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Review Article

The Association between Dairy Consumption and the Risk of Developing Multiple Sclerosis: A Systematic Review and Meta-Analysis

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Abstract

Background: Multiple sclerosis (MS) is a chronic and disabling disease that commonly affects young adults. We aimed to provide a comprehensive review of the current literature on the association between dairy consumption, particularly cow milk, and the risk of developing MS.

Methods: This systematic review and meta-analysis was conducted in accordance with PRISMA guidelines. We searched PubMed, Web of Science, Cochrane Library, and Scopus for peer-reviewed papers published until 2024. Eligible studies included randomized controlled trials, quasi-experimental studies, and observational designs (case-control, cohort, cross-sectional). Studies were excluded if they did not report sufficient data to calculate effect sizes. Study quality was assessed using the Newcastle-Ottawa Scale (NOS). A random-effects meta-analysis was conducted, and heterogeneity was assessed using the I^2 statistic.

Results: Twenty studies met the inclusion criteria. The overall pooled odds ratio (OR) for the association between total dairy consumption and MS risk was 0.96 (95% CI: 0.93–0.99), indicating a weak but statistically significant inverse association. Subgroup analysis of cohort studies, however, showed no significant association (relative risk [RR] = 1.18, 95% CI: 0.95–1.47, $P = 0.41$). Furthermore, cow's milk consumption alone was not significantly associated with MS development (OR = 0.88, 95% CI: 0.46–1.69, $P = 0.21$).

Conclusion: Although pooled results suggest a slight protective effect of overall dairy consumption on MS risk, findings remain inconsistent and inconclusive, especially when considering specific dairy products and study design. Additional longitudinal studies with rigorous methodology are needed to clarify the potential role of dairy in MS pathogenesis.

Keywords: Dairy products; Cow milk; Multiple sclerosis; Meta-analysis

Introduction

Multiple sclerosis (MS) is a chronic, inflammatory, autoimmune disease of the central nervous system that affects about 2.8 million people worldwide, mostly young people and women. Although MS most commonly affects women between the ages of 20 and 40, it can affect people of any gender, including children and the elderly (1-3).

The pathogenesis of MS is complex and multifactorial, ultimately leading to myelin and axonal damage (4). In addition to genetic susceptibility, several environmental factors are thought to contribute to the breakdown of immunological self-tolerance to myelin antigens in the central nervous system (CNS), potentially triggering disease development. Microbial and viral infections, smoking, vitamin D, sun exposure, obesity, and dietary habits may be relevant to its pathogenesis (1, 3, 5). However, the exact role of dietary factors in the pathogenesis of MS remains unclear. Furthermore, the effect of dietary intervention on the inflammatory status and well-being of people with MS has not been associated with any dietary pattern (3, 6).

Dairy products may influence the mechanisms of MS pathology, its development, and disease activity (7, 8). Some studies have reported an increased risk of MS associated with dairy consumption (7-10), while others have suggested a protective effect (11, 12) or no significant association (13, 14). For instance, a retrospective analysis indicated that women who consumed three or more servings of whole milk per day during adolescence had a higher risk of developing MS in adulthood compared to those who consumed less than one serving per day. However, this finding may be confounded by geographic factors, as these women were more likely to reside in northern US states with reduced vitamin D synthesis due to limited sun exposure during the winter months (7).

Conversely, a case-control study conducted in Iran found that individuals who consumed cow's milk during childhood exhibited a reduced risk of developing MS compared to non-consumers (11). Given these conflicting results, we aimed to provide a comprehensive review of the current literature on the association between dairy consumption, particularly cow's milk, and MS risk.

Methods

Design

We carried out a comprehensive search of published studies to locate quantitative data related to the association between dairy products and cow's milk with MS. This review adheres to the guidelines specified in the PRISMA statement, an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses.

Search Strategy

A systematic search was conducted through PubMed, Web of Science, Cochrane Library, and Scopus for peer-reviewed English-language papers published up to 2024, with no restrictions on publication date.

During the database search process, we employed a combination of Medical Subject Headings (MeSH) and specific keywords. We utilized two groups of keywords: Group A) Keywords related to multiple sclerosis, including: " multiple sclerosis “," disseminated sclerosis “, Group B) Keywords related to dairy products, including: " dairy product “, "dairy", " Milk “, “butter”, “Chee”, “cheese”, “yogurt”, “kefir”, “cream”. To conduct the database search, we utilized advanced search functions as follows: first, we combined keywords within each group (A and B) separately using the "OR" operator, creating a comprehensive list of studies relevant to each group. Then, we employed the "AND" operator to merge the results from both groups. This approach allowed us to collect all studies that are relevant to the specific aim of our research. (see supplementary 1 for the entire search strategy). In addition to searching databases, we also searched Google Scholar to include grey literature. Additionally, we carefully examined the references of the included studies to find any other articles that could be potentially relevant.

Inclusion and exclusion criteria

We included studies that described the effects of using dairy and cow dairy products on MS, including randomized controlled trials focusing on mHealth interventions or quasi-experimental, observational (case-control, cohort, cross-sectional), or mixed-method studies. We excluded the review articles, editorials, commentaries, dissertations, conference abstracts, and study protocols.

Review process

Identified records were downloaded to EndNote to identify and remove duplicates. Two reviewers (FA and STA) independently assessed the eligibility of titles and abstracts of identified studies to determine their relevance to the study aims. Studies that did not meet the inclusion criteria were excluded. The same two reviewers then independently screened the full texts of all relevant studies. Any disagreements regarding the inclusion/exclusion of studies were resolved by a third reviewer (PJA). If necessary, the authors of the original articles were contacted for additional information to determine their eligibility based on the inclusion criteria and to assess methodological aspects (Fig. 1).

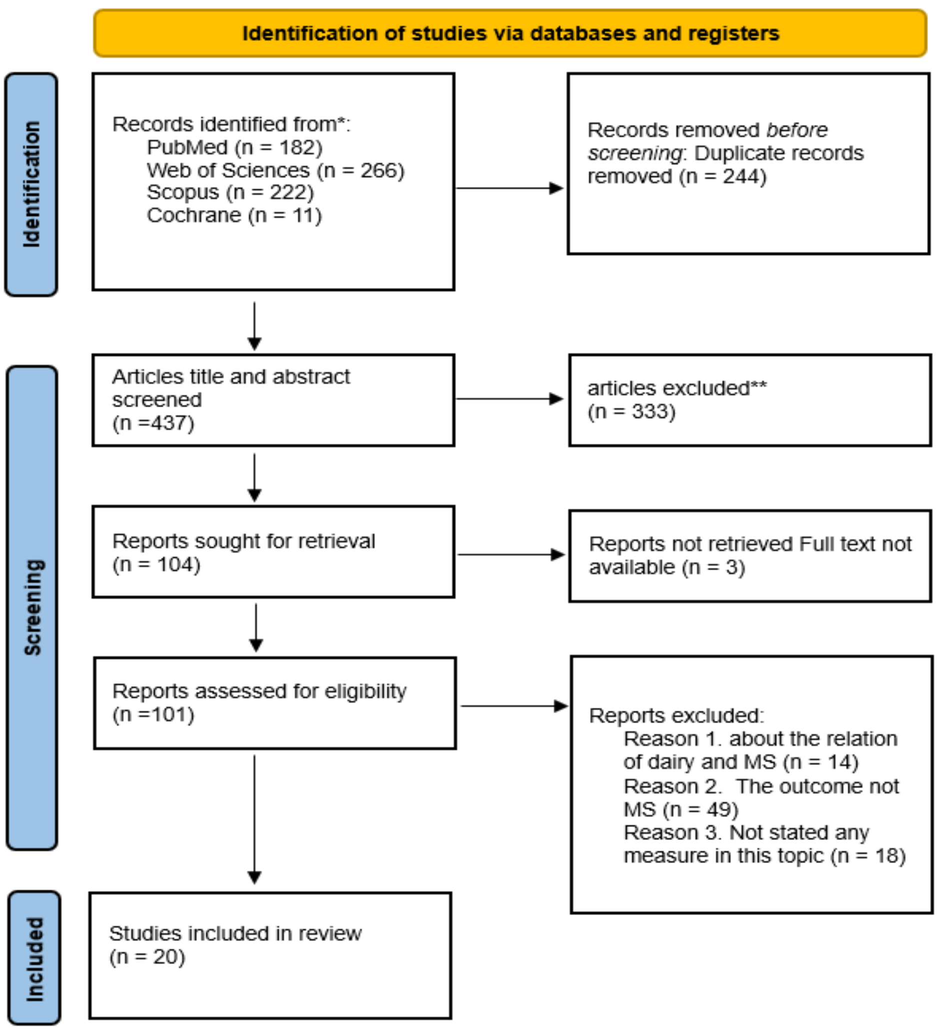

Fig. 1: PRISMA flowchart for selection of articles

Data extraction

Two authors (FA and STA) extracted relevant information from the included studies. Any disagreements that arose during the data extraction process were resolved through consensus discussions with the remaining authors. We utilized a custom-designed Microsoft Excel spreadsheet to collect and organize the extracted data before summarizing and reporting the findings. Extracted data included first author, publication year, country, study design, sample size, study participants, diary product, intervention type, and duration of intervention. We also extracted the main study's outcomes and their effects. This structured approach allowed us to systematically compile the key details from the included studies in preparation for summarizing and presenting the results (Table 1).

Table 1: Summary of the included studies in the systematic review and meta-analysis

Author, Publication Year	Country	Type of diary	sample size	Sex (M/F)	Quality assessment	Measurement Criteria
Abbasi M, 2017 (14)	Iran	Cow milk, Yogurt, Cheese	660 cases 421 controls	(161/919)	7	OR=0.82 (0.34, 1.93)
Zhizhong Zhang, 2021 (15)	Europe	Milk	14802 cases 26703 controls	-	5	OR=0.95 (0.90, 0.99) OR=0.94 (0.90, 0.98)
Papendorf H, 2023 (16)	Australia	Milk, cheese and yoghurt	210 cases	-	6	RR= 1.03 (0.94, 1.12)
Pakpoor J, 2018 (17)	US	Dairy	312 cases 456 controls	(332/436)	7	OR= 0.86 (0.73, 1.02)
Ghazavi Y, 2019 (18)	Iran	Total Dairy	93 cases 94 controls	(33/154)	6	OR=0.98 (0.94, 1.01)
Dieu, D Y R, 2022 (19)	Australia	Total Dairy, Full-fat milk, Yoghurt	272 cases 519 controls	(175/599)	7	OR= 1.00 (0.93, 1.07) OR= 0.99 (0.91, 1.06) OR= 0.89 (0.79, 0.89)
Dehghan M, 2018 (11)	Iran	Milk	120 cases 360 controls	(113/367)	7	OR= 0.33 (0.20, 0.52)
Rezaeimanesh N, 2021 (12)	Iran	Milk,Yogurt,Cheese, Doogh	143 cases 400 controls	(120/423)	7	OR= 0.27 (0.14, 0.53)
Abdollahpour I, 2021 (20)	Iran	Milk,Cheese, Yogurt,Butter	547 cases 1057 controls	(659/945)	7	OR= 0.78 (0.67, 0.91) OR= 0.98 (0.96, 1.00) OR= 0.99 (0.84, 1.11)

Table 1: Continued…

						OR= 0.98 (0.97, 0.99) OR=0.68 (0.55, 0.85)
Noormohammadi M, 2022 (10)	Iran	Cheese	77 cases 148 controls	(58/167)	5	OR= 4.45 (1.70, 11.60)
Simpson- Yap S,2023 (9)	Australia	Dairy	302 cases 282 controls	(120/482)	6	RR= 2.02 (1.25, 3.25)
Marck C H,2021 (21)	Australia	Dairy	1490 cases 1622 controls	(306/1184)	5	OR= 0.03 (0.00, 3.67)
Simpson-Yap S,2022 (22)	Australia	Dairy	403 cases 366 controls	(188/760)	5	OR= 0.63 (0.45, 0.88)
Kirkland H, 2023 (23)	Australia	Dairy	334 cases 346 controls	-	5	OR= 0.99 (0.98, 1.00)
Bagheri - M, 2014 (24)	Iran	Low-fat dairy, High-fat dairy	113 cases 113 controls	-	6	OR= 0.47 (0.27, 0.82) OR= 0.93 (0.45, 1.92)
Shivappa - N, 2016 (25)	Iran	Cow's milk	69 cases 140 controls	(36/171)	5	OR= 1.66 (1.19, 2.31)
Sepcic - J, 1993 (8)	Croatia	Full fat skimmed milk	46 cases 92 controls	-	8	OR= 21.70 (7.12, 66.13)
Pekmezovic - T, 2009 (26)	Serbia	Milk, Cheese, cream, yogurt, butter, ice-cream	110 cases 110 controls	(33/77)	6	OR= 1.10 (0.60, 2.00) OR= 1.00 (0.60, 1.90) OR= 1.20 (0.60, 2.40) OR= 1.10 (0.50, 2.30) OR= 1.70 (1.00, 2.90) OR= 1.80 (1.10, 3.10)
Munger - K.L, 2010 (7)	Boston	Milk, dairy	73938 (379 incidence)	73938 woman	5	RR= 1.11 (0.77, 1.61) RR= 1.14 (0.79, 1.40)
Hadgkiss - E.J, 2015 (13)	Australia	Cow's milk	1417 cases 861 controls	(366/1697)	5	OR= 1.21 (0.95, 1.55)

Quality Assessment

The Newcastle-Ottawa Scale (NOS) checklist was used to assess the quality of articles. This checklist consists of seven items in three sections: 1) study selection, 2) comparability, and 3) outcome. NOS scores of >=7 were considered high quality, scores of 5-6 were considered moderate quality, and a score of <5 was considered low quality. Finally, 20 studies had acceptable quality and were included in the analysis. Two reviewers independently performed the quality assessment of the included studies to ensure reliability and reduce bias. Any disagreements between reviewers were resolved through discussion or consultation with a third reviewer (Table 1).

Data analysis

Stata 14 was used for data analysis. Three categories of heterogeneity, low (≤ 25%), moderate (between 25% and 75%), and high (≥ 75%), were distinguished using I^2 statistics to assess the heterogeneity of study results (27). Both the Egger test and a visual funnel plot were employed to investigate publication bias (28, 29). Odds ratio and Relative risk, the pooled measure of association, were calculated using a random effects model. To ascertain the findings' robustness, a sensitivity analysis was also carried out, in which one study was eliminated at each stage and the outcomes were contrasted with those of the whole analysis.

Results

Overview of search

In the initial search, 681 studies from four databases were identified. Following a review of the title and abstract, 101 studies were determined to be relevant. However, upon a subsequent review of the full text, 81 studies were excluded due to a lack of necessary criteria. We searched Google Scholar to identify relevant papers on our topic. However, no eligible articles were found through this search and screening process. Finally, 20 studies were included in the analysis, with a total sample size of 129548 individuals, consisting of 21899 cases and 107649 controls. Among the studies that reported participants' sex, 82319 were female and 2700 were male. According to the included studies, the age of participants ranged from 18 to 60 years.

Effect size based on OR

The impact of dairy consumption on MS

Dairy consumption was linked to a lower odds of MS (OR; 0.96, 95% CI: 0.93–0.99, *P*-value = 0.001), according to a meta-analysis of 17 studies with 30 parameters that had a total sample size of 54816 (21008 cases and 33808 controls). Fig. 2 illustrates the significant variability among the included studies (I^2 = 81.1%; *P*-value < 0.001).

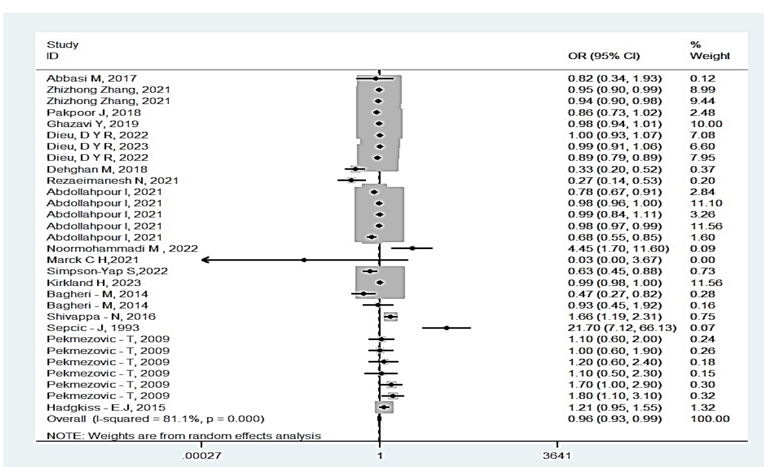

Fig. 2: Impact of dairy consumption on MS based on OR (case-control and cross-sectional study)

The impact of dairy consumption on MS by continent

To investigate the source of heterogeneity, we performed an analysis based on the continent type. The results showed that in Asia, Europe, Oceania and north America continents, impact of Dairy consumption on MS equal (OR; 0.95, 95% CI: 0.90–1, *P*-value = 0.21), (OR; 1.01, 95% CI: 0.85–1.20, *P*-value = 0.32), (OR; 0.97, 95% CI: 0.91–1.03, *P*-value = 0.10) and (OR; 0.86, 95% CI: 0.73–1.02, *P*-value = 0.37) respectively (Fig. 3).

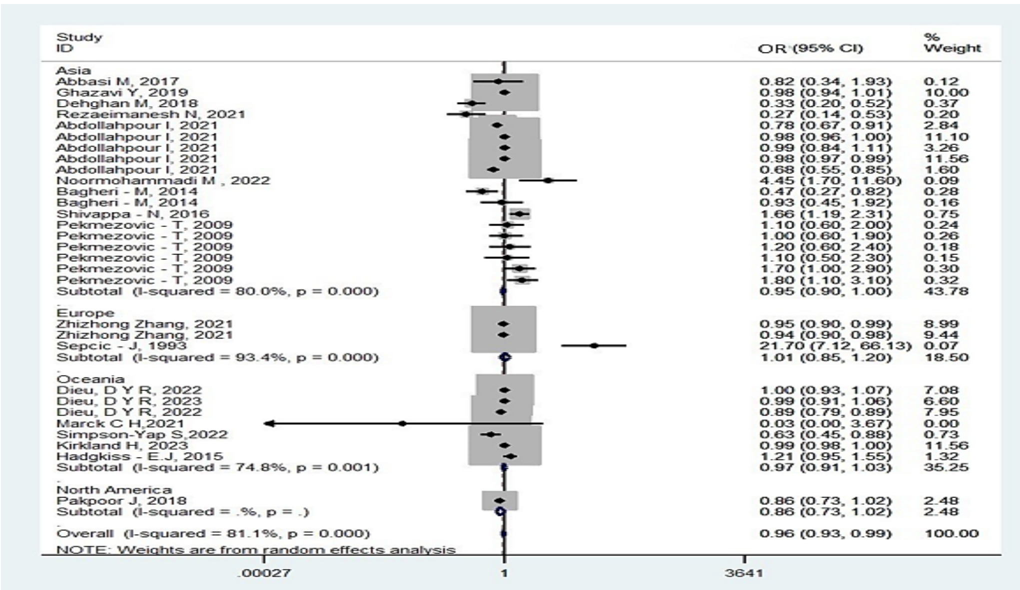

Fig. 3: The impact of dairy consumption on MS by continent based on OR (case-control and cross-sectional study)

Publication bias and Sensitivity analysis

The funnel plot did not show publication bias in the studies that reported the effect of dairy consumption on MS according to the odds ratio (*P*-value>0.05). Also, excluding one study in the sensitivity analysis did not have a significant effect on the results of the effect of dairy consumption on MS according to the odds ratio (Fig. 4).

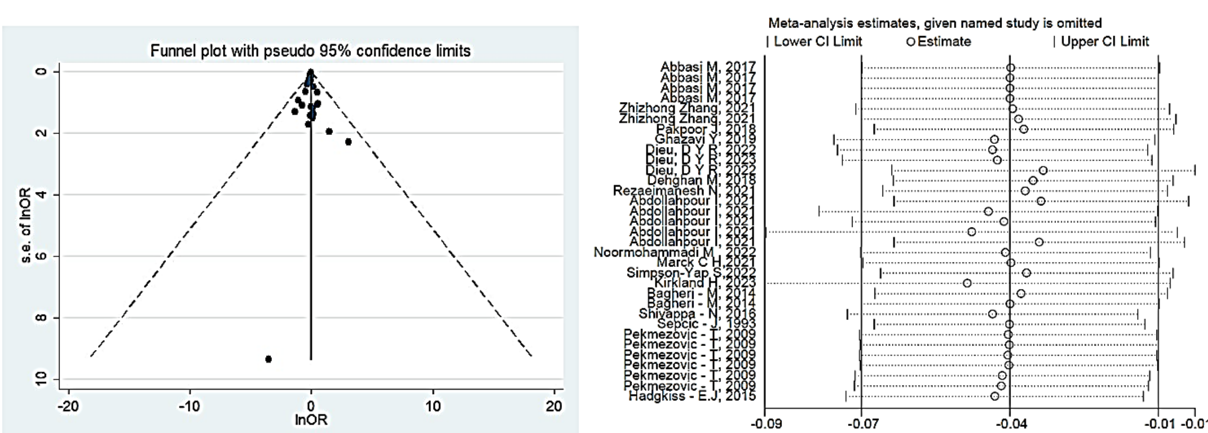

Fig. 4: Funnel plot and Sensitivity analysis for studies the impact of dairy consumption on MS based on OR (case-control and cross-sectional study)

The impact of cow milk consumption on MS

Consuming cow milk was not linked to a higher chance of MS (OR; 0.88, 95% CI: 0.46–1.69, *P*-value = 0.21), according to a meta-analysis of four studies. Fig. 5 illustrates the significant variability across the included studies (I^2 = 90.4%; *P*-value < 0.001).

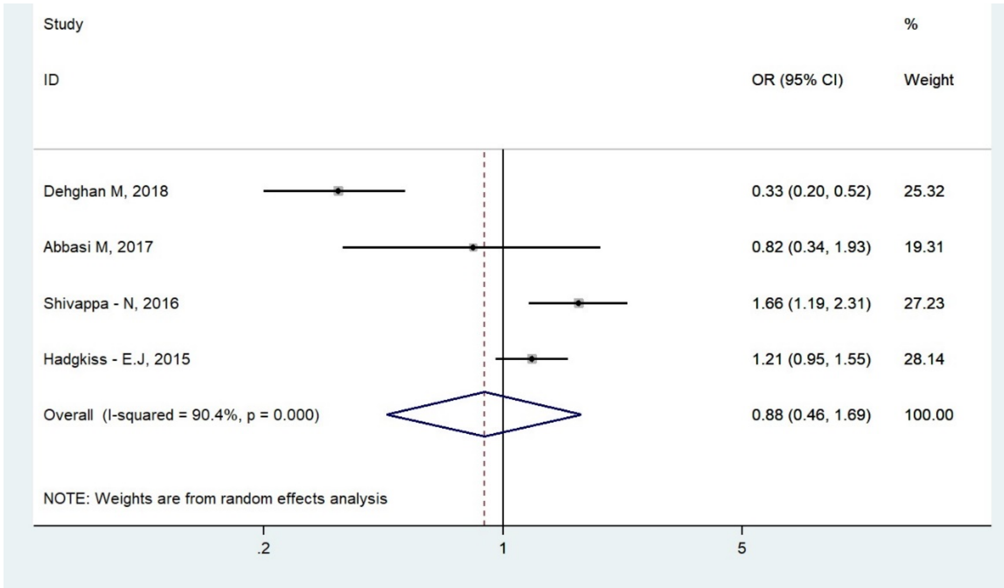

Fig. 5: The impact of cow milk consumption on MS based on OR (case-control and cross-sectional study)

Effect size based on RR

The impact of dairy consumption on MS

A total of four investigations showed that there was no association between dairy consumption and MS risk (RR; 1.18, 95% CI: 0.95–1.47, *P*-value = 0.41). There was a significant amount of heterogeneity across the selected studies (I^2 = 61.1%; *P*-value = 0.052) (Fig. 6).

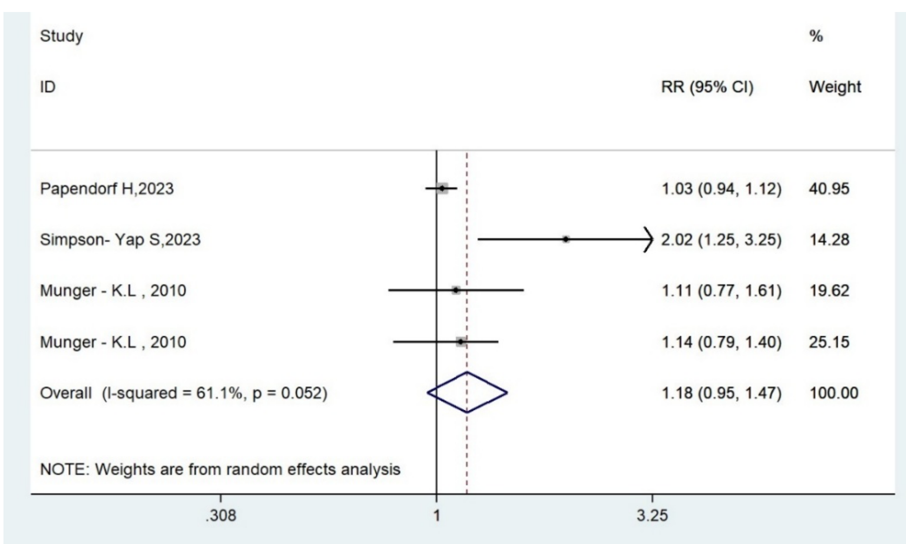

Fig. 6: The impact of dairy consumption on MS based on RR (cohort study)

The impact of dairy consumption on MS by continent

The findings indicated that the influence of dairy consumption on MS was equivalent across the continents of Oceania and North America (RR; 1.38, 95% CI: 0.72–2.66, *P*-value = 0.56 and (RR; 1.13, 95% CI: 0.90–1.41, *P*-value = 0.65), respectively (Fig. 7).

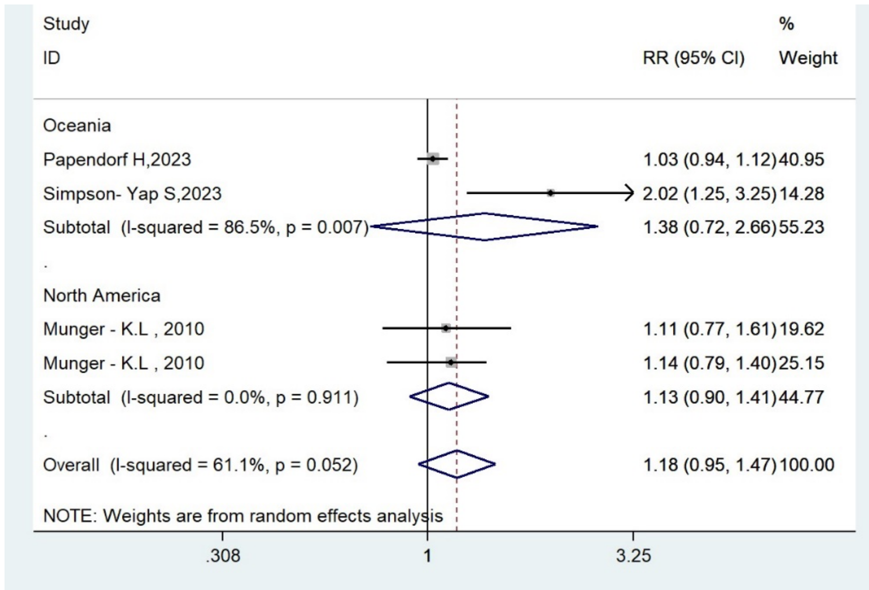

Fig. 7: The impact of dairy consumption on MS by continent based on RR (cohort study)

Publication bias and Sensitivity analysis

According to the relative risk, the studies reporting the impact of dairy consumption on MS did not exhibit publication bias, as indicated by the funnel plot (*P*-value>0.05). The results of the sensitivity analysis regarding the effect of dairy consumption on MS did not significantly change when one study was excluded (Fig. 8).

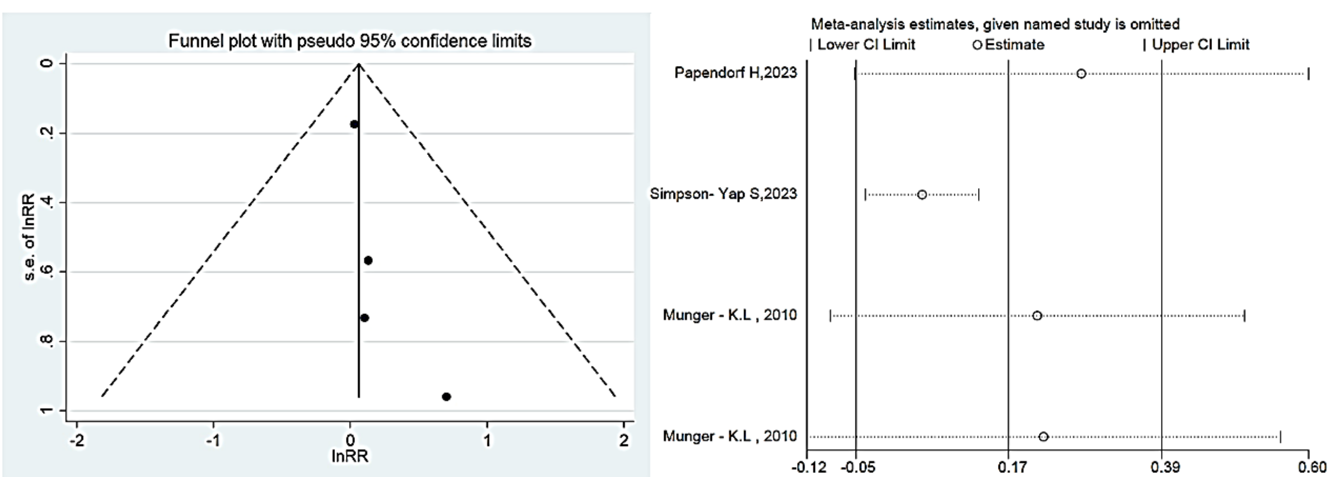

Fig. 8: sensitivity analysis and funnel plot for studies on the effect of dairy consumption on MS based on RR (cohort study)

Discussion

This systematic review and meta-analysis investigated the association between dairy consumption and the risk of developing MS. The findings from case-control and cross-sectional studies suggested a statistically significant association between dairy consumption and a slightly reduced risk of MS. However, the results from four cohort studies showed no significant association between dairy intake and MS risk. Additionally, a meta-analysis of four studies found no evidence linking cow's milk consumption to an increased risk of developing MS.

In this systematic review, several studies demonstrated a protective association between dairy consumption and the risk of developing MS. Higher dairy intake was significantly associated with a lower risk of primary progressive multiple sclerosis (PPMS), with a dose-dependent effect observed (12). Similarly, Abdollahpour et al. highlighted the protective role of nutritional factors during adolescence in the onset of MS, noting that increased consumption of cheese, yogurt, and butter was associated with a reduced risk of MS (20). Furthermore, the risk of MS in offspring may decrease when pregnant women consume 2–3 glasses of milk per day (30). These findings prompt further consideration of the biological mechanisms through which dairy intake might influence MS pathogenesis. From an immunological perspective, components such as vitamin D and specific fatty acids found in dairy products are known to modulate inflammatory responses and may contribute to regulating immune function in MS (1, 31). Additionally, the potential anti-inflammatory properties of dairy may help reduce the neuroinflammation central to MS progression (32).

Some studies have reported an association between dairy consumption and an increased risk of MS. For example, Simpson et al. examined the relationship between diet quality and disability progression in individuals with MS over 7.5 years, finding that dairy consumption was linked to a higher risk of disability progression in MS patients (9). Another study investigated the impact of vitamin D intake during adolescence on the risk of developing MS in adulthood. Although higher vitamin D intake from multivitamins was associated with a non-significant reduction in MS risk, whole milk consumption, which is a significant source of dietary vitamin D, was linked to an increased risk of MS (7). Additionally, consumption of all types of cheese was associated with increased odds of developing MS (10). The mechanisms by which dairy products might influence clinical outcomes in MS remain unclear; however, some evidence suggests that dairy may affect autoimmune responses to myelin antigens (33) or involve molecular mimicry (34).

We also conducted a separate analysis to assess the effect of cow's milk consumption on MS risk, which demonstrated that cow's milk was not associated with an increased likelihood of developing MS. Cow's milk consumption was linked to a reduced risk of MS (11, 15). However, in contrast, Hadgkiss et al. found a strong positive correlation between cow's milk intake and MS prevalence (13).

These discrepancies may be attributed to differences in study design, population characteristics, and patterns of dairy consumption. For example, the geographic and demographic diversity among the studies included in our meta-analysis could reflect varied adaptations to dietary exposures. Addressing these differences requires an understanding of the multifactorial nature of MS, in which genetic susceptibility interacts with environmental and dietary factors, potentially influencing both disease onset and progression in ways that remain incompletely understood.

One proposed biological mechanism is molecular mimicry, the structural similarity between myelin autoantigens and certain dietary proteins, which may trigger autoimmune responses and myelin degradation in MS. In particular, proteins from the milk fat globule membrane of cow's milk have been implicated. The main candidate is butyrophilin, a protein that shares structural similarities with the myelin oligodendrocyte glycoprotein

(MOG). Butyrophilin has been shown to induce antibody cross-reactivity with MOG (17, 18) and stimulate T-cell responses that promote central nervous system inflammation in animal models.

Our analysis revealed notable geographic variations in the impact of dairy consumption on MS risk. For instance, the protective effect was somewhat stronger in North America (OR: 0.86, 95% CI: 0.73–1.02), whereas it was less pronounced in Europe and Asia. These regional differences may be influenced by several factors, including genetic diversity among populations, which can affect both susceptibility to MS and dietary responses. Additionally, environmental factors such as sunlight exposure and the resulting vitamin D synthesis vary significantly with latitude and are known to influence immune function and potentially MS risk. Dietary habits, including the types and processing methods of dairy products consumed, also differ across regions and may impact the bioavailability of nutrients such as vitamin D and omega-3 fatty acids, which are known to modulate inflammatory processes associated with MS (35). Understanding these regional variations is essential for developing tailored dietary recommendations that consider local eating habits and environmental conditions.

Limitations

Although it was based on a systematic review and meta-analysis, the included studies varied considerably in terms of methodology, sample size, population characteristics, and definitions of exposure and outcome. Most of the available data came from observational studies, which may be affected by residual confounding and are not sufficient to determine causal relationships. Additionally, geographic and cultural diversity among study populations may have influenced the results, as variations in genetics, lifestyle, and baseline nutrient intake (such as vitamin D) could confound the association between dairy consumption and MS risk. Furthermore, the possibility of publication bias cannot be ruled out, as studies with significant findings are more likely to be published than those with null results. In some studies, dietary intake was self-reported, which could introduce recall bias and affect the accuracy of exposure assessment.

Conclusion

Although a larger number of studies suggested a potential protective role of dairy consumption in reducing the risk of MS, the observed associations were generally weak and close to the threshold of statistical significance. These conflicting findings highlight the complexity of the relationship and indicate that the role of dairy in MS pathogenesis remains uncertain. Therefore, more rigorous, well-controlled longitudinal studies that account for genetic, environmental, geographic, and dietary factors are needed to clarify whether dairy products contribute to MS risk or offer a protective effect.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of Interests

The authors declare no competing interests.

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