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Review

Hand dysfunction in type 2 diabetes mellitus: Systematic review with meta-analysis

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ABSTRACT

Background: People with type 2 diabetes mellitus frequently show complications in feet and hands. However, the literature has mostly focused on foot complications. The disease can affect the strength and dexterity of the hands, thereby reducing function.
Objectives: This systematic review and meta-analysis focused on identifying the existing evidence on how type 2 diabetes mellitus affects hand strength, dexterity and function.
Methods: We searched MEDLINE via PubMed, CINHAL, Scopus and Web of Science, and the Cochrane central register of controlled trials for reports of studies of grip and pinch strength as well as hand dexterity and function evaluated by questionnaires comparing patients with type 2 diabetes mellitus and healthy controls that were published between 1990 and 2017. Data are reported as standardized mean difference (SMD) or mean difference (MD) and 95% confidence intervals (CIs).
Results: Among 2077 records retrieved, only 7 full-text articles were available for meta-analysis. For both the dominant and non-dominant hand, type 2 diabetes mellitus negatively affected grip strength (SMD: −1.03; 95% CI: −2.24 to 0.18 and −1.37, −3.07 to 0.33) and pinch strength (−1.09, −2.56 to 0.38 and −1.12, −2.73 to 0.49), although not significantly. Dexterity of the dominant hand did not differ between diabetes and control groups but was poorer for the non-dominant hand, although not significantly. Hand function was worse for diabetes than control groups in 2 studies (MD: −8.7; 95% CI: −16.88 to −1.52 and 4.69, 2.03 to 7.35).
Conclusion: This systematic review with meta-analysis suggested reduced hand function, specifically grip and pinch strength, for people with type 2 diabetes mellitus versus healthy controls. However, the sample size for all studies was low. Hence, we need studies with adequate sample size and randomized controlled trials to provide statistically significant results.

1. Introduction

Diabetes mellitus (DM) is a group of metabolic disorders characterized by chronic hyperglycaemia with disturbed carbohydrate, fat and protein metabolism due to absolute or relative deficiency in insulin secretion and/or action [1]. The prevalence of type 2 DM (T2DM) is increasing across the globe. According to the International Diabetes Federation, 415 million adults are estimated to have T2DM. One in 11 adults has T2DM. T2DM is more prevalent in low and middle socio-economic countries [2].

With the increase in prevalence of T2DM, complications associated with the disease also increase. The main reason for complications is poor glycaemic control and diabetes screening, especially in low socio-economic countries, lack of awareness among people, and lack of health care facilities in rural areas [3]. T2DM affects many parts of the body, the most common complications being diabetic cardiovascular problems, retinopathy, nephropathy, and peripheral neuropathy [4]. Peripheral neuropathy with a diabetes origin affects both upper and lower extremities. Throughout the literature, peripheral neuropathy of

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In T2DM, abnormal cross-linking of collagen fibres occurs due to accumulation of advanced glycosylation end-products, which leads to skin thickening and formation of nodules and contractures [6]. Commonly seen hand complications with T2DM are limited joint mobility syndrome, also known as diabetic cheiroarthropathy or stiff hand syndrome, Dupuytren's contracture, flexor tenosynovitis (trigger finger) and carpal tunnel syndrome [7].

Hand complications in patients with T2DM may affect activities of daily living and lead to disabilities in self-care activities. These result in reduced interpersonal interactions, loss of independence, financial burden and overall reduced quality of life [8]. However, we have little research pertaining to hand dysfunction in T2DM. With the increasing life expectancy and steep increase in number of people with T2DM, we need more research on hand function to address the standard of living and self-reliability in general and fine tasks.

With the increase in prevalence of T2DM worldwide and in India, the accompanying complications may disturb activities of daily living and quality of life. Unlike the diabetic foot, complications of hands with T2DM are easily neglected. Only a few studies have assessed hand strength, dexterity and dysfunction in people with T2DM. The reporting of hand dysfunction in these patients lacks agreement among studies. Thus, considering the increasing rate in number of people living with T2DM and the increased life expectancy, a study of hand function may help improve care, independence in activities of daily living and quality of life.

Hence, we performed a systematic review and meta-analysis to provide evidence of the effect of T2DM on hand strength, dexterity and function.

2. Methods

According to the Prisma statement, the review was performed for quality of reporting of a meta-analysis.

2.1. Literature search

We searched MEDLINE via PubMed, Scopus, Science Direct, Web of Science, Cochrane Central register of controlled trials, and CINHAL for articles published in English from June 1, 2017 to June 15, 2017 by using the MESH and keywords "type 2 diabetes mellitus", "hand dysfunction", "hand function", "hand strength", "hand dexterity", including the Boolean operator AND/OR. Full-text articles were selected for the review.

In the meta-analysis, we included articles with the following 3 criteria to achieve a homogenous sample for further analysis:

- participants had T2DM;
- age-matched controls were not diabetic or with impaired glucose tolerance;
- evaluation was of hand grip strength (with the hand Jamar dynamometer), pinch strength (pinch meter), and dexterity (Purdue Pegboard test), with hand function assessed by validated questionnaires.

2.2. Assessment of risk of bias

The included studies were assessed for risk of bias by using the US National Heart, Lung and Blood Institute checklist for observational cohort and cross-sectional studies. In the checklist, 6 questions were applicable to the current study. Questions 1 to of the sample size and adjustment for confounding factors. The quality assessment was performed by 2 independent reviewers. The scoring was Yes, No, cannot determine/not applicable or not reported. The study was rated as poor quality with score < 4; fair with score 4 to 5, and good with all scores ≥ 6. The mean score for the 2 reviewers was considered for each domain.

2.3. Study screening and data extraction

Two authors (GS and AM) independently screened all titles for inclusion. Abstracts of potentially eligible studies were obtained, then full texts. Any discrepancies between the authors were resolved by discussion. Data were extracted by the first author (GS) with the help of a qualified statistician.

3. Statistical analysis

Because all our outcomes were continuous, we calculated mean difference/standardised mean difference (MD/SMD) statistics. For the meta-analysis, we synthesized SMDs because the study authors used different instruments for measuring outcomes. For the studies not included in meta-analyses, we calculated MDs.

Meta-analysis was performed when at least 2 studies were similar in terms of the PICO process and study design providing relevant data. We adopted a random-effects model for the meta-analysis because we anticipated considerable heterogeneity among the studies. To assess heterogeneity, we used the Chi^2 statistic ($P < 0.1$ considered statistically significant) and evaluated heterogeneity with the I^2 statistic ($> 60\%$ considered substantial heterogeneity). Meta-analysis involved use of RevMan 5.2. We present forest plots for all meta-analyses. When meta-analysis was not appropriate, the effect size is presented with 95% confidence intervals (CIs). We performed meta-analysis of the effect of gender and age on grip strength of the dominant hand only because of few studies to analyse the effect size for other outcomes.

4. Results

4.1. Study selection

From the electronic database search, we identified 2077 articles; after removing duplicates and screening for eligibility criteria, 1579 articles were excluded. Overall, 24 full-text articles were eligible for review; 17 did not meet the inclusion criteria (Fig. 1), so finally, 7 articles were included in the final review and meta-analysis. Records were excluded because of inappropriate title and study methodology; no control group; improper study design and outcome measure, statistical analysis, and tools used in the study; inappropriate data; and publication language other than English.

4.2. Study quality

The studies included in the review showed fair quality according to the total score on the US National Heart, Lung and Blood Institute checklist (Table 1). None of the reports stated how the sample size was calculated to detect the clinically significant effect. Various confounding factors were not taken into consideration and could have influenced the outcome of interest.

4.3. Characteristics and recruitment of participants

A total of 761 participants were analysed: 425 in the study groups and 341 in the control groups. People with T2DM and

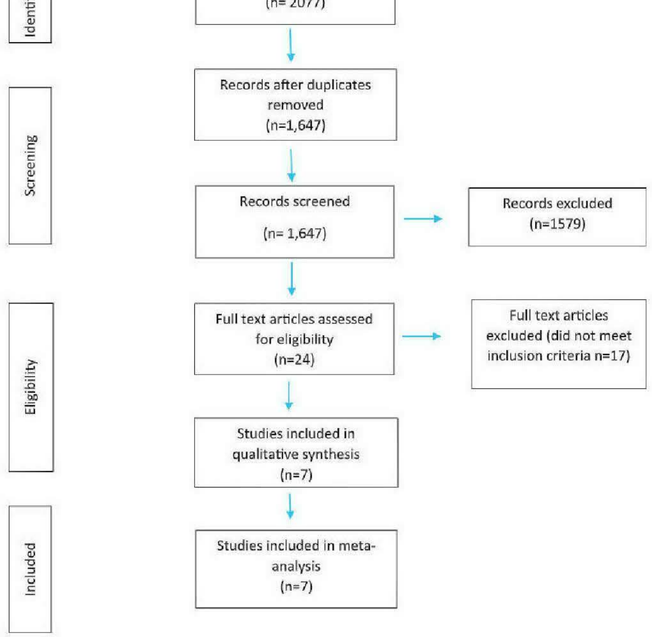

Fig. 1. Flow of the selection of studies for the meta-analysis.

healthy age-matched controls were studied. Characteristics of participants are in the table. Most participants were recruited from hospital and outpatient settings.

4.4. Outcome measures

Each outcome of interest included in the review (Table 1) is discussed in detail below.

4.4.1. Grip strength

Among the 7 studies, 5 reported grip strength for people with T2DM and healthy age-matched controls [9–11,13,14] (Figs. 2–3). Three studies reported means and SDs for dominant and non-dominant hands separately [10,11,13]. Meta-analysis of the dominant hand showed high heterogeneity among the studies ($I^2 = 97\%$) (Fig. 2). We revealed a negative combined effect of grip strength in the dominant hand, indicating a lower mean in the T2DM. Also, meta-analysis of grip strength for the non-dominant hand indicated a negative combined effect of diabetes (SMD: −1.37; 95% CI: −3.07 to 0.33), suggesting low grip strength with T2DM (Fig. 3). The heterogeneity among the studies for the non-dominant hand was also high ($I^2 = 98\%$).

4.4.2. Pinch strength

Three studies reported pinch strength of the dominant and non-dominant hand separately for T2DM and non-diabetes participants [11,13,14]. We found high heterogeneity among the studies, $I^2 = 96\%$ and 97% for the dominant and non-dominant hand, respectively. We found a negative combined mean for both the dominant hand (SMD: −1.09; 95% CI: −2.56 to 0.38) and non-dominant hand (−1.12, −2.73 to 0.49), suggesting reduced pinch strength in study than control groups (Figs. 4–5).

4.4.3. Hand dexterity

Studies used the Purdue Pegboard test-to-test dexterity. Only 2 studies reported dexterity of dominant and non-dominant hand separately for T2DM and non-diabetes participants [12,14]. The meta-analysis revealed no significant difference in hand dexterity in the dominant hand between the study and control groups (SDM: −0.07; 95% CI: −0.51 to 0.36). However, we found a negative combined effect of dexterity for the non-dominant hand (−0.54, −1.43 to 0.35). The heterogeneity among the studies was $I^2 = 0\%$ and 76% for the dominant and non-dominant hand, respectively (Figs. 6–7).

4.4.4. Hand function

Two studies used validated questionnaires to assess hand function in people with T2DM versus healthy controls [12,15]. Yang et al. used the Michigan Hand Outcome Questionnaire to test hand function, with a low score except for the pain dimension indicating poor hand function [12]. Savas et al. used the Duruöz hand index (DHI) self-reporting questionnaire, with a high total score indicating more disability [15]. Hence we could not use these studies for meta-analysis because they were not comparable, but we measured the MD for individual studies. The MDs between the study and control groups for studies conducted by Yang et al. and Savas et al. were −8.7 (95% CI −16.88 to −1.52) and 4.69 (2.03 to 7.35) [12,15]. Therefore, in these 2 studies, hand function was significantly reduced with T2DM as compared with healthy controls or non-diabetics.

Table 1
Characteristics of the studies included in the review.

Study	Study area	No of participants in study group	No of participants in control group	Age of participants, years, mean (SD)	Outcome measures used	Quality assessment
Savas et al., 2007	Turkey	44	60	58.98 (9.07)	Grip strength Pinch strength Duruöz hand index questionnaire	Fair
Cederlund et al., 2009	Sweden	23	35	75 (1.4)	Grip strength Pinch strength Purdue Pegboard test	Fair
Carvalho et al., 2014	Brazil	100	100	64.18 (8.10) (SG) 63.82 (6.58) (CG)	Grip strength	Fair
Mohammed et al., 2014	Egypt	40	40	51 (5.59) (SG) 48.05 (6.73) (CG)	Grip strength Pinch strength	Fair
Cetinus et al., 2005	Turkey	76	47	50.11 (7.6) (SG) 46.9 (10.2) (CG)	Grip strength Pinch strength	Fair
Kaur et al., 2016	India	50	50	54.74 (2.61) (SG) 55.28 (2.83) (CG)	Grip strength	Fair
Yang et al., 2017	Taiwan	92	9	59.4 (9.5) (SG) 52.9 (6.5) (CG)	Perdue Pegboard test Michigan Hand Outcome questionnaire	Fair

SG: study group; CG: control group.

Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Cederlund RI et al 2009	41	23.7	23	39	16.29	35	19.9%	0.10 [-0.43, 0.63]
Centinus E et al 2005	28.92	10.86	76	33.22	10.53	47	20.3%	-0.40 [-0.77, -0.03]
Kaur P et al 2016	20.76	3.55	50	32.9	7.6	50	20.0%	-2.03 [-2.52, -1.55]
Mohamed EK et al 2014	24.9	5.63	40	42.75	4.65	40	19.3%	-3.42 [-4.12, -2.73]
Total (95% CI)			**289**			**272**	**100.0%**	**-1.03 [-2.24, 0.18]**

Heterogeneity: Tau² = 1.85; Chi² = 157.22, df = 4 (P < 0.00001); I² = 97%
Test for overall effect: Z = 1.67 (P = 0.10)

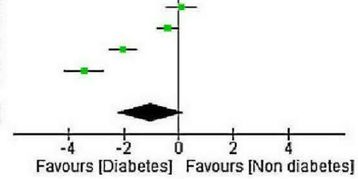

Fig. 2. Forest plot of meta-analysis of grip strength of the dominant hand comparing type 2 diabetes mellitus (T2DM) and healthy controls (negative mean difference indicates higher mean values in controls).

	Diabetes			Non diabetes				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Carvalho F De etal 2004	32.4	12.29	100	28.3	25.92	100	34.1%	0.20 [-0.08, 0.48]
Centinus E et al 2005	27.54	10.51	76	32.05	9.3	47	33.8%	-0.45 [-0.81, -0.08]
Mohamed EK et al 2014	19.07	4.64	40	37.87	4.65	40	32.1%	-4.01 [-4.78, -3.24]
Total (95% CI)			**216**			**187**	**100.0%**	**-1.37 [-3.07, 0.33]**

Heterogeneity: Tau² = 2.20; Chi² = 101.36, df = 2 (P < 0.00001); I² = 98%
Test for overall effect: Z = 1.58 (P = 0.12)

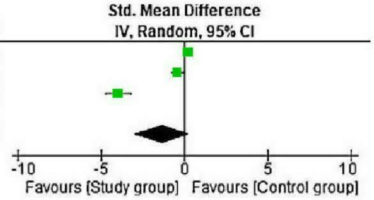

Fig. 3. Forest plot of meta-analysis of grip strength of the non-dominant hand comparing type 2 diabetes mellitus (T2DM) and healthy controls (negative mean difference indicates higher mean values in controls).

	Diabetes			Non diabetes				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Cederlund RI et al 2009	8	5.19	23	8.5	5.93	35	33.3%	-0.09 [-0.61, 0.44]
Centinus E et al 2005	8.47	2.56	76	9.37	1.89	47	34.0%	-0.38 [-0.75, -0.02]
Mohamed EK et al 2014	5.75	1.75	40	11.3	2.11	40	32.7%	-2.84 [-3.46, -2.21]
Total (95% CI)			**139**			**122**	**100.0%**	**-1.09 [-2.56, 0.38]**

Heterogeneity: Tau² = 1.62; Chi² = 52.19, df = 2 (P < 0.00001); I² = 96%
Test for overall effect: Z = 1.45 (P = 0.15)

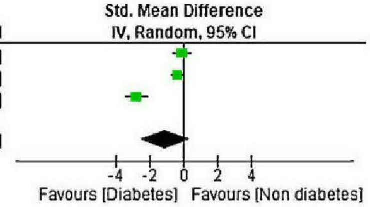

Fig. 4. Forest plot of meta-analysis of pinch strength of the dominant hand comparing type 2 diabetes mellitus (T2DM) and healthy controls (negative mean difference indicates higher mean values in controls).

	Diabetes			Non diabetes				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Cederlund RI et al 2009	8	5.56	23	8	6.74	35	33.3%	0.00 [-0.53, 0.53]
Centinus E et al 2005	8.15	2.5	76	8.92	1.83	47	34.0%	-0.34 [-0.70, 0.03]
Mohamed EK et al 2014	5.52	2.07	40	10.72	1.15	40	32.7%	-3.08 [-3.73, -2.42]
Total (95% CI)			**139**			**122**	**100.0%**	**-1.12 [-2.73, 0.49]**

Heterogeneity: Tau² = 1.95; Chi² = 60.85, df = 2 (P < 0.00001); I² = 97%
Test for overall effect: Z = 1.36 (P = 0.17)

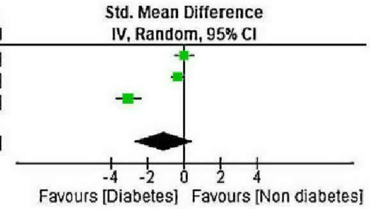

Fig. 5. Forest plot of meta-analysis of pinch strength of the non-dominant hand comparing T2DM and healthy controls (negative mean difference indicates higher mean values in controls).

	Diabetes			Non diabetes				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Cederlund RI et al 2009	10	4.44	23	10	7.41	35	67.6%	0.00 [-0.53, 0.53]
Yang CJ etal 2017	12.1	2.1	26	14.2	18	9	32.4%	-0.23 [-0.99, 0.53]
Total (95% CI)			**49**			**44**	**100.0%**	**-0.07 [-0.51, 0.36]**

Heterogeneity: Tau² = 0.00; Chi² = 0.23, df = 1 (P = 0.63); I² = 0%
Test for overall effect: Z = 0.33 (P = 0.74)

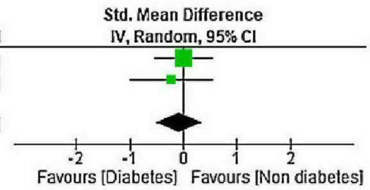

Fig. 6. Forest plot of meta-analysis of hand dexterity of the dominant hand comparing type 2 diabetes mellitus (T2DM) and healthy controls (poor negative mean difference favours neither group).

	Diabetes			Non diabetes				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Cederlund RI et al 2009	10	5.19	23	11	10.37	35	53.3%	-0.11 [-0.64, 0.41]
Yang CJ etal 2017	11.5	2.3	92	13.9	2.5	9	46.7%	-1.03 [-1.73, -0.33]
Total (95% CI)			**115**			**44**	**100.0%**	**-0.54 [-1.43, 0.35]**

Heterogeneity: Tau² = 0.32; Chi² = 4.19, df = 1 (P = 0.04); I² = 76%
Test for overall effect: Z = 1.18 (P = 0.24)

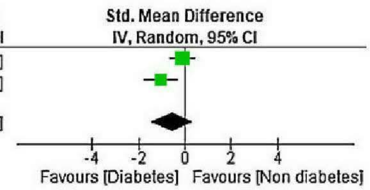

Fig. 7. Forest plot of meta-analysis of hand dexterity of the non-dominant hand comparing type 2 diabetes mellitus (T2DM) and healthy controls (negative mean difference indicates higher mean values in controls).

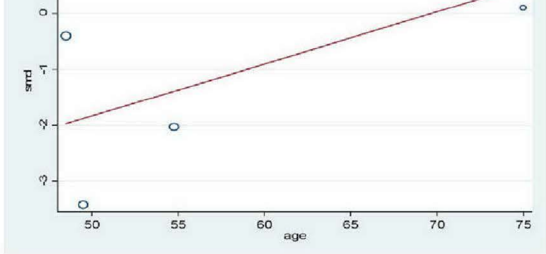

Fig. 8. Meta-regression of effect of mean age on grip strength of the dominant hand.

4.5. *Meta-analysis of grip strength in the dominant hand*

We performed a meta-regression of grip strength in the dominant hand with effect estimates as the dependent variable and mean age as a covariate. Mean age had no effect on the effect estimates (coefficient = 0.09, $P = 0.98$, I^2 residuals = 0%) (Fig. 8), which suggests no effect of age on grip strength measurement in studies. Sub-group analysis of the effect of gender on grip strength of the dominant hand revealed minimal effect of gender (SMD: −1.03; 95% CI: −2.24 to 0.18) (Fig. 9).

5. Discussion

To summarise the result of relevant studies from different geographical areas, our meta-analysis included 7 studies reporting grip and pinch strength as well as hand dexterity and function for people with T2DM versus healthy controls [9–15]. Our results suggest inconsistency and variability among studies in results. We found weak agreement among the studies in reporting our outcomes of interest.

To the best of our knowledge, this is the first meta-analysis reporting on hand function with T2DM. We analysed 3 domains – grip and pinch strength and hand dexterity – which ultimately affect hand function, quality of life, and activities of daily living in people with T2DM.

Our meta-analysis revealed a weak negative mean difference in grip and pinch strength between people with T2DM and healthy controls. Several factors affect hand strength measurements: gender, level of physical activity, age, hand dominance, type of affect strength measurement [14]. However, all the confounding variables were not considered by the studies when assessing strength, which might have influenced the outcome measures and led to varied results.

A number of investigations have involved peripheral neuropathy in lower extremities and its effect on strength. However, few studies have investigated the relation between neuropathy of upper extremities and its effect on strength. Cetinus et al. suggested that low hand strength with T2DM might be due to the severity of the neuropathy, although the authors did not assess this in their study [14,16]. Studies suggested that stiffness of the subcutaneous tissue in the diabetic hand might lead to decreased strength [16].

Dexterity assessed by the Purdue Pegboard test evaluates the gross movement of the fingers, hands, and fine fingertip dexterity necessary in assembling the task. Our meta-analysis of 2 studies of dexterity assessed by the Purdue Pegboard test showed no significant difference in the combined mean for the dominant hand [12,14], which suggests that people with T2DM have good coping strategies to compensate for altered gross motor activity of fingers and hand and fine motor activities of the fingers in the dominant hand. Meta-analysis of the non-dominant hand revealed a negative combined mean, which suggests a poor compensatory mechanism of the non-dominant hand. However, both the studies did not consider confounding factors such as visual co-ordination and involvement of basal ganglia, which might have influenced the dexterity.

Hand function was assessed in 2 studies with 2 validated questionnaires [12,15]. The MD suggested significantly reduced hand function with T2DM. People with T2DM show various disorders of the hand and fingers, which may affect activities of daily living. A study evaluating hand functioning in patients with diabetes and its impact on quality of life in the physical and mental dimensions suggested that impaired hand function leads to lower acceptance of the disease, depression and reduced quality of life [17].

We performed a meta-regression of age and gender on grip strength of the dominant hand to analyse the heterogeneity among the studies, which could have influenced the outcome of interest. Mean age and gender had no influence on grip strength. However, meta-regression of duration of diabetes could not be performed because 2 studies did not report this information.

The limitation of the current analysis was that none of the studies reported a sample size calculation, which might have affected the

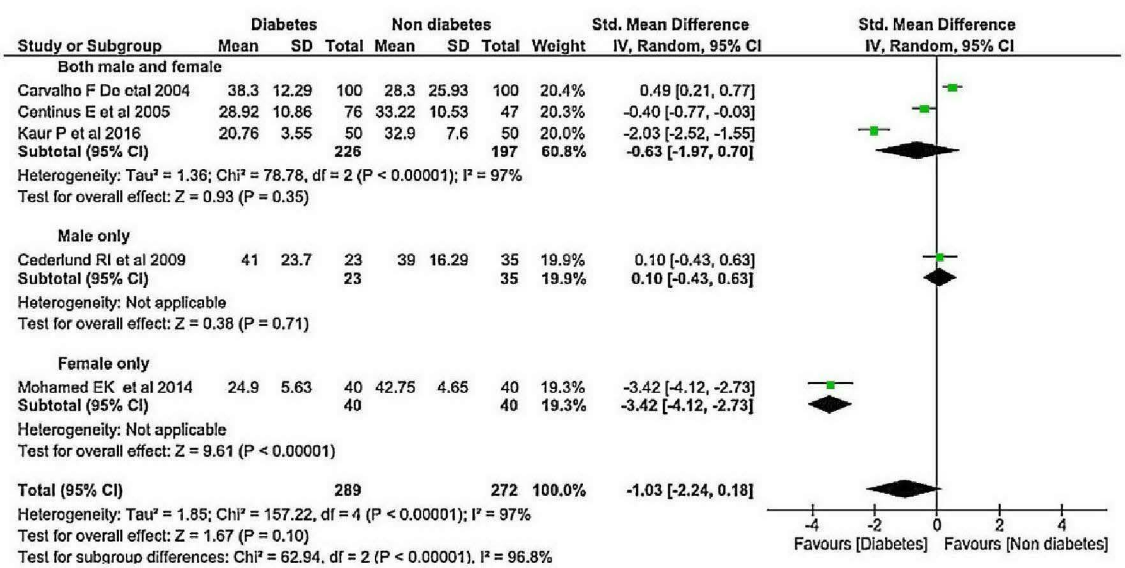

Fig. 9. Meta-analysis of effect of gender on grip strength of the dominant hand.

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