

Clinical effects of Spirulina supplementation on hemoglobin levels in anemic pregnant women: a systematic review and meta-analysis

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<https://doi.org/10.22146/inajbcs.v58i1.23573>

ABSTRACT

Submitted: 2025-08-02
Accepted : 2025-11-21

Anemia during pregnancy continues to pose a significant burden, particularly in low- and middle-income countries (LMICs). Anemia is a major contributor in increasing maternal illness and negative pregnancy outcomes. Spirulina, a nutrient-dense blue-green alga rich in bioavailable iron, has gained attention as a potential nutritional intervention to support hemoglobin improvement in pregnancy. This systematic review and meta-analysis, adhering to PRISMA standards, sought to assess the impact of Spirulina supplementation on improving hemoglobin levels among pregnant women. A single-arm meta-analysis was performed to assess the change in hemoglobin levels before and after Spirulina supplementation, while a comparative meta-analysis evaluated the mean difference in hemoglobin improvement between Spirulina and standard iron supplementation. Four eligible studies involving 1,070 pregnant women were included. The single-arm analysis demonstrated a significant increase in hemoglobin levels following Spirulina supplementation, with a pooled mean difference (MD) of 1.81 g/dL (95% CI: 0.24 - 3.39; $p = 0.024$). In the comparative analysis, Spirulina showed a non-significant trend toward higher hemoglobin than standard iron, with a pooled MD of 1.45 g/dL (95% CI: -0.22 - 3.13; $p = 0.088$). Risk of bias was low to moderate, and the overall certainty of evidence was classified as moderate. These findings suggest that Spirulina may be a promising adjunct for improving maternal hemoglobin, particularly in settings where local cultivation and food-based approaches are preferred. Further high-quality randomized trials are recommended to ascertain its clinical efficacy and inform policy on its integration into maternal nutrition programs.

ABSTRACT

Anemia pada kehamilan merupakan masalah kesehatan masyarakat yang serius, terutama di negara berpenghasilan rendah dan menengah. Anemia merupakan kontribusi meningkatnya risiko morbiditas ibu serta komplikasi kehamilan. Spirulina, mikroalga hijau-biru yang kaya akan zat besi dan nutrisi penting lainnya, telah dikenal sebagai intervensi gizi potensial untuk meningkatkan kadar hemoglobin selama kehamilan. Studi ini bertujuan mengevaluasi efektivitas suplementasi Spirulina dalam meningkatkan kadar hemoglobin pada ibu hamil melalui tinjauan sistematis dan meta-analisis yang dilakukan berdasarkan pedoman PRISMA. Analisis *single-arm* dilakukan untuk menilai perubahan kadar hemoglobin sebelum dan sesudah suplementasi Spirulina, sementara meta-analisis komparatif digunakan untuk membandingkan peningkatan hemoglobin antara kelompok Spirulina dan kelompok kontrol yang menerima suplementasi zat besi standar. Sebanyak empat studi dengan total 1.070 ibu hamil dianalisis. Hasil analisis *single-arm* menunjukkan peningkatan signifikan kadar hemoglobin setelah suplementasi Spirulina, dengan *mean difference* (MD) sebesar 1,81 g/dL (*Confidence interval*/CI 95%: 0,24 - 3,39; $p = 0,024$). Pada analisis komparatif, Spirulina menunjukkan peningkatan yang non-signifikan dibandingkan suplementasi standar, dengan MD sebesar 1,45 g/dL (CI 95%: -0,22 - 3,13; $p = 0,088$). Risiko bias pada studi yang disertakan dinilai rendah hingga sedang, dan tingkat *certainty of evidence* secara keseluruhan tergolong sedang. Hasil ini menunjukkan bahwa Spirulina merupakan intervensi yang memiliki potensi dan menjanjikan untuk meningkatkan kadar hemoglobin pada ibu hamil, khususnya di wilayah yang mendukung budidaya lokal. Penelitian lanjutan dengan uji acak terkontrol yang berkualitas tinggi direkomendasikan untuk memperkuat bukti dan mendukung penerapan Spirulina dalam program gizi maternal.

Keywords:
Spirulina platensis;
maternal anemia;
hemoglobin;
pregnancy;
nutrition

INTRODUCTION

Pregnancy-related anemia is still a major public health issue, particularly in low- and middle-income countries (LMICs), where the prevalence exceeds global averages.¹⁻³ The World Health Organization reports that 36.5% of pregnant women worldwide are affected by it, with even higher rates in Southeast Asia, including Indonesia, where it reaches 48.9% nationally.^{4,5} Anemia in pregnancy is correlated with a host of unfavorable maternal and neonatal outcomes, encompassing preeclampsia, postpartum hemorrhage, preterm birth, and even maternal-perinatal mortality.^{6,7} These outcomes underscore the critical importance of implementing effective, affordable, and well-tolerated strategies to manage anemia in pregnant individuals.⁷

While iron and folic acid supplementation is widely recognized as the standard approach for treating maternal anemia, poor adherence persists, primarily due to adverse effects like gastrointestinal discomfort, nausea, and vomiting.⁸ Moreover, while the Indonesian government provides iron tablets as part of antenatal care, coverage and compliance are suboptimal.⁹ In light of these persistent barriers, there is an increasing interest in alternative nutritional approaches that are better tolerated and potentially more sustainable.^{10,11} Among these, *Spirulina platensis*, a filamentous cyanobacterium widely consumed as a dietary supplement, has garnered attention because of its dense nutrient content.^{12,13}

Spirulina contains highly bioavailable iron, providing up to 28.5 mg per 100 g, making it a potent dietary source for improving hematologic parameters.^{9,10} Additionally, it offers a range of other beneficial components, including proteins, essential amino acids, vitamins, and minerals like

magnesium and calcium.¹⁴ *Spirulina* also harbors antioxidant and anti-inflammatory substances, which may support erythropoiesis and overall immune health during pregnancy.^{15,16} It was shown to increase hemoglobin levels in pregnant women and is generally well tolerated.¹² *Spirulina* is also recognized for its safety by the US Food and Drug Administration (US FDA) and holds promise for sustainable local production.¹⁷ Its versatility in cultivation, thriving in alkaline water and requiring minimal land, positions it as an ideal supplement for food security initiatives in underserved areas.¹⁸ Moreover, unlike synthetic iron supplements, *Spirulina* has been linked to a decreased risk of gastrointestinal side effects, potentially improving compliance and long-term outcomes.¹⁹

Despite these advantages, evidence on the effectiveness of *Spirulina* compared to standard iron supplementation remains limited and inconclusive.^{10,12,20} Current studies vary significantly in design, dosage, population characteristics, and outcome measures, making it difficult to draw definitive conclusions regarding its efficacy.^{9,10,12,20} Furthermore, some trials have evaluated *Spirulina* as a stand-alone intervention, while others have used it in combination with conventional iron therapy, complicating comparisons.⁹ The lack of consensus also extends to the duration of intervention needed to achieve meaningful hematological improvements.

The objective of this review was to review the effect of *Spirulina* supplementation on hemoglobin concentrations in anemic pregnant women using a systematic review and meta-analytical approach. Both single-arm and comparative analyses were carried out to assess hemoglobin alterations after *Spirulina* intake and to determine whether it can serve as an effective alternative or complement to conventional iron supplementation,

particularly in settings where adherence and access to standard therapy remain challenges. By synthesizing existing evidence and quantitatively analyzing changes in hemoglobin concentrations, this review seeks to clarify the role of Spirulina in maternal anemia management and to guide future public health strategies in resource-limited settings.

MATERIAL AND METHODS

This review and meta-analysis followed the PRISMA 2020 guidelines for reporting systematic reviews to ensure methodological transparency and consistency.²¹ Additionally, this research was filed in PROSPERO under the ID CRD420251117350. The objective was to synthesize available evidence on the effect of Spirulina supplementation on hemoglobin levels in pregnant women diagnosed with anemia. An extensive search of the literature was carried out using PubMed, Cochrane Library, ScienceDirect, and Google Scholar to identify studies published through July 2025. Search terms used included “Spirulina,” “pregnancy,” “anemia,” and “hemoglobin.” Two reviewers independently screened titles and abstracts using a standardized form, and disagreements were resolved by a third reviewer. No AI tools were used, and selection was carried out entirely through human review. If a full text was not available, we emailed the corresponding author. If there was no response, the record was excluded and the reason was documented.

Studies were included if they enrolled pregnant women of any gestational age with anemia and reported changes in hemoglobin levels either before and after Spirulina supplementation (single-arm design) or in comparison to standard iron supplementation (comparative design). Trials were eligible when Spirulina was used as monotherapy or as an add-on to

standard iron and folate, provided that background therapy was identical across groups. Studies combining Spirulina with additional active nutrients not matched in the comparator or with unequal background therapy were excluded. The types of studies considered eligible encompassed randomized controlled trials, cohort studies, and quasi-experimental designs, while reviews, animal studies, case reports, and articles lacking extractable data were excluded.

Two reviewers independently extracted relevant data using a standardized form, including study identifiers, country, design, participant characteristics, intervention details (dosage, frequency, duration), control regimen, and hemoglobin values (mean, standard deviation, and sample size). For non-randomized comparative studies, including cohort and quasi-experimental designs with control groups, the Newcastle–Ottawa Scale (NOS) was used. Single-arm pre–post studies were evaluated using the National Institute of Health (NIH) Quality Assessment Tool specifically designed for before-and-after studies lacking a control group. Any disagreements related to study inclusion, data collection, or risk of bias evaluation were addressed through discussion and mutual agreement.

Statistical analysis was performed using the meta package in RStudio. The primary outcome was the mean difference (MD) in hemoglobin levels. A single-arm meta-analysis pooled pre- and post-intervention Hb changes, and a comparative analysis evaluated the difference in Hb improvement between Spirulina and control groups. Parallel-group studies were pooled, combining all eligible study designs into a single comparative meta-analysis. Pooled effect sizes were calculated using the inverse variance method with 95% confidence intervals. Statistical heterogeneity was assessed using the I^2 and τ^2 metrics. A random-effects model was applied

as the primary approach. When heterogeneity was low, with $I^2 < 30\%$, a fixed-effect inverse-variance estimate was additionally reported. The GRADE framework was used to determine the overall certainty of evidence, taking into account factors such as risk of bias, variability among studies, precision of estimates, applicability, and potential for publication bias.

RESULTS

Study selection

A total of 2,583 records were identified across PubMed (37), ScienceDirect (189),

and Google Scholar (2,350), as outlined in the PRISMA flowchart (FIGURE 1). After eliminating 1,971 irrelevant entries, 612 records proceeded to title and abstract screening, where 593 were excluded. Full texts were sought for 19 articles, but 11 could not be retrieved. Of the eight full-text articles reviewed, four were excluded due to either incompatible populations or outcomes. In the end, four studies fulfilled all eligibility criteria. The limited overall yield reflects frequent exclusions for non-pregnant populations, non-interventional designs, absence of hemoglobin outcomes or variance statistics, and several inaccessible full texts.

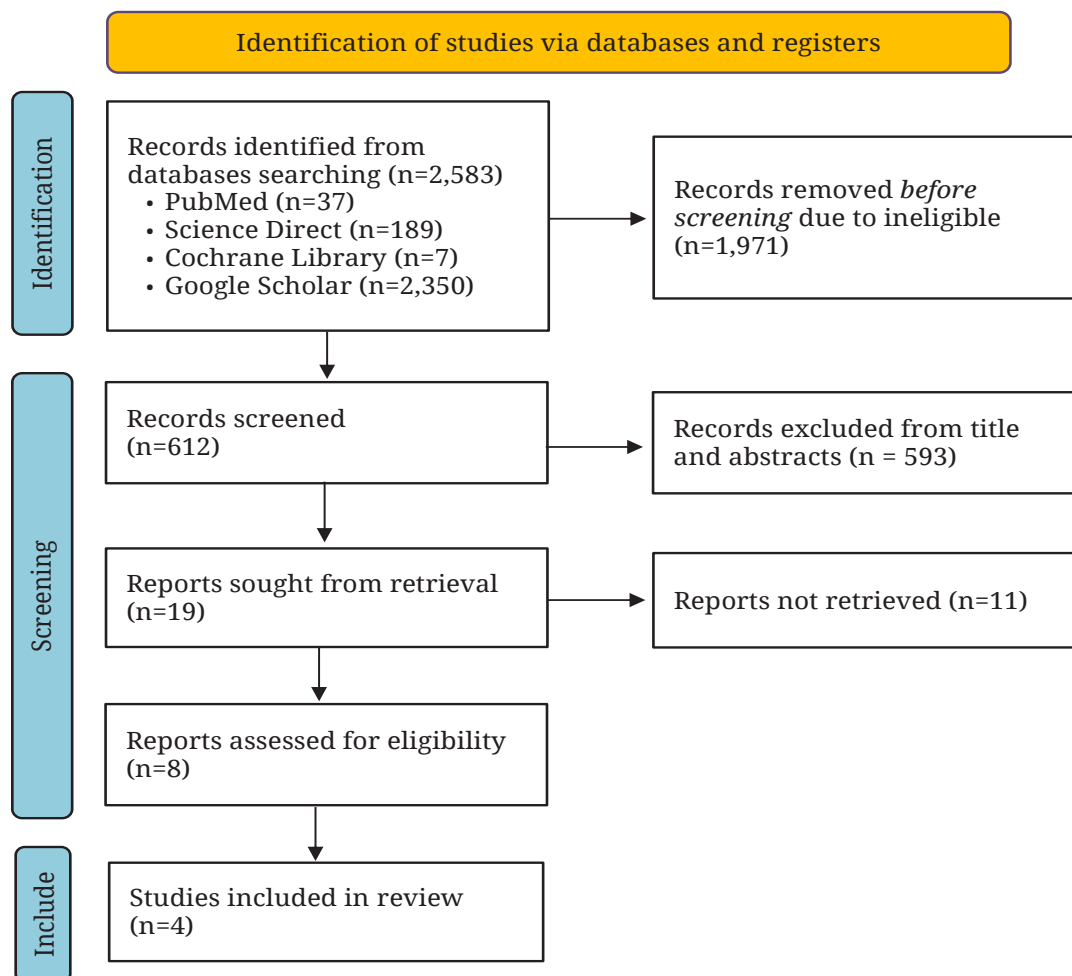


FIGURE 1. Selection process based on PRISMA guideline

Characteristic of selected studies

Baseline characteristics of each study were extracted in TABLE 1. Four studies involving a total of 1,070 pregnant women were included in this review, comprising both quasi-experimental and randomized cohort designs. Study locations ranged from Indonesia to Senegal, with intervention durations of 4 to 8 wk. Participants were anemic pregnant women, generally in the second or third trimester, with baseline hemoglobin ranging from 8 to 11 g/dL. *Spirulina platensis* supplementation was provided in capsule form, typically 300–500 mg per day, either alone or alongside standard iron therapy. Control groups received standard iron or iron–folic acid supplementation. The reported mean age of participants in the intervention groups ranged from 23.45 to 27.87 yr, while control group ages ranged from 24.01 to 32 yr. One study did not report participant age. Sample sizes varied from 30 to 460 participants per group.

The risk of bias assessment was conducted based on the study design. As summarized in TABLE 2, three non-randomized comparative studies, Marlina *et al.*,¹⁰ Niang *et al.*,²⁰ Anggraeni *et al.*,¹² were evaluated using the NOS. All three studies achieved full scores in the selection domain, while comparability and outcome domains showed variability. Niang *et al.*,²⁰ scored highest overall (8/9), indicating good methodological quality, while Marlina *et al.*,¹⁰ Anggraeni

et al.,¹² were rated as moderate due to limited adjustment for confounders and incomplete outcome reporting. The pre-post single-arm study by Nurhayati *et al.*,⁹ was assessed using the NIH Quality Assessment Tool. Of the 11 applicable criteria, the study met 7. It clearly stated its objective, defined eligibility criteria, described the intervention appropriately, and used adequate statistical methods. Notable limitations involved the absence of a comparison group, insufficient justification for sample size, and lack of blinding, and a single pre-post measurement without repeated outcome assessment. Based on this, the study was judged to be of fair quality.

Outcome analysis of selected study

In the single-arm meta-analysis, which included three studies shown in FIGURE 2, Spirulina supplementation resulted in a statistically significant increase in hemoglobin levels. The pooled MD was 1.81 g/dL (95% CI: 0.24 to 3.39) under the random effects model ($p = 0.0243$), and 1.44 g/dL (95% CI: 1.20 to 1.67) under the common effect model ($p < 0.0001$). However, substantial heterogeneity was present ($I^2 = 94.7\%$, $\tau^2 = 1.8698$, $p < 0.0001$), indicating considerable variability in effect sizes across studies. All individual studies showed positive effects, with Marlina *et al.*,¹⁰ reporting the largest mean increase of 3.44 g/dL.

TABLE 1. Summary of included studies evaluating Spirulina supplementation in pregnant women with anemia

Studies, year	Location	Study design	Patient characteristics	Time-line	Number of patients		Age (men ± SD yr)		Regimens	
					I	C	I	C	I	C
Anggraeni <i>et al.</i> ¹²	East Java, Indonesia	Quasi-experimental	Second and third trimester with anemia	4 wk	30	30	27.87 ± 6.68	32 ± 7.15	<i>S. platensis</i> extract capsule 300 mg once/day for 30 d + standard care of iron tablets	Standard care (iron tablets)
Marlina <i>et al.</i> ¹⁰	West Java, Indonesia	Quasi-experimental	Gestational age >20 wk, and anemia range 8-11 g/dL	8 wk	30	30	23.45 ± 2.76	24.01±1.34	<i>S. platensis</i> extract capsule 300 mg once/d for 8 wk	Standard care (iron tablets; 60mg iron)
Niang <i>et al.</i> ²⁰	Dakar, Senegal	Randomized cohort trial	Patient at 28 wk of amenorrhea with anemia	4 wk	460	460	26.6 ± 6.22	26.9 ± 6.13	Spirulina supplementation of 3x500 mg/day	Iron & folic acid supplementation (IFAS) = 90mg ferrous sulfate and 1 mg/d folic acid
Nurhayati <i>et al.</i> ⁹	West Java, Indonesia	Quasi-experimental	Second trimester and anemia range 8-11 g/dL	8 wk	30	No	Not reported	No control	<i>S. platensis</i> extract capsule 300 mg once/day for 8 wk	No control

*I = intervention group; C = comparison group

TABLE 2. Risk of bias for eligible studies evaluating Spirulina supplementation in pregnancy

Study	Risk of bias tool	Domain-level assessment	Overall rating
Marlina <i>et al.</i> ¹⁰	NOS	Selection (4/4), Comparability (1/2), Outcome (2/3)	Moderate
Niang <i>et al.</i> ²⁰	NOS	Selection (4/4), Comparability (2/2), Outcome (2/3)	Good
Anggraeni <i>et al.</i> ¹²	NOS	Selection (3/4), Comparability (1/2), Outcome (1/3)	Moderate
Nurhayati <i>et al.</i> ⁹	NIH (pre-post)	Met 9 of 12 criteria; main issues: no control, no blinding, no sample size calculation	Fair

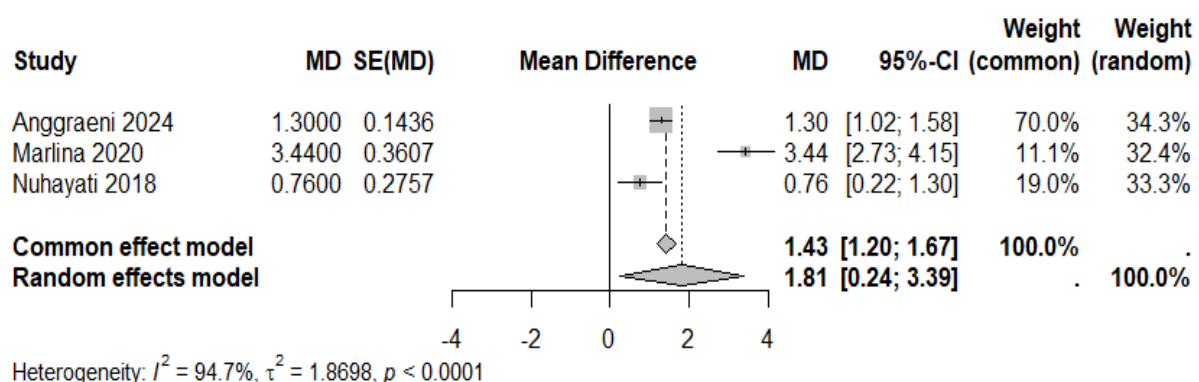


FIGURE 2. Forest plot of single-arm pre-post analysis evaluating the effect of Spirulina on hemoglobin (g/dL) in pregnancy

In the comparative meta-analysis, which pooled data from three studies comparing Spirulina to standard care or iron supplementation, no statistically significant difference in hemoglobin improvement was observed between the groups (MD = 1.45 g/dL; 95% CI: -0.22 to 3.13; p = 0.0881), as shown in FIGURE 3. Heterogeneity was again high ($I^2 = 95.0\%$, $\tau^2 = 1.7135$, $p < 0.0001$), primarily driven by large differences between smaller and larger studies. Marlina *et al.*,¹⁰ demonstrated the most pronounced treatment effect with a mean difference of 3.17 g/dL in favor of Spirulina. In contrast, Niang *et al.*,²⁰ study, which contributed the most weight, showed smaller and non-significant differences between groups.

Using the GRADE approach in TABLE

3, the overall certainty of evidence was rated as moderate for both the single-arm and comparative meta-analyses. In the single-arm analysis, all three studies showed an increase in hemoglobin following Spirulina supplementation, with some variation in effect sizes but consistent direction of effect. For the comparative analysis, three studies demonstrated greater hemoglobin improvement in the Spirulina group compared to standard iron supplementation, even if the null was included in the confidence interval. While heterogeneity was present, no serious concerns were identified regarding indirectness or publication bias, and the evidence was considered directly applicable to the target population.

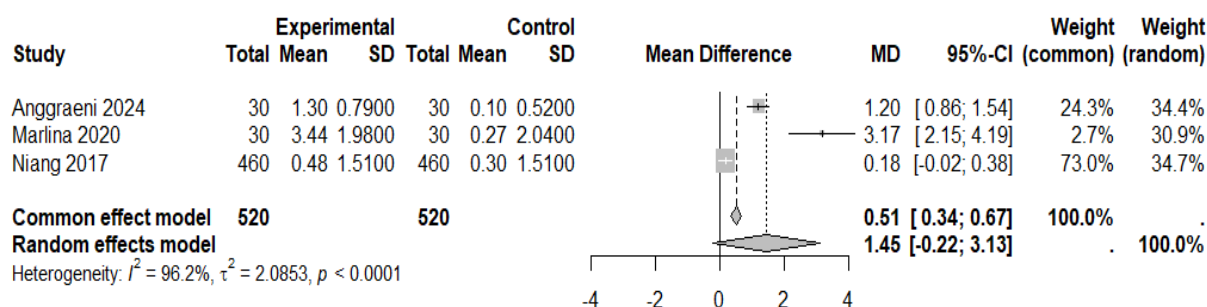


FIGURE 3. Forest plot comparing the mean increase in hemoglobin (g/dL) between Spirulina-treated and control groups

TABLE 3. GRADE summary of evidence certainty for hemoglobin improvement following Spirulina supplementation

Outcome	No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty
Increase in Hb	3	Quasi-experimental & pre-post	Moderate	Serious	Not serious	Serious	Not suspected	●●○○ Moderate
Hb change Spirulina vs Control	3	Quasi-experimental & cohort RCT	Moderate	Serious	Not serious	Serious	Not suspected	●●○○ Moderate

DISCUSSION

This meta-analysis demonstrated a positive effect of Spirulina supplementation on hemoglobin concentrations in anemic pregnant women. The single-arm analysis demonstrated a statistically significant mean increase in hemoglobin of 1.81 g/dL following Spirulina intake, indicating a consistent benefit across studies. The comparative meta-analysis showed no statistically significant difference in hemoglobin increase between Spirulina and standard iron supplementation. This difference in statistical outcome between the two analyses may be because the comparative analysis evaluated the relative effectiveness of Spirulina supplementation compared to standard iron supplementation or no intervention group, providing a more direct estimation of its comparative clinical benefit. While both analyses contribute valuable insights, results from comparative studies generally provide stronger evidence due to the presence of a control group, allowing for direct estimation of the intervention's effect while accounting for confounding variables. In contrast, single-arm studies may overestimate treatment effects as they do not control for natural improvements or external influences. Furthermore, the comparative studies included in this review demonstrated more conservative results, which may be attributed to differences in comparator interventions (varying iron doses and co-supplements) and larger sample sizes. Larger samples generally improve statistical power and may yield more stable but conservative estimates. These factors may have contributed to the attenuation of effect sizes in the comparative analysis.

Based on each study's contribution to the forest plot, the contrasting result in the Marlina *et al.*,¹⁰ study may be partly explained by the comparison

group, which received only 60 mg of elemental iron, whereas the Niang study used a higher 90 mg dose combined with folic acid, potentially leading to a stronger control effect.^{10,20} Additionally, the Marlina *et al.*,¹⁰ study had a smaller sample size and was conducted in a more localized setting, which may have amplified the observed treatment effect due to reduced variability or higher adherence. However, overall, all the examined studies showed a consistent direction of impact, and the certainty of evidence was rated as moderate based on the GRADE assessment.

In addition to its role in improving anemia, Spirulina has also demonstrated potential in addressing chronic energy deficiency (CED) among pregnant women. A study by Kundarti *et al.*,¹¹ found that daily *S. platensis* extract significantly improved nutritional status, as measured by mid-upper arm circumference. After 30 d of supplementation, 67% of the intervention group no longer met the criteria for CED, compared to just 7% in the control group. These findings underscore Spirulina's value as a practical, food-based intervention to combat maternal undernutrition.

Beyond pregnancy, Spirulina supplementation has also demonstrated beneficial effects in various other populations. A recent GRADE-assessed meta-analysis of 17 randomized controlled trials by Lak *et al.*,²² showed that Spirulina significantly reduced body weight, body mass index, and body fat percentage, particularly at doses ≥ 2 g/d and durations >12 wk. These effects were most prominent in obese individuals and older adults, indicating a potential metabolic benefit beyond hematologic parameters. In contrast, a clinical trial in mildly anemic young women conducted by Leal-Esteban *et al.*,²³ did not observe significant improvements in hemoglobin or ferritin levels after 3 mo of daily 3 g Spirulina snack bar supplementation. This discrepancy may be attributed to

short intervention duration, dietary inhibitors in the snack matrix, low iron bioavailability in the product, or the absence of deworming in participants. Nonetheless, the study highlighted Spirulina's acceptability and tolerability, reinforcing its feasibility as a nutritional intervention.

Notably, Spirulina is a blue-green algae recognized for its exceptional nutritional composition, particularly in relation to its iron content, which plays a central role in hemoglobin synthesis.^{24,25} It contains approximately 100 to 170 mg of iron per 100 g, along with high levels of vitamin B12, folic acid, and essential amino acids such as leucine, lysine, and methionine, all of which are essential for red blood cell production.^{17,26} Unlike many plant-based sources, the iron in Spirulina is highly bioavailable and more readily absorbed, partly due to its low phytate content and the absence of compounds that inhibit iron absorption.^{26,27} One of Spirulina most important components is C-phycoerythrin, a biliprotein known for its antioxidant and hematopoietic properties. This compound not only enhances iron uptake but also supports erythropoiesis by stimulating bone marrow activity and mimicking the effect of erythropoietin (EPO), the hormone responsible for promoting red blood cell formation.^{27,28} In addition, Spirulina contains a broad range of micronutrients and vitamins that contribute to improved immune function, reduced inflammation, and protection of red blood cells from oxidative damage.^{17,27} The antioxidant activity of β -carotene, vitamin E, and phycoerythrin can mitigate oxidative stress that contributes to red blood cell breakdown, while also preserving the integrity of developing erythrocytes.^{27,29} Additionally, the immune-modulating polysaccharides in Spirulina may suppress inflammatory pathways that increase the liver-derived hormone hepcidin, which hinders the absorption

of iron during chronic inflammation.^{16,30} The presence of B-complex vitamins, especially folate, B6, and B12, further supports DNA synthesis, erythroid cell division, and red blood cell maturation.^{25,31}

Based on the quantitative nutrient data, Spirulina provides around 55 to 70% high-quality protein by dry weight, which includes all essential amino acids necessary for supporting maternal nutrition and hemoglobin production.³² In comparison to other iron-rich nutritional supplements such as *Moringa oleifera* or iron bisglycinate, Spirulina demonstrates a unique profile by combining highly bioavailable iron with additional bioactive compounds that enhance erythropoiesis and reduce oxidative stress.^{33,34} Unlike *M. oleifera*, which is rich in iron but contains phytates that may inhibit absorption, Spirulina's low phytate content allows for superior iron bioavailability.^{35,36} Furthermore, compared to synthetic iron-folate supplements, Spirulina has been associated with fewer gastrointestinal side effects, which may improve compliance among pregnant women.¹⁹

The findings of this study support the potential role of Spirulina supplementation as an adjunctive strategy for improving hemoglobin levels in pregnant women with anemia, particularly in low-resource settings.^{10,12} Given its high iron content, ease of consumption, and favorable tolerability profile, Spirulina may serve as a practical alternative or complement to conventional iron supplementation, especially in populations with poor adherence to iron-folate tablets. Its potential for local cultivation further enhances its appeal as a sustainable, community-based nutritional intervention. Based on the safety profile, Spirulina is categorized as "Generally Recognized as Safe" by the US FDA, with reported side effects being rare

and generally mild, such as insomnia or gastrointestinal discomfort. Severe adverse events like rhabdomyolysis or anaphylaxis are extremely uncommon and often linked to underlying conditions or co-ingestion with other supplements. However, caution is advised in individuals with autoimmune diseases or those taking cytochrome P450-metabolized medications.¹⁶

Based on the dosing regimens used in the included studies, Spirulina was typically administered in doses of 300–500 mg per d, often in capsule form, over a period ranging from 4 to 8 wk. Significant hemoglobin improvement was observed within this timeframe, suggesting that a daily dose of 300 mg for at least 30 d may be a practical and effective starting point for clinical use, particularly in mild-to-moderate anemia. Spirulina may be integrated into antenatal care either as a stand-alone supplement or in combination with dietary counseling and standard iron-folic acid supplementation. Clinical guidelines may consider including Spirulina as a supplementary nutritional therapy for maternal anemia, supported by further validation through large-scale randomized controlled trials.

Despite promising clinical findings, real-world implementation of Spirulina supplementation in maternal health programs poses challenges. Product standardization, regulatory approval, storage conditions, and pricing models need to be addressed to ensure quality and accessibility.³⁷ Moreover, the acceptability of Spirulina in different cultural contexts may influence its uptake.³⁸ However, successful examples of Spirulina cultivation in community farms in several countries suggest that local production is feasible and may contribute to economic empowerment.^{37,38} Integrating Spirulina into government-run antenatal care initiatives or community-based nutrition programs may be viable,

provided sufficient policy support and implementation research are in place.

This study is among the first meta-analyses to systematically evaluate the impact of Spirulina supplementation on hemoglobin levels in pregnant women using both single-arm and comparative approaches. By including diverse study designs and focusing on clinically relevant outcomes, it provides a comprehensive overview of Spirulina's potential as a nutritional intervention in antenatal care. The dual analysis method strengthens the validity of findings by capturing both within-group effects and between-group comparisons. Moreover, the study applies rigorous methodology, including PRISMA-guided selection, domain-specific risk of bias assessments, and GRADE evaluation of evidence certainty, enhancing transparency and reproducibility. The focus on low- and middle-income countries also increases its relevance to global maternal health policy and nutrition programming.

Despite its strengths, this study has several limitations. Most included studies were non-randomized and quasi-experimental in design, which may introduce inherent bias and limit causal inference. Additionally, due to the limited number of eligible studies, all study designs were combined into a single meta-analysis, potentially increasing methodological heterogeneity. Our search covered PubMed, ScienceDirect, Cochrane Library, and citation chasing via Google Scholar, but we did not search additional databases such as Embase, Scopus, or Web of Science, so some studies may have been missed. The substantial heterogeneity observed across studies may be attributed to differences in study design, sample sizes, baseline hemoglobin levels, Spirulina dosages, intervention durations, and control group regimens, all of which could have influenced the magnitude of hemoglobin response. Limited reporting of participant characteristics, such as

dietary habits and iron status at baseline, restricts subgroup analysis. Future research should prioritize well-designed, large-scale randomized controlled trials to confirm Spirulina's efficacy, define optimal dosing and duration, and explore its long-term effects on maternal and neonatal outcomes. Furthermore, studies examining the integration of Spirulina into public health nutrition strategies and its local production feasibility in low-resource settings are warranted.

CONCLUSION

While our single-arm meta-analysis showed a statistically significant increase in hemoglobin levels following Spirulina supplementation, the comparative analysis found no significant difference compared to standard iron supplementation. Therefore, Spirulina may be considered comparable in efficacy and offers additional value due to its accessibility and nutritional profile, but further large-scale RCTs are needed to confirm superiority or equivalence.

ACKNOWLEDGMENT

The authors express their gratitude to the Faculty of Medicine, Udayana University, Denpasar, Bali for the support provided during this research. No external funding was received from public institutions, commercial entities, or nonprofit organizations.

REFERENCES

1. Stephen G, Mgongo M, Hashim TH, Katanga J, Stray-Pedersen B, Msuya SE. Anaemia in pregnancy: Prevalence, risk factors, and adverse perinatal outcomes in Northern Tanzania. *Anemia* 2018; 2018:1846280. <https://doi:10.1155/2018/1846280>
2. Abdilahi MM, Kiruja J, Farah BO, Abdirahman FM, Mohamed AI, Mohamed J, et al. Prevalence of anemia and associated factors among pregnant women at Hargeisa Group Hospital, Somaliland. *BMC Pregnancy Childbirth* 2024; 24(1):332. <https://doi:10.1186/s12884-024-06539-3>
3. Costa EA, Ayres-Silva JdP. Global profile of anemia during pregnancy versus country income overview: 19-year estimative (2000-2019). *Ann Hematol* 2023; 102(8):2025-31. <https://doi.org/10.1007/s00277-023-05279-2>
4. Balcha WF, Eteffa T, Tesfu AA, Alemayehu BA, Chekole FA, Ayenew AA, et al. Factors associated with anemia among pregnant women attending antenatal care: A health facility-based cross-sectional study. *Ann Med Surg (Lond)* 2023; 85:1712-21. <https://doi.org/10.1097/MS9.0000000000000608>
5. Basrowi RW, Zulfiqqar A, Sitorus NL. Anemia in breastfeeding women and its impact on offspring's health in Indonesia: A narrative review. *Nutrients* 2024; 16(9):1285. <https://doi.org/10.3390/nu16091285>
6. Edelson PK, Cao D, James KE, Ngonzi J, Roberts DJ, Bebell LM, et al. Maternal anemia is associated with adverse maternal and neonatal outcomes in Mbarara, Uganda. *J Matern Fetal Neonatal Med* 2023; 36(1):2190834. <https://doi.org/10.1080/14767058.2023.2190834>
7. Wang R, Xu S, Hao X, Jin X, Pan D, Xia H, et al. Anemia during pregnancy and adverse pregnancy outcomes: A systematic review and meta-analysis of cohort studies. *Front Glob Womens Health*, 2025; 6:1502585. <https://doi.org/10.3389/fgwh.2025.1502585>
8. Banerjee A, Athalye S, Shingade P, Khargekar V, Mahajan N, Madkaikar M, et al. Efficacy of daily versus intermittent oral iron

- supplementation for prevention of anemia among pregnant women: A systematic review and meta-analysis. *EClinicalMedicine* 2024; 74:102742.
<https://doi.org/10.1016/j.eclinm.2024.102742>
9. Nurhayati F, Marlina D. Perbedaan kadar hemoglobin ibu hamil anemia sebelum dan sesudah pemberian ganggang biru hijau. *Prosiding Pertemuan Ilmiah Nasional Penelitian & Pengabdian Masyarakat* 2018; 1(1):551-5.
 10. Marlina D, Nurhayati F. The effectiveness of Spirulina compared with iron supplement on anemia among pregnant women in Indonesia. *Int J Caring Sci* 2020; 13(3):1783-7.
 11. Kundarti FI, Titisari I, Kiswati, Rahayu DE, Riyadi BD. Improving the nutritional status of pregnant women with chronic energy deficiency using Spirulina platensis. *Health Technol J* 2024; 2(4):384-97.
<https://doi.org/10.53713/htechj.v2i4.221>
 12. Anggraeni RP, Kundarti FI, Titisari I. Effect of Spirulina platensis extract (*Arthrospira platensis*) on hemoglobin levels in pregnant women. *EMBRIO* 2024; 16(1):7-17.
<https://doi.org/10.36456/embrio.v16i1.8144>
 13. Prete V, Abate AC, Di Pietro P, De Lucia M, Vecchione C, Carrizzo A. Beneficial effects of Spirulina supplementation in the management of cardiovascular diseases. *Nutrients* 2024; 16(5):642.
<https://doi.org/10.3390/nu16050642>
 14. Liestianty D, Rodianawati I, Arfah RA, Assa A, Patimah, Sundari, *et al.* Nutritional analysis of *Spirulina sp* to promote as superfood candidate. *IOP Conf Ser Mater Sci Eng* 2019; 509:012031.
<https://doi.org/10.1088/1757-899X/509/1/012031>
 15. Wu Q, Liu L, Miron A, Klímová B, Wan D, Kuča K. The antioxidant, immunomodulatory, and anti-inflammatory activities of Spirulina: An overview. *Arch Toxicol* 2016; 90(8):1817-40.
<https://doi.org/10.1007/s00204-016-1744-5>
 16. Finamore A, Palmery M, Bensehaila S, Peluso I. Antioxidant, immunomodulating, and microbial-modulating activities of the sustainable and ecofriendly *Spirulina*. *Oxid Med Cell Longev* 2017; 2017:3247528.
<https://doi.org/10.1155/2017/3247528>
 17. Fernandes R, Campos J, Serra M, Fidalgo J, Almeida H, Casas A, *et al.* Exploring the benefits of phycocyanin: From Spirulina cultivation to its widespread applications. *Pharmaceuticals (Basel)* 2023; 16(4):592.
<https://doi.org/10.3390/ph16040592>
 18. AlFadhly NKZ, Alhelfi N, Altemimi AB, Verma DK, Cacciola F. Tendencies affecting the growth and cultivation of genus Spirulina: An investigative review on current trends. *Plants (Basel)* 2022; 11(22):3063.
<https://doi.org/doi:10.3390/plants11223063>
 19. Nasab SJ, Feizi A, Hajihashemi P, Entezari MH, Sharma M, Adibi P, *et al.* Effects of Spirulina (*Arthrospira*) platensis supplementation on intestinal permeability, antioxidant and inflammatory markers, quality of life, and disease severity in constipated-predominant irritable bowel syndrome: A randomized double-blind, placebo-controlled trial. *Nutr J* 2025; 24(1):64.
<https://doi.org/10.1186/s12937-025-01132-6>
 20. Niang K, Ndiaye P, Faye A, Tine JAD, Diongue FB, Camara MD, *et al.* Spirulina supplementation in pregnant women in the Dakar region (Senegal). *Open J Obstet Gynecol* 2017; 7(1):147-54.
<https://doi.org/10.4236/ojog.2017.71016>

21. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al.* The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* 2021; 372:n71.
<https://doi.org/10.1136/bmj.n71>
22. Lak M, Karimi M, Akhgarjand C, Ghotboddin Mohammadi S, Pam P, Ashtary-Larky D, *et al.* Effects of Spirulina supplementation on body composition in adults: A GRADE-assessed and dose-response meta-analysis of RCTs. *Nutr Metab (Lond)* 2025; 22(1):61.
<https://doi.org/10.1186/s12986-025-00959-4>
23. Leal-Esteban LC, Nogueira RC, Veauvy M, Mascarenhas B, Mhatre M, Menon S, *et al.* Spirulina supplementation: A double-blind, randomized, comparative study in young anemic Indian women. *Clin Epidemiol Glob Health* 2021; 12(5):100884.
<https://doi.org/10.1016/j.cegh.2021.100884>
24. Sahil S, Bodh S, Verma P. Spirulina platensis: A comprehensive review of its nutritional value, antioxidant activity, and functional food potential. *J Cell Biotechnol* 2024; 10(2):1-14.
<https://doi.org/10.3233/JCB-240151>
25. Gaur K, Wal A, Sharma P, Parveen A, Singh P, Mishra P, *et al.* Exploring the nutritional and medicinal potential of Spirulina. *Nat Resour Hum Health* 2024; 4(3):277-86.
<https://doi.org/10.53365/nrfhh/188021>
26. Podgórska-Kryszczuk I. Spirulina—an invaluable source of macro- and micronutrients with broad biological activity and application potential. *Molecules* 2024; 29(22):5387.
<https://doi.org/10.3390/molecules29225387>
27. Sabat S, Bej S, Swain S, Bishoyi AK, Sahoo CR, Sabat G, *et al.* Phytochemistry and pharmacological significance of filamentous cyanobacterium Spirulina sp. *Bioresour Bioprocess* 2025; 12(1):27.
<https://doi.org/10.1186/s40643-025-00861-0>
28. Seyidoglu N, Inan S, Aydin C. A prominent superfood: Spirulina platensis. In: *Superfood and Functional Food: The Development of Superfoods and Their Roles as Medicine*. Rijeka: InTech, 2017.
<https://doi.org/10.5772/66118>
29. Gargouri M, Akrouti A, Magné C, El Feki A, Soussi A. Protective effects of Spirulina against hemato-biochemical alterations, nephrotoxicity, and DNA damage upon lead exposition. *Hum Exp Toxicol* 2020; 39(6):855-69.
<https://doi.org/10.1177/0960327120903490>
30. Nemeth E, Ganz T. Hepcidin and iron in health and disease. *Annu Rev Med* 2023; 74:261-77.
<https://doi.org/10.1146/annurev-med-043021-032816>
31. Rehman M, Naeem R, Biswas S, Sohail M, Khan S, Arif M, *et al.* Synergistic interaction of Spirulina sp. and folic acid-producing bacteria for folate production. *Curr Res Nutr Food Sci* 2024; 12(3):1354-65.
<https://doi.org/10.12944/CRNFSJ.12.3.29>
32. Marjanović B, Benković M, Jurina T, Sokač Cvetnić T, Valinger D, Gajdoš Kljusurić J, *et al.* Bioactive compounds from Spirulina spp. -Nutritional value, extraction, and application in the food industry. *Separations* 2024; 11(9):257.
<https://doi.org/10.3390/separations11090257>
33. Rotella R, Soriano JM, Llopis-González A, Morales-Suarez-Varela M. The impact of *Moringa oleifera* supplementation on anemia and other variables during pregnancy and breastfeeding: A narrative review. *Nutrients* 2023; 15(12):2674.
<https://doi.org/10.3390/nu15122674>

34. Fischer JAJ, Cherian AM, Bone JN, Karakochuk CD. Effects of oral ferrous bisglycinate on hemoglobin and ferritin in adults and children: Systematic review and meta-analysis of randomized controlled trials. *Nutr Rev* 2023; 81(8):904-20.
<https://doi.org/10.1093/nutrit/nuac106>
35. Gallaher DD, Gallaher CM, Natukunda S, Schoenfuss TC, Mupere E, Cusick SE. Iron bioavailability from *Moringa oleifera* leaves is very low. *FASEB J* 2017; 31(S1):786.13.
https://doi.org/10.1096/fasebj.31.1_supplement.786.13
36. Gopalakrishnan L, Doriya K, Kumar DS. *Moringa oleifera*: A review on nutritive importance and its medicinal application. *Food Sci Hum Wellness* 2016; 5(2):49-56.
<https://doi.org/10.1016/j.fshw.2016.04.001>
37. Costa JAV, Freitas BCB, Rosa GM, Moraes L, Morais MG, Mitchell BG. Operational and economic aspects of *Spirulina*-based biorefinery. *Bioresour Technol* 2019; 292:121946.
<https://doi.org/10.1016/j.biortech.2019.121946>
38. Vrenna M, Peruccio PP, Liu X, Zhong F, Sun Y. Microalgae as future superfoods: Fostering adoption through practice-based design research. *Sustainability* 2021; 13(5):2848.
<https://doi.org/10.3390/su13052848>