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Investigating the relationship between vitamin B intake and endometriosis: a systematic review and meta-analysis

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Abstract

Introduction: Vitamin B promotes the inactive metabolism of estrogen and inhibits endometrial growth. Accordingly, the present study aimed to examine the relationship between vitamin B intake and endometriosis.
Materials and Methods: Databases Scopus, PubMed, ProQuest, Web of Science, Cochrane, Embase, and Google Scholar Search Engine were used for articles published until July 18, 2025. Data was entered into SPSS 19 and analyzed using STATA 14.
Results: Generally, administration of vitamins B2 (OR: 0.76, 95% CI: 0.64, 0.90) and B3 (OR: 0.98, 95% CI: 0.96, 1) reduced the risk of endometriosis. However, the relationship between vitamins B1 (OR: 1.04, 95% CI: 0.92, 1.17), B6 (OR: 0.98, 95% CI: 0.89, 1.08), B9 (OR: 1.01, 95% CI: 0.84, 1.21), and B12 (OR: 1.06, 95% CI: 0.98, 1.14) and endometriosis was statistically insignificant. According to the subgroup analysis, vitamin B1 intake in cohort studies increased the risk of endometriosis. Vitamin B2 administration in case-control studies and in the fourth quartile reduced the risk of endometriosis. Vitamin B9 intake, on the other hand, increased the risk of endometriosis in cohort studies and the fourth quartile.
Conclusion: Vitamin B2 and B3 intake reduced the risk of endometriosis in women by up to 24% and 2%, respectively. However, to ensure the validity of the results, further studies on this subject are required.
Registration: This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (ID: CRD420251112519) and Research Registry (UIN: reviewregistry2028) websites.

Introduction

Endometriosis is a common inflammatory disease diagnosed with an abnormal growth of tissue similar to endometrium outside the uterus (1). Endometriosis affects about 10% of women of reproductive age, causing symptoms including pelvic pain, dysmenorrhea, and infertility (2,3). Endometriosis is a multifactorial disease, and its cause is still undetermined (4). Endometriosis affects mental health, quality of life, and costs associated with the treatment of women (5), making it a critical issue.

The current treatment of endometriosis includes medication and surgery, whereas medication may not resolve the primary cause, and surgery may affect fertility (6). Accordingly, researchers try to examine the association between endometriosis and new cases. Considering the effects of diet on immune system modulation, and its antioxidant, estrogen, and anti-inflammatory effects, it may affect the risk of endometriosis

Key point

The results of the present meta-analysis indicated that among the B-group vitamins, vitamins B2 and B3 intake reduced the risk of endometriosis in women. However, there was no statistically significant association between vitamins B1, B6, B9, and B12 and the risk of endometriosis.

(7). On the other hand, studies demonstrated a relationship between micronutrients and endometriosis (8). B-group vitamins regulate the estrogen level of the body and help modulate the symptoms of endometriosis (9). In fact, vitamin B promotes the inactive metabolism of estrogen, supporting the conversion of linoleic acid to gamma-linoleic acid pathway, a critical step in the creation of anti-inflammatory prostaglandins. Such anti-inflammatory prostaglandins can stop the growth of endometrial tissue (10).

One study (11) reported that the relationship between vitamin B1 intake and endometriosis was statistically insignificant, while another (12) showed that the association between vitamin B3 and endometriosis was not significant. However, research (13) demonstrated that vitamin B6 administration reduced the risk of endometriosis, and another (14) indicated that vitamin B2 intake reduced the risk of endometriosis in the second quartile. Considering the inconsistency of the results of the mentioned studies, the current study was carried out using systematic review and meta-analysis methods to present a comprehensive examination.

Materials and Methods

This article was based on the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (15), and its protocol was registered at the PROSPERO (International Prospective Register of Systematic Reviews) and Research Registry websites.

Search strategy

The search was conducted on the databases Scopus, PubMed, Web of Science, ProQuest, Cochrane, Embase, and Google Scholar Search Engine for articles published by July 18, 2025. The search included no limitation in the language and time of the studies. The Medical Subject Heading (MeSH) keywords and their equivalents were used in the search, and operators (AND, OR) were used to combine them. The search strategy in the database Scopus was as follows: (TITLE-ABS-KEY (Vitamin B1 OR Thiamine OR Vitamin B2 OR Riboflavin OR Vitamin B3 OR Niacinamide OR Vitamin B6 OR Vitamin B9 OR Folic Acid OR Vitamin B12 OR Cobalamin) AND TITLE-ABS-KEY (Endometriosis))

PICO components

- **Population:** Research that evaluated the association between vitamin B intake and endometriosis in women.
- **Intervention:** Vitamin B intake.
- **Comparison:** Healthy women.
- **Outcome:** Investigating the association between vitamin B intake and endometriosis.

Inclusion criteria

Research that evaluated the relationship between vitamin B intake and endometriosis.

Exclusion criteria

Low-quality articles, duplicate articles, studies that examined the relationship between women's vitamin B levels and endometriosis, review articles, preprint study, articles without accessible full text, mendelian randomization study, articles that lacked sufficient data.

Quality assessment

Two researcher assessed the quality of articles by the Newcastle-Ottawa Scale (NOS). The scoring method of this 9-question tool is from 0 to 10, where 0 indicates the lowest quality and 10 indicates the highest quality. Studies with scores lower than five were considered low-quality (16).

Data extraction

Two researcher independently extracted data, including sample size, stage of study, index, country, age, year, author's name, and the association between vitamin B intake and endometriosis. Then, using an agreement solution, the two authors addressed the discrepancies.

Statistical analysis

The odds ratio (OR) and rate ratio (RR) logarithms were used to evaluate the effect of vitamin B use on endometriosis. The studies were combined using OR, RR logarithm. To evaluate the heterogeneity, the I^2 index was used, and a random-effects model was employed to combine the results. Data analysis was conducted using STATA 14. Tests with P values < 0.05 were considered statistically significant.

Results

Overall, 141 articles were found. Then, 49 duplicate studies were removed. The abstracts were reviewed, and 8 studies without full text were excluded. Out of the remaining 84 studies, 28 articles that lacked the required data for analysis were removed. A total of 56 studies entered the next step and, 51 articles were excluded due to other exclusion criteria, and six studies remained (Figure 1).

This meta-analysis examined five observational studies, and Table 1 presents a part of the related information.

Findings indicated that in general, there was no statistically significant relationship between the administration of vitamins B1 (OR: 1.04, 95% CI: 0.92, 1.17), B6 (OR: 0.98, 95% CI: 0.89, 1.08), B9 (OR: 1.01, 95% CI: 0.84, 1.21), and B12 (OR: 1.06, 95% CI: 0.98, 1.14) and endometriosis (Figures 2 to 5). However, vitamin B2 (OR: 0.76, 95% CI: 0.64, 0.90) and B3 (OR: 0.98, 95% CI: 0.96, 1) intake reduced the risk of endometriosis (Figures 6 and 7).

Vitamin B1 administration in cohort studies increased the risk of endometriosis. Vitamin B2 intake reduced the risk of endometriosis in case-control studies and the fourth

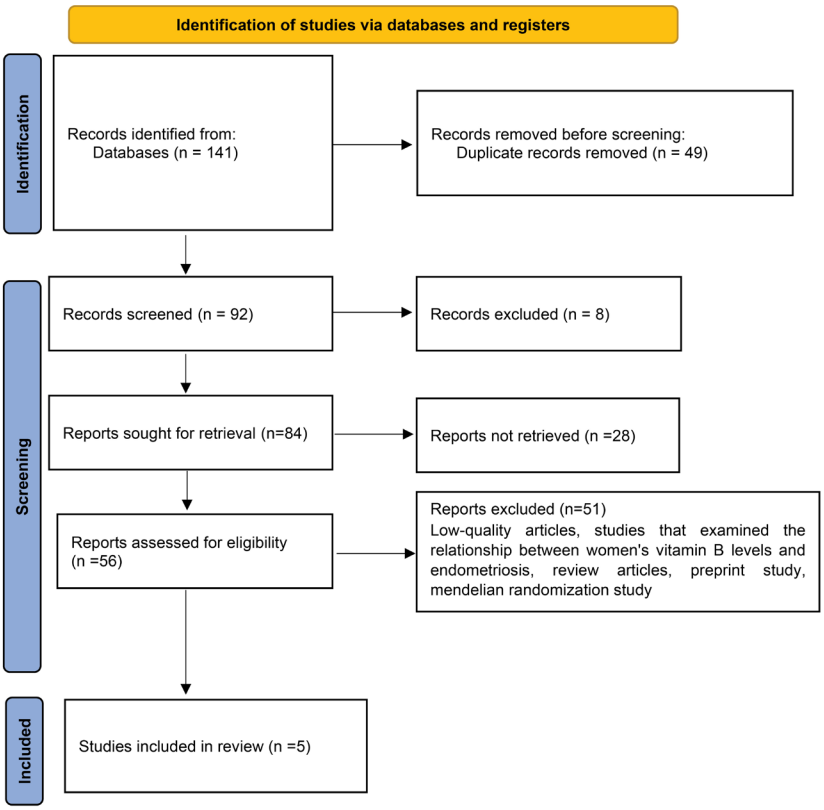

Figure 1. PRISMA flowchart.

quartile. Vitamin B9 increased the risk of endometriosis in cohort studies and the fourth quartile. In other cases, however, there was no statistically significant association between vitamin B intake and endometriosis (Table 2).

Discussion

The results of the present meta-analysis indicated that among the B-group vitamins, vitamins B2 and B3 intake reduced the risk of endometriosis in women. However, there was no statistically significant association between vitamins B1, B6, B9, and B12 and the risk of endometriosis.

According to Zhang et al, vitamin B6 administration increased the risk of endometriosis (OR: 2.39, 95% CI: 1.23–4.66) (18). In a cross-sectional study by Yin et al, vitamin B6 administration increased the risk of endometriosis (OR: 1.18, 95% CI: 1.01 -1.39) (17).

Table 1. Key characteristics of included studies

Author, year	Country	Type of study	Duration of study	Stage of study
Sheng J, 2025 (13)	USA	Cross-sectional	2003-2006	Total
Yin L, 2024 (17)	USA	Cross-sectional	1999–2006	Quartile 2 Quartile 3 Quartile 4
Xu T, 2024 (11)	USA	Cross-Sectional	1999–2006	Quartile 2 Quartile 3 Quartile 4
Darling AM, 2013 (12)	USA	Cohort	1991-2005	Quintile 2 Quintile 3 Quintile 4 Quintile 5
Trabert B, 2011 (14)	USA	Case–Control	1996-2001	Quartile 2 Quartile 3 Quartile 4

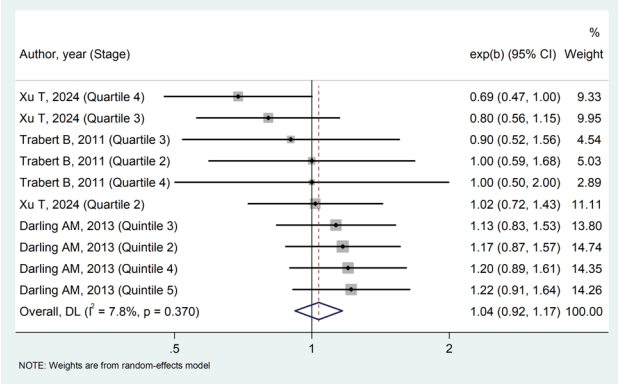

Figure 2. Forest plot association between vitamin B1 use and endometriosis.

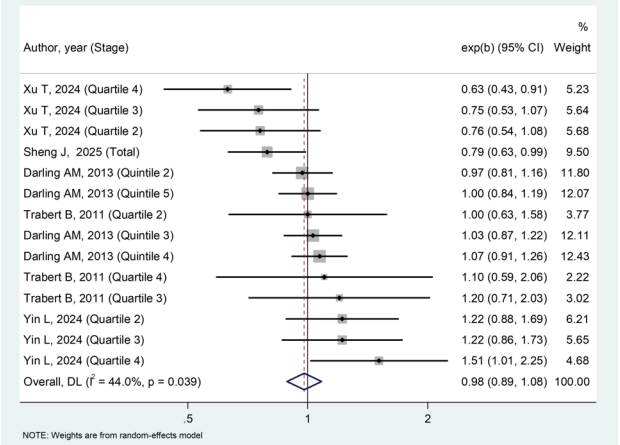

Figure 3. Forest plot association between vitamin B6 use and endometriosis.

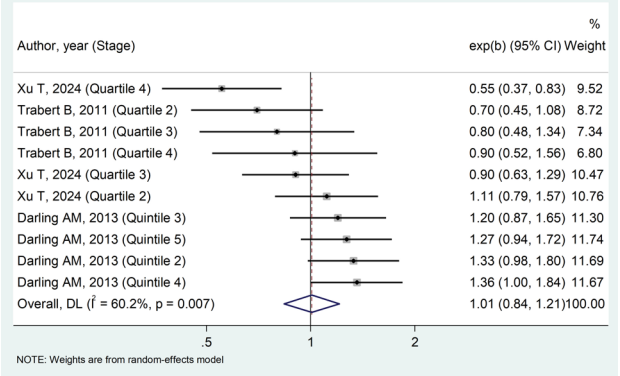

Figure 4. Forest plot association between vitamin B9 use and endometriosis.

These results were not consistent with our findings, as in our study, the association between vitamin B6 and endometriosis was insignificant. The difference in the type of the present research and previous studies may be among the causes of the inconsistent results.

In a cross-sectional study by Sheng et al, findings showed that vitamin B6 (OR: 0.79, 95% CI: 0.62, 0.99) and niacin (OR: 0.98, 95% CI: 0.96, 1.00) administration reduced the risk of endometriosis (13). Their result was not consistent with our findings, as in the present research,

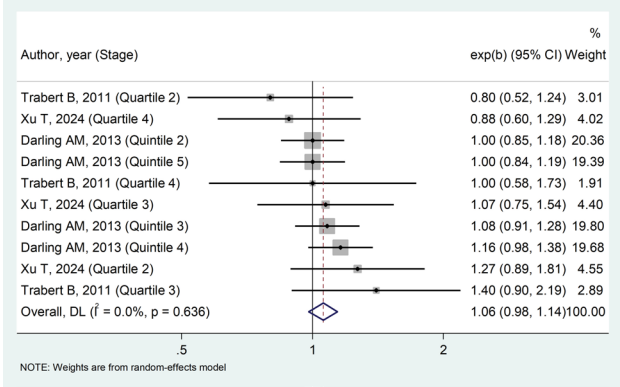

Figure 5. Forest plot association between vitamin B12 use and endometriosis.

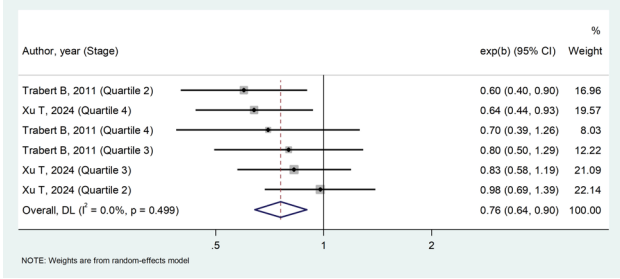

Figure 6. Forest plot association between vitamin B2 use and endometriosis.

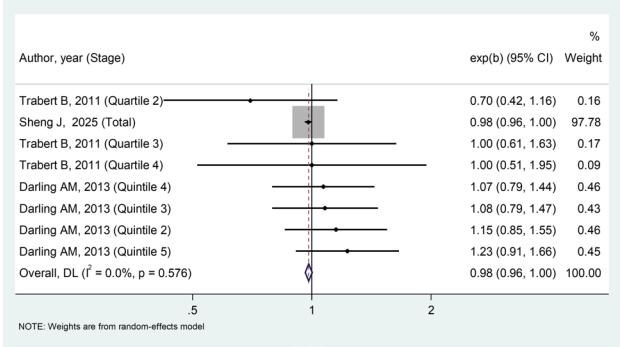

Figure 7. Forest plot association between vitamin B3 use and endometriosis.

the combinative results of cross-sectional studies indicated that there was no significant association between vitamin B6 and endometriosis.

A cross-sectional study by Xu et al revealed that vitamins B1 (OR: 0.81, 95% CI: 0.70, 0.95), B2 (OR: 0.86, 95% CI: 0.74, 0.99), B6 (OR: 0.78, 95% CI: 0.66, 0.91), and folate (OR: 0.77, 95% CI: 0.66, 0.90) administration was associated with a reduction in the risk of endometriosis (11). The findings of this study regarding the administration of vitamins B1, B6, and folate were inconsistent with our results. However, the findings of the two studies regarding the relationship between vitamin B2 and endometriosis were similar.

In a cohort study by Arthur et al in Canada, results indicated that B-group vitamins intake was not associated with the risk of breast or colon cancer. However, consumption of relatively high amounts of folate reduced

Table 2. The association between vitamin B use and endometriosis by subgroups

Subgroups	OR	Low limit	Up limit	P-value	I^2 (%)	Is significant?
Vitamin B1						
Cross-sectional	0.84	0.67	1.04	0.313	14	No
Case-control	0.96	0.69	1.34	0.956	0	No
Cohort	1.18	1.02	1.37	0.986	0	Yes
Quartile 2	1.01	0.76	1.35	0.955	0	No
Quartile 3	0.83	0.61	1.13	0.734	0	No
Quartile 4	0.75	0.54	1.04	0.356	0	No
Quintile 2	1.17	0.87	1.57	---	0	No
Quintile 3	1.13	0.83	1.53	---	0	No
Quintile 4	1.20	0.89	1.61	---	0	No
Quintile 5	1.22	0.91	1.64	---	100	No
Vitamin B2						
Cross-sectional	0.81	0.64	1.03	0.276	22.3	No
Case-control	0.68	0.52	0.90	0.664	0	Yes
Quartile 2	0.77	0.48	1.25	0.076	68.3	No
Quartile 3	0.82	0.61	1.09	0.911	0	No
Quartile 4	0.66	0.48	0.90	0.805	0	Yes
Vitamin B3						
Cross-sectional	0.98	0.96	1	---	0	No
Case-control	0.87	0.64	1.19	0.553	0	No
Cohort	1.13	0.97	1.31	0.912	0	No
Vitamin B6						
Cross-sectional	0.93	0.74	1.17	0.003	69.3	No
Case-control	1.09	0.80	1.47	0.876	0	No
Cohort	1.02	0.94	1.11	0.870	0	No
Quartile 2	0.98	0.73	1.31	0.151	47.1	No
Quartile 3	1.01	0.72	1.42	0.120	52.8	No
Quartile 4	1.01	0.56	1.81	0.006	80.4	No
Quintile 2	0.97	0.81	1.16	---	0	No
Quintile 3	1.03	0.87	1.22	---	0	No
Quintile 4	1.07	0.91	1.26	---	0	No
Quintile 5	1	0.84	1.19	---	0	No
Vitamin B9						
Cross-sectional	0.83	0.56	1.23	0.031	71.1	No
Case-control	0.78	0.59	1.04	0.777	0	No
Cohort	1.29	1.11	1.51	0.948	0	Yes
Quartile 2	0.90	0.57	1.42	0.103	62.4	No
Quartile 3	0.87	0.65	1.17	0.699	0	No
Quartile 4	0.68	0.42	1.09	0.161	49.1	No
Quintile 2	1.33	0.98	1.80	---	0	No
Quintile 3	1.20	0.87	1.65	---	0	No
Quintile 4	1.36	1	1.84	---	0	Yes
Quintile 5	1.27	0.94	1.72	---	0	No
Vitamin B12						
Cross-sectional	1.07	0.87	1.32	0.392	0	No
Case-control	1.04	0.74	1.46	0.212	35.5	No
Cohort	1.06	0.97	1.15	0.571	0	No
Quartile 2	1.03	0.65	1.61	0.109	61.1	No
Quartile 3	1.19	0.90	1.58	0.361	0	No
Quartile 4	0.92	0.67	1.26	0.715	0	No
Quintile 2	1	0.85	1.18	---	0	No
Quintile 3	1.08	0.91	1.28	---	0	No
Quintile 4	1.16	0.98	1.38	---	0	No
Quintile 5	1	0.84	1.19	---	0	No

the risk of endometrial (HR: 0.52, 95% CI: 0.29, 0.93) and ovarian (HR: 0.39, 95% CI: 0.19, 0.80) cancers. Additionally, relatively high vitamin B6 intake reduced the risk of ovarian cancer (HR: 0.49, 95% CI: 0.24,0.9) (19), which was inconsistent with the results obtained in our study.

In a cross-sectional study by Zhao et al, vitamin B2 intake was associated with a reduction in the risk of infertility in women (OR: 0.81, 95% CI: 0.69-0.96) (20), consistent with the present study, which indicated that vitamin B2 was beneficial for women.

According to the results of a meta-analysis by Long et al, the highest level of folate intake compared with the lowest had no association with the risk of endometrial cancer (RR: 0.90, 95% CI: 0.78, 1.05) (21). Based on the findings of a case-control study by Harris et al, the highest quartile of vitamin B6 intake compared with the lowest quartile (OR: 0.76, 95% CI: 0.64, 0.92) reduced the risk of ovarian cancer. However, there was no statistically significant relationship between folate and the risk of ovarian cancer (22). The results of this study regarding folate were consistent with our findings; however, findings concerning vitamin B6 were inconsistent.

Limitations

Subgroup analysis based on the age of women was not possible. All the studies were conducted in the United States of America, and the studies lacked ethnic diversity. The total number of studies was limited.

Conclusion

Based on the achieved results, vitamin B2 and B3 intake reduced the risk of endometriosis in women by up to 24% and 2%, respectively. However, considering the limited number of examined studies, it is recommended that more observational studies be conducted in this regard across different countries to increase the generalizability of the results.

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Authors' contribution

Conceptualization: Amirhosein Moradi, Maryam Farajisani, and Sara Abutalebi Nasrabad.
Data curation: Mehrangiz Ghafari, Maryam Farajisani, and Sadaf Rassouli.
Formal analysis: Ahmadreza Siyasari and Peyman Khajehnabi.
Investigation: Tahmineh Ezazi Bojnordi and Peyman Khajehnabi.
Methodology: Ahmadreza Siyasari and Saba Bazzazi.
Project management: Mehrangiz Ghafari.
Supervision: Amirhosein Moradi.
Validation: Sara Abutalebi Nasrabad and Tahmineh Ezazi Bojnordi.
Visualization: Saba Bazzazi and Sadaf Rassouli.
Writing–original draft: All authors.
Writing–review and editing: All authors.

Ethical issues

This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (International Prospective Register of Systematic Reviews) website with (ID: CRD420251112519) and Research Registry website with (Unique Identifying Number (UIN) reviewregistry2028). Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Conflicts of interest

There are no competing interests.

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