



The association between diabetes and migraine: a systematic review and meta-analysis

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Introduction

Diabetes and migraine are prevalent conditions that can significantly impact quality of life. Existing review suggests a possible connection between the two, though findings have varied.

Objective

This review aims to assess the prevalence and association between diabetes and migraine through a meta-analysis.

Methods

This approach was applied through searches in Scopus, WOS, PubMed, and Google Scholar. A PRISMA checklist was followed. The quality assessment was checked. The included studies investigated either migraine in diabetes patients or diabetes in migraine patients, with no restriction on age groups or timeframes. The meta-analyses were performed using Jamovi 2.3.28 and SPSS Version 28.

Results

Two groups of studies were analyzed. Group 1 (n= 8) assessed migraine prevalence in patients with diabetes. The overall migraine prevalence was 12% (95% CI: 6%- 17%). Type 2 diabetes had a migraine prevalence of 8% (95% CI: 1%- 15%), significantly affected by study demographics and duration of diabetes. Type 1 diabetes showed a lower migraine prevalence (1%). Odds ratios indicated a non-significant decrease in migraine prevalence among diabetes patients overall and a significant decrease for type 1 diabetes.

Group 2 (n= 17) examined diabetes prevalence among migraine patients. The overall odds ratio for diabetes prevalence was 0.86 (p< 0.05), indicating a significant decrease. Specific analyses showed a nearly significant reduction in diabetes prevalence for migraine with aura (OR= 0.78, p = 0.05) and no significant difference for migraine without aura (OR≈ 1, p = 0.95).

Conclusions

The results suggest a generally lower prevalence of migraine among diabetes patients, particularly with type 1 diabetes, while diabetes prevalence is lower among migraine patients, especially those with aura.

Keywords:
Diabetes Mellitus
Migraine
Migraine with aura
Migraine without aura

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Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder that affects millions globally and serves as a major risk factor for cardiovascular diseases, neuropathy, and various other complications. There are two main types: type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM). T1DM usually starts in childhood but can occur in adults, and T2DM is more common in middle-aged and older individuals (1).

Migraine is a neurological disorder characterized by recurrent headaches. It often coexists with various comorbidities, including depression, anxiety, stroke, irritable bowel syndrome, epilepsy, and hypertension (2). It is more frequently reported in females and particularly around age 35 years (3).

Both DM and migraine significantly impact individual health and quality of life. Understanding the relationship between these two conditions is crucial for clinical management and preventive strategies. While prior review (4) have suggested a possible link between these two conditions, the evidence remains inconsistent and fragmented.

This meta-analysis aims to clarify the prevalence and associations of migraine in patients with diabetes, as well as the reverse relationship. Specifically, it explores how migraine prevalence varies across different types of diabetes, such as type 1 and type 2, and examines whether diabetes prevalence differs between patients with migraine with aura (MA) and those with migraine without aura (MO).

Methods

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Data Sources and Searches

On July 15, 2024, a comprehensive search was conducted across Scopus, Medline, PubMed, and Google Scholar using the search terms “diabetes” and “migraine.”

Inclusion and exclusion criteria

The studies included in this review met the following criteria: studies investigated either migraine in diabetes patients or diabetes in migraine patients, with no restriction on age groups or timeframes. Additionally, each study reported the number of patients in each category. The exclusion criteria consisted of studies not published in English, studies with restricted full text availability, and studies that did not provide clear patient numbers for each category.

Study Selection

The eligibility of search results was assessed in two stages: initial screening of titles and abstracts, followed by a full-text review.

Data extraction and Quality Assessment

Data extracted included: the first author name, year of publication, country of study, journal of publication, mean age, sex (female%), type of DM, study design, methods of identification of migraine and DM, total number of patients with diabetes, number of patients with diabetes experiencing migraine, total number of patients without diabetes, number of non-diabetics experiencing migraine, total number of patients with migraine and without migraines, and the number of patients with migraine and without migraines who developed diabetes.

The quality assessment was checked by the Newcastle-Ottawa Quality Assessment Scale (NOS) (Table 1) (5). A rating of seven stars or higher was considered high quality, while ratings below seven stars were considered poor quality.



Data synthesis and analysis

Proportional meta-analysis was performed using Jamovi 2.3.28, while meta-analysis of odds ratios was conducted using SPSS, Version 28.

The initial search identified 882 studies from the Web of Science, 1,036 studies from Scopus, and 1,242 studies from PubMed. A total of 693 duplicates were removed, and 237 studies were excluded for not being in English. 2,236 studies underwent title and abstract screening. Of these, the full texts of 1,267 studies were unavailable, and 448 studies were deemed irrelevant. After full text screening, 492 studies were excluded for irrelevance, and 29 studies were assessed for eligibility. The final analysis was applied to 25 included studies (Figure 1).

Results

Literature search

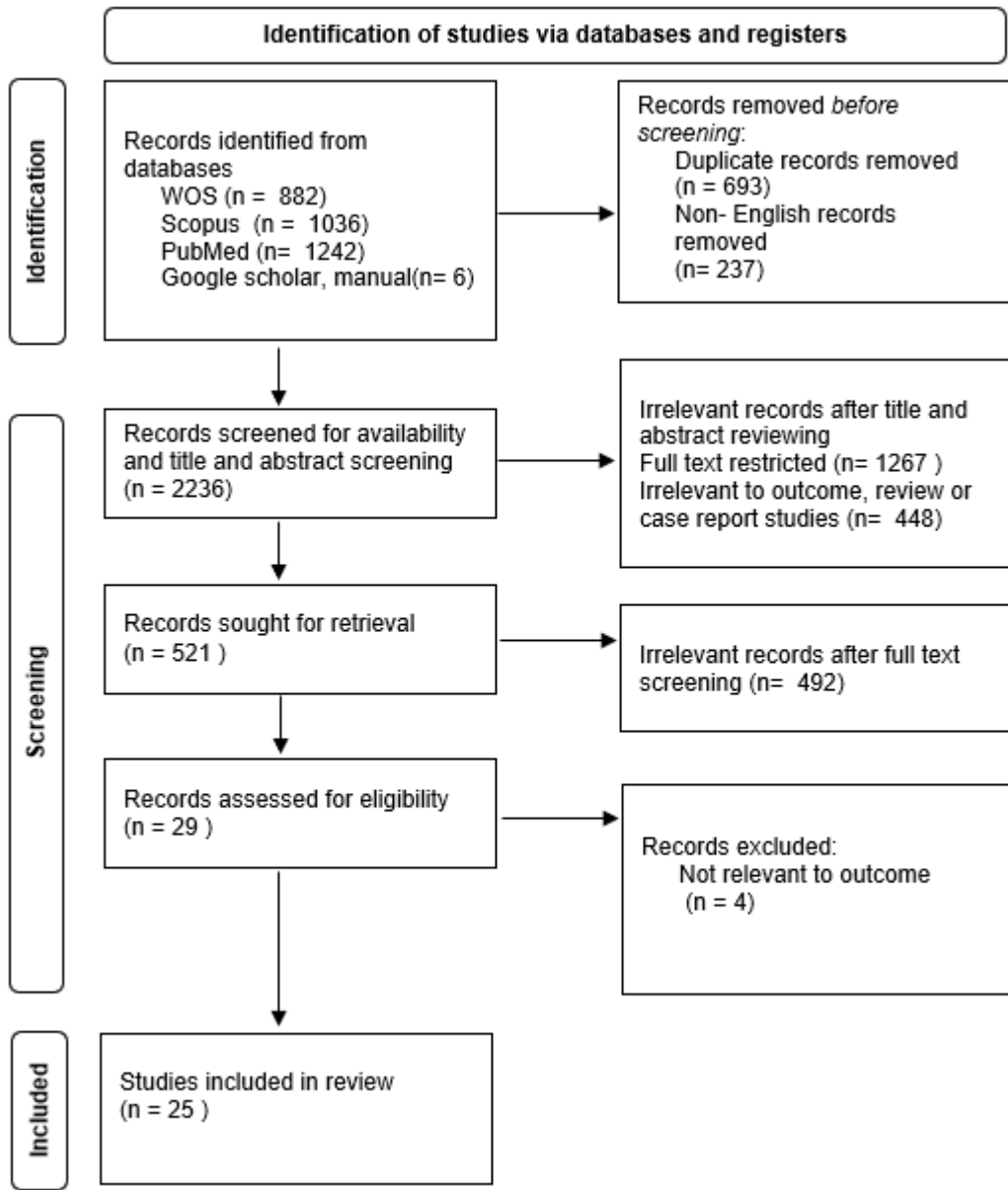


Figure 1. PRISMA Flow Diagram



Characteristics of the included studies

A total of 25 studies (6–30) were included in the final analysis (Tables supplementary 2 and 3). The majority of studies were conducted in the USA and Norway, with five studies from each country. The studies were published between 2007 and 2024, with the Cephalalgia journal featuring the highest number of publications (6 studies).

Group 1: studies screening the prevalence of migraine in patients with diabetes and non-diabetics (Table supplementary 4)

Out of the 25 studies, eight (6–13) (Group 1) focused on the prevalence of migraine in patients with diabetes and non-diabetics:

- Study 1 and Study 6 examined patients with T2DM only.
- Studies 2 and 3 investigate diabetes broadly.
- Studies 4 and 8 covered both type 1 and type 2 diabetes, as well as diabetes in general.
- Studies 5 and 7 separately analyzed type 1 and type 2 diabetes.
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Group 2: studies screening the prevalence of DM in patients with migraine and without migraines

Seventeen studies (14–30) (Group 2) assessed the prevalence of diabetes in patients with migraine and without migraines:

- Study 8 was the only prospective study, focusing on the development of type 2 diabetes in patients with migraine and without migraines.
- Studies 4, 5, 13, 14, and 16 screened for diabetes as a comorbidity, whereas the other studies focused on other conditions and only noted diabetes as part of the medical history.
- Studies 5, 8, and 15 specifically focused on women.
- Studies 3, 4, 6, and 11 distinguished between MA and MO, whereas study 5 focused solely on MA.
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Statistical analysis of Group 1 studies

Prevalence of migraine in patients with any type of DM

In studies that examined diabetes more broadly (studies 2, 3, 4, and 8), the overall prevalence of migraine among patients with diabetes was 12% (95% CI: 6%-17%) (Table 1). The prevalence varied significantly across studies, with the highest percentage observed in study 3c at 21%. Notably, study 3c focused exclusively on females. Excluding study 3c, the overall prevalence of migraine decreased substantially to 9% (95% CI: 5%-13%).

Table 1. Studies that examined the prevalence of migraine in patients with any type of diabetes mellitus

Study ID	Diabetes type	Mean age	%Female	Total number of diabetics	Number of migraine patients	%
study2	any type	15-70	50.4%	2095	185	0.09 [0.08, 0.10]
study3b	any type male	> 40	0%	1598	118	0.07 [0.06, 0.09]
study3c	any type female	> 40	100%	1843	394	0.21 [0.20, 0.23]
study4c	any type	66.3 (11.3)	49.4%	1342	202	0.15 [0.13, 0.17]
study8a	any type	64.7 (14.2)	54.4%	1499	85	0.06 [0.04, 0.07]
						Total 0.12 [0.06, 0.17]



Comparison of migraine prevalence in patients with any type of diabetes versus non-diabetics

In studies 2, 3, 4, and 8, the overall odds ratio for migraine prevalence in patients with any type of diabetes compared to non-diabetics was 0.86 ($p= 0.45$) (Supplementary Figures 1 and 2). This indicates a non-significant decrease in migraine prevalence among patients with diabetes when compared to non-diabetics. Excluding study 3c, the odds ratio decreased to 0.79, but the result remained non-significant ($p= 0.3$) (Supplementary Figures 3 and 4).

Prevalence of migraine in patients with T2DM

For studies examining type 2 diabetes (studies 1, 4b, 5b, 6, 7d, 7f, and 8c), the overall prevalence of migraine in patients with type 2 diabetes was 8%, 95% CI (1%- 15%) (Table 2). The prevalence varied significantly across studies, with the highest percentage observed in study 6, where participants were relatively young (ages 30-42) and 57.8% had diabetes for less than 5 years. Additionally, this study had the highest percentage of female participants (62.6%). Excluding study 6, the overall prevalence of migraine was substantially lower, at 5%, 95% CI (1%- 10%).

Table 2. Studies that examined the prevalence of migraine in patients with type 2 diabetes mellitus

Study ID	Diabetes type	Mean age	Female %	Total number of diabetics	Number of migraine patients	%
Study 1	type 2	62.8 (8.85)	%54.24	1722	125	0.07 [0.06, 0.08]
Study 4b	type 2	67.1 (10.7)	49.2%	1107	173	0.16 [0.13, 0.18]
Study 5b	type 2	52.7 (13.9)	%42.5	93600	930	0.01 [0.01, 0.01]
Study 6	type 2	30-42	62.6%	147	41	0.28 [0.21, 0.35]
Study 7d	type 2	0-50	Not identified	13755	479	0.03 [0.03, 0.04]
Study 7f	type 2	50-more than 70	Not identified	78179	644	0.01 [0.01, 0.01]
Study 8c	type 2	67.1 (10.9)	49.1%	870	40	0.05 [0.03, 0.06]
						Total 0.08 [0.01, 0.15]



Comparison of migraine prevalence in patients with T2DM versus non-diabetics

In studies 1, 4b, 5b, 6, 7d, 7f, and 8c, the overall odds ratio for migraine prevalence in patients with type 2 diabetes compared to non-diabetics was 0.64 (p= 0.12) (Supplementary Figures 5 and 6) when using a random-effects model to account for high heterogeneity. This suggests a non-significant decrease in migraine prevalence among patients with type 2 diabetes compared to non-diabetics. The highest odds ratio was observed in study 7d, which included participants aged 0-50, possibly indicating a shorter duration of diabetes. Excluding study 7d, the odds ratio decreased to 0.52, with a significant p- value of 0.01

(Supplementary Figures 7 and 8). Furthermore, excluding both study 7d and study 6 (which included younger participants with a relatively short duration of diabetes and a higher proportion of female participants), the odds ratio dropped further to 0.45, with a highly significant p- value ≤ 0.001 (Supplementary Figures 9 and 10).

Prevalence of migraine in patients with T1DM

Studies 4a, 5a, 7g, 7h, and 8b specifically examined migraine prevalence in patients with type 1 diabetes. The overall prevalence of migraine in these patients was found to be 1% (Table 3), which is notably lower compared to the prevalence in patients with any type of diabetes (12%) and those with type 2 diabetes (8%).

Table 3. Studies that examined the prevalence of migraine in patients with type 1 diabetes mellitus

Study ID	Diabetes type	Mean age	Female %	Total number of diabetics	Number of migraine patients	%
Study 4a	type 1	56.9 (12.6)	44.4%	81	10	0.12 [0.05, 0.20]
Study 5a	type 1	27.7 (21.9)	40.3%	7883	109	0.01 [0.01, 0.02]
Study 7g	receiving insulin only	0- 50	Not identified	15427	219	0.01 [0.01, 0.02]
Study 7h	receiving insulin only	50-70	Not identified	17288	118	0.01 [0.01, 0.01]
Study 8b	type 1	61.1 (12.0)	43%	179	7	0.04 [0.01, 0.07]
						Total 0.01 [0.01, 0.02]



Comparison of migraine prevalence in patients with T1DM versus non-diabetics

In studies 4a, 5a, 7g, 7h, and 8b, the overall odds ratio for migraine prevalence in patients with type 1 diabetes compared to non-diabetics was 0.44 ($p \leq 0.001$) (Supplementary Figures 11 and 12) when using a random-effects model to address high heterogeneity. This indicates a significant decrease in migraine prevalence among patients with type 1 diabetes compared to non-diabetics, even when including study 7g, which focused on a younger age group. This contrasts with type 2 diabetes, where a significant decrease in migraine prevalence is often associated with a longer duration of diabetes in older age patients.

So, when examining diabetes more broadly, the prevalence of migraine compared to non-diabetics is lower and non-significant. For type 2 diabetes, considering the duration

of the disease shows a significantly lower prevalence of migraine compared to non-diabetics. In contrast, type 1 diabetes is strongly associated with a significant decrease in migraine prevalence compared to non-diabetics.

Studies examining migraine prevalence in type 1 and type 2 diabetes

Studies 4, 5, 7, and 8 examined migraine prevalence in both type 1 and type 2 diabetes. The prevalence of migraine was higher in patients with type 2 diabetes, as observed in studies 4, 7 (age 0-50), and 8. In study 7, for participants aged 50 and older, the prevalence of migraine was nearly equal for both types of diabetes, likely due to the longer duration of diabetes in this age group. Additionally, study 5 reported a lower and nearly equal prevalence of migraine for both types, which may be attributed to the lower proportion of female participants (Table 4).

Table 4. Studies that examined the prevalence of migraine in patients with type1 and type 2 diabetes mellitus

Study ID	Diabetes type	Mean age	Female %	Total number of diabetics	Number of migraine patients	%
Study 4a	type 1	56.9 (12.6)	44.4%	81	10	0.12 [0.05, 0.20]
Study 4b	type 2	67.1 (10.7)	49.2%	1107	173	0.16 [0.13, 0.18]
Study 5a	type 1	27.7 (21.9)	40.3%	7883	109	0.01 [0.01, 0.02]
Study 5b	type 2	52.7 (13.9)	42.5%	93600	930	0.01 [0.01, 0.01]
Study 7d	type 2	0-50	Not identified	13755	479	0.03 [0.03, 0.04]
Study 7f	type 2	50-more than 70	Not identified	78179	644	0.01 [0.01, 0.01]
Study 7g	receiving insulin only	0- 50	Not identified	15427	219	0.01 [0.01, 0.02]
Study 7h	receiving insulin only	50-more than 70	Not identified	17288	118	0.01 [0.01, 0.02]
Study 8b	type 1	61.1 (12.0)	43%	179	7	0.04 [0.01, 0.07]
Study 8c	type 2	67.1 (10.9)	49.1%	870	40	0.05 [0.03, 0.06]



Statistical analysis of Group 2 studies

Studies screening for diabetes in migraine patients compared to those without migraine. In the all seventeen studies that assessed the prevalence of diabetes in migraine patients compared to those without migraine (Table 5), the overall odds ratio was 0.86 ($p < 0.05$) (Supplementary Figures 13 and 14). This indicates a significant decrease in the prevalence of diabetes among migraine patients relative to those without migraine.

Table 5. Group 2 studies that examined the prevalence of diabetes in patients with migraine and those without migraine

Study ID	Diabetes type	Total number of migraine patients	Number of diabetics	total no. of patients without migraine	Number of non-migraine patients with diabetes
Study 1	any type	212836	23679	5863348	680214
Study 2	any type	87809	9836	2628753	303486
Study 3a migraine with aura	any type	168	35	634	148
Study 3b migraine without aura	any type	416	100	634	148
Study 4a migraine with aura	any type	431	6	496	9
Study 4b migraine without aura	any type	826	17	496	9
Study 5 women migraine with aura	any type	1435	24	26423	658
Study 6a migraine with aura	any type	472	70	3294	702
Study 6b migraine without aura	any type	883	166	3294	702
Study 7	any type	983065	169775	55516723	14195626
Study 8	type 2	7839	202	49199	1569
Study 9	type 1 or 2	181	10	1315	108
Study 10	any type	1516	121	9405	953
study11a migraine with aura	any type	79	20	556	115
study11b migraine without aura	any type	116	30	556	115
study12	any type	303	63	5287	1190
study13	any type	72	4	72	3
study14	any type	948	42	3790	199
study15	any type	6857	501	24513	1841
study16	any type	7777	164	23383	518
study17	any type	178	27	923	175

Studies examining MA

For studies 3a, 4a, 5, 6a, and 11a, the overall odds ratio was 0.78 with a p-value of 0.05 (Figure 2). This suggests a nearly significant reduction in the prevalence of diabetes in patients with MA compared to those without migraine.

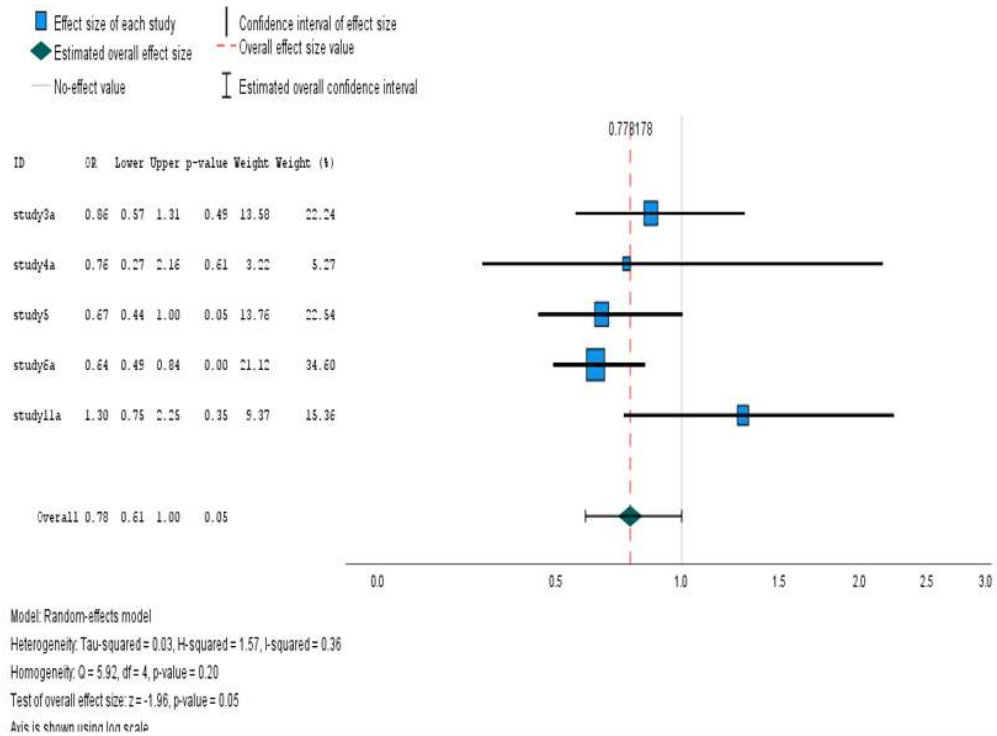


Figure 2. Forest plot illustrating the overall odds ratio for diabetes in patients with migraine with aura.

Studies examining MO

In studies 3b, 4b, 6b, and 11b, the overall odds ratio was close to 1, with a p-value of 0.95 (Figure 3). This indicates no significant difference in the prevalence of diabetes in patients with MO compared to those without migraine.

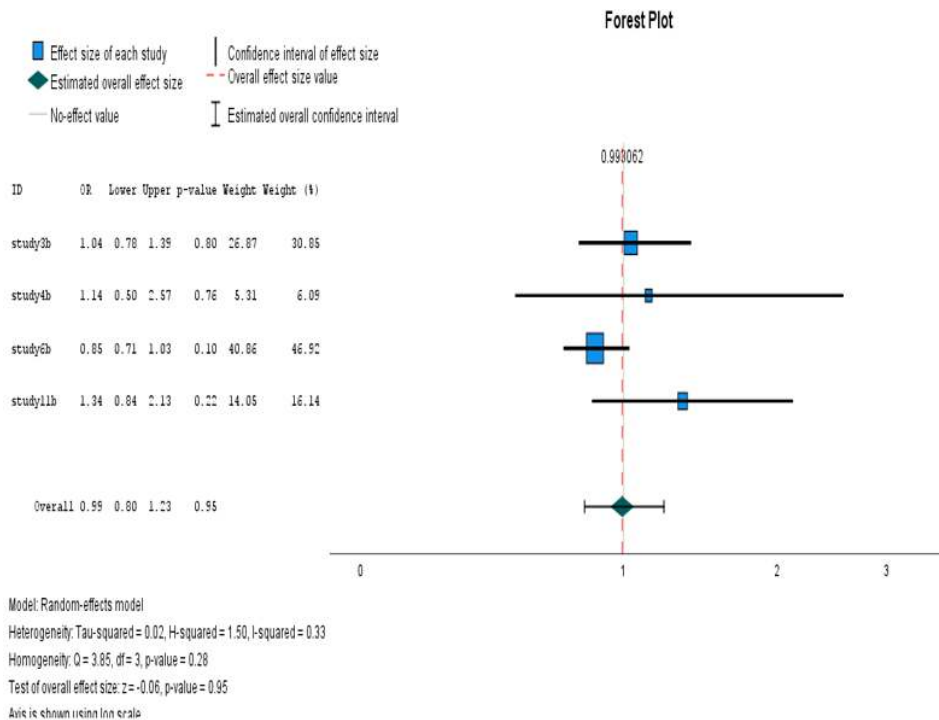


Figure 3. Forest plot illustrating the overall odds ratio for diabetes in patients with migraine without aura



When examining studies that did not specify the type of migraine or focused only on migraine with aura, the prevalence of diabetes mellitus was lower and significant. Conversely, studies focusing solely on migraine without aura showed no significant difference in diabetes prevalence. The studies that did not specify the type of migraine exhibited high heterogeneity ($I^2 = 98\%$, $p < 0.05$), whereas studies specifying MA and those focusing on MO had low non-significant heterogeneity ($I^2 = 36\%$ and 33% , respectively, with p -values of 0.2 and 0.28).

For study 8, a prospective study examining the development of type 2 diabetes in women with active migraine, it was concluded that women with active migraine have a significant lower risk of developing type 2 diabetes ($RR = 0.81$, $p = 0.004$). Additionally, there was a decrease in the prevalence of active migraine before a diabetes diagnosis.

Discussions

This systematic meta-analysis synthesizes findings from twenty-five studies to investigate the association between diabetes and migraine. The studies were categorized into two groups: Group 1 ($n = 8$), which examined migraine in patients with diabetes, and Group 2 ($n = 17$), which explored the prevalence of diabetes in patients with migraine.

For Group 1, studies 2, 3b, 3c, 4c, and 8a included 8377 patients with any type of diabetes, of whom 984 had migraines, resulting in an overall migraine prevalence of 12% (95% CI: 6%- 17%). Studies 1, 4b, 5b, 6, 7d, 7f, and 8c included 189380 patients with type 2 diabetes, with 2432 experiencing migraines, yielding a prevalence of 8% (95% CI: 1%- 15%). Studies 4a, 5a, 7g, 7h, and 8b included 40858 patients with type 1 diabetes, among whom 463 had migraines, resulting in a prevalence of 1% (95% CI: 1%- 2%).

The overall odds ratio for migraine prevalence in patients with any type of diabetes and type 2 diabetes compared to non-diabetics was 0.86 ($p = 0.45$) and 0.64 ($p = 0.12$), indicating a non-significant decrease. In patients with type 1 diabetes was 0.44 ($p < 0.01$), indicating a significant decrease. When considering the duration of diabetes in patients with type 2 diabetes, the overall odds ratio was 0.45 ($p < 0.01$), also indicating a significant decrease. This aligns with previous research suggesting a potential inverse relationship between migraine and diabetes, though the underlying mechanisms remain unclear (6).

For Group 2 studies, the overall odds ratio for diabetes prevalence in patients with migraine was 0.86 ($p < 0.05$), indicating a significant decrease. This finding is consistent with a prospective study (21) indicating a reduced risk of type 2 diabetes among women with active migraines. In studies focusing exclusively on MA (studies 3a, 4a, 5, 6a,

and 11a), the odds ratio was 0.78 ($p = 0.05$), indicating a nearly significant decrease. In contrast, studies focusing on MO (studies 3b, 4b, 6b, and 11b), showed an odds ratio close to 1 ($p = 0.95$), indicating no significant difference. This highlights the need for further investigation into how different migraine types influence diabetes risk.

The results suggest a generally lower prevalence of migraine among diabetes patients, particularly with type 1 diabetes, while diabetes prevalence is lower among migraine patients, especially those with aura.

Despite the insights gained from the current review, there are notable limitations. One key limitation is that this systematic review was conducted by a single author, which may introduce some degree of bias in the selection and interpretation of the data. However, I reviewed and carefully checked the results multiple times to mitigate this limitation and ensure the reliability of the findings. Additionally, the high heterogeneity among the studies, particularly within Group 1, poses another challenge. This variability could be from several factors including the lack of focus on the duration of diabetes, especially in patients with type 2 diabetes. The present study indicates that the duration of type 2 diabetes may impact the prevalence of migraine, particularly in studies that specified the duration or anticipated that participants had diabetes for an extended period. This suggests that the duration of diabetes is a more critical factor than age, a consideration that has often been overlooked in many studies on this topic.

Interestingly, while younger individuals may be more likely to experience migraines regardless of their diabetes status, type 1 diabetes, which typically occurs in childhood, showed a significantly lower prevalence of migraines. This suggests that age is not a critical factor in this context.

Furthermore, the heterogeneity observed in Groups 1 and 2 could be attributed to not specifying the type of migraine, an important aspect that future research should address to better understand the relationship between migraine and diabetes. The study designs employed in these studies varied, with some focusing on different populations or methodologies, which could further contribute to the observed variability in results.

Future studies should prioritize examining the duration of type 2 diabetes. Furthermore, biological studies are needed to investigate whether there are differences in the mechanisms underlying migraine development among type 1, type 2, and other types of diabetes. It is essential to explore whether diabetes itself reduces the likelihood of developing migraines or if migraines have a protective effect against the onset of type 2 diabetes, as suggested by a prospective study (study 8, Group 2).

In summary, future tailored studies should consider not only



age but also factors such as diabetes type, duration of type 2 diabetes, female sex, and the types of migraines in their analyses.

Conclusions

The results suggest a generally lower prevalence of migraine among diabetes patients, particularly with type 1 diabetes, while diabetes prevalence is lower among migraine patients, especially those with aura.

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