Results and Discussion

CHAPTER 4

RESULTS AND DISCUSSION

The results of the present study are reported under the following sections and are discussed in the light of available literature:

Section I — Baseline Data at 20-24 weeks of Gestation : Enrolment profile, Sociodemographic Background, Obstetric History, Health Services Utilization, Anthropometry and Hb

Section II — Efficacy of Home Delivery of Iron Supplements at Different Dose Levels : Coverage, Compliance, A Sub-Study on Compliance, Side Effects, Beneficial Effects

Section III — Effect of Three Different Dose Levels of Iron Supplementation During Pregnancy on Maternal Outcome : Prevalence of Anemia and Hemoglobin Levels, Morbidity Profile, Weight Gain, Gestational Duration, Birthweight

Section IV — Effect of Three Different Dose Levels of Iron Supplementation During Pregnancy on Maternal Weight and Hb at 6 Months Post-partum

Section V — Effect of Three Different Dose Levels of Iron Supplementation During Pregnancy on Infant Outcome at 3 Months and 6 Months of Age

Section I

Baseline Data at 20-24 Weeks of Gestation

Enrollment Profile

The number of subjects enrolled from each area is shown in Table 4.01. Initially 171 pregnant women at 20-24 weeks of gestation were enrolled to participate in the study. However only 120 women could be followed up till delivery, resulting in a dropout rate of 30% during this period (Table 4.02). Dropout rate was even higher for the follow up beyond delivery. Interestingly, larger number of mother-child pairs were available at 6 month post-partum follow up compared to 3 month post-partum. Only 29% of the subjects and their infants were available for follow up at 3 months, while at 6 months, 50% of the mother-child pairs were available. The reasons for drop out were many and varied which are shown in Table 4.03.

The reasons for dropping out of the study before delivery were migration to parental home, which accounted for 1/3rd of the drop outs upto delivery, non co-operation for various reasons and pregnancy complications that accounted for 9.4% and 3.6% of the drop outs respectively. A small percentage of the subjects (2%) preferred treatment from private practitioners. The main reason for the non-

Table 4.01 Areas and number of subjects selected for the study

Name of the area	No. of slums	No. of pregnant women enrolled
Akota	3	28
Anandnagar	3	21
Dharampura	1	27
Sawad	2	13
Savainagar	1	11
Kalyannagar	2	29
Jetalpur	1	23
Kamatipura	1	7
Hariomnagar	1	12
Total	15	171

Table 4.02 Number and percent of pregnant women who were available for follow up

Enrollment profile	Groups			Total	
	I	II	III	N	%
No enrolled	63	49	59	171	100
Socio-economic data available	58	48	57	163	95
Dropouts after baseline data collection	17	8	18	43	25
No. followed till delivery	41	40	39	120	70
No. of mothers available at 6 months	31	26	29	86	50
No. of infants available at 3rd month	21	16	13	50	29
No. of infants available at 6th month	30	26	29	85	50

Table 4.03 Reasons for drop-out of the study in the three iron treatment groups

Reason	Number dropping out			Total	
	Groups				
	I	II	III	N	%
Migration (moved to mother's place/elsewhere)	8	5	5	18	10.5
Could not be traced on follow-up visits	5	1	2	8	4.7
Non co-operation due to various reasons as below:					9.4
Refused to give blood for haemoglobin	1	1	3	5	2.9
Refused to take tablets	1	1	3	5	2.9
Non-cooperation of other family members	2	-	1	3	1.8
Not co-operative to participate in the study	-	-	1	1	0.6
Refused to take tablets and give blood for haemoglobin	1	-	1	2	1.2
Pregnancy complications:					3.6
Medical termination of pregnancy	2	-	-	2	1.2
Pregnancy not confirmed	-	1	1	2	1.2
Miscarriage	1	-	-	1	0.6
Still born infant	-	-	1	1	0.6
Preferred private practitioner	1	-	2	3	1.8
Total No. of Drop-outs	22	9	20	51	29.8

availability of the subjects in the post-partum period was that the mothers migrated either to their parental home or to other places after delivery.

In a similar iron supplementation field trial Sood et al (1975) reported a 30% dropout, chiefly, due to lack of co-operation for withdrawl of blood. Other reasons were premature delivery, leaving the study area and side effects. The ICMR multicentric study on field supplementation trials in pregnant women (ICMR 1992) also reported loss to follow up of 33% due to migration, refusal for withdrawl of blood sample, preferring private practitioners, and non-cooperation. In the iron supplementation trial by Reddiah et al (1989) nine percent of the subjects dropped out due to refusal to give blood samples. Similar findings of a high drop out rate have been reported in other countries like Thailand (22.1%) (Charoenlarp et al 1988), Indonesia (26.6%) (Schultink et al 1993) and Jamaica in the West Indies (32%) (Simmons 1990). The reasons for drop out in these countries were also similar to the ones found in the Indian studies including the present one.

Thus it appears that in India 70% of the underprivileged pregnant women above 20 w of gestation are available at a given time for iron supplementation. If innovative methods of reaching out to the pregnant women who

migrate to their parental homes are devised, 80% of the pregnant women can be brought under the program. However, for universal coverage intensive efforts to persuade the non-cooperative subjects will be required. While the latter two are likely to take a much longer time, it is feasible to reach the 70% using a more accessible delivery system as shown in subsequent sections.

Socio-Demographic Background

Table 4.04 presents the socio-economic and demographic profile of the women in the three groups who were available for follow up till delivery (n=120) while Appendix IX shows the same for the total sample of 163 women. A one way analysis of variance and chi-square tests showed no significant differences in any of the socio-economic variables between the three groups for the total sample of 163 women (see Appendix IX). In order to establish that the group equivalence did not change due to the high drop out rate, the socio-economic parameters of those who were available for follow up until delivery were subjected to one way ANOVA and chi-square tests. No significant differences were seen in any of the parameters except family size showing thereby that the profile of the subjects in the three groups did not change due to the high drop out rate.

Table 4.04 Socio-economic characteristics of the subjects in the three iron treatment groups

Socio-economic characteristics	Groups (Mean ± SE)			F ratio/ Chi Square
	I (41)	II (40)	III (39)	
Family Type %				
Joint	26.8	47.5	33.3	3.92^{NS}
Nuclear	73.2	52.5	66.7	
Family size	4.0 ±0.22	5.3 ±0.35	4.6 ±0.30	5.3286^{*}
Total years of education of the subject	4.3 ±0.66	4.9 ±0.60	4.8 ±0.56	0.4350^{NS}
Total years of education of husband	6.4 ±0.61	7.6 ±0.57	7.4 ±0.46	0.8341^{NS}
Occupation of the subject				
Gainfully employed	14.6	5.0	20.5	4.2^{NS}
Housewife	85.4	95.0	79.2	
Occupation of the husband				
Unskilled labour	14.6	17.5	12.8	1.3^{NS}
Skilled labour	82.9	82.5	84.6	
Unemployed	2.4	-	2.6	
Monthly income (Rs.)	963.9±89.33	1005.0±95.24	991.0±81.73	0.0558^{NS}
Per capita income (Rs.)	276.7±39.37	222.0±30.75	244.7±25.95	0.7173^{NS}
Subject has power to decide to spend money				
Yes	39.0	27.5	48.7	3.7^{NS}
No	61.0	72.5	51.3	

Table 4.04 (contd..)

Socio-economic characteristics	Groups (Mean ± SE) I (41)	II (40)	III (39)	F ratio/ Chi Square
Hours of work outside the house per day	5.0 ±0.63	5.5 ±0.50	5.4 ±0.61	0.4160^{NS}
Nature of work % (those gainfully employed)				
Light	4.9	-	5.1	
Moderate	7.3	5.0	15.4	
Not applicable	87.8	95.0	79.5	
Nature of work at home				
Light	26.8	37.5	30.8	1.1^{NS}
Moderate	73.2	62.5	69.2	
House construction %				
Hut/Kutcha	29.2	22.5	12.8	9.0^{NS}
Semi Pucca	39.0	35.0	25.6	
Pucca	31.7	42.5	61.5	
Toilet facility %				
Individual	43.9	50.0	59.0	2.4^{NS}
Public toilet	43.9	40.0	35.9	
Open defecation	12.2	10.0	5.1	
Source of drinking water				
Safe	100.0	100.0	100.0	-
Environmental sanitation including the house %				
Good	75.6	92.5	89.7	5.6^{NS}
Average	24.4	7.5	10.3	

NS - Not significant
* Significant at p 0.05

For the rest of the discussion in this section, the data presented refer only to the 120 women who were available for follow up till delivery.

Family size and family type

The family size ranged from 2-11 with a mean of 4.6. Thiry six percent of these women lived in a joint family system and the remaining lived in nuclear families.

Education and occupation of the subject and spouse and nature of work

The number of years of education of the subjects ranged from 3-15 years with a mean of 4.7 years. However the mean number of years of education of the spouses was much higher, 7.1 years. A small percentage (13.3%) of the subjects were gainfully employed. Occupation of the spouses revealed that a large percent (83.3%) of the men performed skilled labour, compared to 15% who were unskilled labourers, and 2% who were unemployed.

Both at home and outside, the pregnant women were engaged mostly in moderate type of activities, which involved 25% of the time sitting or standing and 75% of the time spent in specific occupational activities (WHO 1985). None of the subjects was found to engage in heavy physical

labour at any point of time during the study. The most commonly performed activities at work were cleaning utensils, washing clothes, sweeping, mopping, cooking and laundering while the housewives were engaged in cooking, cleaning, washing, fetching water and childcare.

Income

Average monthly income of the families from all sources was Rs.987/- with a mean per capita income of Rs.248/month. Only 38% of the women said they had any autonomy in deciding the pattern of expenditure.

House construction, toilet facility, sanitation of the house and source of drinking water

A sizable section (45%) of the subjects lived in pucca houses, while 33% of them resided in semi-pucca houses and 22% lived in huts or kutcha houses. The availability of toilet facilities was also reasonably good as 51% had individual toilets in the house or attached to the house, and 40% used public toilets. Open defaecation was practised by 9.2% of the women. The environment around the houses and within the house was rated as good in 86% of the households and as average in the remaining. None of the households had an environmental sanitation rating of poor (descriptions of categories are given in Appendix II).

Obstetric History

Information concerning the obstetric history of the women is presented in Table 4.05. One way ANOVA and chi-squares tests were applied to the obstetric history variables. None of these variables showed any significant differences between the three treatment groups. The general obstetric history of the subjects is described below.

Age at menarche, age at marriage

Age of the women ranged from 17-33 years with a mean of 23 years. Mean age at menarche was 14.3 years which is similar to that reported by Shah (1958) in Gujarat (14.8 years) and falls within the range of mean values reported by the ICMR multicentric study (11-14 years) (ICMR 1972). The lowest age at menarche that was reported in this study was 10 years and the highest was 17 years. Age at marriage ranged from 10-26 years with a mean of 17 years which is close to the mean age at marriage of 16.7 years reported in the 1981 country wide census (Census of India 1981). However, the age at marriage of the present study subjects was slightly lower than the mean age at marriage reported in an ICN case study (ICN 1992b) for females in 1981 (18.3 years).

Table 4.05 Obstetric history of the subjects in the three iron treatment groups

Characteristics	Groups (Mean ± SE)			F ratio/ Chi-square
	I (41)	II (40)	III (39)	
Age of the mother	22.8±0.52	22.5±0.48	23.7±0.48	1.5371^{NS}
Age at menarche	14.3±0.19	13.9±0.41	14.43±0.25	1.0179^{NS}
Age at marriage	16.7±0.45	16.9±0.49	17.5±0.38	0.9391^{NS}
Age when first child was born	18.7±0.42	18.5±0.57	19.0±0.44	0.3176^{NS}
Parity	1.74±0.13	1.81±0.1	1.91±0.19	0.2559^{NS}
Previous history of miscarriage				
Yes	24.4	17.5	17.9	0.7575
No	75.6	82.5	82.1	
Previous history of still born children				
Yes	14.6	5.0	7.7	2.4^{NS}
No	85.4	95.0	92.3	
Previous history of premature birth				
Yes	19.5	12.5	15.4	
No	61.0	52.5	66.7	4.2^{NS}
Not applicable	19.5	35.0	17.9	
Closed birth interval				
1st pregnancy	19.5	35.0	17.9	
< 24 months	29.3	17.5	23.1	4.65^{NS}
> 24 months	51.2	47.5	59.0	

NS - Not significant

Birth interval and parity

Twenty three percent of the subjects had a birth interval of less than or equal to 24 months, 52.5% had a birth interval of more than 24 months and for the remaining 24% it was their first pregnancy. Parity ranged from 1-6, with most subjects belonging to 1-3 para. Mean parity of the mothers was 1.4.

History of miscarriage, stillborn children and premature births

Previous history of miscarriage was reported by 20% of the women; 9.1% of the women reported a history of having a stillborn child. History of premature delivery (<36 weeks) was reported by 16% of the women.

Health Services Utilization

The utilization of available health care services by the subjects in the three treatment groups is presented in Table 4.06. No statistically significant differences were found in the extent of utilization of any of the health care services i.e. tetanus toxoid, supplementary food and antenatal care between the three groups.

Table 4.06 Utilization of health care services of the subjects in the three iron treatment groups

Health Care Service Service	Groups (Mean±SE/Percent) I (41)	II (40)	III (39)	F Value
A. Tetanus Toxoid (TT)				
Percent women who received ⩾ 2 doses	95	100	90	-
Percent women who received no TT	5	-	10	
B. Supplementary Food (SF)				
Percent women who received SF	76	88	87	3.32^{NS}
Percent women who did not receive SF	24	22	13	
C. Ante-Natal Visit (ANV)				
Percent women who went for ANV	98	90	85	
Total no. of ANV	4.8±0.41	4.8±0.48	4.1±0.49	0.795^{NS}
Gestational age at 1st visit	21.4±1.11	20.4±1.10	19.9±1.24	0.458^{NS}
Number of ANV before 20th week	1.71 (14)	1.82 (11)	1.73 (15)	0.114^{NS}
Number of ANV between 20-28th week	1.84 (32)	1.90 (31)	1.85 (26)	0.077^{NS}
Number of ANV between 28-36th week	3.03 (38)	3.47 (32)	2.83 (30)	1.829^{NS}
% women with ⩾ 4 ante-natal visits	61	60	51	

NS - Not significant.
Figures in parentheses are percentages.

Tetanus toxoid

A high percentage (93%) of the pregnant women in the present study had taken two or more doses of tetanus toxoid vaccine (TT), compared to an overall figure of 77% reported for rural and urban India (UNICEF 1994). There has been an intensive drive for immunization in the city of Baroda, which is reflected in the highly satisfactory utilization of the TT immunization. Thus most subjects in the present study were protected against tetanus infection.

Supplementary nutrition

Three fourths of the pregnant women (77%) participated in the supplementary nutrition provided at the AWC. The pregnant women are expected to receive the supplementary food for 100 days in the last trimester. However, only 25% of the present subjects took the supplementary food for 50 days or more. Thus, although the receipt of this service was good, full utilization occurred to a much smaller extent.

Ante-natal check ups

The ante-natal medical check ups were taken by the subjects from government or trust hospitals or private hospitals and clinics. In the present study 91% of the women

had ante-natal care with a mean of 4.6 visits during the entire pregnancy. During the entire pregnancy period pregnant women are expected to make at least four ante-natal visits. The situation with respect to ante-natal visits in the present study where 50% to 60% of the subjects had more than 4 ante-natal check ups, is a significant finding when compared to the data from rural and tribal areas in India. It has been observed that pregnant women generally make only 1 or 2 ante-natal visits throughout pregnancy (Gopalan 1989). In the USAID assisted ICDS evaluation (Gopaldas et al 1991) only 3% of the pregnant women were reported to have received three or more health check-ups.

Anthropometry

The mean anthropometric measurements of the subjects in the three different groups and mean Hb are shown in Table 4.07. No significant differences were found in any of the variables i.e. height, weight and MUAC, for the women in the three treatment groups. Mean gestational age of the subjects at entry was also not statistically different between the three groups (Table 4.07).

Table 4.07 Gestational age, anthropometry and hemoglobin of the subjects in the three iron treatment groups

Characteristics	Groups (Mean ± SE)			F ratio
	I (41)	II (40)	III (39)	
Height	151.55±0.87	151.73±0.88	150.17±1.01	0.8400^{NS}
Weight	43.39±1.02	43.31±0.93	44.31±1.20	0.2719^{NS}
MUAC	22.56±0.50	22.23±0.38	23.21±0.52	1.0857^{NS}
Hemoglobin	9.8±0.22	9.5 ±0.21	9.0±0.24	3.1221*
Gestational age	21.46±0.3	21.30±0.3	21.33±0.31	0.0821^{NS}

t' values for Hb

I vs II 1.08^{NS}, I vs III 2.41*, II vs III 1.45^{NS}

* Significant at $< p$ 0.05

Height

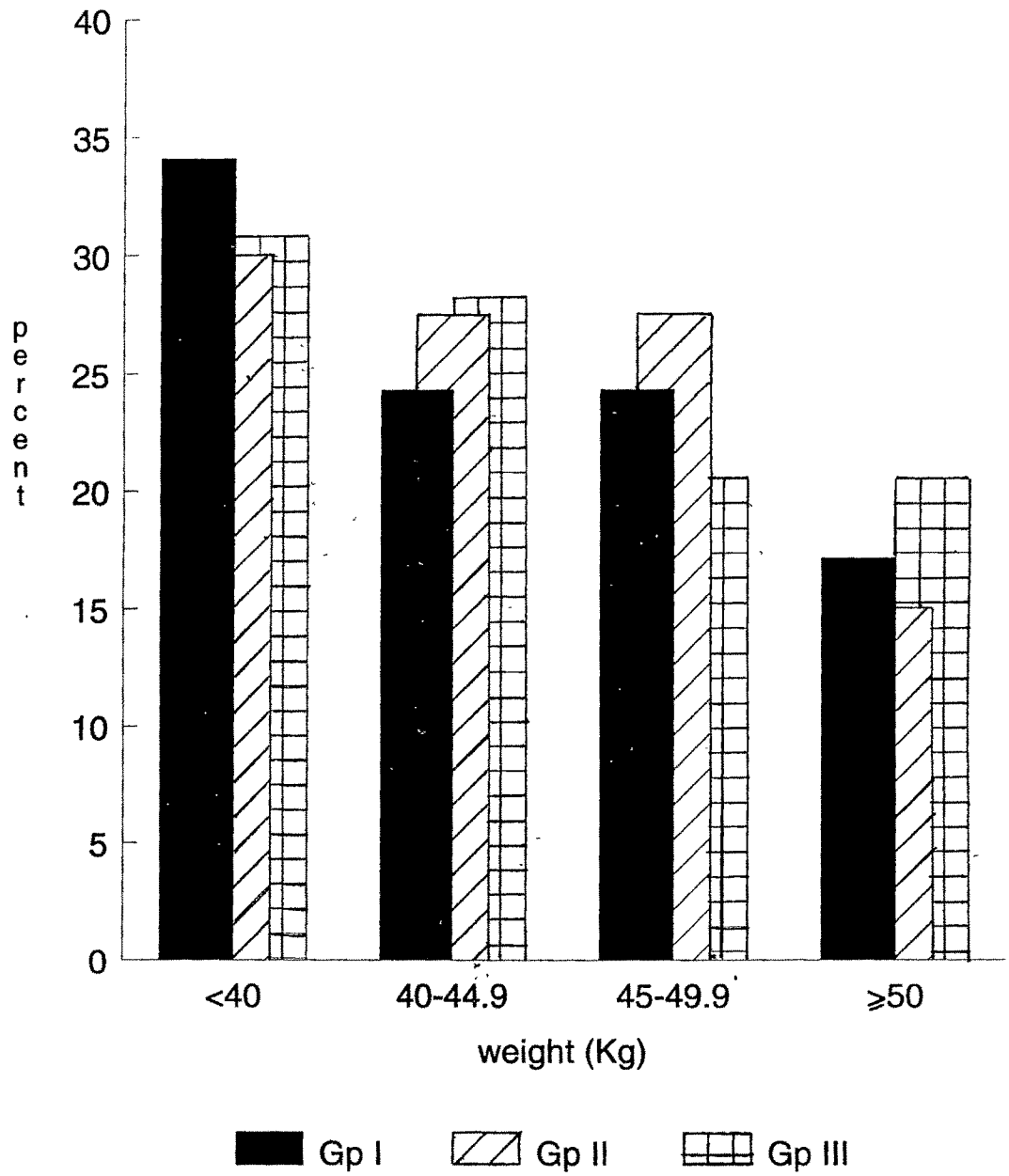
The mean height of the women who completed the study was 151.15 cms, which is similar to the values reported for urban slum dwellers in the ICMR survey in 1972 (152.1 cm) and the NNMB survey in 1984 (150 cm). However the ICMR survey included women aged 20 years and above whereas the present study included some subjects who were below the age of 20 years. The mean height of the subjects in the present study was the same as that reported for the low socio-economic rural and tribal pregnant women from Maharashtra and Gujarat studied by Gopaldas et al (1991) in their USAID assisted evaluation of ICDS in selected districts of these two States. The height range in the present study was 135-165 cm with 2.5% of the women below 140 cm and 10.8% of the women under 145 cm.

Weight

The body weight at entry of the present study subjects ranged from a low of 29.5 kg to a high of 61 kg with a mean of 43.7 kg, which is lower than the mean weight (49.5 kg) reported by Ramachandran (1982) for low socio-economic urban pregnant women in the third trimester (Prema et al 1981b).

The weight distribution, at entry, is shown in Fig 4.01. A chi-square test showed that there was no

Fig. 4.01 Initial weight distribution of the subjects



Chi square 1.0837NS

statistically significant difference in the initial weight distribution into different categories between the three treatments groups.

As can be seen from Fig 4.01, 31.7% of the subjects at entry weighed less than 40 kg while another 26.7% weighed less than 45 kg. Thus about two thirds of the pregnant women in the present study had a low initial body weight. Studies in India (Shah and Shah 1972, Karan and Mathur 1987) have shown that women who weigh less than 40 kg at 20 weeks of gestation are at greater risk of delivering low birth weight infants. Studies in Bangladesh (Chowdhury 1982) have shown much higher rates of neo-natal and post-neo-natal mortalities among infants, if mothers weighed less than 40 kg at some point in pregnancy. One third of the present study subjects at baseline by this weight criterion fell into the at risk category.

Mid upper arm circumference (MUAC)

The MUAC in the present subjects ranged from 18.5 cm to 31.0 cm. The mean was 22.66 cm, which is similar to the mean value reported in a large series of 2404 urban pregnant women by Prema et al (1981b). Recently considerable attention has been focussed on MUAC in relation to pregnancy outcome (Krasovec and Anderson 1991). The MUAC is reported

to increase by 1-4 cm in well nourished pregnant women in developed countries; however in underprivileged pregnant women from the low socio-economic groups in India, no change has been noted in the arm circumference as pregnancy advances (Agarwal et al 1987). Thus, MUAC does not appear to be an appropriate tool for monitoring changes in nutritional status during pregnancy but in view of its simplicity in handling at the field level, and high correlation between MUAC and weight during pregnancy (Tibrewala and Shah 1978), it has been suggested as a screening tool. Currently the search is for a meaningful cut off to determine pregnant women at risk, which it is believed may be somewhere between 20.8 cm to 23.5 cm, though a concensus is yet to be reached. Using the lower range of this cut off, 12.5% of the subjects fell into the at risk category. Using the higher range 67.9% of the present study subjects were at risk.

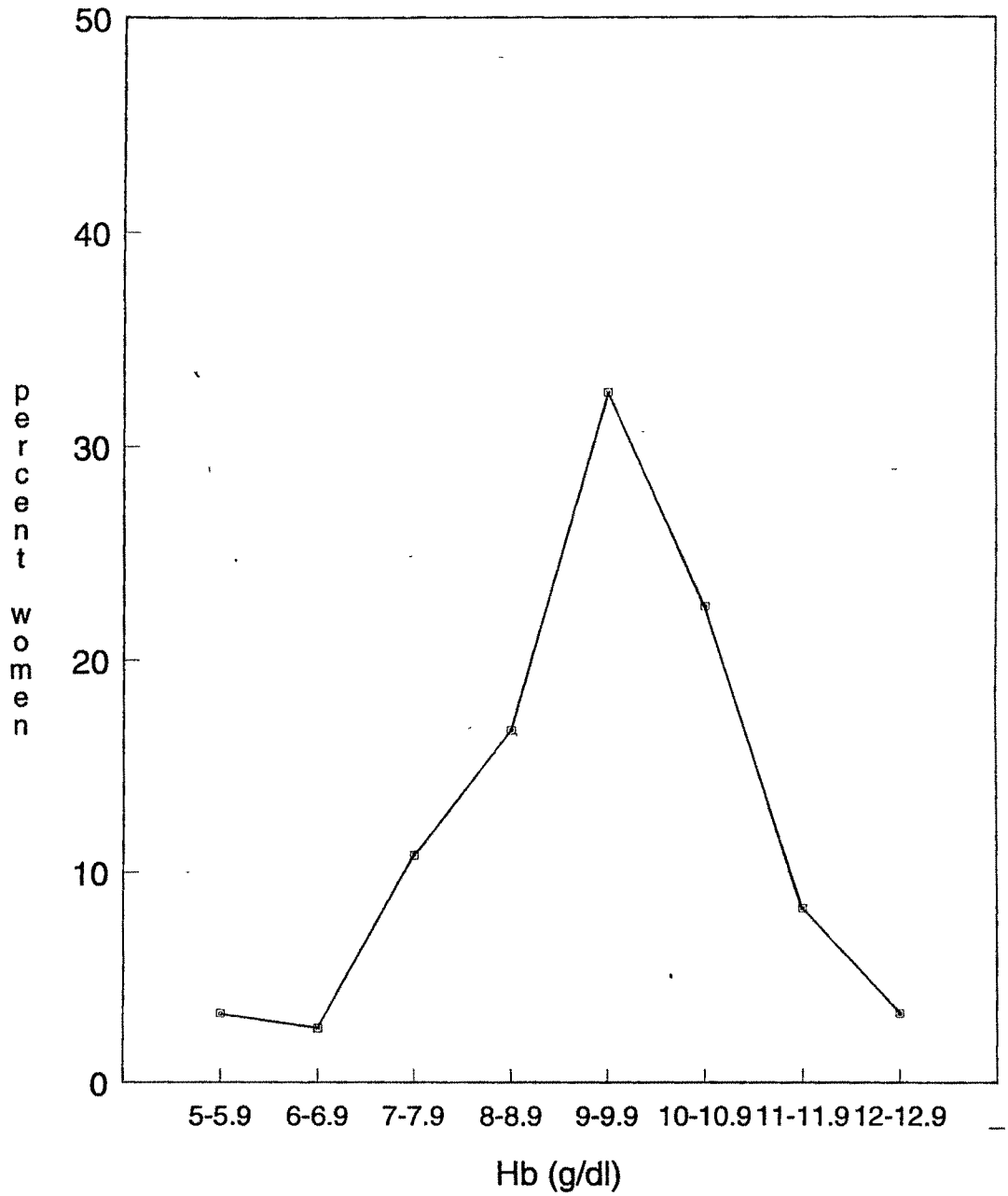
Hemoglobin (Hb) Levels

The mean Hb of the present subjects was 9.1 g/dl. Inspite of the random allocation mean Hb level in Group III was lower than in Group I and Group II, the difference being statistically significant between Group III and Group I. These initial differences in mean Hb levels have been controlled by analysis of covariance, while analyzing the impact of supplementation on Hb levels later. The lowest Hb

recorded in these women was 5.4 g/dl and highest was 12.9 g/dl. The frequency distribution of Hb at 20/24 w gestation is shown in Fig 4.02. As can be seen 5.8% of the women had Hb < 7 g/dl which is classified as severe anemia. Higher figures for prevalence of severe anemia have been reported by others in India, 13.6% (< 8 g/dl) (Prema et al 1981a) and 12.6% (ICMR 1989). Prevalence of anemia according to the WHO cut off of < 11 g/dl was 88.3% which is very similar to the values reported by the ICMR study (1989) in the national evaluation of NNAPP.

The Expert Committee of the Ministry of Health and Family Welfare constituted to review the evaluation of the performance of the Anemia Control Program in India, recommended that pregnant women with Hb < 7 g/dl must be referred to the PHC for active anti-anemia treatment. In the present study it was observed that although severely anemic women were referred by the AWW to be treated at the hospital, the women did not comply. Therefore the women with Hb levels < 7 g/dl were also included in the supplementation trial.

Fig. 4.02 Frequency distribution of initial Hb levels



Section II

Efficacy of Home Delivery of Iron Supplements at Different Dose Levels

Coverage

Iron supplementation was initiated at the 20th or 24th week of gestation and continued till delivery. Inspite of the initial assurances of the subjects that they will remain in the study till delivery and after, as the study progressed, some of the women who were enrolled at 24 week of gestation left for their parental homes at 32 weeks of gestation, thus reducing the duration of their stay in the supplementation trial to only two months. Fortunately the number of such women was very few in the three groups (2.5-5%). All others stayed for a minimum of three months with 50-56% in the different groups remaining in the program for four months. Thus under the Indian field conditions, pregnant women were available for iron supplementation only for a period of 90-120 days. As already stated of the 171 women who were originally enrolled, 120 were available for a follow up till delivery. The tablets in the required numbers could be reached out to all these 120 women through home based distribution. Thus this decentralized delivery system achieved a coverage of 70%.

The Evaluation of the National Program for Anemia Control (ICMR 1989) revealed that only 19.4% of the pregnant women were offered the supplements during their current pregnancy. As against this, a coverage of 70% in the present study is a very remarkable improvement. Modes of delivery in the National Program varied from hospitals, schools and subcenters to home delivery. Although 45% of the women were reported to receive the supplements through home delivery in the NNAPP evaluation, the efficacy was not assessed in terms of coverage with respect to other modes of delivery. Gove et al (1987) observed that higher rates of tablet consumption in Somalia were linked to receipt of the tablets from traditional birth attendants (TBAs) in the homes of the mothers.

As the primary health care system in India, especially the ICDS has a built in component of home visits by the field level functionaries, delivering the tablets through a home based delivery system should pose no problems. The present study has established that once a month visits are adequate, which fits in with the present policy of the ICDS that field functionaries make home visits to the pregnant women atleast once every month.

Other positive features of home based distribution

Home delivery of the supplements provided opportunities for interaction with the mothers and other community members. The once a month contacts gave opportunities to persuade the mothers to regularly consume the supplements. Some of the pregnant women, especially those who experienced marked improvements acted as positive reinforcers in convincing other pregnant women to participate in the iron supplementation programme.

As the study progressed it was interesting to note that other family members were seen to motivate and encourage the pregnant woman to consume the supplements. They also requested a supply of these iron tablets for themselves as they experienced tiredness and felt that it would improve their work performance. It is evident that home delivery does more than achieving good coverage, it gives an opportunity to interact with the women, the family members, and the community to promote healthy attitudes.

Compliance

In the present study compliance was recorded every month by counting the leftover unconsumed tablets in the autoseal covers. Enquiries were also made with the mothers and other family members to ensure that these tablets were

not consumed by anyone other than the subjects or discarded.

The autoseal packing found favour with the subjects as many of them found that the packing helped in preventing the deterioration of the tablets. Misplacement and loss was also reported to be fewer. The packing lent itself to a reasonably good estimate of compliance as the left-over tablets could be counted and recorded.

Two aspects related to tablet consumption have been suggested as the possible determinants of compliance. One is the attitude to tablets per se which includes perceptions such as tablets are hot and liable to cause miscarriages and the other is the discomfort experienced due to iron content of the tablets (WHO 1990, Seshadri et al 1993). Therefore in the present study two measures were used for evaluating compliance. One was tablet consumption per se, regardless of the iron content in the three different groups. The second was the number of doses of iron consumed, equivalent to 60 mg iron per one dose in the three different groups.

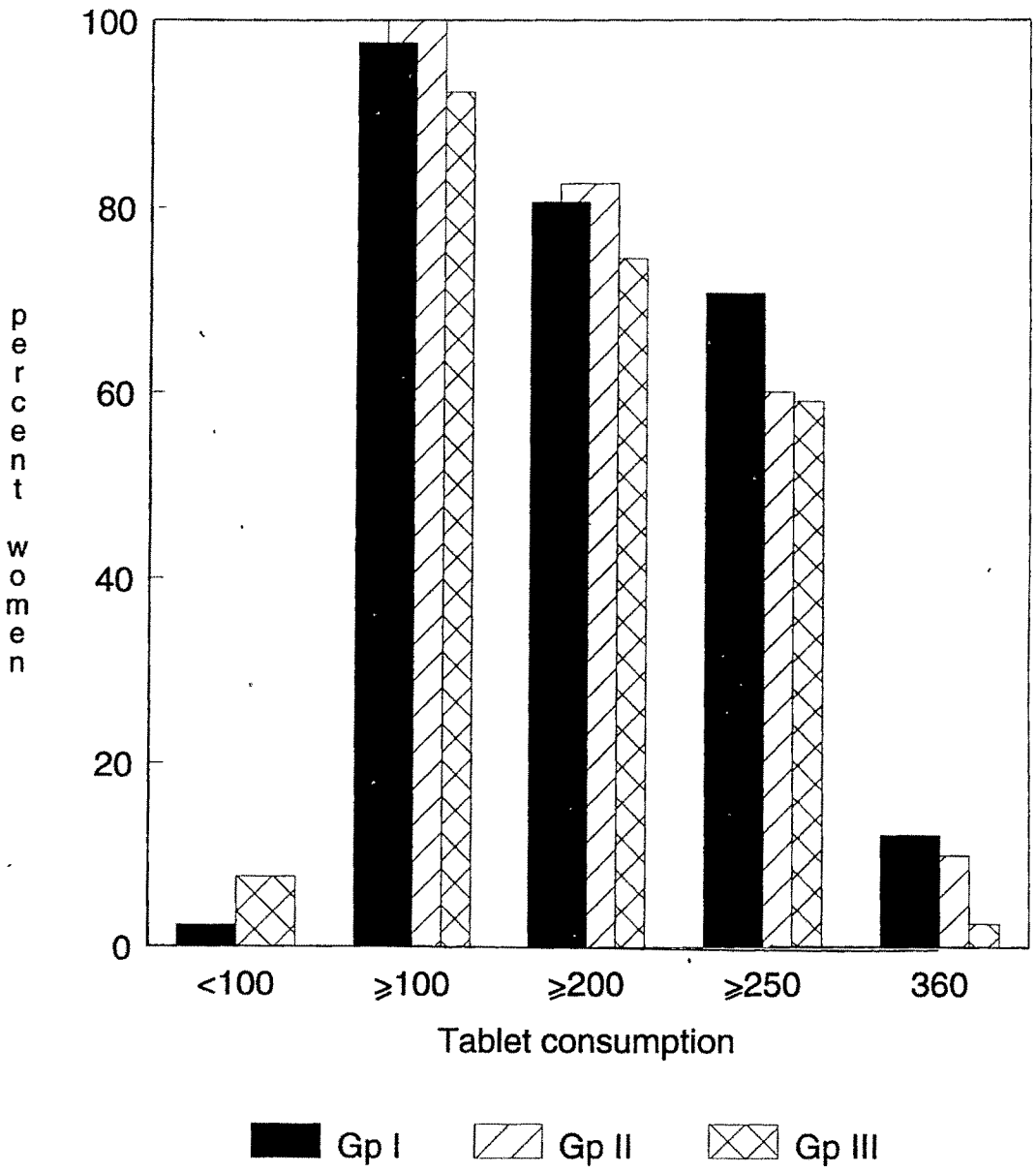
Two cut offs were selected. According to the original NNAPP in India (ICMR 1989) pregnant women are required to receive and consume 100 tablets of 60 mg elemental iron during the last trimester of pregnancy. According to DeMaeyer (1989), women must consume at least 250 tablets of 60 mg elemental iron in one pregnancy to prevent their Hb

levels from dropping below 11 g/dl. Therefore in the present study, consumption of 100 or 250 tablets per se or equivalent 60 mg doses were considered as the cut off levels for determining compliance.

The compliance levels of the women in the three groups with respect to tablet consumption per se is shown in Figure 4.03. Ninety eight percent of the women in Group I, 100% in Group II and 92% in Group III consumed 100 or more tablets during the study period. The target of 250 tablets was achieved by a smaller proportion, 71% of the women in Group I, 60% in Group II and 59% in Group III. Thus, although the belief system concerning tablets as hot existed, it did not appear to be a strong one and with home distribution and counselling once a month, compliance levels were quite high.

When consumption of number of doses of 60 mg iron was computed, it was found that a compliance target of >100 such doses could be achieved in a substantial percentage of the subjects (> 92%) when iron level provided was either 120 mg or 180 mg/day. Only 46% of the women in the 60 mg group consumed more than 100 tablets. The compliance target of 250 doses of 60 mg iron could be achieved only in Group III where 60% of the subjects consumed 250 or more tablets. Given the limitation of the short duration for which

Fig. 4.03 Level of compliance with iron supplements in the three treatment groups



subjects are available the compliance target of 250 mg can be achieved only if a high dose level (≥180 mg/day) is provided.

On further scrutiny, it was seen that length or duration of stay in the program influenced the level of tablet consumption (Fig 4.04). When the women stayed in the program for two months, mean tablet consumption was 128, 180 and 168 in Group I, Group II and Group III respectively. At three months duration mean tablet consumption increased to 220 in Group I, 227 in Group II, and 195 in Group III. The highest consumption of tablets was achieved after supplementation was provided for four months, in all the treatment groups (313 in Group I, 300 in Group II, and 293 in Group III).

That the higher dose level of iron did not affect mean tablet consumption is evident from Fig 4.05 which presents compliance as percent of expected consumption. This was 75-85% in all groups, for different levels of iron and for two different durations, 3 months and 4 months.

These results on coverage and compliance have important implications for the National Anemia Control Program in India. It shows that a decentralized home based distribution of the iron tablets can make the iron supplements accessible to 70% of the pregnant women. It also shows that compliance

Fig. 4.04 Compliance in relation to duration of supplementation

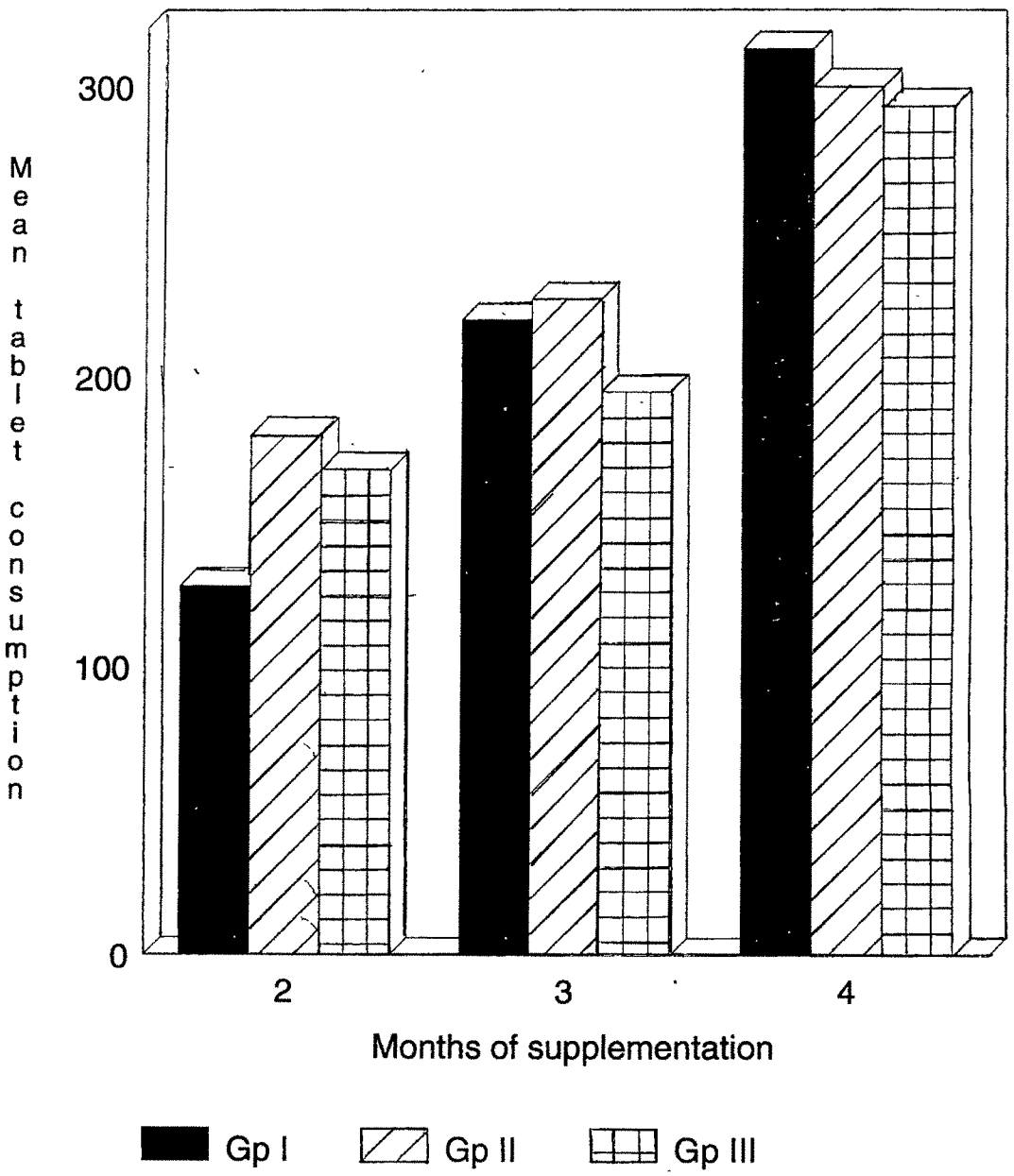
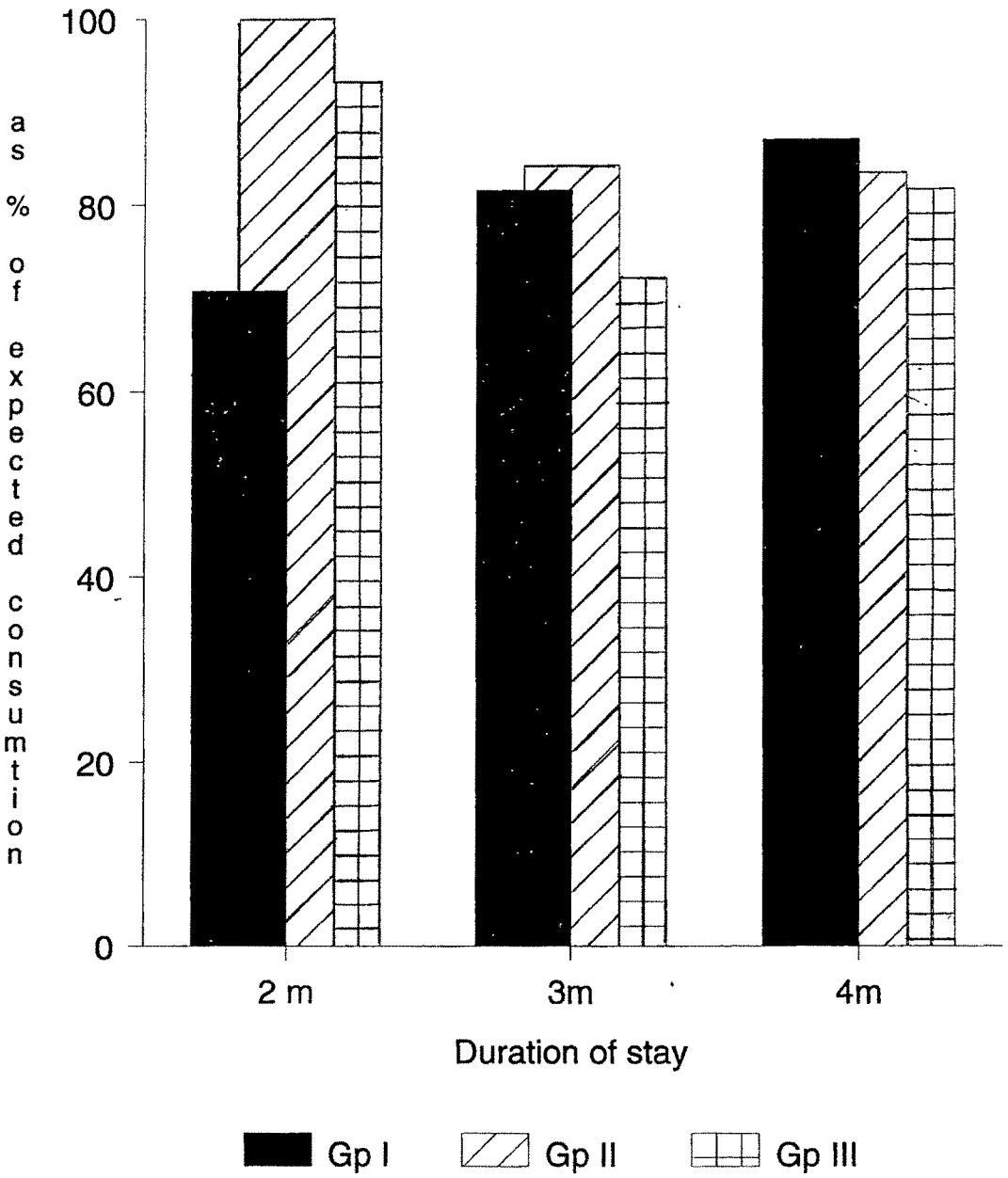


Fig. 4.05 Compliance as percent of expected consumption



levels could be greatly improved by such a distribution system when combined with a monthly follow up and counselling. An important consideration in promoting compliance was a follow up visit within ten days of first delivering the tablets to reassure the mothers and help them to overcome the various problems associated with supplement consumption. This was also found to be important in sustaining their motivation to consume tablets.

The issue of what realistic targets can be set for the anemia control programme in terms of number of doses of iron to be taken is also answered by the present study. Hundred doses of 60 mg elemental iron appears to be the more easily achieveable target but even for this to occur in 90% of the pregnant women, the dose level has to be either 120 mg/day or 180 mg/day. A target of 250 doses of 60 mg iron in about two thirds of the pregnant women population can be achieved only with 180 mg iron/day.

While a majority of the pregnant women in the present study consumed 60 or more tablets/month, there were a few who consumed a much smaller quantity. Those who consumed < 30 tablets/m were considered in this study to be poor compliers. The number and percent of poor compliers is shown in Table 4.08. About 10% of the subjects were poor compliers at the first two contacts of 24 weeks and 28 weeks of

Table 4.08 Reasons for low compliance (< 30 tablets/month) in the three iron treatment groups

Poor Compliers/ Causes	Contacts C_2 (75)	C_3 (113)	C_4 (117)	C_5 (114)
No. of poor compliers	8	12	4	7
Poor compliers as % of total	10.6	10.6	3.4	6.1
Reasons for poor compliance:				
Side effects (%)	62	75	100	57
Other causes (%)	38	25	0	43

Figures in parentheses are number of subjects.

gestation. In the last two contacts the percent poor compliers dropped to 3.4 and 6.1%. The reasons for poor compliance also shown in Table 4.08 indicates that between 24 weeks to 32 weeks of gestation it was indeed the unpleasant side effects that resulted in poor compliance by these women. At the last contact however, 50% of the subjects reported other causes for poor compliance which included miscellaneous ones such as tablets were perceived as unnecessary, forgetting to take the tablets, and objections by their spouse or mother-in-law. In only one case, discontinuation of the supplement was due to the doctor's advice against consuming tablets from other sources.

These data add to the inferences already drawn that with an easily accessible delivery system and periodic counselling, only a small proportion of the subjects remain poor compliers but in this small proportion side effects seem to be a major deterrant to compliance. Additional efforts will be necessary with these subjects in order to increase their level of iron consumption.

There are few studies available in the literature which have investigated compliance systematically in unsupervised field supplementation trials. The national evaluation of the NNAPP in India (ICMR 1989), as mentioned earlier, found that

only 19.4% of the 5779 pregnant women surveyed were offered the supplements. Of those who were offered the supplements only 11.7% consumed 90 or more tablets that was considered effectively complete supplementation. Viewed against this the compliance figures obtained in this present study are very encouraging.

A Sub-Study on Compliance : Efficacy of the Alternate Compliance Measure

Compliance was assessed on monthly basis by two methods; counting the number of tablets remaining in the autoseal pack (compliance = number of pills provided - number left-over) and by counting the number of days for which the calendar was marked. The calendar was tested as an alternative compliance measure as well as a memory device. When visits were made initially, 10 days after commencement of iron supplementation, it was observed that some of the subjects did not display the calendar but instead kept them in an inaccessible place for safe keeping. Therefore in the subsequent visit the women were requested to display the calendar prominently at a place that they could see frequently so that it would act as a reminder.

Percent of women who marked the calendar at each contact for different levels of iron is shown in Table 4.09. In all 53 to 64% of the women made use of the calendar

Table 4.09 Percent of subjects who marked the calendar at each contact

Contact	Groups			Total
	I	II	III	
2nd contact (24 w)	56.5	61.5	42.3	53.3
3rd contact (28 w)	62.5	66.7	51.3	60.17
4th contact (32 w)	82.5	59.0	50.0	64.10
5th contact (36 w)	61.5	60.5	48.6	57.0

during the study period, showing thereby that even with a device such as this, compliance recording can be obtained only from half to two-third of the pregnant women.

Compliance obtained by the markings on the mother retained card (calendar) was compared with compliance as measured by counting the left-over tablets in the autoseal pack. Tablet consumption every month was divided into three categories of ≤ 30, 30-59, 60-90. As can be seen from Table 4.10, there was a great degree of consistency between the two measures. Compliance as percent of women consuming specified number of tablets as mentioned above, was very similar for the two methods, with only slight difference between the two.

Further mean tablet consumption for one month intervals were calculated separately for counting and calendar marking. These data shown in Table 4.11 reveal only small differences in compliance as measured by the two methods. A correlation coefficient was also computed for individual compliance as measured by the two methods (Table 4.12). At all the monthly intervals, as well as for the total study period, a highly significant correlation ($r = 0.7785$) was observed between the two methods showing once again that the calendar marking was a good and reliable alternative that can be used when leftover tablets can not be scrutinized.

Table 4.10 Compliance as number of tablets consumed : Autoseal Pack vs calendar (for only those who marked the calendar)

Range of Tablet Consumption	Percent Women Consuming Specified Range of Tablets					
	Group I		Group II		Group III	
	A	C	A	C	A	C
24 weeks						
87 - 90	61.5	53.8	56.3	50.0	54.5	54.5
60 - 86	30.8	30.8	18.8	6.3	18.2	-
30 - 59	7.7	7.7	25.0	18.8	18.2	27.3
< 30	-	7.7	-	25.0	-	18.2
28 weeks						
87 - 90	72.0	68.0	79.2	79.2	63.2	57.9
60 - 86	20.0	12.0	8.3	8.3	10.5	10.5
30 - 59	8.0	20.0	8.3	4.2	21.1	21.1
< 30	-	-	4.2	8.3	5.3	10.5
32 weeks						
87 - 90	81.8	75.8	78.3	78.3	73.7	73.7
60 - 86	12.1	9.1	17.4	8.7	21.1	15.8
30 - 59	3.0	6.1	-	8.7	5.3	10.5
< 30	3.0	9.1	4.3	4.3	-	-
36 weeks						
87 - 90	62.5	62.5	73.9	65.2	77.8	61.1
60 - 86	33.3	29.2	13.0	-	22.2	16.7
30 - 59	4.2	-	13.0	34.8	-	22.2
< 30	-	8.3	-	-	-	-

A - Autoseal pack
C - Calendar

Table 4.11 Compliance as mean tablet consumption : Autoseal pack vs Calendar
(for only those who marked the calendar)

Contact	Compliance : Mean Tablets Consumed ± SE Groups I		II		III	
	A	C	A	C	A	C
24 W	81.4 ± 4.2 (13)	74.5 ± 6.8	75.3 ± 4.7 (16)	60.8 ± 8.1	71.1 ± 8.6 (11)	62.5 ±10.4
28 W	82.8 ± 2.9 (25)	77.2 ± 4.6	82.0 ± 3.9 (24)	80.0 ± 5.1	84.8 ± 5.3 (19)	69.9 ± 6.3
32 W	84.6 ± 2.5 (33)	76.5 ± 4.7	84.2 ± 3.2 (23)	81.3 ± 4.3	83.8 ± 3.4 (10)	86.4 ± 1.8
36 W	82.0 ± 2.5 (24)	77.4 ± 4.9	83.3 ± 2.8 (23)	74.4 ± 4.6	82.1 ± 4.0 (18)	74.7 ± 5.8

A - Counting the remaining in autoseal pack
C - Calendar marking
Number of subjects in parenthesis.

Table 4.12 Correlation between compliance measured by counting leftover tablets vs calendar marking

Contact	Correlation Coefficient
Contact 2 (24 W)	0.7282**
Contact 3 (28 W)	0.8970**
Contact 4 (32 W)	0.7977**
Contact 5 (36 W)	0.6310**
Total	0.7785**

** Significant at $p < .001$

Reasons for non use of the calendar are shown in Table 4.13. More than a third of the women reported that they just simply forgot to make a mark in the calendar. Other reasons included a crowded work schedule, not enough time to mark, not necessary to mark, out of town, mishandling by the children, or damage to the calendar for various reasons.

Observations indicated that women who marked the calendar regularly were those who hung the calendar in a prominent place, usually near the drinking water pot, which facilitated them to remember to mark the calendar and to remind them to consume the tablet.

One other study available in the literature from Thailand has also shown that a monthly calendar to record daily intake of iron served as a powerful motivational tool to increase iron tablet consumption (Charoenlarp et al 1988). These authors also reported that illustrations showing iron makes pregnant women and their babies stronger on the calendar served as an important educational message.

To sum up, a mother retained was found to provide an estimate of compliance in 50-65% of the women and this estimate was as good as the one obtained by counting the leftover tablets. A mother retained card to identify pregnant women at risk has been shown to work satisfactorily under the Indian condition (Shah 1982). Such a mother

Table 4.13 Reasons for non-use of the calendar at each contact

Reason for not marking the calendar	Contact							
	24 W		28 W		32 W		36 W	
	N	%	N	%	N	%	N	%
Forgot	15	43	15	33	15	36	17	35
Kept safely inside a box and so not available	1	3	4	9	3	7	5	10
Too much work	4	11	8	18	5	12	12	24
Not necessary to mark	7	20	5	11	11	26	3	6
Went to mother's house	1	3	4	10	1	2	4	8
Children tore it up	7	20	5	11	6	14	7	14
Damaged by rain/rodents/ goats	-	-	2	4	1	3	-	-
Lost/ misplaced	-	-	2	4	-	-	1	3
Total	35	100	45	100	42	100	49	100

retained card can also include the provision for recording compliance with iron supplements.

Side Effects

Side effects profile of the supplemented subjects was obtained once every month from 24 weeks to 36 weeks of gestation. Fig 4.06 indicates the percent of women reporting side effects at each contact with different levels of iron treatment. Initially 42% of the women in Group III (180 mg iron) reported one or more side effects compared to only 13% in Group I and 19% in Group II. Thus the higher dose level of iron, 180 mg/day, in the first month of supplementation produced unpleasant side effects in a much higher proportion of the subjects than the 120 mg and 60 mg dose level. However an interesting finding was that the difference narrowed as gestation advanced, and only 10.5% of the women in Group III reported of side effects at 32 weeks of gestation as against 17.5% in Group I and 15.4% in Group II for the same gestational period.

Nature of side effects experienced by the women at each contact are depicted in Table 4.14. The most frequently reported side effects were nausea, vomiting, heartburn and constipation. Other less frequently reported ones were black stools, diarrhoea, abdominal pain, dizziness, skin

Fig. 4.06 Percent subjects reporting side effects in the three iron treatment groups

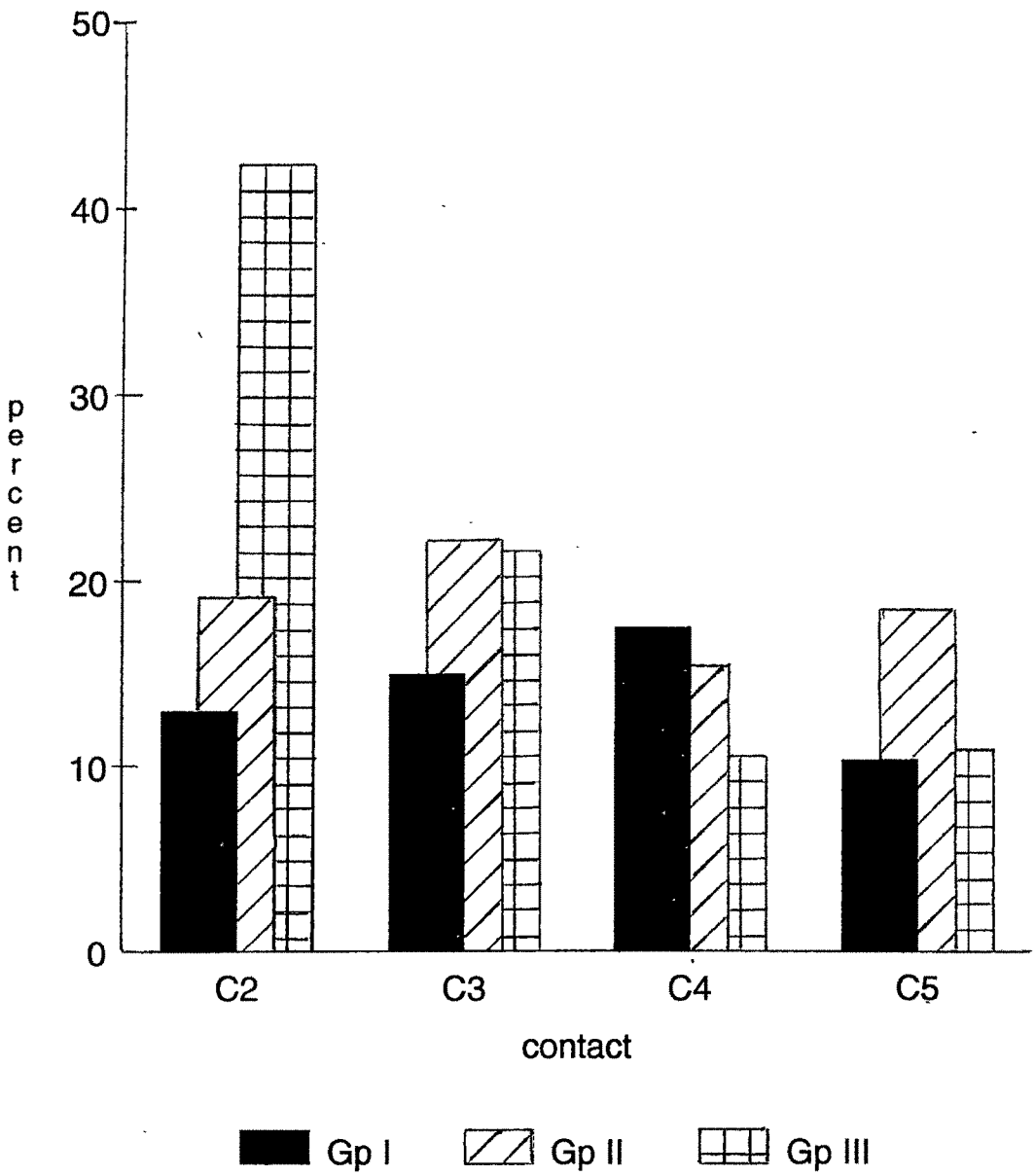


Table 4.14 Nature of side effects reported by the subjects in the three iron treatment groups at different gestational periods

Side Effects	24 W (C_2)			28 W (C_3)			32 W (C_4)			36 W (C_5)		
	I (23)	II (28)	III (28)	I (40)	II (36)	III (37)	I (40)	II (39)	III (38)	I (39)	II (38)	III (37)
Loss of appetite	-	-	-	-	-	-	2.5	-	-	-	-	2.7
Nausea	8.7	7.1	7.1	2.5	5.6	8.1	7.5	2.6	5.3	5.1	-	2.7
Heartburn	4.3	7.1	17.9	7.5	11.1	13.5	7.5	5.1	-	5.1	-	5.4
Vomiting	4.3	3.6	7.1	2.5	2.8	2.7	-	2.6	-	5.1	2.6	-
Constipation	-	-	-	-	5.6	5.4	2.5	2.6	2.6	5.1	10.5	-
Black stools	-	10.7	-	-	-	2.7	-	-	2.6	-	10.5	2.7
Diarrhoea	-	-	-	-	-	-	5.0	-	-	-	-	2.7
Abdominal pain	-	-	7.1	-	-	-	-	-	-	-	-	-
Dizziness	-	-	3.6	-	5.6	2.7	-	-	5.3	2.6	-	-
Skin irritation	-	-	3.6	-	-	-	-	-	-	-	-	-
Cramps	-	-	-	2.5	-	-	-	-	2.6	-	-	-
Feel hot	-	3.6	-	-	-	-	2.5	-	2.6	-	-	2.7

C - Contacts.
Individual side effects do not add up to total as they are mutually exclusive.

irritation and cramps. Only four women reported that the tablets produced heat.

Comparison of mean tablet consumption of the women who reported side effects and those who did not report any side effects is shown in Table 4.15. Mean tablet consumption was found to be lower in women reporting side effects than those who did not report side effects in all the treatment groups, although the difference was statistically significant only for Group I which is surprising in view of the fact that dose level of iron was the lowest in this group. Table 4.15 also shows that Hb rise did not follow a consistent pattern for those reporting side effects vs not reporting in the three iron treatment groups.

Higher incidence of side effects have been reported with increasing levels of iron supplementation by several investigators in controlled trials (Sood et al 1975, Kuizon et al 1983, Charoenlarp et al 1988, Reddiah et al 1989 and ICMR 1992). These were mostly gastro intestinal symptoms of nausea, vomiting, constipation, diarrhoea, and epigastric discomfort. In the ICMR multicentric study (ICMR 1992), with similar dose levels of iron as in the present study, incidence of side effects was 14% in the 60 and 120 mg iron treatment group, compared to 21.3% in the 180 mg group. While these studies reported side effects only once at the

Table 4.15 Mean tablet consumption and mean Hb of the subjects who reported/did not report any side effect during supplementation

Mean ± SE	Group I		Group II		Group III	
	RSE (12)	NSE (29)	RSE (18)	NSE (22)	RSE (19)	NSE (20)
Tablet consumption	217.3 ±20.98	282.4 ±13.73	244.9 ±16.87	274.6 ±12.68	247.0 ±18.64	252.1 ±18.60
t'	2.596*		1.421NS		0.194NS	
Initial haemoglobin	9.3 ± 0.40	10.0 ± 0.26	9.9 ± 0.33	9.1 ± 0.24	8.6 ± 0.34	9.3 ± 0.33
Final haemoglobin	10.4 ± 0.24	11.3 ± 0.21	11.7 ± 0.26	11.4 ± 0.13	11.4 ± 0.21	11.3 ± 0.27
Rise in haemoglobin	1.1	1.3	1.8	2.3	2.8	2.0

RSE - Reported side effects
NSE - Not reported side effects
* Significant at $p<0.05$
NS Not significant

end of supplementation, the present study obtained the side effects profile four times during pregnancy at an interval of one month. The important finding is that at higher dose level of iron percent of women with unpleasant side effects tends to decline as supplementation is continued. That such a decline in subjects manifesting side effects may not be due to a reduction in the amount of iron absorbed is indicated by the lack of a consistently higher Hb levels in the subjects not experiencing side effects.

Simmons (1990) who tested a gastric delivery system for iron found that the incidence of side effects was similar in the placebo and iron treatment groups and there was a general tendency for side effects to diminish with time in all the groups, which is consistent with the observation in the present study.

In order to test the association between the level of iron consumed and the number of unpleasant side effects a Pearson's product moment correlation was computed between the two for each contact. At all contacts the total number of side effects were negatively correlated with the level of iron consumed and this negative correlation was significant for the 24-28 weeks of gestation. These findings need not be interpreted to be at variance with the earlier observation that percent women with any one side effect was higher at

the higher dose level. The two findings apparently relate to two different dimensions of the problem. One is the occurrance of any one side effect in a subject with increasing levels of iron. The other is the number of such side effects with increasing levels of iron. It appears that not all side effects reported by the women increase with increasing level of iron consumed rather they seem to have a tendency to decrease which explains the negative correlation found between the total number of side effects and the level of iron consumed.

Contacts	Correlation coefficient
24 w	-0.1946^{NS}
28 w	-0.2564^{*}
32 w	-0.2065^{NS}
36 w	-0.1381^{NS}

$^{*}p<0.01$ ^{NS} Not Significant

Irregularity in adherance to the treatment regimen has been reported in other iron supplementation trials (Bonnar et al 1969, Senewiratne et al 1974, Alward and Kevany 1984, Shultink et al 1993) as a cause of lack of impact. Many iron supplementation trials have attributed the reasons for non compliance to the manifestation of undesirable side effects, in iron supplementation trials (Kuizon et al 1983,

Charoenlarp et al 1988, DeMaeyer 1989, Reddiah et al 1989, WHO 1990). However the findings of the present study demonstrate that only 10% of the subjects were poor compliers due to side effects, while others who reported side effects continued to ingest the supplements in appropriate dose levels with adequate counselling. That the mean tablet consumption of those who reported side effects was not significantly different in the 120 mg and 180 mg groups also indicates that side effects were not a deterrant to compliance.

Beneficial Effects

Figure 4.07 represents the percent women who reported one or more beneficial effects of iron treatment at different dose levels and at different contacts and Table 4.16 describes the nature of beneficial effects. Two major observations emerge from Fig 4.07. The first is that 60-95% of the subjects reported various beneficial effects of iron therapy. The second is that percent women reporting beneficial effects was seen to rise with increasing duration of therapy only in the 180 mg iron group.

As seen in Table 4.16, general good feeling, feeling energetic, less tiredness, and improved appetite were most frequently reported by the women in all the treatment

Fig. 4.07 Percent subjects reporting beneficial effects in the three iron treatment groups

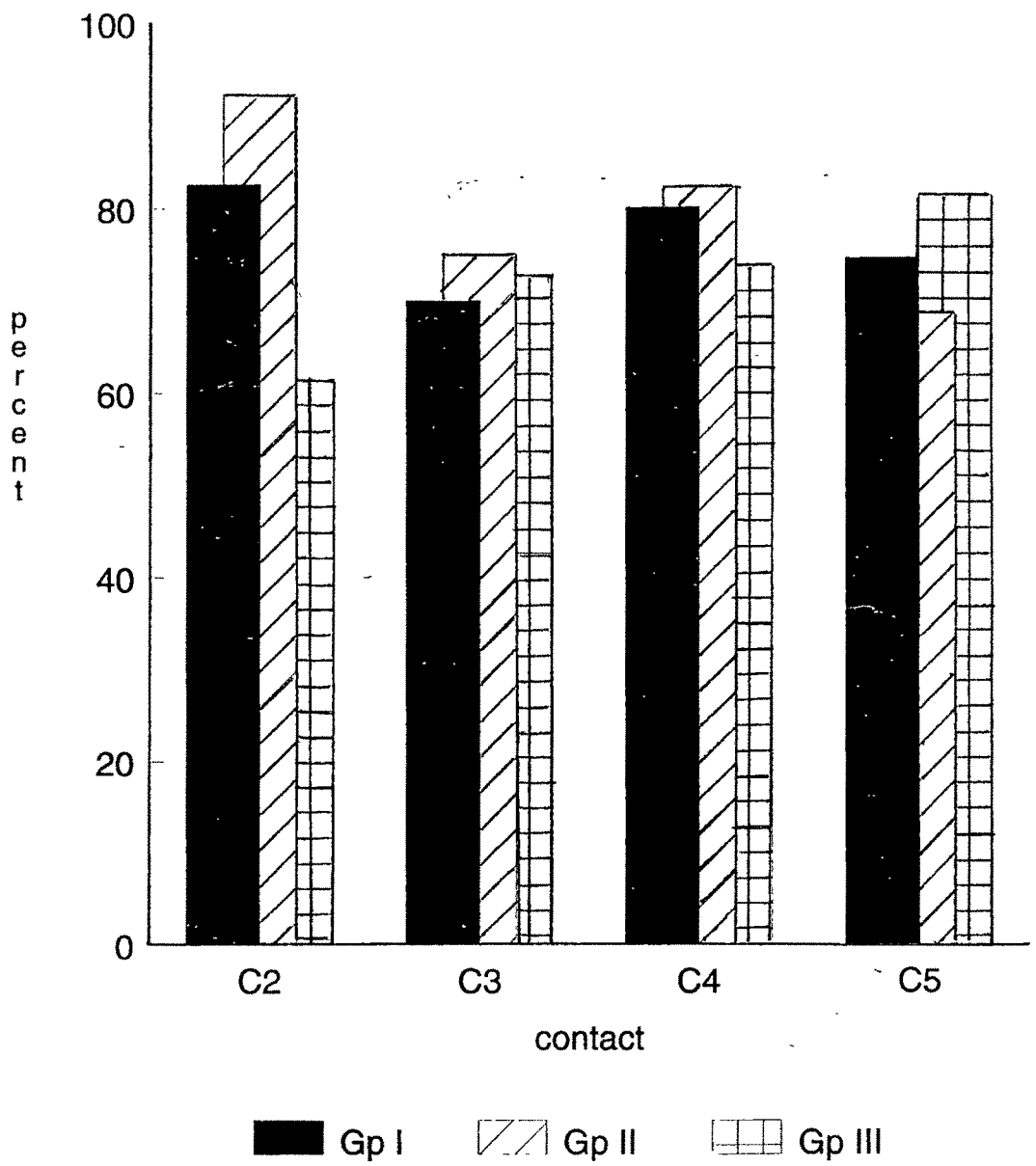


Table 4.16 Nature of beneficial effects reported by the subjects in the three iron treatment groups

Beneficial Effects	24 W (C_2)			28 W (C_3)			32 W (C_4)			36 W (C_5)		
	I (23)	II (28)	III (28)	I (40)	II (36)	III (37)	I (40)	II (39)	III (38)	I (39)	II (38)	III (37)
General good feeling	73.9	89.3	50.0	62.5	75.0	64.9	57.5	79.5	71.1	66.7	68.4	70.3
Feeling energetic	30.4	50.0	25.0	37.5	61.1	56.8	42.5	61.5	55.3	53.8	60.5	62.2
Feel less tired	52.2	53.6	32.1	45.0	52.8	51.4	55.0	66.7	68.4	59.0	63.2	73.0
Improved appetite	26.1	17.9	21.4	17.5	38.9	18.9	25.0	59.0	42.1	25.6	47.4	54.1
Decreased breathlessness	4.3	3.6	3.6	2.5	5.6	-	2.5	2.6	-	-	10.5	10.8
Decreased back-pain	4.3	17.9	17.9	5.0	8.3	18.9	7.5	12.8	31.6	10.3	26.3	40.5
Decreased leg-pain	8.7	14.3	17.9	7.5	19.4	29.7	2.5	28.2	18.4	10.3	21.1	29.7
Improved work capacity	13.0	21.4	3.6	5.0	25.0	16.2	7.5	35.9	28.9	12.8	31.6	40.5
No giddiness	8.7	7.1	-	2.5	5.6	10.8	-	2.6	5.3	5.1	2.6	2.7
No body pain	13.0	3.6	-	5.0	-	-	-	-	-	2.6	-	-
No illness	4.3	-	-	-	-	-	-	-	2.6	2.6	-	2.7
Can sleep better	-	-	3.6	-	-	-	-	-	-	5.1	2.6	-

groups. Comparatively fewer women reported decreased breathlessness and decreased backpain. Lack of symptoms of giddiness, body pain, illness and the ability to sleep better were reported by some of the women.

At each contact, the reported frequency of each beneficial effect between the three groups was subjected to a chi-square analysis results of which are shown in Table 4.17. After four weeks of supplementation a significantly higher percentage of women in Groups I and II reported an improved sense of well being compared to Group III. Improved appetite, decreased back-pain, leg-pain, and improved work capacity were significantly higher in Groups II and III compared to Group I at contacts 3, 4, and 5 i.e. 28th, 32nd and 36th week of gestation, indicating that higher levels of iron were associated with greater recovery from many of the symptoms of anemia.

Statistical comparisons were also made for the frequency of beneficial effects with increasing duration of supplementation at each level of iron intake. Significant differences in some symptoms, chiefly improved appetite, decreased breathlessness, and improved work capacity, were seen with longer duration of supplements only in Group III i.e. 180 mg iron group (Table 4.17).

Table 4.17 Results of chi-square analysis for the frequency of beneficial effects reported in the three iron treatment groups at different contacts

Beneficial Effect	Gestational age 20-24	24-28	28-32	32-36
Level of iron				
General good feeling	7.78687*	1.48725	4.56916	.11411
Improved appetite	0.33110	5.66405*	0.0093	0.93572**
Less back-pain	2.82226	4.21407	8.72636**	9.20382**
Decreased pain in limbs	1.09865	6.30338*	9.78938**	4.49791
Improved work capacity	4.16291	5.98900*	9.52515**	7.57336*
Duration	60	120	180	
Feeling energetic	3.83614	0.46573	8.57973*	
Feel less tired	1.65444	1.71573	11.63528**	
Improved appetite	1.03878	10.58628**	12.48075**	
Decreased breathlessness	1.45539	2.50426	8.29730*	
Improved work capacity	2.01026	1.71285	13.11053**	

* Significant at p<.05 ** Significant at p<.01

Besides these effects, at each contact a record was made of any other beneficial effects that women attributed to the supplementation. Some of them said they found marked differences in their ability to perform certain work tasks, such as manual washing of clothes, fetching water from the hand pump, washing dishes, mopping and taking care of young children. Prior to supplementation the women said they either avoided these tasks or took help from other family members or performed them with consequences such as increased muscular pain and back-ache. While some of these effects may be liable to a certain bias because it was self reporting, there is no objective way of obtaining information on subjective well being like reduced aches and pains. In spite of these limitations, the present study has demonstrated that several beneficial effects are experienced by women which by their own admission motivated them to consume the tablets regularly.

In order to test the association between dose levels of iron and number of beneficial effects for each contact a Pearson's-product moment correlation was computed. A score of one was given for each beneficial effect reported by each subject during one month interval. These associations are shown on the next page.

Contacts	Correlation coefficient
24 w	0.2718*
28 w	0.4586**
32 w	0.4017**
36 w	0.4501**

* Significant at $p<0.01$
** Significant at $p<0.001$

A strong and highly significant positive correlation was noted between dose levels of iron and beneficial effects, this effect being more pronounced at 2, 3 and 4 months of supplementation than at one month.

The highlight of this section is that a very sizable percentage of the subjects attributed beneficial effects in terms of improved health and well being to the iron supplements and therefore these should be emphasized during counselling for iron supplementation programmes.

Section III

Effect of Three Different Dose Levels of Iron Supplementation During Pregnancy on Maternal Outcome

Since this was an unsupervised iron supplementation trial, it was not possible to ensure that all subjects in each group consumed the same amount of total iron. There was some overlap in iron intake between the three groups. Therefore, for studying the impact, two sets of analyses were performed. One set of analyses comprised of comparisons between the three groups and the other comprised of comparisons between sub-groups within each group with the following stipulated levels of iron intake: equivalent to

Group I -- 3600-7200 mg iron (60-120 tablets of 60 mg Fe)

Group II -- 7240-14400 mg iron(120-240 tablets of 60 mg Fe)

Group III-- 14460-21600 mg iron(240-360 tablets of 60 mg Fe)

In the following sections, two notations are utilized : overlapping (OL) for the groups comprising all subjects and non-overlapping (NOL) for the sub-groups comprising those with the above stipulated levels of iron intake. The mean tablet consumption and the mean iron and folic acid intakes for the three different OL and NOL groups is shown in Table 4.18. As seen, the only difference was in the iron intake,

Table 4.18 Mean tablet consumption, mean iron intake and mean folic acid intake in the three iron treatment groups (OL and NOL)

Mean	Group		
	I	II	III
OL			
Mean tablet consumption	263 (41)	261 (40)	249 (39)
Mean iron intake (mg)	5934	10452	14976
Mean folic acid intake (mg)	131.6	130.6	124.8
NOL			
Mean tablet consumption	275 (38)	273 (36)	302 (24)
Mean iron intake (mg)	6166	10919	18125
Mean folic acid intake (mg)	137.8	136.5	151.0

folic acid consumption remaining similar for the three groups.

Prevalence of Anemia

The frequency distribution of the Hb levels of the pregnant women before and after supplementation is illustrated in Fig 4.08. Initially only 3.3% of the women had Hb levels $\geq$12 g/dl, which rose to 25.8% after supplementation. The incidence of severe anemia initially was highest in Group III (12.8%) compared to Group I and Group II (2.4-2.5%). None of the women were severely anemic after the supplementation (Table 4.19 and Fig 4.08). At the end of the iron treatment the lowest Hb observed in the series was 8.6 g/dl and highest was 13.7 g/dl. The shift to the right of the frequency distribution after supplementation is evident as shown in Fig 4.08, bringing out clearly the benefit of iron consumption.

Table 4.19 gives the classification of women by their Hb levels into normal (Hb $\geq$ 11 g/dl), mildly anemic (10-10.9 g/dl), moderately anemic (Hb 7-9 g/dl) and severely anemic (Hb $<$ 7 g/dl) categories for the OL group. Prevalence of anemia before initiating supplementation was 88% in Group I, 90% in Group II and 97% in Group III. At the end of the supplementation period the prevalence of anemia dropped

Fig. 4.08 Frequency distribution of Hb initial and final

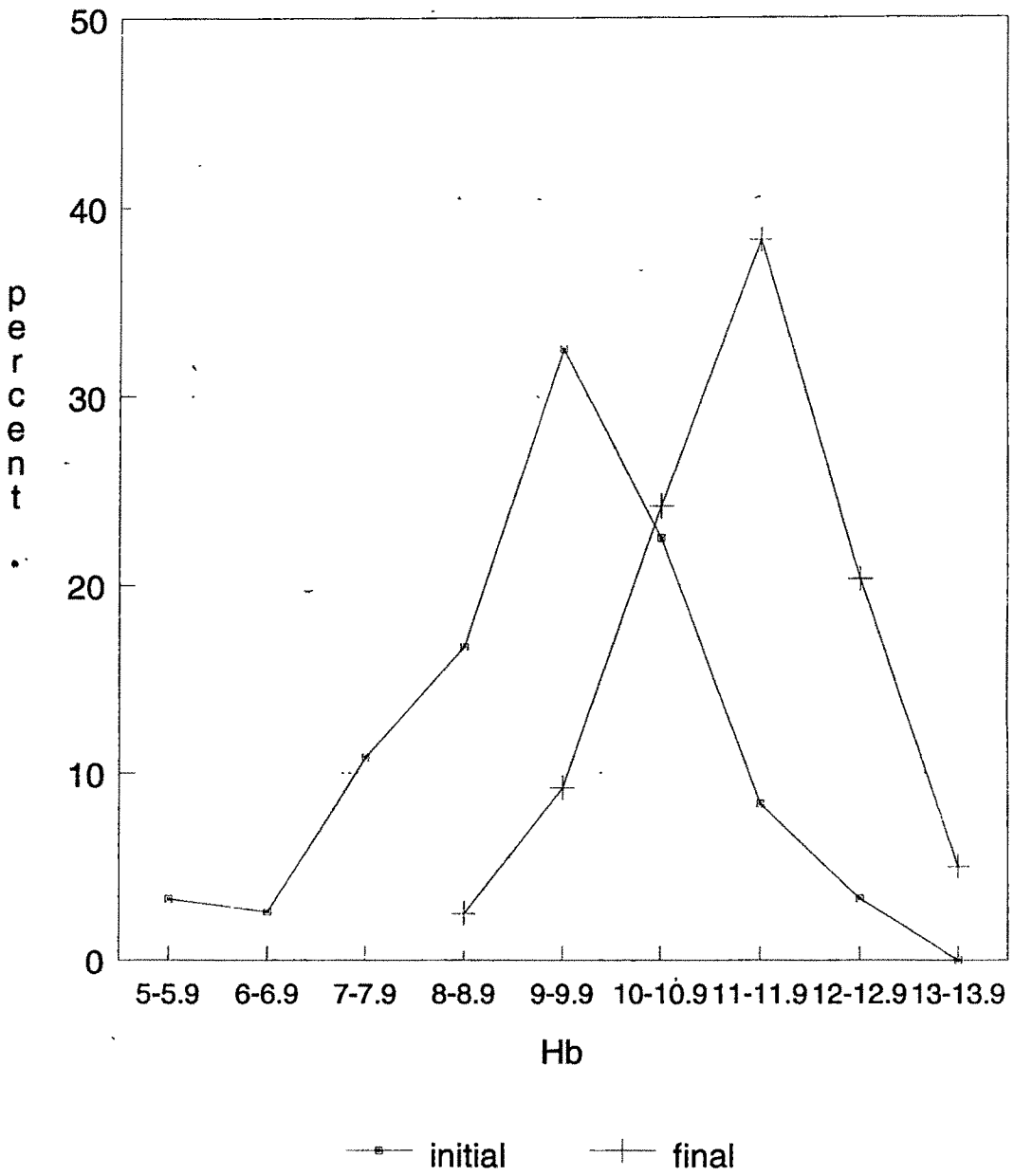


Table 4.19 Percent prevalence of anemia before and after iron therapy in the three iron treatment groups (OL)

Categories based on Hb levels	Groups					
	I (41)		II (40)		III (39)	
	I	F	I	F	I	F
Normal (≥11.0 g/dl)	22.0	46.3	10.0	77.5	2.6	69.2
Mild (10 - 10.9 g/dl)	19.5	36.6	17.5	20.0	30.8	15.4
Moderate (7 - 9.9 g/dl)	56.1	17.1	70.0	2.5	53.8	15.4
Severe (< 7 g/dl)	2.4	-	2.5	-	12.8	-

I - Initial
F - Final

Chi-square 29.41*
* (for final Hb into three categories normal, mild and moderate)
Significant at $p<0.05$

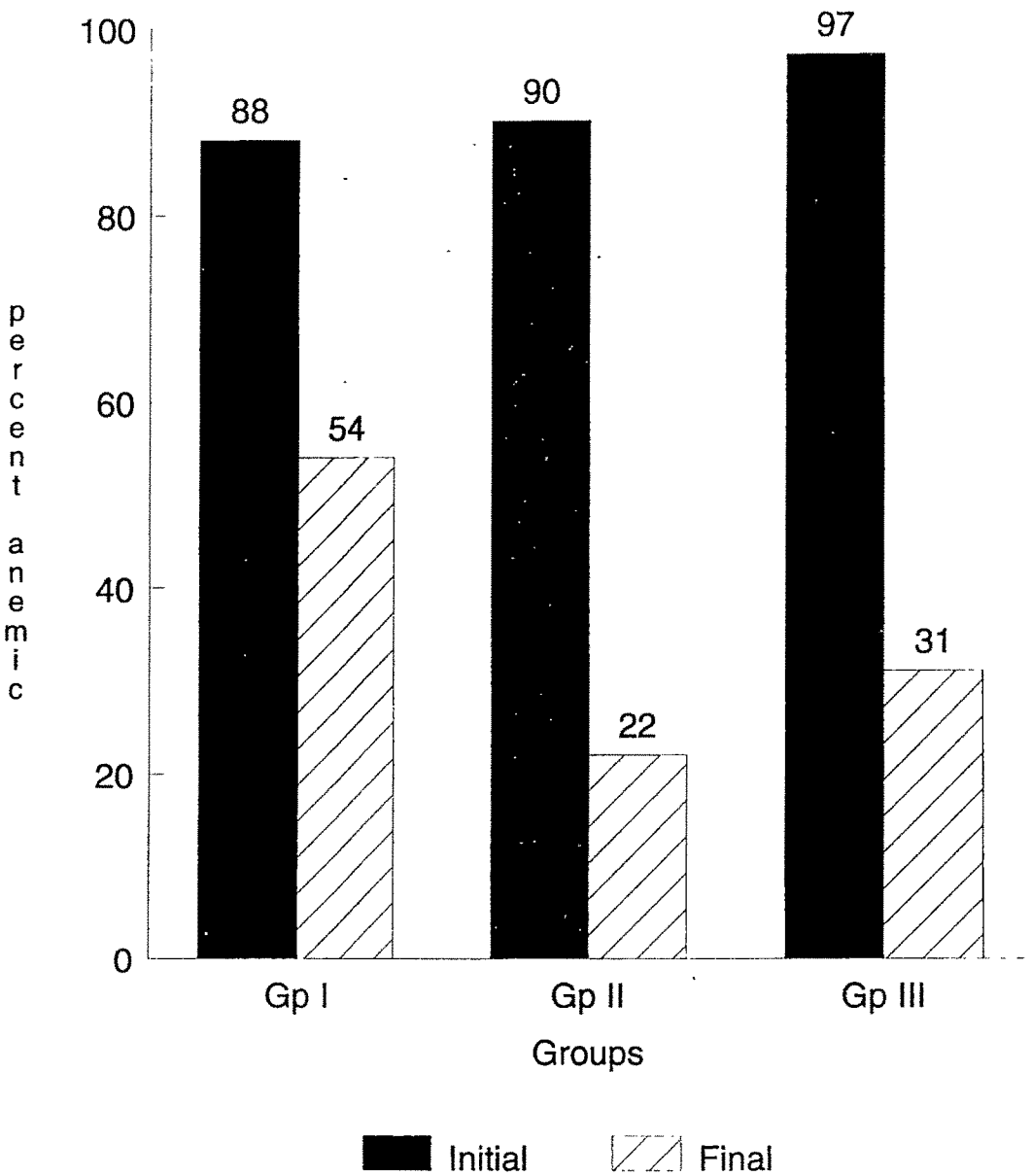
remarkably in Groups II and III (31%) and to a lesser extent in Group I (54%) (Fig 4.09). The magnitude of decrease was 68% in Group II and 67% in Group III compared to only 37% in Group I.

From these results it is seen that a dose level of 120 mg or 180 mg/day was much more effective in reducing the prevalence of anemia compared to 60 mg/day, but no difference was seen between the two higher dose levels, i.e. 120 or 180 mg. Reducing the prevalence of anemia in pregnant women to one third its current level is one of the several goals that has been set by National Nutrition Policy of India (Ministry of Health and Family Welfare, 1991). This was achieved only by the 120 and 180 mg dose level and not by the 60 mg dose level as indicated by the results of the present study. Thus the level of iron (60 mg/day) recommended in the NNAPP appears inadequate and it needs to be raised.

Hemoglobin Levels

The initial mean Hb levels tested by one way ANOVA showed only Group III had significantly lower Hb levels compared to Group I. At the end of the treatment however, the mean Hb levels in the three groups did not differ significantly (Table 4.20). The final mean Hb levels ranged

Fig. 4.09 Prevalence of anemia (Hb < 11g/dl) before and after supplementation in the three iron treatment groups



Chi square 11.856* $p < 0.05$

Table 4.20 Rise in Hb of the subjects in the three iron treatment groups (OL) (mean ± SE)

Hb (g/dl)	Group I (41)	II (40)	III (39)	F Value
Initial	9.8±0.22	9.5±0.21	9.0±0.24	3.1221*
Final	11.1±0.18	11.5±0.14	11.3±0.17	2.249NS
Paired t'	8.99***	11.83***	9.93***	
Rise	1.3 ±0.14	2.0 ±0.17	2.3±0.23	
Rise in Hb/m	0.38±0.04	0.63±0.06	0.67±0.07	

t' value

Initial Hb	Rise in Hb	Rise in Hb/m
I vs II = 0.986NS	I vs II = 3.11*	I vs II = 3.56**
I vs III = 2.46*	I vs III = 3.636*	I vs III = 3.65**
II vs III = 1.56NS	II vs III = 1.02NS	II vs III = 0.51NS

* Significant at p<.05,

** Significant at p<.001,

*** Significant at p<.0001

from 11.1 to 11.5 in the three groups. These findings appeared to indicate that the level of iron did not make a difference as far as final Hb levels were concerned.

However, it is known that final Hb levels depend on the initial Hb and initial Hb levels were significantly different between Group I and Group III. Therefore an analysis of covariance was carried out to remove the effect of initial Hb (Table 4.21). Adjusted final mean Hb levels, after correcting for the effects of initial Hb, were 10.84 g/dl in Group I, 11.53 g/dl in Group II and 11.45 g/dl in Group III, which showed that 120 and 180 mg dose levels produced a significantly higher Hb level at the end of supplementation compared to 60 mg dose level. Once again, no significant difference was noted between the 120 mg and 180 mg groups.

Initial and final Hb levels of the NOL alongwith the rise in Hb for the three groups are shown in Table 4.22. Mean rise in Hb for the OL groups was 1.3 g/dl in Group I, 2.01 g/dl in Group II and 2.30 g/dl in Group III. When rise in Hb was computed for NOL groups, it was very similar to the OL groups (1.3 g/dl in Group I, 2.1 g/dl in Group II and 2.5 g/dl in Group III). The rise in Hb was highly significant ($p<0.0001$) in all the treatment groups as tested by paired t' as well as between three groups with Group II

Table 4.21 Regression coefficients and adjusted means of final Hb in the three iron treatment groups (OL)

Groups	n	Regression coefficient	F ratio	Adjusted Means	F ratio
I	41	0.61		10.836	
II	40	0.36	3.105*	11.534	5.06**
III	39	0.27		11.453	

* p<0.05
** p<0.005

Table 4.22 Rise in Hb of the subjects in the three iron treatment groups : (NOL) (mean ± SE)

Hb (g/dl)	Groups I (38)	Groups II (36)	Groups III (24)	F
Initial	9.7±0.23	9.4±0.23	8.9±0.30	2.1554 NS
Final	11.1±0.18	11.5±0.15	11.5±0.20	2.100 NS
Rise	1.3+0.14	2.1 ±0.19	2.54±0.29	-
Paired t'	9.81***	11.19***	8.7***	

	Rise in Hb	
t' values	I vs II	3.389**
	I vs III	3.850**
	II vs III	1.269 NS

NS - Not significant
*** Significant at p<.0001

and III showing significantly larger rise than Group I, in OL. The difference between Group II and III were, however, not statistically significant.

A rise in Hb of more than 2 g/dl to iron therapy has been suggested as an adequate response in pregnant women (WHO 1993). Forty percent of the women in Group II and 49% in Group III had a rise of 2 g/dl or more compared to only 14.6% in Group I (Fig 4.10). When a cut off of 1 g/dl was used 54% of the women in Group I and 90% of the women in Group II and III (Fig 4.10) had an adequate response indicating that the 60 mg dose level was insufficient.

Three subjects in the series (2.5%) did not respond to iron therapy. Two of these subjects registered a decline of 0.1 g/dl in Hb while the third showed a decline of 0.9 g/dl. The first two subjects were in Group I while the third was in Group III. The initial Hb of all these subjects were higher than 8 g/dl. The final Hb was 10.0, 9.1 and 8.8 g/dl. The reason for non-response in the first two subjects must have been unrelated to iron consumption as they were good compliers. The third subject who showed a decline of 0.9 g/dl was a poor complier and did not consume the tablets regularly. Thus percent non responders was 1.5.

The mean monthly rise at various gestational ages are represented in Fig 4.11. Between 24-28 weeks the monthly

Fig. 4.10 Percent subjects with ≥1g/dl and ≥2g/dl rise in Hb

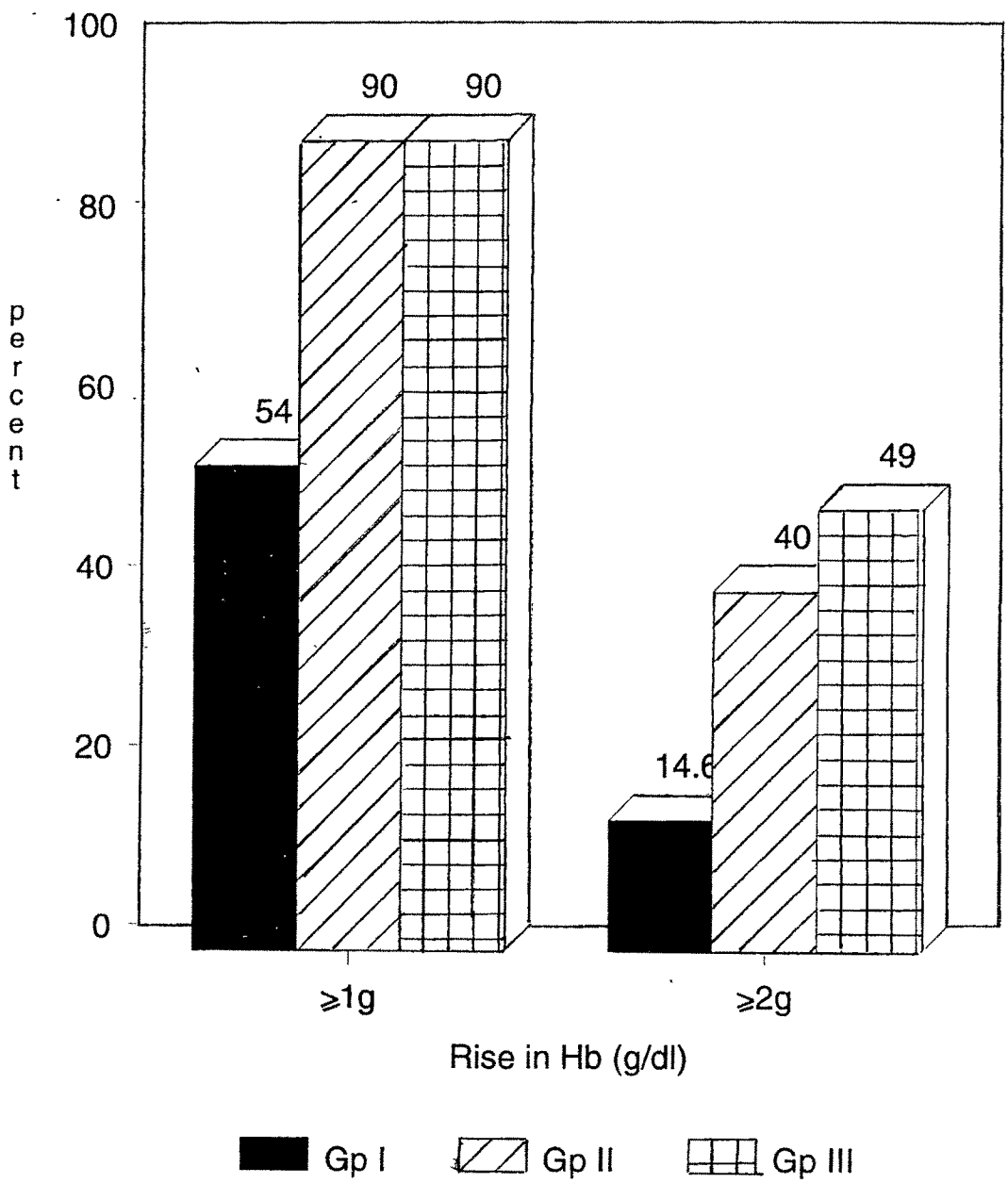
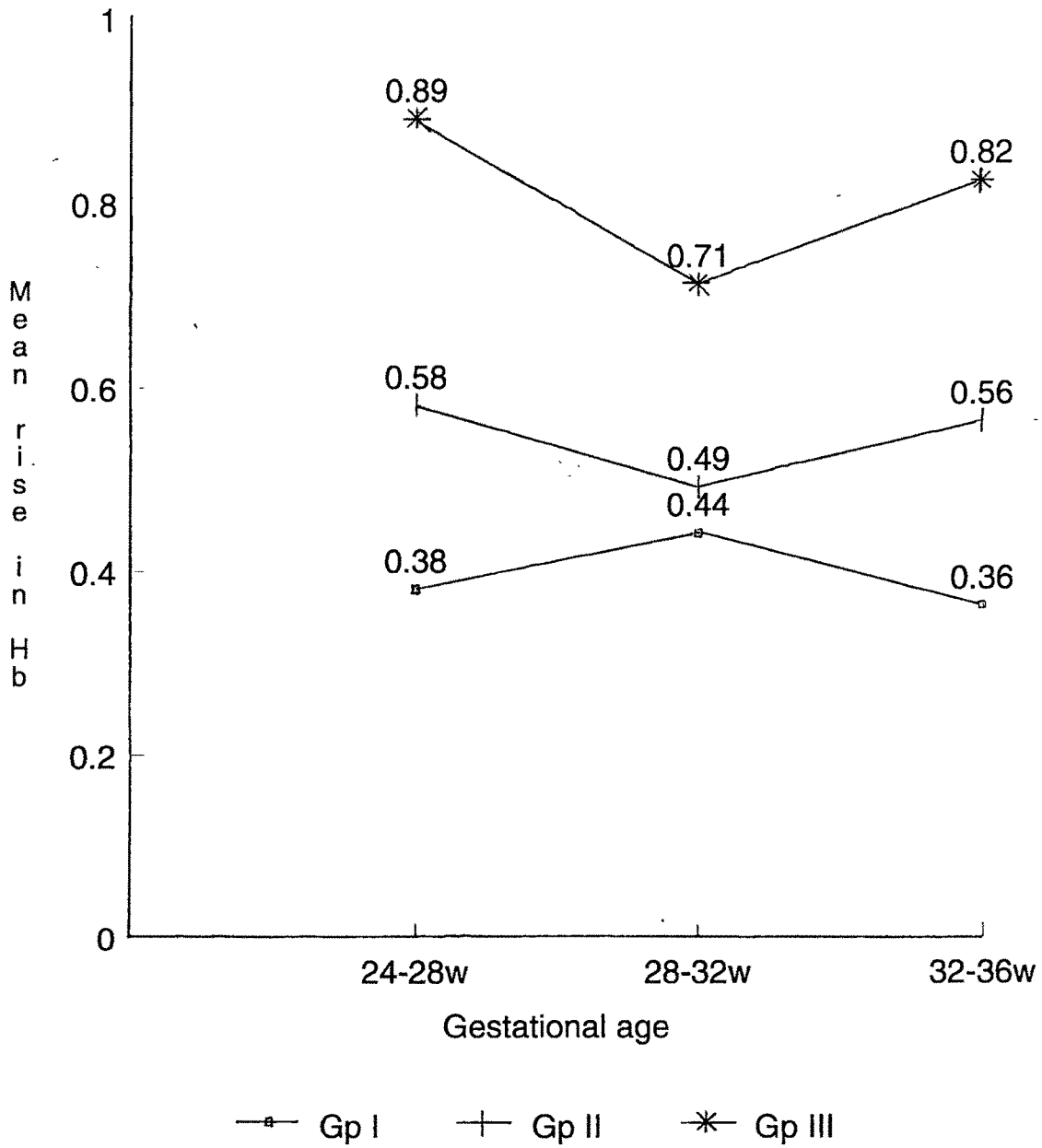


Fig. 4.11 Mean monthly rise in Hb in the three iron treatment groups



rise in Hb was highest in Group III (0.89 g/dl) compared to Group I (0.38 g/dl) and Group II (0.53 g/dl). Between 28-32 weeks of gestation, rise in mean Hb showed a slight decline in Group II and III but not in Group I. Such a decline is expected in view of the increase in plasma volume that has been reported to occur between 20-28 weeks (Rajalakshmi and Raman 1985). During the last month of supplementation (32-36 weeks), there was a drop in the rise in Hb for Group I but Group II and III showed an increase. Rise in Hb was clearly related to the dose level of iron, being highest at all points of time for Group III followed by Group II and was lowest for Group I.

Longer duration of supplementation was seen to contribute to a higher rise in Hb (Table 4.23) but to a very small degree. When the women stayed in the program for 2-3 months the mean rise was 1.16, 2.07 and 2.19 g/dl in Groups I, II and III, compared to 1.4 g/dl, 2.13 g/dl, and 2.52 g/dl in Groups I, II and III when they stayed for a period of four months. As seen from Table 4.23, a substantial proportion of the total rise, 75-86% had already occurred with in 2-3 months in Groups I and III. Further supplementation for another month at the same dose level was responsible for 14-25% of the total rise in Group I and III whereas practically all the total rise in Hb had occurred within 2-3 months in Group II.

Table 4.23 Rise in Hb in relation to duration of supplementation in the three iron treatment groups (mean ± SE).

Duration	Group I	Group II	Group III
OL			
2-3 months	1.16 (20)	2.07 (23)	2.19 (20)
4 months	1.40 (21)	2.13 (17)	2.52 (19)
2-3 months value as % of total rise	84.2	97.1	86.9
NOL			
2-3 months	1.28 (18)	2.17 (19)	2.12 (10)
4 months	1.47 (20)	2.13 (17)	2.85 (14)
2-3 months value as % of total rise	85.7	101.8	74.3

There was a trend towards increased rise in Hb with increasing levels of tablet consumption. Highest rise in mean Hb was recorded when the level of tablets consumed was 250 or more in all the three treatment groups (Table 4.24). This fell progressively with decreasing levels of tablet consumption. Correlation between level of iron intake and rise in Hb was found to be significant ($r = 0.3289^{*}$ $p<0.05$).

In summary given the duration of 3-4 months for which pregnant women were available for supplementation, the 60 mg dose level of iron was consistently inferior to the 120 mg and 180 mg dose levels. Further the 180 mg dose level was only marginally better compared to the 120 mg dose level. These results provide some clear direction to anemia control in pregnant women. With the home delivery of iron, given as three tablets each containing 40 mg elemental iron and 0.5 mg folic acid, there exists a fair chance that prevalence can be reduced to levels that have been set in the National Nutrition Policy. Significantly, the 120 mg dose level given in three divided doses produced much lower side effects in the initial period compared to the 180 mg given as three divided doses. The side effects profile of the 120 mg group was similar to that of the 60 mg group. Thus chances of drop out in the initial period are also fewer which would enhance compliance.

Table 4.24 Mean rise in Hb at different levels of tablet consumption in the three iron treatment groups

Total Consumption		n	Mean ± SE		
			Initial Hb	Final Hb	Rise in Hb
	Group				
< 100	I	1	12.1	12.3	0.2
	II	-	-	-	-
	III	3	7.9±1.27	10.3±0.38	2.4±1.24
	Group				
≥ 100	I	40	9.7±0.22	11.0±0.18	1.3±0.14
	II	40	9.5±0.21	11.5±0.14	2.1±0.18
	III	36	9.1±0.24	11.4±0.18	2.3±0.24
	Group				
≥ 200	I	33	9.7±0.25	11.2±0.17	1.4±0.15
	II	33	9.3±0.22	11.5±0.15	2.2±0.21
	III	29	9.1±0.26	11.6±0.18	2.5±0.26
	Group				
≥ 250	I	29	9.7±0.28	11.2±0.19	1.5±0.17
	II	24	9.4±0.27	11.7±0.15	2.3±0.26
	III	23	9.0±0.31	11.6±0.19	2.6±0.30
	Group				
360	I	5	9.4±0.69	10.8±0.57	1.4±0.35
	II	4	9.4±0.26	11.6±0.12	2.1±0.33
	III	1	10.5	12.0	1.5

In pregnant women with initial Hb similar to the present study, Sood et al (1975) reported a rise of 0.8 g/dl with 60 mg iron, 1.0 g/dl with 120 mg iron and 1.4 g/dl with 240 mg iron when supplemented for 10-12 weeks. While in the study by Sood et al (1975), 54% of the pregnant women consuming 240 mg iron daily were found to be still anemic at the end of the supplementation, in the present study only 22 and 31% of the pregnant women were anemic after supplementation with 120 mg and 180 mg iron respectively. These differences possibly can be attributed to iron being given as multiple divided doses in the present study. Charoenlarp et al (1988) found a higher rise in Hb with longer duration of supplementation in Burmese women, similar to the present study.

Morbidity Profile

The morbidities experienced by the pregnant women fell into three categories: a) infectious or episodic morbidities, b) anemia related morbidities, and c) others. The effect of iron supplementation are discussed under these three categories, for different gestational ages. As noted earlier morbidity profiles were obtained once every month from enrollment till delivery.

Infectious morbidities

Most commonly reported infectious and episodic morbidities were upper respiratory infections such as cough and cold (12.5-32%). Fever and diarrhoea followed this. A few women also reported of malarial fever, throat pain, eye and skin infections and ulcers (Table 4.25).

Agarwal et al (1986) reported a 50% incidence of gastrointestinal and respiratory infections in anemic pregnant women, similar to the incidence of these morbidities seen in the present study. Surveys carried out in Gujarat in 1983 (International Institute of Population Sciences and Population Research Centre, 1985) also reported fever, respiratory problems (cold and cough) and gastro-intestinal problems (diarrhoea, dysentry and constipation) in unsupplemented pregnant women.

Findings of a similar nature have also been reported in the studies conducted by NIN (NIN 1983). These investigators found a significant difference in the prevalence of minor infectious episodic morbidities between the anemic and non-anemic women. Thus in the population of underprivileged pregnant women, the common infectious morbidities relate to the upper respiratory and the gastro intestinal tract, as has been reported for young children living in deprived

Table 4.25 Morbidity profile of the subjects at different gestational periods in the three iron treatment groups - Infectious morbidities

Infectious Morbidity % Women	Gestational period (weeks) < 20			20-24			24-28			28-32			32-36		
	Groups I	II	III	I	II	III	I	II	III	I	II	III	I	II	III
URI	15.3	32.2	24.0	22.0	12.5	18.9	13.5	24.3	17.2	20.5	19.4	23.4	20.5	21.4	13.7
Fever	15.4	-	4.0	12.2	5	21.6	18.9	18.2	5.7	12.8	-	13.3	17.6	7.1	3.4
Diarrhoea	3.8	7.1	-	4.9	2.5	-	2.7	9.1	5.7	5.1	5.6	3.3	5.9	7.1	3.4
Diarrhoea + Fever	3.8	-	4.0	-	-	-	2.7	-	2.9	-	-	-	-	-	-
Fever + URI	7.7	-	4.0	2.4	2.5	2.7	-	3.0	-	-	-	6.7	2.9	-	-
Diarrhoea + URI	-	-	-	-	-	-	-	3.0	-	5.1	2.8	-	-	3.6	-
Fever + URI + Diarrhoea	-	-	-	-	-	-	-	2.5	-	-	-	-	-	-	-
Malaria	7.7	3.6	-	7.3	2.5	2.7	5.4	-	5.7	-	-	-	-	3.6	3.4
Malaria + URI	-	3.6	-	-	-	-	-	-	-	-	-	-	-	7.1	-
Typhoid	-	-	4.0	-	-	-	-	-	-	-	-	-	-	-	-
Others	11.4	-	8.0	2.4	-	8.1	-	-	2.9	5.2	8.4	-	-	3.6	-
No morbidity	53.8	60.7	64	58.5	77.5	62.2	64.9	54.5	62.9	59	72.2	63.3	58.8	64.3	75.9

Others = Throat pain, eye infection, skin problems, ulcers, bleeding gums.
Percentage do not add to 100 due to multiple responses.

circumstances, which appears to be a reflection of the poor quality of the environment they live in.

The number of infectious morbidities experienced during a one month period from 20 weeks - 36 weeks of gestation are presented in Table 4.26. Percent women who experienced more than two morbidities per month decreased from 11.5% at the time of enrollment to 5.9% at the end of the supplementation period in Group I. The trend was reversed for women in Group II for this period as there was an increase from 7.1% to 14.3%. Twelve percent of the women in Group III experienced more than two morbidities at enrollment but none of them reported an incidence of two or more morbidities at the end of supplementation. Thus, there appeared to be no relationship between the number of infectious morbidities vs level of iron consumed.

Table 4.27 presents the mean episodes and the mean duration of infectious morbidities of the subjects in the three groups, at one month intervals from 20 to 36 weeks. Two observations are noteworthy. With increasing gestation there was a fall in mean episodes of infectious morbidities as well as in the mean duration, the latter being more clearly evident in Group I and III but not so consistent in Group II. The second one is related to the effect of the level of iron consumed on morbidities. The mean duration and mean episodes was lowest in Group III (180 mg group) between

Table 4.26 Percent subjects experiencing two or more infectious morbidities, at different gestational periods in the three iron treatment groups

Gestational period (weeks)	Presence/Absence of Morbidities: None			One Morbidity			≥2 Morbidities		
	Group I	Group II	Group III	Group I	Group II	Group III	Group I	Group II	Group III
< 20	53.8	60.7	64.0	34.6	32.1	24.0	11.5	7.1	12.0
20-24th	58.5	77.5	62.2	26.8	15.0	21.6	14.6	7.5	16.2
24-28th	64.9	54.5	62.9	27.0	36.4	34.3	8.1	9.1	2.9
28-32nd	59.0	72.2	63.3	33.3	19.4	26.7	7.7	8.3	10.0
32-36th	58.8	64.3	75.9	35.3	21.4	24.1	5.9	14.3	0

Percent with ≥2 morbidities
Chi-square 23.7996
*Significant at p<0.5

Table 4.27 Mean episodes and mean days of infectious morbidities experienced at different gestational periods in the three iron treatment groups

Gest. Age weeks	Groups I N	I ME	I MD	II N	II ME	II MD	III N	III ME	III MD
< 20	26	0.80	4.46	28	0.71	2.29	25	0.80	5.72
20-24	41	0.75	3.41	40	0.23	1.08	37	0.67	3.89
24-28	37	0.70	2.62	33	0.88	4.33	35	0.69	4.45
28-32	39	0.61	3.10	36	0.50	2.86	30	0.50	1.40
32-36	34	0.58	2.74	28	0.53	2.70	29	0.34	0.89

ME - Mean episodes
MD - Mean no. of days

32-36 weeks of gestation compared to Groups I and II. At other gestational ages, no relationship between the level of iron consumed and the duration or episodes of infectious morbidities was evident. These data need to be interpreted in conjunction with the rise in Hb discussed in the earlier section. The lack of effect of the level of iron consumed on the morbidity profile between 20 and 32 weeks of gestation may be explained on the basis that 75% or more of the total rise in Hb had occurred during this period in all the three groups, producing substantial increases in Hb levels of the subjects. Further rise in Hb during the last month of supplementation was considerable only for Group III, which could possibly account for the difference in mean episodes and duration of morbidities between this Group and Group I and II during this period.

In anemic pregnant women treated with parenteral iron, Prema et al (1982b) reported mean episodes of infectious morbidities to be 1.6/person, compared to only 1.3/person in non anemic pregnant women from the same socio economic background. Commonly reported morbidities were respiratory infection and diarrhoea. The mean episodes of infectious morbidities in the present study was somewhat lower, but the difference seen between the 180 mg and 60 mg iron group particularly in the last month of gestation is similar in

magnitude to what has been reported by Prema et al (1982b) for non-anemic and anemic parenterally supplemented women.

Since morbidities have been reported to decrease Hb levels, an analysis of mean Hb levels in relation to the presence and absence of morbidities was done at the final contact i.e. 32-36 weeks of gestation to know if the decline in Hb occurred even when iron was provided. No differences were seen in the Hb levels between those who experienced infectious morbidities vs the ones who did not in the three groups, both OL and NOL (Table 4.28). The decline in Hb that has been reported to occur due to infectious morbidities was not observed in the present study subjects which seems to indicate that iron supplementation in these pregnant women prevented the fall in Hb that has generally been reported to occur after an episode of infectious morbidity.

To sum up, with increasing oral doses of iron in pregnancy, there occurred a mild reduction in episodes and duration of infectious morbidities only in the final month of supplementation and that only in the 180 mg group. But the morbidities per se had no effect on the Hb levels when iron supplements were provided. Thus the levels of iron in this study for the major part had little effect on the type of infectious morbidities, episodes or duration. At the same time the fear that oral iron supplementation at higher

Table 4.28 Final Hb of the subjects reporting and not reporting infectious morbidities in the three iron treatment groups (mean ± SE)

Final Hb		Groups I (n=41)	II (n=40)	III (n=39)
OL				
IM	Present	10.84±0.31(16)	11.66±0.14(13)	11.32±0.36(10)
	Absent	11.13±0.21(25)	11.41±0.19(27)	11.40±0.21(29)
	t'	0.7746^{NS}	1.059^{NS}	0.1919^{NS}
NOL				
IM	Present	10.97±0.33(14)	11.60±0.17(10)	11.90±0.42(6)
	Absent	11.08±0.22(24)	11.43±0.19(26)	11.43±0.24(18)
	t'	0.2753^{NS}	0.6692^{NS}	0.9716^{NS}

IM - Infectious morbidity

levels may exacerbate infectious morbidities was also not borne out by the results of the present study.

Anemia and work related morbidity

The most commonly reported morbidities under this class were general weakness, tiredness, fatigue, breathlessness, giddiness and back-pain. Some women also reported sleeplessness and chest-pain. At enrollment a larger percent of the women in Group III (88%) reported two or more of these morbidities than in Group I (69%) or Group II (71%). However at the end of the supplementation period 64.7% of the women in Group I still reported 2 or more of these morbidities compared to only 39.3% only in Group II and 41.4% in Group III (Table 4.29), which were statistically significant. These data showed once again that higher levels of iron 120 mg and 180 mg had more beneficial effects in terms of work related morbidities but between the 120 mg and 180 mg, not much of a difference was seen.

Other morbidities

Nausea, vomiting, lucorrhea, pain in pelvic region, head-ache, cramps in lower limbs, increased or decreased micturition and burning during micturition were the other morbidities reported by the subjects. No consistent effect

Table 4.29 Percent subjects experiencing two or more anemia or work related morbidities at different gestational periods in the three iron treatment groups

Gestational period	Number of Anemia/Work Related Morbidity								
	None			One Morbidity			Two or more Morbidities		
	Group			Group			Group		
	I	II	III	I	II	III	I	II	III
< 20th week	15.4	21.4	4.0	15.4	7.1	8.0	69.2	71.5	88.0
20-24th week	14.6	20.0	13.5	24.4	25.0	8.1	61.0	55.0	78.4
24-28th week	13.5	15.2	8.6	16.2	15.2	25.7	70.3	69.6	65.7
28-32nd week	15.4	16.7	6.7	12.8	30.6	26.7	71.8	52.7	66.6
32-36th week	26.5	32.1	31.0	8.8	28.6	27.6	64.7	39.3	41.4

Percent women with 2 morbidities

chi-square 13.1268*

* Significant at $p<0.05$

was seen with different doses of iron supplementation, at different periods of gestation (Table 4.30).

Weight Gain

Mean weights and weight gain characteristics at different gestational ages for the OL and NOL in the three different iron supplementation groups are given in Tables 4.31 and 4.32. There was no significant difference in the mean weight of the mothers in the three groups (OL) either before or after the supplementation period. A further analysis was done to see if the final weight distribution was affected by different levels of iron supplementation. For this analysis, the final weights of the pregnant women were distributed into different weight categories of < 40, 40-45, 45-50, and >50 kg in each of the three groups. These are shown in Fig 4.12. A Chi-square test revealed no significant difference in the weight distribution between the three iron treatment groups.

The weight gain during the study period was statistically significantly different between Group II and III (Table 4.31). Group III and Group I had 1.0 and 0.9 kg higher weight gain than Group II. That the higher weight gain in these groups was not related to initial weight was shown by the observation that mean initial weights were almost identical at entry for the Groups I and II. The

Table 4.30 Other morbidities in the subjects at different gestational periods in the three iron treatment groups

Other Morbidities % Women	Gestational period (weeks)																	
	< 20			24			28			32			36					
	Groups																	
	I	II	III	I	II	III	I	II	III	I	II	III	I	II	III	I	II	III
Nausea	15.4	17.9	20.0	9.8	15.0	5.4	5.4	3.0	11.4	0.0	5.6	-	-	10.7	-			
Heart burn	30.8	21.4	28.0	24.0	22.5	24.3	24.3	6.1	17.1	7.7	11.1	6.7	2.9	7.1	3.4			
Problems in micturition (pain, burning)	23.1	10.7	20.0	22.0	17.5	5.4	24.3	9.1	11.4	15.4	2.8	23.3	13.7	25.0	17.2			
Lucorrhoea	42.3	39.3	40.0	51.2	32.5	37.8	48.6	30.3	28.6	48.7	30.6	20.0	35.3	42.9	24.1			
Piles	3.8	3.6	-	-	5.0	2.7	-	3.0	5.7	-	2.8	10.0	-	-	3.4			
Head-ache	30.8	28.6	28.0	12.2	17.5	21.6	18.9	30.3	20.0	20.5	13.9	10.0	8.8	14.3	10.3			
Oedema	-	-	4.0	7.3	-	8.1	5.4	6.1	2.9	10.3	5.6	6.7	-	3.6	17.2			

Percentage do not add to 100 due to multiple responses.

Table 4.31 Weight gain of the subjects in the three iron treatment groups - (OL) (mean ± SE)

Weight/Weight gain (kg)	Group I (41)	II (39)	III (37)
Initial weight (20-24 w)	43.4 ±1.02	43.3 ±0.93	44.3 ±1.20
Final weight (32-36 w)	49.0 ±1.01 (41)	48.0 ±1.08 (39)	50.0 ±1.40 (37)
Weight gain	5.6 ±0.36	4.7 ±0.35	5.7 ±0.29
Weight gain/month (20-36 w)	1.6 ±0.09	1.4 ±0.09	1.6 ±0.07
Weight gain/week	0.382±	0.326±	0.364±
Weight gain/month (20-28 w)	1.46±0.17	1.51±0.15	1.5 ±0.13
Weight gain/month (28-36 w)	1.78±0.09	1.34±0.13	1.78±0.09

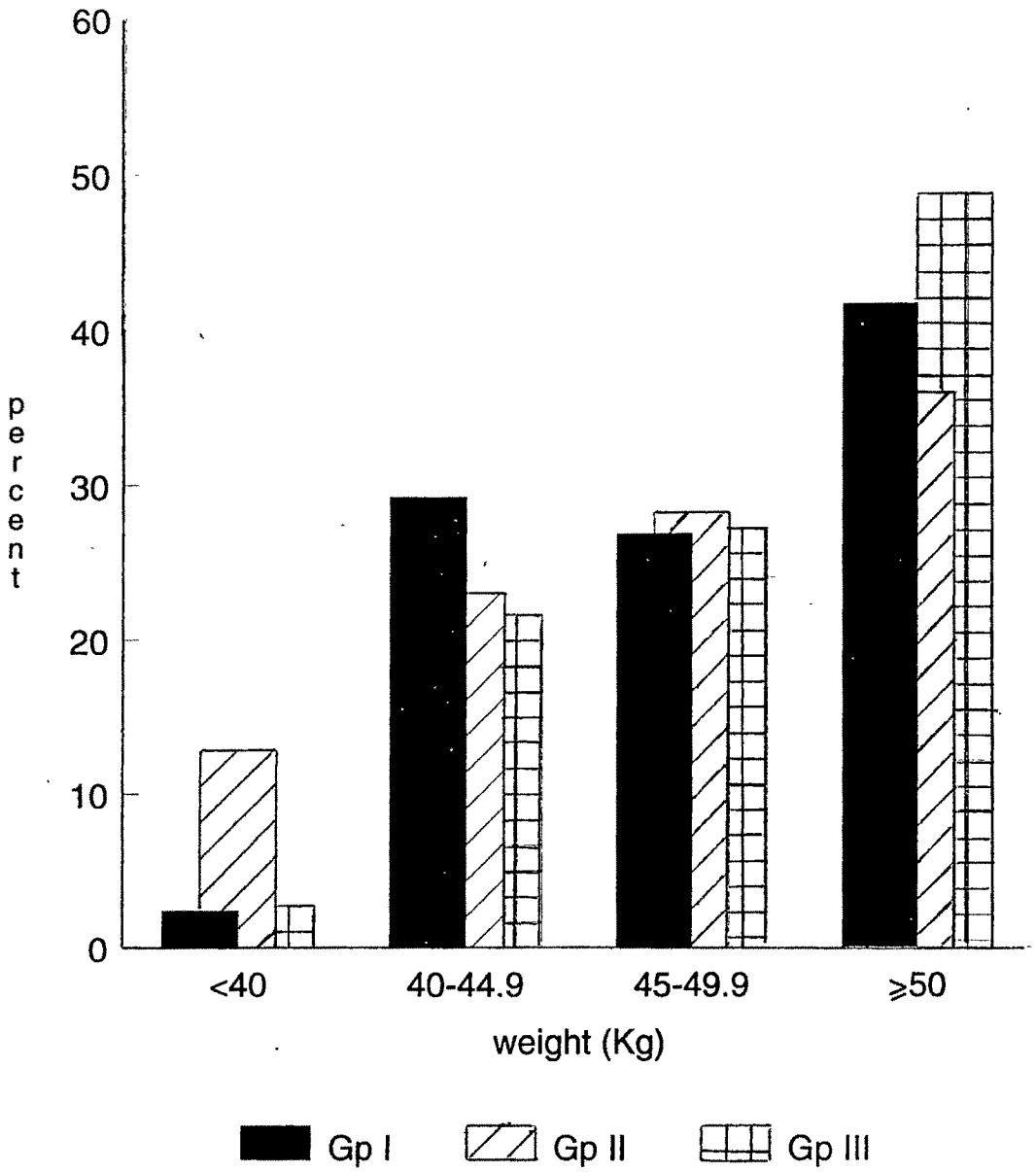
	t' values		
	Initial weight	Final weight	Weight gain
I vs II	0.641^{NS}	0.2745^{NS}	1.80^{NS}
I vs III	0.5967^{NS}	1.235^{NS}	0.22^{NS}
II vs III	1.8926^{NS}	0.98^{NS}	2.20^{*}

* Significant at $p<0.05$.

Table 4.32 Weight gain of the subjects in the three iron treatment groups (NOL) (mean ± SE)

Weight (kg)	Group I (38)	II (36)	III (24)
Initial weight (20-24 w)	43.4 ±1.09	43.7 ±1.00	44.2 ±1.37
Final weight (32-36 w)	49.0 ±1.08	48.4 ±1.16	50.2 ±1.65
Weight gain	5.6 ±0.39	4.7 ±0.37	6.0 ±0.38
Weight gain/month	1.66±0.10	1.40±0.09	1.52±0.09
Weight gain/week	0.387	0.327	0.355

Fig. 4.12 Weight distribution of the subjects after supplementation in the three iron treatment groups

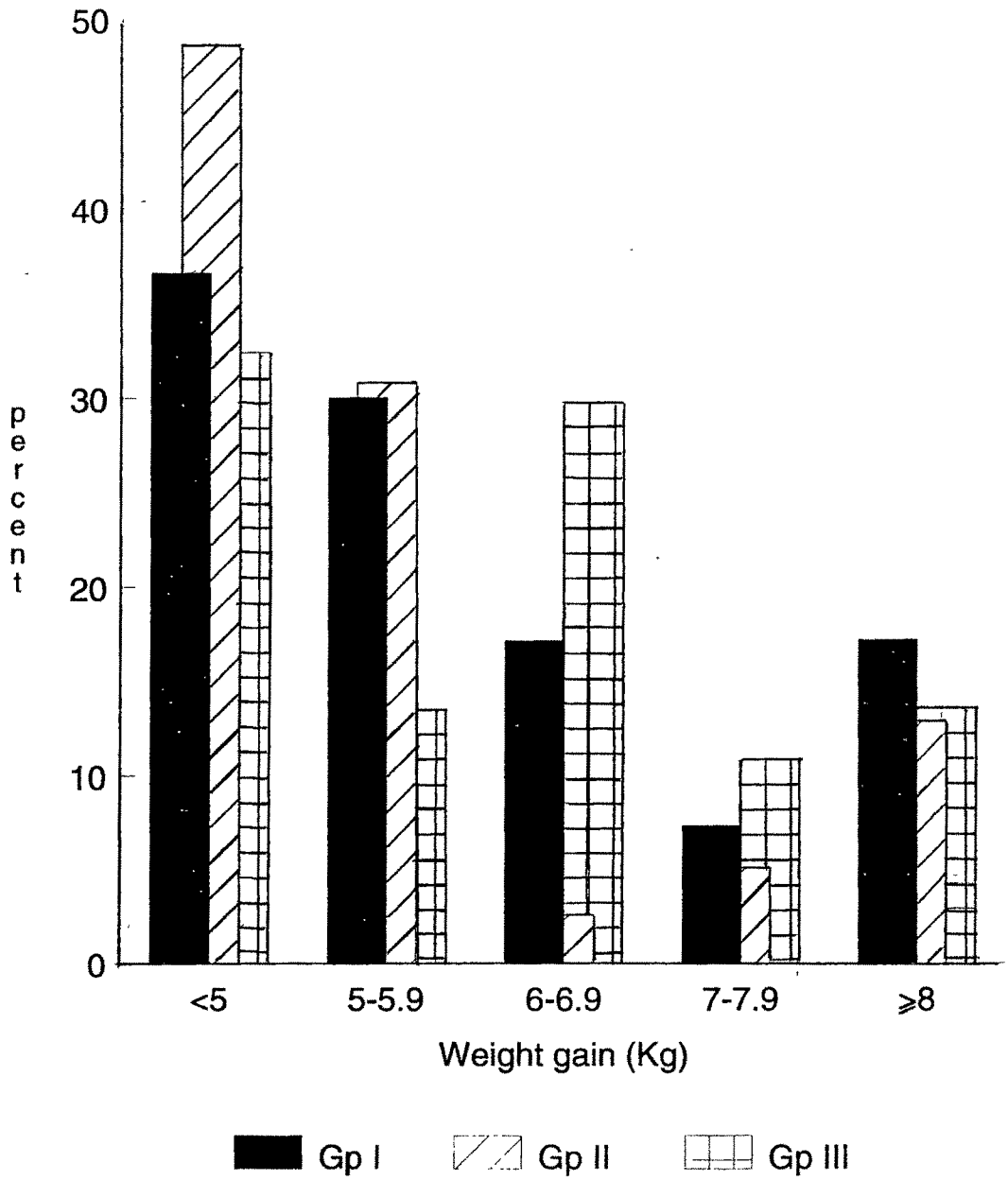


Chi square 1.597NS

weight gain distribution for the three iron treatment groups shown in Fig 4.13 brings out the observation that a larger percent of the subjects in Group II were found to gain less than 5 kg and a very small percent of them gained between 6-6.9 kg, accounting for the lower mean weight gain during the study period in this group. As the subjects remained in the study for varying durations and as pre-pregnancy weights were not available, the total pregnancy weight gain could not be computed. However, rate of weight gain per month or per week has been shown to be a reasonably satisfactory indicator as some studies have demonstrated the weight gain to be linear in the last two trimesters. Therefore mean weight gains were computed separately on per month and per week basis (Tables 4.31 and 4.32). When weight gain per/m was computed separately for 20-28 weeks and 28-36 weeks, Group I and III showed an increased rate of gain in the last two months of gestation whereas in Group II, the weight gain for the two periods remained nearly the same.

The weight gain per week of the present study subjects is similar to the 350-400 g/week reported by Agarwal et al (1987) for rural pregnant women in India. However, they are much higher than the weight gain per week reported by Anderson for pregnant women from Gujarat (210 g/week) and Maharashtra (270 g/week) between 25-35 weeks of gestation (Anderson 1989).

Fig. 4.13 Weight gain distribution of the subjects in the three iron treatment groups



Chi square 12.834* $p < 0.05$

Weight gain in well nourished pregnant women from the developed countries has been shown to be 400 g/week. Using this as a cut off, about 50% of the subjects in Group I and III were found to have a satisfactory weight gain while only 30% in Group II was in this category (Fig 4.14).

While the level of iron supplementation in the present study did not seem to have any significant impact on the weightgain of the subjects, whether unsupplemented women will have a lower weightgain can not be answered by the present study, as a placebo control group could not be included for ethical reasons.

Only two studies were available on the effect of iron supplementation on weight gain in pregnant women, one of which (Guldholt et al 1991) did not report any significant difference in the weight gain of pregnant women supplemented with either 15 mg or 100 mg iron. The other which reported a positive impact of iron supplementation on weight gain was not a randomized study (Vijayalakshmi and Shobana 1982).

During the course of the study, several women reported that they had improved appetite which they attributed to the tablet consumption. An analysis was done to see if improved appetite via better food intake led to better weight gains. These analyses shown in Table 4.33 revealed that weight gain tended to be higher for those with improved appetite in

Fig. 4.14 Weight gain per week (≥400g) of the subjects in the three iron treatment groups

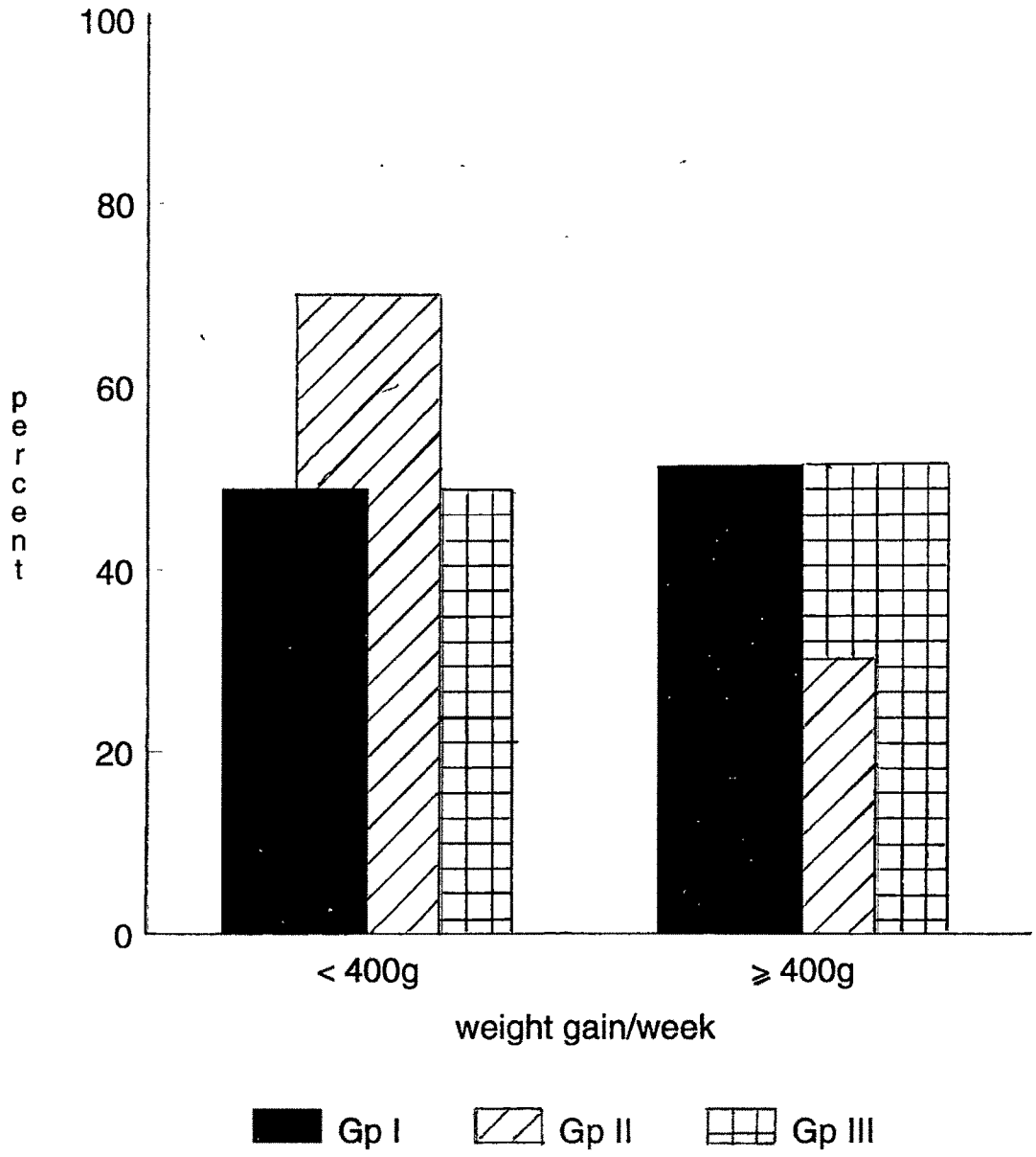


Table 4.33 Weight gain (mean ± SE) of the subjects who reported improved appetite due to iron supplementation in the three iron treatment groups

Mean weight gain (kg)/ month	Group I	II	III
Reported improved appetite	1.78±0.15 (19)	1.33±0.10 (31)	1.59±0.09 (27)
Not reported improved appetite	1.52±0.12 (22)	1.63±0.19 (9)	1.49±0.13 (12)
t' value	1.3535^{NS}	1.3973^{NS}	0.6325^{NS}

^{NS} Not significant

Group I and III but were not statistically significant. Group II was an outlier as it did not show this trend.

Summing up the results on weight changes in the present study it is seen that none of the weight gain parameters, namely total weight gain during this period, rate of weight gain and weight distribution was different between the three iron treatment groups although Group II came out consistently poorer.

The low weight gain of the subjects in Group II despite their having reported improved appetite could be attributed to two reasons. Improved work performance, as reported by the women could have resulted in increased energy expenditure resulting in lower weight gain. Another probable reason was that women belonging to Group II had lower per capita income (although not statistically significant) and higher family size compared to women in Group I and Group III; so despite their improved appetite, the lower PCI and higher family size could have resulted in lower availability of food. Agarwal et al (1987) substantiated this probability as pregnant women with higher PCI (> Rs.140) had higher weight gain, in the second and third trimester than those with lower PCI (< Rs.139).

In undernourished pregnant women with initial weight of 44.5 kg, and height of 151 cm, a weightgain of 17 kg has

been recommended in order to correct the initial deficit (+6.5 kg) and for a weightgain of about 10-12 kg (Krasovec and Anderson 1991). The highest weight gain in the present study was only 12 kg, and thus it appears that unless the pre-pregnancy weights can be improved recommendations of the kind cited above may be practically unachieveable.

Gestational Duration

Mean gestational duration of the mothers in the three groups did not differ significantly and was 39.29, 38.58, and 39.18 weeks in Groups I, II and III (Table 4.34). When the criterion used for defining premature delivery was 36 weeks, it was found that none of the women in Group I had premature deliveries compared to 5.2% in Group II and 2.6 in Group III. Incidence of premature delivery with a 37 week cutoff was 9.7%, 5.2% and 7.9% in Groups I, II and III respectively. The rest of the women delivered between 37-42 weeks of gestation, except one woman in Group III who delivered after 42 weeks of gestation.

Reports in the literature indicate that anemia contributes to increased incidence of premature delivery. Positive outcomes in terms of increased gestational duration were reported in two of the 17 controlled iron supplementation trials reviewed by Hemminki and Starfield

Table 4.34 Mean gestational duration and percent premature deliveries in the three iron treatment groups

Gestational Duration	Group I	Group II	Group III	F ratio
	(41)	(38)	(38)	
Gestational duration (weeks) (mean ± SE)	39.29±0.24	38.58±0.32	39.18±0.34	1.6193^{NS}
Percent premature delivery				
< 36 weeks	-	5.3	2.6	
< 37 weeks	9.8	5.3	7.9	
37 - 42 weeks	90.2	89.4	86.9	
> 42 weeks	-	-	2.6	

(1978). In the present study, there was no apparent effect of increased levels of iron supplementation on the gestational duration and the incidence of premature delivery.

Findings of the present study correlate well with that of Mitchell and Lerner in USA (1992), who demonstrated that supplementation with 100 mg iron and 1.6 mg folic acid resulted in a mean gestational duration of 39 weeks and 8.6% incidence of premature delivery (< 37 weeks). In an ongoing study in this Department on the evaluation of the anemia control programme in Baroda, women who received no iron supplementation had a mean gestational duration of only 35.2 weeks. The restoration of Hb to normal levels (i.e.> 11 g/dl) in a substantial proportion in the present study subjects and higher level of folic acid (1.5 mg/day) administered in the present study may have contributed to the normal gestational duration seen.

A multiple regression analysis was run with gestational duration as the dependent variable and age, initial weight of the mother, weight gain, number of years of education of the mother, environmental sanitation score, type of housing, number of antenatal visits, number of episodes of infectious morbidity, per capita income, iron intake, folic acid intake, and rise in Hb as independent variables. Only weight

gain and parity were found to be significantly associated with gestational duration in the present study and together they explained 12.8% of the variation in gestational duration, while 87.3% of the variability remained unexplained (Table 4.35, Fig 4.15). These findings are consistent with Kramer's observations (Kramer 1987) that the cause of the majority of premature births are unexplained.

Two women in Group II and one woman in Group III delivered stillborn babies. Of these only one woman had poor weightgain, was a poor complier and as the bread-winner of the family she was involved in moderate work activity till delivery. The other two women had normal weight gain (> 5 kg) and normal Hb (> 11 g/dl) but still delivered still-born babies.

Birth Weight

Birth weights, as mentioned already were obtained from hospital records as 99% of the deliveries took place in a hospital. For the two deliveries that occurred at home the birth weights were obtained with in 48 hours. The mean birth weights of the infants in the three different iron supplementation groups is shown in Table 4.36 separately for male and female babies. The same Table provides percent infants with birth weight less than 2.5 kg. The highest (4

Table 4.35 Regression analysis of factors affecting gestational duration

Variables	B	SE B	t'
Parity	0.40130	0.15781	2.543***
Weight gain	0.77847	0.31991	2.433***
Constant	37.15936	0.58820	63.174*
R^2		0.12779	

*
*** $p < 0.02$
$p < 0.001$

Fig. 4.15 Results of multiple regression analysis of factors affecting gestational duration

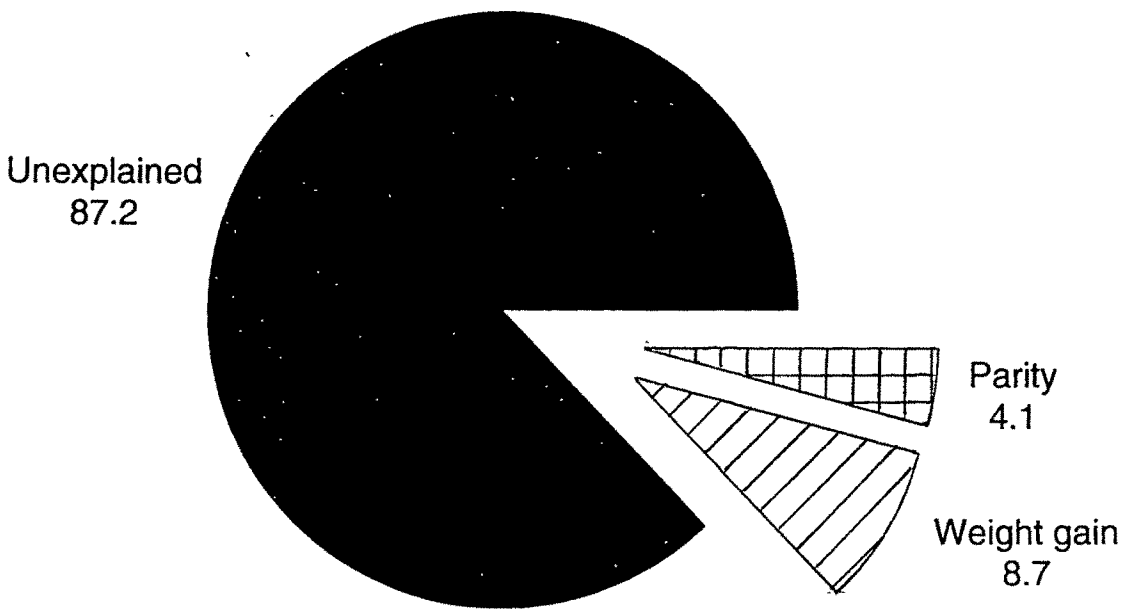


Table 4.36 Birthweight (mean ± SE) and percent low birthweight in the three iron treatment groups (OL and NOL)

	Groups I	II	III	F Value
OL				
Mean birthweight (kg) All infants	2.70±0.06 (41)	2.72±0.06 (38)	2.85±0.07 (38)	1.5976^{NS}
Males	2.8 ±0.07 (28)	2.82±0.09 (21)	2.89±0.08 (24)	
Females	2.55±0.09 (16)	2.59±0.08 (17)	2.79±0.13 (14)	
Percent low birth weight (< 2.5 kg) All infants	22	23.7	13.2	
Males	7.3 (3)	10.5 (4)	5.3 (2)	
Females	14.6 (6)	13.2 (5)	7.9 (3)	
NOL				
Mean birth weight	2.7±0.06 (38)	2.71±0.07 (34)	2.81±0.08 (23)	0.6226^{NS}
Percent low birth weight (< 2.5 kg)	21.1 (8)	26.5 (9)	8.7 (2)	

NS - Not significant
Number of subjects in parentheses

kg) and lowest (1.8 kg) birth weight were both recorded in women supplemented with 120 mg iron during pregnancy (Group II).

Although, no statistically significant difference was evident in the mean birth weights of infants born to mothers in the three iron supplementation groups, infants in Group III had a higher birth weight by about 150 g, compared to Group I and II. This was seen for both male and female babies, although the difference was higher for the female babies (240 g vs 150 g).

Incidence of low birthweight was lowest in Group III (13.2%), compared to Groups I and II (22% and 24% respectively). A higher percent of the female infants were found to fall in the low birth weight category than the male infants in all the three iron treatment groups.

In a commentary on birthweight and ethnicity Barron (1983) reported that birthweight of male infants was 150 g greater than female infants, similar to the present study, where male infants in all the treatment groups had higher birth- weights and lower incidence of low birthweight than female infants.

Mean birthweight of the infants in the three different treatment groups in NOL category did not differ from that of

the OL (Table 4.36). However the incidence of low birthweight was considerably lower in the non-overlapping Group III, in comparison to the total sample of the women belonging to Group III (8.3 vs 13.2). Thus the higher level of iron supplementation (180 mg) during pregnancy had a small effect on the birthweight of the infants and a somewhat more pronounced effect on low birthweight incidence.

Very few studies have addressed the issue of birthweight in randomized iron supplementation trials. Prema et al (1982) demonstrated that pregnant women treated with Imferon had significantly higher birthweight (2.890 kg) than those who were untreated (2.734 kg). Results of the present study with oral iron supplements at 180 mg are very similar to that of the parenteral iron group.

In the study by Sood et al (1975) no particular trend was found with increasing levels of iron supplementation during pregnancy on birthweight. Infants of mothers supplemented with placebo or 240 mg iron had similar mean birthweight of 2.7 kg. However, non-compliance with consumption of the supplements at the 240 mg level may have resulted in more than 50% of the pregnant women continuing to remain anemic. This could possibly explain the finding of a lack of effect of iron on birth weight in this study.

Similar findings were reported in Denmark and Dublin as no variations in birthweight were recorded for women supplemented with different levels of iron (Guldholt et al 1991, Alward and Kevany 1984).

As birth weight is strongly affected by gestational duration the mean birthweight in the three groups was tabulated only for those completing 36 weeks of gestation. The higher birth weight and lower percent lower birth-weight infants in Group III was evident even after adjusting for gestational duration (Table 4.37).

A multiple regression analysis was carried out as birthweight is known to be affected by a number of factors. Birth weight was taken as the dependent variable and initial weight, weight gain, gestational duration, age of the mother, parity, sex, total years of education of the mother, environmental sanitation score, type of housing, per capita income, number of antenatal visits, episodes of infectitious morbidity, level of iron intake, folic acid intake, and rise in Hb, as independent variables. Sex of the baby and weight of the mother at entry were the two factors that were significantly correlated with birth weight and entered the multiple regression equation (Table 4.38 and Fig 4.16). Together they explained 39.6% of the variation in birth weight. Although gestational duration was significantly

Table 4.37 Birthweight (mean ± SE) and percent low birthweight of full term infants (36 w) in the three iron treatment groups

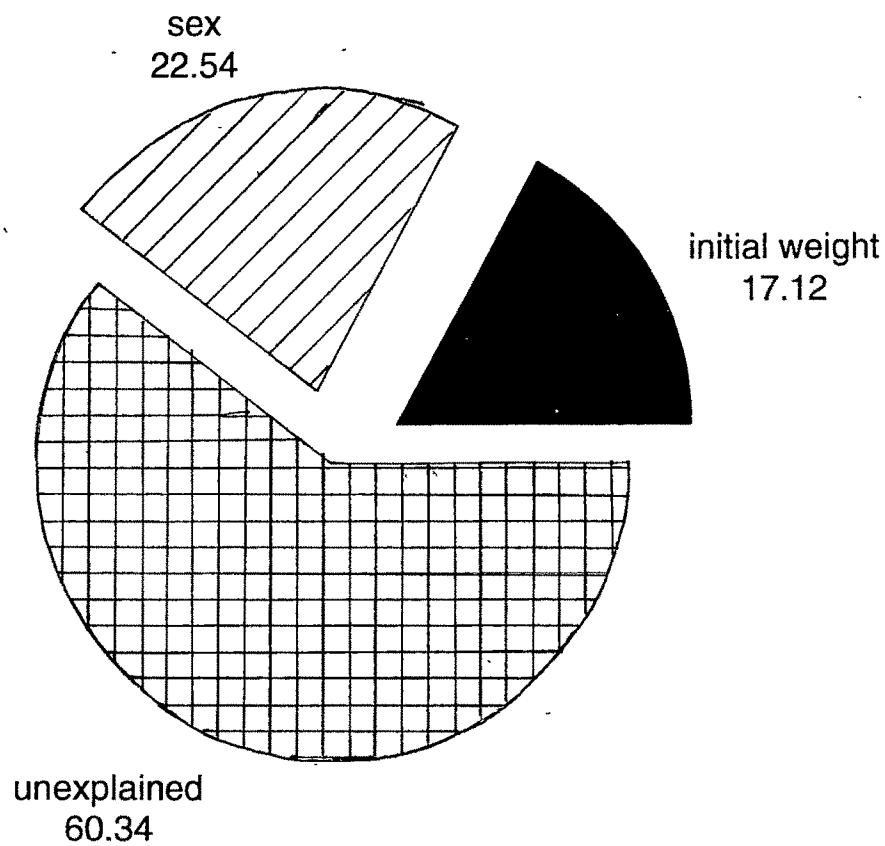
Gestational Duration (36-42 w)	Group I	Group II	Group III
All infants	2.70±0.06 (41)	2.73±0.07 (36)	2.86±0.07 (36)
Males	2.80±0.07	2.86±0.10	2.89±0.08
Females	2.55±0.09	2.59±0.08	2.81±0.14
Percent low birth weight (<2.5 kg)	22	22.2	13.9
Males	12	15.8	8.7
Females	37.5	29.4	23.1

Table 4.38 Regression analysis of factors affecting birthweight

Variables	B	SE B	T
Initial weight	0.02459	4.9801	4.938**
Sex of the infant	-0.18907	0.06694	-2.824*
Constant	1.94331	0.24224	8.022**
R^2		0.396668	

** p<0.0001
* p<0.01

Fig. 4.16 Results of multiple regression analysis of factors affecting birthweight



correlated with birth weight (r = 0.3271), it did not emerge as a variable in the multiple regression, which is probably due to the fact that the gestational duration was higher than 36 weeks for most of the subjects in the present study.

Barron (1983) also reported correlations between birthweight and gestational duration and sex. Kirksey et al (1991) found that the best predictors of birth weight were pre-pregnancy weight, gestational duration and weight gain, which was also demonstrated by Singh et al (1992). Badole et al (1992) found a progressive increase in the birthweight with increasing gestational duration. Initial weight and weight gain was also demonstrated to have an impact on birthweight, by other investigators (Gueri et al 1982, Agarwal et al 1991).

Incidence of low birthweight in India is estimated to be about 33% (UNICEF 1994). Figures obtained in this study after iron supplementation were much lower, the lowest being observed for the 180 mg iron group compare to the reported estimates. Reduction of low birth weight infants to less than 10% occurred only in the 180 mg group.

Section IV

Effect of Different Dose Levels of Iron Supplementation During Pregnancy on Maternal Weight and Hb at 6 Months Post-partum

Maternal Weight

Despite all attempts to make a post-natal follow up of all the subjects who were available till delivery, only 41% of the original sample was available at 3 months and 71% were available at 6 months postpartum. Many of the women migrated after delivery to their natal homes or other places.

The mean weight at entry and at 6 months post-partum for the available subjects in the three groups is shown in Table 4.39. Despite the 29% drop out, the mean body weight at entry was not statistically different for the three different groups. A trend that seems to be of some importance is that at 6 months postpartum, women in Group I had lost 1.17 kg compared to their weight at 20/24 weeks of gestation while the women in Group II and III maintained similar weight as at 20 weeks of gestation.

None of the iron supplementation trials in the literature have followed up the pregnant women in the

Table 4.39 Weight and Hb of the subjects at 6 months postpartum in the three iron treatment groups (mean ± SE)

	Group I	Group II	Group III	t' value
Weight				
Initial weight (kg) (20-24 w)	42.85±1.11 (31)	44.02±1.25 (26)	43.88±1.51 (29)	I vs II = 1.64^{NS} I vs III = 1.22^{NS} II vs III = 0.19^{NS}
6 months postpartum	41.68±1.1 (31)	44.40±k1.3 (26)	44.01±1.6 (29)	I vs II = 1.5972^{NS} I vs III = 1.200^{NS} II vs III = 0.1892^{NS}
Hemoglobin (g/dl)				
Initial (20-24 w)	9.77±0.25 (26)	9.57±0.30 (26)	9.07±0.28 (28)	I vs II = 1.44^{NS} I vs III = 0.99^{NS} II vs III = 0.05^{NS}
6 months postpartum	10.79±0.25 (26)	11.27±0.22 (26)	11.12±0.22 (28)	I vs II = 1.72^{NS} I vs III = 1.0^{NS} II vs III = 0.4^{NS}

Number of subjects in parentheses.
NS Not Significant

postpartum period for anthropometric measurements. However, data on lactating women at ≤ 6 months have shown a mean weight of 42.1 kg in rural pregnant women (NIN 1982), almost similar to the mean weight of women supplemented with 60 mg iron in the present study. Longitudinal studies on weight characteristics in the post-partum period have shown that women tend to lose weight during the lactation period, about 2 kg in the 18 months of lactation (NIN 1980). The present findings show that much of this loss appears to occur in the first six months as seen in Group I. Interestingly, supplementation with 120 or 180 mg iron seems to have arrested the weight loss, providing a further rationale for supplementing women with higher levels of iron during pregnancy.

Hemoglobin

The mean Hb levels at 6 months postpartum and the prevalence of anemia at the same point of time presented in Tables 4.39 and 4.40 bring out some interesting findings. For comparison the initial Hb levels of these subjects at 20 weeks gestation is also presented in the same Table 4.39.

As seen, the level of iron supplementation during pregnancy had a clear impact on the Hb levels at 6 months postpartum, the group that received higher levels had higher

Table 4.40 Prevalence of anemia at 6 months postpartum in the three iron treatment groups

Prevalence of Anemia	Group I		Group II		Group III	
	N	%	N	%	N	%
Normal (above 11 g/dl)	10	38.5	19	73.1	18	64.3
Mild (10 - 10.9 g/dl)	7	26.9	4	15.4	6	21.4
Moderate (7 - 9.9 g/dl)	9	34.6	3	11.5	4	14.3
Severe (< 7 g/dl)	0.0	0.0	0.0	0.0	0.0	0.0
All cases - anemic	16	61.5	7	26.9	10	35.7
Total	26	100.0	26	100.0	28	100.0

Chi-square = 29.91* $p < 0.05$

mean Hb levels. Other studies available in the literature (Sood et al 1975, Aung Than Batu et al 1976, Kuizon et al 1980) have followed up supplemented pregnant women for a much shorter period of time perinatally (1-3 months) but have shown that women supplemented during pregnancy tend to have higher levels of Hb perinatally compared to unsupplemented women.

The picture with respect to prevalence of anemia is even more convincing. A significantly higher percentage of the women in Group II and Group III were normal at 6 months postpartum compared to Group I. While 61.5% of the women in Group I were anemic (Hb $<$ 11 g/dl) only 26.9% and 35.7% in Group II and III were anemic at 6 months postpartum. However, it should be noted that severe degree of anemia was absent in all the three groups at 6 months postpartum (Table 4.40).

The higher levels of Hb and lower prevalence of anemia in Groups II and III appear to be due to increased levels of storage iron that has been reported in pregnant women provided with higher levels of iron daily. Serum ferritin levels have been shown to be the highest in pregnant women receiving $\geq$ 120 mg elemental iron per day (Thane Toe and Thein Than 1982, Reddiah et al 1989, Charoenlarp et al 1988).

In terms of both the maternal outcome parameters, weight and Hb the dose levels of 120 mg and 180 mg iron are far better than the 60 mg dose level. Between the two higher levels no differences are seen. The delivery of iron and folic acid supplements, whatever the level of iron, calls for an accessible and efficient delivery system. When efforts are made to deliver iron and provide ante-natal care, selection of dose level of iron should be such as to prevent the women from lapsing into anemia after delivery. The results of the maternal outcome in the peri-natal period in this study indicate that 120 mg iron is adequate for this and is not different from the 180 mg level but the latter produces more unpleasant side effects initially.

Section V

Effect of Different Dose Levels of Iron Supplementation During Pregnancy on Infant Outcome at Three Months and Six Months of Age

At 3 months post-partum only 41% of the mother infant pairs were available for follow-up however at 6 months 71% of them were available.

Diet Pattern

At three months, majority of the women (>85%) in all the three groups exclusively breast-fed their infants (Table 4.41). Five of the mothers had introduced small quantities of top milk (cow or buffalo milk). Twenty six percent of the women stated that the infants were also given tonics occasionally, which were ayurvedic, gripe-water or multi-vitamin tonics. These were however given in small amounts only when the child fell ill. Proprietary baby food was introduced by only one mother, but the child had not taken a liking to it and so it was discontinued. There was no significant difference in the percent infants exclusively breast-fed vs given other foods at 3 months of age between the three iron treatment groups.

During the 6th month follow up it was observed that 40% of the mothers still exclusively breast-fed their infants, 50% continued breast-feeding along with other foods while 10% of the mothers had ceased to breastfeed their infants altogether (Table 4.41). No difference was evident in the type of feeding practices between the three iron treatment groups. A similar percentage of infants in each group was exposed to foods other than breast milk.

Two women gave only top milk to their infants as they were employed and therefore did not find it feasible to

Table 4.41 Feeding practices of the infants at 3rd month and 6th month in the three iron treatment groups

Feeding Practices %		Group I	II	III
Age 3 m	N	21	16	13
Exclusively breastfed		90.0	88.0	85.0
Breast-fed + Top milk		9.5	12.5	7.7
Breastfed + Commercial baby food		0.0	0.0	7.7
Age 6 m	N	30	26	29
Exclusively breastfed (BF)		43.3	34.6	41.3
Continued to breastfeed and introduced other foods:		53.2	53.3	44.7
BF + TM		3.3	11.5	13.8
BF + Commercial baby food		3.3	3.8	0.0
BF + Tonic		6.7	23.1	0.0
BF + Tonic + Solids		10.0	3.8	3.4
BF + Solids		23.3	7.7	17.2
BF + TM + Solids		3.3	3.8	3.4
BF + TM + Tonic		3.3	-	6.9
Discontinued BF only top milk:				
Top milk only (TM)		0.0	3.8	3.4
TM + Solids		3.3	7.7	10.3

BF - Breast-fed
TM - Top milk

breastfeed the child. Commercial baby food was introduced to two other infants, but were given infrequently as it was expensive. Fortunately breast feeding of these infants was continued. The solid foods given were thin gruels, porridge, khichadi (rice and dal preparation), and roti in milk and biscuit.

None of the tonics given by the mothers to their infants contained iron as a component. Thus the feeding practices survey indicated that the proportion of infants in each group fed solid foods or other animal milk was similar and that none received iron from any extraneous sources.

Anthropometry

Height

Mean height of the infants at the third month was 59 cm in Group I, and 62 cm in Group II and Group III (Table 4.42). Male infants were taller than the female infants in all the treatment groups. However the female infants in Groups II and III were taller than the male infants in Group I.

At six months, heights of the male infants (Table 4.42) were found to be 2.8 and 3.4 cm more in Groups II and III compared to Group I. Heights of the female infants were also

Table 4.42 Height of the infants in the three iron treatment groups at 3 months and 6 months of age (mean ± SE)

Height (cm)	Groups I	II	III
Age 3 m			
All infants	59.56±0.91 (21)	62.01±1.05 (16)	62.16±0.96 (13)
Male	59.97±1.41 (11)	63.66±0.98 (8)	62.26±1.26 (5)
Female	59.11±1.19 (10)	63.35±1.72 (8)	62.10±1.42 (8)
Age 6 m			
All infants	62.81±0.78 (30)	65.00±0.39 (26)	66.18±0.93 (29)
Male	63.53±0.92 (16)	66.38±1.26 (15)	66.04±1.28 (18)
Female	61.99±1.3 (14)	64.40±1.53 (13)	66.40±1.33 (11)

Figures in parentheses number of infants.

t' values

	3m	6m
I vs II	1.76^{NS}	2.51^{*}
I vs III	0.105^{NS}	2.79^{NS}
II vs III	1.969^{NS}	1.17^{NS}

* Significant at $p < 0.05$

found to be different between the groups (62 cm, 64 cm, and 66 cm in Groups I, II and III respectively). The mean heights of the female infants in Group II and III were found to be higher than the mean height of the infants in Group I.

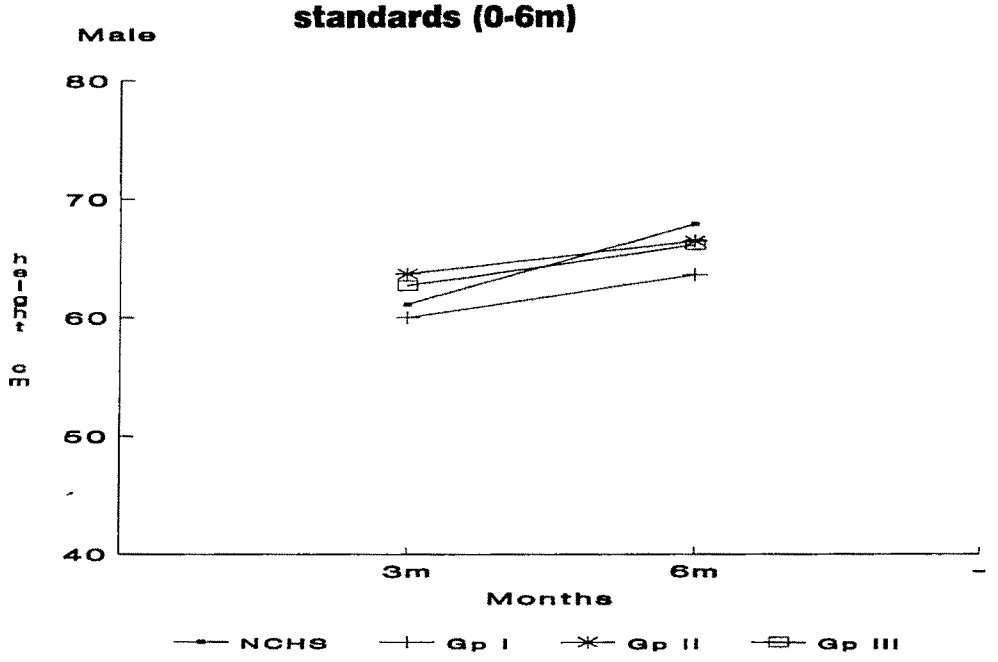
The mean heights of the infants at 3 months and 6 months of age in the three groups along with the NCHS standards are shown in Fig 4.17. The slope of the height curve for the infants in the present study was in general lower compared to the NCHS height curves. Among the male infants, the ones in Group II did better while among the female infants, the Group III was better. Though measurements were obtained only at two points, it is clear from the graph that the growth in height of the infants in the 60 mg group, both males and females, trailed behind that of the infants in 120 mg and 180 mg group.

Weight

Both male and female infants in the higher iron dose groups i.e. II and III weighed more than the infants in 60 mg group, at 3 months as well as at 6 months (Table 4.43).

Mean weights of the infants at the sixth month showed that infants in Group II weighed 470 g more than infants in Group I and 190 g more than infants in Group III. The female infants in Groups II and III had similar mean weight (6.82

Fig. 4.17 Growth pattern in height of the infants in comparison with NCHS standards (0-6m)



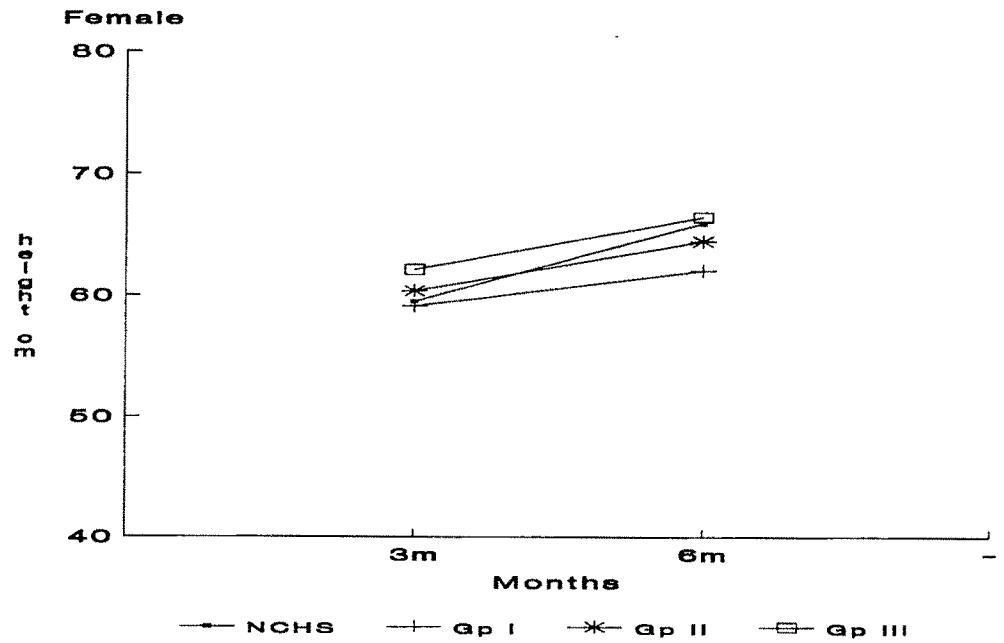


Table 4.43 Weight of the infants in the three iron treatment groups at 3 months and 6 months of age (mean ± SE)

Weight (Kg)	Groups I	II	III
Age 3 m			
All infants	5.22±0.21 (21)	5.58±0.20 (16)	5.35±0.24 (13)
Male - Birthweight	2.68±0.11	3.02±0.15	2.81±0.28
3rd month	5.49±0.24 (11)	6.11±0.25 (8)	5.45±0.36 (5)
Female-Birthweight	2.53±0.11	2.51±0.12	2.84±0.17
3rd month	4.92±0.33 (10)	5.05±0.18 (8)	5.29±0.33 (8)
Age 6 m			
All infants	6.46±0.20 (30)	6.93±0.22 (26)	6.84±0.19 (29)
Male - Birthweight	2.82±0.11	2.90±0.14	2.88±0.10
6th month	6.82±0.20 (16)	7.03±0.31 (13)	6.85±0.23 (18)
Female-Birthweight	2.58±0.11	2.56±0.10	2.77±0.15
6th month	6.05±0.33 (14)	6.82±0.31 (13)	6.82±0.35 (11)

Figures in parentheses number of subjects.

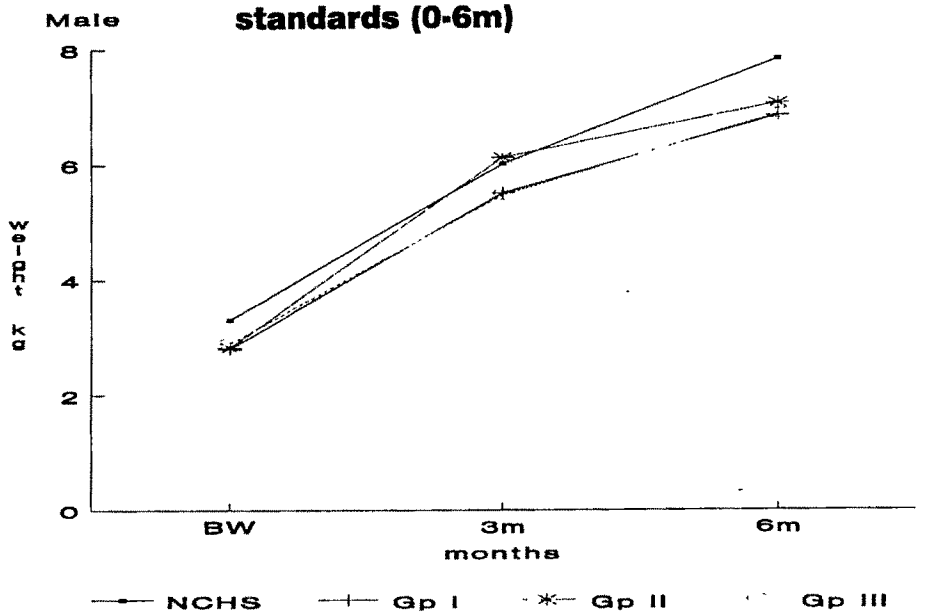
t' values

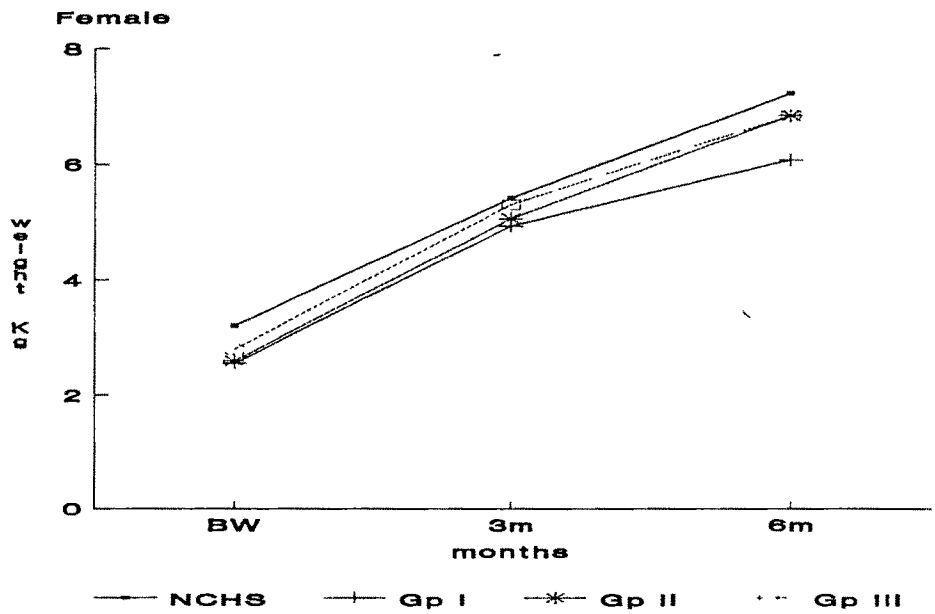
	3m	6m
I vs II	1.24^{NS}	1.58^{NS}
I vs III	0.41^{NS}	1.38^{NS}
II vs III	0.749^{NS}	0.31^{NS}

kg) at 6 months which was higher than the male infants of 6 months in Group I. These findings indicate a favourable outcome of higher level of iron supplementation during pregnancy on the heights and weights of the infants, with 120 mg dose level being as good as the 180 mg dose level as far as the growth responses were concerned. The 60 mg dose level was associated with lower height and weights at 3 months and 6 months.

Comparison of the weights of these infants at 3rd and 6th month with that of the NCHS standards revealed that the growth pattern of the male infants whose mothers were supplemented with 120 mg of iron followed closely the 50th percentile of the NCHS standards upto 3 months of age (Fig. 4.18) while that of 60 mg and 180 mg were below the NCHS standard. Between 3 months and 6 months growth rate was found to be lower than the NCHS standard. Weitht of the female infants in the 120 mg and 180 mg group closely followed the NCHS standards between 0-3 months and between 3-6 months. The female infants of 60 mg group also followed the NCHS between 0-3 months but faltered thereafter. An interesting observation was that the female infants seemed to benefit more from higher level of iron supplementation during pregnancy, a finding which will need to be confirmed.

Fig. 4.18 Growth pattern in weight of the infants in comparison with NCHS standards (0-6m)





Prevalence of Anemia and Hemoglobin Levels

Hb estimations were made only at 6 months, as the women were reluctant to allow the infants to be pricked earlier. The hemoglobin measurements carried out on the infants at the sixth month is represented in Table 4.44. Mean Hb of infants in Group II and III was higher than of infants in Group I, although the difference was found to be statistically significant only between Group I and Group II. Similar to the findings in mothers, at 6 months post-partum, a lower incidence of anemia was found in Group II (41.6%) and Group III (60%), compared to Group I (67.9%) which was much more marked for moderate anemia (8.3% and 16%) in Groups II and III compared to 50% in Group I (Table 4.44). Absence of severe anemia in all the treatment groups has significant implications for the growth and development of the infants.

Iron status of the mother has been shown to be closely associated with the iron status of the infant, as the fetus is reported to extract iron in proportion to maternal serum levels (Singla et al 1978). The effect of iron supplementation during pregnancy at different dose levels on the iron status of the infant has not been addressed adequately in therapeutic trials. Kuizon et al in Philippines (1980) and Zittoun et al in France (1983) did

Table 4.44 Mean Hb and prevalence of anemia in infants at 6 months of age in the three treatment groups (mean ± SE and %)

Infant Hb/ prevalence of anemia	Groups			t' values		
	I (28)	II (24)	III (25)	I vs II	I vs III	II vs III
Hb (g/dl)	10.22 ± .31	11.10 ± .26	10.94 ± .24	2.13*	1.64NS	1.44NS
Normal (11 g/dl)	32.1	58.3	40.0			
Mild (10-10.9 g/dl)	17.9	33.3	44.0			
Moderate (7-9.9 g/dl0	50.0	8.3	16.0		chi square*** 58.908	
Severe (7 g/dl)	0.0	0.0	0.0			
All cases - anemic	67.9	41.6	60.0			

*** Significant at p<0.001

not find any significant difference between the Hb levels of infants, whose mothers were supplemented with different levels of iron during pregnancy, and those supplemented with placebos. However, Sood et al in India (1975) found a small difference in the Hb of the infants between the placebo group (9.86 g/dl) and in the iron treated group (10.01-10.16 g/dl). Milman et al (1987) found that the serum ferritin of mothers recommended 200 mg of iron with folic acid and B_{12} during pregnancy corresponded to the serum ferritin levels of the 5 day old infants ($r = 0.36$). In India, Raman et al (1990) found that infants of mothers who were given 120 mg elemental iron per day for 100 days had higher serum ferritin at 6 months of age compared to infants of mothers who were not supplemented. These authors therefore concluded that iron supplementation during pregnancy conferred the benefit of higher iron stores to the infant at birth and later. The findings of the present study are consistent with the observations made by Raman et al (1990) as infants of mothers supplemented with higher dose levels of iron during pregnancy in this study were found to have higher Hb levels at 6 months of age post-natally.

As with several previous observations made in this study, the 120 mg and 180 mg dose levels run parallel as far as their effects on post-natal Hb levels are concerned and are more effective than 60 mg dose level.

Morbidity Profile

In view of the suggested relationship between anemia and morbidity, this study investigated the morbidity profile of the infants at 3 months and 6 months of age. It is important to recall here that exposure to any pathogenic agents was similar in all the three iron treatment groups, as a similar percent of infants were introduced to topmilk and solids on all three groups.

A clear trend towards reduced incidence of morbidity was found in infants whose mothers were supplemented with higher levels of iron during pregnancy (Table 4.45, Figs 4.19 and 4.20).

Mean days of morbidity in the first three month period although not significant was much lower in Group III 1.62, compared to Group I and II 2.7 (Table 4.45). The most common morbidity experienced was URI (23-29%), which occurred alone or with others (Fig 4.21). Only 31% of the infants had one or more incidence of morbidity in Group III, compared to 57% in Group I and 44% in Group II (Fig 4.19) which was significantly different.

Morbidity between the third and sixth month showed that significantly higher percent of the infants in Group I, 70%, had one or more morbidities compared to 50% in Group II and

Table 4.45 Morbidity profile of the infants in the three iron treatment groups

Morbidity		Groups I	II	III
Age 3 m	N	21	16	13
Percent with morbidity		57.3	43.9	30.8
Percent without morbidity		42.7	56.2	69.2
Mean days of morbidity		2.76±0.85	2.75±0.91	1.62±0.89
Age 6 m	N	30	26	29
Percent with morbidity		70.0	50.0	44.8
Percent without morbidity		30.0	50.0	55.2
Mean days of morbidity		4.67±1.11	2.85±0.76	1.79±0.48

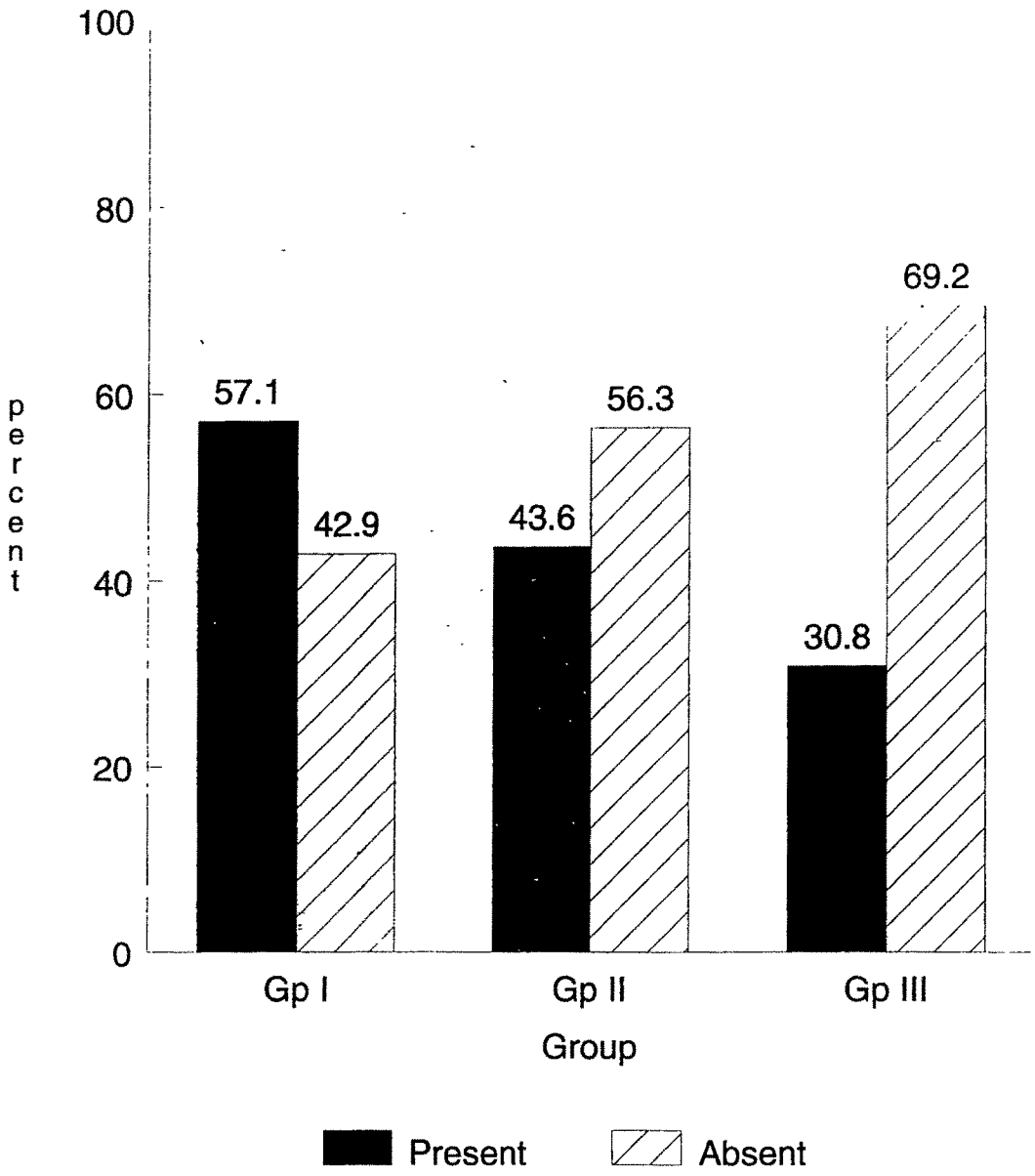
Mean days of morbidity

t' values

	3m	6m
I vs II	0.008^{NS}_{NS}	1.35^{NS}_{*}
I vs III	0.93^{NS}_{NS}	2.38^{NS}_{NS}
II vs III	0.89^{NS}	1.31^{NS}

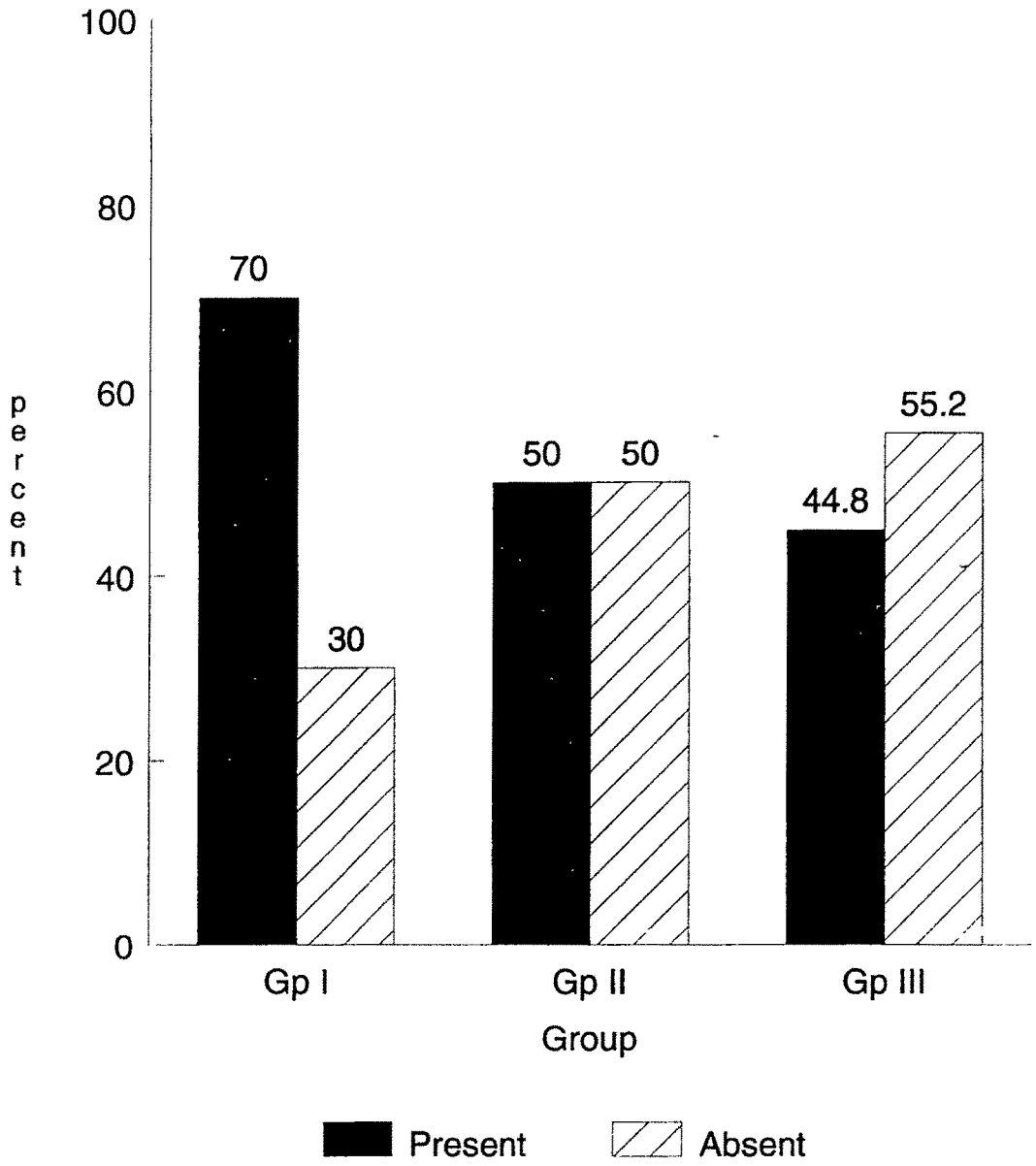
* Significant at $p < 0.05$

Fig. 4.19 Presence or absence of morbidities among infants in the three iron treatment groups (0-3m)



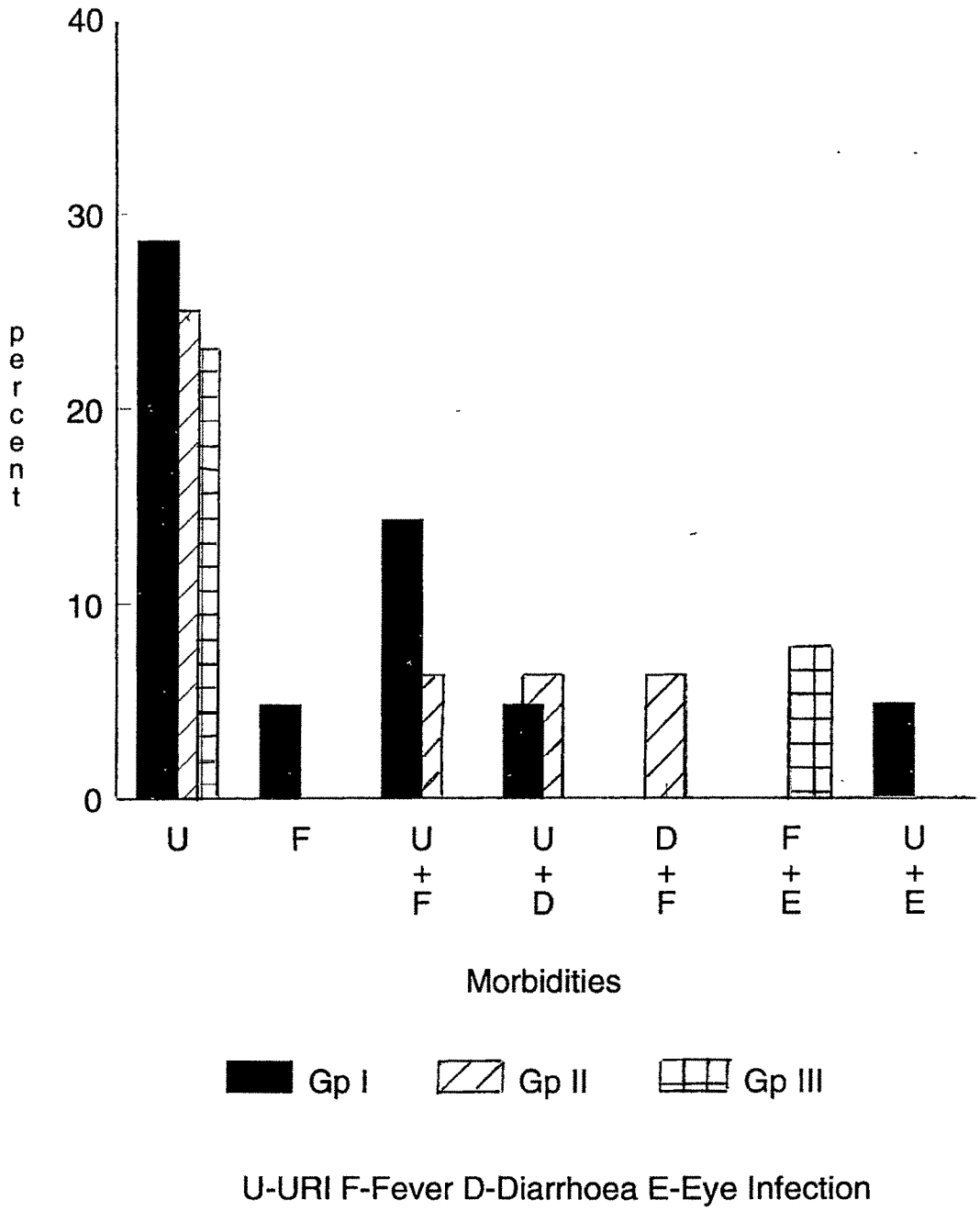
Chi square 14.06* P < 0.05

Fig. 4.20 Presence or absence of morbidities among infants in the three iron treatment groups (3-6m)



Chi square 14.29* P< 0.05

Fig. 4.21 Types of infectious morbidities among infants in the three iron treatment groups (0-3m)



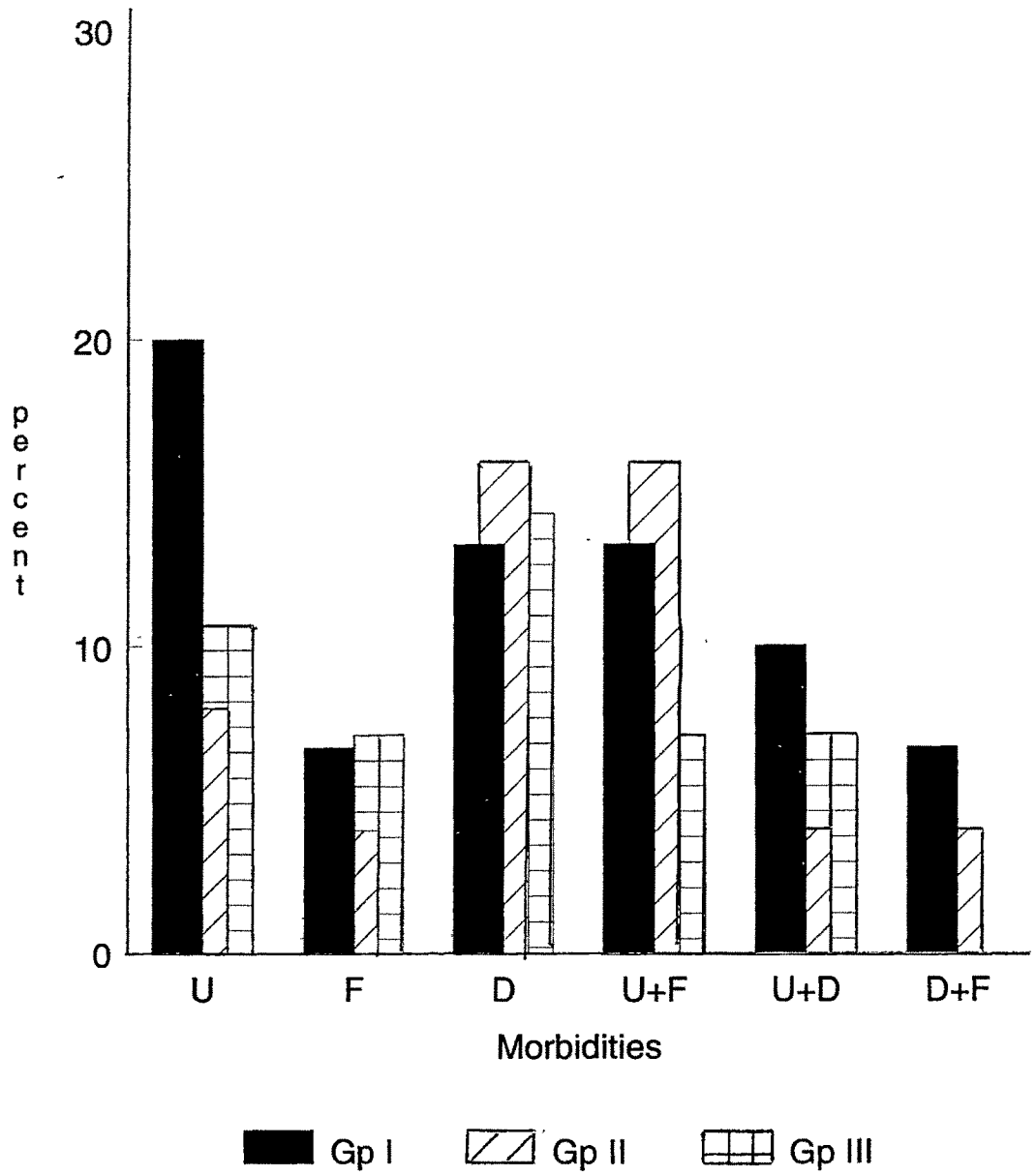
45% in Group III (Table 4.45 and Fig 4.20). Incidence of URI, diarrhoea, and fever were found to be the highest (Fig 4.22).

Mean days of morbidity of the infant as reported by the mother was lowest for Group III (1.8 days), followed by 2.9 days for Group II, and 4.7 days for infants in Group I, the differences being statistically significant between Groups I and III.

During the follow up study subjective reports of the mothers tallied with the above findings. Some of the mothers from the higher dose level groups observed that these infants were healthier than their siblings. Their perception of "health" meant absence of illness, adequate weight gain, and a child who had a good appetite and played actively.

Lower incidence of fever, respiratory and gastrointestinal infections have been found in term and preterm infants supplemented with iron (Andelman and Sered 1966, MacKay 1928). However studies which have followed up the morbidity profile of infants born to mothers supplemented with iron during pregnancy are not available in the literature. The present study indicates a pronounced beneficial effect in the morbidity profile of infants supplemented with higher levels of iron as indicated by lowered mean episodes, and lower mean days of morbidity during the six month follow up.

Fig. 4.22 Types of infectious morbidities among infants in the three iron treatment groups (3-6m)



U-URI F-Fever D-Diarrhoea