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The prevalence of obstructive sleep apnea in patients with type 2 diabetes: a systematic review and meta-analysis

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Abstract

Background: Obstructive Sleep Apnea (OSA) is one of the diseases related to diabetes. Considering the varying prevalence of OSA in patients with type 2 diabetes in different parts of the world, in order to aggregate the results and come to a general review about the topic mentioned, the current study performed a systematic review and meta-analysis of OSA in patients with type 2 diabetes.

Methods: In this study, the international databases (PubMed, Scopus, Web of science, and Cochran library) were searched without time limit using keywords diabetes, obstructive sleep apnea, and prevalence or epidemiology. Homogeneity was investigated among studies using Cochran Q test and I^2 index. Given the heterogeneity of studies, random effect model was used to estimate the prevalence of OSA. Meta-regression was used to investigate the effect of quantitative variables on the prevalence of OSA. Comprehensive Meta-analysis (CMA) software was used for data analysis.

Results: Twenty studies were included in the meta-analysis. In these 19 studies, the total number of patients with type 2 diabetes was 10,754, with a mean age of 58.6 ± 4.1 years. Final estimation of OSA prevalence was calculated to be 56.0%. The results of meta-regression showed the prevalence of OSA increased with a rise in the mean age, the percentage of male sex, body mass index, and sample size.

Conclusion: Given the high prevalence of OSA in patients with type 2 diabetes, weight control can partly mitigate their problems and possibly reduce OSA prevalence.

Keywords: Meta-analysis, Obstructive sleep apnea, Prevalence, Systematic review, Type 2 diabetes

Introduction

Type 2 diabetes is a chronic disease in which the body is unable to use and store glucose and instead of being converted into energy, glucose returns to the bloodstream and causes various symptoms (Srinivasan et al. 2018a). The prevalence of diabetes worldwide is estimated to be 4.6%, having a significantly increasing trend over the past two decades (Shaw et al. 2010). Moreover, the prevalence of type 2 diabetes in Iran has been reported to be 24%, indicating 4% annual increase over the past 20 years (Aamir et al. 2019). It is necessary to try to understand the factors associated with diabetes in order to prevent the increasing problems of these patients (Botros et al. 2009). Identification of potentially changeable risk factors for diabetes is still a clinical and public health priority (Nagayoshi et al. 2016). Obstructive Sleep Apnea (OSA) is one of the diseases related to diabetes; the two diseases

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are too common and both have common risk factors like obesity (Nannapaneni et al. 2013; Altaf et al. 2016; Mok et al. 2017).

There is a two-way relationship between OSA and diabetes; diabetes is one of the risk factor for OSA and OSA is a risk factor for diabetes (Jehan et al. 2018). The prevalence of OSA is different in independent studies. A study in China estimated the prevalence of type 2 diabetes to be 38.0% (Srinivasan et al. 2018b). This rate has been reported to be 86.0% in another study in the U.S (Foster et al. 2009). Further, in two independent studies in Iran, the prevalence rates of OSA in patients with type 2 diabetes has been reported to be 74.0 and 54.0% (Nasseri et al. 2015; Sadeghniiat-Haghighi et al. 2015). To the best of our knowledge, a meta-analysis study has not yet examined the prevalence of OSA in type 2 diabetic patients. So, due to differences in the prevalence of OSA in patients with type 2 diabetes, in order to summarize the results and gain an overview of the topic, the present study was aimed to carry out a systematic review and meta-analysis of the prevalence of OSA in patients with type 2 diabetes. The results of this study are hoped to be used by the healthcare policymakers.

Materials and methods

The present systematic review and meta-analysis investigated the prevalence of OSA in patients with diabetes based on the articles published in English journals without time limitation. In this study, the articles published in journals available in the international databases, including PubMed, Scopus, Web of Science, and Cochran library were used. The articles were searched using the keywords diabetes, obstructive sleep apnea, and prevalence or epidemiology. Searching strategies were as follows:

> ((diabetes [Title/Abstract]) AND "obstructive sleep apnea"[Title/Abstract] AND prevalence [Title/Abstract])
> ((diabetes [Title/Abstract]) AND "obstructive sleep apnea"[Title/Abstract] AND epidemiology [Title/Abstract])

In order to reduce bias, the articles were searched independently by two researchers (the first and second authors), and in case of disagreement over a study, that article was judged by the supervisor of the research team (the fifth author). At first, all extracted articles were fed into the Endnote software and then the duplicate articles were deleted using the *duplicate* command. In the next step, the titles and abstracts of all papers were reviewed by the researchers and unrelated articles were removed. The remaining articles were evaluated based on the inclusion criteria using the STROBE checklist. The inclusion criteria were articles published until 27.9.2018 and being written in English and existence of title and keywords in the abstract. In these articles, the criteria for diagnosing OSA was apnea–hypopnea index $\geq$5 or a positive score in more than two categories of the Berlin questionnaire. Type 2 diabetic patients included those whose diagnosis had been confirmed and were treated with hypoglycemic drugs. The exclusion criteria were topics irrelevant to the subject matter, case reports, duplicate studies, uncertain method and sampling method, and lack of access to the full text of the studies. Data of the selected articles, such as title, first author's name, year of publication, place of study, participants' mean age, participants' sex percentage, sample size, and number and percentage of patients with type 2 diabetes who had OSA were extracted and recorded. In addition, since a questionnaire was used in some studies to diagnose OSA and sleep monitoring devices were used in others, in order to investigate the effect of diagnostic method on the prevalence of OSA in patients with type 2 diabetes, the information about the diagnostic method was extracted and used to analyze the results in each study.

Article selection

Searching the databases started on October 27, 2018 without time limitation. A total of 961 articles were extracted from the databases, 406, 89, 454, and 12 articles from PubMed, Cochran library, Scopus and Web of science, respectively. Of these, 341 articles were duplicate and were excluded. Of 620 articles, 569 articles were excluded because they were irrelevant to the research subject, so 51 articles remained for analysis (full text). Of these 51 full text articles, 9 articles were in non-English language. In 13 studies, target populations were diabetic patients at high risk and in 5 articles, patients with type 1 diabetes were examined. The content of one of the articles was repetitive and 2 articles examined the prevalence of diabetes in patients with OSA, so they were excluded from the study. Two other articles were also excluded because they used reading medical document method and the OSA diagnostic tool was not explained. The full text of all the studies included in the final stage was available. The Joanna Briggs Institute Prevalence Critical Appraisal Tool was used to evaluate the quality of these articles. This tool has 10 items and each item has four options including "yes, no, unspecified, and not applicable". The yes option is awarded one point and the other options are awarded zero points. The rating range is between zero and 10 (Munn et al. 2014). Studies that scored equal to or higher than 5 were included in the current study. Eventually, 18 articles were included in the meta-analysis. Since two groups of Asian and European

subjects were separately examined in one of the articles, the data were separately fed into the software; in fact, the data of 19 studies were fed into the software (Fig. 1).

Statistical analysis

Comprehensive Meta-analysis (CMA) software was used to analyze the data. The prevalence of OSA was extracted from the articles. Then, the variance of each study was determined by binomial distribution. Weighted mean was used to combine the prevalence of various studies. Each study was weighted proportional to its variance inverse. Heterogeneity between studies was reviewed using the heterogeneity test Cochran Q and I^2 index. According to the heterogeneity of the studies, random effects model was used to estimate the prevalence. The impact of omission of each study was assessed by sensitivity analysis. To investigate the publication bias, the funnel plot and Begg and Mazumdar's rank correlation test were used. To examine the effect of OSA evaluation tool on the prevalence, two groups of questionnaires and devices were compared. Meta-regression was also used to study the effect of quantitative variables, including age, year of study, sample size, body mass index, and gender percentage. All tests were performed with 95% confidence.

Results

Eighteen articles were included in the meta-analysis. According to the STROBE checklist, the articles included in the meta-analysis had good quality. Since one of the articles had been conducted on the Asian and European patients, its data were recorded in two separate studies; hence, 19 studies were analyzed. The total number of patients with type 2 diabetes in these 19 studies was 10,754, with a mean age of 58.6 ± 4.1 years. The highest and lowest prevalence rates of OSA were belonged to Israel (90.3%) and Saudi Arabia (15.2%), respectively (Donovan et al. 2017; Kalakattawi et al. 2017).

The OSA diagnostic tool was a questionnaire in eight studies, while it was a sleep monitoring device in 12 studies (Table 1). After initial calculations, the heterogeneity of the studies was significant based on the heterogeneity indices ($Q = 1922.946$ and $I^2 = 99.012$) ($P < 0.001$). For this reason, the random effects model was used in all

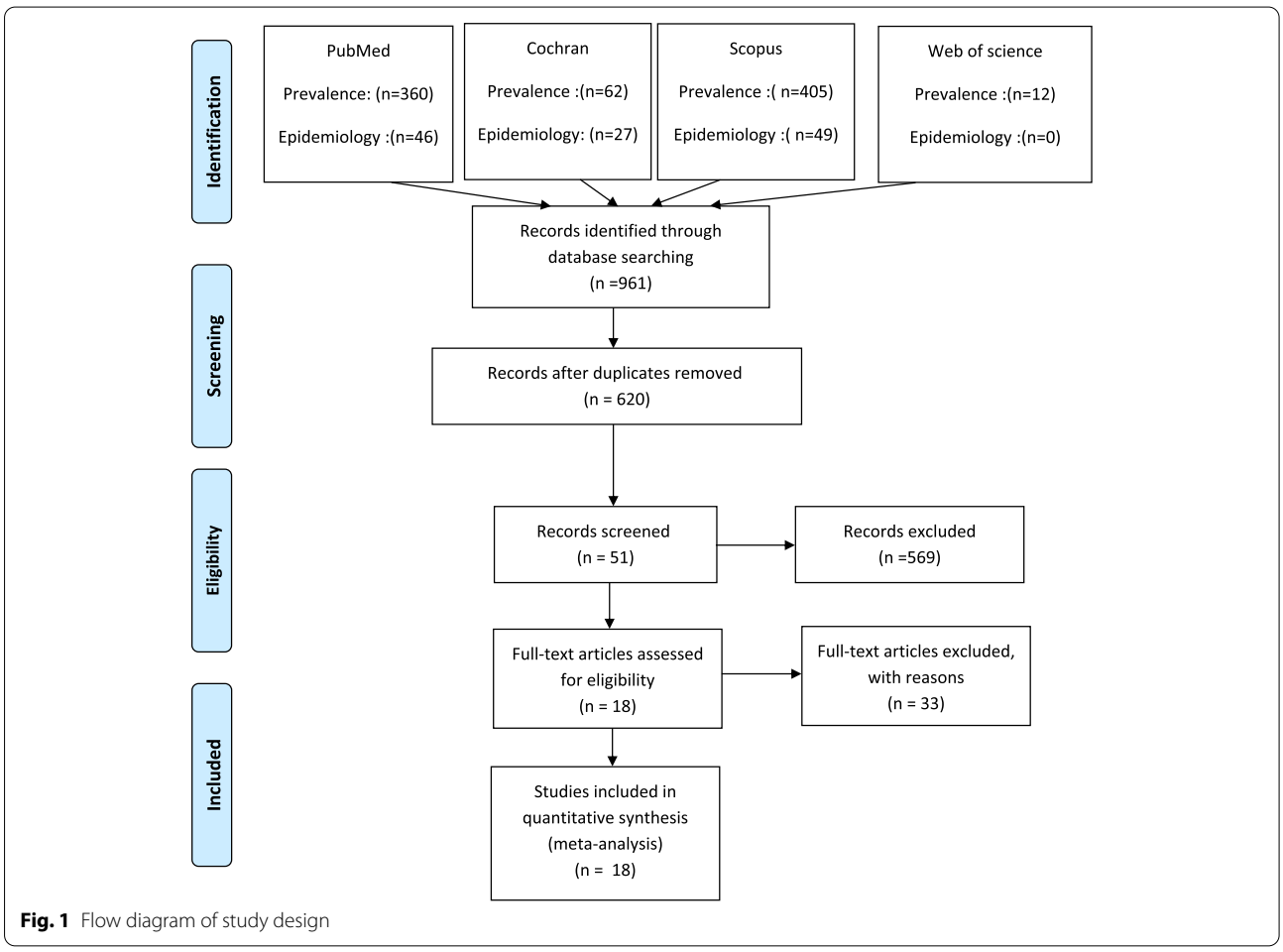

Fig. 1 Flow diagram of study design

Table 1 Specifications of the included studies

Author Name	Year of study	Place of study	OSA diagnostic tool	Sample size	Prevalence (%)	Average age	Men (%)[a]	Mean of BMI[ab]	Quality assessment
Kalakattawi et al.	2017	Saudi Arabia	Questionnaire	197	15.2	56.1	0.44	_	7
Lam et al.	2010	Hong kong	Device	824	53.9	57.4	0.62	26.0	8
Lecome et al.	2012	France	Questionnaire	3894	85.0	66.0	0.58	–	8
Nasseri et al.	2015	Iran	Questionnaire	173	54.0	55.4	–	27.9	10
Obaseki et al.	2014	Nigeria	Questionnaire	117	27.0	63.0	0.44	27.5	8
Ozol et al.	2011	Turkey	Questionnaire	237	47.3	58.6	0.53	30.3	6
SHim et al.	2011	South Korea	Questionnaire	784	15.8	54.0	0.50	24.8	9
Sokwalla et al.	2017	Kenya, Africa	Questionnaire	223	44.4	56.8	0.46	28.8	9
Tahrani et al.	2012	UK	Device	234	65.0	58.5	0.67	34.4	7
Vale et al.	2015	Portugal	Device	23	60.0	62.2	0.30	29.2	7
Viswanathan et al.	2017	Chennai	Device	203	23.6	54.0	0.71	29.1	8
Westlake et al.	2016	Prague	Device	294	72.0	64. 7	0.59	31.1	7
Zhang et al.	2016	China	Device	880	60.0	60.5	0.53	25.1	10
Zhang et al.	2015	China	Device	337	66.7	54.5	_	26.5	10
Burgess, K.R	2013	Queensland and New South Wales	Device	1109	71.0	53.0	0.62	31.8	8
Amin et al. (Asians)	2017	South Asians	Device	105	51.0	54.5	0.58	30.7	9
Amin et al. Europeans)	2017	Europeans	Device	129	75.2	59.3	0.57	37.4	9
Donovan et al.	2017	Israel	Questionnaire	818	90.3	63.5	_	32.5	8
Sadeghniiat et al.	2015	Iran	Questionnaire	173	74.0	61.6	0.44	28.8	9

[a] Cells that are empty have not been reported in the relevant articles

[b] Body Mass Index

subsequent stages. The results of funnel plot and Begg and Mazumdar's rank correlation test showed no publication bias (Fig. 2). The final estimate of the prevalence of OSA was calculated to be 56.0% (Fig. 3). In order to analyze the sensitivity, each study was excluded from the analysis and the final estimate of OSA prevalence was calculated, which had no significant effect.

Regarding the heterogeneity of the results of the studies, meta-regression models were used to find the influential factors (heterogeneity). The results showed the prevalence of OSA elevated significantly with an increase in the mean age in studies ($p < 0.001$). The results of meta-regression showed a statistically significant relationship between the prevalence of OSA and sample size, and that the prevalence of OSA increased with an increase in the sample size ($p < 0.001$). However, the year of study did not have a significant effect on the prevalence of OSA. Meta-regression was also used to examine the effect of sex percentage on the prevalence of OSA. The results showed the prevalence of OSA increased with a rise in the male percentage ($p < 0.001$). The results also revealed that with increasing BMI, the prevalence of OSA increased ($P < 0.001$). The graphs for meta-regression are shown in Fig. 4. The results showed that the prevalence of OSA in the studies using questionnaire was not significantly different from that of the sleep monitoring devices (Fig. 5).

Discussion

This systematic review and meta-analysis was aimed to determine the prevalence of OSA in patients with type 2 diabetes. The results showed that the total number of patients with type 2 diabetes in this study was 10,754, with a mean age of 58.6 ± 4.1 years. In our study, the final estimate of the prevalence of OSA was calculated to be 56.0%. The prevalence of OSA in patients with type 2 diabetes varied from country to country, ranging from 15.2 to 90.3% (Lam et al. 2010; Ozol et al. 2011; Shim et al. 2011; Tahrani et al. 2012; Burgess et al. 2013; Lecomte et al. 2013; Obaseki et al. 2014; Nasseri et al. 2015; Sadeghniiat-Haghighi et al. 2015; Vale et al. 2015;

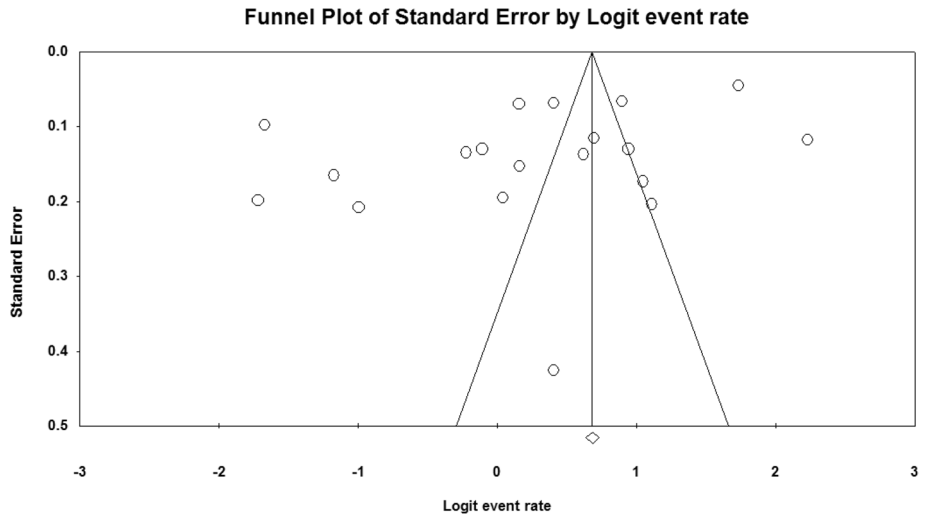

Fig. 2 Funnel plot for checking publication bias

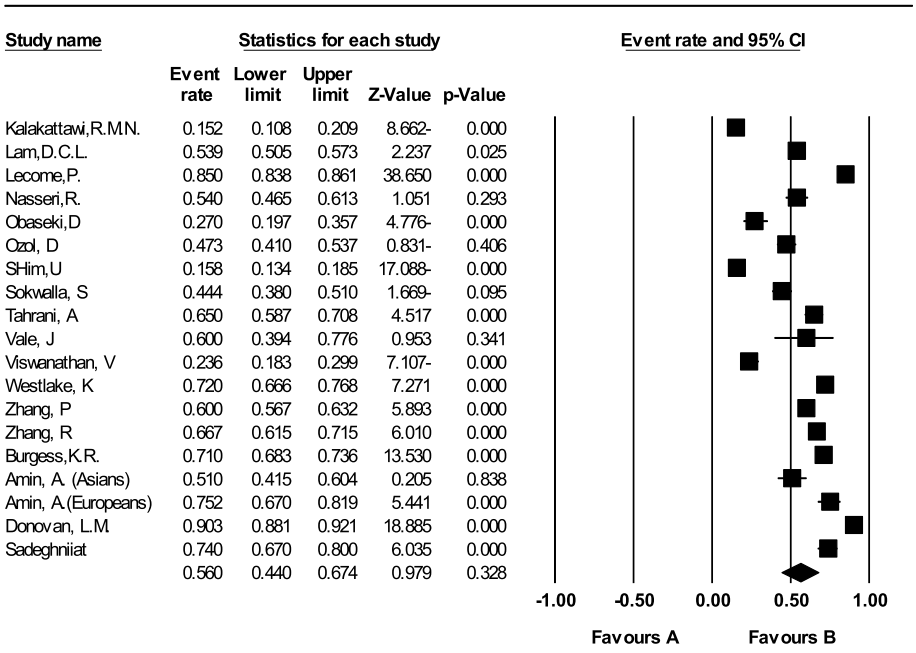

Fig. 3 Forest plot for the prevalence of OSA in type 2 diabetic patients

Zhang et al. 2015, 2016; Westlake et al. 2016; Amin et al. 2017; Donovan et al. 2017; Kalakattawi et al. 2017; Sokwalla et al. 2017; Viswanathan et al. 2017). The highest and lowest prevalence of OSA were related to Israel (90.3%) and Saudi Arabia (15.2%), respectively (Donovan et al. 2017; Kalakattawi et al. 2017). The prevalence of OSA in adults is estimated at 1 billion people worldwide, with a prevalence of more than 50.0% in some countries (Benjafield et al. 2019), which is much lower than the results of our study. In fact, our findings show that OSA is more common in people with type 2 diabetes than in non-diabetic group people.

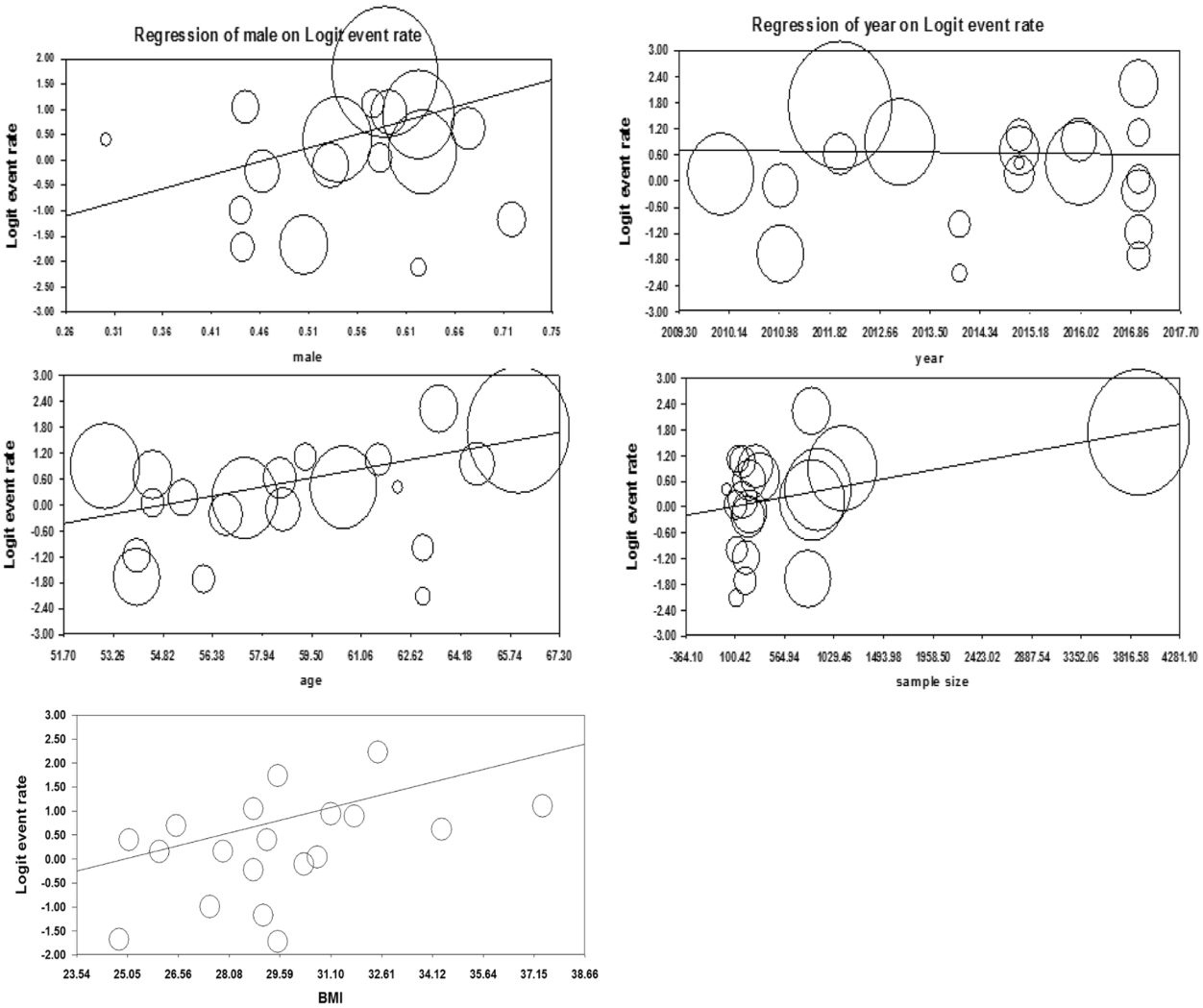

Fig. 4 Scatter plot for the relationship between OSA and Percent of men, year of stydy, age, BMI, and sample size

The variables sample size, age, and gender were introduced as factors causing heterogeneity in the meta-regression analysis. Studies with a larger sample size were more prevalent. The prevalence of OSA also increased as the number of men rose in the studies. This relationship was also observed for age so that the prevalence of OSA increased significantly with an increase in mean age. Evidence suggests that age and male gender are the factors that increase the vulnerability of patients with OSA (Durán et al. 2001; Punjabi 2008). The results of a study in Saudi Arabia (2017) indicated that the risk of prevalence of OSA increased with an increase in the age of the diabetic patients (Kalakattawi et al. 2017). Another study in China (2015) showed that the chance of OSA prevalence elevated with an increase in the age of the diabetic patients (Zhang et al. 2015).

In our study, the results showed that with increasing BMI, the prevalence of OSA increases. This finding is consistent with previous studies (Schwab et al. 2003, JP, J 2014; Basoglu et al. 2015; Dong et al. 2020). Evidence suggests that obesity is a common cause of OSA and diabetes (Nannapaneni et al. 2013; Altaf et al. 2016). Lifestyle modification and weight control are vital factors, especially in the male patients with diabetes (Kline et al. 2011). Changing the lifestyle and performing routine exercises can help to prevent obesity and decrease the risk of OSA in patients with type 2 diabetes (Kline et al. 2011; Hargens et al. 2013; Miller et al. 2015).

In order to diagnose OSA, some studies used questionnaires, including STOP-BANG, The Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and BERLIN questionnaire and some other studies used devices such as Alice PDX, PSG, Apnealink,

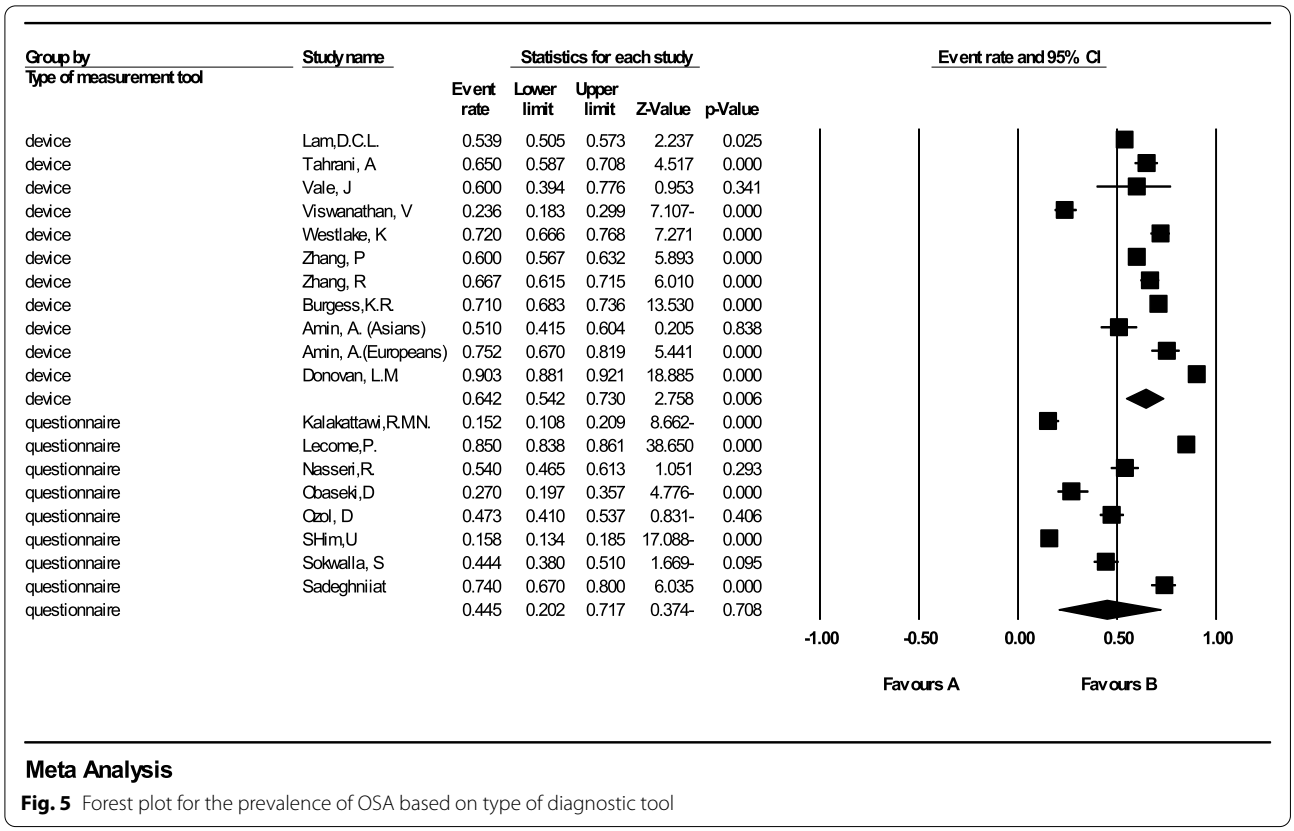

Fig. 5 Forest plot for the prevalence of OSA based on type of diagnostic tool

and night sleep monitors. The results showed no significant difference in the prevalence of OSA between studies using the questionnaire and those using sleep monitoring devices. According to Gantner et al. (2010), the accuracy of the BERLIN questionnaire was lower in OSA diagnosis than in PSG and Apnealink devices. Given the high prevalence of OSA in patients with type 2 diabetes and the cost-effectiveness of the questionnaire, diabetics can be tracked using a screening questionnaire and polysomnography in the first and second steps, respectively. With the early diagnosis of the diabetic patients' problems, solutions and treatments for these patients can be considered (Gantner et al. 2010). Regarding the high prevalence of OSA in patients with type 2 diabetes and the presence of risk factors such as old age and male gender, it is important to take health and medical planning into account to decrease the prevalence of OSA.

This study faced three limitations. The first limitation was the lack of uniform distribution of studies in different parts of the world. Lack of information, such as the OSA report by gender, was the second limitation. The third limitation was the lack of search for gray resources due to lack of access.

Conclusion

The prevalence of OSA was estimated to be 56.0%. The results of meta-regression showed that the prevalence of OSA increased with an increase in the mean age, male gender percentage, BMI, and sample size. Since screening diabetic patients with OSA has not been performed in many parts of the world and there is no accurate information on the prevalence of OSA in patients with type 2 diabetes, it seems that more precise national planning is needed to screen the prevalence of OSA in the country and other parts of the world.

Abbreviations

ESS: Epworth Sleepiness Scale; OSA: Obstructive sleep apnea; PSQI: Pittsburgh Sleep Quality Index.

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Authors' contributions

BA, MJ, AK, AS, MJ and SMA contributed in designing the study, BA, SMA, and AK collected the data, and analyzed by BA. The final report and manuscript were written by BA, AK, AS, MJ and SMA. All authors read and approved the final manuscript.

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Availability of data and materials
The identified datasets analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by research ethics committee of Kermanshah University of Medical Sciences.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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