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Role of Fortified Cereals as Supplementary Food During the Complementary Feeding Period for Infants and their Impact on Iron Deficiency Status: A Retrospective Case Series with a Follow-up of 6 Months

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1. ABSTRACT

This case report assessed eleven (11) Indian infants selected from published data to evaluate the effect of nutrient-fortified (rice-based) supplementation from six months of age for a 6-month weaning period. Anthropometric measurements (weight and length/height) and Body Mass Index (BMI) based on the Z-score were evaluated at four-time points at 6-weeks intervals and correlated with nutrient intake (energy, fat, carbohydrates, protein, iron, and vitamin A), haemoglobin, serum ferritin, and serum soluble Transferrin Receptor (sTfR). Of the 11 subjects, 5 were exclusively breastfeeding and 6 were on mixed feeding. On enrolment, all patients presented the following characteristics: mild/borderline anaemia (Hb at 10.3 g/dL ± 1.55 g/dL); mean gestational age of 36.45 ± 1.57 weeks, mean birth weight was 2.72 kg ± 0.31 kg, and male-to-female distribution was 6:5. Post 6-months follow-up with the multi-nutrient fortified feeds including iron, the Hb concentration increased to 11.5 μg/dL ± 1.3 μg/dL at 12-months. There was a significant correlation between Hb and serum ferritin, soluble transferrin receptor, and mean corpuscular volume. The individual composite score on the Bayley-III assessment (including cognitive and motor function) showed that 27% of the infants (3/11) at 6-months were below average [mean score: ≤ 70] and at 12-months all the infants were found to be average [mean score:100]. While supplementation is used for therapeutic purposes where anaemia has

progressed to the severity necessitating treatment, fortified cereals are used to prevent the risk. Thus, good nutritional fortified feeds are of profound importance during the rapid growth and development of infants.

2. Keywords: Infants; Fortified infant cereal; Anaemia; Iron deficiency; Haemoglobin

3. INTRODUCTION

A common issue in public health, Iron (Fe)-Deficiency Anaemia (IDA) is more prevalent in Low- and Middle-Income Nations (LMICs) affecting 293.1 million children. According to the latest reports published by the World Health Organization (WHO), almost two billion people, or 25% of the world's population, are anaemic, with roughly half of them having IDA [1-3]. Among these, approximately 165 million are young children, with the highest prevalence found in Southeast Asia (over 35%) [4]. Infants and toddlers aged 6 months -24 months had the highest IDA rates. In India, the recent Comprehensive National Nutrition Survey (CNNS) has shown an Fe-deficiency prevalence (with micronutrient deficiencies) of 30% to 40% in children aged between 12 months -48 months old. The prevalence of Fe-deficiency-linked anaemia in 6 months -23 months of children, which is not separately detailed in the National Family Health Survey-5 (NFHS-5) (2019-21), is estimated to be about one-third of the overall high rates of anaemia and has seen a substantial rise (about 10% -15%) from the NFHS-4 survey [1,5,6].

Among the various dynamic factors that potentially contribute to anaemia, Fe deficiency is the most common cause of anaemia globally, along with other macro- (i.e., carbohydrates, proteins, lipids, etc.) and selected micronutrient (i.e., Zn, Cu, Mg, vitamins A, B12, C, D, and folate) deficiencies [7-9]. Anaemia caused by deficiencies in Fe, vitamin B12, or folate is relatively well characterized and generally common, while anaemia resulting from other micronutrient deficiencies, such as vitamin A, is not clearly understood. Consequently, if Complementary Foods (CF) do not provide adequate amounts of bioavailable Fe and other nutrients, young children are at high risk of developing ID and IDA and are susceptible to impaired neurophysiological, motor, cognitive, and social-emotional development [10]. In many LMICs, such as India, CF generally contains home-made local staple foods (cereals, roots/tubers) only; however, these feeds often does not display minimum dietary diversity and nutrient density and possess a low concentration and/or bioavailability of Fe, and thus, are unable to deliver satisfactory Fe to the growing child [11]. A systematic review and meta-analysis conducted by previous researchers indicated that multi-micronutrient fortified milk and cereal products can be an effective option to reduce anaemia in children, especially up to 3 years of age, in LMICs [12-15]. However, systematic evidence and cohort analyses on the consumption of fortified infant cereals from developing countries, such as India, are limited. Taking a cue from the lack of available data and detailed analytical evidence on commercially fortified cereal products, a comprehensive study [13] suggested that consuming a micronutrient-fortified infant cereal daily for six months during complementary feeding promoted a better Fe status while reducing the risk of anaemia and ID and was associated with superior neurodevelopmental scores. As a follow-up to this study, we present a series of representative cases of infants with borderline to mild anaemia based on Hb, ferritin, and transferrin receptor levels. The objective of this study was to re-evaluate the efficacy of these fortified cereals with special reference to the daily iron intake, Hb, ferritin, and soluble transferrin receptor concentrations, as well as other micro- and macro-nutrients (i.e., carbohydrates, proteins, lipids, and vitamin A) in Indian infants.

4. METHODOLOGY

In this case series, 11 infants with mild or borderline anaemia (Hb < 100 g/L or 10 g/dL) were selected from the published multicenter study data of infants in tertiary-care paediatrics outpatient clinics in India in 2018 [11]. The six months follow-up was evaluated to assess the additional effects of Fe intake and Hb level at the end of the study period. Breastfeeding and mixed feeding of infants continued throughout the complementary feeding period.

Anthropometric measurements (weight and length/height) and Body Mass Index (BMI) based on the Z-score were evaluated at four time points at 6-weeks intervals and correlated with nutrient intake. Every 6-weeks follow-up data were evaluated based on Fe intake and other nutrients and weight gain till 9 months -12 months. Nutrient intake was evaluated using a 24-h dietary recall by a trained paediatrics dietitian from the infant's parent or caregiver at each study visit. Breast milk intake during the 24-h dietary recall period was assessed as the frequency of breastfeeding. The daily intake of energy, macronutrients (fat, carbohydrates, and protein), and selected micronutrients (Fe and vitamin A) from CF at twelve months of age (excluding nutrients from breast milk) were calculated using Indian Food Composition Tables. Additionally, Hb estimation was performed as part of a normal examination done/ordered by the paediatrician. According to the WHO classification, a child was considered anaemic and normal if the Hb levels were <11 g/dl and ≥ 11 g/dl, respectively. The correlation of Hb status with daily Fe intake, MCV, serum ferritin, and serum soluble Transferrin Receptor (sTfR) was assessed. Of the 11 infants in the case series, five were reported individually, and all the data were expressed as frequencies and proportions for categorical variables and mean and Standard Deviations (SDs) for continuous variables. Chi-square and unpaired t-tests were used to assess significant differences across the study variables. Multivariate logistic regression analysis was performed to examine the simultaneous impact of several factors on the anaemia status of the child. Statistical significance was set at $p < 0.05$.

5. CASE PRESENTATION

5.1. Case Report 1

A healthy single-birth male infant at 37 weeks of gestation, aged 6 months, with a birth weight of 3 kg, visited the well-baby clinic in April 2017. The infant was exclusively breastfed and was subsequently introduced to solid feeds with micronutrient-fortified infant cereal, along with continuation of breastfeeding until 12 months of age, as per the dietitian's guidance.

The Hb level at baseline was 10.0 g/dL and during the follow-up at 12 months increased to 12.7 g/dL. Congruently, it resulted in a serum ferritin drop of 12.45 ng/ml and the soluble transferrin receptor showed a marginal decrease of 0.68 mg/L. Over the course of the monitoring period, the Fe intake transiently increased from 8 µg/dL at 6 months to 9.60 µg/dL at 7.5 months. This increment might be due to the increased bioavailability of iron present in breast milk. With the decreased frequency of breastfeeding but with the addition of complementary feed, the daily Fe intake further increased to 10.60 µg/dL at 12 months, which was well above the Recommended Dietary Allowances (RDA) and Estimated Average Requirements (EAR). His weight increased from 6.64 kg at 6 months to 9.1 kg at 12 months of age (change in WAZ: -0.38) and the length was increased by 8.1 cm (change in WHZ: 0.96 and change in HAZ: -2.57). Concomitant decreases in BMI and

Body Mass Index-for-age Z score (BAZ) by 1.3 kg/m^2 and 1.71 kg/m^2, respectively. As per the dietitian's 24-h recall on energy intake and macro- and micronutrient level calculations, macronutrients over 6 months were not significantly increased, although they were above the RDA limits. The weight was at the 50th centile IAP growth chart at 12 months of age, and the effect of iron fortification in the diet led to an increase in Hb levels, which has important ramifications for other parameters of holistic development. The individual score on the Bayley-III assessment showed that at 6-months it was below average [mean score: ≤ 70] and at 12-months it became average [mean score:100]; it included cognitive and motor function. A summary of this case is presented in Table 1.

5.2. Case Report 2

A female child born to an upper-lower class family residing in an urban area at 36 weeks of gestation and with a birth weight of 2.6 kg was enrolled at 6 months of age with a weight and length of 7.96 kg and 63 cm (WAZ = 0.71; HAZ = -1.21, and BAZ = 1.87) and Hb levels were 10 g/dL. The dietitian demonstrated the complementary feeding technique of micronutrient-fortified infant cereal with a daily amount of 50 g/day until 12 months of age, along with breast milk and formula-feeding, and any other home-made feeds as and when advised by the dietitian. At an interval of 6 weeks, the mother with the infant visited the clinic and the dietitian performed a dietary recall of the last three days, calculated the amount consumed, and computed the macro- and micronutrient intake to assess the adequacy of the consumption. At the end of 6 months of reassessment, there was an increase in Hb level by 0.6 g/L (10.6 g/dL at 12 months of age) and an increase in daily iron intake from 3.84 at 6 months to 5.65 µg/dL to 12 months, well above the RDA; serum ferritin dropped by 23.58 ng/ml and soluble transferrin receptor showed a marginal decrease by 0.02 units. At 12 months of age, her weight had increased to 11.3 kg (WAZ= 0.8). Likewise, the length of the subject increased by 9 cm (WHZ showed a marginal increase of 0.94), HAZ was -3, and BMI was 21.8 kg/m^2 and BAZ 3.54. Analysis of nutrient intake showed that daily carbohydrate, lipid, and protein intakes increased by 60.17 g/d, 6.25 g/d, and 3.86 g/d, respectively. The energy intake increased by 333.37 Kcal/d. Hb levels showed a borderline increase and maintained the same percentile in the growth curve from the baseline percentile. The individual score on the Bayley-III assessment maintained the composite score as an average, both at baseline and at 6-months. A summary of this case is presented in Table 1.

5.3. Case Report 3

A female child, 37 weeks gestational age, belonging to an upper-middle-class family from an urban area, with a birth weight of 2.98 kg, was enrolled at 6 months of age. The weight was 6.3 kg (WAZ = -1.22), and the height was 60 cm. The infant was exclusively breastfed until 6 months of age and was introduced to solid feeds with micronutrient-fortified infant cereal and regular homemade feeds until 12 months of age, according to the dietitian's guidance. The Hb level increased to 11.1 g/dL at 12 months of age (against baseline 10.7 g/dL), and it resulted in a serum ferritin drop by 7.82 ng/ml and soluble transferrin receptor showed a marginal increase by 0.02 units. The daily iron intake increased from 2.92 µg/dL to 4.61 µg/dL. Her weight increased to 8.01 kg at 12 months of age (change in WAZ: -0.83) and her height increased by 13 cm (change in WHZ: -1.78 and HAZ: -0.12). Concomitant decreases in BMI and BAZ by 2.5 kg/m^2 and 0.91, respectively. Analysis of nutrient intake showed that daily energy, carbohydrate, lipid, and protein intake increased by 347.3 Kcal/d, 53.89 Kcal/d, 6.57 Kcal/d, and 7.47 g/d, respectively. While the iron-fortified diet led to an increase in Hb levels, adequate intake of key macronutrients helped in favourable development scores and overall growth improvement (Table 1). The individual score on the Bayley-III assessment maintained the composite score as an average, both at baseline and at 6-months.

5.4. Case Report 4

A 6-month-old male term-infant, 36-week gestational age, had a routine visit to the outpatient department in June 2017 for a regular check-up. The birth weight was 2.8 kg, belonging to urban upper-middle socioeconomic status, and breastfeeding was already complemented by solid foods. After the initial baseline visit, he received 50 g/day of a micronutrient-fortified cereal throughout the six months of intervention, in addition to the habitual complementary feeding regimen.

The haematology results confirmed the Hb level at baseline of 10.8 g/dL (6-months) increased to 11.3 g/dL at 12-months. The serum ferritin increased from 36.72 μg/dL (6-months) to 87.12 μg/dL (12-months) due to inflammation as the CRP was raised from 0.15 mg/L to 7.5 mg/L but no additional treatment was given for the same. Daily iron intake increased from 0.70 μg/dL *v*. 5.63 μg/dL. Further clinical findings revealed the following: vit. A increased to 287.47 μg/d (as against a baseline of 25.5 μg/d); and 16-, 4-, 2-, and 2.5-fold increases in energy, protein, carbohydrate, and lipid, respectively at 12-months. His weight increased to 11.2 kg at 12 months of age (WAZ: 0.21) and his height increased by 10 cm (change in WHZ= 0.08 and HAZ= -1.36). The BMI remained unchanged, and BAZ increased by 0.82. The individual scores on the Bayley-III assessment showed that at 6-months it was below average [motor: 47·5 (S.D. 5·2); cognition: 74·4 (S.D. 8·2)] and at 12-months it became average [motor: 72·9 (S.D. 8·4); cognition: 85·2 (S.D. 8·1)].

5.5. Case Report 5

A healthy singleton birth infant at 37 weeks of aged 6 months with a birth weight of 2.55 kg and Z scores (WAZ: -0.93, HAZ: -1.37, and BAZ: -0.16) visited the paediatricians outpatient department in January 2018 at the well-baby clinic with a weight of 6.77 kg. The infant was exclusively breastfed and was subsequently introduced to solid feeds, including micronutrient-fortified infant cereal, until 12 months of age at 50 g/day. The Hb level at baseline (6-months) was 11.1 g/dL and post-follow-up haematological analysis showed an increased to 11.7 g/dL. The serum ferritin dropped by 13.83 μg/L (33.01 ng/ml at 6-months *v*. 19.18 ng/ml at 12-months) and soluble transferrin receptor remained unchanged. Serum ferritin and MCV showed a positive correlation, and MCV increased from 78 to 89 μm^3. During the monitoring period, the daily Fe intake increased significantly from 1.43 μg/dL to 6.30 μg/dL with a simultaneous increase in the daily energy (361.35 Kcal/d to 640.56 Kcal/d) and daily protein (8.94 g/d to 21.83 g/d) uptake. Also, vitamin A levels increased from 43.97 μg/d to 304.59 μg/d, along with the daily carbohydrate and lipid intake till the study-end period. The weight increased to 8.6 kg at 12 months of age (change in WAZ: -1.06) and his height increased by 10 cm (change in WHZ and HAZ: -0.65 and -1.75, respectively). When the BMI decreased from 17.1 to 16.1, the BAZ score marginally increased by 0.08. Analysis of nutrient intake showed that carbohydrate and lipid intake increased by 51.39 and 2.47 g/day, respectively (Table 1). The individual score on the Bayley-III assessment maintained the composite score as an average, both at baseline and at the 6-months follow-up. Additionally, details on the summary of the cases can be found in Supporting Information.

6. DISCUSSION

Several scientific studies and clinical practices have pointed out that fortification has better compliance and proposed this as a strategy to be used as a preventive, long-term sustainable mass approach in addition to regular homemade feeds to meet the nutritional needs during the critical period of 6-23 months of age [12,13]. At the end of the intervention, we were able to confirm earlier observations that a multi-nutrient fortified infant cereal is an efficacious way to prevent the progression of anaemia and the lack of micronutrients in infants aged 6-23 [11]. In recent years, nutritional research in developing countries has largely focused on iron, vitamin A, and iodine deficiencies, and there have been relatively few investigations on the prevalence of other micronutrient deficiencies and issues. A preliminary examination of the literature revealed that there is significant health concern regarding the lack of micronutrients in infants aged 6 months - 23 months. The prevalence of anaemia was found to be over 60% among infants, while approximately 20 % - 30% suffered from iron deficiency. Moreover, national surveys indicated that 70 % - 80% of the infants were deficient in vitamin A, 13% were deficient in vitamin B12, 22% were deficient in folate, and 60% - 65% were found to have zinc deficiency. These findings highlight the urgent need to address this issue and to implement appropriate interventions to improve the health outcomes of this vulnerable population [14]. Anaemia affects most infants, young children, and women in developing countries, and it is mostly assumed that anaemia is caused by iron deficiency [1-5,11]. Thus, it is a fact that the many existing, large-scale iron-supplementation programs would be effective for the prevention and treatment of anaemia if adequate amounts of iron were consumed. However, the predicted and actual prevalence of deficiencies of other micronutrients required for haemoglobin synthesis are high in population groups, such as rural Indian children studied in previous studies [15-18].

This case series of infants showed that anaemia at 6 months of age was mostly due to iron deficiency, as assessed by the serum ferritin, serum soluble transferrin receptor level, and Mean Corpuscular Volume of the RBCs. Because the values of iron status indicators between normal and iron-deficient individuals are known to overlap, a combination of iron indicators was used in this study to improve the accuracy of the detection of individuals with iron deficiency. The prevalence of iron deficiency anaemia in the present study appears to be higher than the levels reported in other Asian countries but lower in Western countries, including the USA, UK, and Denmark [19]. The present findings are in general agreement with results from other studies that have also reported that the intake of a fortified infant cereal is critical to meet the increased energy, nutrition, and micronutrient demand beyond 6 months of age [12,20-23]. Data on the nutrient intake of Indian infants are scarce on how commonly used complementary foods may not meet the high iron requirement at this age [24,25]. Multi-nutrient fortification appears to be the most practical and feasible approach for anaemia prevention and control, although anaemia has a multifactorial etiology. The present case series provides preliminary evidence regarding the benefits of multi-nutrient-fortified cereals in the Indian context, and similar effects have been reported by others [11,12,15,19,20-22]. It has also been concluded that fortification would have an impact on morbidity and mortality, although a conclusive answer cannot yet be provided [26]. Food fortification is the best sustainable approach to prevent iron deficiency as it has the potential to reach all sections of society; it is not dependent on the cooperation of the individual, the initial cost is low, and the maintenance expenses may be less than that of medicinal iron supplementation, in cases where supplementation is used for preventive purposes. As per the Copenhagen Consensus and ex-ante analysis of FSSAI, such fortification interventions are associated with a high benefit-to-cost ratio (9:1) for the overall health outcomes of infants. In addition, existing evidence suggests that such an intervention yields maximum improvements at a lower baseline Hb level [27].

To be more effective and acceptable, fortification should be performed on commonly used foods [28,29]. For instance, cereals are used worldwide as staple foods, especially in the Indian subcontinent. Cereals are considered functional foods because their benefits are beyond basic nutrition and are useful for fortification. Therefore, fortified cereals providing a low to moderate dose of Fe are a pertinent approach in an Indian setting where childhood anaemia is a major public health problem. Homemade complementary foods are key from a familial and cultural perspective for a smooth transition to family food and for building lifelong food habits. In addition, delayed introduction and/or inappropriate complementary feeding practices, such as inadequate dietary diversity, meal frequency, runny consistency, and inappropriate food choices, are important attributes that influence early-stage child growth development.

7. CONCLUSION

This is the first-of-its-kind case series to our knowledge from a developing country like India confirming the association between fortified cereals providing adequate Fe status in early life and its supportive role in age-appropriate growth, weight-for-age, and weight-for-length Z-scores, no significant impact on BMI and increased intake of key macro- and/or micro-nutrients positively impacting neuro and cognitive development. These key findings not only contribute novel information to this field of research, but can also be applied to public health programs, especially in countries where double-burden malnutrition is prevalent. Furthermore, the prompt risk assessment and early intervention of anaemia in tertiary health units and individual homes in low-resource settings are of considerable social importance and warrant the use of relatively inexpensive, non-invasive, and reliable tests that are likely to be better received by children. One such test, the ‘Non-invasive Screening of Anemia (NISA) color shade card’ would be helpful for medical practitioners as well as for overall community health in a larger population of real-world experience [30]. A larger community-based study should be conducted using this color shade card to identify borderline anaemia and address nutritional interventions accordingly.

8. SUPPLEMENTARY MATERIALS

8.1. Summary of the cases and Table S1-S3: Demographic and baseline characteristics, anthropometric measures, and change in daily macro and micro-nutrient intake and Hb, SFRS, and SSTRS from baseline to 6 study-end period, respectively.

Table 1: Summary of the five cases.

Case 1	Parameters/Baseline	6 months	12 months
Case 1 [Gestational age: 37 weeks; Sex: Male; Birthweight: 3 kg; Location/Demography: Urban; SES SCALE: Lower-middle]	Weight (Kg)	6.64	9.1
	Height (Cm)	63.9	72
	WAZ[1]	-1.1	-1.48
	WHZ[2]	-0.65	0.31
	HAZ[3]	-0.94	-3.5
	BMI[4]	16.3	17.6
	BAZ[5]	-0.74	0.97
	Hb (g/l)	100	127

	Serum ferritin (ng/ml)	24.52	12.07
	SSTRS (mg/l)	2.18	1.5
	MCV (fL)[6]	69.1	88
	Energy (kCal)	501	475.5
	Protein (g)	26.2	19.2
	Carbohydrate (g)	84.3	64.8
	Fat/Lipid (g)	9	7.35
	Fe (µg/dL)	8	3.6
	Vitamin A (µg/d)	66.8	139.6
	Bayley-III score		
Case 2 [Gestational age: 36 weeks; Sex: Female; Birthweight: 2.6 kg; Location/Demography: Urban; SES SCALE: Upper-lower]	Weight (Kg)	7.96	11.3
	Length (Cm)	63	72
	WAZ[1]	0.71	0.8
	WHZ[2]	1.96	2.9
	HAZ[3]	-1.21	-3
	BMI[4]	20.1	21.8
	BAZ[5]	1.87	3.54
	Hb (g/l)	100	106
	Serum ferritin (ng/ml)	74.47	50.89
	SSTRS (mg/l)	1.56	1.54
	MCV (fL)[6]	73.5	75.6
	Energy (kCal)	164.8	498.17
	Protein (g/d)	5.36	9.22
	Carbohydrate (g/d)	20.36	80.53
	Fat/Lipid (g/d)	6.88	13.13
	Fe (µg/dL)	3.84	5.65
	Vitamin A (µg/d)	66.8	260.8
	Bayley-III score		
Case 3 [Gestational age: 36 weeks; Sex: Female; Birthweight: 2.98 kg; Location/Demography: Urban; SES SCALE: Upper-middle]	Weight (Kg)	6.3	8.01
	Height (Cm)	60	73
	WAZ[1]	-1.22	-2.05
	WHZ[2]	0.76	-1.02
	HAZ[3]	-2.54	-2.66
	BMI[4]	17.5	15
	BAZ[5]	0.38	-0.53
	Hb (g/l)	107	111
	Serum ferritin (ng/ml)	23.69	15.87
	Serum soluble transferrin receptor (mg/l)	1.62	1.64
	MCV (fL)[6]	80.2	76.5

	Energy (kCal)	222	569.3
	Protein (g/d)	7.27	14.74
	Carbohydrate (g/d)	30.58	84.47
	Fat/Lipid (g/d)	7.85	14.42
	Fe (µg/dL)	2.92	4.61
	Vitamin A (µg/d)	157.5	217.18
	Bayley-III score		
Case 4 [Gestational age: 36 weeks; Sex: Female; Birthweight: 2.98 kg; Location/Demography: Urban; SES SCALE: Upper-middle]	Weight (Kg)	8.4	11.2
	Length (Cm)	64	74
	WHZ[2]	2.1	2.18
	HAZ[3]	-1.7	-3.06
	BMI[4]	20.5	20.5
	BAZ[5]	2	2.82
	Hb (g/l)	108	113
	Serum ferritin (ng/ml)	36.72	87.12
	SSTRS (mg/l)	1.78	1.65
	MCV (fL)[6]	76.2	79
	Energy (kCal)	198.51	729.45
	Protein (g/d)	2.56	32.06
	Carbohydrate (g/d)	25.49	80.81
	Fat/Lipid (g/d)	9.59	26.4
	Fe (µg/dL)	0.7	5.63
	Vitamin A (µg/d)	25.5	287.47
	Bayley-III score		
Case 5 [Gestational age: 37 weeks; Sex: Female; Birthweight: 2.55 kg; Location/Demography: Urban; SES SCALE: Lower-middle]	Weight (Kg)	6.77	8.6
	Height (Cm)	63	73
	WAZ[1]	-0.93	-1.99
	WHZ[2]	-0.02	-0.67
	HAZ[3]	-1.37	-3.12
	BMI[4]	17.1	16.1
	BAZ[5]	-0.16	-0.08
	Hb (g/dL)	11.1	11.7
	Serum ferritin (ng/ml)	33.01	19.18
	SSTRS (mg/l)	1.32	1.32
	MCV (fL)[6]	78	89
	Energy (kCal)	361.35	640.56
	Protein (g/d)	8.94	21.83
	Carbohydrate (g/d)	52.96	104.35
	Fat/Lipid (g/d)	12.71	15.18
	Fe (g/dL)	1.43	6.3
	Vitamin A (µg/d)	43.97	304.59

	Bayley-III score		

[1]weight-for-age Z score; [2]weight-for-height Z score; [3]height-for-age Z score; [4]Body mass index; [5]BMI-for-age Z score; [6]Mean corpuscular volume.

Table S1: Demographic and baseline characteristics.

		Cereal intervention group
Gestational Age (weeks)	Mean ± SD	36.45 ± 1.57
	Median (min, max)	37 (32, 38)
Birth weight (Kg)	Mean ± SD	2.72 ± 0.31
	Median (min, max)	2.70 (2.03, 3.10)
BMI (Kg/m^2)	Mean ± SD	17.45 ± 1.98
	Median (min, max)	17.10 (15.10, 20.50)
Socioeconomic Scale	Upper middle	1 (9.09%)
	Upper Lower	7 (63.64%)
	Lower middle	3 (27.27%)
Location	Rural	1 (9.09%)
	Sub-urban	1 (9.09%)
	Urban	9 (81.82%)
Sex	Male	6 (54.55%)
	Female	5 (45.45%)
Type of Breast Feeding	Breastfeeding with commercial fortified formula	6 (54.55%)
	Exclusive breastfeeding	5 (45.45%)

Table S2: Disposition of anthropometric measures.

Case Number	**ID**	**weight-for-age Z score**		**weight-for-height Z score**		**height-for-age Z score**		**BMI-for-age Z score**	
		Baseline	**Final visit**	**Baseline**	**Final visit**	**Baseline**	**Final visit**	**Baseline**	**Final visit**
1	9101001	-1.47	-3.99	-0.49	-1.78	-1.7	-5.29	-0.62	-1
2	9101011	-1.22	-2.05	0.76	-1.02	-2.54	-2.66	0.38	-0.53
3	9101015	-1.14	-2.36	1.82	0.65	-3.57	-5.29	1.37	1.47
4	9101032	-1.82	-2.07	-0.94	-0.77	-1.65	-3	-1.16	-0.22
5	9101037	0.71	0.8	1.96	2.9	-1.21	-3	1.87	3.54
6	9101038	-0.37	-1.27	-1.57	0.53	1.57	-3.43	-1.69	1.23
7	9101040	0.52	0.21	2.1	2.18	-1.7	-3.06	2	2.82

8	9101048	-1.02	-2.18	-1.04	-1.18	-0.33	-2.66	-1.14	-0.69
9	9101056	-0.93	-1.99	-0.02	-0.67	-1.37	-3.12	-0.16	-0.08
10	9101057	0.63	-1.17	1.27	0.69	-0.46	-3.39	1.19	1.3
11	9103001	-1.1	-1.48	-0.65	0.31	-0.94	-3.5	-0.74	0.97

Table S3: Change in daily macro and micro-nutrient intake and Hb, SFRS, and SSTRS from baseline to 6 study-end period.

	Baseline (6 months)	**Final visit (12 months)**	**p-value**
	Median (IQ1, IQ3)	**Median (IQ1, IQ3)**	
Iron (mg/d)	3.84 (1.71, 6.19)	6.30 (4.61, 7.87)	0.091
Vitamin A (µg/d)	66.80 (29.72, 188.87)	260.80 (242.38, 304.59)	0.05
Protein (g/d)	8.94 (5.36, 13.44)	21.27 (14.74, 21.91)	0.008**
Energy (Kcal/d)	319.50 (198.51, 501.00)	623.03 (569.30, 640.56)	0.008**
Carbohydrate (g/d)	42.29 (25.49, 84.30)	93.93 (80.81, 98.59)	0.008**
Lipid (g/d)	9.59 (7.85, 12.71)	15.24 (14.41, 20.27)	0.041*
Hb (g/L)	106 (103, 111)	113 (109, 124)	0.004**
SFRS (ng/ml)	33.15 (24.52, 51.51)	29.02 (15.87, 50, 89)	0.075
SSTRS (mg/L)	1.56 (1.32, 1.94)	1.59 (1.33, 1.65)	0.262
MCV	75 (71.30, 78)	79 (75.60, 82.60)	0.05
MCH	23.80 (22.20, 24.50)	25.10 (23.50, 26.20)	0.045*

8.2. Author Contributions: Writing - original draft preparation: M.M.; Writing - review and editing: M.M., S.A., and N.U.R.; All authors have read and agreed to the published version of the manuscript.

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8.4. Conflicts of Interest: The authors declare no conflict of interest.

9. SUMMARY OF THE CASES

Figure 1, Tables S1 and S2 present the general features of the demographic and baseline characteristics, and anthropometric measures, respectively. Tables S1 and S2 present the general features of the demographic and baseline characteristics, and anthropometric measures, respectively.

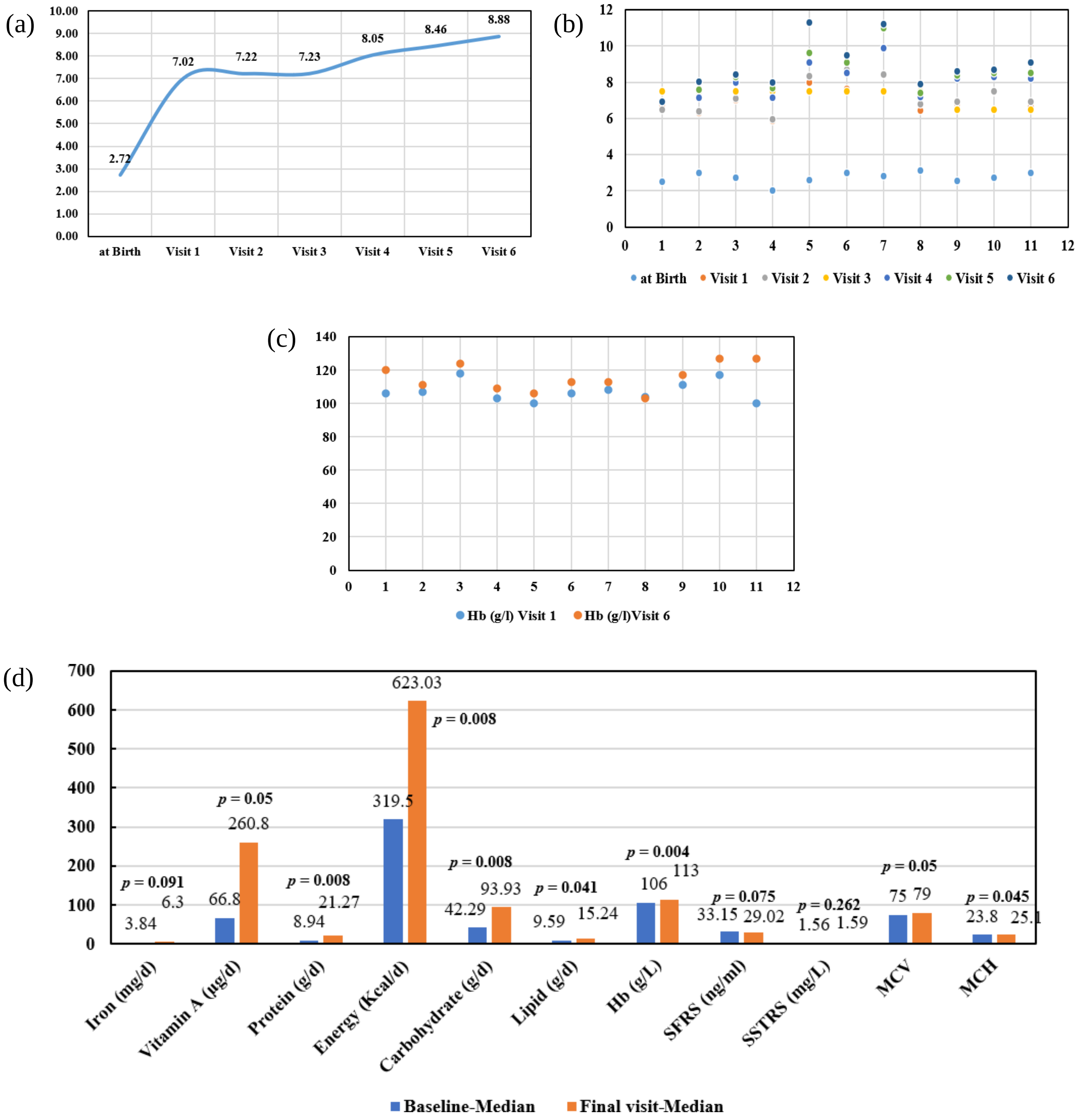

Figure 1: (a) Visit-wise changes in mean weight for all the cases; (b) Case- and visit-wise weight profile; (c) Mean Hb profile across all the cases, and (d) Changes in daily macro- and micro-nutrient intake and other biochemical parameters.

Dietary outcomes and differences in micronutrient intake for reducing the risk of micronutrient deficiencies and growth markers across groups

As reported in Table S3, median (IQ1, IQ3) daily energy intake experienced a significant increase from baseline *vis-à-vis* final visit 319.50 (198.51, 501.00) *v.* 623.03 (569.30, 640.56) kcal/d, respectively; p = 0.008) at 12 months of age. This is equivalent to the Estimated Average Requirement (EAR) as per the guidelines laid down by ICMR-NIN 2020 for infants in the age–6-12 months (530-680 Kcal/d). Because there is no RDA for energy, the EAR for energy is equivalent to the Estimated Energy Requirement (EER). Also, the protein profile for all the cases significantly increased two-fold [i.e., 8.94 g/d (5.36, 13.44) *v.* 21.27 g/d (14.74, 21.91)], 50.63% more than that of %RDA daily requirement for the infants in the age range of 6-12 months (8 g/d -10.5 g/d).

In addition, intakes of vitamin A from baseline [66.80 µg/d (29.72, 188.87)] in all the cases compared with the final visit [260.80 µg/d (247.38, 304.59)] showed improvement and thus the homemade CF along with fortified infant cereal feeds could fulfil about 75% of the daily RDA. Similarly, intakes of carbohydrates experienced a nearly 2-fold increase across cases (baseline: 42.29 g/d (25.49, 84.30) *v.* 93.93 g/d (80.81, 98.59) and this increase was 2- to 4-times in cases 1, 2, 4, 5, 7, 9 and 10 and case 8 had an increase of 7-times from baseline to study-end. Continuing this trend lipid profiles (total fat, linoleic acid, and α-linoleic acid) were also significantly higher (p =0.041) from baseline [9.59 g/d (7.85, 12.71] to study-end [15.24 g/d (14.41, 20.27].

The median daily iron intake of the study subjects at baseline was 3.84 g/dL (1.71, 6.19) and at study-end was 6.30 g/dL (4.61, 7.87). Iron intake was satisfactory, with all participants meeting the Indian RDA for iron. Cases 7 and 10 had an intake ≥ 5-fold increment from baseline to the study end. At the end of the study, all female and male subjects had an iron intake that exceeded the RDA's recommended level, while at baseline, only 60% of female subjects and 66.67% of male subjects achieved this.

All subjects except case 8 showed an improvement in Hb level. All 11 subjects had mild- to border-line anaemic infants at baseline, among which almost all subjects (91%) had an increase in Hb level, and almost 50% of the cases showed approximately ≥ 12 g/dl at the end of the study. Almost all cases (82%) showed a decrease in ferritin levels, except for cases 3 and 7, which showed an increase from baseline to the study end, probably underlying inflammation as the CRP level increased. With regard to soluble transferrin, approximately 37% of the cases showed an increase in the serum soluble transferrin receptor. Overall, the individual composite score on the Bayley-III assessment (including cognitive and motor function) maintained its composite score as an average post-12-months study-end period.

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