

Original Research Article

Impact of use of iron fortified iodised salt beyond 12 months on haemoglobin levels

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ABSTRACT

Background: Use of iron fortified iodised salt (IS) for 12 months, resulted in improvement in haemoglobin (Hb) in women, children and men. There is no published data on impact of DFS use beyond 12 months on Hb levels.

Methods: A community based open randomised study to assess impact of use of DFS on Hb was discontinued after 12 months due to COVID 19 related lockdown. These families used IS for six months during lockdown; they were willing to continue using the salt provided for further one year. These families were re-randomized into three groups and given the assigned salt for further 12 months and Hb, ferritin and C-reactive protein (CRP) were estimated at 12 months.

Results: Improvement in the mean Hb was 0.5 g/dl in women who had used IS earlier and DFS under second randomisation and 0.3 g/dl in those who had used DFS under first and second randomisation. Mean Hb at 30 months was higher in those who had used DFS for 24 months as compared to those who had used IS for 18 months and DFS for 12 months. The deterioration in mean Hb following discontinuation of DFS for 6 and 18 months was small.

Conclusions: DFS use for the second year resulted in a further increase in Hb in those who had used DFS earlier. The relatively small deterioration in mean Hb following discontinuation of DFS might at least be in part due to the impact of nutrition and health education and access to health and nutrition services.

Keywords: Haemoglobin, Ferritin, CRP, Iron-fortified iodized salt, IS DFS use beyond 12 months, Impact of DFS use

INTRODUCTION

Prevalence of anaemia in India is high across all age, sex and physiological groups.^{1,2} Iron deficiency, mainly due to low dietary of iron intake and poor bio-availability of iron from Indian diets, is the major factor responsible for the high prevalence of anaemia.³ Anaemia Mukh Bharat programme envisages a three-pronged strategy of dietary diversification, iron folic acid supplementation and iron fortification for improving haemoglobin (Hb) status of the population.⁴ Fortification of iodised salt with iron (double fortified salt - DFS) has been shown to be a feasible, affordable and sustainable method of bridging the gap in iron intake and improving Hb status.⁵ Food Safety and Standards Authority of India (FSSAI) has approved two formulations of DFS⁶. Research studies in India and

elsewhere have shown that consumption of DFS for 6 to 12 months results in improvement in Hb and ferritin.⁷⁻¹¹ There are no published data on impact of use of DFS for two years or longer on Hb levels. It is important to find out the magnitude of improvement in Hb during the second and subsequent years of use of DFS before it is introduced into the programmes for long term use.

Our institution was conducting a community based, three-armed open randomised study of two formulations of DFS and iodised salt (control arm) to assess the impact of use of DFS for 18 months on Hb and ferritin.¹¹ The trial was disrupted at 12 months, due to COVID 19 related lockdown between April and October 2020. When the travel restrictions were eased in October 2020, we contacted the families and assessed the impact of stopping

DFS use for six months. Discontinuing use of DFS for six months resulted in some fall in Hb; even after discontinuation DFS use for six months Hb levels in DFS users were higher as compared to IS users.¹² It is important to find out the impact of longer duration of discontinuation of DFS use on Hb levels.

Families who had participated in the earlier study and were still residing in the area were willing to continue to use salt provided for a further period of 12 months. The families were re-randomised into three groups and were provided with DFS and IS for a further period of 12 months to assess the impact on Hb status of continued use of DFS beyond 12 months and discontinuation of DFS use for 18 months.

METHODS

A community based open randomized three-arm study (one arm IS and two arms two formulations of DFS) to assess the impact of use of DFS on Hb status was conducted in three purposively chosen blocks in South Delhi. From the census of households in the area the first 750 families who fulfilled the inclusion criteria and consented to participate in the study were allocated to one of the three groups [250 each in group 1 (IS), group 2 (DFS ferrous sulphate DFS FS), and group 3 (DFS ferrous fumarate DFS FF)] using a computer-generated random allocation. The families had completed 12 months use of IS or either one of the DFS as per the random allocation.¹¹ Due to COVID 19 related lockdown the supply of salts could not be done between April to September 2020.

In October 2020, the research team went back to the community. Many families had moved out during the lockdown; but those who belonged to Delhi or could not go back to villages remained in the area. These families were contacted and the importance of obtaining information on the impact of continuing the use of DFS beyond 12 months and discontinuing use of DFS for 18 months on Hb levels were explained to them. We also explained to them that as a large number of the families had left during lockdown, there was a need for re-randomization of the salt provided to them and they may no longer receive the salt assigned to them earlier. Almost all the families provided informed consent for using the salt provided to them after re-randomization for a period of 12 months and providing blood samples at 0, 6 and 12 months of use of the allocated salt. The families in the three groups as per first randomisation were re-randomised (Figure 1).

These low middle income families faced hardships during and after lockdown in finding employment with adequate remuneration. Men worked in different parts of Delhi where they could find employment and did not consistently eat at home. As schools were closed many children stayed at times in Delhi with parents and at times went back to grandparents in villages. Women who were mostly homemakers stayed at home and ate home cooked food continuously. Blood samples at 0, 6 and 12 months were

collected from women from the following three groups of families.

In group 1, women those who had used IS for 12 months, continued using IS for 6 months during lockdown and were given DFS for the next 12 months: in this group the effect of DFS use for 12 months for the first time in the present study was assessed.

In group 2, women who had used DFS for 12 months and used IS for 6 months during lockdown and later restarted using DFS for 12 months: in this group the effect of continued use of DFS beyond 12 months with a break of 6 months during lockdown was investigated.

In group 3, women who had used DFS for 12 months, used IS for six months during lock down and continued to use IS for 12 months: in this group the impact of discontinuing the use of DFS for 18 months was investigated.

In all the blood samples Hb, ferritin and CRP assays were done. Hb estimations by cyanmethaemoglobin method were carried out at our institution on the day the samples were collected; technicians who undertook Hb estimation were blinded to the group from which the samples were drawn. All samples were coded and after processing they were stored in deep freeze until analysis. Ferritin assay was done by electrochemiluminescence immunoassay (ECLIA) and CRP estimation was done using enhanced immunoturbidimetry assay using COBAS 6000 in a laboratory certified by the National Accreditation Board for Testing and Calibrating of Laboratories, India. The laboratory fared well in the external quality assurance programmes; internal quality assurance tests showed that there was excellent concordance in measurement of parameters between coded duplicate samples. Technicians who undertook ferritin and CRP assays were given coded samples and did not know the group from which the samples were collected.

Data entry, data cleaning and data analysis

Data entry was done in Microsoft excel; data cleaning was done using Microsoft excel and statistical package for the social sciences (SPSS). Data analysis was done with SPSS version 27 and Stata version 15.

Mean Hb, ferritin and CRP levels were computed in all the groups at all-time points. Impact of the salt used on Hb, ferritin and CRP on pre- and post-use were assessed by paired t test. P values <0.05 were considered statistically significant.

RESULTS

Changes in mean Hb, ferritin and CRP after use of salt as per 2nd random allocation for 12 months in paired samples are given in Table 1. There was some improvement in the mean Hb in all the three groups. The mean Hb was highest in the group of women who had received DFS for 12

months twice and IS in between for 6 months. The improvement in the mean Hb was 0.5 g/dl in the group of women who had consumed IS earlier for 18 months and had then consumed DFS for 12 months; this was statistically significant. The improvement in the mean Hb was 0.3 g/dl in the group of women who had used DFS earlier for 12 months, used IS for 6 months during lockdown and then used DFS for 12 months; and in the group of women who had earlier consumed DFS for 12 months and subsequently consumed IS for 18 months. The difference in the mean Hb between 0 and 12 months in these two groups was not statistically significant. The changes in the mean ferritin and mean CRP between 0 and 12 months were small and varied between the three groups (Table 1).

Mean Hb levels in women in the three groups assigned to them during the first randomisation at the time of enrolment to the study, at 12 months of use of the salt

provided in the first randomisation and after 6 months of IS use during lockdown is given in Table 2. There was some improvement in Hb in all the groups after use of the assigned salt for 12 months. The improvement in Hb after 12 months of use of DFS was higher as compared to the improvement in those using IS for 12 months. There was a small fall in Hb in both IS and DFS users when they had used IS during lockdown. Women who had used IS for 18 months had a lower mean Hb at 18 months (10.7 ± 1.35 g/dl) as compared to those who had earlier used DFS for 12 months and later used IS for 6 months (11.2 ± 1.52 g/dl).

There was a statistically significant rise in Hb between 0 and 18 months both in women who had used IS for 18 months (0 month 10.4 ± 1.57 and 18 months 10.8 ± 1.42 g/dl) and those who had used DFS for 12 months and later IS for 6 months (0 month 10.6 ± 1.63 and 18 months 11.0 ± 1.54 g/dl).

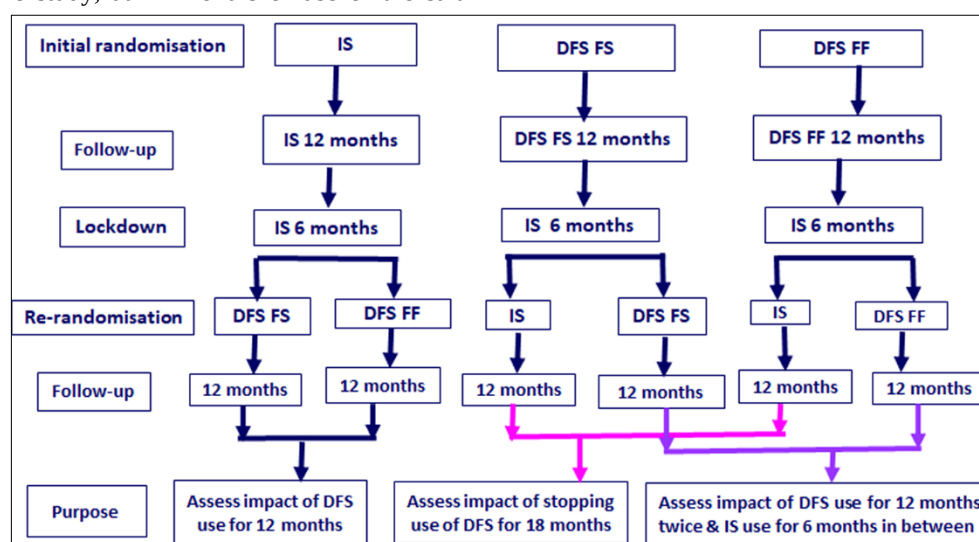


Figure 1: Study design.

Table 1: Impact of salt used in the last 12 months on Hb levels in women (second randomisation).

Prior salt use		Second randomisation 12 months				
1st randomisation 12 months	Lockdown 6 months	Salt provided	Parameter	0 months	12 months	Paired T test
IS	IS	DFS (FS+FF)	Hb (g/dl)	10.7 ± 1.51 (86)	11.2 ± 1.26 (86)	0.01
DFS (FS+FF)	IS	DFS (FS+FF)		11.1 ± 1.59 (82)	11.4 ± 1.37 (82)	NS
DFS (FS+FF)	IS	IS		10.8 ± 1.37 (67)	11.1 ± 1.34 (67)	NS
IS	IS	DFS (FS+FF)	Ferritin (ng/ml)	36.2 ± 32.20 (80)	35.2 ± 28.96 (80)	NS
DFS (FS+FF)	IS	DFS (FS+FF)		41.8 ± 43.50 (74)	42.9 ± 40.79 (74)	NS
DFS (FS+FF)	IS	IS		44.1 ± 38.29 (61)	37.1 ± 35.01 (61)	NS
IS	IS	DFS (FS+FF)	CRP (mg/l)	3.3 ± 3.72 (80)	2.2 ± 2.49 (80)	0.03
DFS (FS+FF)	IS	DFS (FS+FF)		3.1 ± 3.39 (74)	3.1 ± 3.02 (74)	NS
DFS (FS+FF)	IS	IS		3.0 ± 3.06 (61)	2.6 ± 2.52 (61)	NS

Table 2: Impact of salts used on Hb levels in women (first randomisation).

Salt used and duration	0 month (g/dl)	12 month (g/dl)	Paired t test
IS for 12 months	10.7±1.42 (114)	11.1±1.27 (114)	0.03
DFS (FS+FF) for 12 months	11.0±1.45 (214)	11.4±1.32 (214)	0.003
	12 months	18 months	
IS for 18 months	10.9±1.21 (63)	10.7±1.35 (63)	NS
DFS for 12 months and IS for 6 months	11.3±1.36 (127)	11.2±1.52 (127)	NS
	0 month	18 months	
IS for 18 months	10.4±1.57 (129)	10.8±1.42 (129)	0.03
DFS for 12 months and IS for 6 months	10.6±1.63 (199)	11.0±1.54 (199)	0.01

DISCUSSION

Prevalence of anaemia in Indians across all age, sex and physiological groups is the highest in the world. The high prevalence of iron deficiency and anaemia in India is mainly due to inadequate iron intake and poor bio-availability of iron from habitual Indian diets.³ Over the last two decades there had been some reduction in the prevalence of anaemia in all groups but the pace of decline is slow.¹³⁻¹⁷ Anaemia Mukht Bharat programme aims to accelerate the reduction in prevalence of anaemia using a three-pronged strategy of dietary diversification, iron folic acid supplementation to vulnerable groups and iron fortification of food stuffs for improving Hb status of the population.⁴ DFS has been shown to be a feasible, affordable and sustainable method of bridging the gap in iron intake.^{5,18,19} Research studies have documented that use of DFS for 12 months was associated with improvement in Hb levels.⁷⁻¹¹ There are no published data from research studies on impact of DFS use beyond 12 months on Hb. Several states (Tamil Nadu, Chhattisgarh, UP, MP) have provided DFS to families through PDS for some years; there are no published data from these state level interventions on offtake, consistent use of DFS and impact of use of DFS on Hb and ferritin levels. It is important to obtain these data on efficacy of DFS use beyond one year, so that programme evaluations on use of DFS can compare the improvement in mean Hb and reduction in the prevalence of anaemia from research studies to changes in these parameters under service conditions. When large scale national programmes are implemented, it is inevitable that there may be periodic disruption in supplies and some discontinuation in use of the DFS. It is important to document the impact of such disruption of varying duration on Hb levels, so that these could be factored in while undertaking the impact evaluation of the DFS programme.

Our institution was conducting a community based, three-armed open randomized study of two formulations of DFS and iodised salt (control arm) to assess the impact use of DFS use on Hb and ferritin.¹¹ At the end of first year of use of DFS the mean Hb levels in women were higher.¹¹ The trial was disrupted after 12 months of use of assigned salt by the families due to COVID 19 related lockdown. We requested the families telephonically to purchase iodised salt from the market and use it until such time as we were

able to resume supply of the assigned salt. Many families had moved out of the area or gone back to the villages during the lockdown. When the travel restrictions were eased in October 2020, we went back to the area and found that there were families who had stayed in Delhi during the lockdown, bought iodised salt from the market and used it. We discussed with them the importance of assessing their Hb levels after the six-month use of iodised salt and obtained blood samples from women from these families. Discontinuing use of DFS for six months resulted in some fall in Hb in all the three groups; the fall in Hb levels in DFS users were higher as compared to IS users.¹²

There is no published data on the magnitude of improvement in the Hb levels when DFS was used for the second year. Earlier studies have reported that initial Hb levels and prevalence of anaemia prior to use of DFS, influenced the impact of DFS use on Hb levels at 12 months.¹¹ It is important to find out the magnitude of improvement in Hb levels in the second year when women who had higher mean Hb levels at the end of first year used DFS for the second year. We discussed with the families the importance of continuing the study for 12 more months. We informed them that there will be a re-randomization and many of them will not get the salt they were using earlier. They were willing to continue using the assigned salt for the next twelve months and providing blood samples at 6 and 12 months of use of the assigned salt.

The study was continued for a further period of 12 months and the impact on Hb and ferritin status of: women who used DFS for 12 months twice with use of IS for 6 months in between, discontinuation of DFS use after 12 months and used IS for 18 months, and those who had used IS for 18 months and used DFS for 12 months was assessed.

Changes in mean Hb, ferritin and CRP in paired samples at 0 and 12 months after second random allocation (after 12 months of use of salt as per initial random allocation, use of purchased IS for 6 months during lockdown) is shown in Table 1. The improvement in the mean Hb was highest in women who had used IS for 18 months earlier and then used DFS for 12 months. The magnitude of improvement in mean Hb in first time DFS users in second randomisation was comparable to the magnitude of

increase in Hb in mean Hb in women who had used DFS in the first randomisation (Table 2).

It was reassuring that even in the second year of use of DFS there was a trend for continued improvement in the mean Hb. The observed improvement in mean Hb in women who had earlier used DFS for 12 months, used IS for 6 months during lockdown and then used DFS for 12 months was lower as compared to women who had used DFS for the first time for 12 months under the second randomisation (Tables 1 and 2). This might partly be due to the fact that women who had earlier used DFS had a higher mean Hb at 0 month of second randomisation. Our earlier study had shown that women who were anaemic responded to DFS use with higher magnitude of improvement in the mean Hb.

In the study women there was a small increase in the mean Hb over a period of 30 months in all the groups irrespective of the type of salts that they had received over this period (Tables 1 and 2). The research staff visited these families every month for checking the amount of salt consumed during the month and giving them the salt needed for the next month. During these visits, the research staff provided nutrition and health education to these women.

One topic of discussion was steps that the family should take to improve vegetable intake and ensuring consistent consumption of home food cooked with the salt provided in the study. The family was also informed about the ongoing interventions available in their block for improving health and nutritional status of women and children. As and when they faced difficulties in accessing these services the research team tried to facilitate access to these services. These were small interventions but were done consistently because the research teams felt that it was part of their responsibility. These might be to some extent responsible for the small but consistent improvement in mean Hb in women across the groups even when women were using IS for 18 months continuously. This might also explain the lack of progressive deterioration in Hb in DFS users who had used IS for 18 months subsequently.

Strength of the study

This community based randomised study provided the data on Hb levels when IS and DFS were used for varying periods of time over a thirty-month period, and impact of discontinuing DFS use for 6-18 months. These data can provide the benchmark against which the data from programme evaluations on impact of use of DFS on Hb under service conditions can be compared.

Limitations

Due to COVID 19 related lockdown and the socio-economic disruptions that followed, there was severe attrition in the number of families participating in the study.

CONCLUSION

Use of DFS for one year and beyond resulted in improvement in the mean Hb levels in women. Improvement in the mean Hb in women who had used IS earlier and DFS in second randomisation was 0.5 g/dl; improvement in mean Hb in women who had used DFS under first and second randomisation was 0.3 g/dl. Mean Hb at 30 months was higher in those who had used DFS for 24 months as compared to those who had used IS for 18 months and DFS for 12 months. The deterioration in mean Hb following discontinuation of DFS for 6 and 18 months was relatively small. Hb levels in all the groups were higher at 18 and 30 months of participation in the study and use of different salts as compared to the initial levels (0 month) at the beginning of the study. This might at least be in part due to the nutrition and health education that women from all the groups received and partly due to research staff helping them to access to health and nutrition services. It is therefore important to continue nutrition education regarding dietary diversity, improve access to health and nutrition services as envisaged in Anaemia Mukh Bharat initiative. As and when DFS becomes accessible and available at affordable cost and is used by families there will be acceleration in the pace of improvement in Hb and reduction in anaemia in all age and sex groups.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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