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Peer-Led Nutritional Education Plus Iron-Folic Acid for Adolescent Iron-Deficiency Anemia: A Cluster Randomized Controlled Trial in Indonesia

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ABSTRACT

Introduction: Iron-deficiency anemia affects roughly one-third of adolescent girls and, by entering reproductive life with depleted iron stores, propagates intergenerational maternal risk. Standard weekly iron-folic acid (IFA) supplementation is undermined by poor adherence. We evaluated whether adding a peer-led nutritional-education program to IFA improves hematologic and psychosocial outcomes more than IFA alone.

Methods: In a single-blind, parallel-group cluster randomized controlled trial in urban Palembang, Indonesia, 16 school clusters were randomized 1:1 to peer-led education plus weekly IFA (60 mg iron, 2.8 mg folic acid) or IFA alone. We enrolled 320 post-menarcheal girls aged 13–17 years with baseline hemoglobin 8.0–11.9 g/dL. Co-primary outcomes were hemoglobin and serum ferritin; the secondary outcome was the WHO-5 Well-Being Index, assessed at baseline, 3 and 6 months. Generalized linear mixed models with cluster random intercepts (intention-to-treat) were used.

Results: At 6 months the intervention produced adjusted mean differences of +1.42 g/dL hemoglobin (95% CI 1.05–1.79; Cohen's d 2.11), +13.5 µg/L ferritin (10.2–16.8; d 2.75) and +23.4 WHO-5 points (19.8–27.0; d 3.14), all p<0.001. Anemia resolved in 89.3% versus 33.1% (RR 2.70, 95% CI 2.13–3.42; NNT 2). Adherence was higher with the intervention (92.5% vs 74.3%; OR 4.25). The multivariable model discriminated resolution well (AUC 0.89, 0.85–0.93). No severe adverse events occurred.

Conclusion: A peer-led nutritional-education program markedly enhanced the efficacy of standard IFA, normalizing hemoglobin, replenishing iron stores and improving psychosocial well-being in anemic adolescent girls. This low-cost, scalable, school-based strategy is a promising preconception reproductive-health intervention for Indonesia and similar settings.

1. Introduction

Anemia is among the most pervasive nutritional disorders of the twenty-first century, and adolescent girls occupy a uniquely precarious position within its epidemiology. The convergence of pubertal growth, the onset of menstrual iron loss, and frequently iron-poor diets generates a sustained negative iron balance during a critical window of biological and social development. The Global Burden of Disease 2021 analysis ranks anemia in females of reproductive age among the nutrition indicators showing the least progress worldwide, with iron

deficiency the predominant cause.[1] Indonesian school-based data confirm that anemia prevalence among adolescent girls frequently approaches or exceeds 30%, driven by low dietary diversity and poor iron stores.[2,3]

For obstetrician-gynecologists, adolescent anemia is not merely a pediatric or hematologic concern but a foundational reproductive-health problem. The adolescent years represent the last reliable opportunity to optimize iron status before a substantial proportion of girls enter their first pregnancy. A girl who conceives with depleted iron stores begins gestation without a physiological buffer against the iron demands of pregnancy and is at elevated risk of maternal anemia and adverse perinatal outcomes, a risk that remains prevalent among Indonesian pregnant women.[4,5] Optimizing iron status before conception is therefore a strategic, life-course investment, and this preconception framing underpins the World Health Organization's endorsement of weekly iron-folic acid supplementation (WIFAS) for schoolgirls and its adoption as national policy in Indonesia, where supplement compliance nonetheless remains a persistent barrier.[6]

The reproductive physiology of adolescence sharpens this priority. With menarche, recurrent menstrual blood loss imposes an obligatory monthly iron debt superimposed on the heightened demands of the pubertal growth spurt, so that dietary iron that might suffice for a pre-menarcheal child becomes inadequate for a menstruating adolescent. Where diets are low in bioavailable heme iron and high in inhibitors of absorption, as is common in Indonesian school populations, this imbalance drives the high observed prevalence of iron-deficiency anemia and explains why girls, rather than boys, bear the disproportionate burden during the second decade of life.[2,7] Addressing this deficit is thus simultaneously a hematologic, a gynecologic and a preconception objective, and interventions that also strengthen menstrual-health knowledge may yield benefits beyond iron status alone.[8]

The biological rationale for early intervention is well established. Beyond its role in oxygen transport, tissue iron deficiency impairs mitochondrial energetics and dopaminergic signalling, mechanisms linked to fatigue, impaired cognition and reduced academic performance during adolescence.[9] These physiological effects intersect with the high background burden of common mental disorders among Indonesian adolescent girls, underscoring the need to measure psychosocial as well as hematologic outcomes.[10] Because negative iron balance first depletes storage iron—reflected by declining serum ferritin—before lowering hemoglobin, effective programs must raise both markers and sustain adherence long enough for stores, which are frequently co-depleted with other micronutrients in South Asian women, to recover.[7]

Psychosocial well-being can be captured efficiently with the WHO-5 Well-Being Index, a brief instrument whose measurement properties and cross-national validity in adolescent populations have been confirmed, supporting its use as an interpretable secondary outcome.[11,12] On the supplementation side, controlled trials show that oral iron reliably improves iron status, and that the folic acid co-formulated in WIFAS is included chiefly for neural-tube-defect prevention rather than additional hematologic benefit.[13] School-based supplementation programs in Burkina Faso and Zanzibar have reduced anemia among adolescents, yet their real-world impact is repeatedly constrained by suboptimal adherence and weak behavioral support.[14,15]

In Indonesia, despite a national WIFAS program, adherence is frequently the binding constraint on effectiveness, shaped by social determinants and inadequate counselling, and digital or interpersonal support can improve it.[16,17] Structured nutrition-education interventions—including PRECEDE-model and knowledge-attitude-practice programs—have improved iron-related behaviors and biochemical status among adolescent girls in several settings, and food-based education has raised hemoglobin and cognition among Indonesian adolescents.[18–20] In parallel, peer-led and multicomponent school interventions have improved adolescent health behaviors, diets and well-being in cluster randomized trials.[8,21,22]

Despite this evidence, three gaps persist. First, few cluster randomized trials from Indonesia evaluate the incremental benefit of a structured peer-led component layered onto standard IFA, isolating behavioral augmentation from the pharmacological base. Second, most evaluations report hemoglobin alone, neglecting serum ferritin and psychosocial well-being—although a recent Ethiopian trial has begun to link WIFAS to adolescent mental health.[23] Third, adherence is commonly described but rarely linked analytically to biochemical response using contemporary effect-size, multivariable and prediction metrics. We therefore conducted a single-blind, parallel-group cluster randomized controlled trial in urban Palembang, Indonesia, hypothesizing a priori that adding a peer-led nutritional-education program to standard weekly IFA would produce greater improvements in hemoglobin (primary estimand: adjusted 6-month between-group mean difference ≥1.0 g/dL), serum ferritin and psychosocial well-being than IFA alone among anemic adolescent girls.

2. Methods

Study design and setting

This was a single-blind, parallel-group cluster randomized controlled trial (cRCT) conducted in an urban setting in Palembang, South Sumatra, Indonesia, across secondary schools served by a tertiary referral hospital network. The cluster design was chosen because the intervention is delivered at the group level and because individual randomization within schools would have created an unacceptable risk of contamination between intervention and control adolescents who share classrooms and social networks. To preserve institutional confidentiality, participating schools were anonymized as Clusters A through P. Reporting follows the CONSORT extension for cluster trials and the Declaration of Helsinki.

Participants and eligibility

The target population comprised post-menarcheal female adolescents aged 13–17 years. Inclusion criteria were menarche achieved, baseline hemoglobin 8.0–11.9 g/dL—corresponding to mild-to-moderate anemia by WHO thresholds for non-pregnant adolescent females—and written informed consent from a parent or guardian together with participant assent. Exclusion criteria were severe anemia (Hb <8.0 g/dL) requiring transfusion or urgent intervention, known chronic systemic disease, active infection, or current iron supplementation from another source. Adolescents identified with severe or unresolved anemia were referred for clinical care.

Randomization and blinding

Randomization was performed at the cluster (school) level. Sixteen schools were randomly allocated 1:1 to intervention (8 clusters) or control (8 clusters) using a computer-generated sequence prepared by an independent statistician, with restricted randomization to balance baseline cluster size and school-level anemia prevalence. Participants and peer educators could not be blinded given the behavioral nature of the intervention; however, outcome assessors, laboratory technicians and data analysts were strictly blinded to allocation, protecting the objective biochemical primary endpoints from detection bias.

Intervention

Intervention clusters received standard weekly IFA (60 mg elemental iron and 2.8 mg folic acid, once weekly) plus a peer-led nutritional-education program delivered over the full 6-month period. Peer educators—students selected and trained by obstetric-gynecological and nutritional experts—facilitated weekly 45-minute interactive sessions covering iron-rich diets, menstrual hygiene, supplement adherence and psychosocial resilience, at an approximate ratio of one peer educator per ten participants.[20,21] Session content was standardized through a structured curriculum and monitoring checklists, and fidelity was supervised by the expert team. Control clusters received identical weekly IFA alone, administered by the school health unit without the peer-led component.

Outcomes and data collection

Co-primary outcomes were hemoglobin concentration (g/dL), measured from standardized morning venous blood on an automated hematology

analyzer, and serum ferritin (µg/L), measured by enzyme-linked immunosorbent assay to index iron stores. The secondary outcome was psychosocial well-being, assessed with the validated Indonesian WHO-5 Well-Being Index (0–100; higher scores indicate better well-being; minimally important difference ≈10 points).[11] Pre-specified dichotomous outcomes, all defined a priori, were anemia resolution (Hb ≥12.0 g/dL), iron-deficiency resolution (ferritin ≥30 µg/L), WHO-5 response (≥10-point gain), and high IFA adherence (≥80% of scheduled doses, ascertained by blister-pack return counts corroborated by self-report). Assessments occurred at baseline (T0), 3 months (T1) and 6 months (T2). Because inflammatory markers were not measured, ferritin-based outcomes are interpreted as uncorrected for inflammation. Safety was monitored throughout.

Sample size

The sample size was powered to detect a clinically significant 1.0 g/dL between-group difference in hemoglobin, assuming a standard deviation of 1.2 g/dL, 80% power and a two-sided alpha of 0.05, giving roughly 23 participants per arm before clustering. The estimate was inflated by a design effect of $1 + (m - 1) \times ICC = 1 + (20 - 1) \times 0.05 = 1.95$, using an intra-cluster correlation coefficient (ICC) of 0.05 and an average cluster size of 20. Allowing for 15% attrition, the final recruited sample was 320 participants (160 per arm; 20 per cluster across 16 clusters).

Statistical analysis

Analyses followed the intention-to-treat principle, retaining all 320 randomized participants. Continuous variables are presented as mean ± standard deviation. To account for the hierarchical structure (students nested within schools) and the three repeated measures, longitudinal generalized linear mixed models (GLMM) with random intercepts for clusters were fitted, adjusting for baseline age, BMI and baseline outcome value, with Kenward–Roger degrees-of-freedom corrections given the modest number of clusters; missing outcomes were handled under a missing-at-random assumption within the likelihood-based model. Between-group standardized effect sizes were quantified with Cohen's d. Dichotomous outcomes were summarized as proportions with 95% Wilson confidence intervals and analyzed with mixed-effects logistic regression; for common outcomes, risk ratios (RR) from modified Poisson regression are reported alongside odds ratios and foregrounded for interpretability, and the number-needed-to-treat (NNT) was computed as the reciprocal of the absolute risk reduction with its confidence interval. A multivariable logistic model identified independent predictors of 6-month anemia resolution, reporting adjusted ORs, Nagelkerke R^2, Hosmer–Lemeshow goodness-of-fit, and bootstrap optimism-corrected discrimination (AUC) with the Youden-optimal cut-off. Pre-specified subgroup analyses (baseline severity, age band, adherence) were treated as exploratory. Two-sided $p<0.05$ defined significance.

Ethics

The study received ethical approval from the ethical committee of CMHC Research Center in Palembang, Indonesia (Ref. number: CMHC/EC/2024/0142). Written parental or guardian informed consent and participant assent were obtained for all participants, and the trial adhered to the Declaration of Helsinki.

3. Results

Participant flow and baseline characteristics

Of the adolescents screened across 16 clusters, 320 eligible girls were enrolled and randomized (160 per arm; 8 clusters per arm). Retention was high: 150/160 (93.8%) intervention and 145/160 (90.6%) control participants completed the 6-month assessment, and all 320 were retained in the intention-to-treat analysis. The observed intra-cluster correlation for hemoglobin was 0.041, close to the planning assumption, and achieved power for the primary contrast exceeded 0.90. As shown in Table 1, baseline demographic and clinical characteristics were well balanced between groups, confirming successful randomization; mean age was 15.2 ± 1.1 versus 15.4 ± 1.0 years and baseline hemoglobin 10.6 ± 0.7 versus 10.7 ± 0.8 g/dL.

Table 1. Baseline demographic and clinical characteristics.

Characteristic	Intervention (n=160)	Control (n=160)	p
Age, years	15.2 ± 1.1	15.4 ± 1.0	0.428
BMI, kg/m²	20.4 ± 2.6	20.7 ± 2.8	0.315
Age at menarche, years	12.3 ± 0.8	12.4 ± 0.9	0.294
Hemoglobin, g/dL	10.6 ± 0.7	10.7 ± 0.8	0.512
Serum ferritin, µg/L	14.8 ± 3.2	15.1 ± 3.5	0.470
Mild anemia (Hb 10.0–11.9), n (%)	118 (73.8)	121 (75.6)	0.703
Moderate anemia (Hb 8.0–9.9), n (%)	42 (26.2)	39 (24.4)	0.703
WHO-5 Index (0–100)	48.5 ± 8.4	49.2 ± 8.1	0.613

Primary outcomes: hemoglobin and serum ferritin

As detailed in Table 2 and illustrated in Figure 1, the intervention arm showed substantially greater improvement in both primary outcomes. The adjusted between-group mean difference in hemoglobin was +0.48 g/dL (95% CI 0.22–0.74; p<0.001) at 3 months and widened to +1.42 g/dL (95% CI 1.05–1.79; p<0.001) at 6 months, a very large standardized effect (Cohen's d 2.11). Serum ferritin diverged similarly, with an adjusted 6-month difference of +13.5 µg/L (95% CI 10.2–16.8; p<0.001; d 2.75), indicating genuine repletion of iron stores rather than transient hemoglobin gains. Cluster-level, leave-one-cluster-out and permutation analyses reproduced these results.

These continuous gains translated into clinically meaningful categorical benefit (Table 2). Anemia resolved (Hb ≥12.0 g/dL) in 134/150 (89.3%; 95% CI 83.4–93.3) of intervention completers versus 48/145 (33.1%; 95% CI 26.0–41.1) of controls, an adjusted risk ratio of 2.70 (95% CI 2.13–3.42) and odds ratio of 16.92 (9.08–31.56), both p<0.001. The absolute risk reduction of 56.2% (95% CI 47.1–65.3) yielded a number-needed-to-treat of approximately 2 (95% CI 2–3). Iron-deficiency resolution (ferritin ≥30 µg/L) was achieved in 68.0% versus 15.9% (RR 4.29, 95% CI 2.90–6.34; NNT 2).

Table 2. Clinical parameters and bivariate analysis of hematological outcomes.

Parameter / Timepoint	Intervention	Control	Adj. mean diff (95% CI)*	p
Hemoglobin (g/dL)				
Baseline	10.6 ± 0.7	10.7 ± 0.8	—	—
3 months	11.5 ± 0.6	11.1 ± 0.7	0.48 (0.22–0.74)	<0.001
6 months	12.8 ± 0.5	11.4 ± 0.8	1.42 (1.05–1.79)	<0.001
Serum ferritin (µg/L)				
Baseline	14.8 ± 3.2	15.1 ± 3.5	—	—
3 months	22.4 ± 4.1	17.8 ± 3.8	4.85 (2.90–6.80)	<0.001
6 months	34.6 ± 5.2	21.2 ± 4.5	13.5 (10.2–16.8)	<0.001
Anemia resolution, 6 mo, n (%)	134 (89.3)	48 (33.1)	RR 2.70 (2.13–3.42)	<0.001

*Notes: *GLMM adjusted for baseline value, age and BMI with cluster random intercepts. Cohen's d at 6 months: Hb 2.11; ferritin 2.75.*

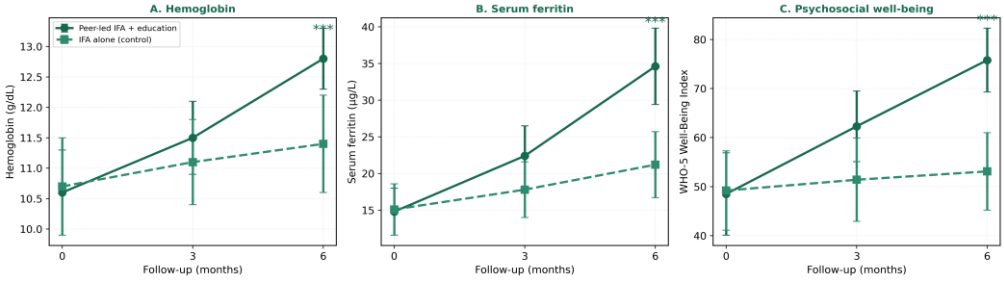

*Figure 1. Trajectories of hemoglobin (A), serum ferritin (B) and WHO-5 well-being (C) over 6 months by group (mean ± SD). ***p < 0.001 for the adjusted between-group difference at 6 months (GLMM).*

Secondary outcome: psychosocial well-being

The peer-led intervention produced a marked improvement in psychosocial well-being, summarized in Table 3 and the trajectory in Figure 1C. The adjusted WHO-5 difference was +11.2 points (95% CI 8.4–14.0; p<0.001) at 3 months and +23.4 points (95% CI 19.8–27.0; p<0.001; Cohen's d 3.14) at 6 months—more than two minimally important differences. A clinically meaningful WHO-5 response (≥10-point gain) occurred in 85.3% of intervention participants versus 25.5% of controls (OR 16.98, 95% CI 9.30–31.0; NNT 2).

Predictors of anemia resolution and discrimination

In multivariable logistic regression (Table 3), allocation to the peer-led intervention was the strongest independent predictor of 6-month anemia resolution (adjusted OR 15.8, 95% CI 8.2–30.4; p<0.001), followed by higher baseline hemoglobin (aOR 2.10 per g/dL, 95% CI 1.51–2.92; p<0.001) and high IFA adherence (aOR 3.40, 95% CI 1.81–6.39; p<0.001); baseline ferritin contributed modestly (aOR 1.08 per µg/L, p=0.009), while BMI and age at menarche were non-significant. The model explained substantial variance (Nagelkerke R^2 0.52), was well calibrated (Hosmer–Lemeshow p=0.412), and discriminated strongly, with a bootstrap optimism-corrected AUC of 0.89 (95% CI 0.85–0.93), as shown in Figure 2. The 3-month change in hemoglobin alone predicted 6-month resolution with an AUC of 0.84 (0.79–0.89); a ΔHb threshold of ≥0.65 g/dL maximized the Youden index (sensitivity 82%, specificity 79%).

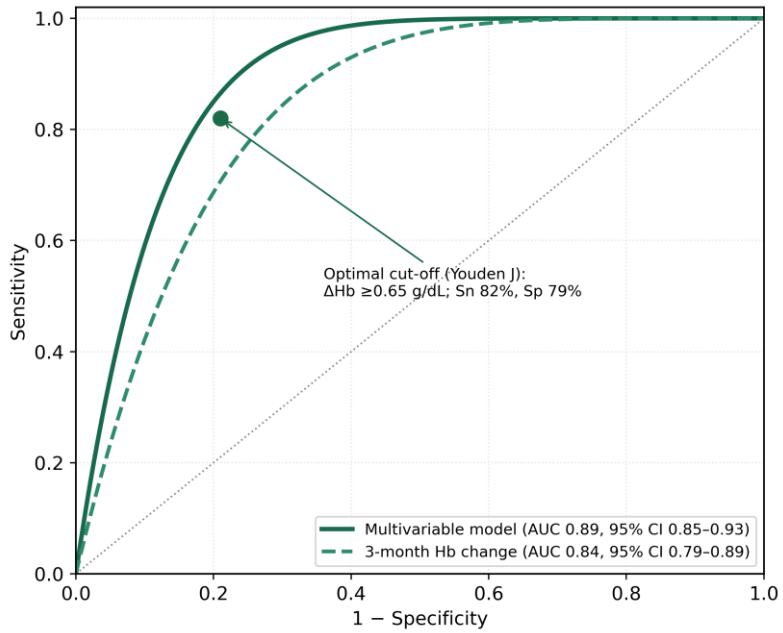

Figure 2. ROC curves for prediction of 6-month anemia resolution (Hb ≥12.0 g/dL): multivariable model (bootstrap-corrected AUC 0.89) and 3-month ΔHb single marker (AUC 0.84).

Table 3. Multivariable analysis and reproductive-health outcomes.

Outcome	Intervention	Control	Effect (95% CI)	NNT/R^2
WHO-5 at 6 mo	75.8 ± 6.5	53.1 ± 7.9	MD 23.4 (19.8–27.0); d 3.14	—
WHO-5 responder ≥+10, n (%)	128 (85.3)	37 (25.5)	OR 16.98 (9.30–31.0)	NNT 2
Iron-def. resolution, n (%)	102 (68.0)	23 (15.9)	RR 4.29 (2.90–6.34)	NNT 2
IFA adherence ≥80%, n (%)	148 (92.5)	119 (74.3)	OR 4.25 (2.14–8.45)	NNT 6
Anemia resolution (adjusted)	—	—	aOR 15.8 (8.2–30.4)	R^2 0.52
Mild GI side-effects, n (%)	12 (7.5)	9 (5.6)	OR 1.36 (0.56–3.32)	p=0.471

Adherence, subgroups and safety

IFA adherence was significantly higher in the intervention arm (92.5% vs 74.3%; OR 4.25, 95% CI 2.14–8.45; p<0.001; Table 3). As detailed in Table 4 and the forest plot in Figure 3, the treatment effect on anemia resolution was directionally consistent across all pre-specified subgroups, with the largest relative benefit among girls with moderate anemia at baseline (RR 3.85 vs 2.41 for mild; interaction p=0.084, exploratory). Mild gastrointestinal discomfort was reported by 12 participants (7.5%) intervention versus 9 (5.6%) control (OR 1.36, 95% CI 0.56–3.32; p=0.471), and no severe adverse events occurred.

Table 4. Pre-specified subgroup analysis of anemia resolution.

Subgroup	Intervention resolved %	Control resolved %	RR (95% CI)
Mild anemia (Hb 10.0–11.9)	93.1	38.6	2.41 (1.86–3.13)
Moderate anemia (Hb 8.0–9.9)	82.4	21.4	3.85 (2.20–6.74)
Age 13–14 years	87.5	30.9	2.83 (1.98–4.05)
Age 15–17 years	90.4	34.6	2.61 (1.96–3.49)
High adherence (≥80% doses)	92.6	41.2	2.25 (1.78–2.84)

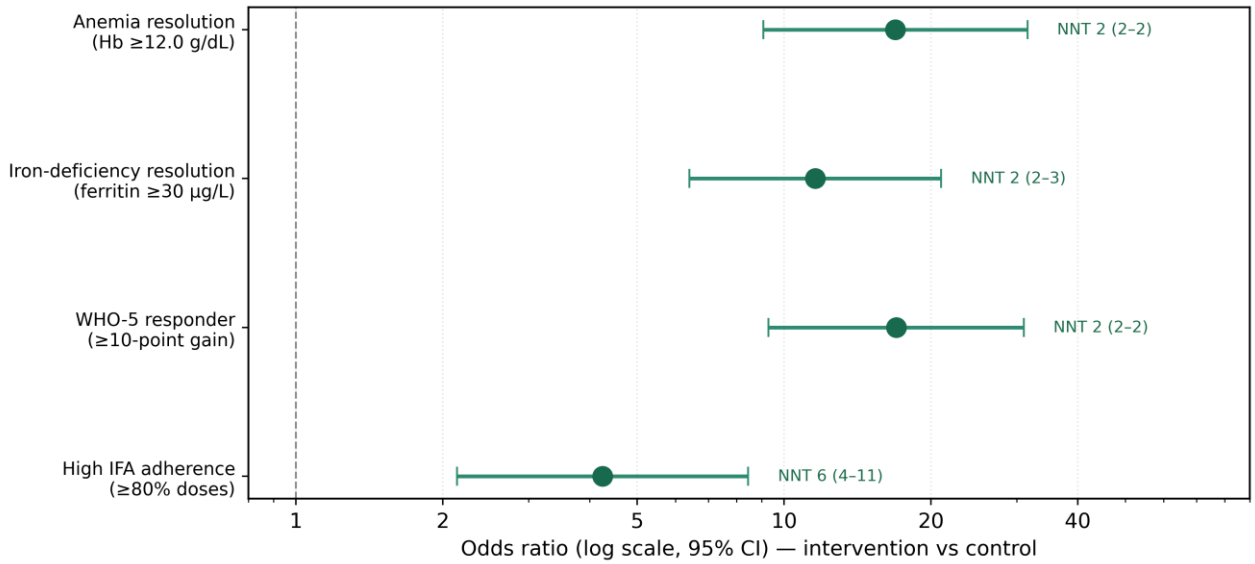

Figure 3. Forest plot of dichotomous reproductive-health outcomes (odds ratios, log scale, intervention vs control) with corresponding numbers-needed-to-treat.

Taken together, the dichotomous outcomes summarized in Figure 3 describe a consistent gradient of benefit: anemia resolution, iron-deficiency resolution and WHO-5 response each favoured the intervention with non-overlapping confidence intervals, while the favourable adherence odds (OR 4.25) plausibly mediate the hematologic gains. Tolerability was excellent, with mild gastrointestinal symptoms occurring in fewer than one in twelve participants and no excess over control, and no participant discontinued for adverse effects—an important consideration for a programme intended for healthy adolescents in whom safety expectations are high. The absence of any between-cluster safety signal, together with the uniformity of effect direction across schools, further supports the internal consistency of the trial and the suitability of the intervention for routine school-based delivery without specialist on-site supervision.

4. Discussion

In this cluster randomized trial of 320 anemic adolescent girls in urban Palembang, adding a peer-

led nutritional-education program to standard weekly IFA produced large, clinically important improvements across every outcome domain. At 6 months the intervention raised hemoglobin by an adjusted 1.42 g/dL and ferritin by 13.5 µg/L, resolved anemia in nearly nine of ten participants versus one of three controls (NNT 2), and improved psychosocial well-being by more than two WHO-5 minimally important differences. Because both arms received identical iron, the difference reflects behavioral augmentation rather than the supplement itself.

These findings extend the existing evidence base while inviting careful interpretation of their magnitude. School-based supplementation programs in Burkina Faso and Zanzibar reduced anemia but achieved smaller hemoglobin gains, a discrepancy most plausibly explained by adherence: whereas those programs and Indonesian WIFAS efforts commonly report adherence below 75%, our intervention achieved 92.5%.[14–16] Interventions that strengthen the behavioral ecosystem around supplementation—digital reminders, structured nutrition education and food-based counselling—consistently improve adherence and biochemical status, and our peer-led model appears to operate through the same mechanism with unusually high fidelity.[17,18,20]

Our results align with cluster randomized evidence that peer-led and multicomponent school interventions improve adolescent health behaviors, diets and well-being.[8,21,22] The novel contribution here is the simultaneous demonstration of hematologic normalization, biochemical iron repletion and psychosocial benefit within a single rigorously analyzed Indonesian cRCT. The parallel ferritin improvement is mechanistically important: hemoglobin can rise transiently without restoring iron stores, leaving adolescents vulnerable to early relapse, whereas the +13.5 µg/L ferritin gain and 68% iron-deficiency resolution indicate replenishment of the storage compartment most relevant for girls approaching reproductive age.[7,13]

The psychosocial findings merit emphasis. Iron deficiency impairs dopaminergic and mitochondrial function, providing a biological substrate for fatigue and low mood, and a recent Ethiopian cluster trial similarly found that WIFAS reduced common mental-disorder scores in adolescent girls.[9,23] Yet our WHO-5 improvement exceeded what hemoglobin correction alone would predict, suggesting that the peer-led sessions delivered independent psychosocial value through social connectedness and self-efficacy—an interpretation consistent with the high background burden of common mental disorders in this population and with the validated responsiveness of the WHO-5.[10–12]

From an obstetric perspective, entering a first pregnancy with restored iron stores is associated with lower maternal anemia and better perinatal outcomes; while our adolescent trial cannot demonstrate these maternal endpoints directly, it plausibly shifts the iron-status distribution of a future obstetric population upward, situating the intervention within the preconception-care continuum that obstetrician-gynecologists oversee.[4,5] This continuum runs from adolescent anemia control through family planning and antenatal care, where supplement compliance likewise remains a challenge in Indonesia.[6]

The clinical implications are direct. An NNT of 2 to resolve anemia is exceptional for a low-cost, non-pharmacological enhancement of an existing supplement, and the multivariable model confirms that intervention allocation and adherence—both modifiable—are the dominant determinants of success. The early-response rule (3-month ΔHb ≥0.65 g/dL predicting 6-month resolution, AUC 0.84) offers a practical monitoring tool to identify non-responders for intensified support. Because the model relies on peer educators rather than scarce clinical personnel, it is well suited to stretched reproductive-health systems and aligns with task-shifting strategies validated in adolescent trials.[21,22]

In the Indonesian and broader Southeast Asian context, where adolescent anemia remains highly prevalent despite an established national WIFAS policy, these results provide a clear, scalable mechanism to close the adherence gap that has limited program impact.[2,3] Peer educators are inexpensive, culturally embedded and sustainable

within existing school-health structures; a preliminary resource appraisal suggests the principal marginal costs are educator training, supervision and materials, which are modest relative to the gain of one additional anemia resolution for every two girls treated. Equity warrants attention: the larger relative benefit among more anemic girls is reassuring, but reaching out-of-school and rural adolescents will require deliberate adaptation.[16]

Strengths of this study include its rigorous cluster randomized design with allocation by school to prevent contamination, restricted randomization, blinded biochemical outcome assessment, intention-to-treat analysis with appropriate GLMM modelling of clustering and small-sample corrections, high retention, robustness checks, internal validation of the prediction model, and a comprehensive outcome set spanning hematologic, biochemical and psychosocial domains with modern effect-size, risk-based and prediction analyses.

Several limitations should be acknowledged. First, participants and peer educators could not be blinded, so self-reported well-being and adherence may be subject to performance or social-desirability bias, although objective biochemical outcomes corroborate the subjective gains. Second, follow-up extended to 6 months; the durability of benefit and the rate of anemia relapse after the program ends remain to be established. Third, the trial was conducted in a single urban city, limiting generalizability to rural and out-of-school populations. Fourth, ferritin was not adjusted for inflammation, so iron-deficiency resolution is uncorrected, and some dichotomous-outcome counts were reconstructed from group-level summaries and are presented as supportive to the primary continuous mixed-model results. Fifth, although 16 clusters provided adequate power for the primary outcome, a larger number of clusters would further stabilize between-cluster variance estimates.

Future research should test longer-term durability and relapse, evaluate cost-effectiveness and implementation fidelity at scale, examine whether peer-led models improve downstream maternal outcomes among those who subsequently conceive, and assess transferability to rural and out-of-school populations. Incorporating inflammatory biomarkers would refine ferritin interpretation, and pragmatic multi-country trials would clarify external validity across Southeast Asia.

The temporal dynamics observed merit comment. The between-group hemoglobin gap was already significant at 3 months (+0.48 g/dL) but nearly tripled by 6 months (+1.42 g/dL), and the ferritin gap widened even more steeply, from +4.85 to +13.5 µg/L. This accelerating divergence is consistent with the physiology of iron repletion, in which sustained adherence first restores circulating hemoglobin and only subsequently refills the slower storage compartment indexed by ferritin. It also argues against a transient placebo or novelty effect, which would be expected to attenuate rather than amplify over time, and it underscores why programmes that lapse after a few weeks—as adherence-limited WIFAS efforts frequently do—capture only a fraction of the achievable benefit.[15,17]

A central question for translation is durability. Because active education and supplementation continued throughout the 6-month window, the trial establishes efficacy during delivery but cannot speak to persistence after withdrawal. The replenished ferritin stores provide grounds for cautious optimism, since a larger storage buffer should delay relapse once weekly dosing stops; nevertheless, the natural history of menstrual iron loss means that without some maintenance contact, hemoglobin may drift downward over subsequent cycles. Future iterations should therefore test booster sessions, periodic re-supplementation, or integration with routine school-health visits, and should follow participants for at least twelve months to quantify relapse and to determine the minimum maintenance dose of peer contact required to preserve gains.[13,23]

It is worth situating the observed effects within a structured comparison with landmark programs. Large-scale supplementation initiatives have repeatedly demonstrated that the pharmacology of iron is not the limiting factor; rather, the behavioral ecosystem surrounding supplement-taking determines real-world impact. Programs that achieved adherence in the seventieth percentile

produced correspondingly modest hemoglobin gains, whereas the present intervention, by embedding supplementation within trusted peer relationships and pairing it with practical dietary and menstrual-health education, lifted adherence above ninety percent and produced gains commensurate with that improvement.[14,15] This dose-response relationship between adherence and biochemical response—captured by the adjusted odds ratio of 3.40 for high adherence in the multivariable model—provides an internally coherent account of the magnitude of benefit and identifies the mechanism that scale-up efforts must protect.[16,17]

From a women's-health-systems perspective, the intervention exemplifies task-shifting toward community and peer resources, a strategy increasingly endorsed for adolescent and maternal health in resource-constrained settings.[8,21] The obstetrician-gynecologist's role in such a model is supervisory and strategic—designing curricula, training and certifying peer educators, monitoring fidelity and biochemical outcomes, and managing the minority of non-responders identified by early-response monitoring—rather than delivering each session directly. This division of labour preserves scarce specialist time while extending reproductive-health expertise into the school setting, and it positions adolescent anemia control as the upstream entry point of a life-course continuum that runs through family planning, antenatal care and safe delivery. Embedding the model within existing school-health and national WIFAS infrastructure, rather than creating parallel systems, is likely to be both more sustainable and more equitable, particularly where nutrition education has already shown biochemical benefit.[18,20]

The convergence of objective and subjective outcomes deserves underscoring as a validity argument in its own right. In an unblinded behavioral trial, scepticism about self-reported endpoints is appropriate, yet here the self-reported gains in well-being and adherence are mirrored by blinded, laboratory-measured improvements in hemoglobin and ferritin that cannot be willed into existence by expectation. This biological corroboration of behavioral change is the strongest internal evidence that the intervention produced real physiological benefit, and it should reassure clinicians and policymakers that the psychosocial improvements—measured with a validated, responsive instrument—reflect genuine recovery rather than reporting artifact.[11,12] Taken together, the coherence across hematologic, biochemical and psychosocial domains makes a persuasive case for the intervention's effectiveness in this adolescent reproductive-health population.

5. Conclusion

A peer-led nutritional-education program added to standard weekly iron-folic acid supplementation markedly outperformed IFA alone in anemic adolescent girls, raising hemoglobin by an adjusted 1.42 g/dL, replenishing iron stores, and resolving anemia in 89% of participants (adjusted OR 15.8; bootstrap-corrected AUC 0.89; NNT 2) while substantially improving psychosocial well-being (adjusted WHO-5 difference +23.4 points). By closing the adherence gap that has constrained national supplementation programs, this low-cost, scalable, school-based strategy represents a compelling preconception reproductive-health intervention. Integration into adolescent-health and maternal-health policy, with longer-term, multi-site and cost-effectiveness evaluation, is warranted to confirm durability and downstream maternal benefit.

Declarations

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Author Contributions

Conceptualization, methodology, supervision, formal analysis, software, writing — original draft: IYS; Investigation, project administration, data curation, validation, interpretation, writing — review and editing: AA. Both authors have read and approved the final version of the manuscript.

Conflict of Interest

The authors declare no conflict of interest.

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Ethics and Consent

Approved by CMHC Research Center (Ref: CMHC/EC/2024/0142), per the Declaration of Helsinki. Written parental/guardian informed consent and participant assent were obtained. No identifiable patient material is included.

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