily antenatal iron supplementation were less likely to have iron deficiency and iron-deficiency anaemia at term as defined by the current cut-off values.

Coverage of iron supplementation was very high among pregnant women in Sri Lanka under the current antenatal care programme. It was observed that almost all pregnant women in the study have been given iron supplements either from the Government antenatal clinics or from the private health care centres. In Sri Lanka, iron supplements are given to all pregnant women irrespective of their baseline iron status. Overall, a pregnant woman needs about 2 to 4.8 mg of iron per day (28). Since the absorption of iron in the gut is only 10%, a pregnant woman must consume 20 to 48 mg of dietary iron to absorb this quantity of iron daily. An average vegetarian diet does not provide more than 10 to 15 mg of iron per day. Thus, the amount of iron absorbed from diet is usually insufficient to meet the demands imposed by pregnancy and this demand cannot be met without supplementation. The total maternal need for extra iron averages close to 800 mg (elemental iron) during pregnancy (29) and the total extra dietary iron requirement is 8000mg. Some studies suggested that the net iron requirement associated with pregnancy is about 630 mg (30, 31) which means that 6300mg of iron should be given

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during pregnancy. Furthermore, there are different opinions regarding iron requirement during pregnancy and according to Scholl, T.O., the maternal requirement of iron increases to approximately 1000 mg on average and the increased requirement needs to be supported by a higher maternal iron intake (32). According to the findings of the present study, it was shown that the total iron intake during pregnancy was adequate and there was no significant difference in the iron status of pregnant women depending on the type of iron supplements obtained.

There are several limitations in this investigation. Even though we inquired on iron deficiency anaemia (IDA), several other conditions that can mimic such as thalassaemia, mixed deficiency and ongoing blood loss such as haemorrhoids are not inquired. Therefore, their influence on the final outcome cannot be fully refined focusing on IDA alone. Furthermore, conditions which can affect the serum ferritin (inflammation/urosepsis) were not assessed in this study.

CONCLUSION

This prospective study gives a better understanding of maternal iron status during pregnancy in the study population. Although the prevalence of anaemia was low, when compared to national figures, the serum ferritin which is a better indicator of iron status, illustrated that iron deficiency was high in early pregnancy. Prevalence of anaemia increased significantly ($p<0.001$) with the advancement of the pregnancy and it is comparable to many of the regional studies.

In conclusion, the overall iron intake was adequate and the maternal iron status was satisfactory. A higher prevalence of iron deficiency in early pregnancy should be addressed. The generated results did not prove any benefit over the generic preparations given by the government clinics. Awareness should be created regarding the importance of maintaining good pre-pregnant iron stores among targeted populations such as adolescent females and those who are in the reproductive age group through continued health education programmes.

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