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The prevalence of type 2 diabetes in patients with COVID-19: a systematic review and meta-analysis

ABSTRACT

Background. A strong link between morbidity and mortality from COVID-19 and diabetes mellitus is reported by many studies. The present study estimated the pooled prevalence of diabetes in patients with COVID-19.

Material and methods. International scientific databases were searched until 15 April 2020. There was no limitation in time and language of the published papers. Quality assessment of studies was performed using the Newcastle-Ottawa Scale (NOS) checklist. The random effects model was used to report the pooled prevalence with 95% confidence interval (CI).

Results. The pooled prevalence of diabetes in patients with COVID-19 was 14% (95% CI: 11.17). Due to high heterogeneity (I^2 of 93.4%, $P < 0.001$), three subgroups were analyzed based on study location, age and sex. The prevalence of diabetes (P) was higher among male patients ($P = 16\%$, 95% CI: 0.12, 0.20), patients aged ≥ 65 years ($P = 19\%$, 95% CI: 0.08, 0.31). The prevalence of diabetes was 15% (95% CI: 0.10, 0.20) among patients in Wuhan, China and 10% in patients in other cities in China (95% CI: 0.06, 0.15), and 39% in patients from other countries (95% CI: 0.04, 0.74).

Conclusion. According to the results of this systematic review, the prevalence of diabetes in patients with COVID-19 is higher in other countries compared to China. The prevalence of diabetes among COVID-19 patients was also significantly higher in men and elderly. This evidence may be useful for health policy-makers to design suitable preventive and therapeutic interventions in patients with diabetes and COVID-19. (Clin Diabet 2020; 9; 5: 271-278)

Key words: COVID-19, diabetes mellitus, prevalence, systematic review

Introduction

The outbreak of the new coronavirus disease (COVID-19) from Wuhan, China, began in December 2019 [1] and has been declared as a global emergency by the World Health Organization [2]. People with diabetes mellitus (DM) usually present a more severe morbidity and mortality from COVID-19 [3, 4]. Studies have shown that underlying conditions such as cardiovascular diseases, diabetes, hypertension, and chronic obstructive pulmonary disease (COPD) can exacerbate COVID-19 [5, 6]. There is a significant difference in the mortality of COVID-19 in people with diabetes compared to patients free of diabetes. This proportion varies from 9.7% to 85.54% [7, 8]. A two-fold increase in the chance of COVID-19 mortality among people with diabetes is also reported [9]. Diabetes is one of the most common diseases in the world [10] and its association with COVID-19 disease has been confirmed by many studies [11]. However, the reliability of these findings might be confounded by low sample size and scale of the studies. To get more convincing results, we

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conducted a systematic review and meta-analysis for estimation of the prevalence of diabetes in patients with COVID-19. Notwithstanding, we used both types of diabetes (including diabetes mellitus and type 1 diabetes) in our review of the literature.

Material and methods

Searching strategy

International scientific databases including Web of science, Scopus and PubMed were searched until 15 April 2020. In the PubMed search, we used the following combination of key terms: diabetes mellitus OR diabetes type 2 OR diabetes OR diabetes type 1 AND COVID-19 OR "SARS COV-2" AND prevalence. In the Web of science and Scopus, we used a combination of key terms: COVID-19, SARS COV-2, coronavirus and diabetes, diabetes mellitus.

Inclusion/exclusion criteria

All cross-sectional studies reporting prevalence of diabetes in patients with COVID-19 were eligible for the study. There was no limitation in the time and language of the published papers. Exclusion criteria included other types of observational studies (including letter to the editor, review articles, and case reports), books, editorials, conference abstracts, and notes. These studies did not include the minimum data required for extraction.

Data collection

To ensure the correct selection of articles according to the inclusion criteria, two researchers (MFG and NA) were responsible for selecting articles independently. In cases of a disagreement, it was decided through negotiations with the third person (HM). First, all articles related to the prevalence of diabetes as well as articles related to COVID-19 were collected. At this stage, screening was conducted on all articles based on the keywords in their title or abstract. Then, full-text of articles reporting the prevalence of diabetes in patients with COVID-19 were assessed thoroughly. The following variables were extracted from the selected studies: name of the first author, study location, sample size, number of people with diabetes and COVID-19, median age, gender, type of diabetes and diagnosis method for COVID-19. Quality assessment of studies was performed using the Newcastle-Ottawa Scale (NOS) checklist. Using the Newcastle-Ottawa Scale (NOS), we used selection and outcome domains with the following items: representativeness of the sample, determining the sample size, assessing the outcome, and statistical tests [12]. The evaluation was done independently by three researchers (MFG and NA and

SN). Any disagreement between the researchers were resolved through negotiation.

Heterogeneity assessment and statistical analysis

Heterogeneity of studies was determined by the forest plot diagram and statistical tests. The statistical tests included Chi-square, X^2 , I^2 and Tau² [13, 14]. The random effects model was used to report the results with 95% confidence interval (CI). We used Stata 14 software to analyze the data.

Results

Search and selection

A total of 216 articles were retrieved initially including 187 records in the PubMed database, 18 records in the Web of science database, 11 records in the Scopus database. After the duplication removal, a total of 182 articles remained including 176 in the PubMed database and 6 in the Web of science database. After reviewing the title and abstracts, 23 articles that reported the prevalence of diabetes in people with COVID-19 were entered the data extraction phase and the rest of the articles were excluded. Using the NOS checklist, the quality of 23 articles was evaluated and finally 20 articles (total sample size of 5515) were entered into the meta-analysis. The studies included cross-section and case series. Of the 20 studies that entered into the meta-analysis, most were conducted in Wuhan, China ($n = 12$, 60%) and six (28.5%) were conducted in other parts of China and only two (10%) in other countries (France and the United States) (Figure 1).

Heterogeneity test

According to the results of the chi-square test, heterogeneity of studies was significantly high, yielding an I^2 of 93.4% ($P < 0.001$). Although we could not combine these studies, we reported an estimate of the prevalence of diabetes in patients with COVID-19. As a result, to reduce heterogeneity, we divided the included studies into subgroups based on study location, age, and gender.

Estimate of prevalence

The prevalence of diabetes in patients with COVID-19 was 14% (95% CI: 11,17%) (Figure 2). The lowest prevalence of diabetes in patients with COVID-19 (2.7%) was reported by Wang, Xiaobing et al. [15] in Wuhan, China, and the highest prevalence (58%) was reported in Washington DC, the US [16] (Figure 3). The mean (\pm SD) of prevalence in the remaining studies was 17% (\pm 12%) (Tables 1, 2). In this study, the Egger test was used to diagnose publication bias, and the Egger test was significant ($P = 0.001$) and had a confidence

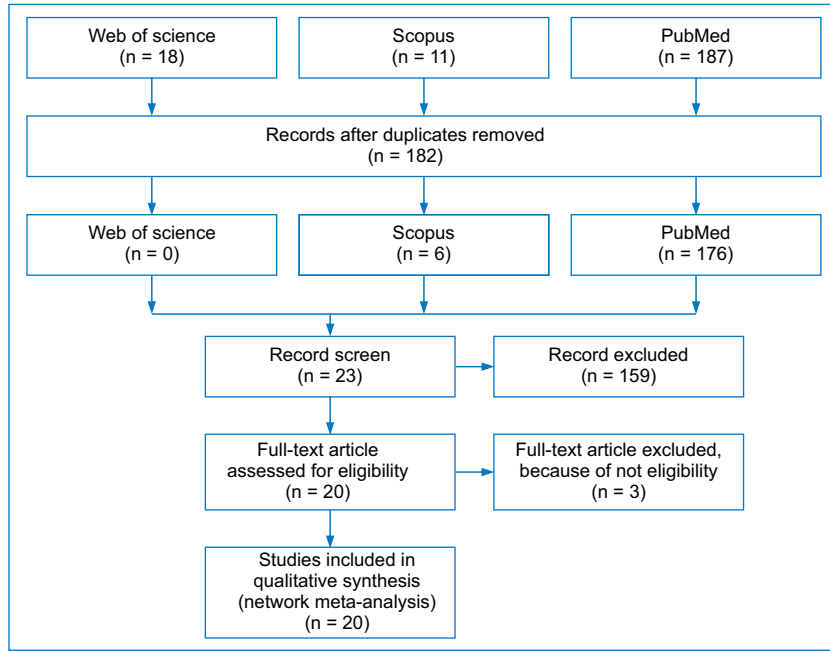


Figure 1. PRISMA flow diagram of the included studies

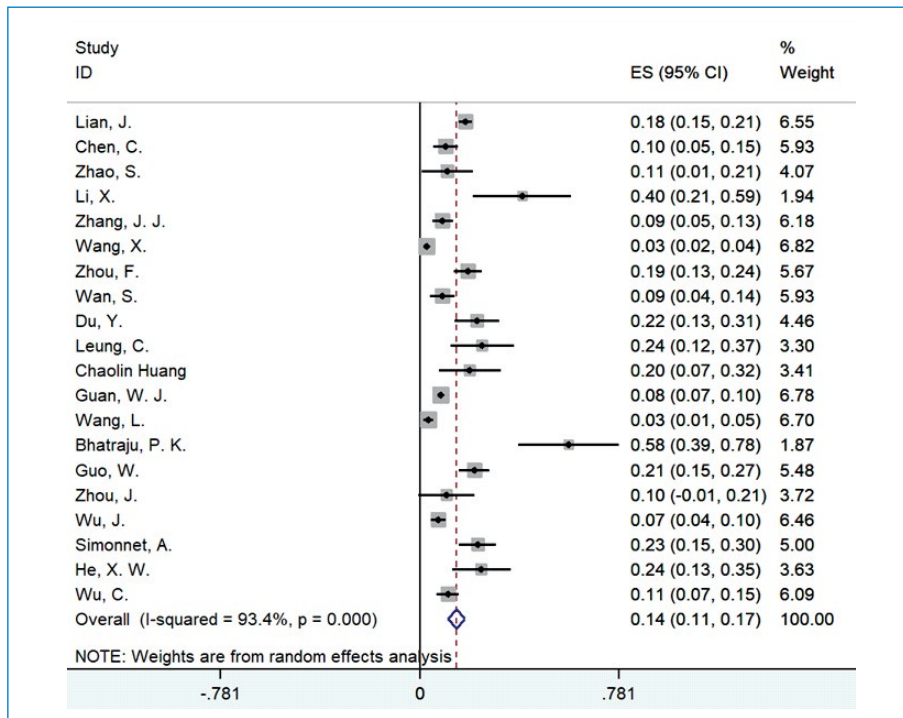


Figure 2. Funnel plot for prevalence of diabetes in patients with COVID-19. % heterogeneity = 93.4% (95% CI); P for heterogeneity = 0.001

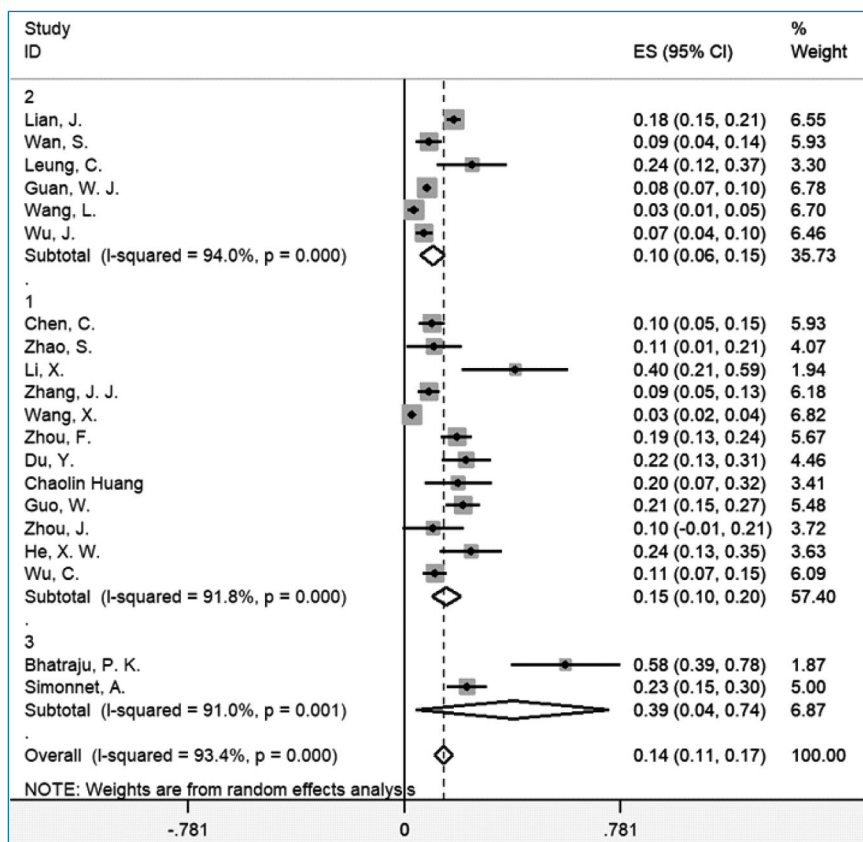


Figure 3. The results of meta-analysis of prevalence of diabetes in patients with COVID-19 according to study location. 1 — Wuhan, China; 2 — other place in China; 3 — other countries (France and Washington in the United States)

interval of 2.28 to 5.85, indicating a publication bias (Figs 6, 7).

Discussion

Currently, the geographical spread and mortality of COVID-19 disease, as well as the rapid transmission of the disease, have raised concerns among countries [17]. So far, there is not any confirmed medication for COVID-19 while the situation gets worsen in those with diabetes. In this subgroup of patients, COVID-19 progresses rapidly, and respiratory failure can occur in a short time, which probably leads to death [18, 19]. The most common symptoms among diabetic patients with COVID-19 were fever (85.6%), cough (68.7%) and fatigue (39.4%). The most common comorbidities included high blood pressure (17.4%), hypertension (17.4%), diabetes (3.8%), and coronary heart disease (3.8%). A recent study and meta-analysis of 24 studies confirmed that fever and cough are the most common symptoms in COVID-19 patients with diabetes mellitus [20]. Our study showed that the prevalence of diabetes in patients with COVID-19 was 14%. However, a systematic review of 1556 patients in 24 studies by Andrea Lovato et al. on the prevalence of diabetes in patients with COVID-19 showed that the prevalence in

these patients was 3.8% [20]. This difference may be due to differences in sample size, location of the study, data collection technique, and the sex and age of the patients. In our study, the prevalence was very different, from 2% [15] in China to 58% [16] in Washington. Due to the high heterogeneity, we preferred to classify these studies according to subgroups.

Due to the change in the prevalence of diabetes in people with COVID-19 in different regions, we divided the geographical areas into three categories: Wuhan in China, other cities in China and other countries. The prevalence of diabetes in Wuhan, China (15%) was higher than other Chinese cities (10%). In countries like the United States and France, it was more than twice as high as in China (39%). Another risk factor for unchanged COVID-19, which has been the subject of numerous studies, is gender [21, 22]. Our study found that more than 50 percent of diabetic patients with COVID-19 were men. Older age is another factor that has led to a higher incidence of diabetes in people with COVID-19 [22]. Our study identified age over 65 as a risk factor and found that 20 percent of elderly patients with COVID-19 had diabetes. Obviously, one must be very careful in interpreting these results because our study has several limitations. The main limitation of the study was related to the low quality of

Table 1. Characteristics of the included studies in systematic review of the prevalence of diabetes in patients with COVID-19*

ID	First author	Study location	Type of diabetes	N. of COVID-19 patients with diabetes	Sample size	Prevalence of diabetes in patients with COVID-19	Median age	IQR	N. of males	N. of females
1	Lian J.	Wuhan, China	Diabetes	141	788	0.18	41.15	30-52	407	381
2	Chen C.	Wuhan, China	Diabetes	15	150	0.10	57	41-72	84	66
3	Zhao S.	Wuhan, China	Diabetes	4	37	0.11	41	21-61	14	23
4	Li X.	Wuhan, China	Diabetes	10	25	0.40	73	55-100	10	15
5	Zhang J.J.	Wuhan, China	Diabetes mellitus	17	140	0.09	57	25-87	72	119
6	Wang X.	Wuhan, China	Diabetes	27	1012	0.03	50	39-58	524	488
7	Zhou F.	Wuhan, China	Diabetes	36	191	0.19	56.0	46.0-67.0	119	72
8	Wan S.	China	Diabetes	12	135	0.09	47	36-55	72	63
9	Du Y.	Wuhan, China	Diabetes	19	85	0.22	65	51-79	62	23
10	Leung C.	China	Diabetes	11	45	0.24	70.6	52.0-80.5	30	15
11	Chaolin Huang	Wuhan, China	Diabetes	8	41	0.20	49.0	41.0-58.0	30	11
12	Guan W.J.	Mainland China	Diabetes	130	1,590	0.08	48.9	32-64	904	674
13	Wang L.	China	Diabetes	11	339	0.03	71	63-79	166	173
14	Bhatraju P.K.	Washington	Diabetes mellitus	14	24	0.58	64	46-82	15	9
15	Guo W.	Wuhan, China	Diabetes	37	174	0.21	59	49-67	76	98
16	Zhou J.	Wuhan, China	Type 2 diabetes	3	NA	0.10	69	54-81	NA	NA
17	Wu J.	China	Diabetes	20	280	0.07	43.12	24-62	129	151
18	Simonnet A.	French	Diabetes	28	124	0.23	60	51-70	90	34
19	He X.W.	Wuhan, China	Diabetes	13	54	0.24	68	59.8-74.3	34	20
20	Wu C.	Wuhan, China	Diabetes	22	201	0.11	51	43-60	128	74

NA — not available

*All studies were published in 2020

Table 2. Subgroup analysis for prevalence of diabetes in patients with COVID-19*

Variable	Prevalence	95% CI	I ² (%)	P value*
Geographic area (Figure 3)				
Wuhan, China	0.15	0.10–0.20	91.8	< 0.001
Other places in China	0.10	0.06–0.15	94.0	< 0.001
Other countries (France and the United States)	0.39	0.04–0.74	91.0	< 0.001
Gender (Figure 4)				
Male < 50 %	0.12	0.06–0.17	89.5	< 0.001
Male ≥ 50 %	0.16	0.12–0.20	94.9	< 0.001
Age (Figure 5)				
Median age < 65	0.13	0.1–0.17	94.4	< 0.001
Median age ≥ 65	0.19	0.08–0.31	90.3	< 0.001

*P value for heterogeneity test

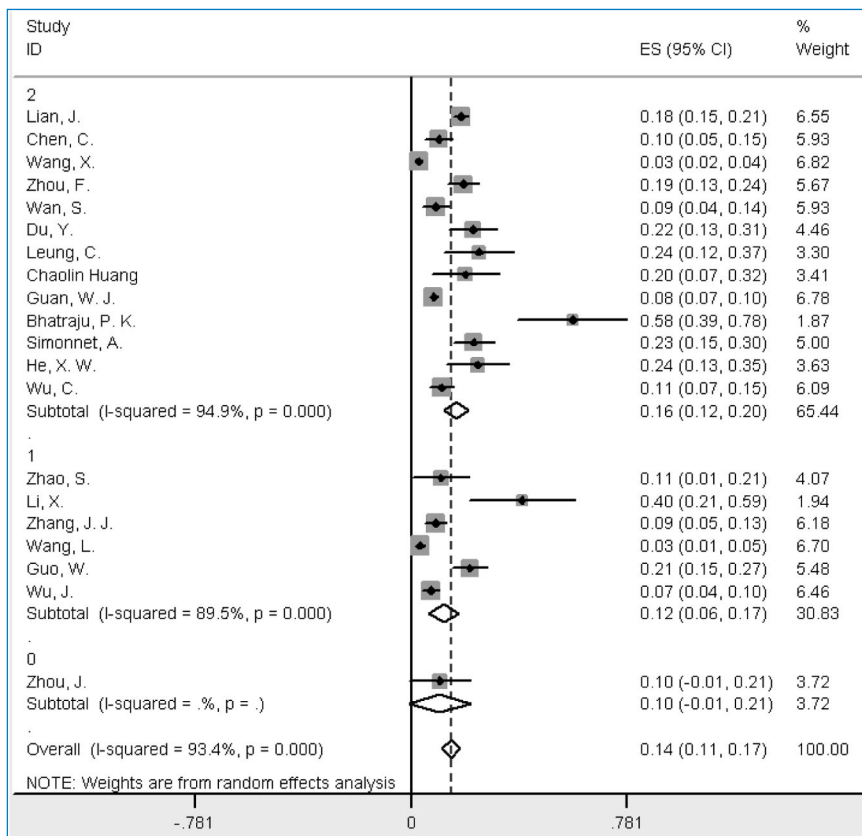


Figure 4. The results of meta-analysis of the prevalence of diabetes in patients with COVID-19 according to gender. 1 — male < 50%; 2 — male ≥ 50%; 0 — **NA (not available)

included evidence (most of the studies were retrospective) and it may not represent the general population. The sample size was also small in some instances, which may affect the results. The next point was that the different examinations and grades were not uniform for the severe and non-severe patients in the included studies. Also, some studies included patients with more than

one common disease. The quality of the studies was not similar, which may affect the results. In addition, most of the studies were conducted in China, and we studied only two countries except China. One of the strengths of the study is that so far, no comprehensive study has been conducted to summarize the prevalence of diabetes in people with COVID-19.

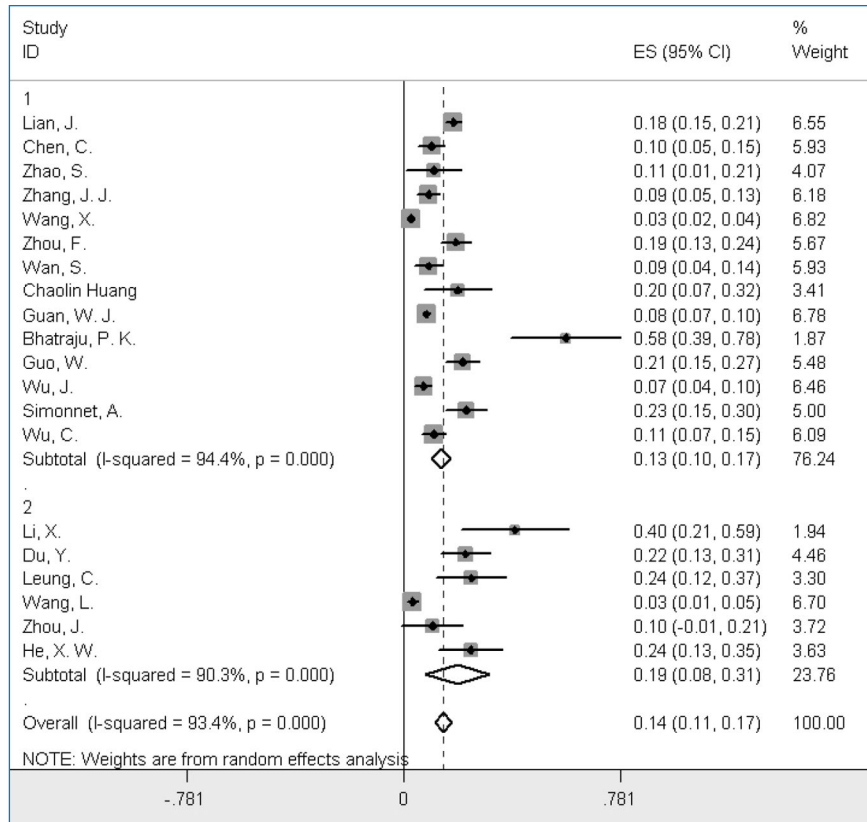


Figure 5. The results of meta-analysis of the prevalence of diabetes in patients with COVID-19 according to age. 1 — median age < 65; 2 — median age ≥ 65

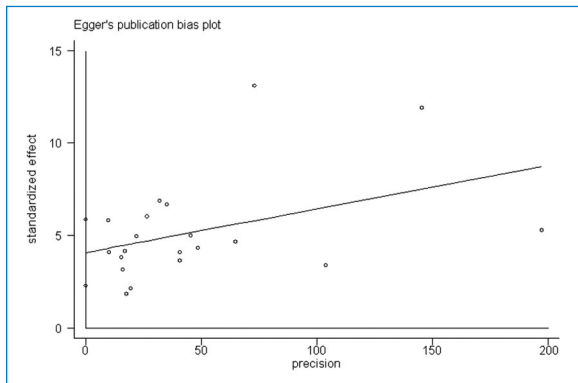


Figure 6. The Egger test for diagnosing publication bias for prevalence of diabetes in patients with COVID-19

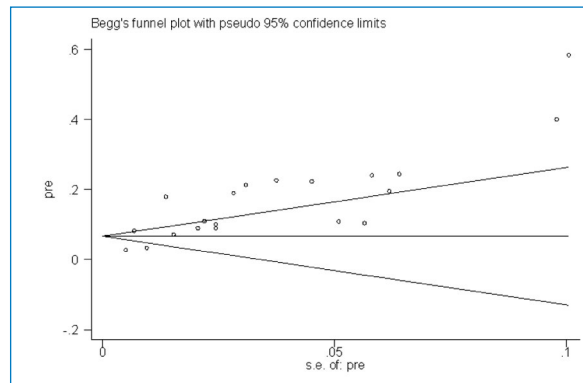


Figure 7. The Begg test for diagnosing publication bias for prevalence of diabetes in patients with COVID-19

Conclusion

The results of this systematic review showed that diabetes in patients with COVID-19 is not negligible. The prevalence of this disease in different areas can vary depending on lifestyle. According to the results of this systematic review, the prevalence of diabetes in patients with COVID-19 is higher in other countries compared to China. The prevalence of diabetes among

COVID-19 patients was also significantly higher in men and elderlies. This evidence may be useful for health policymakers to design suitable preventive and therapeutic interventions in cases with comorbidity of diabetes and COVID-19. It seems that diabetes is an important underlying condition that should be taken into account when developing and implementing interventions to reduce the burden of COVID-19.

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Conflict of interest

The authors declare no competing interests.

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