Evaluation of effectiveness of iron-folate supplementation and anthelminthic therapy against anemia in pregnancy--A study in the plantation sector of Sri Lanka

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Abstract (Abstract):
Intervention measures against anemia available to plantation workers during pregnancy include fortified food supplements and iron-folate supplements. The effectiveness of these supplements is discussed.

Full text:
INTRODUCTION
Nutritional anemia is an important health problem in many developing countries, including Sri Lanka, and it leads to decreased capacity for physical work (1). The prevalence of anemia is very high during pregnancy and was estimated to be 59 in 1980 in developing countries (2). It is a major cause of maternal morbidity and mortality and it also affects the outcome of pregnancy (3).

Several intervention measures are available to pregnant women in Sri Lanka, including female plantation workers. Monthly antenatal clinics are held on plantations and pregnant women are examined by a Medical Assistant/Public Health Midwife for clinical evidence of anemia (ie, pallor of tongue) and their weight change is monitored. The Ministry of Health in Sri Lanka provides the following free of charge to all pregnant women: 1) a vitamin-mineral fortified food supplement (thriposha); 2) oral iron-folate supplements (ferrous sulphate containing 60 mg elemental Fe and 0.25 mg folic acid); and 3) one course of mebendazole, an oral anthelminthic agent, after the first trimester of pregnancy.

Despite the availability of intervention measures, we observed a high prevalence of anemia and protein-energy deficiency among plantation workers during 10-26 wk of gestation. Hemoglobin concentrations <110 g/L were noted in 58.4% of 309 subjects, whereas protein-energy deficiency as indicated by low (< 18.5) body mass index (BMI; in kg/m sup 2 ) was observed in 30.9% and midupper arm circumference values <23 cm were observed in 73.2% of these subjects. Subclinical deficiencies of vitamin A and zinc, as indicated by low concentrations of vitamin A (0.70 mu-mol/L, <20 mu-g/dL) and zinc (< 8 mu-mol/L) in the serum, were also noted in 46.2% and 45.8% of the subjects, respectively, during the same period of gestation (LDR de Silva and TMS Atukorala, unpublished observations, 1991). It is important to ascertain the effectiveness of the above-mentioned interventions in improving nutritional status when delivered under field conditions, so that effective intervention measures can be identified.

This report presents data on a study done to evaluate the effectiveness of intervention measures given to pregnant plantation workers to improve their nutritional status and the outcome of pregnancy.

SUBJECTS AND METHODS
One hundred ninety-five pregnant plantation workers (14-24 wk gestation; mean +/- SD 19.6 +/- 6.3 wk) aged 17-45 y (mean age 25.1 +/- 4.9 y) were selected randomly from the largest plantation and neighboring plantations in five of six regions belonging to Sri Lanka State Plantations Corporation. Tea was grown on these plantations, which were situated in the hilly areas of Sri Lanka. Selection of the largest plantation in each region was based on the fact that these plantations had a higher number of pregnant women and had better facilities for conducting the study. The number of subjects studied had to be limited because of difficulties in transporting blood samples from plantations in remote areas to the laboratory for processing and analysis. Only women who did not have other known disease were included in the study. One hundred and thirty subjects were reassessed ==14 wk later, at >32 wk gestation (mean period of gestation 33.1 +/- 3.7 wk). Laboratory data on 65 subjects
who had delivered babies by the second assessment were not included. The subjects studied were mainly tea pluckers. Their mean (+/-SD) monthly income per family was 1608 +/- 652 Rupees (range 1000-3750 Rupees/mo), equivalent to ==$40.00. There was no significant difference in the income between plantations. Although their income varied depending on the availability of work, it was sufficient to purchase food. The main food items were purchased, whereas some vegetables were grown by the workers on community plots, or around their own quarters. The average number of women of childbearing age working on the plantations studied during the 2-y period of study was 7120 and there were 508 and 553 pregnancies, respectively, per year. Fifty-nine percent of female plantation workers in this age group were literate. The prevalence of anemia among nonpregnant women in the plantation sector has not been studied. Some sociodemographic information regarding the subjects studied is given in Table 1. (Table 1 omitted) The parity of the subjects studied ranged from 1 to 6 with a mean (+/-SD) of 2.30 +/- 1.28.

The nutritional status of subjects was assessed initially and reassessed ==14 wk later by using anthropometric and biochemical indexes. The weight and height of all subjects was measured (without shoes) at each assessment by using calibrated scales to an accuracy of +/-0.5 kg and +/-0.5 cm, respectively, and the midupper an circumference was also measured by using a specially designed tape measure to an accuracy of +/-0.1 cm according to the methods described by Jelliffe (4). Triceps-fatfold thickness was not measured in our study. Because these subjects do not usually attend antenatal clinics in the first trimester of pregnancy and prepregnancy body weights were not available, the rate of weight gain during pregnancy was calculated according to the formula given below:

\[(\text{Equation omitted})\]

where weight 2 and weight 1 are weights at 32-40 and 14-24 wk gestation, respectively. The anthropometric measurements were carried out by the same investigator (TMSA) to avoid any interobserver measurement error. The outcome of pregnancy was also noted from records available at health centers in plantations. Each pregnant woman receives two 750-g packets of the fortified food supplement (thriposha) per month at antenatal clinics located on each plantation and is advised to consume 50 g/d, either alone or mixed into other food preparations. This quantity would provide an average energy content of 753 kJ (180 kcal), 10 g high-quality protein, 9 mg Fe, and 20 mg ascorbic acid (data provided by the manufacturer). Mothers were aware of the high palatability of thriposha and all mothers collected it, if it was available at antenatal clinics. Each subject was interviewed individually at both assessments (in the absence of plantation staff) regarding the intake of supplements. Mothers were asked whether they received the fortified food supplement (thriposha) at every visit to the antenatal clinic and also whether they took it daily. Data on attendance at antenatal clinics and collection of supplements were obtained from entries in mother’s health records.

The Ministry of Health, Sri Lanka, supplies iron-folate supplements (ferrous sulphate containing 60 mg elemental Fe and 0.25 mg folic acid) to antenatal clinics, and all mothers are given these supplements (after the first trimester of pregnancy) when they attend antenatal clinics. The number of tablets given per mother and the recommended dose frequency was either one or two tablets per day in most clinics. Either 30 or 60 tablets were given per month whereas a few received 90 tablets/mo. The mothers were told that the tablets contained iron, and to take one tablet once daily, one tablet twice daily, or one tablet thrice daily (in a few instances), but no other educational message was given. The number of tablets taken per day depended on the recommended dose frequency and on individual preferences. A sample of iron-folate tablets was shown to each mother (interviewed individually, in the absence of plantation staff) and they were asked whether they took the tablets daily and whether they started taking the tablets from the first visit to the antenatal clinic or later. The number of iron-folate tablets taken per day was deduced by questioning each mother regarding the time of the day at which she took the tablets (morning, afternoon, and/or night). When anthelminthic therapy (AHT) was given, mothers were told that it is treatment given for worms and all mothers took it if they were given the tablets. Mothers were asked whether they were given AHT and whether they took it. This was cross-checked by
examining the mother's health records. Few subjects received parenteral iron therapy (Imferon; MEDISCA, Milano, Italy) and were excluded from the study if they did.

A venous blood sample (10 mL) was collected between 0900 and 1100 from each subject (==3 h after the morning meal) and an aliquot (3 mL) was placed in a bottle containing anticoagulant and used for estimating hemoglobin and erythrocyte protoporphyrin, whereas the remainder was collected into a bottle without anticoagulant. Blood was transported to the laboratory in a refrigerated box. The blood collected without anticoagulant was centrifuged and the serum was separated within 6 h of blood collection, divided into aliquots, and stored at -20°C until analyzed. An aliquot of anticoagulated whole blood was stored at 4°C and its hemoglobin concentration was estimated within 24 h of blood collection (5), whereas the remainder was stored at -20°C; its erythrocyte protoporphyrin concentration was estimated within 3 d of blood collection (6). The iron concentration and total iron-binding capacity of the serum was determined within 2 wk of blood collection by using reagent kits obtained from Sigma Chemicals, St Louis (procedure no. 565) and the percentage transferrin saturation was calculated. The ferritin concentration of the serum was determined within 3 mo of blood collection by using the sandwich enzyme immunoassay method of Linpisarn et al (7).

This project was approved by the Ethical Review Committee of the Faculty of Medicine, University of Colombo, Sri Lanka, and subjects gave informed consent.

Statistical analyses

Statistical analyses were carried out on an Apple Macintosh Computer by using Data Desk Professional 3.0 and Exstatix 1.0.1 programs (8). The methods used were Student's t test, paired t test, analysis of variance, and two-variable and multiple-regression analyses. Because the serum ferritin concentrations showed a skewed distribution, Wilcoxon's signed-rank test and Kruskal-Wallis tests were used, whereas log-transformed values of ferritin concentration were used in multiple-regression analysis.

RESULTS

The mean (+/-SD) BMI of subjects at first assessment (14-24 wk of gestation) was 19.7 +/- 1.9 (n = 195), and 27.2% had BMI values <18.5. Birth weight of newborns was 2.69 +/- 0.44 kg, and 21.9% had birth weights <2.5 kg, whereas 36.9% had birth weights between 2.5 and 2.7 kg. The nutritional status of subjects reassessed after 14 wk (n = 130) is given in Table 2. (Table 2 omitted) The mean rate of weight gain during the period between the two assessments was 0.25 +/- 0.18 kg/wk, and 46.9% of the subjects had rates of weight gain <0.2 kg/wk. There was also a significant decrease in midupper arm circumference during this period (P <0.01).

Although all women should have received the food supplement (thriposha), 24 subjects (12.3%) had not received any food supplement, whereas 31.3% (n = 61) of the subjects had received it for <10 wk during pregnancy and 30.7% (n = 60) and 25.7% (n = 50) had received it for 10-17 wk and >17 wk, respectively (Table 3). (Table 3 omitted) Mothers who received the food supplement were advised to consume 50 d, but there was considerable variation in the amount consumed and this amount was difficult to quantify.

There was no significant association between the access to the food supplement and the rate of weight gain (r sup 2 = 2.6%, F = 2.82, n = 130, P >0.05) or change in midarm circumference (r sup 2 = 2.2%, F = 2.42, P >0.05). There was also no significant relationship between access to the food supplement by pregnant women and birth weights of their newborns (r sup 2 = 0.7%, n = 195, F = 0.96, P >0.05). Further, the association between the change in hemoglobin concentration and access to the food supplement during pregnancy was also not statistically significant (r sup 2 = 2.2%, n = 130, F = 2.22, P >0.05).

The prevalence of anemia (hemoglobin <110 g/L) at first and second assessments among mothers who were followed up was 65.4% and 59.2%, respectively. Of the 130 mothers who were followed up, 14 mothers (10.8%) did not take iron-folate supplements during pregnancy because of undesirable side effects. The dose frequency could not be determined in one subject. Nausea, vomiting, and constipation were the common side effects. The amount of supplements taken varied from one tablet daily, one tablet twice daily, or one tablet thrice daily in a few subjects (n = 13). There was no significant difference in age, parity, period of gestation, or access to the
food supplement (thriposha) among the groups (Table 4). (Table 4 omitted) Hemoglobin concentrations at 32-40 wk of gestation were significantly higher than values at 14-24 wk of gestation (P <0.05) only in the group of subjects who took one tablet daily (Table 4). Taking one tablet per day caused a significant positive change in hemoglobin as compared with unsupplemented subjects (t = 2.19, P <0.05), whereas there was no significant difference between those taking one tablet daily and those taking two tablets daily.

The erythrocyte protoporphyrin concentrations at second assessment were significantly lower than initial values (P <0.02) in the group of subjects who took one tablet of iron-folate supplement daily, but not in those who did not take supplements or in those who took more than one tablet daily (Table 4). The change in serum ferritin concentration among subjects who took different amounts of supplements was not statistically significant. Further, the number of iron-folate tablets taken per day had no significant effect on the rate of weight gain during pregnancy, or birth weights of their newborns. To determine whether taking more than one tablet per day had a beneficial effect on subjects with initial hemoglobin concentrations <80 g/L, the change in hemoglobin concentration during pregnancy was compared in subjects who took one, two, or three tablets per day. There was no significant difference among the groups (n = 31, F = 1.77, P = 0.187).

Sixty-two subjects took iron-folate supplements for <= 17 wk, whereas 53 subjects took the supplement for >17 wk during pregnancy. There was no significant difference in age, parity, period of gestation, or duration of intake of thriposha between these two groups of subjects (Table 5). (Table 5 omitted) Hemoglobin concentrations at 32-40 wk of gestation were significantly higher than initial values (P <0.01) only in the group supplemented for >17 wk (Table 5). A significant positive change in hemoglobin during pregnancy was noted in the group supplemented for >17 wk when compared with unsupplemented subjects (t = 3.01, P <0.01), or those taking supplements for <= 17 wk (t = 2.71, P <0.01). Further, the erythrocyte protoporphyrin concentration and the ratio of protoporphyrin to hemoglobin were significantly lower (P <0.05) in the group supplemented for a longer period. However, there was no significant difference between initial and final ferritin concentration in the serum in both groups. To determine whether there is a difference in each group between subjects taking one or two tablets per day, the change in hemoglobin was compared within each group. Those taking three tablets per day were excluded because the number of subjects in each group was small. There was no significant change in hemoglobin resulting from different dose frequencies within each group (duration <= 17 wk: F = 3.46, P = 0.064; duration >17 wk: F = 0.56, P = 0.54).

Only 44.3% of the iron-folate-supplemented subjects had received one course of AHT between first and second assessments, whereas none had received it before the first assessment. The subjects who did not take iron-folate supplements had also not taken AHT. The hemoglobin concentration and iron status were compared in subjects who took only iron-folate supplements with those who received AHT in addition to supplements--AHT group (Table 6). (Table 6 omitted) There was no significant difference in age, parity, period of gestation, or duration of intake of thriposha between the two groups. Hemoglobin concentrations at 32-40 wk of gestation were significantly higher than initial values in the AHT group (P <0.001), but not in the group of subjects who received only iron-folate supplements. A significant positive change in hemoglobin was noted in subjects who received AHT in addition to supplements, when compared with those who received only iron-folate supplements (t = 5.98, P <0.001). A significant decrease in erythrocyte protoporphyrin concentration (t = 2.18, P <0.05) and the ratio of protoporphyrin to hemoglobin (t = 2.53, P <0.02) and a significant increase in serum ferritin concentration (Kruskal-Wallis test for two groups, H = 8.56, P <0.005) was also noted in the AHT group when compared with the untreated group. To determine whether there is a difference within groups due to differences in duration of supplementation, the change in hemoglobin concentration was compared in those supplemented for <= 17 wk with those supplemented for >17 wk. There was no significant difference within the group given only supplements (F = 0.3, P = 0.57) and in the group given AHT (F = 3.54, P = 0.06).

The influence of several independent variables [hemoglobin concentration at 14-24 wk of gestation (Hb1), duration and dose of iron folate supplementation, and receipt of AHT] on hemoglobin concentration at 32-40 wk
of gestation (Hb2) was assessed by multiple-regression analysis. A significant positive correlation was noted (R² = 23.5%, F = 10.5, P = 0.000). The regression equation is given below:

\[ Hb2 = 4.96 + 0.432 \times Hb1 + 1.62 \times AHT - 0.30 \times \text{number of iron tablets} + 0.04 \times \text{iron duration} \]

A significant partial correlation was noted between Hb2 and Hb1 (t = 5.46, P = 0.000), duration of iron supplementation (t = 2.17, P = 0.032), and AHT (t = 4.15, P = 0.0001). But, there was no significant effect of the number of iron-folate supplements taken per day on Hb2. Similarly, a significant positive correlation (R² = 11.6%, F = 4.99, P = 0.003) existed between the log-transformed values of ferritin concentration at second assessment and initial ferritin concentration (P = 0.025) and AHT (P = 0.001), but the association with dose frequency or duration of iron-folate supplementation was not significant.

**DISCUSSION**

Our study was an attempt to assess the effectiveness of intervention measures available to pregnant plantation workers as a component of routine antenatal care, and not to determine the effects of supplements under controlled conditions. The consumption of the fortified food supplement (thriposha) during pregnancy had no significant beneficial effect on maternal weight gain, change in midarm circumference, or hemoglobin concentration. Further, there was no significant effect on birth weight of newborns. In contrast, in an East Java pregnancy study, giving energy supplements during the last trimester of pregnancy resulted in a modest improvement in birth weight (9). Further, it was effective in promoting postnatal growth and reducing malnutrition in preschool children (10). A significant beneficial effect on maternal weight gain and intrauterine growth was also observed when protein-energy supplements were given to pregnant Asian mothers at nutritional risk living in Birmingham, UK (11).

It is important to note that the data mentioned above refer to controlled studies in which supplementation was carried out in a specific area under supervision. In contrast, in our study the food supplement was given as a component of routine antenatal care and its intake was dependent on availability of the food supplement at antenatal clinics and mother's attendance at the clinic. It was observed that 43.6% of pregnant plantation workers studied had either not received the food supplement, or received it for <10 wk during pregnancy. Thus, the duration of intake of the supplement was probably too short to cause a significant effect. The FAO/WHO/UNU consultation on energy and protein requirements have recommended an additional energy intake of 1200 kJ (285 kcal/d) if the same activity pattern is maintained (12). It is possible that the energy increment provided by the food supplement was insufficient to meet the additional demands of pregnancy and the high energy cost of their occupational activities (such as climbing mountains, plucking tea leaves, and carrying baskets of tea leaves). Therefore, it may be necessary to increase the energy content of the food supplement. Further, it is likely that the food supplement was often shared with other members of the family, so that the energy and nutrients received by pregnant women were less than expected. Thus, optimal benefit from the food supplement would more likely be achieved by having an "on site" feeding program at places of work, creches, homes, or other meeting places, or by providing a family food package. Iron-folate supplements were available at antenatal clinics and good compliance was noted among the subjects studied, although some complained of side effects. Compliance could be increased further if the beneficial effects of supplements and their side effects were explained to each mother when the tablets were given, because this was not done in the antenatal clinics. The dose recommended by the Ministry of Health, Sri Lanka, and the World Health Organization (2) is two tablets per day. The dose frequency depended on the number of tablets given per month and on individual preferences. Taking one tablet of iron-folate supplement per day caused a significant positive change in hemoglobin concentrations, but there was only a slight improvement in the iron status. Increasing the amount taken to two tablets per day did not cause any significant additional benefit with respect to hemoglobin concentrations or to iron status. Only a few subjects claimed to have taken three tablets per day. The difference between groups could not be due to differences in age, parity, or period of
gestation because there were no significant differences among the groups. The varied response to higher dose frequency could be partly due to the fact that coexistent energy-protein deficiencies limited the utilization of iron in some subjects. In fact, the mean rate of weight gain during the interval between two assessments was only 0.25 +/- 0.18 kg/wk, and 46.9% had rates of weight gain <0.2 kg/wk. It is also likely that the suboptimal vitamin A status noted among these subjects (LDR de Silva and TMS Atukorala, unpublished observations, 1991) may have limited the utilization of iron. A cross-sectional study on the iron and vitamin A status of pregnant women in West Java, Indonesia, showed a relationship between the metabolism of vitamin A and that of iron (13).

It is possible that subjects who claimed that they took more than one tablet per day may not have taken the higher amounts regularly. A more practical approach would be to advise that the iron supplements be taken once daily, possibly at nigh before sleeping because this would minimize side effects. In a recent study on the efficiency of an established program for iron supplementation during pregnancy at a community health center in Jakarta, Indonesia, 45 women who attended the normal pregnancy-care program were studied over a 2-mo period (14). They received 30 tablets of iron supplements per month (containing 60 mg elemental Fe in each tablet). Of the 33 women who continued to participate in the study, 21 claimed to have taken the supplements but only 12 had a positive stool test for iron. These workers have suggested that the dose of iron supplements should be increased because the compliance is low. Further studies are needed to determine whether tablets containing 120 mg elemental Fe once daily would be more effective than 60 mg/d. In a WHO-sponsored collaborative study on iron supplementation in Burma and in Thailand, administration of 120 or 240 mg Fe as ferrous sulphate to anemic women of reproductive age resulted in a significant increase in the concentration of both hemoglobin and serum ferritin, but there was no significant difference in serum ferritin concentration with the increase in dose (15).

Iron-folate supplementation for >17 wk during pregnancy caused a more positive change in hemoglobin than did the shorter period of supplementation. This difference could not be attributed to differences in parity, period of gestation, or intake of the food supplement, because they were similar in the two groups. Further, there was no significant difference within groups due to a difference in number of tablets taken per day or to AHT. Unlike hemoglobin or serum ferritin, the free erythrocyte protoporphyrin concentration increases in iron deficiency and decreases when iron is available and protoporphyrin is used for erythropoiesis (1). The significantly lower erythrocyte protoporphyrin concentrations at 32-40 wk of gestation than at first assessment suggest that the availability of iron for erythropoiesis increased when supplements were taken for >17 wk. Thus, increasing the duration of supplementation had a greater benefit than did increasing the dose frequency. However, there was no significant improvement in iron stores. This is probably because blood loss due to hookworm infection prevented any net storage of iron.

One course of AHT after the first trimester of pregnancy in addition to iron-folate supplements resulted not only in a marked increase in hemoglobin concentrations, but also in a significant improvement in iron status. Thus, AHT greatly improved the beneficial effects of iron-folate supplements. Whether AHT alone (without iron-folate supplements) would cause an improvement in iron status could not be determined because none of the subjects received only AHT. In our study, samples of stools were not tested for hookworm infection. However, studies carried out by E Sorenson and MM Ismail (unpublished observations, 1992) have shown a high prevalence of mild hookworm infection among Sri Lankan plantation workers of childbearing age. It is important to note that 73.2% of the subjects lived in crowded dwellings and sanitary facilities were not available to 33.3% of the subjects. Similar beneficial effects of AHT would be expected among women living in urban slums or rural women with no toilet facilities. These studies also highlight the need to adopt measures to prevent hookworm infection, such as more effective health education and improvement of sanitary facilities. A few studies on experimental animals have shown that AHT may have teratogenic effects when it is given during early pregnancy (16), but a similar effect has not been conclusively shown in humans. Further, the teratogenic effects, if any, are unlikely to occur if AHT is given after the first trimester of pregnancy.
In our study, supplementation with thriposha did not have a significant effect on nutritional status or outcome of pregnancy. It is likely that greater benefit could be obtained from thriposha by increasing its energy value and also by an on-site feeding program. Our data suggest that an increase in the duration of iron-folate supplementation during pregnancy conferred a greater benefit than did an increase in the dose frequency. AHT in addition to iron-folate supplements not only caused a greater increase in hemoglobin, but also a marked improvement in iron status. Therefore, iron-folate supplementation for >17 wk during pregnancy together with AHT (after the first trimester) is suggested for this population and others living under poor conditions. Our thanks to the Social Development Division of the Sri Lanka State Plantations Corporation and managers and health staff of the respective plantations for providing facilities to conduct the study. We also thank Chandralal de Silva (Dutch Norwegian Technical Assistance Team) for assistance with data analysis.

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REFERENCES

Subject: Pregnancy; Nutrition; Medical research; Iron; Food additives; Anemia;

Publication title: The American Journal of Clinical Nutrition

Volume: 60

Issue: 2

Pages: 286

Publication year: 1994

Publication date: Aug 1994

Year: 1994

Publisher: American Society for Clinical Nutrition, Inc.

Place of publication: Bethesda

Country of publication: United States

Publication subject: Nutrition And Dietetics, Medical Sciences

ISSN: 00029165

Source type: Scholarly Journals

Language of publication: English

Document type: Feature

Accession number: 02048768

ProQuest document ID: 231916915

Document URL: http://search.proquest.com/docview/231916915?accountid=1468

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Last updated: 2014-05-21

Database: Research Library