

A Community-Based Trial on The Comparison of Efficacy, Safety and Cost Effectiveness of Ferrous Sulphate and Ferrous Ascorbate for Anaemia in Pregnancy In Madhya Pradesh, India

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ABSTRACT

Background: Anaemia has significant impact on health of the fetus as well as that of mother. Increased need of iron during pregnancy especially after 2nd trimester makes iron supplementation mandatory. Ferrous ascorbate is known to exist intact inside the gastrointestinal tract due to the stable chelation of iron with ascorbate. This compound does not dissociate due to any of the food inhibitors. The aim is to study the effectiveness of Ferrous Ascorbate and Ferrous sulphate in terms of compliance and cost effectiveness of management of anaemia in pregnancy.

Methodology: Study design: Quasi Experimental study, Study area: District Vidisha, Study participants: Pregnant women of first trimester registered during the study period in the selected Anganwadis/ Gram Arogya Kendra (GAK), Sample size: 240 antenatal mothers.

Results: Baseline mean haemoglobin was 11.31±1.05 gm/dl. The mean increase in Ferrous Sulphate was 0.55 gm/dl, and in Ferrous ascorbate was 1.27 gm/dl. Ferrous Sulphate was less compliant than Ferrous ascorbate, and has higher efficacy and lesser side effects. Only Rs. 10.2 additional cost per antenatal mothers for increase of ≥1gm% in Hb will be borne by government if Ferrous Sulphate is replaced by Ferrous Ascorbate.

Conclusions: Study results show statistically significant difference in rise of haemoglobin amongst the antenatal mothers consuming Ferrous ascorbate over Ferrous Sulphate.

Key words: Ferrous ascorbate, Ferrous Sulphate, Oral iron supplementation, Antenatal mothers, Cost effective analysis

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INTRODUCTION

Iron deficiency is a major problem worldwide in women of all age groups but especially in reproductive age. Anaemia has a substantial impact on both the fetus and the mother's health. Increased need of iron during pregnancy especially after 2nd trimester makes iron supplementation mandatory.¹ Both Oral and parenteral iron preparations are used in prevention and treatment of anaemia but Oral iron preparations are preferred to treat mild to moderate iron deficiency anaemia. Oral iron preparations include Ferrous Sulphate, Fumarate, succinate while newer preparations include Ferrous ascorbate.²⁻⁵

Ferric forms of iron are poorly soluble in alkaline solutions and hence they have to be transformed into Ferrous forms before they are absorbed.⁶ The oral route is preferred to replace iron stores and mild to moderate iron deficiency anaemia are treated using oral iron supplements³. Bivalent iron salts, such as Ferrous Sulphate, Ferrous fumarate, and Ferrous gluconate, are more commonly employed in clinical practice than Ferric iron forms.⁷

The Ferrous form of iron offers therapeutic benefits over the ferric type.⁸ None of the dietary inhibitors cause this molecule to dissociate. Iron gets absorbed easily in vivo from Ferrous ascorbate than from Ferrous Sulphate.⁹ Also, a recent study reported that behaviour problems and low intelligence were significantly high among anaemic children and that children with iron deficiency anaemia (IDA) were more prone to low attention and being hyperactive.¹⁰

In the year 2015-16 a committee was formed in National Health Mission, Madhya Pradesh (NHM MP) where the consumption and compliance of IFA (Ferrous Sulphate) was evaluated in the entire state of Madhya Pradesh according to NFHS 4 data. It was concluded by committee members that the consumption and compliance was low and it should be replaced with a better Ferrous salt. Hence the guidelines were made in the state that those females who show less compliance with Ferrous Sulphate should be shifted to Ferrous ascorbate (then chosen IFA for replacement). To study whether there was any difference in consumption and compliance with Ferrous ascorbate after implementation of guidelines, a research proposal was made to observe the difference in an aspirational district of Madhya Pradesh namely Vidisha, with the objective to study the effectiveness of Ferrous Sulphate and Ferrous Ascorbate in management of anaemia in pregnancy, to evaluate the compliance of pregnant women towards oral iron therapy and to study the cost effectiveness of Ferrous Sulphate and Ferrous Ascorbate.

METHODOLOGY

A Quasi Experimental study under the guidance of NHM, MP was conducted in aspirational district Vidisha of MP from December 2020 till December 2021.

Pregnant females of first trimester were registered during the study period in Anganwadi Centers (AWC)/ Gram Arogya Kendra (GAK) which are village level health unit for universal health coverage. Pregnant females with Hb >9 gm/dl; Gestational period of <12 weeks and who have not started iron tablets of randomly selected GAK or villages were enrolled in the study.

Pregnant females with Hb <9 gm/dl, antenatal women who were started on IFA supplementation, history/diagnosis of any other forms of anaemia, chronic GI illnesses and patients on IV Iron or with a history of recent blood transfusion were excluded from the study.

$$\text{Sample size formula: } n = \frac{2S_p^2[Z_{1-\alpha/2} + Z_{1-\beta}]^2}{\mu_d^2},$$

$$S_p^2 = \frac{S_1^2 + S_2^2}{2}$$

where S_1^2 =Standar deviation in the first group, S_2^2 =Standar deviation in the second group, μ_d^2 =Mean difference between the samples, α - Level of Significance, $1-\beta$ - Power

Sample size: The sample size was calculated based on a study⁽⁶⁾, in which mean increase in Hb in group I (ascorbate group) was 12.4 ± 0.5 and mean increase in Hb in group II (Sulphate group) was 12.2 ± 0.7 . With taking Alpha error 5% and power 90%, a sample size of 194 was estimated. Ten percent was added considering lost to follow up and another 10% added considering non-respondents. The sample size came out to be $239=240$. The expected number of first trimester pregnant females in each AWC\GAK was around 1-3 in number (average 2). Thus, 120 AWC\ GAK were covered to complete the sample. Out of these 120 AWC\GAKs was equally divided into six blocks of the district i.e., 17 Anganwadi centers per block, covering 40 first trimester pregnancies per block and were selected using lottery method. Study plan: Two teams comprising of two investigators (1 faculty and 1 PG) had visited the study area which constituted of one baseline and four follow up rounds, starting from tracking the antenatal mother from third month to seventh month. In the first visit enrolment of antenatal mothers was done in their respective Anganwadi centre and baseline haemoglobin was taken using HemoCue device and other socio demographic variables were recorded and oral Ferrous Sulphate (60mg elemental iron) was distributed for one month. Hb levels were recorded on each follow up which was done monthly, and were compared with the Hb value of previous month. The antenatal mothers who were compliant to Ferrous Sulphate and showed rise in Hb >1gm% were continued on Ferrous Sulphate, and were followed up till 7th month of pregnancy. If no improvement in the Hb level i.e., <1gm/dl was observed, they were shifted to Ferrous ascorbate, in every follow-up. The compliance of Ferrous ascorbate was assessed by taking in-

to consideration that out of 30 at least 25 days IFA was consumed. If still no improvement was observed the participants was referred for IV iron sucrose and blood transfusions. During the follow up, participants were advised to report immediately if there were any adverse effects, like nausea, vomiting, metallic taste, constipation and diarrhoea. Information regarding compliance and reasons for non-compliance if any was also obtained from study participants and was evaluated. Subsequently 1st follow up was done in 4th month of pregnancy, 2nd follow up was done in 5th month of pregnancy, 3rd follow up in the 6th month and 4th follow up will be done in 7th month of pregnancy. Descriptive analysis was done by comparing the rise in haemoglobin in each group and calculating mean haemoglobin changes in each follow up. Cost effectiveness and net utilization for both the drugs was assessed. Informed signed consent was obtained from the study participants after explaining the nature and purpose of study and ensuring confidentiality and privacy. Participants

were informed the right to abstain from research at any point of time. Permission from Institutional Ethics Committee with Ethics Committee Registration no.ECR/1055/INST/MP/2018EC/NEW/INST/2020/98 9 was taken for conducting this research, approval letter no: 24001/MC/IEC/2020 dated 5.10.2020.

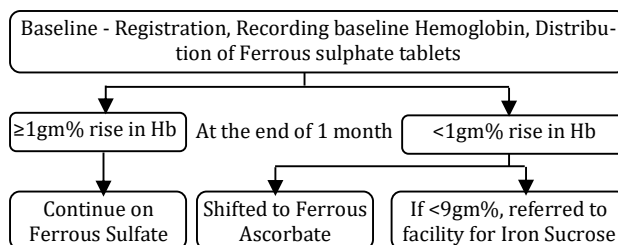


Figure 1: showing the criteria of shifting the participants from Ferrous Sulphate to Ferrous ascorbate in each follow up

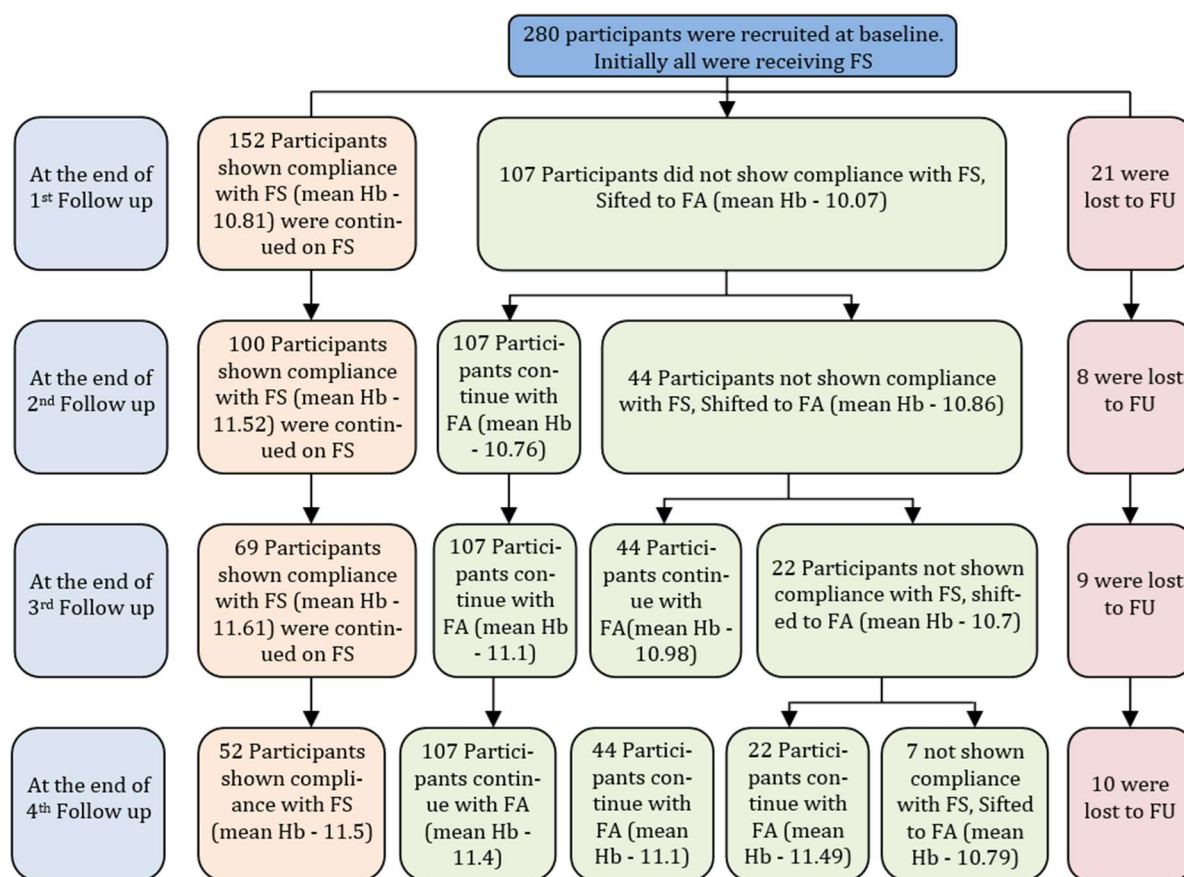


Figure 2: showing the detailed study process with number of participants recruited at baseline and further shifting to Ferrous Sulphate and Ferrous ascorbate with their respective mean Hb in parenthesis in subsequent follow ups (blue colored showing the Ferrous Sulphate (FS), red color showing the Ferrous ascorbate (FA) and green color depicts the lost to follow up (FU)

RESULTS

Table 1 shows the socio-demographic profile of the antenatal mothers. Majority of the antenatal mothers belong to the age group of 21-25 years (57.33%),

were Hindu by religion (92.67%) and 69.39% of them were housewives. Most of them were educated up to middle school (42.67%) and about 17.24% were illiterate. Around 61% of antenatal mothers belonged to lower middle class.

Table 1: Socio-demographic profile of the antenatal beneficiaries (n=232)

Variable	Frequency (%)
Age (in years)	
≤20	51 (21.98)
21-25	133 (57.33)
26-30	40 (17.24)
> 30	8 (3.45)
Religion	
Hindu	215 (92.67)
Muslim	17 (7.33)
Sikh	0 (0)
Christian	0 (0)
Education	
Illiterate	40 (17.24)
Primary	22 (9.48)
Middle	99 (42.67)
High School	51 (21.98)
High Secondary	18 (7.76)
Graduate	1 (0.43)
Post Graduate	1 (0.43)
Occupation	
House wife	161 (69.39)
Others	72 (31.03)
Gravida	
Primi	89 (38.36)
Multi	143 (61.63)
Type of housing	
Kachha	123 (53.02)
Semi Pucca	51 (21.98)
Pucca	58 (25)
Socio-economic status	
Lower	29 (12.5)
Lower middle	142 (61.2)
Middle	38 (16.4)
Upper middle	23 (9.9)
Total	232 (100)

Table 2 shows, at the beginning of the study, baseline haemoglobin was found to be in normal range in 48.3% of the antenatal mothers, 39.2% mothers had mild anaemia and 12.5% were in moderate range. At

the end of the final follow up the proportion remarkably increased in normal range amongst 74.13% of antenatal mothers.

Figure 3 shows the pattern of consumption of FA and FS along with loss to follow up (LFU). There has been substantial decrease in consumption of Ferrous Sulphate over the subsequent follow-ups, from 280 (100%) consumers in baseline it curtailed to 52 (21.48%) antenatal mothers consuming FS, whereas there was consecutive increment in antenatal mother who consumed FA. Starting with 107 (38.21%) antenatal mothers consuming FA in first follow-up, the total antenatal on FA in final follow-up rose up to 180 (74.38%). Total loss to follow-up at the end of the study was 48 (17.14%) antenatal mothers. The most common reason for lost to follow up was that the participant went to maternal home, in few cases there were miscarriage and abortions.

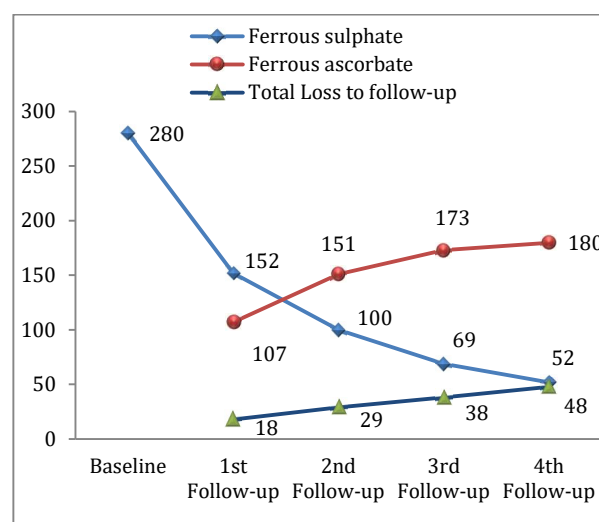


Figure 3: Distribution of antenatal mothers on FS, FA and total LFU in each follow-up (n)

Table 2: Anaemia as per classification in Antenatal mothers during follow up

Classification of Anemia	Baseline (%)	1st follow-up (%)	2nd follow up (%)	3rd follow up (%)	Final follow up (%)
Normal (≥11gm %)	112 (48.3)	120 (51.7)	143(61.63)	146(62.93)	172(74.13)
Mild (10-10.9gm %)	91 (39.2)	71 (30.6)	65(28.01)	69(29.74)	50(21.55)
Moderate (7.1-9.9gm %)	29 (12.5)	41 (17.7)	24(10.34)	17(7.32)	10(4.31)
Total	232 (100)	232 (100)	232 (100)	232 (100)	232 (100)

1st Follow-up: at the end 4th month of Gestational period; 2nd Follow-up: at the end 5th month of Gestational period; 3rd Follow-up: at the end 6th month of Gestational period; Final follow-up: at the end 7th month of Gestational period

Table 3: Change in mean Haemoglobin (gm/dl) level during subsequent visits (gm/dl)

Iron preparation	Hb (gm/dl) - Mean ± SD					Overall rise in mean Hb per month	Difference in Hb recorded in last FU from baseline
	Baseline	1 st FU	2 nd FU	3 rd FU	4 th FU		
Ferrous Sulphate	11.31±1.05	11.81±0.73	11.52±0.82	11.61±0.83	11.5±0.68		
Mean difference		0.86	-0.29	0.09	-0.11	0.55/4=0.13	0.55
Ferrous Ascorbate		10.07±0.75	10.76±0.94	11.04±0.78	11.33±0.83		
Mean difference			0.69	0.28	0.3	1.27/3=0.42	1.27

FU - Follow up; SD- Standard Deviation

Table 4: Correlation between iron preparations and Haemoglobin during final follow up (n=232)

Final follow up	<11 gm/dl (%)	>11 gm/dl (%)
Ferrous Sulphate	6 (2.58)	46 (19.82)
Ferrous Ascorbate	73 (31.46)	107 (46.12)

χ^2 15.127; p-value <0.001 (significant)

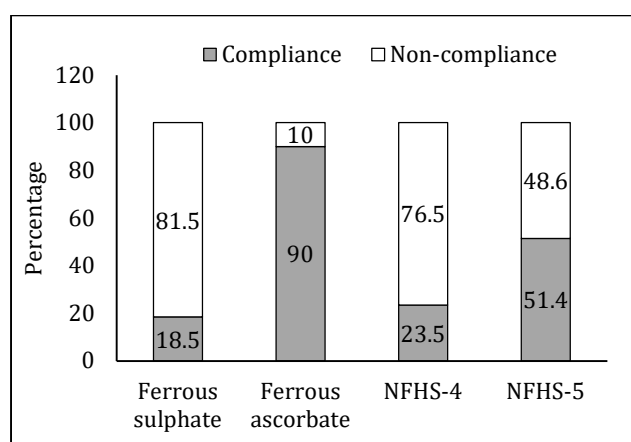


Figure 5: Comparison of compliance in study with NFHS data

Table 3 illustrates change in mean haemoglobin level during subsequent visit due to Ferrous Sulphate and Ferrous Ascorbate from 12 weeks to 28 weeks of gestation. Baseline mean haemoglobin of antenatal mothers was found to be 11.31 gm/dl. Antenatal mothers who consumed Ferrous Sulphate tablet for 4 months resulted in rise of mean haemoglobin by 0.55 gm/dl from baseline to final visit. Whereas antenatal mothers who consumed Ferrous ascorbate tablet for only 3 months showed rise of mean haemoglobin by 1.27 gm/dl from baseline. Ferrous ascorbate is effective in increase in haemoglobin than Ferrous Sulphate.

Table 4 shows significant statistical difference in haemoglobin in final follow up in those consuming Ferrous Sulphate than those consuming Ferrous

ascorbate, with p value <0.01.

Figure 4 shows proportional distribution of compliance and side effects amongst antenatal mother for both Iron preparations.

Figure 5 Shows comparison of compliance of different IFA with NFHS 4 and NFHS 5 data. The study findings showed that Ferrous Sulphate was found to be less compliant (18.5%) as compared to Ferrous ascorbate (90%) which had a better compliance, has higher efficacy and lesser side effects in benefit of antenatal mothers.

Consumption of iron folic acid has increased from 23.5% (NFHS-4) to 51.4% (NFHS-5) i.e., overall, 27% increase, ranking third in the country after West Bengal (34%) and Chandigarh (29%). This might be the outcome of distribution Ferrous ascorbate in different districts of Madhya Pradesh, implying that the compliance is remarkably better with Ferrous Ascorbate.^{11,12}

Cost Effective Analysis

Cost effective Analysis is a type of economic evaluation that compares the costs and outcomes of health programs or treatments when the interventions have a common health outcome but differ in effectiveness. The cost-effectiveness ratio (CER) or the cost per unit of benefit of the health care intervention (e.g., medicine A) is compared with the alternative intervention (e.g., medicine B).^{13,14}

Cost of one tablet of FA is Rs. 0.81 therefore cost of 90 tablets is Rs.72.9 and cost of one tablet of FS is Rs. 0.13 hence cost of 90 tablets of FS is Rs. 11.7.

Taking haemoglobin level of 14 gm/dl as 100 percent level achieved, change in mean Hb due to Ferrous ascorbate is 1.27 gm/dl which is about 9 percent increase in haemoglobin. While change in mean Hb due to Ferrous Sulphate is 0.42 gm/dl which is 3 percent increase in Hb.

Table 5: Complaints of Antenatal mothers during consumption of Ferrous Sulphate and Ferrous Ascorbate in each follow up (FU) (n=232)

Complaints#	1st FU		2nd FU		3rd FU		Final FU	
	FS (%)	FA (%)	FS (%)	FA (%)	FS (%)	FA (%)	FS (%)	FA (%)
Nausea	62 (26.7)	0	44 (18.9)	11 (4.7)	19 (8.1)	15 (6.4)	29 (12.5)	1 (0.4)
Vomiting	55 (23.7)	0	37 (15.9)	7 (3)	20 (8.6)	6 (2.5)	22 (9.4)	0
Gastritis	36 (15.5)	0	48 (20.7)	9 (3.8)	43 (18.5)	13(5.6)	4 (1.7)	2 (0.8)
Metallic taste	35 (15)	0	41 (17.7)	7(3)	38 (16.3)	10(4.3)	26 (11.2)	8 (3.4)
Constipation	12 (5.2)	0	20 (8.6)	3 (2)	27 (11.6)	6 (2.5)	12 (5.1)	5 (2.1)
Dark stools	30 (12.9)	0	40 (17.2)	0	36 (15.5)	2 (0.8)	17 (7.3)	2 (0.8)
No complaint	35 (15.1)	0	11 (4.7)	81 (34.9)	8 (3.4)	143 (61.6)	7 (3)	171 (73.7)

#Multiple responses; FU – Follow up; FS – Ferrous Sulphate; FA – Ferrous Ascorbate

Table 6: Cost-Effective Analysis of Ferrous Ascorbate and Ferrous Sulphate

	Ferrous ascorbate	Ferrous Sulphate
Total cost of tablets (90 days)	90x 0.81 =INR72.9	90x0.13 =INR 11.7
Benefit of drug {change in mean Hb(gm%) over period of 90 days}	1.27	0.42
Proportional change in Hb (%)	9	3
Average Cost-Effective Ratio (ACER)	72.9/9=8.1	11.7/3=3.9

Table 6 describes the average cost-effectiveness ratio for Ferrous ascorbate and Ferrous Sulphate is Rs. 8.1 and Rs. 3.9 per 1% rise in Hb, respectively.

The incremental cost per extra antenatal mothers with $\geq 1\%$ increase in Hb (gm%) is calculated as;⁽¹⁴⁻¹⁷⁾

Incremental Cost-Effective Ratio

$$ICER = \frac{\text{Cost of Drug A} - \text{Cost of Drug B}}{\text{Benefit of Drug A} - \text{Benefit of Drug B}} = \frac{72.9 - 11.7}{9 - 3} = 10.2$$

Extra cost per antenatal mothers for $\geq 1\%$ increase in Hb with Ferrous ascorbate in comparison to Ferrous Sulphate: Rs. 10.2/- if consumed for 90 days.

Net utilization (Figure 6)

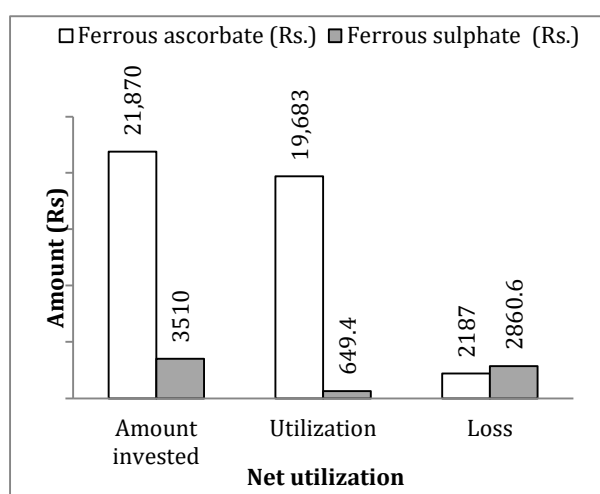


Figure 6: Comparison of net utilization and net loss according to compliance of iron salts for 100 antenatal women

Ferrous Sulphate:

Number of tablets required in one pregnancy is 270, cost of 1 Ferrous Sulphate tablet is 0.13/- therefore cost of Ferrous Sulphate tablets for 100 ANC will be = $100 \times 270 \times 0.13 = \text{Rs. } 3510/-$

Non-compliance according to our study for Ferrous Sulphate is 81.5%. Hence, loss due to non-compliance is Rs. 2860.6/- and amount utilized is $3510 - 2860 = \text{Rs. } 649.4/-$

Ferrous ascorbate:

Number of tablets required in one pregnancy is 270, cost of 1 Ferrous Ascorbate tablet is Rs. 0.81/- therefore cost of Ferrous Ascorbate tablets for 100 ANC will be = $100 \times 270 \times 0.81 = \text{Rs. } 21870/-$

Non-compliance according to our study for Ferrous Ascorbate is 10%.

Hence loss due to non-compliance is Rs. 2187/- and amount utilized is $21870 - 2187 = \text{Rs. } 19683/-$

DISCUSSION

In the present study, majority 57.33% of the antenatal mothers belonged to the age group of 21-25 years, 92.67% were Hindu by religion and 69.39% of them were house wives. Most of them were educated up to middle school (42.67%). The major source of drinking water for the household was common hand pump (51.29%). Most of them (61.2%) belonged to lower middle class.

The baseline hemoglobin among the 48.3% antenatal mothers was in normal range, 39.2% mothers had mild anemia and 12.5% were in moderate range. Baseline mean hemoglobin of antenatal mothers was found to be 11.31 gm/dl. Antenatal mothers who consumed Ferrous Sulphate tablet for 4 months resulted in rise of mean hemoglobin by 0.55 gm/dl from baseline to final visit. Whereas antenatal mothers who consumed Ferrous Ascorbate tablet for only 3 months showed rise of mean hemoglobin by 1.27 gm/dl from baseline. According to this study finding Ferrous Ascorbate was found to be more effective in increasing the hemoglobin in comparison to Ferrous Sulphate. The results of this study were similar to the study conducted by **Eesha A et. al**¹⁸ where those who were given Ferrous ascorbate revealed significant rise in Hb (1.569 gm %) which was greater than Ferrous Fumarate (1.097 gm %) and Iron polymaltose complex (0.48 gm %). Another study conducted by **Mistry N et. al**¹⁹ observed a significant increase in hemoglobin in both Ferrous Sulphate (9.129 ± 1.098 gm/dl) and Iron Peptone + Ferrous Ascorbate groups (9.490 ± 1.909 gm/dl). The rise in hemoglobin is more with Ferrous ascorbate than with Ferrous Sulphate because of better bioavailability and lesser side effects of Ferrous ascorbate.

Berber I et al⁸ observed that with the Ferrous preparation, women with IDA who received oral ferric protein succinylate tablets (n = 30) and Ferrous glycine Sulphate tablets (n = 34) for three months saw higher mean Hb (0.95 vs 2.25 g/dL) and hematocrit (2.62 vs 5.91%) levels.

Major complaints reported by participants in this study were nausea, vomiting, gastritis and metallic taste followed by dark stools and constipation. The complaints were more amongst antenatal mothers consuming Ferrous Sulphate as compared to Ferrous Ascorbate. Similar findings were observed by **Kriplani A et al**²⁰ a comparative evaluation of Ferrous sulfate (100 mg), fumarate (100 mg), ascorbate (100 mg), sodium feredetate (33 mg), and Ferrous bisglycinate (30 mg) in antenatal women, maximum side effects were reported with Ferrous fumarate (51 AEs) followed by Ferrous sulfate (40 AEs), Ferrous bisglycinate (26 AEs), Ascorbate (18 AEs), and sodium feredetate (10 AEs). **Langstaff et. al**²¹ were majority of events were gastrointestinal in nature: constipation was reported in 11% in the standard FS group and abdominal pain in 18%. **Mistry N et. al**¹⁹ also reported similar finding that the most common

side effects were nausea (31.9%), followed by constipation (27.6%) and heart burn (25.5%). Others like metallic taste, vomiting, headache and epigastric pain were less common. The evidence of good efficacy and excellent safety and tolerability of Ferrous Ascorbate can be attributed to chemical state including a better bioavailability and utilization of iron. In the Ascorbate preparation, iron is maximally absorbed due to: inhibition of conversion of Ferrous into ferric ion, leading to better absorption, inhibition of the effect of phytates, phosphates and oxalates on iron absorption and inhibition of formation of insoluble iron complexes that interfere with absorption.^{22,23}

All of this leads to better absorption and less free radical generation and also prevention of conversion of Ferrous to ferric state and hence better tolerability than other forms of iron salts. This ultimately leads to less gastrointestinal side effects. If still not tolerated, it can be given with food.

Present study findings showed that Ferrous Sulphate was found to be less compliant (18.5%) as compared to Ferrous Ascorbate (90%), the reason for better compliance with Ferrous Ascorbate is lesser side effects as observed by antenatal mothers with this drug. Consumption of iron folic acid in Madhya Pradesh has increased from 23.5% (NFHS-4) to 51.4% (NFHS-5). Overall, 27% increase in IFA consumption in MP, ranking third in the country after West Bengal (34%) and Chandigarh (29%). This increased consumption of IFA in MP, is the outcome of distribution Ferrous Ascorbate in aspirational districts of Madhya Pradesh, implying that the compliance is remarkably better with Ferrous Ascorbate.

Cost effective analysis was demonstrated considering both health results (rise in Hb) and the cost for medical care. Extra cost per antenatal mothers for ≥ 1 gm% increase in Hb with Ferrous Ascorbate in comparison to Ferrous Sulphate: Rs. 10.2/- if consumed for 90 days. As observed by **Panchal PJ et. al**²⁴, the mean total cost of therapy in patients treated with Ferrous Ascorbate group was Rs. 1269.6/- and in Ferrous Sulphate group was Rs. 409.7/-. **Esha A et. al**¹⁸ reported that the average cost-effectiveness ratio (ACER) of Iron polymaltose complex, Ferrous Fumarate, Ferrous Ascorbate was Rs. 281.12/-, Rs. 60.16/- and Rs. 184.21/- per increase in Hb gm%.

However study conducted by **Murugesan et. al**²⁵ observed the average cost effectiveness ratio, with respect to Group 1 (Ferrous Sulfate), Group 2 (Ferrous Ascorbate), Group 3 (Ferrous Fumarate), and Group 4 (Inj. Iron Sucrose), is Rs. 675, Rs. 1782.9, Rs. 1110.7, and Rs. 786.7 per increase in Hb%, respectively. Thus, Ferrous sulfate can be considered as cost effective with a cost effectiveness ratio of Rs. 675 per % increase in hemoglobin.

With better adherence and rise in mean Hemoglobin among Ferrous Ascorbate consumers will go a long way in decreasing dependency on parenteral iron.

The benefits will be weighed in terms of reduced out of pocket expenditures, travel costs of patients, wage loss and facility load.

Cost of treatment incurred by health system per month is two times higher with Ferrous Ascorbate as compared to Ferrous Sulphate. However, Ferrous Ascorbate might be costly but, the net benefit is more in comparison to Ferrous Sulphate. Hence introduction of Ferrous Ascorbate is a good option for antenatal mothers, which has better compliance, higher efficacy and lesser side effects.

CONCLUSION & RECOMMENDATIONS

The present study concluded that the Ferrous ascorbate is a better choice for oral iron supplement in the treatment of iron deficiency anemia in the antenatal mothers as compared to Ferrous Sulphate. Study results shows difference in rise of hemoglobin amongst the antenatal mothers consuming Ferrous Ascorbate over Ferrous Sulphate. Ferrous Sulphate had more side effects. Ferrous Ascorbate was better tolerated but more expensive as compared to Ferrous Sulphate.

Compliance with IFA is the most important measure to reduce anaemia burden in the community, as these findings show that ensuring compliance with IFA tablets reduces the prevalence of anemia. It is also evident that side effects of Ferrous Sulphate are very common and pregnant women show poor compliance with Ferrous Sulphate in comparison to Ferrous Ascorbate so it is recommended that non-compliant antenatal mothers get Ferrous Ascorbate and this intervention should be scaled up in the remaining districts of Madhya Pradesh and other states.

With better adherence and rise in mean Hemoglobin among Ferrous Ascorbate consumers will go a long way in decreasing dependency on parenteral iron. The benefits will be weighed in terms of reduced out of pocket expenditures, travel costs of patients, wage loss and facility load. Cost of treatment incurred by health system per month is two times higher with Ferrous Ascorbate as compared to Ferrous Sulphate. However, Ferrous Ascorbate might be costly but, the net benefit is more in comparison to Ferrous Sulphate. Hence introduction of Ferrous Ascorbate is a good option for antenatal mothers, which has better compliance, higher efficacy and lesser side effects.

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REFERENCES

- Saha L, Pandhi P, Gopalan S, Malhotra S, Saha PK. Comparison of efficacy, tolerability, and cost of iron polymaltose complex with Ferrous sulphate in the treatment of iron deficiency anemia in pregnant women. *MedGenMed Medscape Gen Med*. 2007 Jan 2;9(1):1.
- Antenatal iron supplementation [Internet]. [cited 2023 Feb 7]. Available from: <https://www.who.int/data/nutrition/nlis/info/antenatal-iron-supplementation>
- World Health Organization. Guideline: daily iron and folic acid supplementation in pregnant women [Internet]. Geneva: World Health Organization; 2012 [cited 2023 Feb 7]. Available from: <https://apps.who.int/iris/handle/10665/77770>
- World Health Organization. Guideline: Intermittent iron and folic acid supplementation in non-anaemic pregnant women [Internet]. Geneva: World Health Organization; 2011 [cited 2023 Feb 7]. Available from: <https://apps.who.int/iris/handle/10665/75335>
- Global nutrition monitoring framework: operational guidance for tracking progress in meeting targets for 2025 [Internet]. [cited 2023 Feb 7]. Available from: <https://www.who.int/publications-detail-redirect/9789241513609>
- Iron Deficiency and Other Hypoproliferative Anemias | Harrison's Principles of Internal Medicine, 21e | AccessMedicine | McGraw Hill Medical [Internet]. [cited 2023 Feb 6]. Available from: <https://accessmedicine.mhmedical.com/content.aspx?bookid=3095§ionid=263547538>
- Santiago P. Ferrous versus ferric oral iron formulations for the treatment of iron deficiency: a clinical overview. *Sci World J*. 2012;2012.
- I B, H D, Ma E, I A, E K, I K. Evaluation of ferric and Ferrous iron therapies in women with iron deficiency anemia. *Adv Hematol* [Internet]. 2014 [cited 2023 Feb 7];2014. Available from: <https://pubmed.ncbi.nlm.nih.gov/25006339/>
- [cited 2023 Feb 7]. Available from: <http://pharmaceuticalcompanyindia.in/advantages-of-Ferrous-ascorbate-on-other-forms-of-iron-salts/>
- Ganguly S, Dewan B, Philipose N, Samanta T, Paul DK, Purkait R. Comparison between Ferrous Ascorbate and Colloidal Iron in the Treatment of Iron Deficiency Anemia in Children from Kolkata, India. *J Adv Med Med Res*. 2012 Mar 14;195-205.
- Final Compendium of fact sheets_India and 14 States_UTs (Phase-II).pdf [Internet]. [cited 2023 Feb 7]. Available from: [http://rchiips.org/nfhs/NFHS-5_FCTS/Final%20Compendium%20of%20fact%20sheets_India%20and%2014%20States_UTs%20\(Phase-II\).pdf#toolbar=0&navpanes=0](http://rchiips.org/nfhs/NFHS-5_FCTS/Final%20Compendium%20of%20fact%20sheets_India%20and%2014%20States_UTs%20(Phase-II).pdf#toolbar=0&navpanes=0)
- MadhyaPradesh.pdf [Internet]. [cited 2023 Feb 7]. Available from: <http://rchiips.org/nfhs/NFHS-4Reports/MadhyaPradesh.pdf>
- Edlin R, Round J, Hulme C, McCabe C. Cost-effectiveness analysis and efficient use of the pharmaceutical budget: the key role of clinical pharmacologists. *Br J Clin Pharmacol*. 2010 Sep;70(3):350.
- Cost-Effectiveness Analysis | POLARIS | Policy and Strategy | CDC [Internet]. 2021 [cited 2023 Feb 7]. Available from: <https://www.cdc.gov/policy/polaris/economics/cost-effectiveness/index.html>
- Rakanita Y, Syamsunarno MRAA, Sinuraya RK, Suradji EW, Abdulah R, Suwantika AA. Cost-Effectiveness of Ferrous Fumarate-Folic Acid and Ferrous Gluconate-Multivitamins in a High Prevalence Area of Iron Deficiency Anemia in Indonesia. *Ther Clin Risk Manag*. 2021;17:1075-81.
- Gafni A, Birch S. Incremental cost-effectiveness ratios (ICERs): The silence of the lambda. *Soc Sci Med*. 2006 May 1;62(9):2091-100.
- Drug and Therapeutics Committee Training Course. Session1: Drug and Therapeutics Committee- Overview. Participants Guide. Rational Pharmaceutical Management Plus Program; 2001
- Eesha A, Yogita K, Manju T, Girija W, Vijaya P. Pharmacoeconomic evaluation of Ferrous ascorbate, Ferrous fumarate and iron polymaltose complex in 14 to 24 weeks of gestation. *Inte J Health Sci Res*. 2015;5(11):339-44.
- Mistry N, Joshi H, Sood S, Shah S, Malhotra S. Efficacy and tolerability of Ferrous sulphate vs iron peptone+ Ferrous ascorbate in pregnancy: An observational study. *Natl J Integr Res Med*. 2018;9(5).
- Kriplani A, Pal B, Bhat V, Swami O. Ferrous Ascorbate: Current Clinical Place of Therapy in the Management of Iron Deficiency Anemia. *J South Asian Fed Obstet Gynaecol*. 2021 Sep 9;13(3):103-9.
- Langstaff RJ, Geisser P, Heil WG, Bowdler JM. Treatment of iron-deficiency anaemia: a lower incidence of adverse effects with Ferrum Hausmann than Ferrous sulphate. *Br J Clin Res*. 1993;4.
- Tolkien Z, Stecher L, Mander AP, Pereira DIA, Powell JJ. Ferrous sulfate supplementation causes significant gastrointestinal side-effects in adults: a systematic review and meta-analysis. *PloS One*. 2015;10(2):e0117383.
- Habib F, Alabdin EHZ, Alenazy M, Nooh R. Compliance to iron supplementation during pregnancy. *J Obstet Gynaecol J Inst Obstet Gynaecol*. 2009 Aug;29(6):487-92.
- Panchal PJ, Desai MK, Shah SP, Solanki MN. Evaluation of efficacy, safety and cost of oral and parenteral iron preparations in patients with iron deficiency anemia. *J Appl Pharm Sci*. 2015;5(3):066-72.
- Murugesan S. Comparative study on efficacy, tolerability, and cost of different iron supplements among antenatal women with iron-deficiency anemia. 2022;13(04).