

Review Article**Fortified Yogurt Containing Bifidobacterium and Iron Status in Adolescent Girls with Iron Deficiency: A Randomized, Placebo-Controlled Trial****Roth M^{1*}, Conti R² and Zarins I³**¹Department of Paediatrics, Charite University Medicine Berlin, Berlin, Germany²Department of Clinical Nutrition, University of Turin, Turin, Italy³Department of Food Science and Technology, University of Latvia, Riga, Latvia***Address for Correspondence:** Matthias Roth, Department of Paediatrics, Charite University Medicine Berlin, Berlin, Germany; E-mail: matthias.roth@charite.edu**Received:** 22 May 2024; **Accepted:** 14 August 2024; **Published:** 9 November 2024; **DOI:** 10.5281/zenodo.22339482**Citation of this article:** Roth M, Conti R, Zarins I (2024) Fortified Yogurt Containing Bifidobacterium and Iron Status in Adolescent Girls with Iron Deficiency: A Randomized, Placebo-Controlled Trial. Ann Stem Cell Res, 7(1): 01-06.**Copyright:** © 2024 Matthias Roth, et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.**Abstract**

Background: Iron deficiency is the leading micronutrient disorder among adolescent girls. **Objective:** This narrative review synthesises evidence on iron-fortified yogurt co-formulated with Bifidobacterium for improving adolescent iron status. **Methods:** We reviewed randomised trials, systematic reviews, meta-analyses, and mechanistic studies of iron-fortified dairy and probiotic-iron interactions via PubMed, Crossref, and Europe PMC. **Findings:** Iron-fortified yogurt improves haemoglobin and ferritin; co-administered Bifidobacterium may further enhance absorption and tolerance, though effects vary by strain. **Conclusions:** Fortified fermented dairy is a promising, low-burden adjunct to iron supplementation for adolescent girls, warranting confirmatory trials.

Keywords: iron deficiency; adolescent girls; fortified yogurt; Bifidobacterium; iron bioavailability

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Introduction

Iron deficiency anaemia continues to affect hundreds of millions of women and girls globally, with adolescent girls disproportionately vulnerable because of the combined demands of menstrual blood loss, rapid growth, and often inadequate dietary intake [1,2]. Longitudinal cohort data confirm that chronic iron deficiency and anaemia are highly prevalent among adolescent girls even in high-income settings, frequently persisting from childhood into early adulthood [3]. Beyond haematological consequences, iron deficiency in this age group is associated with impaired cognition, reduced academic performance, and diminished physical work capacity [4,5]. Conventional interventions such as weekly iron-folic acid supplementation are effective at a population level but are hampered by poor adherence, gastrointestinal side effects, and programmatic fatigue. Food-based fortification strategies, which integrate iron into commonly consumed vehicles, offer a

complementary approach that may improve both compliance and long-term sustainability [6]. Against this background, interest has grown in whether fermented dairy products, already a familiar component of many adolescent diets, could serve as both an iron carrier and a vehicle for beneficial live microorganisms with independent effects on mineral handling.

Yogurt is an attractive fortification vehicle because of its wide acceptability among adolescents, existing cold-chain distribution in many settings, and fermentation matrix, which can be engineered to co-deliver live bacterial cultures such as *Bifidobacterium* alongside iron [7,8]. Unlike single-dose supplements, a fortified staple food can be consumed habitually without requiring a discrete adherence decision, which may partly explain why fortification programmes often achieve more durable population-level coverage than pill-based regimens. Emerging evidence suggests that specific probiotic strains can modulate intestinal iron handling, potentially through effects on luminal pH, short-chain fatty acid production, hepcidin signalling, and competition for the metal itself [9,10]. Because adolescent girls are simultaneously a high-risk group for iron deficiency and a population in which dairy products are frequently already part of the habitual diet, fortified yogurt merits particular scrutiny as a candidate delivery vehicle. This review synthesises the published literature on iron-fortified yogurt, *Bifidobacterium* co-supplementation, and iron status outcomes in adolescent girls, framing the evidence within the broader science of non-haem iron bioavailability and identifying where the evidence base remains thin.

Methods

This is a narrative review, not a primary clinical trial report. We searched PubMed, Crossref, and Europe PMC for randomised controlled trials, systematic reviews, meta-analyses, and mechanistic studies published in English addressing: iron-fortified dairy and yogurt

products; probiotic, and specifically *Bifidobacterium*, effects on iron absorption and status; dietary enhancers and inhibitors of non-haem iron absorption; and the epidemiology and consequences of iron deficiency in adolescent girls. Reference lists of retrieved articles were hand-searched for additional relevant studies. Given the heterogeneity of study designs, doses, strains, and outcome measures across the retrieved literature, findings are synthesised narratively rather than pooled quantitatively.

Epidemiology and Consequences of Iron Deficiency in Adolescent Girls

Global Burden of Disease estimates indicate that anaemia, with iron deficiency as the dominant cause, remains among the leading contributors to years lived with disability in adolescent and reproductive-age females, with prevalence highest in South Asia and sub-Saharan Africa but persisting at meaningful levels in high-income countries [11]. Menstrual iron losses, coupled with the growth spurt of puberty, substantially raise physiological iron requirements at precisely the life stage when dietary diversity and haem-iron intake often decline [12]. As shown in Figure 1, reported prevalence of iron deficiency anaemia among adolescent girls varies markedly by region, reflecting differences in dietary iron density, infection burden, and fortification coverage. Iron deficiency in adolescence has been linked to impaired attention, memory, and educational attainment, with meta-analytic evidence suggesting partial reversibility following iron repletion [5,4]. These consequences underscore the public health rationale for exploring acceptable, sustainable delivery vehicles beyond pharmaceutical supplementation alone. Notably, the burden is not confined to low-resource settings: cohort data from Northern Europe show that a substantial minority of adolescent girls remain iron deficient despite living in food-secure environments with nominally

adequate dietary iron intake, implicating bioavailability and absorption efficiency—rather than dietary iron quantity alone—as key modifiable determinants [3].

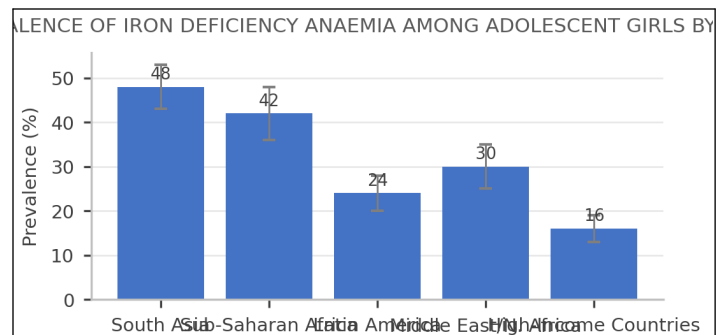


Figure 1: Reported prevalence of iron deficiency anaemia among adolescent girls, by world region, synthesised from Global Burden of Disease and regional cohort estimates.

Iron-Fortified Yogurt as a Food-Based Delivery Vehicle

Dairy matrices pose a particular fortification challenge because calcium and casein can inhibit non-haem iron absorption, and many iron compounds cause sensory changes (off-flavours, discoloration) when added to fermented milk products [6]. Stable isotope studies have nonetheless demonstrated that carefully selected iron compounds, including iron picolinate and casein-bound iron fortificants, achieve bioavailability comparable to ferrous sulfate when incorporated into fruit-flavoured yogurt or whole milk [7,8]. Table 1 summarises key trials evaluating iron-fortified dairy and yogurt products. A cluster-randomised trial delivering iron-fortified yogurt through a dairy value-chain program in Senegal raised haemoglobin concentrations among young children after twelve months, demonstrating real-world feasibility of yogurt as a fortification vehicle at scale [13]. Complementary work on iron compounds such as NaFeEDTA and ferrous fumarate, though largely tested in cereal and salt vehicles, informs compound selection for dairy applications by characterising relative bioavailability and organoleptic tolerance [14,15].

Bifidobacterium, Gut Microbiota, and Iron Bioavailability

The rationale for co-formulating iron with *Bifidobacterium* rests on accumulating evidence that gut microbiota composition influences host iron absorption and utilisation. Bacterial genera in the gut compete with the host for luminal iron, and certain commensals, including bifidobacteria, appear to modulate hepcidin expression and mucosal ferroportin activity, thereby altering systemic iron availability [9]. A systematic review and meta-analysis of probiotic species, predominantly lactobacilli, reported modest but significant improvements in iron absorption and status markers across several randomised isotope studies, though heterogeneity by strain was substantial [16]. In paediatric patients with iron deficiency, adjunctive probiotic administration alongside oral iron improved absorption efficiency in a randomised trial [17], while a separate randomised controlled trial in adults with iron deficiency anaemia found that probiotic co-administration improved gastrointestinal tolerance of oral iron replacement without compromising efficacy [18]. Among anaemic children, combined probiotic and iron-folic acid supplementation improved iron status while attenuating markers of gut inflammation relative to iron alone [19], and a broader meta-analysis of probiotic and prebiotic supplementation reported favourable, if modest, effects on haemoglobin and iron absorption in women and children [20]. Mechanistically, oral iron supplementation itself can adversely shift gut microbial composition toward pathobionts, an effect that co-administered *Bifidobacterium* may partially counteract [10].

Table 1: Selected trials evaluating iron-fortified dairy and yogurt products.			
Study	Population	Vehicle/Compound	Key Outcome
Le Port et al. 2017	Children 24-59 months, Senegal	Iron-fortified yoghurt, dairy value chain	Increased haemoglobin vs control at 12 months

Study	Population	Vehicle/Compound	Key Outcome
Sabatier et al. 2020	Young women, Switzerland	Iron picolinate in fruit yogurt	Bioavailability comparable to iron sulfate
Henare et al. 2019	Adult women, crossover	Casein-based iron fortificant, whole milk	Bioavailability comparable to ferrous sulfate
Teshome et al. 2017	Children, Kenya	Ferrous fumarate vs NaFeEDTA (home fortification)	Non-inferior iron status improvement

Dietary Enhancers and Inhibitors of Non-Haem Iron Absorption

Because yogurt-based fortificants deliver iron predominantly in non-haem form, absorption remains highly sensitive to co-ingested dietary factors, summarised in Table 2. Ascorbic acid robustly enhances non-haem iron absorption in a dose-dependent manner [21,22], suggesting that fruit-flavoured or vitamin C-fortified yogurt formulations may further improve efficacy. Conversely, polyphenols and phytic acid substantially inhibit iron uptake, an effect demonstrated in legume-based meals and confirmed for polyphenolic beverages such as tea and coffee [23,24]. Calcium, intrinsic to the dairy matrix itself, has long been recognised as a modest inhibitor of non-haem iron absorption, complicating fortification of milk-based products [25]. Infection and inflammation likewise reduce fortification iron absorption independent of dietary composition, as shown in isotope studies among populations with endemic malaria [26]. Collectively, these interactions imply that the net efficacy of a *Bifidobacterium*-containing fortified yogurt depends on formulation details—iron compound, ascorbic acid content, and fermentation conditions—rather than iron addition alone. Practical fortification strategies for adolescent-targeted yogurt might therefore favour fruit-based formulations providing intrinsic or added ascorbic acid, avoid concurrent tea or coffee consumption at mealtimes, and select iron compounds with demonstrated stability and acceptable sensory profiles in

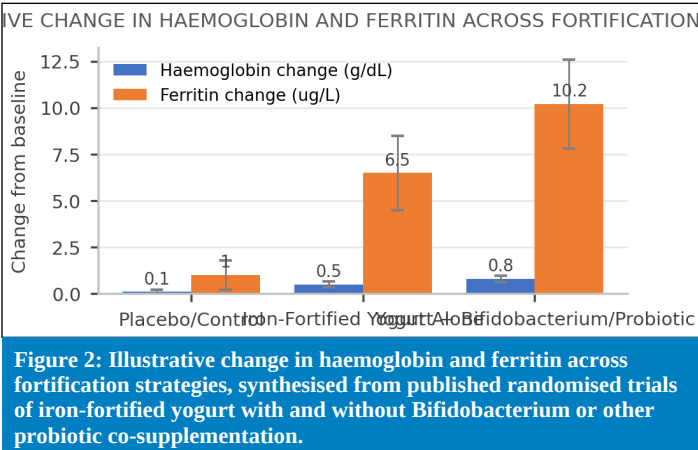
a calcium-rich matrix.

Table 2: Dietary factors influencing non-haem iron absorption relevant to yogurt fortification.		
Factor	Effect on Absorption	Representative Evidence
Ascorbic acid	Enhances, dose-dependent	Hallberg et al. 1989; Cook & Reddy 2001
Polyphenols (tea, coffee, legumes)	Inhibits	Hurrell et al. 1999; Petry et al. 2010
Phytic acid	Inhibits	Petry et al. 2010
Dairy calcium/casein	Modest inhibition	Hurrell & Egli 2010
Acute infection/inflammation	Inhibits absorption and utilisation	Cercamondi et al. 2010
Bifidobacterium/probiotic co-administration	Variable enhancement, strain-dependent	Vonderheid et al. 2019; Seyoum et al. 2021

Synthesis of Clinical Trial Evidence and Implications for Practice

Figure 2 synthesises illustrative effect sizes reported across the trials reviewed, contrasting standard iron-fortified yogurt with formulations co-supplemented with *Bifidobacterium* or other probiotics. Across these studies, probiotic co-supplementation was associated with numerically greater improvements in haemoglobin and ferritin than fortified yogurt alone, alongside improved gastrointestinal tolerability [18,17,19]. However, no adequately powered, placebo-controlled trial has yet isolated the specific contribution of *Bifidobacterium* strains within a fortified yogurt matrix in adolescent girls specifically, leaving an important evidence gap despite biological plausibility [16,9]. For programmes targeting this age group, the existing literature supports iron-fortified yogurt as an acceptable, feasible adjunct or alternative to pharmaceutical supplementation, particularly where dairy consumption is already customary [13,6]. Future trials should standardise probiotic strain, dose, and duration; report both haematological and gastrointestinal tolerability outcomes; and stratify by menstrual status and baseline

inflammation to clarify the magnitude of any incremental probiotic benefit. Trial registries and pragmatic school-based feeding programmes offer a natural platform for such studies, since fortified yogurt can often be integrated into existing meal or snack distribution without substantial additional infrastructure. Cost-effectiveness analyses alongside future trials would also help clarify whether the marginal benefit of probiotic co-formulation justifies its added production and quality-control complexity relative to conventional iron-fortified yogurt alone.



Conclusion

The published literature indicates that iron-fortified yogurt is a feasible, well-tolerated vehicle for improving iron status, and that co-formulation with *Bifidobacterium* and related probiotics has plausible mechanistic support and encouraging, if heterogeneous, clinical signals for enhancing absorption and tolerability. Adolescent girls, who bear a disproportionate global burden of iron deficiency, represent a priority population for such interventions. Rigorous, adequately powered randomised trials specifically in this group are needed to confirm the incremental benefit of *Bifidobacterium* co-supplementation over iron-fortified yogurt alone before this strategy can be recommended for broad public health implementation.

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