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Determinants of compliance to antenatal micronutrient supplementation and women's perceptions of supplement use in rural Nepal

Bharati Kulkarni[1], Parul Christian[2,*], Steven C LeClerq[2] and Subarna K Khatry[3]
[1]National Institute of Nutrition, Hyderabad, India: [2]Department of International Health, Center for Human Nutrition, Bloomberg School of Public Health, 615 N. Wolfe Street – W2041, Baltimore, MD 21205, USA: [3]Nepal Nutrition Intervention Project, Sarlahi, Kathmandu, Nepal

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Abstract

Objective: We examined factors affecting compliance to antenatal micronutrient supplementation and women's perceptions of supplement use.
Design: Randomized controlled supplementation trial of four alternative combinations of micronutrients given during pregnancy through to 3 months postpartum. Women were visited twice weekly to monitor compliance and to replenish tablets by female study workers. At 6 weeks postpartum women with live births (n 4096) were interviewed regarding their perceptions of the supplement. Median compliance calculated as percentage of total eligible doses received by women was high (84 %).
Setting: Rural southern Nepal.
Subjects: Pregnant women.
Results: Women with high compliance (above the median of 84 %) were likely to be older, less educated, poorer, undernourished, belong to lower caste and of Pahadi (hill) ethnicity compared with women with low compliance (at or below the median of 84 %). Smoking and drinking alcohol in the past week during pregnancy were strongly associated with low compliance. The major reason for irregular intake was forgetting to take supplements. A higher proportion of the high compliers liked taking the supplements but only half of them were willing to purchase them in the future. A large proportion of women (91 %) perceived a benefit from taking the supplement such as improved strength and health, whereas only about 10 % perceived any side-effects which were not a major barrier to compliance.
Conclusions: The present analysis highlights that poor, undernourished, uneducated women can have high compliance to antenatal supplementation if they are supplied with the tablets and reminded to take them regularly, and counselled about side-effects.

Keywords
Micronutrients
Pregnancy
Supplements
Compliance
Nepal

Micronutrient deficiencies during pregnancy are common in developing countries such as Nepal. Data from the 2006 Nepal Demographic Health Survey indicated that about one in three (36 %) women in Nepal is anaemic[1]. Studies carried out in rural Nepal indicate deficiencies of Zn, Fe, vitamins A, D, E, B_6, B_{12} and riboflavin during early pregnancy to be common[2,3]. Simultaneous deficiencies of two or more micronutrients affected >80 % of women in early pregnancy in these studies. Dietary deficits of micronutrient-rich foods such as meat, fish, dairy products, fruits and green leafy vegetables could help explain the high prevalence of micronutrient deficiencies in Nepal and other South-East Asian countries[4,5]. High amounts of phytate in cereal-based diets that inhibits mineral absorption add to the problem[6]. Maternal micronutrient deficiencies may be an important cause of adverse obstetric outcome such as fetal loss, stillbirth and low birth weight[7–9]. The effect of micronutrient supplementation on pregnancy outcome is presently a topic of considerable research interest. A number of studies have been carried out in developing countries which show equivocal results[10–12]. The present body of work on multiple micronutrient interventions is not sufficient to draw conclusions on their effects on neonatal well-being[13,14]. However, a few studies have indicated beneficial effects of maternal multiple micronutrient supplementation on early infant mortality and birth outcomes[15,16].

WHO, UNICEF and the International Nutritional Anemia Consultative Group recommend distribution of Fe and folic acid supplements to pregnant women[17]. Many

*Corresponding author: Email pchristi@jhsph.edu

developing countries have national programmes for Fe and folic acid supplementation to pregnant women, but these programmes have been shown to fail in reaching a large proportion of women and coverage rates have been low[18]. Studies in developing countries have indicated that the major barrier to effective supplementation programmes is inadequate supply[19]. Other barriers include poor compliance owing to side-effects, inadequate counselling and dislike of the taste[20,21]. Facilitators of compliance include women's recognition of improved physical well-being, better appetite, and increased perception of benefits for the fetus[22].

It is important to assess the determinants of compliance to supplementation and women's perceptions of supplement use to examine the possible effectiveness of antenatal micronutrient supplementation as a programme. A controlled setting of a community trial provides an opportunity to examine determinants of compliance since supply of supplements and logistics of delivery are designed to be optimal. The present study therefore assessed determinants of compliance to antenatal micronutrient supplementation and women's perception of supplement use in a randomized controlled trial in rural Nepal.

Experimental methods

The Nepal Nutrition Intervention Project Sarlahi 3 (NNIPS-3) study was a cluster-randomized, double-blind, controlled trial conducted in the rural plains district of Sarlahi, Nepal. The objective of this study was to examine the effects of prenatal and postnatal maternal micronutrient supplementation on birth weight, fetal loss and early infant mortality. Details regarding the study area, subjects and supplementation are published elsewhere[10]. Some of the relevant details are described below.

The study area, comprising thirty village development communities with a total population of ~200 000, was divided into 426 smaller communities called 'sectors' which served as the units of randomization. Randomization was done in blocks of five within each village development community. The sectors were randomly assigned to one of five treatment arms. To identify pregnancies in early gestation, all eligible women of reproductive age (married women, 15–45 years of age who were not menopausal, sterilized or not already breastfeeding an infant <12 months of age) in the study area were visited every 5 weeks and asked about their menstruation in the past 30 d. Pregnancy was ascertained with a urine test (human chorionic gonadotrophin antigen test; Clue®, Orchid Biomedical Systems, Goa, India) among women who reported not menstruating in the past 30 d. Women who tested positive were enrolled after obtaining consent. At enrolment, newly identified pregnant women were administered a baseline interview to obtain data on 30 d and 7 d frequencies of symptoms of morbidity, 7 d frequency of intake of selected foods, alcohol and tobacco use, 7 d work history, and information on household socio-economic status and previous pregnancy history. Anthropometric measurements including weight, height and mid upper-arm circumference (MUAC) were taken at enrolment. Similar interviews were repeated at 32 weeks of gestation and 6 weeks postpartum. During the postpartum interview, questions regarding the intake of the supplement (described below in detail) were added. Women's perceptions of the supplement, its use and reasons for not taking the supplement were also assessed as described below. Perceived side-effects due to the supplements were also ascertained at this visit.

Supplement

The five supplement arms in the study were: (i) folic acid (400 μg); (ii) folic acid–Fe (60 mg); (iii) folic acid–Fe–Zn (30 mg); (iv) folic acid–Fe–Zn plus eleven other micronutrients (10 μg vitamin D, 10 mg vitamin E, 1·6 mg thiamin, 1·8 mg riboflavin, 20 mg niacin, 2·2 mg vitamin B_6, 2·6 μg vitamin B_{12}, 100 mg vitamin C, 65 μg vitamin K, 2·0 mg Cu, 100 mg Mg), all with vitamin A; and (v) vitamin A alone (1000 μg retinol equivalents) as the control. At the outset of the study, each pregnant woman received a small bottle containing fifteen supplement caplets, with instructions from the staff to take one caplet each day. Women were subsequently visited twice each week by the sector distributors, who replenished the caplets, monitored their consumption and did pill counts, and collected data on pregnancies and their outcomes. The supplements were identical in shape, size and colour. The supplements were to be taken daily from the time of pregnancy detection through to 3 months postpartum in the case of a live birth or through to 5 weeks after a miscarriage or stillbirth. All the pregnant women in the study received counselling on antenatal care and nutrition at the time of enrolment. The women were encouraged to visit health posts and to take Fe supplements during pregnancy. The policy in Nepal is for all pregnant women visiting health posts to receive Fe supplements, although coverage and adherence are poor[1].

Women's perceptions

At 6 weeks postpartum, women who had a live birth were visited in their homes by trained interviewers and were asked about their perceptions of supplement use during pregnancy and lactation. Specifically, they were asked whether they liked taking the supplement and whether they would take it in a future pregnancy, if offered. They were also asked whether members of their family such as husband and mother-in-law, who might influence their decision, approved their intake of the supplement. Women were also asked whether they took the supplements regularly in order to assess the perception of their own compliance. Women who responded that they did not take the supplements regularly were probed further

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for the reasons. They were asked if their responses fitted in any of the six coded reasons. They were then also asked an open-ended question regarding reasons for not taking the supplements and all responses were recorded in their own words. These responses were later classified and coded for analysis. Women were also asked whether they suffered from any of seven side-effects due to the supplement and whether they stopped taking the supplement as a result of the side-effects. Those who said that they stopped taking the supplement were further asked whether they resumed taking the supplement later on. Women were also asked whether they perceived any benefit or harm as a result of the supplementation. Those who said 'yes' were asked to specify the perceived benefit or harm due to the tablets. All responses were recorded in their own words and were later classified and coded for analysis. They were also asked whether they were willing to buy the tablets and what price they were willing to pay for the tablets.

The study was approved by the ethical review committees of the Ministry of Health in Nepal and the Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA.

Statistical analyses

For the present analysis, which included only live births, data on compliance were analysed for 4096 women. Descriptive statistics of the baseline characteristics of these women, such as age, parity, education, socio-economic status, history of fetal loss and anthropometry (height, weight, MUAC), were calculated. The number and proportion of women with night blindness, other morbidities, and smoking and alcohol use in the third trimester of pregnancy were calculated. For each participant, compliance was calculated as percentage of the total eligible doses consumed during pregnancy through the postpartum period. Median compliance was 84 % (interquartile range 60–94 %) and did not differ by allocation code. Similarly, prevalence of side-effects did not differ by treatment[10]. Thus, all data in the present analysis were combined across treatment groups. The prevalence of Fe–folic acid supplement use during pregnancy through the local primary health-care system was low at 2·5 % and this was unlikely to impact the present analyses. Compliance at or below the median (≤84 %) was classified as 'low' compliance and compliance above the median (>84 %) was classified as 'high' compliance. Differences in various characteristics among the two compliance groups were assessed using Student's *t* test for continuous variables and the χ^2 test for categorical variables. Variables examined included age, parity, gestational age at enrolment, history of stillbirth, weight, height, MUAC, BMI (kg/m^2), literacy, husband's occupation, caste, ethnicity, tobacco/alcohol use, and indicators of socio-economic status such as land ownership and type of house construction. A stepwise multiple logistic regression model was developed to identify determinants of high compliance in this population. Variables significant at $P < 0{\cdot}05$ were retained in the model. Perceptions regarding the supplement and its use were also examined by high *v.* low categories of compliance and tested using the χ^2 test. Statistical analysis was carried out using the STATA statistical software package version 10 (Stata Corporation, College Station, TX, USA).

Results

Comparison of subject characteristics by compliance strata showed that women in the high compliance group were significantly older (23·4 *v.* 22·6 years, $P < 0{\cdot}001$) and a lower proportion were primiparas (23·0 % *v.* 30·4 %, $P < 0{\cdot}001$) compared with those in the low compliance group (Table 1). Gestational age at enrolment or previous history of stillbirth did not differ by compliance category. High compliers were slightly more undernourished than the low compliers. Mean height of high compliers was lower than that of the low compliers (150·0 *v.* 150·5 cm, $P = 0{\cdot}01$) and there was a trend of lower weight among the high compliers compared with the low compliers (43·4 *v.* 43·7 kg, $P = 0{\cdot}06$).

Overall, the proportion of women who were literate (able to read and write) was very low (20·9 %) and did not differ between the two compliance groups. In the high compliance group, a higher proportion of women's husbands were farmers or unskilled or contracted labourers, indicating poorer socio-economic status than women from the low compliance group (81·0 % *v.* 75·9 %, $P < 0{\cdot}001$). A higher proportion of women belonging to the Pahadi ethnicity (36·5 % *v.* 22·7 %, $P < 0{\cdot}001$) were in the high compliance group. The high compliance group owned less land and owned houses that were constructed with poor-quality materials. A significantly higher proportion of low compliers smoked and drank alcohol during pregnancy.

The multiple logistic regression analysis revealed that after adjusting for each other, variables significantly associated with high compliance were older age, later gestational age at enrolment, lower height and literacy (Table 2). Other variables found to be significantly associated with high compliance included husbands being farmers or unskilled labourers, lower caste, and lower rates of smoking and alcohol use during pregnancy.

A majority of the women (87 %) reported that they liked taking the supplements, although a higher proportion of high than low compliers said this (95·4 % *v.* 77·1 %; Table 3). A higher proportion of women in the high compliance group perceived the supplements to be beneficial (63·1 % *v.* 42·9 %), whereas the proportion perceiving harm was lower in the high *v.* the low compliance group (1·6 % *v.* 8·2 %). When women were asked about the specific perceptions of benefit, the major benefits

Table 1 Characteristics of the study subjects by compliance status: pregnant women, rural southern Nepal, participating in the Nepal Nutrition Intervention Project Sarlahi 3

	Low compliers (*n* 2057)		High compliers (*n* 2023)		
	Mean	SD	Mean	SD	*P* value*
Age (years)	22·6	5·7	23·4	5·6	<0·001
Gestational age at enrolment (weeks)	11·5	5·3	11·4	5·1	0·40
Weight (kg)	43·7	5·6	43·4	5·4	0·06
Height (cm)	150·5	5·6	150·0	5·4	0·01
BMI (kg/m^2)	19·3	2·1	19·2	2·0	0·62
MUAC (cm)	22·0	1·8	21·8	1·8	0·87
	n	%	*n*	%	
Parity					
0	628	30·4	466	23·0	<0·001
1–3	992	48·0	1060	52·2	
>3	446	21·6	504	24·8	
Previous stillbirth	90	6·2	115	7·2	0·28
Literate	433	21·2	415	20·5	0·52
Any schooling	430	20·8	379	18·7	0·08
Husband literacy	1033	50·7	1062	52·5	0·20
Husband's occupation					
Farmer, unskilled labourer	1568	75·9	1644	81·0	<0·001
Business/service	498	24·1	386	19·0	
Caste					
Hindu – higher	299	14·5	341	16·8	0·04
Hindu – lower/non-Hindu	1767	85·5	1689	83·2	
Ethnicity†					
Pahadi	463	22·7	739	36·5	<0·001
Madheshi	1572	77·1	1279	63·2	
Land ownership					
<0·2 ha	817	39·5	782	38·5	0·002
0·2–5·5 ha	962	46·6	1031	50·8	
>5·5 ha	287	13·9	217	10·7	
House construction material					
Thatch/grass/sticks	1786	86·4	1774	87·4	0·37
Cement/wood	280	13·5	256	12·6	
Roof material					
Thatch/grass	361	17·5	434	21·4	0·002
Tile/tin/cement	1705	82·5	1596	78·6	
Smoked tobacco in past 7 d	898	43·5	613	30·2	<0·001
Drank alcohol in past 7 d	721	34·9	423	20·8	<0·001

MUAC, mid upper-arm circumference.
*Differences in characteristics among the two compliance groups were assessed using Student's *t* test for continuous variables and the χ^2 test for binary variables. Compliance and age, *n* 4096; gestational age at enrolment, *n* 4028; parity, *n* 4061; history of fetal loss, *n* 3049; anthropometry, *n* 3865; literacy, education and socio-economic variables, *n* 4061.
†Pahadis are people from the hills of Nepal who have settled in the plains and Madheshis are peoples of Indian origin who have migrated across the border.

included gain in strength (40–50 %) and improvement in health (20–25 %). Other benefits perceived by women included having a healthier baby, improved appetite, improvement in night blindness, increased blood and milk flow. A very small percentage of women (14·0 % in the low and 4·5 % women in the high compliance group) said that they suffered from adverse health or side-effects as a result of the supplementation.

Importantly, about 90 % of women in the high compliance group and 75 % women in the low compliance group said that they would take the supplement in future pregnancy, if offered. However, only half of the women were willing to buy the tablets, with a higher proportion of high compliers indicating willingness (53 % *v.* 44 %). Among those willing to buy tablets, about <10 % were willing to pay up to Nepali paisa 10 (100 paisa = 1 Nepali rupee; Nepali rupees 60 = 1 US dollar) and about a third each were willing to pay Nepali paisa 11–50 or Nepali paisa 51–100 per tablet.

Women's own perception regarding regularity of their intake ranged between 60 % and 75 %, with 60 % of the low compliers reporting their intake as irregular and 75 % of high compliers reporting their intake as regular (data not shown). When women who perceived their intake of the supplement as irregular were asked for reasons of not taking the tablets, 39 % said that they forgot to take the supplement (Fig. 1). Another 16 % of women reported the cause of not taking the supplement as going to parents' home for delivery. These women did not receive supplements from project distributors who did not know their parents' home address, which in some cases was located in a different village. About 13 % said that they did not take the tablets due to the side-effects they were perceived to cause, whereas 10 % said that they did not

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Table 2 Odds ratios and 95 % confidence intervals* for determinants of high *v.* low compliance to supplementation: pregnant women, rural southern Nepal, participating in the Nepal Nutrition Intervention Project Sarlahi 3

Variable	Adjusted OR	95 % CI	*P* value
Age (years)	1·03	1·02, 1·04	<0·001
Gestational age at enrolment (weeks)	1·03	1·01, 1·04	<0·001
Height (cm)	0·98	0·97, 0·99	0·002
Literate†	0·71	0·58, 0·87	0·001
Husband's occupation – business/service‡	0·76	0·64, 0·89	0·001
Lower caste§	1·31	1·04, 1·66	0·02
Madheshi ethnicity‖	0·36	0·29, 0·76	<0·001
Smoked tobacco in the past 7 d	0·62	0·50, 0·76	<0·001
Drank alcohol in the past 7 d	0·57	0·45, 0·73	<0·001

*Using stepwise multiple logistic regression analysis to predict the odds of high compliance.
†Defined as the ability to read or write.
‡Farmer/unskilled labourer was the referent category.
§Caste was categorized as Hindu castes of Brahmins and Chhetris as higher castes *v.* Hindu castes of Vaishya, Shudra and non-Hindus as lower castes. Higher caste was the referent category.
‖Pahadis are people from the hills of Nepal who have settled in the plains and Madheshis are peoples of Indian origin who have migrated across the border. Pahadi was the referent category.

Table 3 Perceptions of women regarding supplement use during pregnancy and lactation by compliance status*: pregnant women, rural southern Nepal, participating in the Nepal Nutrition Intervention Project Sarlahi 3

	Low compliers		High compliers	
	n	%	*n*	%
Perception towards supplement				
Liked the supplement	1317	77·1	1874	95·4
Did not like the supplement	329	19·3	41	2·1
Was indifferent (neither liked nor disliked the supplement)	56	3·3	45	2·3
Didn't know	6	0·4	4	0·2
Husband approved of supplement	1413	87·0	1851	94·4
Mother-in-law approved of supplement	1049	64·6	1390	70·9
Perception of benefit or harm caused by supplement				
Benefit	697	42·9	1238	63·1
Harm	133	8·2	32	1·6
Neither benefit nor harm	326	20·1	291	14·8
Both benefit and harm	13	0·8	16	0·8
Didn't know	454	28·0	383	19·5
Types of perceived benefits				
Improved health	187	22·7	306	24·7
Gained strength	345	41·9	595	48·0
Increased appetite	50	6·1	100	8·1
Baby was healthier	63	7·6	87	7·0
Cured night blindness	18	2·2	25	2·0
Increased blood	7	0·8	16	1·3
Increased breast milk	2	0·2	6	0·5
Types of perceived harm				
Caused health problem to self	115	14·0	56	4·5
Caused health problem to the baby	3	0·4	1	0·1
Willing to take supplement in future pregnancy	1227	75·5	1751	89·3
Willing to pay per tablet	711	43·8	1041	53·1
Willing to pay up to 10 paisa	86	12·1	61	5·9
Willing to pay 11–50 paisa	216	30·4	366	35·2
Willing to pay 51–100 paisa	235	33·1	367	35·2
Willing to pay but amount unspecified	174	24·4	247	23·7

*Differences in perceptions in the two compliance groups were assessed using the χ^2 test; all $P<0·001$ except for categories of types of perceived harm, where $P>0·05$.

like the tablets. About 7 % perceived that the supplement caused harm, whereas 4 % and 3 %, respectively, said they did not take them around the days when they delivered a baby or because they were taking some other medicine. Other reasons were provided by <1 % each of the women.

Overall, only 10 % of the women reported any side-effects. A higher proportion of low compliers perceived side-effects compared with the high compliers (13·3 % *v.* 5·1 %; Table 4). Nausea and abdominal pain were the most commonly reported symptoms. Other side-effects were vomiting, black stools, diarrhoea and constipation. About 50 % of the women in each group who perceived side-effects stopped taking the supplement. About 13 % of them stopped taking the tablets for less than a week, 6–8 % stopped for 7–29 d and 30 % stopped for more than a month. These proportions were not significantly

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different in the two compliance groups. However, only 40 % of the women in the low compliance group resumed taking the tablets compared with 74 % of women in the high compliance group.

Discussion

In the context of a randomized controlled trial of micronutrient supplementation with high overall compliance, we found that women who were older, poorer, less educated, undernourished, belonging to lower castes and of Pahadi ethnicity were likely to have high compliance. Richer, more educated women, who may have had adequate knowledge and resources to avail of antenatal services on their own, on the other hand, may not have perceived that the supplements provided any benefit and were less likely to be compliant. In the trial we had two supervisory visits by project staff to monitor compliance and replenish supplements, a strategy that has poor programmatic relevance. This was one of the reasons to assess women's perceptions of the supplement and their willingness to use them in the future.

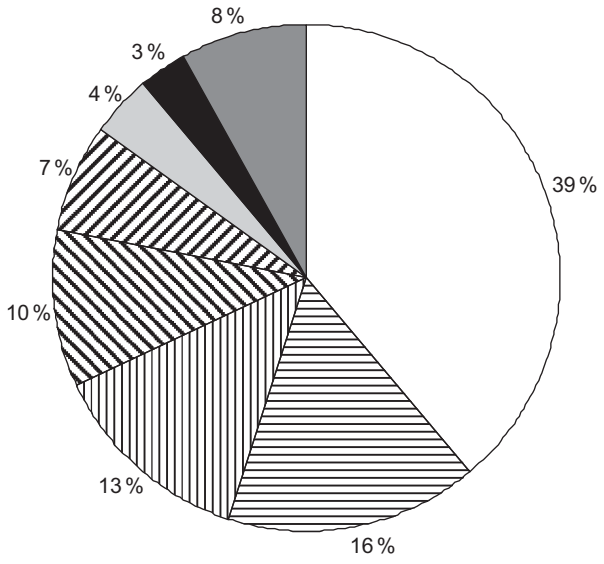

Fig. 1 Reasons reported by 1520 women for not taking tablets regularly among those who perceived not taking them regularly: □, forgot to take; ▤, was at parents' home; ▥, due to side-effects; ▧, did not like tablets; ▨, would cause harm; ▫, did not take around delivery; ■, taking other medicines; ▪, other. 'Other' reasons included family did not allow, bad taste or smell of tablet, tablet being too big, fear of baby being big, misplacing the supplement bottle, due to festival, change in residence and unknown reason (all prevalences <1 %)

We found high compliers to be older and to have more children. Earlier studies conducted in programmatic settings have not reported these relationships[20,21]. Perhaps, in the present study, women who had more children had a longer exposure to the messages of antenatal supplements that may have improved their compliance. But more likely, many younger, primiparous women went to their parents' home for delivery for 2–3 months during which they were not reached for supplement distribution by the study workers. This reason, however, is unlikely to have relevance for programmes, but was more specific to the context of the present trial.

High compliers were less educated and poorer as indicated by husband's occupation, land ownership and type of housing, similar to what we previously reported in a study involving vitamin A supplementation to pregnant women in which characteristics that predicted higher coverage rates included older age, higher parity, previous child deaths and lower socio-economic status[23]. In a study in Indonesia that assessed determinants of community-based periodic vitamin A supplementation programmes in children also indicated that coverage was higher in villages which were economically less developed[25]. In that study it was shown that the highest performance was achieved by village distributors who were less educated and represented the local status quo rather than more upwardly mobile, highly educated ones[24]. However, a weekly Fe–folic acid supplement delivered with social marketing to pregnant women in Cambodia found that compliance to the supplement was higher among women of higher socio-economic status[25] and an Fe supplementation study in infants in southern

Table 4 Perceived gastrointestinal side-effects due to supplementation by compliance group*: pregnant women, rural southern Nepal, participating in the Nepal Nutrition Intervention Project Sarlahi 3

	Low compliers (*n* 1624)		High compliers (*n* 1961)	
Side-effect	*n*	%	*n*	%
Nausea	81	5·0	38	1·9
Vomiting	49	3·0	18	0·9
Diarrhoea	27	1·7	9	0·5
Constipation	27	1·7	9	0·5
Pain in abdomen	58	3·6	28	1·4
Black stools	37	2·3	42	2·1
Any other	41	2·5	16	0·8
Any one of the above	215	13·3	99	5·1

*Differences in perceived side-effects in the two compliance groups were assessed using the χ^2 test; all $P<0{\cdot}001$ except black stools, where $P>0{\cdot}05$.

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Israel found that maternal education was positively related to higher compliance to the supplement[26]. In general, associations with schooling and literacy and compliance are likely to be setting-specific.

Although there was a higher proportion of upper caste women in the high compliance group when compared with the low compliance group, belonging to lower caste predicted higher compliance in the multiple logistic regression analysis. It is possible that the relationship of caste to compliance in the univariate analysis was confounded by other variables included in the multiple logistic regression model. Smoking and alcohol consumption during pregnancy were strong predictors of poor compliance. These have been shown to be associated with poor health behaviours including lower compliance with the prescribed treatment[27,28]. Fe supplement use among pregnant Danish women was also negatively associated with smoking during pregnancy[29], as observed in the present study.

A majority of the women (87 %) liked taking the supplement and supplement use was largely approved by the family members. Similarly, a large proportion of women perceived benefits due to the supplements and few perceived any adverse health effects. Benefits reported by women included increased strength, improvement in health, increased blood and having a healthy baby. Perception of benefits was found to be an important determinant of high compliance to the supplement, which has been observed in previous studies in the Philippines as well as in the MotherCare project carried out in eight developing countries[20,22]. As micronutrient deficiencies are widespread in this region and anaemia and other micronutrient deficiencies lead to fatigue, loss of appetite and sense of poor health, it is possible that women felt that they gained strength due to the supplements. This indicates the 'hidden hunger' for these important nutrients in this population. More women in the low compliance group perceived the supplement to cause some harm (14·0 % *v.* 4·5 %), but largely the adverse effect was perceived to be felt to themselves and not the baby, and could be related to the gastrointestinal side-effects.

While a large proportion of women expressed willingness to take similar supplements in a future pregnancy, only half of them were willing to buy them or pay very small amounts of money for them, suggesting that perhaps cost is the biggest barrier to access to micronutrient supplements in this population.

The most frequently quoted reason (~40 %) for irregular intake of the supplement was that they 'forgot to take the tablet'. In studies carried out in the Philippines on compliance to Fe supplementation this was also found to be the most common reason for low compliance[20]. However, unlike in the Philippines study, women in the present study received regular counselling and supervision through twice weekly visits. This reveals the difficulty of ensuring daily, regular consumption of antenatal supplements. Alternative strategies of communication to ensure that women as well as their families understand the importance of not forgetting to take their supplements are needed. For example, Fe–folic acid supplementation programmes in Cambodia as well as Vietnam utilized social marketing and community mobilization approaches to educate women about the benefits of taking Fe and folic acid regularly[27,30].

Perceived side-effects were reported as a reason for not taking the supplement regularly by ~10 % of the women. This proportion is similar to that reported by some earlier studies in the Philippines, Mali and Tanzania and as part of qualitative research carried out by the MotherCare project in eight developing countries[19,20,31,32]. Contrary to the belief that women stop taking tablets due to side-effects, the major barrier to effective supplementation programme was inadequate supply[19]. Also, in our study, although the proportion of women who stopped taking the supplement as a result of the side-effects was not different in the two compliance groups, the percentage who resumed taking the supplement was significantly higher in the high *v.* the low compliance group (74 % *v.* 40 %), indicating that resumption of supplement consumption following side-effects may be an important determinant of compliance. In a study in Senegal, counselling by midwives to pregnant women regarding the transient nature of side-effects with Fe–folic acid supplements and specifically explaining to them that the tablets would improve health were also important determinants of compliance[33]. During pregnancy many of the side-effects such as nausea, vomiting, constipation and abdominal pain are likely to be mistaken to result from the supplement[34].

In conclusion, our study provides important information on determinants of compliance and women's perceptions of supplement use in a rural community in Nepal. Considering the current move towards multiple micronutrient supplementation, these findings can help inform policy and programme development for the effective control of micronutrient deficiencies in pregnant women in the South Asian context.

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References

1. Ministry of Health, UNICEF & World Health Organization (1998) *Nepal Family Health Survey Data (Nepal Micronutrient Status Survey)*. Kathmandu: Ministry of Health, Child Health Division, HMG/N, New ERA, Micronutrient Initiative, UNICEF Nepal and WHO.
2. Jiang T, Christian P, Khatry SK, Wu L & West KP Jr (2005) Micronutrient deficiencies in early pregnancy are common, concurrent, and vary by season among rural Nepali pregnant women. *J Nutr* **135**, 1106–1112.
3. Christian P, Jiang T, Khatry SK, LeClerq SC, Shrestha SR & West KP Jr (2006) Antenatal supplementation with micronutrients and biochemical indicators of status and subclinical infection in rural Nepal. *Am J Clin Nutr* **83**, 788–794.
4. Rao S, Yajnik CS, Kanade A *et al.* (2001) Intake of micronutrient-rich foods in rural Indian mothers is associated with the size of their babies at birth: Pune Maternal Nutrition Study. *J Nutr* **131**, 1217–1224.
5. National Nutrition Monitoring Bureau (2002) *Diet and Nutritional Status of Rural Population*. Hyderabad: National Institute of Nutrition.
6. Hallberg L, Brune M & Rossander L (1989) Iron absorption in man: ascorbic acid and dose-dependent inhibition by phytate. *Am J Clin Nutr* **49**, 140–144.
7. Fall CH, Yajnik CS, Rao S, Davies AA, Brown N & Farrant HJ (2003) Micronutrients and fetal growth. *J Nutr* **133**, 5 Suppl. 2, 1747S–1756S.
8. Costello AM & Osrin D (2003) Micronutrient status during pregnancy and outcomes for newborn infants in developing countries. *J Nutr* **133**, 5 Suppl. 2, 1757S–1764S.
9. Ladipo OA (2000) Nutrition in pregnancy: mineral and vitamin supplements. *Am J Clin Nutr* **72**, 1 Suppl., 280S–290S.
10. Christian P, Khatry SK, Katz J, Pradhan EK, LeClerq SC, Shrestha SR, Adhikari RA, Sommer A & West KP Jr (2003) Effects of alternative maternal micronutrient supplements on low birth weight in rural Nepal: double blind randomised community trial. *BMJ* **326**, 571.
11. Christian P, West KP, Khatry SK, Leclerq SC, Pradhan EK, Katz J, Shrestha SR & Sommer A (2003) Effects of maternal micronutrient supplementation on fetal loss and infant mortality: a cluster-randomized trial in Nepal. *Am J Clin Nutr* **78**, 1194–1202.
12. Ramakrishnan U, González-Cossío T, Neufeld LM, Rivera J & Martorell R (2003) Multiple micronutrient supplementation during pregnancy does not lead to greater infant birth size than does iron-only supplementation: a randomized controlled trial in a semirural community in Mexico. *Am J Clin Nutr* **77**, 720–725.
13. Haider BA & Bhutta ZA (2006) Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev* issue 4, CD004905.
14. Christian P, Osrin D, Manandhar DS, Khatry SK, de L Costello AM & West KP Jr (2005) Antenatal micronutrient supplements in Nepal. *Lancet* **366**, 711–712.
15. Supplementation with Multiple Micronutrients Intervention Trial (SUMMIT) Study Group, Shankar AH, Jahari AB, Sebayang SK *et al.* (2008) Effect of maternal multiple micronutrient supplementation on fetal loss and infant death in Indonesia: a double-blind cluster-randomised trial. *Lancet* **371**, 215–227.
16. Zagré NM, Desplats G, Adou P, Mamadoultaibou A & Aguayo VM (2007) Prenatal multiple micronutrient supplementation has greater impact on birth-weight than supplementation with iron and folic acid: a cluster-randomized, double-blind, controlled programmatic study in rural Niger. *Food Nutr Bull* **28**, 317–327.
17. Stoltzfus RJ & Dreyfuss ML (1998) *Guidelines for the Use of Iron Supplements to Prevent and Treat Iron Deficiency Anemia*. Washington, DC: International Life Sciences Institute.
18. Mukuria A, Aboulafia C & Themme A (2001) *The Context of Women's Health: Results from the Demographic and Health Surveys, 1994–2001. Comparative Reports* no. 11 2005. Calverton, MD: ORC Macro.
19. Galloway R & McGuire J (1994) Determinants of compliance with iron supplementation: supplies, side effects, or psychology? *Soc Sci Med* **39**, 381–390.
20. Lutsey PL, Dawe D, Villate E, Valencia S & Lopez O (2008) Iron supplementation compliance among pregnant women in Bicol, Philippines. *Public Health Nutr* **11**, 76–82.
21. Schultink W, van der Ree M, Matulessi P & Gross R (1993) Low compliance with an iron-supplementation program: a study among pregnant women in Jakarta, Indonesia. *Am J Clin Nutr* **57**, 135–139.
22. Galloway R, Dusch E, Elder L *et al.* (2002) Women's perceptions of iron deficiency and anaemia prevention and control in eight developing countries. *Soc Sci Med* **55**, 529–544.
23. Katz J, West KP Jr, Wu L, Khatry SK, Pradhan EK, Christian P, LeClerq SC & Shrestha SR (2002) Determinants of maternal vitamin A or β-carotene supplementation coverage: village-based female distributors in Nepal. *Am J Public Health* **92**, 1105–1107.
24. Tarwotjo I, West KP Jr, Mele L, Nur S, Nendrawati H, Kraushaar D & Tilden RL (1989) Determinants of community-based coverage: periodic vitamin A supplementation. *Am J Public Health* **79**, 847–849.
25. Kanal K, Busch-Hallen J, Cavalli-Sforza T, Crape B & Smitasiri S; Cambodian Weekly Iron–Folic Acid Program Team (2005) Weekly iron–folic acid supplements to prevent anaemia among Cambodian women in three settings: process and outcomes of social marketing and community mobilization. *Nutr Rev* **63**, 12 Pt 2, S126–S133.
26. Amsel S, Boaz M, Ballin A, Filk D & Ore N (2002) Low compliance of iron supplementation in infancy and relation to socioeconomic status in Israel. *Pediatrics* **110**, 410–411.
27. Ahmed AT, Karter AJ & Liu J (2006) Alcohol consumption is inversely associated with adherence to diabetes self-care behaviours. *Diabet Med* **23**, 795–802.

28. Bazargan-Hejazi S, Bazargan M, Hardin E & Bing EG (2005) Alcohol use and adherence to prescribed therapy among under-served Latino and African-American patients using emergency department services. *Ethn Dis* **15**, 267–275.
29. Nordeng H, Eskild A, Nesheim BI, Aursnes I & Jacobsen G (2003) Guidelines for iron supplementation in pregnancy: compliance among 431 parous Scandinavian women. *Eur J Clin Pharmacol* **59**, 163–168.
30. Khan NC, Thanh HT, Berger J, Hoa PT, Quang ND, Smitasiri S & Cavalli-Sforza T (2005) Community mobilization and social marketing to promote weekly iron–folic acid supplementation: a new approach toward controlling anaemia among women of reproductive age in Vietnam. *Nutr Rev* **63**, 12 Pt 2, S87–S94.
31. Aguayo VM, Koné D, Bamba SI, Diallo B, Sidibé Y, Traoré D, Signé P & Baker SK (2005) Acceptability of multiple micronutrient supplements by pregnant and lactating women in Mali. *Public Health Nutr* **8**, 33–37.
32. Ekström EC, Kavishe FP, Habicht JP, Frongillo EA Jr, Rasmussen KM & Hemed L (1996) Adherence to iron supplementation during pregnancy in Tanzania: determinants and hematologic consequences. *Am J Clin Nutr* **64**, 368–374.
33. Seck BC & Jackson RT (2007) Determinants of compliance with iron supplementation among pregnant women in Senegal. *Public Health Nutr* **3**, 1–10.
34. Milman N, Byg KE, Bergholt T & Eriksen L (2006) Side effects of oral iron prophylaxis in pregnancy – myth or reality? *Acta Haematol* **115**, 53–57.

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