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Investigating the association between diabetes and carpal tunnel syndrome: A systematic review and meta-analysis approach

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Abstract

Introduction

In recent years, several studies have reported on the relationship between diabetes and carpal tunnel syndrome (CTS). However, due to their contradictory results, a systematic review and meta-analysis were conducted to investigate this subject.

Methods

This study is a systematic review and meta-analysis of studies published in ISI Web of Science, Scopus, PubMed, Cochrane, Google Scholar, and Embase databases. Heterogeneity in the studies included in the meta-analysis was evaluated using statistical tests such as the Chi-square test, I^2, and forest plots. Publication bias was assessed using Begg's and Egger's tests.

Results

This investigation analyzed data from 42 studies conducted between 1985 and 2022, with a total of 3,377,816 participants. The meta-analysis demonstrated that the odds ratio (OR) of CTS in participants with a history of diabetes compared to those without was 1.90 (95% CI: 1.64–2.21; P-value < 0.001). Given that publication bias was observed in this study (Begg's test P-value = 0.01), the modified OR was calculated with consideration of missed studies, which was 1.68 (95% CI: 1.45–1.94; P-value < 0.001).

Conclusion

The results of this study suggest that diabetic patients have 90% higher odds of developing CTS compared to non-diabetic individuals, which is statistically significant.

Introduction

Carpal Tunnel Syndrome (CTS) is the most common focal mononeuropathy caused by median nerve compression, with a global prevalence of 2.7–5.8% [1–6]. This syndrome affects between 7% and 16% of the adult population and is the leading cause of sick leave and work disability [7]. Certain conditions that can cause this syndrome include metabolic disorders, collagen vascular diseases, obesity, kidney failure, contraceptive use, and endocrine disorders such as hypothyroidism [1, 2, 4, 8]. Moreover, diabetes, trauma, heavy manual, and repetitive work, tumors, amyloidosis, and sarcoidosis have all been identified as potential risk factors for CTS [1, 4, 9]. Symptoms of CTS include numbness, especially at night, and nerve pain, as well as neuropathic pain with localized compression of the median nerve in the wrist [10]. Whilst the sensory symptoms of this syndrome are often confined to the fingers, they can extend to the wrist, forearm, and even the entire hand. CTS becomes more common between the ages of 45 and 64 and in women than men (10% versus 1%) [2, 8].

Diabetes is a chronic multisystem disease characterized by high blood and urine glucose levels due to insufficient insulin production or use [11, 12]. In 2019, 79% of all adults with diabetes (463 million) lived in developing countries, with that figure expected to rise to 84% (700 million) by 2045 [13–15]. Diabetes has an estimated prevalence of 6.4% worldwide, with a predicted prevalence of 7.7% by 2030 [14]. Diabetes is one of the leading causes of disability worldwide. Its prevalence has risen due to population growth, aging, and lifestyle changes [4, 12, 16].

CTS has been reported to occur in up to 15% of diabetic patients. Reports suggest that the lifetime risk of developing CTS in a diabetic patient is approximately 85%, although previous research has yielded conflicting results regarding the association between diabetes and CTS [17–20].

Numerous studies have been conducted worldwide in recent years to investigate the relationship between diabetes and CTS, with a significant proportion of them demonstrating that diabetes increases the risk of developing CTS [3, 5, 21–26]. However, there are also studies that suggest that there is no association between diabetes and the occurrence of CTS [17, 27–34]. For instance, Wiberg et al. (2022) investigated the association between diabetes and CTS in a UK population-based cohort of over 400,000 people. They reported odds ratios of 2.31 (95% CI: 2.17–2.46) for the association between diabetes and CTS [35]. However, in a study conducted with Low et al. investigated the association between diabetes and CTS in the US, observed that adjusted odds ratio was equal to 0.84(95%CI: 0.65–1.09; P = 0.20) [36].

Due to the inconsistencies in determining whether diabetes increases the risk of CTS or not, systematic review and meta-analysis studies are one of the best ways to draw a definite conclusion and answer the scientific question. This study aims to investigate the association between diabetes and CTS by means of the systematic review and meta-analysis method, using the results of research studies conducted in this field.

Materials and methods

Type of study and search strategies

In this systematic review and meta-analysis research, we utilized the principles of Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) when writing the report. We conducted a comprehensive search of published articles in databases including Pubmed, ISI Web of Knowledge, Cochrane, Embase, Google Scholar, and Scopus until the end of 2022. Our search criteria included diabetes as an exposure, and carpal tunnel syndrome as an outcome.To conduct the search, we utilized study keywords and their synonyms based on Mesh (Medical Subject Headings). Only studies including human subjects and published in the English language were considered. We followed the related instructions and guides provided

to search in each of the databases. Additionally, the sources of articles resulting from the search were manually reviewed to find more studies on this topic.

Inclusion and exclusion criteria of study

As previously stated, the articles selected for inclusion in the study must have used case-control, cross-sectional, or cohort study designs. The main objective of the study was to investigate the association between diabetes and CTS and to determine the effect size of this relationship, with a 95% confidence interval (CI) presented in the article or calculated based on the information provided. Additionally, articles in the form of letters to the editor, editorial, protocol, review, meta-analysis, and ecological articles were excluded from the analysis.

Specifications of study data collection tool

After collecting the articles, we entered their bibliographic information and abstracts into the Endnote version 8 reference management software. We diagnosed and removed any duplicate papers using this software, and then rechecked the titles of the remaining articles. In the next step, we reviewed the titles and discarded any articles not related to the purpose of the research. Among the remaining articles, we carefully reviewed the abstract and full text of each article to ensure that it was related to the purpose of the study, and removed any irrelevant items. To increase credibility, the process of searching and selecting articles was conducted by two independent researchers. In cases of disagreement between the two researchers, a third researcher was consulted to reach a consensus on the selection of the final articles.

Data extraction

For each study, information such as the title, study type, article quality, first author's name, year of publication, country of study, gender and age range of participants, sample size, duration of follow-up, number of exposed and non-exposed groups in cohort studies, number of case and control groups in case-control studies, diabetes status of participants, and relative effect size (risk ratio, hazard ratio, or odds ratio) along with the 95% CI were collected from the related articles. The adjusted variables included in the multivariate model were also noted.

Two researchers independently extracted the desired data, and any disagreements were resolved through discussion with a third researcher. Articles that did not provide sufficient data to calculate the standard error for estimating the effect size were excluded from the study. Moreover, the latest findings from studies that had published their results multiple times were included in this systematic review.

Evaluation of the quality of the articles

The Newcastle-Ottawa checklist was used to evaluate the quality of the articles, given its ability to provide a quantitative score. Based on the study method and corresponding checklist, the articles were divided into three categories: low quality, moderate quality, and good quality.

Statistical methods

For studies where the effect size was calculated and presented separately for different time or seasonal periods, we used the meta-analysis method to calculate a total effect size from the presented values and considered it in the analysis. Additionally, for studies where the effect size was not reported, but information about exposure and outcome was available, we estimated the effect size and the relevant 95% confidence interval (CI) and included it in the meta-analysis.

To assess the presence of heterogeneity in the studies included in the meta-analysis, we used statistical tests (Chi-square test and I^2 to report a quantitative amount of heterogeneity) and graphical methods (forest plot). The Chi-square test was used to investigate differences in the results of the studies entered in the meta-analysis, and the results of this test determined the type of model (fixed or random). We used the met-regression model to determine the factors related to heterogeneity in the results, taking into account variables such as study sample size, article quality evaluation score based on the Newcastle-Ottawa, study design, sex ratio (male-to-female) of participants, and year of the study.We also used sensitivity analysis to evaluate the effect of omitting each study on the final result. Funnel plots and Begg's and Egger's tests were used to assess publication bias. We used the Metatarium command to estimate the effect size of the relation in the missing studies. All analyses were performed using Stata statistical software (version 15.0, Stata Corp, College Station, TX), and the significance level in this study was considered to be less than 0.05.

Results

Articles included in the study

As shown in Fig 1, an electronic search of databases using keywords in the title or abstract yielded 2060 articles, of which 563 duplicates were removed, resulting in 1497 articles. After scrutinizing each title, 1448 articles were excluded as being unrelated to the research topic, leaving 49 potentially relevant papers. Upon further examination, one article was excluded due to a lack of access to the full text, four articles were excluded due to a lack of effect size reporting, one article was excluded as a review, and one article was excluded due to the calculation of the time of occurrence, leaving a total of 42 articles to be included in the study (Fig 1).

Characteristics of selected studies

This review included a total of 42 articles investigating the association between diabetes and the occurrence of carpal tunnel syndrome, with a combined study population of 3,377,816 participants between 1991 and 2022 [3, 5, 17, 19, 21–34, 36–59]. Geographically, 15 studies with 1,332,085 participants were conducted in America, 12 studies with 19,792 participants were carried out in Europe, and 15 studies with 1,019,692 participants were conducted in Asia. In terms of study types, the review included 23 case-control, 12 cross-sectional, and 7 cohort studies. Among the 42 articles, 18 were categorized as being of low quality, 16 were categorized as being of medium quality, and 8 were categorized as being of good quality, as shown in Tables 1–3.

Association between diabetes and CTS

The results of the meta-analysis of the 42 studies showed that the odds ratio (OR) of CTS in participants who had a history of diabetes compared to those who did not was 1.90 (95% CI: 1.64–2.21; P-value <0.001). In other words, the results of this meta-analysis demonstrate that diabetes increased the odds of carpal tunnel syndrome by 90%, which is statistically significant (Fig 2).

Evaluation of publication bias

In investigating the relationship between diabetes and the occurrence of CTS using Begg's test (P-value = 0.01), there is a publication bias. No publication bias was observed using the Egger's test (P-value = 0.65). The corresponding funnel diagram can be seen in Fig 3.

In light of Begg's test indicating a publication bias in this study, we used the Metatarium command to estimate the effect size of the relationship between diabetes and CTS in the

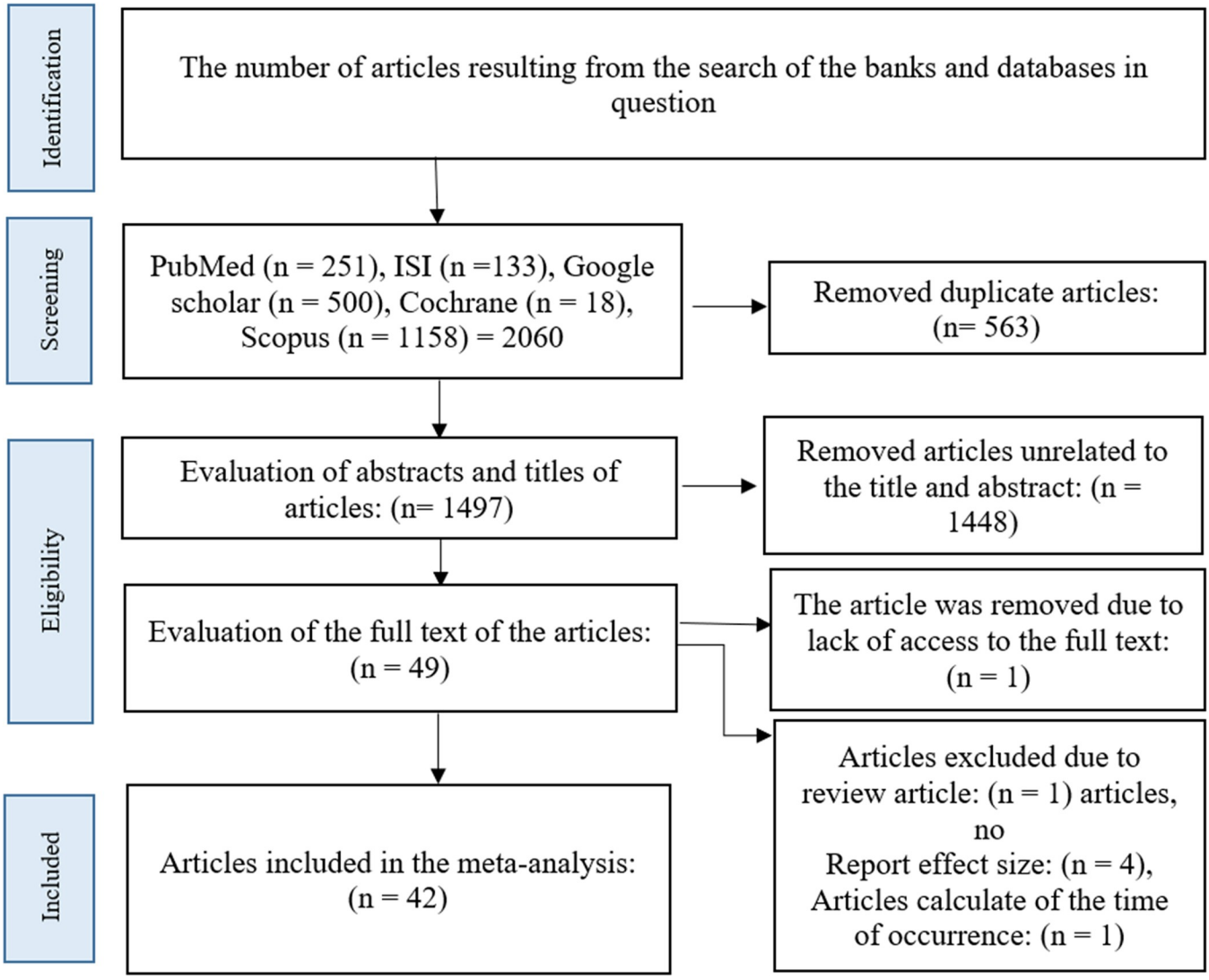

Fig 1. Diagram of selected studies for meta–analysis.

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missing studies and included it in the final calculations (Fig 4). Based on the results of the four missing studies estimated in this phase, the final modified odds ratio was 1.68 (95% CI: 1.45–1.94; P-value≤0.001).

Meta-regression and sensitivity analysis

A meta-regression was performed with the following variables included to investigate the cause of heterogeneity in study results: year, study design, sample size, quality of study based on the Newcastle-Ottawa, and sex ratio (male to female) of participants. According to the meta-regression results, the sex ratio (male to female) was the only variable that significantly contributed to the heterogeneity in the results of the studies analysed. Studies with a higher proportion of men (male to female ratio greater than 1) had a lower odds ratio of CTS occurrence than studies with a higher proportion of women (Table 4).

Table 1. Characteristics of meta–analysis studies to investigate the relationship between diabetes and CTS.

Number	*Publication first author*	*Year*	*Study setting*	*Study design*	*OR*	*Quality assessment*
1	Rocks MC [25]	2022	USA	Case-control	1.77 (1.62–1.93)	5
2	Rydberg M [26]	2022	Sweden	Cross-sectional	3.35 (2.51–4.48)	3
3	Kim JH [34]	2021	South Korea	Cross-sectional	1.75 (0.47–6.51)	4
4	Low J [36]	2021	USA	Cross-sectional	0.84 (0.65–1.09)	6
5	Naha U [51]	2021	USA	cross sectional	0.95 (0.32–2.79)	5
6	Rhee SY [55]	2021	South Korea	Cohort	1.04 (0.97–1.11)	6
7	Rydberg M [56]	2020	Sweden	Cohort	2.52 (1.99–3.19)	7
8	Shen PC [57]	2019	Taiwan	Case-control	1.32 (1.25–1.40)	4
9	Bhanderi D [38]	2017	India	Case-control	0.84 (0.47–1.50)	4
10	Hou WH [44]	2017	Taiwan	Cross-sectional	1.34 (1.19–1.50)	3
11	Kim YH [48]	2017	Korea	Cross-sectional	1.47 (0.75–2.90)	4
12	Hou WH [43]	2016	Taiwan	Case-control	1.31 (1.22–1.40)	5
13	Oktayglu P [52]	2015	Case-control	case control	6.92 (3.77–12.71)	4
14	Hendriks SH [42]	2014	Netherlands	Case-control	1.77 (1.22–2.57)	3
15	Musolin K [19]	2014	USA	Cross-sectional	1.54 (1.03–2.31)	4
16	Harris-Adamson C [41]	2013	USA	Cohort	1.08 (1.03–2.31)	5
17	Pandey A [53]	2013	India	Case-control	3.45 (1.58–7.53)	4
18	Wessel LE [59]	2013	Washington	Cohort	1.88 (1.08–3.25)	5
19	Evanoff B [33]	2013	USA	Cohort	2.06 (0.48–9.21)	5
20	Kidwai SS [47]	2013	Pakistan	Case-control	4.94 (1.65–14.80)	3
21	Karadag O [45]	2012	USA	case control	7.01 (1.86–26.40)	3
22	Tseng CH [5]	2012	Taiwan	Cohort	3.58 (3.05–4.20)	7
23	Ravindran Rajendran S [54]	2011	Chandigarh	Case-control	5.66 (1.24–25.87)	4
24	Shiri R [32]	2011	Finland	Cross-sectional	1.10 (0.61–1.99)	9
25	Plastino M [24]	2011	Case-control	case control	8.36 (4.65–15.03)	7
26	Mattioli S [49]	2009	Italy	case control	2.60 (0.74–9.17)	5
27	Melchior M [50]	2006	France	Cross-sectional	1.92 (0.95–3.89)	6
28	Mondelli M [31]	2006	Italy	Case-control	5.51 (0.26–116.79)	4
29	Gell N [40]	2005	Michigan	Cohort	7.28 (1.27–41.62)	8
30	Geoghegan JM [3]	2004	UK	Cross-sectional	1.79 (1.24–2.58)	5
31	Ardic F [30]	2003	Turkey	Case-control	0.48 (0.02–9.01)	3
32	Karpitskaya Y[46]	2002	Washington	Case-control	3.05 (1.08–8.61)	5
33	Cagliero E [17]	2002	USA	case control	1.56 (0.67–3.63)	4
34	Ferry S [29]	2000	UK	Case-control	1.83 (0.68–4.95)	4
35	Solomon DH [58]	1999	Washington	Case-control	1.40 (1.14–1.71)	3
36	Awada A [23]	1998	Saudi Arabia	Case-control	4.51 (2.91–6.99	3
37	Atcheson SG [37]	1998	USA	Cross-sectional	3.98 (0.88–17.95)	4
38	Chammas M [39]	1995	France	Case-control	0.06 (0.02–0.19)	5
39	Florack TM [22]	19922	USA	Cross-sectional	5.63 (1.17–27.09)	3
40	De krom M [28]	1990	Netherlands	Case-control	2.34 (0.50–10.88)	4
41	Wieslonder G [27]	1989	Sweden	Case-control	1.42 (0.27–7.43)	5
42	Dieck GS [21]	1985	USA	Case-control	2.90 (1.30–6.48)	5

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Sensitivity analysis

Sensitivity analysis was carried out by removing each study from the analysis one by one during each run. However, the estimated OR did not vary considerably, indicating that the meta-analysis results were robust (Table 5).

Table 2. Demographic composition of the participants in the included studies.

Number	*Publication first author*	*Year*	*Sample size*	*Men/women*	*Age average*	*With CTS/without CTS*	*With diabetes/without diabetes*
1	Rocks MC [25]	2022	997541	408487/589054	52.52	5726/991815	59166/938375
2	Rydberg M [26]	2022	1099543	545735/553808	-	30475/106068	56207/1014336
3	Kim JH [34]	2021	43	23/20	60.4	19/24	14/29
4	Low J [36]	2021	322092	20503/23018	-	1775/320317	43521/278571
5	Naha U [51]	2021	292	292	-	41/251	138/154
6	Rhee SY [55]	2021	476586	264686/211900	-	7258/469328	963/60516
7	Rydberg M [56]	2020	30446	12099/18347	57	1204/29242	1378/29067
8	Shen PC [57]	2019	41871	21307/20564	-	31928/9943	19494/22377
9	Bhanderi D [38]	2017	411	87/324	47.6	137/274	66/345
10	Hou WH [44]	2017	114186	57816/56370	-	-	57093/57093
11	Kim YH [48]	2017	230	81/119	52.81	105/125	41/189
12	Hou WH [43]	2016	201348	107392/93956	-	9025/192323	33571/167855
13	Oktayglu P [52]	2015	216	93/123	45.94	96/120	87/129
14	Hendriks SH [42]	2014	1591	558/1003	53.31	997/594	158/1433
15	Musolin K [19]	2014	318	94/224	39	127/191	17/301
16	Harris-Adamson C [41]	2013	3515	1860/1654	-	190/3007	122/3075
17	Pandey A [53]	2013	400	199/201	52.45	37/363	200/200
18	Wessel LE [59]	2013	300	300	-	84/216	-
19	Evanoff B [33]	2013	711	458/253	30.6	31/680	24/687
20	Kidwai SS [47]	2013	413	143/270	50.11	23/390	210/203
21	Karadag O [45]	2012	100	22/78	49.59	19/81	11/89
22	Tseng CH [5]	2012	47406	21951/25455	-	15802/31604	662/46744
23	Ravindran Rajendran S [54]	2011	409	204/205	52.92	13/396	206/203
24	Shiri R [32]	2011	6254	6254	51.9	238/6016	353/5880
25	Plastino M [24]	2011	245	125/120	-	117/128	136/109
26	Mattioli S [49]	2009	567	97/470	48.6	220/356	15/461
27	Melchior M [50]	2006	2656	1549/1107	-	79/2577	43/2613
28	Mondelli M [31]	2006	145	145	39.6	70/75	2/143
29	Gell N [40]	2005	432	134/298	37.47	29/403	6/426
30	Geoghegan JM [3]	2004	16955	4735/12221	-	3391/13564	494/16461
31	Ardic F [30]	2003	115	33/82	57.12	2/113	78/37
32	Karpitskaya Y [46]	2002	614	248/366	49.51	514/100	62/552
33	Cagliero E [17]	2002	300	186/114	50	32/268	200/100
34	Ferry S [29]	2000	2528	2528	41.9	1264/1264	17/2511
35	Solomon DH [58]	1999	4244	1096/3148	-	627/3740	849/3395
36	Awada A [23]	1998	240	68/132	-	100/100	30/170
37	Atcheson SG [37]	1998	297	-	-	193/104	16/281
38	Chammas M [39]	1995	240	162/78	-	44/196	120/120
39	Florack TM [22]	19922	246	33/213	-	106/140	10/236
40	De krom M [28]	1990	501	164/337	-	28/473	17/484
41	Wieslonder G [27]	1989	177	177	-	34/143	8/169
42	Dieck GS [21]	1985	1083	1083	-	40/1043	90/977

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Subgroup analysis

To determine the reason for the heterogeneity, subgroup analysis was performed and studies based on sample size (more or less than 10,000 participants), study design, study location, time period, sex ratio (male/female) of participants, qualitative evaluation score of articles, and the

Table 3. Adjusted variables in the studies that investigate the relationship between diabetes and CTS.

Publication first author	*Year*	*Study setting*
Kim JH	2021	Age, sex, WFR
Low J	2021	Age, sex, tobacco use, obesity, hypothyroid, CKD
Rhee SY	2021	Age, sex, BMI, Rheumatoid arthritis, Raynaud's syndrome
Rydberg M	2022	Age, sex, BMI, Hypertension, smoking, Alcohol consumption, Antihypertensive treatment
Bhanderi D	2017	Age, sex, education, smoking, current tobacco chewing, past smoking, past tobacco chewing, family history, obesity, Short Stature
Hendriks SH	2014	Sex, age, BMI
Harris-Adamson C	2013	Sex, age, and BMI
Pandey A	2013	Age, sex
Wessel LE	2013	Age, sex, smoking
Evanoff B	2013	Age, BMI, sex
Kidwai SS	2013	Age, sex
Tseng CH	2012	Sex, age, occupation, urbanization, income, uremia, Vit. B6 deficiency, RA, hypothyroidism, obesity, hypertension, diabetes, Gout, Acromegaly
Ravindran Rajendran S	2011	Age, sex, job types
Shiri R	2011	Age, sex, education, somatisation, hand grip with high forces, and work using vibrating tools
Plastino M	2011	Sex
Mattioli S	2009	Socio-occupational status, BMI, height, age, center
Melchior M	2006	Age
Mondelli M	2006	Age, BMI, hobbies, Oral contraceptives, other diseases, Current job length
Geoghegan JM	2004	BMI, diabetes, thyroxine, rheumatoid, OA, HRT, COCP, Smoking, Corticosteroids
Ferry S	2000	Age, date of birth
Solomon DH	1999	Age, gender, inflammatory arthritis, diabetes, hypothyroidism, hemodialysis, corticosteroid use, Estrogen replacement use
Chammas M	1995	Age, sex

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state of adjustment of confounding variables in the study were assessed. The odds ratio of CTS in people with diabetes compared to people without a history of diabetes was reported as 2.04 (95% CI: 1.69–2.46) in case-control studies, 1.61 (95% CI: 1.20–2.17) in cross-sectional studies, 2.06 (95% CI: 1.10–3.86) in cohort studies, 1.69 (95% CI: 1.33–2.15) in America, 2.04 (95% CI: 1.37–3.05) in Europe, 1.78 (95% CI: 1.43–2.23) in Asia, 1.95 (95% CI: 1.30–2.92) in studies before 2010, 1.88 (95% CI: 1.59–2.23) in studies after 2010, 1.75 (95% CI: 1.28–2.40) in adjusted studies(the role of confounding variables is controlled), 1.94 (95% CI: 1.65–2.29) in unadjusted studies, 2.37 (95% CI: 1.59–3.53)in studies with a sample size of less than thousand participants, 1.65(95% CI: 1.39–1.94) in studies with sample size a larger or equal to thousand participants, 2.35(95% CI: 1.86–2.98) in studies with a gender ratio of less than one, 1.36(95% CI: 1.14–1.63) in studies with a gender ratio equal to or greater than one, 2.49 (95% CI: 1.88–3.92) in studies categorized in good quality group, 1.41 (95% CI: 1.19–1.68) in studies categorized in moderate quality group, and 2. 16 (95% CI: 1.24–3.74) in studies categorized in poor quality group (Table 6).

Discussion

The purpose of this study was to investigate the relationship between diabetes and the occurrence of CTS. In this study, it was observed that compared to people without diabetes, the

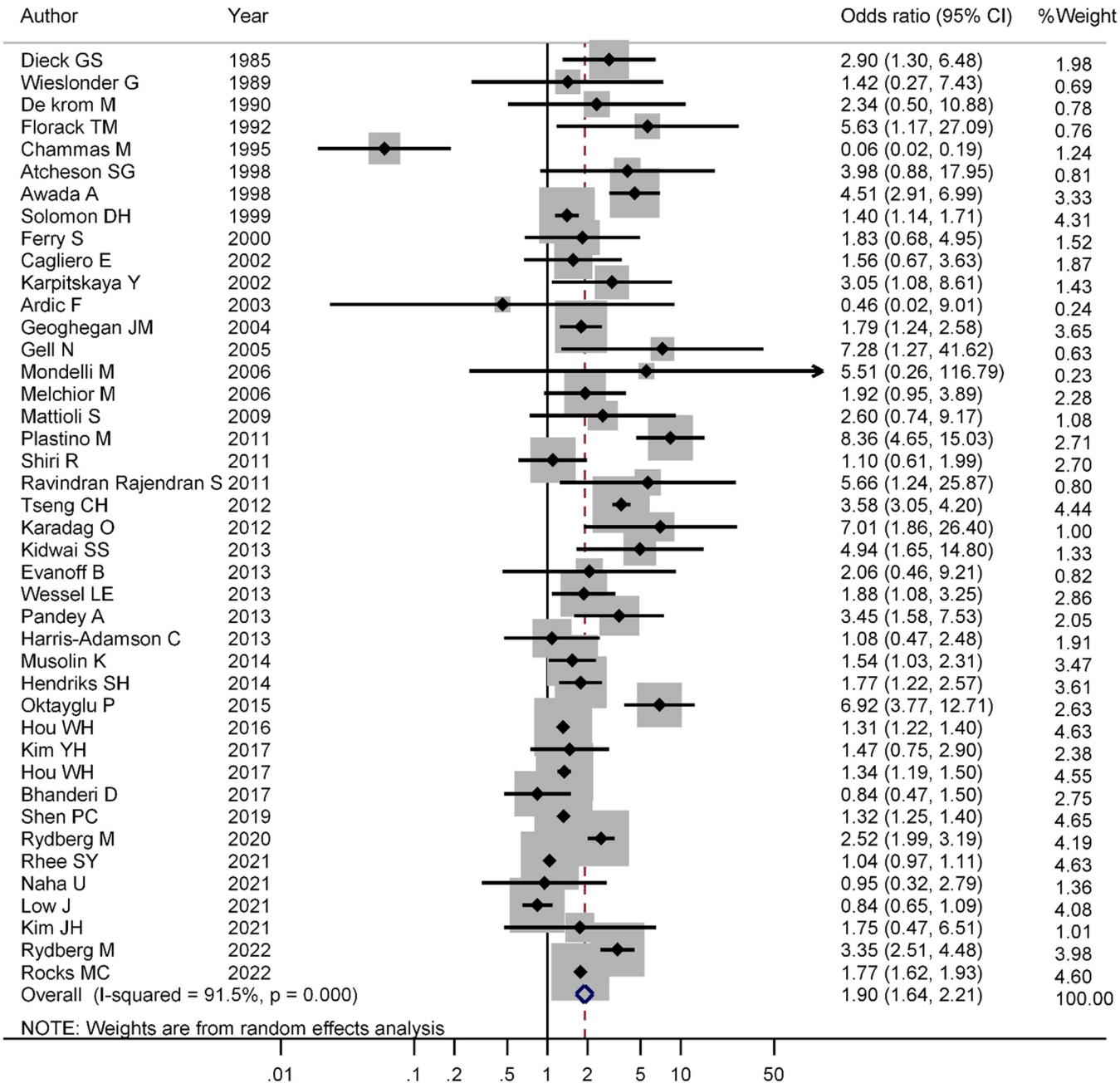

Fig 2. Forest plot of the relationship between diabetes and CTS.

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odds ratio of the occurrence of CTS in diabetic paitents is equal to 1.90 (95% CI: 1.64–2.21; P-value <0.001). Since in this study, the heterogeneity between the results of the studies included in the analysis is 91.5%, the meta-regression approach was used to identify the root of the heterogeneity. According to the meta-regression results, the sex ratio was the only variable that significantly contributed to the heterogeneity in the results of the studies analysed. So, studies with a higher proportion of men had a lower odds ratio of carpal tunnel syndrome occurrence than studies with a higher proportion of women.

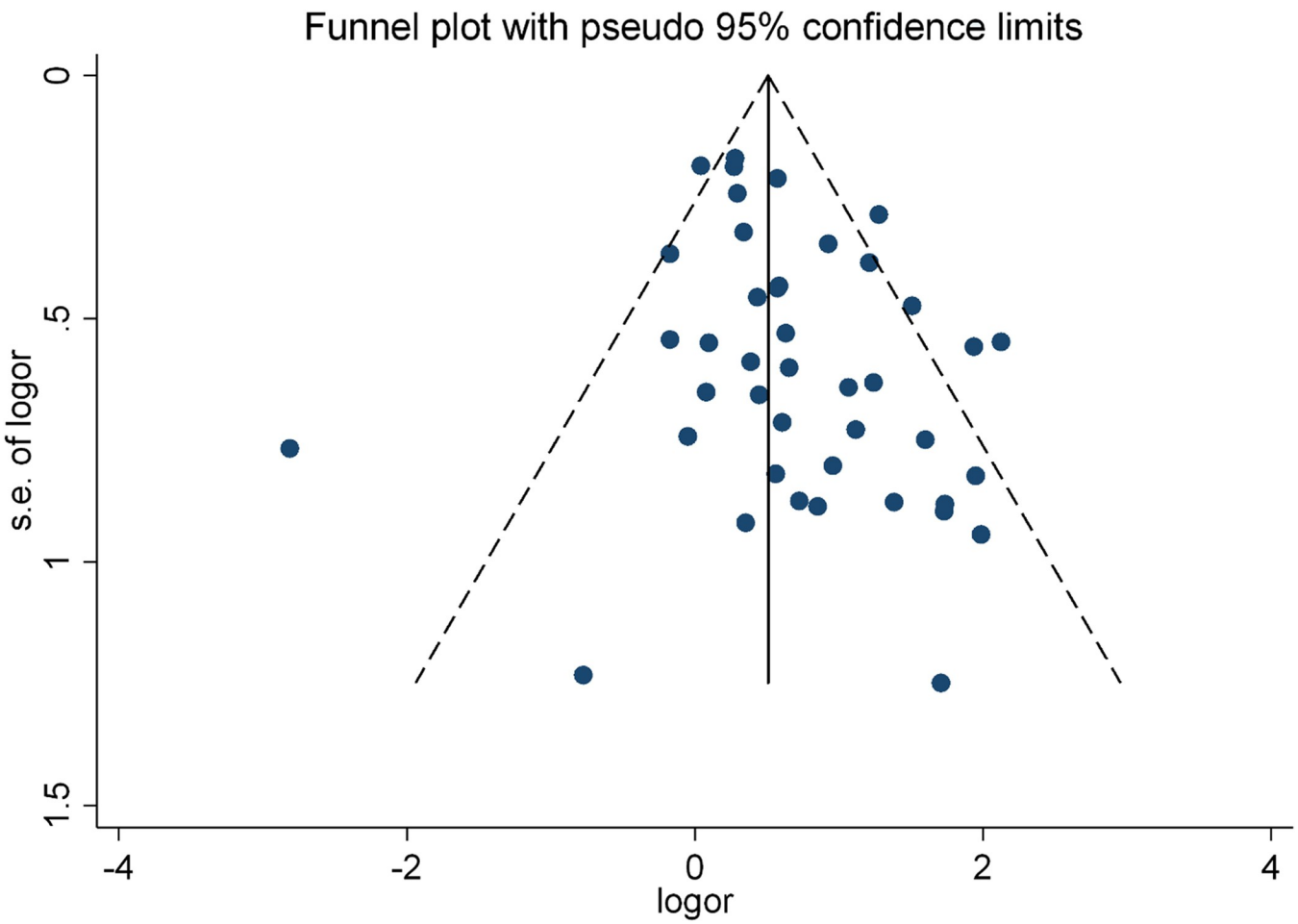

Fig 3. Funnel plot for evaluation of publication bias in investigating the relationship between diabetes and CTS.

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This study uncovered the presence of publication bias, which aims to amplify the dissemination of research findings indicating an increased risk of carpal tunnel syndrome in individuals with diabetes.To address this, we attempted to estimate the effect size of the missing studies and included it in our calculations. By estimating the effect size of diabetes on the occurrence of CTS and considering the results of the four missing studies, we arrived at a final modified odds ratio of 1.68 (95% CI: 1.45–1.94; P-value$\leq$0.001). Despite controlling for the effect of publication bias in the final meta-analysis, diabetes still poses an increased risk of CTS occurrence.

In a systematic review and meta-analysis conducted by Pourmemari MH and Shiri R, in 2016 on the relationship between diabetes and CTS, it was found that the crude odds ratio was 1.97 (95% CI: 1.56–2.49), while the adjusted odds ratio for confounding variables was 1.69 (95% CI: 1.45–1.96). In addition, in this study, no difference was observed between type 1 and type 2 diabetes in the development of CTS, in fact, both type 1 and type 2 diabetes are related to the occurrence of CTS [4]. The results of this study are consistent with the findings of our study.

A large population-based investigation revealed that diabetic individuals have a higher incidence of CTS, with an odds ratio of 1.51 that is independent of other risk variables. The increased prevalence of CTS in diabetic individuals may begin up to ten years before the

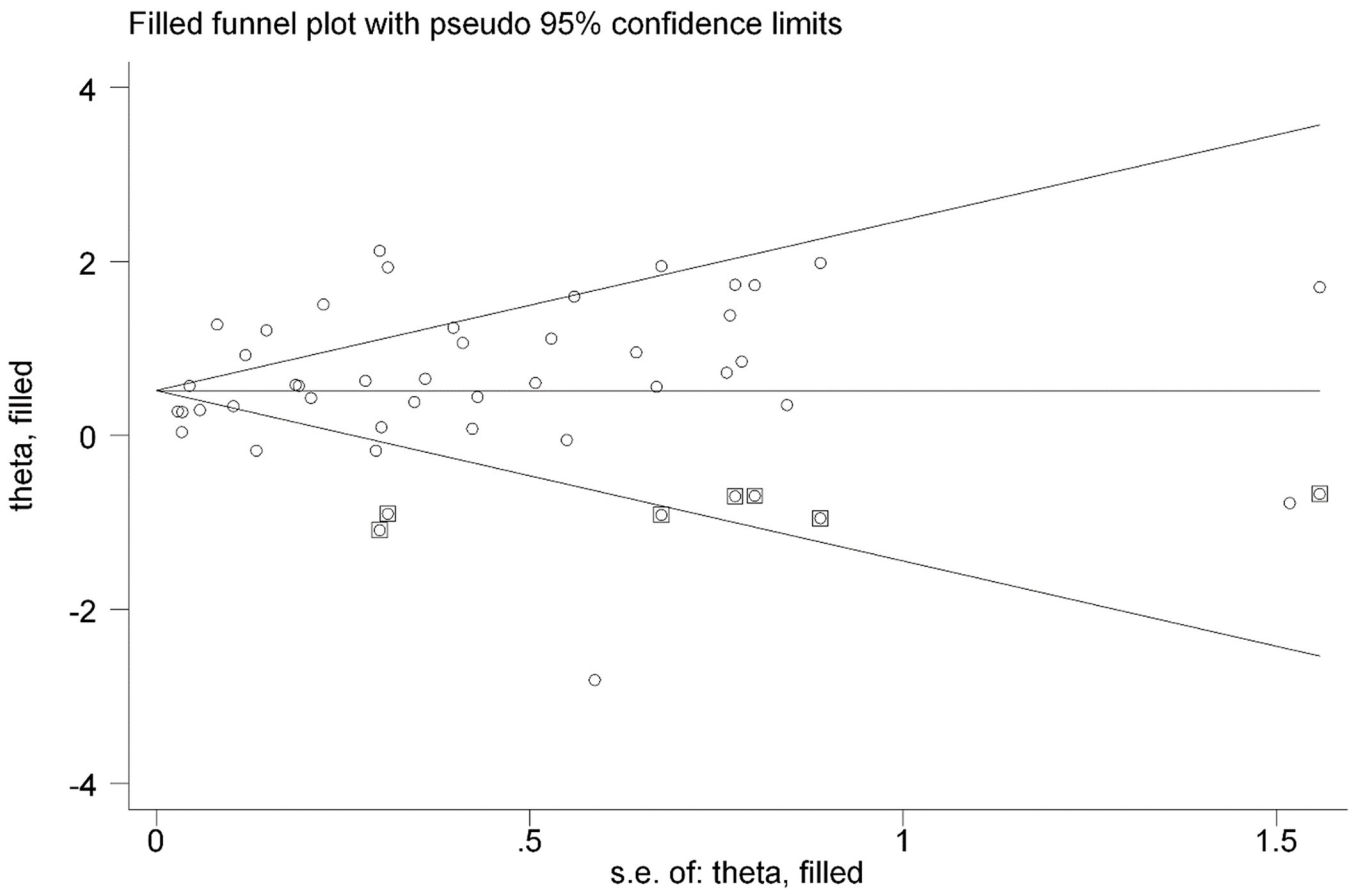

Fig 4. The results of the four missing studies estimated using the Metatarium command.

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diagnosis of diabetes [60]. Bilateral CTS has been observed to be more common in diabetic individuals, with its prevalence linked to increasing age and body mass index [61]. Therefore, it appears that in diabetic individuals, the presence of special conditions and characteristics such as older age and higher body mass index create a positive interaction, leading to the occurrence of CTS and its higher prevalence in this group.

Table 4. Meta–regression results in the studies that investigate the relationship between diabetes and carpal tunnel syndrome.

Meta-regression					**Number of obs = 38**	
REML estimate of between-study variance					**Taue2 = 0.4471**	
% residual variation due to heterogeneity					**I-suuared_res = 87.71%**	
Proportion of between—study variance explained					**Adj R-squared = 1.76%**	
Joint test for all covariates					**Model F (5,32) = 1.42**	
With Knapp-Hartung modification					**Prob>F = 0.2431**	
logor	***Coef.***	***Std. Err.***	***t***	***p ||t||***	***[95% Conf. Interval]***	
Year	0.2241241	0.2812747	0.80	0.431	0.3488138	0.797062
Sample size	-0.3452252	0.2802587	-1.23	0.227	0.9160934	0.2256431
Sex ratio	-0.6181865	0.2963283	-2.09	0.045	1.0221788	-0.0145855
Study design	-0.0615807	0.1565388	-0.39	0.697	0.3804398	0.2572784
Quality assessment	0.065364	0.1864653	0.35	0.728	0.3144533	0.4451814
-cons	1.671189	0.6622751	2.52	0.017	0.3221792	3.020199

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Table 5. Results of sensitivity analysis for the assessment of the relationship between diabetes and CTS.

Publication first author	*Year*	*OR (95% CI)*
Rocks MC	2022	1.91 (1.63–2.24)
Rydberg M	2022	1.85 (1.59–2.15)
Kim JH	2021	1.90 (1.63–2.21)
Low J	2021	1.96 (1.69–2.29)
Naha U	2021	1.92 (1.65–2.23)
Rhee SY	2021	1.96 (1.68–2.28)
Rydberg M	2020	1.87 (1.61–2.18)
Shen PC	2019	1.95 (1.64–2.32)
Bhanderi D	2017	1.94 (1.67–2.26)
Hou WH	2017	1.94 (1.65–2.27)
Kim YH	2017	1.91 (1.64–2.22)
Hou WH	2016	1.95 (1.65–2.30)
Oktayglu P	2015	1.83 (1.58–2.12)
Hendriks SH	2014	1.90 (1.63–2.22)
Musolin K	2014	1.91 (1.64–2.23)
Harris-Adamson C	2013	1.92 (1.65–2.23)
Pandey A	2013	1.87 (1.61–2.18)
Wessel LE	2013	1.90 (1.63–2.21)
Evanoff B	2013	1.90 (1.63–2.20)
Kidwai SS	2013	1.87 (1.61–2.18)
Karadag O	2012	1.88 (1.61–2.18)
Tseng CH	2012	1.82 (1.58–2.08)
Ravindran Rajendran S	2011	1.88 (1.62–2.19)
Shiri R	2011	1.93 (1.66–2.24)
Plastino M	2011	1.82 (1.57–2.11)
Mattioli S	2009	1.89 (1.63–2.20)
Melchior M	2006	1.90 (1.63–2.21)
Mondelli M	2006	1.89 (1.63–2.20)
Gell N	2005	1.88 (1.62–2.19)
Geoghegan JM	2004	1.90 (1.63–2.22)
Ardic F	2003	1.90(1.64–2.21)
Karpitskaya Y	2002	1.88 (1.62–2.19)
Cagliero E	2002	1.91 (1.64–2.21)
Ferry S	2000	1.90 (1.63–2.21)
Solomon DH	1999	1.93 (1.65–2.25)
Awada A	1998	1.84 (1.58–2.13)
Atcheson SG	1998	1.89 (1.62–2.19)
Chammas M	1995	1.98 (1.70–2.29)
Florack TM	1992	1.88 (1.62–2.19)
De krom M	1990	1.89 (1.63–2.20)
Wieslonder G	1989	1.90 (1.64–2.21)
Dieck GS	1985	1.88 (1.62–2.19)

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Research has indicated that CTS does not predict diabetes, but rather, diabetes predicts CTS [62]. According to the study conducted with Perkins et al., the prevalence of clinical CTS was 14% in diabetic patients without diabetic peripheral neuropathy (DPN), 30% in those with DPN, and 2% in the general population. They also found that CTS, is common in individuals with distal sensory peripheral neuropathy [63].

Table 6. Subgroup analysis of the association between diabetes and CTS.

Characteristics		*Number of studies*	*OR (95% CI)*	*P-value*
Study design	Case-control	23	2.04 (1.69–2.46)	≤0.001
	Cross-sectional	12	1.61 (1.20–2.17)	≤0.001
	Cohort	7	2.06 (1.10–3.86)	0.02
Study location	America	15	1.69 (1.33–2.15)	≤0.001
	Europe	15	2.04 (1.37–3.05)	≤0.001
	Asia	12	1.78 (1.43–2.23)	≤0.001
Time period	Before 2010	17	1.95 (1.30–2.92)	≤0.001
	After 2010	25	1.88 (1.59–2.23)	≤0.001
Sample size	<1000	25	2.37 (1.59–3.53)	≤0.001
	≥1000	17	1.65(1.39–1.94)	≤0.001
Adjustment of confounding variables	No	20	1.94(1.65–2.29)	≤0.001
	Yes	22	1.75(1.28–2.40)	≤0.001
Sex ratio	Unknown	8	1.69(1.24–2.30)	≤0.001
	<1	23	2.35(1.86–2.98)	≤0.001
	≥1	11	1.36(1.14–1.63)	≤0.001
Quality assessment	Good quality	5	2.49 (1.88–3.29)	≤0.001
	Moderate quality	27	1.41 (1.19–1.68)	≤0.001
	Poor quality	10	2.16 (1.24–3.74)	≤0.001

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While the adverse effects of diabetes on peripheral nerves have been extensively studied, the mechanism by which diabetes increases the risk of CTS is still being investigated. Median nerve neuropathy is a common complication of diabetes. Patients with diabetes who are not exposed to nerve compression have been found to have a reduction in myelinated nerve fibre and endoneurial capillary densities, which may lead to median nerve neuropathy [64]. In addition, advanced glycation end-products have been found to increase production of circulating inflammatory cytokines in patients with diabetes, while vascular endothelial growth factor may cause impaired microvascular circulation, resulting in demyelination and axonal degeneration in the median nerve [65, 66]. However, further research is still needed to fully understand the underlying mechanisms of CTS caused by diabetes.

Our study consisted of 42 observational studies (case-control, cross-sectional, and cohort). The results of this study can be highly beneficial for health professionals in making well-informed decisions and adopting evidence-based preventive measures for patients with diabetes. In this research, subgroup analysis was used to present the results in greater detail. However, this study has some limitations. One of the most important limitations of this study is that all the studies included in the analysis are observational. One limitation of observational studies is the presence of confounding variables when examining the relationship between exposure and outcome. While these studies attempt to control for confounding variables through methods such as matching or statistical methods like classification or regression models, there is still the possibility of residual confounders in these studies. Therefore, caution should be exercised when interpreting the results of observational studies and meta-analyses based on these studies. Consequently, it is not possible to infer causal inference relationships between exposure and outcome in these studies, and should only interpret the relationship between variables [67].

Conclusion

This study observes that diabetes is related to the occurrence of CTS, with diabetic patients having a 90% higher odds of developing the condition compared to non-diabetic individuals.

Therefore, health policies and recommendations should pay special attention to the risk of CTS in diabetic people. Periodic evaluations should also be considered for diabetic patients to prevent the occurrence of this disorder and its related disabilities.

Supporting information

S1 File.
(DOCX)

Author Contributions

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Writing – review & editing: Hadi Raeisi Shahraki, Lusine G. Khachatryan, Abdollah Mohammadian-Hafshejani.

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