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Efficacy of Sprinkles and Iron Folic Acid Tablets to Control Anaemia during Pregnancy

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instructed to sprinkle the entire contents on to whatever semi-solid food is being served in the household (e.g. cooked rice, porridge, etc). The sachet with the encapsulated iron and other micronutrients is called 'Sprinkles'. For women who are accustomed to adding condiments to food (like salt or pepper), the addition of Sprinkles will not likely be a major change from normal eating habits. However, before embarking on a trial of effectiveness, we are obliged to assess the efficacy of this new intervention compared to the currently recommended iron/folic acid tablets. The study is a cluster-randomized trial carried out in 42 clusters from Gazipur district to see the efficacy of Sprinkles and IFA tablets.

SUBJECTS AND METHODS

STUDY SETTINGS AND SUBJECTS

The subjects were pregnant women aged 14-45 years who had a gestational age between 14-22 weeks and were permanent residents of the Kaliganj *upazilla* of Gazipur district in Bangladesh. The subject's written consent to participate in the study was sought. Recall of LMP approximated the gestational age in weeks; gestational age is estimated from the first day of the LMP. Therefore, any women already on iron supplementation prior to the study, and who were severely anemic (<70g/L) were excluded. The sample size for the study was calculated on the basis of an expected difference of 5g/L for Hb between 2 intervention groups. Thus, after correction of an allowance of 35% drop out during the follow-up, we recruited 490 subjects from two intervention groups. The ethical committee of Medical Research Council, Dhaka, Bangladesh, approved the study protocol.

STUDY DESIGN AND INTERVENTION

A cluster-randomized trial was used and all the clusters were randomly assigned to 1 of 2 intervention groups; the IFA group (60 mg of elemental iron, 400 µg of folic acid) or the Sprinkles group (60 mg of elemental iron, 400 µg of folic acid, 30 mg of vitamin C, and 5mg of Zn). At 14-22 gestational week, each recruited woman received a sachet containing 20 tablets/Sprinkles sachets. Enrolled subjects were followed up at bi-weekly intervals up to 34 gestational weeks and given 15 IFA tablets/sprinkles sachets at the end of every follow-up visit. At the end of the trial (34 gestational week), all the subjects were provided with a 3 mo ·· ·pply of IFA tablets/Sprinkles.

DATA COLLECTION

The enrolled subjects were followed up bi-weekly. The field staff made ≥7 visits during the whole pregnancy period to supervise the consumption of the supplements to ensure maximum compliance. There was some variability in the visiting schedule depending on the enrollment. Few women enrolled at 14 weeks and few were up-to 22 weeks of gestational age. The subjects were advised to take one tablet/sprinkles daily for the benefit of their health and that of the baby, and were advised lunch just before being given the supplement to ensure that it was not taken on an empty stomach. The field staff maintained a record of consumption of the supplement for each subject as a measure of compliance. During recruitment, semi-structured interviews were conducted to collect information on the women's reproductive history, socioeconomic status, and recorded anthropometric measurements.

Anthropometry

Anthropometrics measurement included weight and height recorded at baseline using a standard technique. Height was measured by using a wooden scale to the nearest 1 cm and weight was taken using the UNISCALE to the nearest 100 g.

Hb measurement

Hb was measured in the field setting from capillary blood via a finger prick using the portable HEMOCUE B-haemoglobin photometer (Hemocuo®, Angelholm, Sweden) and standard techniques (Cohen 1998). The accuracy of the Hemocuo was checked daily with control cuvettes provided by the manufacturer with each machine. At base line, 24, 28 and 32 weeks of gestation Hb were measured. In this study, anaemia was defined using the WHO cut-off for Hb (Hb<110g/L), 100-109g/L as mild anemia, 70-99g/L as moderate anemia and <70g/L as severe anemia (WHO 1998, WHO 2000).

Adherence/compliance

Compliance was assessed by calculating the percent of recommended sachets given to the subjects throughout the intervention period. Every two weeks, field workers counted the number of used (empty) and unused (full) Sprinkles sachets remaining and recorded the numbers on a pre-tested semi-structured questionnaire. They took back all tablets/sprinkles sachets remaining from the last visit and provided them with another 15 tablets/sprinkles sachets. However, during the first round of recruitments, field workers gave them 20 tablets/sprinkles sachets so that these extra 5 tablets/sprinkles sachets could be available for use throughout the rest of the intervention period.

Side effects

After two weeks of supplementation, interviews were conducted at home, including open-ended questioning on any morbidity and gastrointestinal symptoms during the last one week. Probing regarding heartburn, nausea, vomiting, diarrhea, and constipation followed this. Side effects information was collected at 24, 28 and 32 weeks of gestational age.

Acceptability

Subjects' attitude about IFA and Sprinkles were examined at 34 weeks of gestation using a semi-structured questionnaire and also using qualitative assessment tools, FGDs.

Socio Economic Status (SES)

Three indicators of socioeconomic status were coded: i.Exposure to formal schooling of women (never enrolled at school 0, some schooling=1) ii.Household landholding (landholding <1 acre=0, >1 acre=1), and iii.Perceived economic status (deficit household economy some period last year=0, not deficit=1). A SES was constructed using the addition of these three indicators, ranging from 0 to 3. The score 0-1 was labeled as "lower" socioeconomic group, and the score 2-3 was labeled as "higher" socioeconomic group (Hyder 2002).

STATISTICAL ANALYSIS

Statistical analysis was carried out by using SPSSWIN (version 11.0) with a univariate analysis of simple-frequency distribution of the selected variables. Descriptive analysis was used to see the differences across groups. Changes from baseline to different stages of gestational week

were observed. We looked at relevant factors to see whether and/or when they influenced the Hb levels, using OLS regression (Stata 9.1).

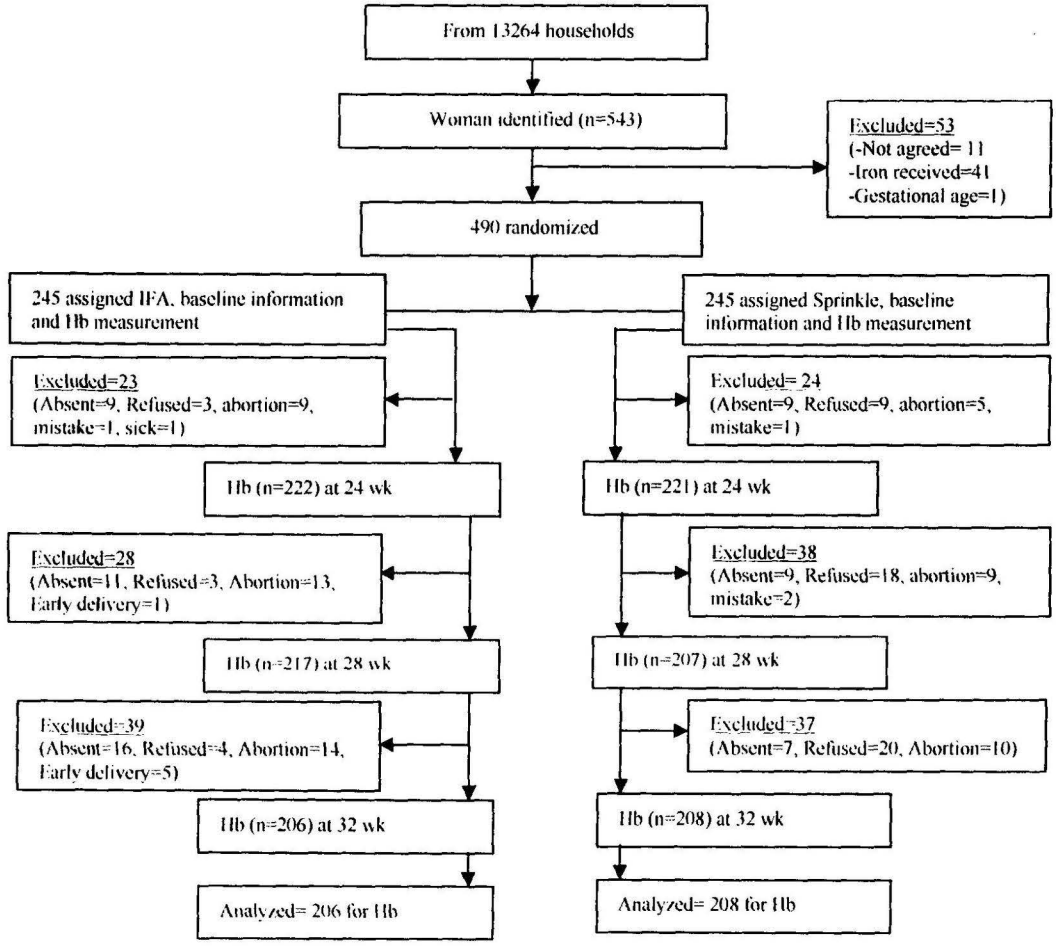
RESULTS

STUDY SUBJECTS

Of the 490 women recruited to the study, 206 (42%) subjects from the IFA group and 208 (42.4%) from Sprinkles group completed the 20 weeks study protocol (Fig-1). Seventy-six out of 490 subjects were lost in follow-up for the following reasons: refused to give a second blood sample, absentees on the day of blood collection, abortion, miscarriage or early delivery and in few cases, interviewers made a mistake.

The number of subjects lost to follow-up was not significantly different between the two groups.

Figure 1. A trial profile



BASELINE

A comparison of the subjects between two groups is given in Table 1. The mean age, ht, wt, and BMI of the subjects who were a part of the Sprinkles group were similar to those subjects who were in the IFA group. Mean age of the mother was 22 years (range 14-46 years), being on their first (44%), second (27%), third (14%) or more (15%) pregnancy. All of them were in their second trimester (14-22 gestational week). Sixty per cent of the households were functionally landless, 16% of the women perceived themselves as economically deficit and 88% of the women had attended school for at least a year. Mean Hb was 111g/L (95% CI 110-112) and 47% (95% CI 42-51) of the women were anemic. The anemia was mild in 22% and moderate in 21% of the study women. None of them had severe anemia. There was no association of anemia prevalence with age, parity, nor any of the social economic status variables except in group (IFA or Sprinkles) allocations. The Hb concentration of the subjects who were in the Sprinkles group were comparable with that of the subjects who were in the IFA group; however the Sprinkles group had Hb concentrations (109g/L) lower than those of the IFA group (112g/L).

AFTER SUPPLEMENTATION

Haemoglobin level

The distribution of haemoglobin concentration in the two supplemented groups before and after intervention is shown in Table 3. At baseline, haemoglobin concentrations were not similar in the two intervention groups, with an overall mean value of 111.27±14.6 g/L. In both supplemented groups, the haemoglobin concentration had decreased from baseline level in the 24th gestational week by 3 g/L in the IFA group and nearly 1g/L in the Sprinkles group. This change in haemoglobin concentration was not significantly different between the groups. After the 24th gestational week, in both supplementation groups, there was a slight increase in Hb levels, although it was not above their respective baseline. It was found in both supplementation groups, where women were anemic at baseline, responded 13-17 times more frequently in increasing of Hb levels compared to those that were not anemic at baseline (Table 4). Other possible contributing factors like supplementation group, age, BMI, SES, and compliance, all have a positive impact on increasing Hb levels; though not significant. Only history of abortion had a negative impact on increasing Hb levels, although it is not significant.

Side effects and compliance

In IFA and Sprinkles groups, more than 85% of the women reported the occurrence of gestational side effects (heart burn, nausea, vomiting, diarrhea, and/or constipation) during the supplementation period. Constipations were reported more frequently in both groups, while the occurrence of vomiting and diarrhea were reported less frequently. None of the suspected side effects differed between the supplementation regimens (Table 5). The compliance of the IFA group was comparable with that of the subjects in the Sprinkles group. However, the Sprinkles group had a lower compliance than those of the IFA groups ($p < 0.00$). Over time, the compliance was increased in both groups. The difference was about 7% (for IFA 10% and for Sprinkles 5%) (Table 6). Presence or absence of any side effects during the 24-28 gestational weeks affected the overall compliance rate in the two groups. Subjects that reported having side effects had low compliance rates compared to those subjects without side effects. On the other hand, compliance did not differ between 24-28 gestational weeks among the socioeconomic strata, but it differed during the 32nd gestational week between the socioeconomic strata. The lower socioeconomic group had 70%, while the higher socioeconomic group had 65% compliance ($p<0.05$).

Acceptability

A total of 445 women participated in the acceptability survey, 216 in the IFA and 229 in the Sprinkles regimens. There were significant differences that were observed between the comparison groups with respect to the women's perceptions about supplementation in terms of changes in appetite, taste, and smell. More than 82% of the women from the Sprinkles group and 92% of the IFA group found that Sprinkles or IFA could change their appetite affirmatively.

> *The IFA tablet increased my appetite. After taking lunch, and then the tablet, I would feel hungry again within 2 hours. I stopped taking the tablets because I think it made me want to eat more, but I don't have extra food in the house.* (A mother of IFA regimen)

> *I didn't face any side effects such as heartburn, vomiting, nausea....rather I feel that it increased my appetite* (A mother of Sprinkles regimen).

About 85% of the women in the Sprinkles group and 55% of the women in the IFA group had experienced somewhat to severe bad taste while they had supplementation (Table 7). Only 10 cases were found who reported that they never missed their dose schedule. The most cited reason for not taking Sprinkles or IFA tablets was forgetfulness (70-90%). Other reasons mentioned were that women were out of the home, and due to some side effects. (Table-8).

During FGD most of the women (25/32) said that they were encouraged to do so by other members of the family or community, especially by their husbands. Five reported that they were neither encouraged nor discouraged to take the supplements; and two reported that they are discouraged to do so. All (32/32) women found that the supplements had a beneficial effect on their pregnancy. Among the benefits, the most frequently reported were supplements eliminating some pregnancy side effects such as headaches, dizziness, nausea and/or vomiting (20/32), feeling healthy (18/32), increased appetite (22/32) and work improvement (25/32).

> *I went to sleep for the night without taking the tablet...my husband brought me a tablet and a glass of water and woke me and told me to take it...* (A mother from IFA group)

> One mother from Sprinkles regimen mentioned "*I didn't feel bad by taking it...rather I feel good. If I miss a day, after a couple of days, I feel weak. Whenever I took, I felt good.*"

Commonly the mothers preferred to mix the Sprinkles only into a small area of the food so that it can be consumed in the first 3 mouthfuls, so that they do not have to taste it during the whole meal. The subjects mentioned that it tasted sandy (unanimous opinion) and sour. Common food items mixed with Sprinkles are rice and curry, banana, and biscuits. Dry biscuit is also smashed and mixed with Sprinkles (a little water is sometimes added) and then it is consumed. However, they felt the major problem was consuming the Sprinkles, as it did not work well with rice. One mother said food is their only recreation/enjoyment i.e. the whole day they wait/look forward to their meal, so they do not want to sacrifice the taste by compromising it with something that will change the taste, opinionating that they would prefer any other option. Since the food system in rural areas is rice-based, if there is a problem with Sprinkles complementing rice, then there are very few other options. However, on an average, more than 90% of women (Sprinkles 84-86% and IFA 99%) reported that they will use and buy Sprinkles or IFA tablets in the future if it is available in the market.

DISCUSSION

The study was conducted to evaluate the relative efficacy of two different models of iron supplementation. We found in this study that the prevalence of anemia was 47%, similar to BBS findings (BBS/UNICEF 2004), although this is high compared to HKI findings (HKI 2006). After 10-14 weeks of supplementation, both IFA and Sprinkles groups did not show any significant changes in Hb levels. Nevertheless, women with anemia at the start of the study showed a significant increase in hemoglobin concentration after supplementation. Therefore, the satisfactory index of iron deficiency Ferritin concentrations would be one that does not change during pregnancy, which was not done in this present study.

Determined on the basis of Hb level by Hemocue machine and according to protocol, Sprinkles is not inferior to IFA because none of the regimens could increase Hb concentration after supplementation. This is also despite a significant difference between the two intervention groups at baseline and also after supplementation. The literature indicates (Juan P 2004) that the levels of 90-100g/L, after gestational week 30, have no effect on premature delivery and low birth weights, whereas Hb levels <90g/L and >130g/L, by week 26, are associated with these outcomes. Thus, it is suggesting that optimal birth weight and overall health of the newborn is achieved when maternal Hb levels remain between 90 and 130g/L throughout pregnancy. However, on average, after supplementation the Hb level was 111g/L (CI 109-112g/L). Some possible factors may explain why prevalence of anemia did not decline in this study:

During pregnancy, a common assumption is that the prevalence of anemia increases from the first to the third trimester, but this is partially false. It depends on the expansion of the maternal plasma volume, a normal physiological response to pregnancy. Although the maternal red blood cell mass also increases during gestation, its expansion and the expansion of the plasma volume are not synchronous (Theresa 1994). Thus, Hb concentrations decline throughout the first and second trimesters, and then rise again nearer to term. Depending on the stage of gestation when anemia is assessed, it may be more or less difficult to distinguish women who are truly anemic from those whose anemia is physiological and occurs because of hemodilution (Theresa 1994). Moreover, the women recruited at a later stage of gestation in this study had a shorter interval between the time of initial measurement and the last measurement.

Although there was a good compliance in taking supplementation, nearly half of the women still remained anemic. This suggests that they did not take all the tablets/sprinkles given to them. In addition, 67% of the women claimed to have taken all iron tablets, but this could not be confirmed by any other biochemical test, such as the stool test. Hb levels markedly increased only in the women who were anemic (<110g/L) at the start of the study, which is similar to Schultink's findings. This may indicate that the dose the women received was not high enough to increase Hb if the initial Hb concentration was >110g/L.

Another factor that may have reduced improvements in the iron status of the pregnant women is the daily amount of iron provided by the supplements given with rice, which contain high amounts of phytate, a potent inhibitor of iron absorption (Gibson *et al.* 1998, Lutter and Rivera 2003, Schultink W 1993).

Previous studies suggested that if supplements were ingested in an empty stomach, it might accentuate gastrointestinal side effects (Juan P 2004). In our study, women reported

more side effects compared to another study (Hyder 2002). Gastrointestinal side-effects are considered to be one of the main reasons for limited compliance (Hyder 2002). Our findings support that gastrointestinal side-effects have an influence on compliance, especially up to the 28th week of gestational age.

Another significant point for discussion is whether routine iron supplementation produces a greater change in the iron status of pregnant women who are the most iron deficient (<110g/L), or whether all expectant mothers derive an equal benefit from supplementation. That is, should there be a routine iron supplementation of all pregnant women? Existing data indicate that severely iron-deficient individuals from both supplementation regimens are more efficient in absorbing iron and hence would derive more of a benefit from iron supplementation than less iron-deficient individuals.

References

Ahmed F, Moududur Rahman Khan, Mohammad Akhtaruzzaman, Rezaul Karim, Geoffrey Christopher Marks, Cadi Parvin Banu, Badrun Nahar, and Gail Williams (2005). Efficacy of twice-weekly multiple micronutrient supplementation for improving the hemoglobin and micronutrient status of anemic adolescent schoolgirls in Bangladesh. *Am J Clin Nutr* 2005; 82: 829 -35.

Allen L, Gillespie S: What works? A review of the Efficacy and Effectiveness of Nutrition interventions. ACC/SCN Nutrition Policy Paper Sries, 5 2001, 19(UNACC/SCN, ADB): 43-54.

BBS/UNICEF (2004). Anemia prevalence survey of urban Bangladesh and rural Chittagong hill tracts-2003. May. Dhaka: BBS

Cohen. AR and J. Seidl-Friedman, HemoCue system for hemoglobin measurement. Evaluation in anemic and nonanemic children. *Am J Clin Pathol*, 1998. 90 (3): p. 302-5.

Galloway R, McGuire J. Determinants of compliance with iron supplementation: supplies, side-effects, or psychology. *Soc Sci Med* 1994;39:381-90.

Gibson, R.S., Ferguson, E.L. & Lethrfeld, J. (1998) Complementary foods for infant feeding in developing countries: their nutrient adequacy and improvement. *Eur J Clin Nutr*, 52, 764-70.

Hallberg L, Bengtsson G, Garby L, Lennartsson J, Rossander A, Tibblin E: An analysis of factors leading to a reduction in iron deficiency in Swedish women. *Bull WHO* 1979, 947-954.

HKI NSP Bulletin 16, April 2006

HKI/IPHN (1999) HKI/IPHN. Iron deficiency anaemia throughout the lifecycle in rural Bangladesh. Dhaka: Helen Keller International and Institute of Public Health Nutrition, 1999.

Hyder S, Persson L, Chowdhury M, Lonnerdal B, Ekstrom L. Anaemia and iron deficiency Prevalence of anaemia and iron deficiency during pregnancy in rural Bangladesh. 2004 *Public Health Nutrition* 7(8), 1065-1070.

Juan P. Pena-Rosas, Malden C. Nesheim, Maria N. Garcia-Casal, D.W.T. Cromton, Diva Sanjur, Fernando E. Viteri, Edward A. Frongillio, and Paulina Lorenzana (2004) Intermittent iron supplementation Regimens are able to maintain safe maternal haemoglobin concentrations during pregnancy in *Vnezuela. J. Nutr.* 2004; 134: 1099-1104.

Lutter, C.K. & Rivera, J.A. (2003) Nutritional status of infants and young children and characteristics of their diets. *J Nutr*, 133, 2941S-9S.

Roodenburg AJ: Iron supplementation during pregnancy. *Eur j Obstet Gynecol Reprod Biol* 1995, 61 (1): 65-71.

SM Ziauddin Hyder, Lars Ake Persson, AMR Chowdhury and Eva-Charlotte Ekstrom (2002) Do side-effects reduce compliance to iron supplementation? A study of daily and weekly-dose regimens in pregnancy. *J Health Popul Nutr* 2002 June; 20(2): 175-179.

Theresa o Scholl and Mary L Hediger (1994) Anemia and iron-deficiency anemia: compilation of data on pregnancy outcome. *Am J Clin Nutr* 1994;59 (suppl): 492S-501S.

WHO (1992) World Health Organization (1992) The prevalence of anemia in women: A tabulation of available information. Maternal Health and safe motherhood and nutrition programs. WHO, Geneva, Switzerland.

WHO (1998) World Health Organization (1998) The world health report 1997: conquering suffering, enriching humanity. WHO, Geneva, Switzerland.

Winichagoon P: Prevention and control of anemia: Thailand experiences. J Nutr 2002, 132 (4 Suppl): 862S-6S.

Zubia Mumtaz, Saquib Shahab, Naila Butt, M. Abdur Rab and Aime DeMuynck (2000): *J Nutr* 2000; 130: 2697-2702

Malnutrition. The global picture, 2000, World Health Organization: Geneva.

Ritsuko Aikawa, Masamina Jimba, Khan C Nguen, Yun Zhao, Colin W Binns and Mi Kuang Lee (2006) Why do adult women in Vietnam take iron tablets?. *BMC Public Health* 2006, 6:144

Werner Schultink, Marrianne vad der Ree, Paul Matulessi, and Rainer Gross (1993) Low compliance with an iron-supplementation program: a study among pregnant women in Jakarta, Indonesia. *Am J Clin Nutr* 1993; 57:135-9

Appendixes

Table 1. Anthropometric and socio-demographic characteristics of the study participants at baseline by intervention group

Indicators	Supplementation groups		Total (n=490)	*P* value
	IFA (n=245)	Sprinkles (n=245)		
Age (y)	22.34±5.25	22.06±5.07	22.20±5.16	.541
Ht (cm)	150.15 ±5.80	150.07±5.61 (244)	150.11±5.70 (489)	.877
Wt (kg)	46.47 ±6.45	45.93 ±7.66	46.20±7.08	.392
BMI (kg/m^2)	20.60±2.56	20.36±2.85(244)	20.48±2.71 (489)	.379
Hb (g/L)	112.89±14.8	109.64±14.2	111.27±14.6	.014
Anemic (%)	43.5 (100)	56.5 (130)	46.9 (230)	.004
Gestational week	17.48±2.69	17.63±2.57	17.55±2.63	.525
Family size (n)	4.88±2.31	5.00±2.54	4.94±2.43	.578
SES (%) Lower	23.3 (57)	25.7 (63)	24.5 (120)	.300

Table 2. Some socio economic indicators of the study participants at baseline by intervention group

Indicators	Groups		Total (n=490)	*P* value
	IFA (n=245)	Sprinkles (n=245)		
Educational level (%)				.951
-Illiterate	.8	1.6	1.2	
-Can sign only	11.0	11.0	11.0	
-Passed I-V	27.3	28.2	27.8	
-Passed VI-IX	47.8	47.3	47.6	
-Passed SSC/HSC	11.8	10.2	11.0	
-Passed degree or above	1.2	1.6	1.4	
Holding cultivable land (%)				.310
- No land	58	62.9	60.4	
- Have land	42	37.1	39.6	
Health problem (%)				.156
-No health problem	9.4	12.2	10.8	
-Mild	72.7	74.3	73.5	
-Moderate	18.0	12.7	15.3	
-Severe	0	0.8	0.4	

Table 3. Mean Hb (g/L) level at different gestational age by groups.

Indicators	Groups				Total	95% Conf. Interval
	IFA	95% Conf. Interval	Sprinkles	95% Conf. Interval		
-Baseline	112.89	111.02 - 114.75	109.64	107.85 -111.44	111.27	109.97-112.56
-24 week	109.36	107.62-111.11	108.78	107.07-110.49	109.07	107.86-110.29
-28 week	110.47	108.82-112.11	109.76	107.87-111.64	110.12	108.88-111.36
-32 week	112.49	110.91-114.07	109.65	107.88-111.43	111.07	109.87-112.26

Table 4. Changes of Hb at different gestational week

Factors	Coef.	Std. Err	t	P>|t|	[95% conf. interval]	
a. Hb level changes from baseline to 24th week of GW						
-Group (1=Sprinkles)	1.27	1.38	0.92	0.358	-1.44	3.98
-Anemic at baseline	13.58	1.25	10.84	0.000	11.11	16.04
-GW while recruited	0.50	0.24	2.09	0.037	.030	0.976
-Age (y)	0.25	0.15	1.62	0.106	-.053	0.557
-Abortion history (1=yes)	-0.055	1.51	-0.00	0.997	-2.98	2.97
-BMI	0.065	0.23	0.28	0.783	-0.398	0.529
-SES	0.952	1.61	0.59	0.556	-2.22	4.12
-Compliance	0.01	0.03	0.36	0.722	-.054	.078
b. Hb level changes from baseline to 28th week of GW						
-Group (1=Sprinkles)	1.63	1.39	1.17	0.243	-1.11	4.38
-Anemic at baseline	15.11	1.27	11.87	0.00	12.61	17.62
-GW while recruited	0.46	0.24	1.91	0.057	-0.013	0.947
-Age (y)	0.30	0.15	1.94	0.053	-0.003	0.615
-Abortion history (1=yes)	-2.02	1.54	-1.43	0.155	-5.24	0.833
-BMI	0.122	0.24	0.50	0.615	-0.357	0.603
-SES	0.144	1.62	0.09	0.92	-3.05	3.341
-Compliance	0.05	0.03	1.57	0.117	-0.013	0.12
c. Hb level changes from baseline to 32nd week of GW						
-Group (1=Sprinkles)	-0.22	1.45	-0.15	0.87	-3.08	2.63
-Anemic at baseline	16.51	1.33	12.35	0.000	13.885	19.14
-GW while recruited	0.94	0.25	3.67	0.000	0.437	1.44
-Age (y)	0.219	0.163	1.34	0.181	-0.102	0.540
-Abortion history (1=yes)	-2.60	1.60	-1.62	0.106	-5.76	0.55
-BMI	-0.04	0.255	-0.17	0.869	-0.544	0.46
-SES	3.10	1.70	1.83	0.069	-0.238	6.450
-Compliance	0.07	0.03	2.17	0.030	0.007	0.15

Table. 5. Frequency of reported possible side-effects

Indicators	Groups		Total	*P* value
	IFA (n)	Sprinkles (n)		
24th week				
-Heartburn	45.3 (111)	44.1 (108)	44.7 (219)	.428
-Nausea	49.8 (122)	43.7 (107)	46.7 (229)	.102
-Vomiting	28.6 (70)	26.1 (64)	27.3 (134)	.306
-Diarrhea	27.3 (67)	25.3 (62)	26.3 (129)	.341
-Constipation	57.6 (141)	62.0 (152)	59.8 (293)	.178
Any of the five	86.9 (213)	86.9 (213)	86.9 (426)	.553
28th week				
-Heartburn	41.5 (90)	43.5 (90)	42.5 (180)	.375
-Nausea	42.9 (93)	45.9 (90)	44.3 (188)	.298
-Vomiting	17.1 (37)	20.3 (42)	18.6 (79)	.232
-Diarrhea	21.7 (47)	13.0 (27)	17.5 (74)	.013
-Constipation	53.5 (116)	60.4 (125)	56.8 (241)	.090
Any of the five	86.6 (188)	87.4 (181)	87.0 (369)	.460
32 week				
-Heartburn	41.3 (85)	45.7 (95)	43.5 (180)	.210
-Nausea	53.4 (110)	46.2 (96)	49.8 (206)	.084
-Vomiting	21.8 (45)	18.8 (39)	20.3 (84)	.254
-Diarrhea	26.7 (55)	20.2 (42)	23.4 (97)	.074
-Constipation	49.0 (101)	51.4 (107)	50.2 (208)	.347
Any of the five	85.4 (176)	84.1 (175)	84.8 (351)	.408

Table 6. Compliance by group, side-effects and socioeconomic status

Compliance by groups (Mean±SD)				
	IFA (n)	Sprinkles (n)	Total	*P* value
-24 week	66.60±16.77 (207)	52.11±21.36 (208)	59.34 ±20.51 (415)	.000
-28 week	71.00±15.91 (239)	55.31±22.22 (237)	63.19±20.83 (476)	.000
-32 week	76.05± 13.50 (233)	57.53±22.48 (231)	66.83± 20.69 (464)	.000
Compliance by side effect				
	Yes (n)	No (n)		
-24 week	58.25± 20.89 (358)	66.15 ± 16.55 (57)	59.34±20.51 (415)	.007
-28 week	65.17± 19.92 (369)	71.48 ± 16.12 (54)	63.19± 20.83 (476)	.027
-32 week	66.89 ± 20.60 (351)	71.55± 16.16 (63)	66.83 ±20.69 (464))	.089
Compliance by socioeconomic status				
	Lower	Higher		
-24 week	60.93±19.28 (94)	58.87±20.86 (321)	59.34 ±20.51 (415)	.393
-28 week	65.73± 20.07 (116)	62.37±21.03 (360)	63.19±20.83 (476)	.132
-32 week	70.57±18.20 (113)	65.63±21.32 (351)	66.83± 20.69 (464)	.027

Table 7. Acceptability by groups

Indicators	Group		Total (n=445)	P value
	IFA (n=216)	Sprinkles (n=229)		
Changes in appetite				.001
-Not increased appetite	7.4 (16)	17.5 (40)	12.6 (56)	
-Somewhat increased	44.9 (97)	48.9 (112)	47.0 (209)	
-Absolutely increased	47.7 (103)	33.6 (77)	40.4 (180)	
Any experience in taste				.000
-Experienced severe bad taste	43.5 (94)	41.9 (96)	42.7 (190)	
-Somewhat bad taste	13.0 (28)	44.5 (102)	29.2 (130)	
Any experience on smell				.000
-Experienced severe bad smell	2.8 (6)	13.5 (31)	8.3 (37)	
-Somewhat bad smell	16.7 (36)	32.3 (74)	24.7 (110)	
-Had no bad experience on smell	80.6 (174)	54.1 (124)	67.0 (298)	
Willing to use	99.1 (214)	86.5 (198)	92.6 (412)	.000
Willing to buy	99.1 (214)	84.3 (193)	91.5 (407)	.000

Table 8. Reasons of not taking the supplementation (multiple answers considered)

Reasons	Group	
	IFA (n=209)	Sprinkles (n=226)
Fail to remember	89.5 (187)	72.6 (164)
Out of home	28.7 (60)	4.0 (9)
Unwell	13.9 (29)	16.8 (38)
Not interested	5.3 (11)	0.9 (2)
Diarrhea/ constipation	14.4 (30)	12.8 (29)
Did not like taste after mixing Sprinkles	-	63.3 (143)
Did not like color after mixing Sprinkles	-	50.4 (114)
Did not like smell after mixing Sprinkles	-	50.4 (114)