Review Article

Moringa oleifera supplementation for anemic pregnant women: A Systematic Review and Meta-analysis

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ABSTRACT

Objective

Iron supplements are often suggested to anemic pregnant women during antenatal care. *Moringa oleifera* (Moringa) is rich in essential nutrients and commonly used as an alternative supplement to overcome anemia in pregnancy. There is sparse evidence of its efficacy as an anemia treatment. Thus, this systematic review and meta-analysis aimed to assess the effectiveness of Moringa's supplementation for anemic pregnant women.

Materials and Methods

We searched the Cochrane Central Register of Controlled Trials, MEDLINE, and Epistemonikos for all randomized controlled trials (RCTs) reporting anemic pregnant ladies receiving Moringa. We independently screened the titles and abstracts of identified trials before the full text of relevant trials were evaluated for eligibility. We then independently extracted data on the methods, interventions, outcomes, and risk of bias from the included trials. Primary outcome measures were hemoglobin level and erythrocyte index levels while secondary outcomes were hematocrit level, ferritin level, and baby's weight.

Results and Discussion

Fifteen trials with a total of 808 anemic pregnant women were analyzed using two comparisons. Moringa had increased hemoglobin level (MD 0.42, 95% CI 0.14 to 0.71; I^2 statistic = 78%) when used as an adjunct to standard treatment as well as when it was used alone (MD 0.65, 95%CI 0.40 to 0.90; I^2 statistic = 0%; $p < 0.05$). Furthermore, Moringa has increased MCH level (MD 0.84, 95%CI 0.11 to 1.56; I^2 statistic = 0%; $p = 0.02$) and ferritin level (MD 18.80, 95%CI 7.53 to 30.07; $p = 0.001$) when used as an adjunct to standard treatment. However, it does not affect the MCV ($p = 0.52$), MCHC ($p = 0.15$), and hematocrit l ($p = 0.88$) for both comparisons. ***Conclusion.*** Moringa may increase hemoglobin levels when used in anemic pregnant women either as an adjunct therapy or alternative therapy to iron supplements, with no severe adverse event that could disrupt the intervention. Nevertheless, further research is needed to determine Moringa's precise dose and ideal preparation that will impact hemoglobin levels.

Keywords

anemia; folic acid, iron; *Moringa oleifera*; pregnant PROSPERO registration number: CRD42022304292

INTRODUCTION

Anemia is a public health issue and commonly affects reproductive-age women globally [1,2]. It affects 1.8 billion people worldwide, or almost a quarter (23.2%) of the global population [3]. Data from 2019 show that in developed nations, 16.6% of women who are expecting suffer from anemia, while in developing countries and Malaysia, the figures are 44.9% and 31%, respectively [4]. The Centers for Disease Control and Prevention defines anemia in pregnancy as having levels of hemoglobin under 11 g/dL or hematocrit of less than 33% in the first and third trimesters; in the second-trimester figures of less

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than 10.5 g/dL and 32%, respectively [5,6].

Anemia in pregnant women is most commonly caused by a lack of iron. Iron deficiency anemia (IDA) occurrence is influenced by age, gender, socio-demographics, and parity [5,7]. However, deficiency in vitamin B complex, vitamin B9, vitamin B12, and vitamin C also leads to anemia in pregnancy [8]. Anemia in pregnancy heightens preterm delivery risk, resulting in low birth weight (LBW) babies, and raises the rate of perinatal death [1,6,9,10]. Pregnant women with anemia are at risk of having children with learning disabilities and memory problems that could last until adulthood [6]. These women could also suffer from exhaustion, elevated heart rate, intolerance to physical exertion, and poor work performance [6]. Their low blood reserves pose a risk of blood transfusion during delivery and make them vulnerable to preeclampsia, placental abruption, heart problems, and ultimately a higher risk of death [1,6].

By the year 2025, the World Health Assembly has targeted a 50% reduction in the incidence of anemia in pregnancy [11]. In order to reduce the rate of LBW infants, anemia in pregnancy, and iron deficiency, the World Health Organization (WHO) has strongly recommended daily doses of folic acid and iron for pregnant women [12]. As prophylaxis, folic acid 400mg daily and elemental iron 30–60 mg is recommended throughout pregnancy, while pregnant women with anemia are recommended to take a high dose of elemental iron at 120 mg daily to increase their hemoglobin level to normal [13].

The common side effect of high-dose iron is gastrointestinal distress; which results in a maximum of 50% of patients stopping treatment, and this leads to significant treatment failure and unnecessary follow-up investigations [14]. A review in Cochrane demonstrated the effectiveness of daily low-dose iron supplements in treating pregnancy anemia, and there were reduced gastrointestinal side effects in comparison with a higher dose treatment [14]. Another study however showed no significant difference in the effects of intermittent or daily iron supplements on IDA at term [15].

Moringa *(Moringa oleifera Lam. moringaceae)* is an Indian herb native and commonly used in tropical and subtropical nations to treat cholera, anemia, anxiety, skin infections, asthma, bronchitis, chest congestion, and skin infections in addition to malnutrition [9,16]. Moringa is also used to treat inflammation, hypertension, ulcers, epilepsy, high cholesterol, renal disease, and diabetes [17]. Moringa leaves maintain their nutritional value after being cooked or when processed into a dry powder for long-term storage outside a refrigerator. Its leaves when boiled or in powder form have bio-available iron content thrice the amount found in raw leaves [17]. It was reported that the most common traditional medicine side effect is stomach pain [18], however, moringa appears to have no ill effects as shown in previous studies on humans. The plant is prepared differently when used as food or medicine [17,19]. It contains high amounts of vital elements i.e. iron (Fe), calcium (Ca), β-carotene, protein, vitamins A, B, C, D, E, and K (thiamine, riboflavin, niacin, pantothenic acid, biotin, vitamin B6, vitamin B12, and folate) and is also rich in antioxidants in the form of vitamin C (ascorbic acid), flavonoids, phenolics and carotenoids [20]. Its various micronutrients make it ideal for use in treating malnutrition and other health problems in mothers, children, and pregnant women [10].

A previous study has shown the extent of daily supplements with folic acid and iron in pregnant women who are enrolled in prenatal care programs to avert or treat anemia [15]. Another study proved the effectiveness of iron-folic acid supplements and other supplements in alleviating pregnancy health issues [13]. Using the extract of moringa leaves as a natural supplement to iron intake can treat anemia as hemoglobin concentration is improved [9]. Thus, this review paper aims to report on moringa's effectiveness as a supplement for anemic pregnant women, whether it is used as a supplement to standard treatment or used in comparison with iron supplements.

MATERIALS AND METHODS

Our systematic review was conducted according to the protocol previously published in the International Prospective Register of Systematic Review (PROSPERO) with trial number CRD42022304292. This review was carried out in accordance with the guidelines for Cochrane Systematic Reviews, and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Ethical approval was obtained in May 2022. The quality of evidence for all outcomes was assessed according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) guidelines [21].

Search strategy

We searched the Cochrane Central Register of Controlled Trials, MEDLINE, and Epistemonikos from 1966 to

January 2022. The search keywords included "*Moringa oleifera"*, "kelor leaves", "anemia", "low hemoglobin", "pregnant" and "antenatal", with Boolean operators of AND and OR. We also searched for ongoing trials through the World Health Organization International Clinical Trials Registry Platform and ClinicalTrials.gov.

Identification of included studies

We looked at randomized control trials (RCTs) that compared Moringa oleifera with a placebo or no treatment at all. Both blinded and open-label trials were included. The participants were pregnant women in all trimesters with hemoglobin less than 11g/dL. The intervention included Moringa in various preparation forms such as leaf extract, dried powdered leaves, flour, biscuits, soup, or honey via oral consumption. The comparator was a placebo or an adjunct to standard treatment. We included trials that were written in both English and Malay to increase the number of trials that were included.

Selection criteria

We independently screened the titles and abstracts from the searches and acquired full-text articles if they fit the eligibility criteria. We evaluated the eligibility of each trial independently and listed the reasons why they were excluded. We resolved any disagreements between the review authors through discussion. If further information is required, we contact the authors.

Data extraction

We independently extracted the characteristics of the trials (study setting, inclusion, and exclusion criteria), participants' features (age and weeks of gestation), methodology (method of randomized participants and duration of intervention given), description of the intervention (including dose and preparation type) and all outcomes into data extraction forms.

Outcomes The primary outcome was measured according to hemoglobin level and erythrocyte index levels consisting of mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). Meanwhile, the secondary outcomes were hematocrit level, ferritin level, and baby's weight.

Assessment of risk of bias

The risk of bias was assessed based on random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, completeness of outcome data, selectivity of outcome reporting, and other biases [22]. The risk of bias was categorized as low, unclear, or high. Any disputes were discussed and resolved.

Statistical analysis

The statistical analysis was carried out using the Review Manager software (Review Manager, 2011). The mean differences (MDs) with 95% confidence intervals (CI) were calculated for all the included trials with continuous outcomes. The encountered dichotomous outcomes were analyzed using risk ratio (RR) and 95% confidence intervals (CI). The results were reported using fixed-effect and random-effect models [22] utilizing inverse variance. The measures were pooled in meta-analysis and forest plots were drawn.

The presence of heterogeneity was evaluated in two stages. First, apparent heterogeneity at face value was observed by comparing populations, settings, interventions, and outcomes. Second, statistical heterogeneity was calculated using I^2 statistic[22]. The Cochrane Handbook for Systematic Reviews of Interventions described the method for analyzing heterogeneity [22]: 0% to 40% might not be significant, 30% to 60% may represent moderate heterogeneity, 50% to 90% may represent substantial heterogeneity and 75% to 100% would be considerable heterogeneity.

The principles of the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) approach were used for evaluating the quality of evidence in systematic reviews adopted by The Cochrane Collaboration. The GRADE system defines four levels of quality, the highest of which is for randomized trial evidence. It can be degraded to moderate, low, or even extremely poor-quality evidence, depending on the existence of the following four conditions: (i) limitations in the design and implementation of available studies, (ii) indirectness of evidence, (iii) unexplained heterogeneity or inconsistency of results, (iv) imprecision of results, and (v) publication bias. We used the GRADEpro software to reflect the quality of evidence for each outcome. The assessment is summarized in 'Summary of findings (SoF) table (GRADEpro 2014).

RESULTS

Study selection and characteristics

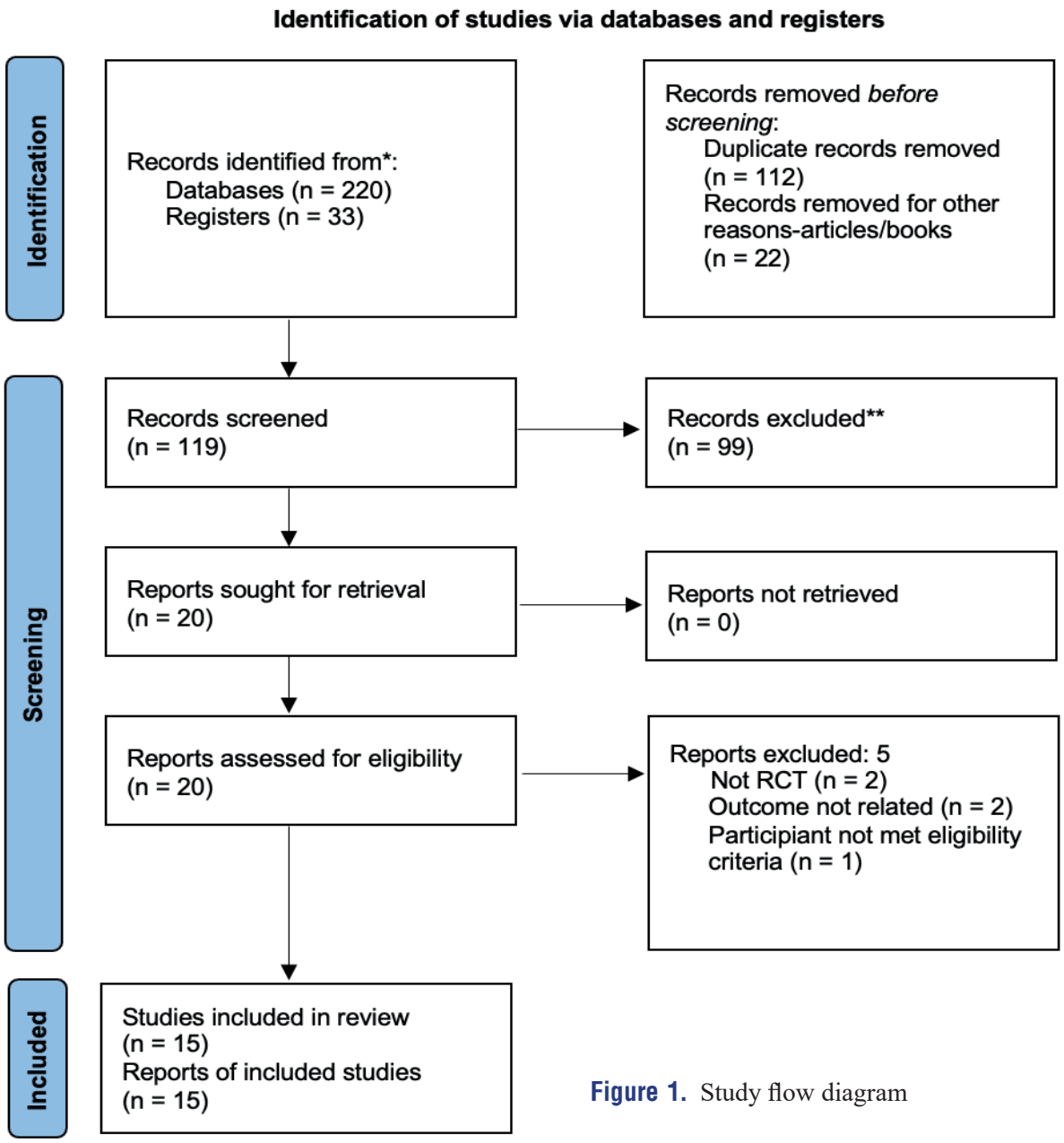

Figure 1. Study flow diagram

A total of 220 records from electronic databases and 33 papers from other sources were retrieved, as illustrated in Figure 1. From 20 trials reviewed, five were excluded: one trial fulfilled the exclusion criteria [10], one trial is a pre-experimental research design [23], two trials had no related outcome [24,25] and one trial was related to non-anemic pregnant women [25]. Therefore, the remaining 15 trials consisting of 808 anemic pregnant women with hemoglobin levels less than 11g/dL [19,26-39] were included in this review.

The characteristics of the included trials are summarized in Table 1. All trials were conducted in Indonesia and none of it declared funding. One trial reported the exclusion of pregnant women who have diabetes, hypertension, preeclampsia or eclampsia, and heart disease [35].

Table 1. Characteristics of included trials

Author (year)	Study design	Participants / Sample size (drop-outs)	Duration of intervention	MO Form/ Dosage	Comparison	
					Control	Standard treatment (given to all participants)
Andira 2020	Randomised, DB	20-32 weeks pregnant Intervention: 21(0) Control: 21(0)	60days	Leave extract in capsule/ 500mg/day	Placebo(starch flour) 500mg	Iron supplement
Hastuty 2020	Randomised, DB	20–32 weeks pregnant Intervention: 19(0) Control: 19(0)	60days	Leave extract in capsule/ 500mg/day	Placebo (starch flour) 500mg	Iron supplement
Iskandar 2015	Randomised, DB	12–20 weeks pregnant Intervention: 33(0) Control: 31(0)	90 days	Leave extract in capsule/ 1 capsule/day	Placebo	Iron supplement
Loa 2021	Quasy research type	First and third trimesters Intervention: 25(0) Control: 25(0)	60 days	Biscuits/ 2 pieces/day	-	Iron supplement Fe 2x250mg
Manggul 2021	Quasy experimental design	20 - 32 weeks pregnant Intervention: 45(10) Control: 45(10)	60 days	Biscuits/ 2 pieces/day	-	Iron supplement Fe 2x250mg
Mutmaina 2021	Randomised, DB	20-27 weeks pregnant Intervention: 20(0) Control: 20(0)	8 weeks	Honey/ 15mls daily	Regular honey 15mls od	Iron supplement
Nur 2020	Quasy experiment with randomised, DB	Pregnant women Intervention: 20(0) Control: 20(0)	8weeks	Leave extract in capsule/ N/A	-	Iron supplement
Rismawati 2021	Quasy experimental design	Pregnant with anemia Intervention: 15(0) Control: 15(0)	Not mention	Leaves capsule/ N/A	-	Iron supplement
Yulni 2021	Randomised, DB	Pregnant with anemia Intervention: 24 (0) Control: 21(0)	2 months	Moringa capsule/ N/A	Placebo starch powder	Iron supplement
Laiskodat 2021	Quasy experimental design	Third trimester Intervention: 16(0) Control: 16(0)	14days	Soup/ Once daily	-	Iron supplement
Sitohang 2018	Randomised, DB	Pregnant women with anemia Intervention: 53(4) Control: 53(9)	3months	Biscuits/ N/A	-	Iron supplement
Hadju 2020	Randomised, DB	29–31 weeks pregnant, Intervention: 20(1) Placebo: 20(1)	2 months	Leaf powder in capsule 2 capsules twice (2g)/ day	IFA 4capsule (60mg elemental iron + 400mcg FA)	N/A
Mandasari 2020	Randomised, DB	20 - 32 weeks pregnant Intervention: 21(0) Control: 21(0)	60 days	Leave extract in capsule/ 500mg/day	Tablet Fe	N/A
Nurdin 2018	Randomised, DB	12-24 weeks pregnant Intervention: 62 Control: 68 92 dropped out	12 weeks	Extract in capsule/ N/A	IFA	N/A
Yusnidar 2020	Randomised, DB	28 weeks pregnant Intervention: 19(0) Control: N/A	60 days	Leaf flour capsule/ 2 capsules twice (2g)/ day	Tablet Fe (60mg iron + 500mg FA)	N/A

*DB - Double-blind, IFA- Iron folic acid

Participants in the trials were grouped randomly into intervention and control groups. For ten trials, the intervention was the Moringa leaf in capsule form either extract, flour, or dried powdered [19,26-28,31,34-36,38,39]. The other three trials used Moringa biscuits [30,32,37], one trial used Moringa honey 15mls per day [33], and one trial used Moringa leaf soup once per day [29]. Three trials used Moringa extract at the dose of 500 mg per day [26,27,31], one trial used Moringa leaf powder at the dose of 2g per day [19], two trials only mentioned prescription without dosage, which are two capsules of Moringa leaf powder twice per day [39], one capsule leave extract per day [28] while four trials did not mention prescriptions nor dosage [34-36,38]. The duration of intervention in three trials was 90 days [28,35,37] and ten trials in 60 days [19,26,27,30-34,38,39], one trial in 14 days [29] while one trial did not mention the duration of the intervention [36].

Eleven trials use *Moringa* as an adjunct to the standard treatment [26-30,32-34,36-38]. Iron supplements as the standard treatment for anemic pregnant women were given to both the intervention group and control group. The standard treatment consists of Tab Ferrous 500 mg daily in two trials [30,32], Tab Ferrous with 60 mg elemental iron daily in three trials [26,27,38], and an unknown dosage of Tab Ferrous daily in two trials [33,36]. Four trials only mentioned iron supplements without further details [28,29,34,37].

Five of 11 trials compared *Moringa* as an adjunct against iron supplement and placebo [26-28,33,38]. The placebos were 500 g starch powder [26-28,38], and 15 mls regular honey [33]. Six other trials were compared against iron supplements alone [29,30,32,34,36,37]. Meanwhile, four trials compared *Moringa* alone against iron supplementation [19,31,35,39] in which iron supplements were iron-folic acid capsules [19,35,39] and tablet ferrous [31].

Risk of bias assessment

The risk of bias assessment is shown in Figure 2 and Figure 3.

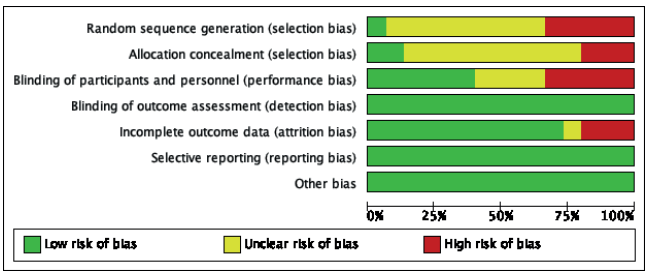

Figure 2. The risk of bias graph

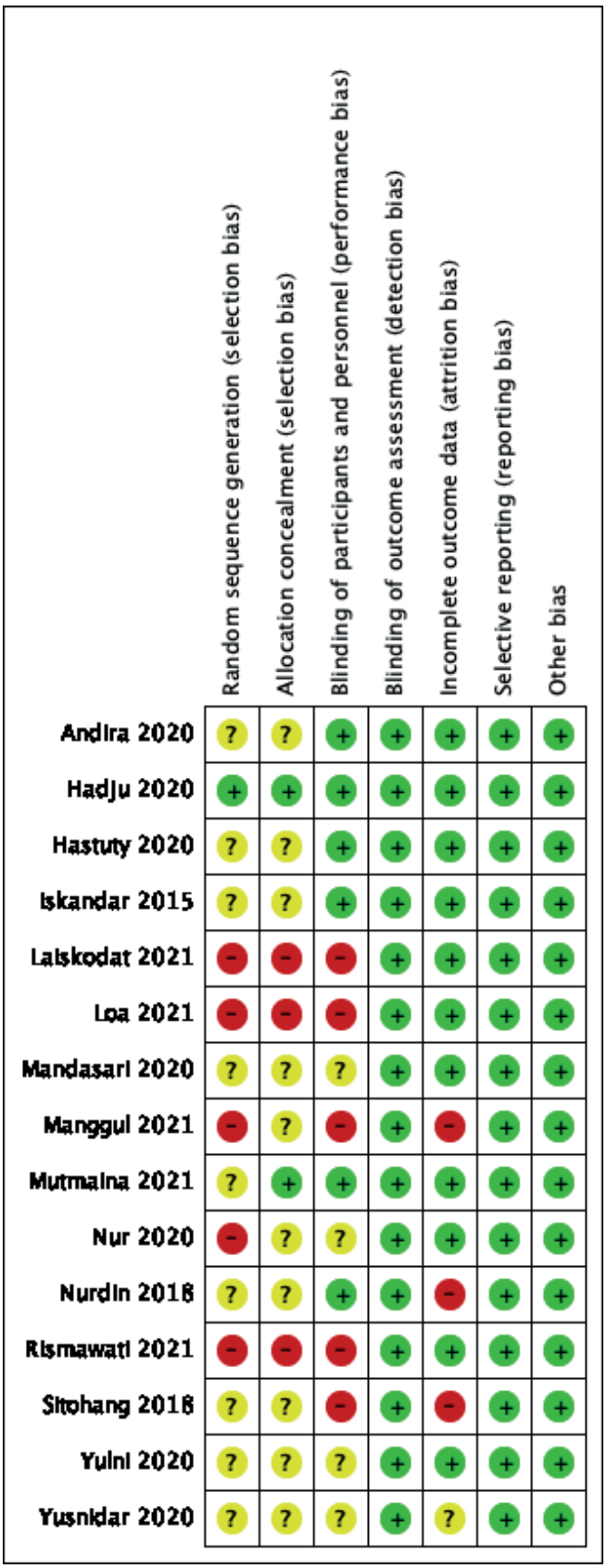

Figure 3. Risk of bias summary

The risk of bias assessment shows that one trial has a low risk of selection bias in which randomization was generated by hand [19]. Nine trials have an unclear risk of selection bias as the randomization method was not mentioned [26-28,31,33,35,37-39]. Another five trials were at high risk of selection bias as these trials used quasi-experimental research types [29,30,32,34,36].

The allocation concealment was judged as low risk in two trials. The participants were allocated to either an intervention or control group depending on the papers they chose in box [19,33]. Three trials have a high risk of bias as the researcher divided the participants into two groups [29,30,36]. Meanwhile, another ten trials had unclear risks as no detailed method was mentioned by the author [26-28,31,32,34,35,37-39].

There were six trials with a low risk of performance bias as researchers, participants and enumerators did not know the difference in the supplement given [19,26-28,33,35]. Five studies were deemed to have a high risk of performance bias [29,30,32,36,37], whereby three trials used Moringa biscuits for their intervention group while the control group did not [30,32,37], one trial used Moringa leaf soup as an intervention [29] and one trial Moringa leaf capsule was only given to the intervention group [36]. Four trials have an unclear risk of performance bias as the author did not describe further in the studies [31,34,38,39]. It was determined that detection bias was at low risk in all studies because participants' blood samples were collected after the intervention and evaluated and the baby's weight was measured after delivery. Thus, the measurements were unlikely to be influenced.

Eleven trials have low-risk attrition bias as they carried out the intention-to-treat analysis [19,26-31,33,34,36,38], three trials have high-risk attrition bias as they follow per-protocol analysis [32,35,37] while another one trial has unclear risk attrition bias because they did not clearly mention their sample size [39]. Two of these trials reported missing data due to non-compliance with the intervention and refused to continue further [32,35]. Besides, another trial did not report the missing data [37]. All fifteen trials reported the outcomes as specified in their methods section. We detected no other potential sources of bias.

Outcomes

Two comparisons were evaluated in this review by; (i) comparing *Moringa oleifera* as an adjunct to standard treatment versus the control group and (ii) comparing *Moringa oleifera* versus iron supplements.

Comparison 1: *Moringa oleifera* as an adjunct to standard treatment versus the control group

Moringa as an adjunct to standard treatment has increased hemoglobin level (MD 0.42, 95% CI 0.14 to 0.71; I^2 statistic = 78%; p = 0.003; six trials, 281 participants, very low quality of evidence) (Figure 4, Table 2) [28,29,32,33,36,38] compared to the control group. Three trials showed no difference in increment of hemoglobin level (RR 1.72, 95% CI 0.51 to 5.77; p = 0.38; three trials, 170 participants, very low quality of evidence) (Figure 5, Table 2) [29,37,38] compared to the control group. A paper was not included in the meta-analysis because it did not report the SD of hemoglobin level [34]. Subgroup analysis based on the Moringa preparations and duration of Moringa supplementation is not feasible due to a limited number of studies.

For the erythrocyte index level, Moringa has an increased MCH (MD 0.84, 95%CI 0.11 to 1.56; I^2 statistic = 0%; p = 0.02; three trials, 132 participants, low-quality of evidence)(Figure 6, Table 2). However, there is no difference in MCV (MD 0.44, 95%CI -0.92 to 1.81; I^2 statistic = 0%; p = 0.52; three trials, 132 participants, low-quality of evidence) and MCHC (MD 0.75, 95%CI -0.26 to 1.76; I^2 statistic = 71%; p = 0.15; three trials, 132 participants, very low quality of evidence when used as an adjunct to standard treatment compared to the control group) [27,30,33].

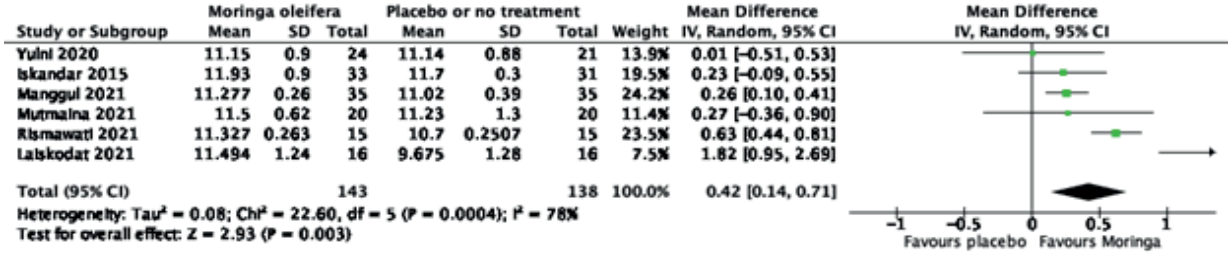

Figure 4. Forest plot of comparison between *Moringa oleifera* as an adjunct to standard treatment versus the control group for the outcome hemoglobin level (g/dl)

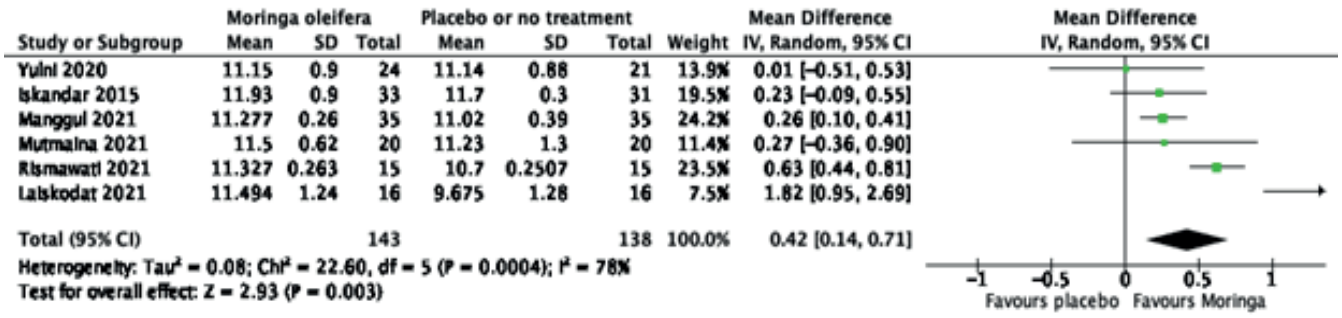

Figure 5. Forest plot of comparison between Moringa oleifera as an adjunct to standard treatment versus the control group for the hemoglobin level (g/dl) outcome increment.

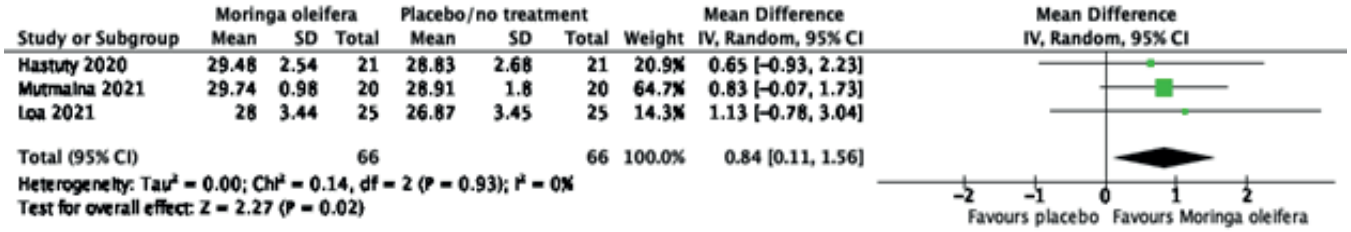

Figure 6. Forest plot of comparison between Moringa oleifera as an adjunct to standard treatment versus the control group for the outcome MCH.

Table 2. Summary of the findings, including GRADE quality assessment for comparison between *Moringa oleifera* as an adjunct to standard treatment versus the control group

***Moringa oleifera* as an adjunct to standard treatment for anemia in pregnant women**								
Patient or Population: Anemic pregnant women **Setting: Outpatient Clinic** **Intervention: *Moringa oleifera*** **Comparison: Placebo/standard**								
Outcome	**Anticipated absolute effects**		**Relative effect (95% CI)**	**Study event rates (%)**		**No of participants (studies)**	**Certainty of evidence (Grade)**	**Comments**
	Risk with placebo	**Risk difference with Moringa oleifera as an adjunct to standard treatment**		**With placebo**	**With Moringa oleifera as an adjunct to standard treatment**			
Increment in hemoglobin level (g/dL)	272 per 1,000	196 more per 1,000 (from 133 fewer to 1,000 more)	RR 1.72 (0.51 to 5.77)	22/81 (27.2%)	34/89 (38.2%)	170 (3 RCTs)	Very low	Risk of bias: serious Inconsistency: serious Indirectness: not serious Imprecision: serious
Hemoglobin level (g/dl)	The mean hemoglobin level (g/dl) was 0	MD 0.42 higher (0.14 higher to 0.71 higher)	-	138	143	281 (6 RCTs)	Very low	Risk of bias: serious Inconsistency: serious Indirectness: not serious Imprecision: serious
Hemoglobin level by the duration of supplement (g/dl)	The mean hemoglobin level by the duration of supplement (g/dl)	MD 0.37 higher (0.03 higher to 0.7 higher)	-	123	128	251 (5 RCTs)	Very low	Risk of bias: serious Inconsistency: serious Indirectness: not serious Imprecision: serious

Moringa oleifera as an adjunct to standard treatment for anemia in pregnant women								
Patient or Population: Anemic pregnant women **Setting: Outpatient Clinic** **Intervention: *Moringa oleifera*** **Comparison: Placebo/standard**								
Outcome	**Anticipated absolute effects**		**Relative effect (95% CI)**	**Study event rates (%)**		**No of participants (studies)**	**Certainty of evidence (Grade)**	**Comments**
	Risk with placebo	**Risk difference with Moringa oleifera as an adjunct to standard treatment**		**With placebo**	**With Moringa oleifera as an adjunct to standard treatment**			
MCV (fL)	mean MCV (fL) was 0	MD 0.44 higher (0.92 lower to 1.81 higher)	-	66	66	132 (3 RCTs)	Low	Risk of bias: serious Inconsistency: not serious Indirectness: not serious Imprecision: serious
MCH (pg/cell)	The mean MCH (pg/cell) was 0	MD 0.84 higher (0.11 higher to 1.56 higher)	-	66	66	132 (3 RCTs)	Low	Risk of bias: serious Inconsistency: not serious Indirectness: not serious Imprecision: serious
Hematocrit level	The mean hematocrit level was 0	MD 0.13 lower (1.75 lower to 1.49 higher)	-	52	54	106 (2 RCTs)	Very low	Risk of bias: serious Inconsistency: serious Indirectness: not serious Imprecision: serious
Ferritin level (µg/ml)	The mean ferritin level (µg/ml) was 0	MD 18.8 higher (7.53 higher to 30.07 higher)	-	31	33	64 (1 RCT)	Very low	Risk of bias: serious Inconsistency: serious Indirectness: not serious Imprecision: serious

CI: confidence interval; **MD:** mean difference, **RR:** risk ratio

For secondary outcomes, Moringa has increased ferritin level (MD 18.80, 95%CI 7.53 to 30.07; p = 0.001; one trial, 64 participants, very low quality of evidence) but showed no significant difference in hematocrit level (MD -0.13, 95%CI -1.75 to 1.49; I^2 statistic = 71%; p = 0.88; two trials, 106 participants, very low quality of evidence) and the baby's weight (MD 0.04, 95%CI -0.16 to 0.24; p = 0.69; one trial, 64 participants, very low quality of evidence) as an adjunct to standard treatment compared to control group [28].

One trial reported that respondents felt the benefits of consuming Moringa honey such as increased appetite, the body feeling fresher and calmer, and overcoming pregnancy problems such as insomnia, flu, coughs, and nausea [33].

Comparison 2: *Moringa oleifera* versus iron supplementation

Moringa has increased hemoglobin level (MD 0.65, 95%CI 0.40 to 0.90; I^2 statistic = 0%; p < 0.05; two trials, 386 participants, moderate-quality of evidence) (Figure 7, Table 3)[19,35] and improved the baby's weight (MD 0.45, 95%CI 0.20 to 0.70; p < 0.05; one trial, 38 participants, low-quality of evidence) [19] compared to iron.

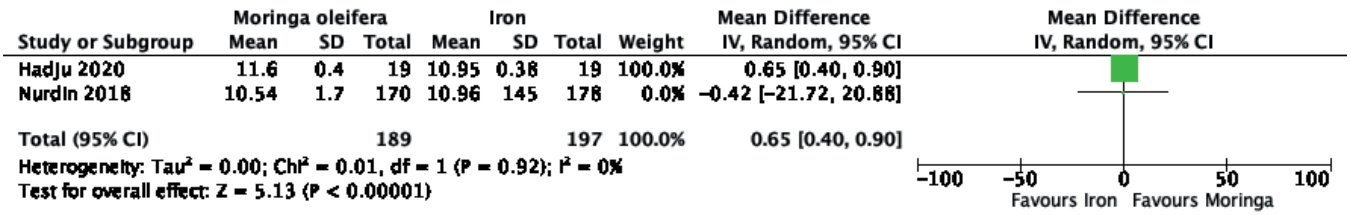

Figure 7. Forest plot of comparison between *Moringa oleifera* versus iron for the hemoglobin level (g/dl).

Table 3. Summary of the findings, including GRADE quality assessment for comparison between *Moringa oleifera* versus iron.

***Moringa oleifera* compared to iron supplement for anemic pregnant women**								
Patient or Population: Anemic pregnant women								
Setting: Outpatient Clinic								
Intervention: *Moringa oleifera*								
Comparison: Iron								
Outcome	**Anticipated absolute effects**		**Relative effect (95% CI)**	**Study event rates (%)**		**No of participants (studies)**	**Certainty of evidence (Grade)**	**Comments**
	Risk with placebo	**Risk difference with *Moringa oleifera* as an adjunct to standard treatment**		**Risk with iron**	**Risk with Moreinga oleifera**			
Hemoglobin level (g/dl)	The mean hemoglobin level was 0	MD 0.65 higher (0.4 higher to 0.9 higher)	-	197	189	386 (2 RCTs)	Moderate	Risk of bias: not serious Inconsistency: not serious Indirectness: not serious Imprecision: serious
Weight of baby (kg)	The mean baby's weight was 0	MD 0.45 higher (0.2 higher to 0.7 higher)	-	19	19	38 (1 RCT)	Low	Risk of bias: not serious Inconsistency: serious Indirectness: not serious Imprecision: serious

CI: confidence interval; **MD:** mean difference

DISCUSSION

Summary of the main result

The design of this review included RCTs addressing the effectiveness of *Moringa oleifera* use in pregnancy anemia. From the identified trials, 11 were found to have used moringa to supplement the standard treatment; results from these studies show that moringa raised levels of hemoglobin in pregnant women in comparison with controls. The limited number of studies however precluded carrying out subgroup analysis of preparation and duration of supplementation. Only a few studies documented the dosage of moringa used, thus the optimum dosage of moringa could not be ascertained. Moringa was also found to have raised the erythrocyte index level in terms of MCH value and ferritin level when it supplemented standard treatment. At the same time, hematocrit level and baby weight did not show significant differences. A couple of studies comparing Moringa with iron supplements showed a hemoglobin level increase and baby weight was also enhanced. No adverse events were reported throughout any of the trials, therefore moringa may be regarded safe when administered medicinally.

Overall Completeness and Applicability of the Evidence

The moringa's effectiveness and role in the treatment of pregnancy anemia were assessed by the author using a thorough study of the literature. From the 15 trials, three were excluded and not pooled because the data analysis was incomplete [34,36,39]. Most of the trials were conducted in lower-middle socioeconomic countries; thus, overall results do not give an overview of the actual population. The studies included in the review all shared the feature of limited sample size, making their findings unsuitable for application in the review. The optimum dosage of moringa that yielded positive results could not be ascertained as well; there were multiple preparations in limited studies. In the first comparison, there were discrepancies in intervention duration. Two of the studies only carried out a 12-week intervention [28,37], seven reported 8-week interventions [26,27,30,32-34,38], and a lone trial documented 2 weeks of intervention [29]. In all trials, hemoglobin levels showed an increase; these differences cannot be considered valid because the data is incomplete. None of the studies' participants reported adverse effects, which means moringa can be deemed to have a good efficacy profile.

Quality of the Evidence

The evidence quality in the main findings ranged from extremely poor to low. A majority of the studies considered had vague selection bias as they did not document details of random sequencing and allocation concealment. Only one study documented its participant

selection procedure [19]. Blinding in treatments was complicated and limited. This is because moringa soup and moringa biscuits could not be properly blinded in the intervention due to their form in comparison with any intervention in capsule form. This results in a high-risk bias in reporting however it would not be greatly impacted by the lack of blinding, as the majority of the outcome's changeable components are biochemical in nature. In three studies, there was a high attrition bias because they disregarded the intention-to-treat analysis. The results of these studies show significant heterogeneity, which the small number of studies could not explain [32,35,37]. The high imprecision in all outcomes was also shown to be the result of the reviewed trials having small sample sizes.

Potential Biases in the Review Process

Publication bias was minimised by searching various databases and further references were discovered by checking the reference lists in the included trials. One article had been translated into English from the Malay original. There is doubt about how relevant data taken from all trials are to this review even though the journal databases had been searched vigorously. A team of two persons assessed the trials and data independently from each other to minimise any potential bias during the review.

Agreements and Disagreements with Other Studies or Reviews

No previous systemic review and meta-analysis have specifically investigated moringa's effects when used on pregnancy anemia. A previous literature review of moringa exists but it did not apply any particular method [10]. The author assessed a total of seven studies from 2013 to 2018 using moringa extract as an intervention. These studies did not discuss their methods in acceptable detail. These trials used samples ranging from anemic women to pregnant women and postpartum women. This review included one trial from the seven[28] whose author concluded moringa has benefits to support pregnancy and prevent adverse pregnancy outcomes.

CONCLUSION

Implication for practice

Moringa oleifera may increase the hemoglobin levels slightly when used in anemic pregnant women either as an adjunct therapy or alternative therapy to iron supplements. Therefore, women with anemia who could not tolerate iron supplements due to their side effects might alternatively use Moringa to improve their hemoglobin levels. No severe adverse event was reported that contributed to the discontinuation of the intervention during the trials.

Implication for research

If further studies were to be conducted, data on the randomization method and blinding should be reported clearly to increase the quality of evidence and the bigger sample size needed, thus improving its applicability. Besides that, all participants need to be investigated for the cause of anemia first as iron deficiency anemia would benefit better from Moringa supplementation than other causes of anemia. Further research is required to determine the precise dose and ideal preparation of Moringa that will impact hemoglobin levels.

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Conflict of Interest

All authors declared that they have no conflict of interest.

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ETHICAL CLEARANCE

Not applicable

AUTHORS CONTRIBUTION

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