REVIEW ARTICLE

Food Fortification in India: A Literature Review

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Abstract

Background: India has a high prevalence of micronutrient deficiency-related health risks, which can be improved by food fortification. **Objectives:** To identify and analyze single or multiple micronutrient (MMN) food-fortification studies for their efficacy and effectiveness in India. **Methods:** Papers from searching 10 databases were independently screened by two researchers. Data were abstracted to summarize food fortification results on biological markers, anthropometry, clinical, morbidity, cognition, dietary intake, and physical performance. **Results:** Forty-seven papers, of which 25 were randomized controlled trials, were included for analysis. Children ≤12 y were the main population (n=38). Food vehicles were cereals (n=6), oils and salts (n=18), and other (e.g., school meals (n=23)). Improvements in ≥1 biological markers were reported in all 35 papers (22 MMN, 9 Iron, 4 Iodine) with interpretable results. More specifically, iron or hemoglobin improvements were noted in all papers fortifying with MMN or solely iron. Iodine nutriture was improved in all salt iodization papers. Eight of 14, 6 of 7, 2 of 6, 4 of 6, 1 of 4, and 1 of 1 papers with interpretable results showed ≥1 positive result of fortification in anthropometry, clinical signs, morbidity, cognition, dietary intake, and physical performance, respectively. **Conclusion:** Research in India suggests food fortification improves biological markers, particularly iron and hemoglobin when fortifying with MMN or iron. MMN fortification saw more health impacts than using single fortificants. Iodine status was improved through salt iodization. Existing government nutrition programs, especially those that target children, are good avenues for food fortification implementation.

Key Words

Food fortification; micronutrient

Introduction

India shares a disproportionate number of micronutrient deficiency-related health risks (e.g., neural tube defects (NTDs) [1], blindness [2], and anemia [3]), which affect over 2 billion people worldwide [4]. Previous reviews [5,6] in India stress food fortification as a strategy for improving health, highlighting research of iron, B-vitamin, and vitamin D deficiency on Indian populations.

Food fortification is used in many countries for improving nutrition [7]. Salt iodization around the world has consistently benefited reducing iodine deficiency disorders [8]. All countries that have evaluated folic-acid fortification of flour have shown a decrease in NTDs [9-18]. Evidence shows that fortifying with iron, vitamin A, and multiple micronutrients (MMN) increases hemoglobin levels and reduces the prevalence of anemia [19,20].

India's history of fortification began in 1953 when fortification of hydrogenated vegetable oil (vanaspati) with vitamin A and D [21] was mandated. Mandatory salt iodization began in 1998. However, in 2005-2006, only 51% of households used adequately iodized salt [3]. In 2000, wheat flour fortification started in West Bengal. Since then, 11 other states introduced fortification, though many initiatives have halted due to change in leadership or logistical constraints [22].

The Indian government has recommended food fortification in the 10th, 11th, and 12th Five-year Plans as a strategy to improve nutrition through existing government nutrition programs: Integrated Child Development Services (ICDS, targets pre-school children and pregnant or lactating women) [23], Mid-Day Meal (MDM, targets school children) [24], and Public Distribution System (PDS, targets poor, underserved communities) [25].

Aims & Objectives

The purpose of this review was to identify and analyze food fortification studies for their efficacy and effectiveness in India.

Material and Methods

Literature Search

A literature search (Table 1, [26-35]) to find food fortification research in India was conducted across ten databases.

Inclusion and Exclusion Criteria

Published trials, with full-text English-language version, with post-intervention data in at least one outcome measure (biological markers, anthropometry, morbidity, cognition, clinical signs, physical performance, and dietary intake) describing the results of fortification of foods with one or more micronutrients on the population of India were included.

Reviews, conference abstracts, and letters to the editor were excluded. Papers about fortification at the point of use (e.g., home fortification, micronutrient powders) and papers about biofortified crops, genetically modified foods, foods fortified with foods, drug fortification, macronutrient fortification, fortified oral rehydration salts, fortification of enteral/parenteral feeds, fortification with pre- and pro-biotics, ready to use therapeutic foods (RUTF), spreads, breast milk fortification and human milk fortifiers were also excluded. In vitro bioavailability papers were excluded, as well as ex-ante analyses.

Selection Process

After duplicates were removed, papers were independently screened for relevance by two reviewers in a multi-stage process (Figure 1). Papers were reviewed, first the titles alone and then by titles and abstracts, and then categorized as relevant, irrelevant, or cannot determine relevance.

Any disagreements were resolved by discussion and full text obtained for papers not marked as irrelevant. Full texts were read independently for final evaluation of pertinence and to obtain additional papers relevant for the review. All papers marked as relevant at this stage underwent data extraction independently by the two reviewers and after discussion, summarized into a standardized form.

Data Extraction

Two reviewers independently extracted the following from each full-text paper: Study design (e.g., randomized controlled trials, cross-sectional), age of subjects at baseline, initial number of subjects selected and those who had end-point data reported (in the case of discrepancies in either number, the smaller number was reported), population characteristics (e.g., pregnancy status, gender), Indian state in which the study took place, food vehicle used for micronutrient fortificant(s), micronutrients added, intended micronutrient dosage and frequency, and duration of the intervention. A narrative of statistically significant results along with important remarks on study design or data were noted.

Data Analysis

For each outcome measure, it was noted if there was a statistically significantly positive or negative effect of food fortification, no significant effect, or an un-interpretable result (e.g., missing statistical comparison between intervention and control groups). Results were reviewed as a whole in each outcome category, and then stratified into three subgroup analyses: age, micronutrients, and food vehicle.

Results

Literature Search

An initial 1037 papers were reviewed. After screening (Figure 1), 48 papers were selected and data were extracted from 47 papers for the review; one paper [36] described the study design details of results from another [37], and therefore both papers were counted as one.

The papers reported studies conducted in one or more of 13 Indian states. Intervention trials with at least one experimental group (i.e., received fortified food) and one control group (i.e., received no intervention or received unfortified food) made up 41 papers, with 25 randomized controlled trials, and for the other 16 it was unclear if randomization occurred. Cross-sectional designs were reported in 6 of the papers, all of which included endpoint data from large-scale samples of a population to monitor effectiveness of iodized salt.

The majority of papers (n=42) reported on children (e.g., preschoolers, low income, Mid-Day Meal

Program participants). Children aged 0-5 y, 6-12 y, and y were the focus in 10, 28 and 9 papers, respectively.

Food vehicles used were cereals (e.g., wheat flour, rice (n=6)), oils and salts (e.g., ground nut oil, salt (n=18)), and other (e.g., school meals, beverages (n=23)). All cereal food vehicle papers fortified with only iron. The majority of papers discussed MMN fortification (n=29). Single fortificants were iron (n=9), iodine (n=6), vitamin A (n=2) and other ((n=1), where fortificant(s) added was unclear [38]).

Effects on Biological Markers

Thirty-seven papers provided results of fortification on biological markers (Table 2, [37-83]). In 35 of these (22 MMN, 9 iron, 4 iodine), the results were interpretable, and all had at least one result that indicated a positive effect of fortification. Markers of iron or hemoglobin were the most-reported positive results. Salt (n=14) was one of the most common food vehicles for positive results. Soley iron as the fortificant, or solely iodine as the fortificant, resulted in positive outcomes in all papers for iron, and iodine nutriture, respectively.

Effects on Anthropometry

Fourteen out of 20 papers provided interpretable results on anthropometry (Table 2). Height (n=11) and weight (n=10) were the most reported results. All papers with at least one positive effect on an anthropometric outcome were MMN fortification (n=8).

No papers on solely iodine fortification reported on anthropometry.

Effects on Clinical Outcomes

Seven of 11 papers provided interpretable results on effects of food fortification on clinical outcomes, of which 6 were positive. The outcomes that were most positively associated with fortification were angular stomatitis (n=3), goiter (n=2) and bitot's spots (n=1) (Table 2).

No papers reported negative effects on clinical symptoms, and no papers on iron fortification reported on clinical outcomes.

Effects on Morbidity

Six of 10 papers provided interpretable results on morbidity (Table 2). Diarrhea (n=4), fever (n=4), and respiratory illnesses (n=3) were the most reported measures. In 2 of the 10 papers, there was a positive effect of fortification on at least one morbidity measure, and both were MMN fortification papers using a prepared beverage as the vehicle.

Four papers (2 MMN and 2 iron) reported no effect on morbidity.

Effects on Cognition

Six of 7 papers provided interpretable results on effects of food fortification on cognition (Table 2); all were in the 6-12 y age group. Four papers showed a positive effect of fortification on at least one cognition outcome and all were MMN fortification.

Two papers reported no effect of fortification. No paper reported negative effects on cognition.

Effects on Dietary Intake

Four papers provided results on effects of fortification on total dietary intake, of which 1indicated a positive effect on dietary intake of iron through fortification of salt with solely iron (Table 2).

Three papers (all MMN) reported no effect of fortification on dietary intake. No paper reported negative effects.

Effects on Physical Performance

One of two papers provided interpretable results of fortification on physical performance. One indicated a positive effect of MMN fortification. The other paper was an iron-fortified rice and did not have interpretable results. Both papers were in the 6-12 y age group.

Discussion

This paper is the first review of food-fortification research in India. Food fortification shows an overall positive impact, with 42 out of the 47 identified research papers reporting at least one health benefit in the following outcome categories: biological markers, anthropometry, clinical signs, cognition, morbidity, dietary intake, and physical performance.

MMN Fortification

All papers with interpretable results for MMN fortification reported at least one positive outcome on biological markers. Findings are consistent with previous reviews [84]. Iron (n=19), hemoglobin (n=22), vitamin A (n=6), iodine (n=9), vitamin B12 (n=7), folate (n=7), and other B complex vitamins (n=6) were the most reported positive results. One MMN paper [61] was the only one in the review to report a negative effect on a biological marker, specifically a decrease in median urinary iodine. This could have been due to high iodine losses in the micronized ground ferric pyrophosphate (MGFePP) salt with high moisture content [61].

All papers which showed at least one positive outcome in anthropometry had study durations of longer than 9 months and were MMN fortification.

Most of these also included zinc as an added fortificant and reported linear growth benefits, as described by other researchers [85,86]. The two MMN papers which reported no effect of fortification on anthropometry had shorter study durations of 4 months each.

All positive effects from MMN papers on clinical outcomes were reported on angular stomatitis or goiter. Papers with positive results on angular stomatitis included at least vitamin B2 and iron as fortificants, and papers with positive results on goiter included at least iodine as a fortificant.

The effects of MMN fortification on morbidity were overall equivocal, similar to findings in other reviews [20,84]. However, it should be noted that the only positive results in morbidity across the review were in two out of the five MMN papers that reported morbidity measures. Both papers used MMN fortification including zinc; this is consistent with a previous review that zinc supplementation aids in prevention of diarrhea and pneumonia [87].

Four out of five MMN fortification papers reported a positive impact of at least one cognitive domain in fluid reasoning, short-term memory measures, and concentration tests, which is consistent with previous research [5,88,89]. Three MMN papers reporting positive results on short-term memory measures included iron or zinc as a fortificant, which is consistent with a study that zinc and iron supplementation improve verbal and nonverbal short-term memory [90]. Few positive effects of MMN fortification were noted on long-term memory or IQ tests, and previous reviews have found the same [5,84].

Physical performance was reported in one paper [39], and had positive results in whole body endurance, aerobic capacity and step test, which is supported by research [91,92] that micronutrient supplementation, particularly with iron and B complex vitamins, largely affects aerobic exercise.

Iron Fortification

Iron as the sole fortificant resulted in improvements in at least one iron and or/hemoglobin biological marker for all papers; this is consistent with earlier reviews [19,20,93,94]. Similar to previous publications, iron fortification did not provide evidence supporting anthropometric [85,95] or morbidity [96] effects. One paper measured cognition, and reported no significant effect of fortification [69]. Previous reviews suggest beneficial effects of fortification on cognition particularly in anemic or iron deficient anemic children, and especially to those who were given treatment early in infancy [90,97].The iron-depleted children from the review paper mentioned above [69] were in the 6-12 age group, which may have been too old to reverse any cognitive damage from early life iron deficiency. No iron fortification paper identified in this review reported physical performance outcomes, though previous studies have shown iron benefits on aerobic exercise [91,92,98].

Iodine Fortification

The results observed in this review support the National Iodine Deficiency Disorders Control Program's (NIDDCP) vision of improved iodine nutriture through government-mandated salt iodization in India. All papers with interpretable results for sole iodine fortification were large-scale program assessments of salt iodization and showed improvements in iodine status, which is consistent with previous reviews [20]. No iodine fortification papers identified in this review looked at anthropometric outcomes, but a previous review showed significant positive effects of iodized salt on Indian children's weight for age Z score (WAZ) [99]. No papers in this review looked at cognition and iodine fortification, but it is well established that iodine deficiency during intra-uterine life impairs cognitive and psychomotor development [100].

Vitamin A Fortification

Two papers focused solely on vitamin A fortification and neither provided many interpretable results, with the exception of one that noted improvement in clinical signs of bitot's spots [83]. A previous review reported benefits of vitamin A supplementation on serum retinol concentration and hemoglobin levels [20]. Other studies looked primarily at large doses of vitamin A supplementation and found little to no impact on linear growth [85], and no effect on morbidity or mortality [101].

Program Implications

Evidence in support of Indian government nutrition programs were seen in the reviewed literature. Three papers reporting on trials supported by ICDS or MDM food fortification intervention all saw improvements in at least one biological marker. The majority of papers in the review were conducted on children 12 y, and this further suggests food fortification as a method employed by ICDS and MDM to reach that target population. Though a handful of papers had low-income or underprivileged subjects, no papers explicitly discussed any efforts of food fortification intervention through PDS.

Strengths and Limitations

This review is the first comprehensive examination of food-fortification research in India. Due to the wide scope, limitations arose from heterogeneity of publications and their study designs. Nonetheless, the data retrieved from a systematic search of 10 databases and organized in table form provide a holistic evidence of the effect of single and MMN fortification on health indicators in the Indian population.

Earlier reviews on India focused on specific micronutrient deficiencies [5,6,102], or provided highlights of food fortification research in India as a small part of a larger research question regarding fortification in all of Asia [99,103]. Other non-India food fortification reviews focus only on one, or on one specific combination of micronutrients [84,88,93,94,99,104], target population [20,84,85,94,104,106], food vehicle [105,106], outcome measure [55,84,85,88,93,94,104,105], or fortification/supplementation strategy [85,93].

This review is the first to provide a comprehensive overview of results of food fortification trials in India, is in line with the findings of other publications on Indian and non-Indian populations, and contributes additional important conclusions on food fortification research in India.

Conclusion

Food fortification offers many health benefits to the Indian population. The type of micronutrient is strongly linked to expected benefits. Evidence was strong for improvements in hemoglobin or iron markers when fortifying foods with a MMN fortificant containing iron or solely iron. Zinc as a component of MMN fortification resulted in positive effects on anthropometry, common morbidity symptoms, and short term cognitive measures, which is consistent with previous reviews on zinc supplementation. Clinical signs of angular stomatitis and goiter improved when vitamin B2 and iron, and iodine were part of the MMN fortificants, respectively. Sole iron fortification did not result in improved cognition in Indian school-children, and is not supportive of earlier findings that iron improves cognitive domains. Sole iron fortification did not show an effect on anthropometry or morbidity, and is consistent with previous reviews. Iodized salt showed consistent positive results on iodine status in the Indian population, and is a marker of the success of the universal salt iodization program. Previous reviews suggest benefits of iodine supplementation on anthropometry and cognition, though no papers were identified in India on these outcomes. Vitamin A fortification research is limited on the Indian population.

Observed results show that food fortification is a promising solution to improving health in India. Existing programs, particularly those that target children, are good avenues for implementation.

Authors Contribution

PL: Wrote manuscript, analyzed data extracted from papers and summarized into diagrams/tables. Retrieved citations, independently reviewed all citations, extracted key information from studies, sorted through discrepancies with other independent reviewer. RB: Critically reviewed and approved manuscript. Wrote the introduction. HP: Independently reviewed all citations, extracted key information from studies, sorted through discrepancies with other independent reviewer, critically reviewed and approved manuscript, and conceptualized study.

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Tables

TABLE 1 DATABASE SEARCH STRATEGY WITH DOCUMENTS FOUND JULY 17TH, 2013

Database	Search Strategy	Documents
PubMed [26]	(("Food, Fortified"[Mesh] OR fortif*) AND india) AND Humans[Mesh]	289
EMBASE [27]	'india'/exp AND fortif* AND [humans]/lim	103
BIOSIS Previews [28]	india fortif*	152
IndMED [29]	fortification OR fortify OR fortified	38
CABabstracts [30]	india fortif* subject_facet:"Homo"	183
Web of Science [31]	india fortif*	159
CINAHL [32]	india AND fortif* and search related texts, within full text	47
POPLINE [33]	india fortif* filter by Asia	50
AGRICOLA [34]	india fortif* and search related words	8
Dissertation Abstracts [35]	(LOC.exact("INDIA") OR SU.exact("INDIA") OR SU.exact("INDIA 90340") OR PER.exact("INDIA")) AND fortif*, nutrition, public policy, public health, agriculture, gender, nursing, zinc subjects	15
Database	Search Strategy	Documents
PubMed [26]	(("Food, Fortified"[Mesh] OR fortif*) AND india) AND Humans[Mesh]	289

EMBASE [27]	'india'/exp AND fortif* AND [humans]/lim	103
BIOSIS Previews [28]	india fortif*	152
IndMED [29]	fortification OR fortify OR fortified	38
CABabstracts [30]	india fortif* subject_facet:"Homo"	183
Web of Science [31]	india fortif*	159
CINAHL [32]	india AND fortif* and search related texts, within full text	47
POPLINE [33]	india fortif* filter by Asia	50
AGRICOLA [34]	india fortif* and search related words	8
Dissertation Abstracts [35]	(LOC.exact("INDIA") OR SU.exact("INDIA") OR SU.exact("INDIA 90340") OR PER.exact("INDIA")) AND fortif*, nutrition, public policy, public health, agriculture, gender, nursing, zinc subjects	15

TABLE 2: SUMMARY OF FORTIFICATION PAPER RESULTS ON DIFFERENT OUTCOMES

Micronutrient	Food Vehicle	Age (y) Dur(mo)	Author Year State (Program)	Biological Markers	Anthropometry	Clinical	Morbidity	Cognition	Dietary Intake	Physical Performance
MMN ; Vit (A, B1, B2, B3, B5, B6, B7, B9, B12, C, D), Ca, Cu, Fe, I,Mg, Zn	Other (choco-malt beverage powder)	6-12 4	Vaz M. 2011 [39] Karnataka	✓iron, vit (B1, B2, B3, B6, B9, B12, C)	O height, weight	✕	✕	✕	O energy, fat, protein, carbohydrates	✓WB endurance, aerobic capacity, step test O visual reaction time, 40-m sprint, handgrip strength, static forearm endurance
MMN; Vit D, Ca	Other (laddoo)	0-5 12	Ekbote VH 2011 [40] Pune	✓serum iPTH O 25OHD	✓TBLH BMC O height	✕	✕	✕	O Ca, P, Ca:P	✕
MMN; Vit (A, B9), Fe	Other (khichdi)	0-5 6	Varma JL 2007 [41] West Bengal (ICDS)	✓ SF, anemia, ID, IDA O Hb, serum retinol, %low vit A	?	✕	✕	✕	✕	✕
MMN; Vit (A, B1, B2, B3, B6, B9, B12, C, D, E), Cu, Fe, I, Zn	Other (dhal)	6-12 8	Osei AK 2010 [42] Uttarakhand	✓serum (retinol, folate, ferritin), %low (serum folate, vit B12), anemia, vit B12, total body iron O %low serum (retinol, zinc,	?	✕	O%(diarrhea, fever, cough, runny nose, vomiting)	✕	✕	✕

				ferritin), IDA						
MMN; Vit (A, B9, C), Fe	Other (hard candy)	0-5 3	Anand K 2007 [43] Haryana (ICDS)	✓Hb, SF ○ serum (retinol binding protein, retinol)	✕	✕	✕	✕	✕	✕
MMN; Vit (A, B9, C) Fe, I	Other (biscuits)	≥13 4	Goyle A 2012 [44] Rajasthan	✕	○ weight, height, BMI	✕	✕	✕	✕	✕
MMN; Vit (A, B1, B2, B3, B6, B9, C, D), Ca, Fe,I, Zn	Other (beverage reconstituted in milk)	6-12 14	Sivakumar B 2006 [37] Andhra Pradesh	✓plasma (ferritin, PTH, TSH), RBC folate, vit (A, B2, C, D) ○ Hb, vit (B6, B12), Ca, P	✕	✕	✕	✕	✕	✕
MMN; Vit (A, B9, C) Fe, I	Other (biscuits)	≥13 4	Anuradha G 2010 [45] Rajasthan	✓Hb, serum iron	✕	✕	✕	✕	✕	✕
MMN; Vit (A, B9, C) Fe, I	Other (biscuits)	≥13 4	Goyle A 2011 [46] Rajasthan	✓vit A ○ serum protein	✕	✕	✕	✕	✕	✕
MMN; Vit (A, C, E), Cu, Fe, Se, Zn	Other (milk powder)	0-5 12	Sazawal S 2007 [47] National Capital Territory of India	✕	✕	✕	✓diarrhea, ALRI, high respiration rate, severe illness, high fever, measles, antibiotic doses consumed ○ dysentery, severe respiratory illness	✕	✕	✕
MMN; Vit (A, B2, B9, B12,C),Fe, Zn	Other (beverage)	6-12 12	Thankachan P 2013 [48] Karnataka	✓Hb, SF, vit (A, B12, C), folate, BIS, sTfR, ZnPP, ID, IDA, %low vit (C, B12) ○ serum zinc, anemia	?	✕	?	✕	✕	✕
MMN; Vit B2, Fe	Other (school noon meal)	6-12 6	Malavika V 2009 [49] Tamil Nadu	✓Hb, anemia	✕	✓angular stomatitis	✕	✕	✕	✕

MMN; Vit (A, B9, C) Fe, I	Other (biscuits)	≥13 4	Goyle A 2011 [50] Rajasthan	✓UI	✕	✕	✕	✕	✕	✕
MMN; Vit (A, B1, B2, B3, B5, B6, B7, B9, B12, C, D, E, K), Ca, Cu, Fe, I, Mn, P, Se, Zn	Other (milk powder and cooked cereal food)	0-5 12	Nita B 2001 [51] National Capital Territory of India	✕	✓weight change ○ WHZ, weight, height, height change, %low height	✕	○ diarrhea, ALRI –fever, dysentery	✕	✕	✕
MMN; Vit (A, B2, B6, B9, B12, C), Ca, I, Fe, Zn	Other (biscuit and milk powder)	6-12 12	Muthayya S 2009 [52] Karnataka	✓Hb, ferritin, BIS, vit (B9, B12), anemia, ID, %low vit B12	✓linear growth ○ MUAC, %(stunting, underweight)	✕	✕	✓fluid reasoning ○ short term memory	✕	✕
MMN; Vit (A, B2, B3, B5, B6, B9, B12, C, E), Ca, Fe	Other (school meal)	6-12 9	Vinodkumar M 2006 [53] Tamil Nadu	✓Hb, serum vit (A, B12), vit B9 ○ serum vit E	✓height ○ weight	? angular stomatitis	✕	✕	✕	✕
MMN; Vit A, Ca, Fe	Other (biscuits)	0-5 6	Jyothi LA 2006 [54] Karnataka	?	✕	?	?	✕	✕	✕
MMN; Vit (A, C, E),Cu, Fe, Se, Zn	Other (milk powder)	0-5 12	Sazawal S 2010 [55] National Capital Territory of India	✓Hb, Hct, SF, ZnPP, RCDW, sTfR, ID, mean BIS, TIBC ○ plasma zinc	✓weight velocity, height velocity, WHZ, WAZ, HAZ	✕	✕	✕	✕	✕
MMN; Vit (A, B1, B2, B3, B6, B9, B12, C, D), Ca, Fe, I, Zn	Other (beverage reconstituted in milk)	6-12 14	Sarma KV [56] 2006 Andhra Pradesh	✕	✓height, height velocity, BMI ○ weight, HAZ, WAZ, weight velocity, HAZ velocity, WAZ velocity	○ bitot's spots, angular stomatitis, cheilosis, glossitis, bleeding gums, tooth caries, mottled enamel, goiter 1, goiter 2	✓duration of sickness ○ episodes of morbidity (fever, cough and cold, diarrhea, ear infection)	✕	✕	✕

MMN; Vit (A, B1, B2, B3, B6, B9, B12, C, D), Ca, Fe, I, Zn	Other (beverage reconstituted in milk)	6-12 14	Vazir S 2006 [57] Andhra Pradesh	✕	✕	✕	✕	○ increment in memory scores, school marks, IQ, verbal quotient, performance quotient, letter cancellation	✕	✕
MMN; Vits (A, B1, B2, B3, B6, B9, B12, C, D), Ca, Fe, I, Zn	Other (beverage reconstituted in milk)	6-12 14	Shatrugna V 2006 [58] Andhra Pradesh	✕	✓height, weight, FFM, % fat, WB-BMC, WB-bone area, BMD at neck of the femur ○ neck (BMC, area), hip (area BMC, BMD), spine (BMC, area, BMD), WB-BMD	✕	✕	✕	✕	✕
MMN; Vit (A, B2, B3, B5, B6, B9, B12, C, E), Ca, Fe	Other (school lunch meal)	6-12 12	Vinodkumar M 2008 [59] Tamil Nadu	✓Hb, Hct, RBC	✕	✕	✕	✓BVRT, CRT, Mann-Suiter picture recall, delayed response learning, digit forward, letter cancellation ○ personal information, digit backward, CPM	✕	✕
MMN; Fe, I	Oil/Salt (salt)	6-12 24	Brahmam GNV 2000 [60] Andhra Pradesh	✓median UI, T4	✕	✓% goiter	✕	✕	✕	✕
MMN; Fe, I	Oil/Salt (salt)	6-12 10	Andersson M 2008 [61] Karnataka	✓SF, body iron, sTfR, ZnPP, Hb –median UI	✕	✕	✕	✕	○ iron	✕
MMN; Fe, I	Oil/Salt (salt)	6-12 3	Vijayalakshmi P 2003 [62] Tamil Nadu	✓PCV, RBC	✕	✕	✕	✕	✕	✕
MMN; Vit (A, B1, B2, B3, B6, B9,	Oil/Salt (salt)	6-12 9	Vinodkumar M 2009 [63] Tamil Nadu	✓Hb, serum (vit A, vit B12,	✕	✓angular stomatitis	✕	✓memory tests	✕	✕

B12), Fe, I, Zn				zinc, folic acid), ferritin, BIS, sTfR, anemia, IDA ○ CRP, AGP						
MMN; Vit (A, B1, B2, B3, B5, B6, B9, B12), Fe, I	Oil/Salt (salt)	6-12 12	Vinodkumar M 2009 [64] Tamil Nadu	✓Hb, Hct, RBC, UI ○ serum Vit A	✓weight, weight change	? angular stomatitis	✕	✕	✕	✕
MMN; Vit (A, B1, B2, B3, B5, B6, B9, B12), Fe, I	Oil/Salt (salt)	6-12 12	Kumar MV 2007 [65] Tamil Nadu	✓Hb, Hct, RBC, UI ○ serum Vit A	✕	✓angular stomatitis	✕	✓BVRT, CRT, Mann-Suiter picture recall, delayed response learning, letter cancellation ○ personal information, digit (backward, forward), CPM	✕	✕
MMN; Fe, I	Oil/Salt (salt)	6-12 4	Umadevi P 2006 [66] Tamil Nadu	✓serum (iodine, phosphorus, iron) UI, urinary (creatinine, calcium, phosphorus) Hb, %transferrin saturation, TIBC ○ serum calcium	✕	✕	✕	✕	✕	✕
Iron	Cereals (wheat flour)	6-12 7	Amalrajan V 2012 [67] Karnataka	✓Hb, SF, sTfR ○ median urinary zinc, ZnPP, CRP	✕	✕	✕	✕	✕	✕
Iron	Cereals (rice)	6-12 7	Moretti D 2006 [68] Karnataka	✓SF, BIS, sTfR	?	✕	○ infectious disease	✕	✕	✕
Iron	Cereals (whole wheat flour)	6-12 7	Muthayya S 2012 [69] Karnataka, Maharashtra	✓anemia, ID, IDA, Hb, SF, sTfR,	○ weight, height	✕	✕	○ cognitive performance	✕	✕

				ZnPP, BIS ○ CRP						
Iron	Cereals (rice)	6-12 6	Zimmerman MB 2006 [70] Karnataka	✓SF, ZnPP, ID, median blood lead ○ sTfR	✕	✕	✕	✕	✕	✕
Iron	Cereals (rice)	6-12 8	Radhika MS 2011 [71] Andhra Pradesh (MDM)	✓ferritin, ID ○ CRP, Hb, anemia, IDA	○ height, weight, %underweight, %stunting, %wasted	✕	✕	✕	✕	✕
Iron	Cereals (rice)	6-12 6	Thankachan P 2012 [72] Karnataka	✓Hb, vit B12, plasma homocysteine, % low zinc, ZnPP, anemia, whole blood thiamine ○ SF, sTfR, serum (retinol, zinc), ID, IDA, % low vit A	○ height, weight	✕	○ common morbidity symptoms	?	✕	?
Iron	Oil/Salt (salt)	≥13 4	Jain M 1987 [73] Haryana	✓Hb, PCV, MCH concentration, serum iron, TIBC ○ RBC count, MCV, MCH content	✕	✕	✕	✕	✓iron	✕
Iron	Oil/Salt (salt)	6-12 12	Kapil U 2006 [74] Andhra Pradesh	✓Hb, anemia	✕	✕	✕	✕	✕	✕
Iron	Oil/Salt (salt)	≥13 12	149 Working Group on Fortification of Salt with Iron 1982 [75] Andhra Pradesh, National Capital Territory of India, Tamil Nadu, West Bengal	✓Hb ? anemia	✕	✕	✕	✕	✕	✕
Iodine	Oil/Salt (salt)	6-12	Kapil U 1996 [76] National Capital	✓UI	✕	✕	✕	✕	✕	✕

			Territory of India (USI)							
Iodine	Oil/Salt (salt)	6-12 180	Jagirdar PB 2000 [77] Maharashtra (USI)	?	✕	?	✕	✕	✕	✕
Iodine	Oil/Salt (salt)	6-12 144	Sooch SS 1973 [78] Punjab (USI)	✕	✕	✓goit er	✕	✕	✕	✕
Iodine	Oil/Salt (salt)	≥13 60	Kapil U 2004 [79] Tamil Nadu (USI)	✓UI	✕	✕	✕	✕	✕	✕
Iodine	Oil/Salt (salt)	≥13 180	Kapil U 2005 [80] Andhra Pradesh, Karnataka, Pondicherry, Tamil Nadu (USI)	✓UI	✕	✕	✕	✕	✕	✕
Iodine	Oil/Salt (salt)	≥13	Kapil U 2006 [81] Kerala (USI)	✓UI	✕	✕	✕	✕	✕	✕
Vit A	Oil/Salt (ground nut oil)	0-5 7	Jayakumar YA 2001 [82] Tamil Nadu	✕	?	✕	?	✕	✕	✕
Vit A	Oil/Salt (ground nut oil)	0-5 7	Sivan YS [83] 2002 Tamil Nadu	?	?	✓bit ot’s spots	?	✕	✕	✕
Other	Other (bread)	0-5 6	Kumari S 1985 [38] National Capital Territory of India	✕	⁻PEM grade I	✕	✕	✕	✕	✕

Figures

FIGURE 1 PAPER SELECTION PROCESS

(*reviewers discussed discrepancies together; ~, article not in English language (n=1), couldn't find full text (n=10))