



■ Original Article

Maternal Vitamin D Supplementation for the Prevention of Respiratory Tract Infections in Offspring: A Meta-Analysis

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Background: Vitamin D may enhance immune system function and provide a protective effect against infections. Feto-maternal circulation plays an important role in supplying the developing fetus with nutrients and antibodies for its development and health during pregnancy and for its early years of life after birth. This meta-analysis aimed to determine the effectiveness of maternal vitamin D supplementation in preventing respiratory tract infections (RTIs) in children.

Methods: We searched the Central and MEDLINE databases and went through all the reference lists in the related articles. We also searched for ongoing trials at <http://www.who.int/ictrp/en/> and www.clinicaltrials.gov. Randomized controlled trials comparing vitamin D supplementation with a placebo or no treatment in pregnant women published in the English language up to March 2019 were included. Two reviewers extracted data independently using a predefined protocol and assessed the risk of bias using the Cochrane risk of bias tool, with differences agreed upon by consensus. The predefined primary outcome was the number of offspring who had RTIs. The secondary outcome was the presence of measurable serum immunoglobulin E levels.

Results: Three trials involving 3,224 participants (mother-child pairs) met the inclusion criteria and were included in this review. The present analysis reported that maternal supplementation with vitamin D had no effect on RTIs among children (n=1,486 offspring; risk ratio, 0.95; 95% confidence interval, 0.82-1.11; random effects; I² statistics, 0%).

Conclusion: Maternal vitamin D supplementation had no effect on RTIs in children. Therefore, consideration of other prevention methods in this regard is recommended.

Keywords: Vitamin D; Pregnant Women; Respiratory Tract Infections; Children; Infants

Received: February 16, 2021, Revised: April 19, 2021, Accepted: May 10, 2021

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INTRODUCTION

Respiratory tract infections (RTIs) are a group of infectious diseases divided anatomically into the upper and lower respiratory tracts. Upper RTIs include the common cold, laryngitis, pharyngitis/tonsillitis, acute rhinitis, and acute otitis media. Acute bronchitis, bronchiolitis, pneumonia, and tracheitis are common lower RTIs. This group of infections is a common affliction that causes discomfort and debilitation and significantly contributes to absenteeism from school among children and from work among parents, who may end up contracting the infections without proper preventive measures when they have to stay at home for their child's care. Acute RTIs are a major cause of morbidity and mortality globally among all population groups, including children.¹⁻³⁾

RTIs may be viral or bacterial. Most common colds are caused by *rhinoviruses*.^{4,5)} Other known pathogens, such as *coronavirus*, contributed to 10%–15% of the cases, *influenza* to 5%–15%, *parainfluenza* to 5%, and *respiratory syncytial virus* and *metapneumovirus* to 5%.⁴⁾ The common bacterial RTIs are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*.⁶⁾

RTIs can present as a range of symptoms, such as cough, fatigue, and secretory (e.g., nasal congestion) and pain symptoms (e.g., sore throat, headache, muscle pain).⁷⁾ They are also associated with troublesome complications that may be unbearable for young children who contract it. The symptoms of RTIs are usually persistent and may last longer than 2 weeks. In a study on children aged 6 months to 12 years, 26% still had symptoms 7 days from onset and 6% after 14 days.⁸⁾ Cough is the most common persistent symptom, lasting from 15.3 to 28.6 days. The approach for the treatment of RTIs is based on etiology and is predominantly focused on symptom relief.²⁾

Vitamin D is a seco-sterol that is produced endogenously in the skin from sun exposure or can be obtained from natural foods.⁹⁾ It is an important micronutrient for bone growth and immune function. Its deficiency leads to rickets, and it has been linked to various infections, including RTIs. Several studies have reported an association between vitamin D deficiency and infection among children. These interrelations are considered to be related to the role of vitamin D in regulating the immune system.¹⁰⁾ According to Hossein-Nezhad and Holick,⁹⁾ maternal supplementation with 2,000 and 4,000 IU/d of vitamin D during pregnancy improved maternal and neonatal vitamin D status. Maternal supplementation can positively affect the immune system of children to fight infections during their early lives. *In vitro* and *in vivo* studies have shown that vitamin D plays an important role in the innate immune system. The innate immune system provides frontline protection against infectious agents.¹¹⁾ Activated T and B lymphocytes have vitamin D receptors, and thus, their immunological activities are regulated by 1,25-dihydroxyvitamin D.⁸⁾

Maternal vitamin D status during pregnancy may modulate the development of the fetal immune system and infant susceptibility to infections.¹²⁾ A significant correlation was found between maternal and vitamin D levels in cord blood as 25-hydroxyvitamin D (25(OH)D) could cross the placenta.¹³⁾ Thus, maternal supplementation of vita-

min D is considered to strengthen the immune system of children and protect them from respiratory infections in their early lives.

The side effects were used for secondary analysis when intoxication occurred, involving a markedly high level of serum 25-hydroxycholecalciferol (>150 mg/dL). These side effects are characterized by hypercalcemia, hypercalciuria, and hyperphosphatemia.^{14,15)} We tested the supplementation of vitamin D (4,000 IU/d) in adults and reported that the dose effectively increased 25(OH)D from high to normal concentrations and remained in the serum within the physiologic range.

We hypothesized that preventive measures, such as maternal vitamin D supplementation, might reduce the number of children contracting RTIs, thus improving their quality of life and providing them with better health conditions for their growth. This meta-analysis aimed to determine the effectiveness of maternal vitamin D supplementation in preventing RTIs in children.

METHODS

This review was conducted according to the Cochrane Handbook for Systematic Reviews of Interventions¹⁶⁾ and the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) assessment for quality of evidence.¹⁷⁾ The review protocol was registered in PROSPERO (International Prospective Register of Systematic Reviews; registration no., CRD42019131597).

1. Eligibility Criteria

Randomized controlled trials (RCTs) published in the English language, comparing vitamin D supplementation with the control group, were searched. Trials that involved healthy pregnant women and their offspring until the age of 3 years in either sex and only physician-diagnosed RTIs were included. The participants were given daily vitamin D supplementation taken orally or as a bolus at any dosage until the birth of their child. Studies that provided interventions to both the mother and the born infants were excluded.^{18,19)} The findings from the intervention group with those from the placebo or no treatment control group were compared.

2. Search Strategies

The Cochrane Central Register of Controlled Trials in Central (Issue 4, 2019) and MEDLINE were searched. The following search terms were used: vitamin D, pregnant women, maternal supplementation, RTIs, infants, and children. The reference lists of the identified RCTs and review articles were checked to find unpublished trials or trials that were not identified by electronic searches. Moreover, ongoing trials using the World Health Organization International Clinical Trials Registry Platform <http://www.who.int/ictrp/en/> and www.clinicaltrials.gov were searched.

3. Trial Selection

Two authors (Z.S. and A.S.F.M.L.) independently scanned the titles and abstracts from the searches and obtained full-text articles when

they met the eligibility criteria or when information to assess eligibility was insufficient. Two authors (Z.S. and N.M.N.) independently assessed the eligibility of the trials and documented the reasons for exclusion. Any disagreements were resolved among the review authors through discussion, and the authors were contacted when clarification was needed.

4. Data Extraction

From each of the selected studies, two authors (A.S.F.M.L. and M.I.) extracted information pertaining to the study setting, participant characteristics (gestational age, state of health, child's age, etc.), methodology (number of participants randomized and analyzed, duration of follow-up), method for diagnosing RTIs, dose of vitamin D supplementation, frequency of vitamin D administration, method of outcome assessment, occurrence of RTIs among child participants, and serum immunoglobulin E (IgE) level in the offspring. The predefined primary outcome was the number of offspring who had RTIs. The secondary outcome was the presence of measurable serum IgE level.

5. Risk of Bias Assessment

Two authors (Z.S. and A.S.F.M.L.) assessed the risk of bias 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.²⁰⁾ Any disagreements were resolved through discussion.

6. Statistical Analyses

The predefined outcomes for trials with categorical outcomes using risk ratios (RRs) and 95% confidence intervals (CIs) were measured, as well as the risk differences and 95% CIs. For the outcomes with numerical values, data using the mean difference and 95% CI were analyzed. A random-effects model was used to report the findings. The heterogeneity of the trials was assessed in two steps. First, the obvious

heterogeneity was assessed by comparing populations, settings, interventions, and outcomes. The statistical heterogeneity was then evaluated using the I^2 statistic. The guidelines outlined in the "Cochrane Handbook for Systematic Reviews of Interventions" were utilized to interpret heterogeneity.¹⁶⁾ A sensitivity analysis was performed to investigate the effect of the risk of bias on the sequence generation and allocation concealment of the included studies. The included trials were checked for the unit of analysis errors, which were not encountered during the study. If the studies were sufficient, funnel plots were used to assess the possibility of reporting biases or small study biases, or both.

7. Quality of Evidence

The principles of the GRADE approach were used to evaluate the quality of evidence. The GRADE approach specifies four levels of quality, the highest of which is for randomized trial evidence. It can be downgraded to moderate-, low-, or even very-low-quality evidence depending on the presence of four factors: limitations in the design and implementation of available studies, indirectness of evidence, unexplained heterogeneity or inconsistency of results, and imprecision of results.

The GRADEpro software (www.gradepr.org) was used to reflect the quality of evidence for each outcome. The assessment is presented together with a summary of findings (SoF) table. The following outcomes are included in the SoF table: the number of offspring with RTIs and the presence of measurable serum IgE level.

8. Patients and Public Involvement

Patients and the public were not involved in the design or planning of the study.

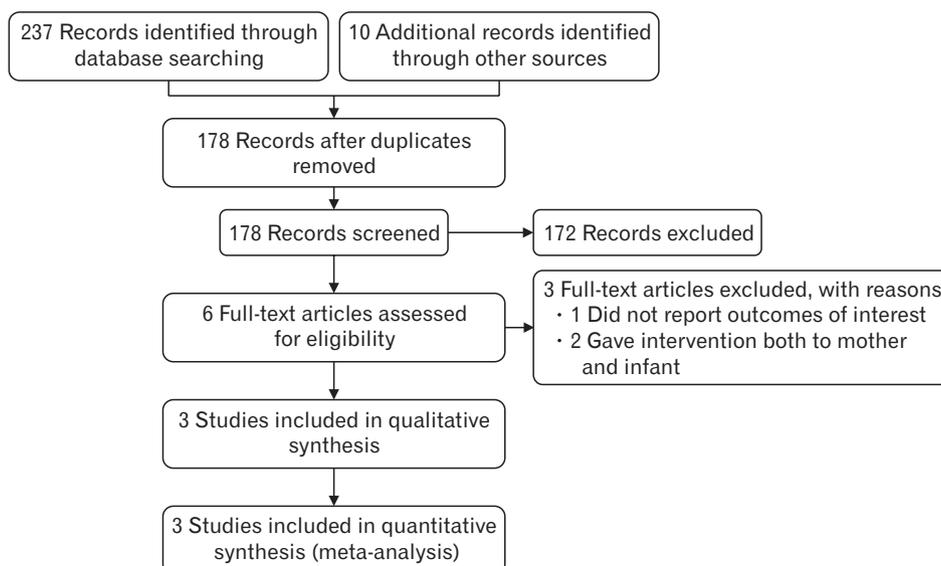


Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of study selection.

RESULTS

1. Trial Selection

A total of 237 records identified through database and electronic searches were retrieved, and 10 additional records from other sources were identified (Figure 1). After removing the duplicates, 178 records were screened. The full texts of the six articles were assessed for eligibility. Three articles were excluded for the following reasons. One trial did not report the outcomes of interest,²¹⁾ and two trials provided intervention to both mother and infant participants from birth until 6 months old.^{18,19)} Three trials were included and analyzed for qualitative and quantitative syntheses.

2. Characteristics of the Included Studies

Three studies with a total of 3,224 participants (mother–infant pairs) were included,^{22–24)} among which 1,679 were mothers and 1,545 were infants. All three trials declared funding from private sources and public research funds.^{22–24)} Table 1 summarizes the characteristics of the included trials.

3. Participants

All three trials were conducted in high-income countries, namely, Denmark,²²⁾ the United States,²⁴⁾ and the United Kingdom,²³⁾ and recruited participants from healthcare settings. Participants with gestational age above week 26 or taking more than 600 IU/d of vitamin D (cholecalciferol) were excluded in one trial.²²⁾ Two trials reported the exclusion of participants due to known sarcoidosis, osteomalacia, renal dysfunction, tuberculosis, or any endocrine, cardiovascular, or nephrological disorders.^{22,23)} The inclusion criteria for the participants were healthy pregnant women with a prespecified gestational age for each trial and their born child. Only one trial included pregnant women or their partners (biological father of the child) who had a history of asthma, allergic rhinitis, or eczema and were nonsmokers as inclusion criteria.²⁴⁾

4. Intervention

The eligible participants in the trials were randomized into the intervention and control groups. In the trial by Goldring et al.²³⁾ in 2013, two different doses of vitamin D were given. The participants were randomized from 27 weeks of gestation to receive either a daily dose of vitamin D of 800 IU or a bolus of 200,000 IU. In another trial, all women received vitamin D (4,000 IU/d) as part of their usual pregnancy care.²⁴⁾ The intervention group was supplemented with an additional dose of vitamin D (2,400 IU/d), and the control group was given matching placebo tablets.²²⁾ The intervention was given from 24 weeks of gestation²²⁾ and at a range of 10–18 weeks of gestational age in one trial.²⁴⁾ About 4,000 IU was supplemented to the intervention group alongside a prenatal vitamin containing 400 IU vitamin D. The women in the control group received a placebo and prenatal vitamin containing 400 IU of vitamin D. The supplements were administered orally in all three trials.

5. Outcomes

All three trials reported their primary outcomes. One trial monitored the offspring every 3 months by telephone and scheduled an annual in-person assessment of the child's health by the study staff.²⁴⁾ One trial reported an assessment at 3 years of age by investigators, using a validated health questionnaire and clinical assessment with primary healthcare records obtained from the participants' general practitioner.²³⁾ Another trial assessed their participants with scheduled visits, acute visits, and daily diary card monitoring to capture symptom burden between visits.²²⁾ This trial also reported the mean number of episodes of RTI per year. The presence of measurable IgE levels was reported in two trials and was measured when the offspring were 6 and 18 months of age²²⁾ and at 3 years of age.²⁴⁾

6. Risk of Bias Assessment

The risk of bias assessment is shown in Figures 2 and 3. Figure 2 presents the proportion of studies as low, unclear, or high risk of bias for each bias indicator. Figure 3 shows the risk of bias indicators for each study.

Table 1. Characteristics of the included studies

Author (year)	Country	No. of patients	Intervention (dose/IU)	Frequency	Comparison	Gestation age at the start of trial (wk)	Outcome	Method of assessment	No. of offspring assessed
Goldring (2013)	UK	180	vD (800 IU, daily); vD in bolus (200,000 IU, once)	Daily or once	No treatment	27	Number of offspring who had RTIs	Validated health questionnaire and clinical assessment by a blinded investigator	158
Chawes (2016)	Denmark	623	vD (2,400 IU)	Daily	Placebo	24	Number of offspring who had RTIs; presence of measurable serum IgE level; episodes of RTIs	Scheduled and acute visits to the pediatricians and daily diary card monitoring	581
Litonjua (2016)	USA	876	vD (4,000 IU)	Daily	Placebo	10–18	Number of offspring who had RTIs; presence of serum IgE level	Over the phone monitoring every 3 months and annually in person for 3 years by the study staff	806

vD, vitamin D; RTIs, respiratory tract infections; IgE, immunoglobulin E.

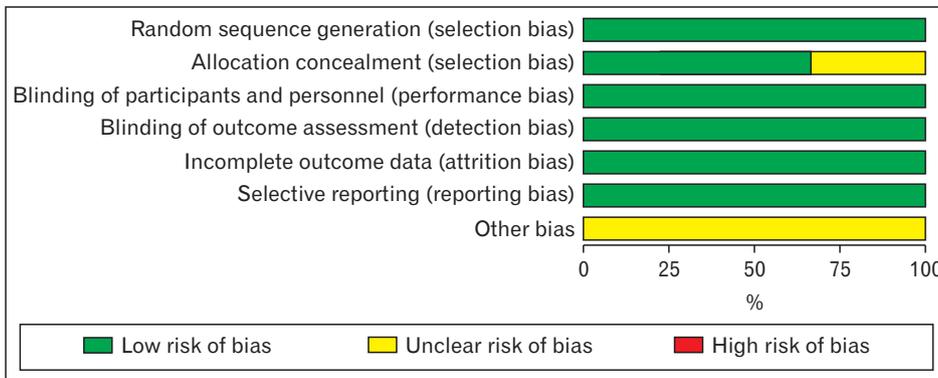


Figure 2. Risk of bias graph: evaluation of each risk of bias item presented as percentages across all included studies.

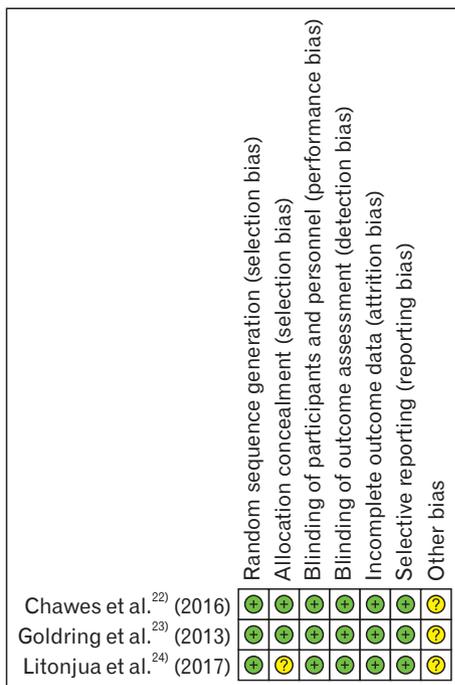


Figure 3. Risk of bias summary: evaluation of each risk of bias item for each included study.

1) Allocation

The randomization method used was described in all trials. Two trials used a computer-generated list of random numbers,^{22,23)} and one trial reported using a system that automates the random assignment of treatment groups using stratified permuted blocks with randomly varied block sizes.²⁴⁾ On the method described above, the allocation intervention was evaluated as low risk. The concealment of allocation was of low risk in two studies.^{22,23)} One trial did not report any method of concealment, and thus, it was evaluated as an unclear risk of concealment allocation bias.²⁴⁾

2) Blinding

Two trials used a placebo control,^{22,24)} and one trial did not provide any treatment to the control group.²³⁾ The participants, the person responsible for the participants' care, and the outcome assessor were blinded

in all three trials and evaluated as having a low risk of blinding. One trial reported the unblinding of eight randomizations during pregnancy.²²⁾ Four of them were due to intrauterine death; the reasons for the other four cases were not reported. The participants were unblinded and were excluded from the primary analysis.

3) Incomplete outcome data

Three trials measured the primary outcomes and were included in the meta-analysis. The primary outcome was assessed for the first 3 years of life for the child participants. Two trials measured secondary outcomes. One trial measured the presence of measurable IgE levels at 6 and 18 months of age.²²⁾ Another trial assessed the outcome at 3 years of age. The rate of withdrawal was low for all three trials and balanced between the intervention and control groups.

4) Selective reporting

All trials reported the outcomes as prespecified in the Methods section and answered the objectives.²²⁻²⁴⁾ Two trials were registered in Clinical-Trials.gov,^{22,24)} and one trial was registered in Controlled-Trials.com.²³⁾

5) Other potential sources of bias

Any other potential sources of bias were not detected.

7. Clinical Outcomes

1) Number of offspring who had RTIs

Three trials reported the number of offspring who had RTIs in their first years of life (three trials, 1,486 participants; RR, 0.95; 95% CI, 0.82–1.11; random effects; I² statistics, 0%) (Figure 4).²²⁻²⁴⁾ The overall quality of evidence was moderate (Table 2).

2) Presence of measurable serum IgE levels

Two trials reported measurable serum IgE levels in child participants. One trial assessed these data when the child was 3 years old.²⁴⁾ Another trial measured these data when the child was 6 and 18 months old (two trials, 1,373 participants; RR, 1.14; 95% CI, 0.98–1.58; random effects; I² statistics, 49%) (Figure 5).²²⁾ The I² value did not change with the fixed effects. The overall quality of evidence was moderate (Table 2).

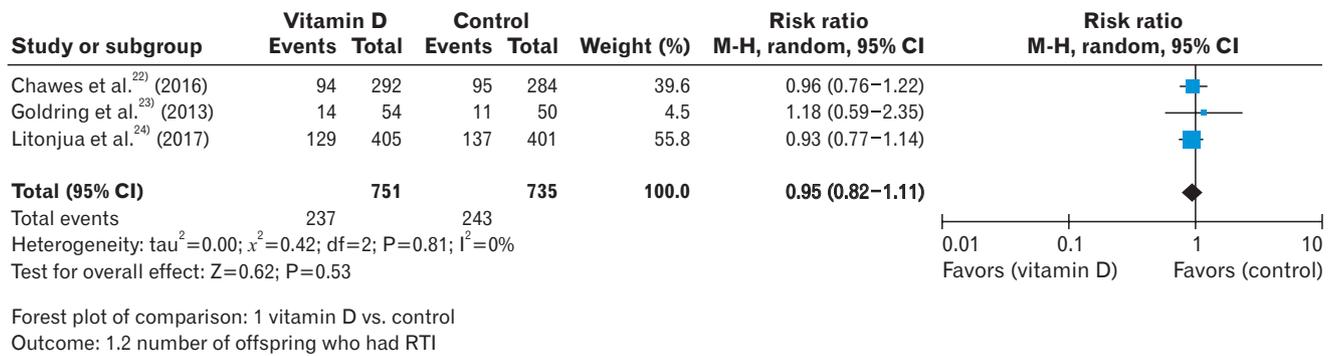


Figure 4. Individual and pooled effect size (risk ratio and confidence interval [CI]) of respiratory tract infections (RTIs) in offspring of mothers treated with vitamin D during pregnancy compared to control according to the random-effect model. M-H, Mantel-Haenszel; df, degrees of freedom.

Table 2. Summary of the findings including the GRADE quality assessment

Outcomes	Study population: anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with vitamin D				
No. of children who had RTIs	331 per 1,000	314 per 1,000 (271–367)	RR 0.95 (0.82–1.11)	1,486 (3 RCTs)	⊕⊕⊕⊕ moderate [†]	Risk with vitamin D calculated from the mean risk across the intervention group from the three trials
Presence of measurable serum IgE level	418 per 1,000	477 per 1,000 (347–661)	RR 1.14 (0.83–1.58)	1,373 (2 RCTs)	⊕⊕⊕⊖ moderate [†]	Risk with vitamin D calculated from the mean risk across the intervention group from the two trials

Vitamin D compared with placebo for RTIs in offspring: (1) patient or population: pregnant women and their offspring; (2) setting: healthcare settings; (3) intervention: vitamin D; and (4) comparison: placebo. GRADE (Grading of Recommendations, Assessment, Development and Evaluation) working group grades of evidence: (1) high certainty: We are very confident that the true effect lies close to that of the estimate of the effect. (2) Moderate certainty: We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. (3) Low certainty: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect. (4) Very low certainty: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

CI, confidence interval; RTIs, respiratory tract infections; RR, risk ratio; RCTs, randomized controlled trials; IgE, immunoglobulin E.

*The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[†]Imprecise because of the wide confidence interval.

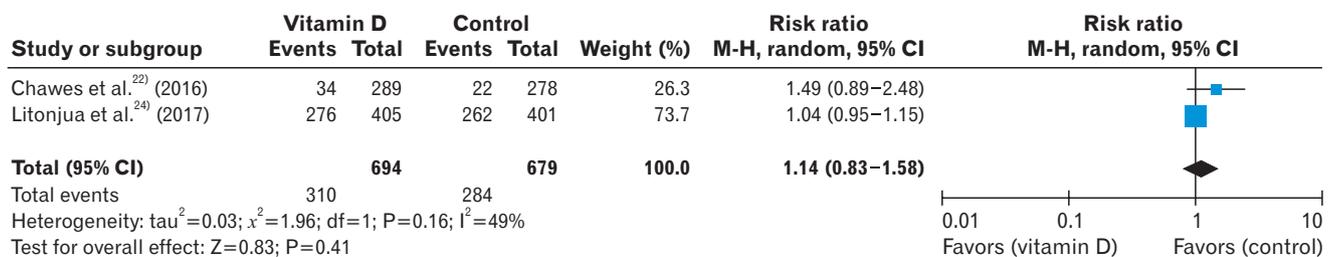


Figure 5. Individual and pooled effect size (risk ratio and confidence interval [CI]) of measurable serum immunoglobulin E (IgE) levels in offspring of mothers treated with vitamin D during pregnancy compared to control according to the random-effect model. M-H, Mantel-Haenszel; df, degrees of freedom.

3) Episodes of RTIs

This outcome was reported in one trial.²²⁾ No difference was found in the mean±standard deviation between the intervention and control groups (5.2±2.62 versus 5.2±5.57).

8. Sensitivity Analysis

For all three outcomes, no change was found in the effect sizes and CI after removing the trial with an unclear risk of concealment allocation and random sequence generation.

9. Adverse Events

Included RCTs did not report any of the adverse events.

DISCUSSION

1. Summary of the Main Results

This review was designed to include all RCTs addressing the effectiveness of maternal vitamin D supplementation during pregnancy to prevent their children from contracting RTIs during their first 3 years of life. The three identified trials formed a group addressing several comparisons and a variety of outcomes, resulting in several trials contributing to each of our predefined outcomes. In total, 31.6% of the young children in the intervention group contracted RTIs in comparison with 33% of the control group during the 3-year follow-up period. Proving the effectiveness of maternal vitamin D supplementation in preventing RTIs in children in a larger population is insignificant. This is due to the limited number of RCTs conducted on this topic, which involved a small population size.

The intervention group did not have a better effect than that in the control group in terms of the presence of measurable serum IgE level. Moreover, no significant difference was observed between the intervention and control groups in the episodes of RTIs among the children throughout the 3-year follow-up period. The documented results may not be precise in assuming the same effect on a large population due to the limitations encountered in this study. More RCTs involving a larger population size may report substantially different results. As all three trials were conducted in high-income countries, data from low-income countries could have different results by considering the hygienic and living condition factors in young children's susceptibility to infections.²⁵⁾

No predicted adverse events, such as renal stones or hypercalcemia, were reported in the included studies. The dosage of vitamin D used in these trials can be concluded to be safe for pregnant women.

2. Agreements and Disagreements with Other Studies or Reviews

Three other systematic reviews have examined the preventive effects of vitamin D supplements on RTIs.^{1,3,10,26)} However, among the reviews, only one was conducted on maternal vitamin D supplementation and the resulting wheezing in children.¹⁾ The review included four RCTs, three of which were included in this review. One other trial was excluded because it provided intervention to the participants' children. This review supports the preventive role of vitamin D during pregnancy in offspring wheeze. However, wheezing is a broad condition that may occur due to asthma. The other two reviews found a reduction in the development of RTIs in various population groups taking vitamin D supplements. Charan et al.²⁶⁾ included five RCTs, two of which tested vitamin D supplementation in a pediatric age group and were analyzed separately. Both RCTs reported a significant reduction in RTIs in the intervention group. One review included data on the preventive role of vitamin D in RTIs in different population groups from 25 RCTs,

seven of which included a pediatric age group.³⁾ However, none of these trials were included in our study because they did not meet our inclusion criteria. The review proved the protective role of vitamin D supplements against RTIs, with vitamin D deficiency experiencing the most benefit. All three reviews found a reduction in the development of RTIs with the use of vitamin D supplements as a preventive measure. Although not all of these reviews analyzed trials that provided vitamin D supplementation during pregnancy with subsequent RTIs in offspring, the positive effect of vitamin D on the immune system was implied for our review. We found no other systematic review that reported our prespecified secondary outcomes.

3. Quality of Evidence

The quality of trial evidence was moderate. Generally, a low or unclear risk of bias was found in most trials in most domains. No evidence of selective reporting bias was found, although we could not exclude this for all the included trials because only one of the trials had published protocols.²⁴⁾ All three trials were prospectively registered in a clinical trial registration database. The risk of attrition bias was low in all included studies. The rate of withdrawal was low in all studies and accounted for less than 10% of the total participants. In addition, the withdrawals were with reasons, and from the reasons stated, we believe that the withdrawals had no direct correlation with the intervention done. All three trials declared funding from various sources. In our meta-analysis, we encountered no heterogeneity in the primary outcome. We performed a random-effects meta-analysis in which no heterogeneity was found. A wide level of CI was found, and the sample size of the population was small, thus causing a downgraded quality in the imprecision value of the evidence. The result may not be imprecise enough to be implicated in a large population. Our secondary outcomes showed substantial heterogeneity, with an I^2 value of 49%. We were unable to perform additional sensitivity analyses because only two trials contributed to this outcome. The removal of one of the studies did not show any changes in the effect estimate. Therefore, the overall level of evidence contributing to this review, as assessed using the GRADE approach, is of moderate quality.

4. Potential Biases in the Review Process

We attempted to reduce publication bias by checking the reference lists of all related studies for further references and by searching multiple databases. We restricted the search to English publications only. Therefore, we cannot be certain that we identified all trials in this area, which may have led to language and systematic biases in the conclusion. A funnel plot to detect bias or heterogeneity was not constructed because of the limited number of studies contributing to each outcome. None of the included trials reported any outcomes. The included studies showed the same direction of effect, and thus, we encountered no heterogeneity between the studies. However, differences were observed in the primary outcome measurements. The diagnosis of RTIs is subjective, and although attempts were made in all the included studies for the primary outcome to make it more objective, the defi-

nitions used varied across the studies. The outcome assessor across the studies used different methods of assessment, namely, validated health questionnaires, daily diary card monitoring, and assessment of the primary healthcare records of the offspring obtained from their general practitioners.

In conclusion, based on the currently available trials, vitamin D supplementation during pregnancy seems to have no effect in preventing RTIs in children. Therefore, using other methods to prevent RTIs in the offspring of mothers supplemented with vitamin D are recommended. Further studies should be conducted to investigate the effectiveness of maternal vitamin D supplementation in preventing RTIs in children. Studies examining the use of vitamin D supplementation during pregnancy should include the proportion of RTIs as an outcome and provide detailed safety data. Data on antibiotic usage or other treatments for RTIs, serum IgE levels, and other pro-inflammatory markers should also be collected. Data on the start of vitamin D supplementation during gestation and the dosage of vitamin D are also essential and should be included.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGMENTS

We would like to thank Scribendi Inc. (www.scribendi.com) for English language review. The authors would also like to acknowledge Mr. Amran Mamat and Ms. Nurul Azurah Mohd Roni, librarians from Hamdan Tahir Library, for their assistance with database searches.

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