Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 2463–2468

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Prevalence of obstructive sleep apnea in patients with type 2 diabetes: A systematic review and meta-analysis

Arezoo Fallahi [a], Dashty Ismil Jamil [b], Elnaz Beghban Karimi [c], Vajiheh Baghi [d], Reza Ghanei Gheshlagh [e, *]

[a] Social Determinants of Health Research Center, Research Institute for Health Development, Kurdistan University of Medical Sciences, Sanandaj, Iran
[b] Department of Health and Hospital Administration, Lebanese French University, Erbil, Kurdistan, Iraq
[c] Imam Reza Hospital, Tabriz University of Medical Sciences, Tabriz, Iran
[d] Be'sat Hospital, Kurdistan University of Medical Sciences, Sanandaj, Iran
[e] Clinical Care Research Center, Research Institute for Health Development, Kurdistan University of Medical Sciences, Sanandaj, Iran

ARTICLE INFO

Article history:
Received 29 May 2019
Accepted 27 June 2019

Keywords:
Obstructive sleep apnea
Diabetes
Prevalence
Systematic review

ABSTRACT

Obstructive sleep apnea (OSA) is highly prevalent among patients with diabetes, intensifying the complications of the disease. Various studies in Iran have reported different prevalence rates. This systematic review and meta-analysis was performed to determine OSA prevalence in patients with type 2 diabetes in Iran. In this study, we evaluated five articles published in Persian and English. The articles were searched using the keywords of obstructive sleep apnea, sleep disordered breathing, sleep apnea, OSA, diabetes mellitus and Iran and all possible combinations of these terms in national databases of Scientific Information Database (SID) and Magiran and international databases of Google Scholar, Web of Science, PubMed and Scopus with no time limit. Data were analyzed using the meta-analysis and random effects model. In addition, the heterogeneity between studies was assessed using I^2 statistic, and data analysis was performed in Stata version 11. In this study, five articles with a total sample size of 2360 were evaluated. According to the results, the prevalence of OSA in diabetic patients was reported to be 54.50% (95% Confidence Interval [CI]: 39.90–69.09). In addition, the results were indicative of a lower prevalence of OSA in men (63.26%; 95% CI: 43.26–83.26), compared to women (66.22%; 95% CI: 57.60–74.84). According to the results of the study, there was a high OSA prevalence in patients with type 2 diabetes. Therefore, it is crucial to recognize diabetic patients at risk of OSA to decrease the adverse effects of this condition.

1. Introduction

The latest estimates show a global prevalence of 382 million (8.3%) people with diabetes (known as a global epidemic) in 2013, expected to rise to 592 million (10.1%) by 2035 [1]. The sixth leading cause of death in the United States, diabetes is associated with a high incidence rate of cardiovascular, cerebrovascular and renal diseases. In addition, the risk for death among people with diabetes is about twice the healthy individuals [2,3]. In Iran, the total prevalence of diabetes is 7.7%, and 16.8% of the Iranian people have impaired fasting glucose [4]. Poor diabetes control can lead to complications such as cardiovascular diseases, stroke, blindness, renal failure, lower limb loss by amputation, and even mortality [5].

Obstructive sleep apnea (OSA) is one of the common problems in diabetic patients that can complicate the condition of these individuals and is associated with poor blood glucose control [6–8], which leads to macro and microvascular complications in patients [9]. In general, OSA is defined as the cessation of airflow for ten or more seconds occurring during sleep due to upper airway collapse and correlating with conditions such as frequent arousals, sleep fragmentation, and intermittent hypoxemia [10,11]. Therefore, diabetic patients constantly complain about fatigue, excessive daytime sleepiness, and morning headaches [12]. This impairment results in the activation of the sympathoadrenal system, oxidative stress, systemic inflammation, and change in adipokines, which increase the risk of cardiovascular diseases, hypertension, and metabolic syndrome [13]. While OSA remains undiagnosed in most

* Corresponding author. Tel: +98 9144050284; fax: +98 8736237511.
E-mail addresses: Arezofalahi91@gmail.com (A. Fallahi), Dashty@lfu.edu.krdEmam (D.I. Jamil), Elnaz.karimi123@yahoo.com (E.B. Karimi), Vajihehbaghi@gmail.com (V. Baghi), Rezaghanei30@yahoo.com (R.G. Gheshlagh).

https://doi.org/10.1016/j.dsx.2019.06.030
1871-4021/

patients, one in five adults and half of the overweight people have this condition [14].

According to the literature, there is a correlation between OSA and hypertension, atherosclerosis [15] and depression [16]. Recognized as prevalent diseases, OSA and diabetes have similar risk factors, including high age and obesity [3]. Therefore, it is no surprise to see both disorders in a patient. A 10% increase in weight accelerates the risk of OSA by six times [17]. Various studies performed in Iran to evaluate the OSA prevalence in patients with type 2 diabetes have yielded conflicting results. Given the fact that understanding the current status of this condition is one of the preliminary steps taken toward its elimination, this study aimed to estimate the overall prevalence of OSA in Iranian patients with diabetes.

2. Methodology

2.1. Search strategy

In this systematic review and meta-analysis, we evaluated the prevalence of OSA in patients with type 2 diabetes according to the protocol of preferred reporting items for systematic review and meta-analysis (PRISMA) [18]. The documents collected were the result of a search on the Internet and manual search in the library of Kurdistan University of Medical Sciences. To find relevant articles, we searched the national databases of scientific information database (SID) and MagIran and the international databases of Web of Science, Scopus, and PubMed without time limitation. The keywords included obstructive sleep apnea, sleep disordered breathing, sleep apnea, OSA, diabetes mellitus, and Iran. In addition, backward (evaluation of the list of selected articles references) and forward (evaluation of studies pointed out in the selected articles) citation searching methods were carried out to have access to a greater number of articles.

2.2. Study selection and data extraction

First, all articles related to the prevalence of frequency of OSA in patients with type 2 diabetes were collected by two individuals separately. Inclusion criteria were observational studies, Persian or English language, and access to the full text of articles. Moreover, unrelated articles, gray literature, interventional studies, review studies, and repetitive studies were excluded from the research. To avoid bias, two researchers separately searched and selected articles, evaluated the quality of methodology of articles, and extracted the data. In case of disagreement on a research, the opinion of the corresponding author, who had experience in this field, was employed. The desired information of the selected articles, including the name of the corresponding author, year of publication, research setting, total sample size, the mean age of the participants, duration of the disease, and prevalence of OSA, were recorded on the data extraction sheets. The methodological quality of articles were assessed based on 10 items selected from STROBE Checklist (title and abstract, aims and hypotheses, research setting, inclusion criteria, sample size, analytical methods, descriptive statistics, interpretation of results, research limitations, and funding) [19].

2.3. Data analysis

In this systematic review and meta-analysis, point estimation and 95% confidence interval (CI) of the OSA prevalence were calculated according to the binomial distribution. In addition, heterogeneity between studies was assessed by Cochran's Q test with a level of significance below 0.1 and I^2 statistic. According to the recommendation by Higgins and Thompson, the I^2 statistic was divided into three classes of below 25% (low heterogeneity), 25–75% (moderate heterogeneity) and above 75% (considerable heterogeneity) [20]. Given the heterogeneity among the selected articles, the pooled prevalence was estimated using the random effects model. In addition, we applied the univariate meta-regression test to assess the association between OSA and the variables of the publication year, the mean age of the samples, and the sample size of the studies. Pooled prevalence was also calculated based on the type of screening tool using the subgroup analysis. Sensitivity analysis was used to examine the role of each study in the pooled prevalence. To determine whether all studies performed on OSA in patients with type 2 diabetes have been published and entered into the research, we used a funnel plot based on Egger's weighted regression analysis [21]. Data analysis was performed in Stata version 11.

3. Results

In this research, all studies performed on OSA were evaluated systematically with no time limitation. In the primary search of the national and international databases, we found 128 articles. However, 123 irrelevant studies were excluded during the identification and screening phase, thereby leading to the entrance of six articles into the research. (Fig. 1).

The total sample size was 2360 (a mean of 472 individual in each research), and the lowest and highest sample sizes were related to studies by Ghofraniha ($n = 80$) and Emra ($n = 1234$), respectively. In addition, all selected articles had a medium methodological quality. (Table 1).

Results were indicative of the lack of significance of publication bias ($P = 0.948$) (Fig. 2). According to the results of sensitivity analysis, the removal of each study did not lead to a significant change in the pooled prevalence of OSA.

In Iranian patients with type 2 diabetes, the pooled prevalence of OSA was reported at 54.50% (95% CI: 39.90–69.09) (Fig. 3). Results of subgroup analysis of OSA prevalence based on the type of OSA screening tools showed that the OSA prevalence reported by the Berlin questionnaire (56.98%; 95% CI: 38.82–75.15) was higher, compared to Stop-Bang tool (50.28%; 95% CI: 3.54–97.03). Moreover, the OSA prevalence was lower in male patients (63.26%; 95% CI: 43.26–83.26), compared to female individuals (66.22%; 95% CI: 57.60–74.84) (see Fig. 4).

According to the meta-regression results, there was no relationship between OSA and variables of body mass index (BMI) ($p = 0.372$), articles' publication year ($p = 0.306$), the mean age of the subjects ($p = 0.684$), and mean duration of diabetes ($p = 0.729$).

4. Discussion

The present systematic review and meta-analysis was performed to estimate the pooled prevalence of OSA in patients with type 2 diabetes in Iran. According to the results, more than half of the Iranian diabetic patients (54.50%) suffered from OSA, which is consistent with the results obtained by Einhorn et al. (2007), in which the prevalence of OSA in patients with diabetes was reported to be 48% [27]. In a study by Shim et al. (2011), 50.8% of the patients with diabetes were at high risk of OSA, according to the Berlin Questionnaire [28]. In another study in Jordan, 48.5% of the patients with diabetes were at high risk of OSA [29]. In China, research reported the diagnosis of OSA in 60% of hospitalized diabetic patients [11].

All studies showed a high prevalence of OSA in patients with diabetes. Studies also demonstrated that the association between OSA and diabetes is bidirectional, meaning that the neuropathy of

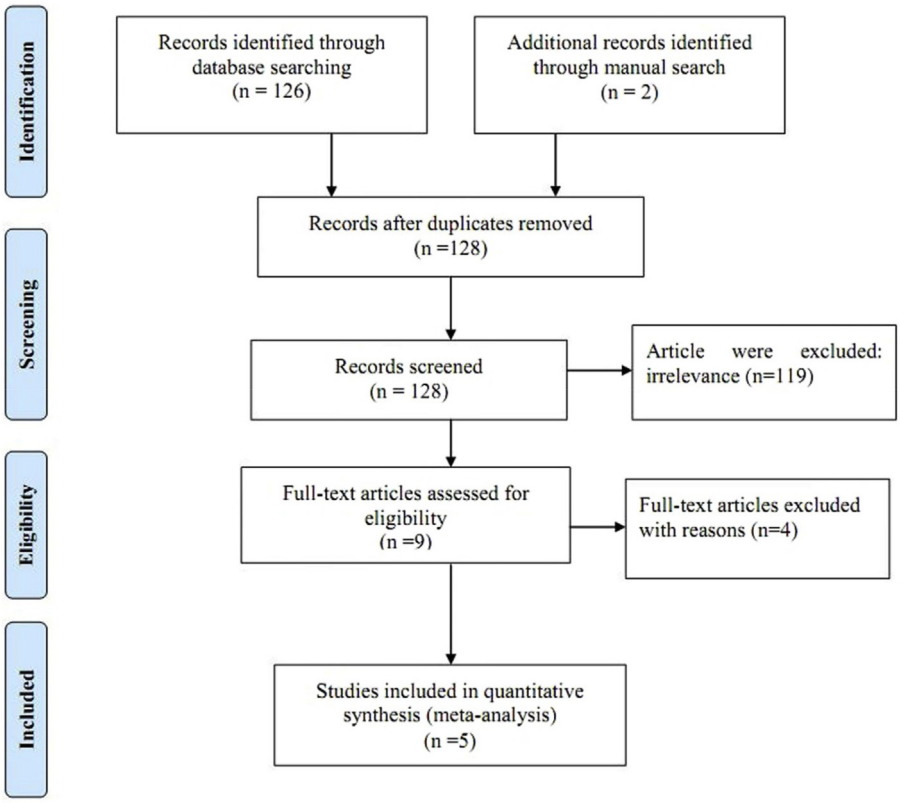

Fig. 1. Flowchart of the process of screening and selection of selected articles.

Table 1
Specifications of selected articles.

Prevalence (%)			Scale	City	Duration (year)	BMI	Sample size		Age	Year	First Author
Women	Men	Total					M/F	Total			
73.4	44.6	50.5	Berlin	Isfahan	7.5	28.9	372/862	1234	53.4	2012	Amra [22]
64.6	85.8	74	STOP-BANG	Tehran	7	28.8	77/96	173	51.6	2015	Sadeghniiat Haghighi [23]
44.4	52.6	46	Berlin	Saghez	–	30.8	19/81	100	55.5	2015	Hemmati Maslakpak [24]
_	–	56.4	STOP-BANG	Mashhad	8.3	26	35/45	80	57	2017	Ghofraniha [25]
75.9	68.3	73.6	Berlin	Sabzevar	8.6	29.4	230/543	773	58.4	2018	Shourideh-Yazdi [26]

BMI: Body mass index.

diabetes can affect the central control respiration, and upper airway neural reflexes result in OSA [30]. Moreover, nighttime hypoxia caused by OSA is correlated with glucose intolerance and insulin resistance [31,32]. In a study, Foster reported that 86.6% of patients with diabetes suffered from OSA [33]. The results were also indicative of a higher OSA prevalence in women, compared to men. Generally, OSA has been seen as a male disease due to higher involvement of men, compared to women [34]. Hormonal factors, differences in fat distribution in the body, and pharyngeal anatomy and function are the cause of the difference in the prevalence of OSA in men and women.

Due to hormonal effects, women are less affected by OSA before menopause. Nevertheless, there is an equal rate of OSA in men and women after menopause [35]. Regarding the prevalence of diabetes in this group of patients, the selected articles reported different results varying in the range of 46–74% [23,24]. This difference in the results might be related to the features of the evaluated population (e.g., gender, level of obesity, and race) and OSA determination methods. In a cross-sectional study, Amin et al. (2017) evaluated OSA in South Asians and white Europeans with diabetes, reporting OSA prevalence rate of 51.4% and 75.2% in the mentioned individuals, respectively [36]. The meta-regression results demonstrated that the OSA prevalence had an ascending trend with increased mean age, duration of disease, and BMI of the subjects (which was not significant).

High age and obesity are the mutual causes of OSA and diabetes, in a way that increase of age and gaining weight increase the risk of diabetes and OSA [3]. Results obtained by Saad et al. (2019) were indicative of the significant association between age and risk of OSA in patients with diabetes [29]. Change in the pharynx structure, lengthening of the soft palate, and increased deposition of fat in the parapharyngeal area is among the causes of the high prevalence of OSA in the elderly [37,38].

Researchers believe that aging increases the risk of underlying diseases for patients with diabetes. In addition, the possibility of the emergence of diabetes complications increases by aging, which can have adverse effects on the sleep condition of patients with diabetes. During 2012–2018 (the time period of publication of the

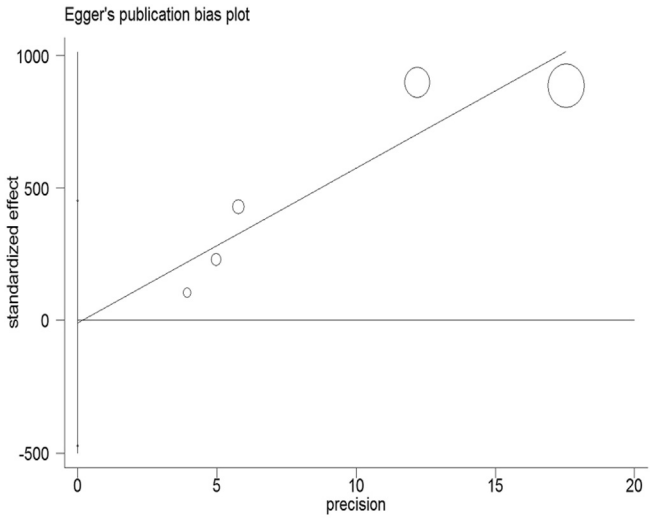

Fig. 2. The publication bias in the estimation of OSA in patients with type 2 diabetes. Size of circles shows the sample size of articles.

selected articles), there was an increase in the prevalence of OSA. It seems that more familiarization with OSCA and better use of screening tools by patients at risk of this condition are the major causes of this increased rate.

One of the major limitations of the study was lack of full report of necessary information by some studies. On the other hand, a strength point of the current research was its exquisite nature since the evaluation of OSA in patients was carried out for the first time and the relevant results can be beneficial for healthcare authorities of the country.

5. Conclusion

According to the results of the present study, there was a high OSA prevalence in patients with type 2 diabetes. In addition, the prevalence of OSA was higher in women, compared to men. Given the fact that OSA could worsen the complications of diabetes and complicate the disease control protocol, it is crucial to recognize diabetic patients at risk of OSA and propose strategies to control and reduce the condition.

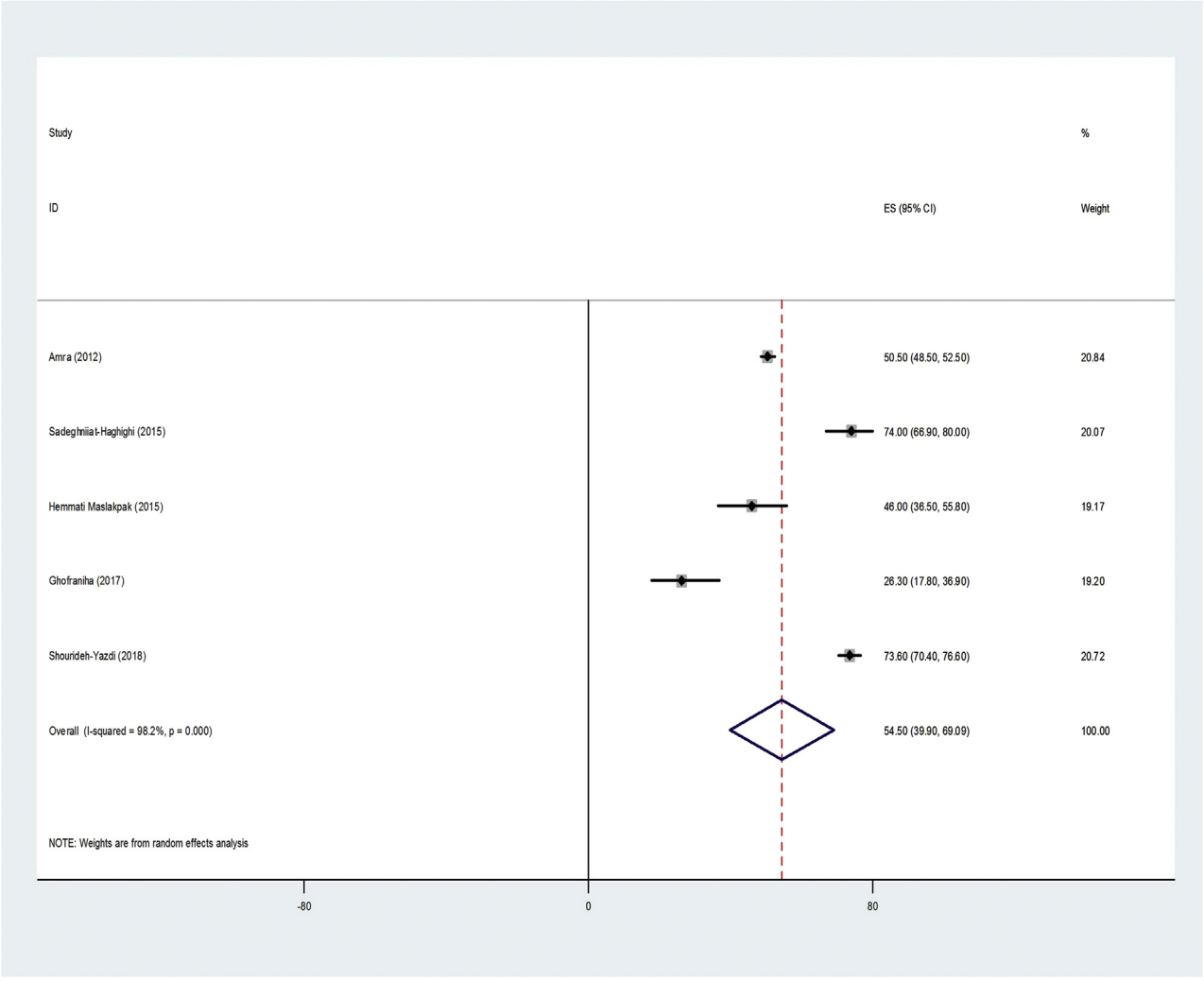

Fig. 3. OSA prevalence and its 95% confidence interval in patients with type 2 diabetes based on the name of the corresponding author and year of publication according to the random effects model. The point in the middle of each line segment shows the prevalence of medication errors in each study, whereas the rhombus shape demonstrates the prevalence of medication errors for all studies conducted in Iran.

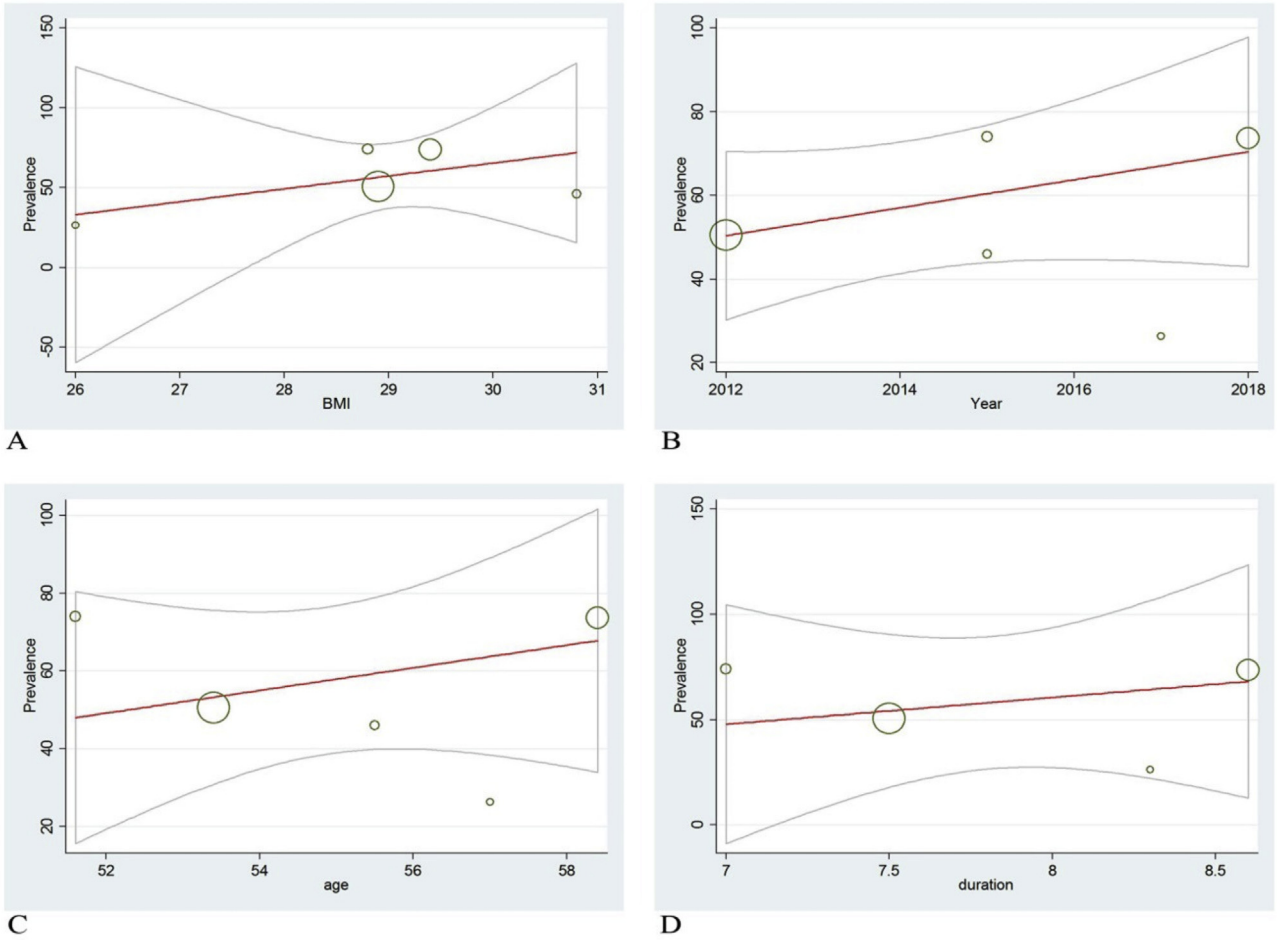

Fig. 4. Meta-regression results. Relationship between OSA in patients with type 2 diabetes and BMI (A), year of article publication (B), the mean age of subjects (C), and mean duration of diabetes (D).

Funding

The authors report that there was no funding source for the work that resulted in the article or the preparation of the article.

Disclosure (authors)

The authors declare no conflicts of interest.

Acknowledgements

The authors appreciate all the researchers whose articles were used in the present research.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.06.030.

References

[1] Tahrani AA, Ali A. Obstructive sleep apnoea and type 2 diabetes. Eur Endocrinol 2014;10(1):43–50. https://doi.org/10.17925/EE.2014.10.01.43.
[2] Mahmood K, Akhter N, Eldeirawi K, Christman JW, Carley DW, Herdegen JJ. Prevalence of type 2 diabetes in patients with obstructive sleep apnea in a multi-ethnic sample. J Clin Sleep Med 2009;5(03):215–21.
[3] Reichmuth KJ, Austin D, Skatrud JB, Young T. Association of sleep apnea and type II diabetes: a population-based study. Am J Respir Crit Care Med 2005;172(12):1590–5. https://doi.org/10.1164/rccm.200504-637OC.
[4] Esteghamati A, Gouya MM, Abbasi M, Delavari A, Alikhani S, Alaedini F, et al. Prevalence of diabetes and impaired fasting glucose in the adult population of Iran: national survey of risk factors for non-communicable diseases of Iran. Diabetes Care 2008;31(1):96–8. https://doi.org/10.2337/dc07-0959.
[5] Rafique G, Azam S, White F. Diabetes knowledge, beliefs and practices among people with diabetes attending a university hospital in Karachi, Pakistan. East Mediterr Health J 2006;12(5):590–8.
[6] Mok Y, Tan CW, Wong HS, How CH, Tan KLA, Hsu PP. Obstructive sleep apnoea and Type 2 diabetes mellitus: are they connected? Singap Med J 2017;58(4):179–83. https://doi.org/10.11622/smedj.2017027.
[7] Hermans MP, Ahn SA, Mahadeb YP, Rousseau MF. Sleep apnoea syndrome and 10-year cardiovascular risk in females with type 2 diabetes: relationship with insulin secretion and insulin resistance. Diabetes Metab Res Rev 2013;29(3):227–34. https://doi.org/10.1002/dmrr.2387.
[8] Aronsohn RS, Whitmore H, Van Cauter E, Tasali E. Impact of untreated obstructive sleep apnea on glucose control in type 2 diabetes. Am J Respir Crit Care Med 2010;181(5):507–13. https://doi.org/10.1164/rccm.200909-1423OC.
[9] Siwasaranond N, Nimitphong H, Manodpitipong A, Saetung S, Chirakalwasan N, Thakkinstian A, et al. The relationship between diabetes-related complications and obstructive sleep apnea in type 2 diabetes. J Diabetes Res 2018;2018. https://doi.org/10.1155/2018/9269170.
[10] Ghanei Geshlagh R, Hemmati Maslakpak M, Ghoci S. Sleep apnea and metabolic syndrome in hemodialysis patients. Urmia Med J 2011;22(4):339–45 [In Persian].
[11] Zhang P, Zhang R, Zhao F, Heeley E, Chai-Coetzer CL, Liu J, et al. The prevalence and characteristics of obstructive sleep apnea in hospitalized patients with type 2 diabetes in China. J Sleep Res 2016;25(1):39–46. https://doi.org/10.1111/jsr.12334.
[12] Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, et al. Prevalence of obstructive sleep apnea in the general population: a systematic review. Sleep Med Rev 2017;34:70–81. https://doi.org/10.1016/j.smrv.2016.07.002.

[13] Rajan P, Greenberg H. Obstructive sleep apnea as a risk factor for type 2 diabetes mellitus. Nat Sci Sleep 2015;7:113–25. https://doi.org/10.2147/NSS.S90835.
[14] Tasali E, Mokhlesi B, Van Cauter E. Obstructive sleep apnea and type 2 diabetes: interacting epidemics. Chest 2008;133(2):496–506. https://doi.org/10.1378/chest.07-0828.
[15] Botros N, Concato J, Mohsenin V, Selim B, Doctor K, Yaggi HK. Obstructive sleep apnea as a risk factor for type 2 diabetes. Am J Med 2009;122(12):1122–7. https://doi.org/10.1016/j.amjmed.2009.04.026.
[16] Farajzadeh M, Hosseini M, Mohtashami J, Chaibakhsh S, Tafreshi MZ, Ghanei Gheshlagh R. The association between obstructive sleep apnea and depression in older adults. Nurs Midwifery Stud 2016;5(2). e e32585, https://doi.org/10.17795/nmsjournal32585.
[17] Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. J Am Med Assoc 2000;284(23):3015–21. https://doi.org/10.1001/jama.284.23.3015.
[18] Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 2009;151(4):264–9. https://doi.org/10.7326/0003-4819-151-4-200908180-00135.
[19] Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med 2007;147(8):573–7. https://doi.org/10.7326/0003-4819-147-8-200710160-00010.
[20] Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2000;15(11):1539–58. 21, https://doi.org/10.1002/sim.1186.
[21] Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315(7109):629–34.
[22] Amra B, Bahaee FS, Amini M, Golshan M, Fietze I, Penzel T. Sleep apnea symptoms in diabetics and their first degree relatives. Int J Prev Med 2012;3(2):95–101. PMID: 22347605.
[23] Sadeghniiat-Haghighi K, Mohajeri-Tehrani MR, Khajeh-Mehrizi A, Fathi F, Saremi-Rasouli F, Ghajarzadeh M, et al. Obstructive sleep apnea and excessive daytime sleepiness among patients with type 2 diabetes mellitus: a single-center study from Iran. Int J Diabetes Dev Ctries 2015;35(2):189–93. https://doi.org/10.1007/s13410-014-0281-0.
[24] Hemmati Maslakpak M, Ghanei R, Ghaderi C. Sleep apnea, sleep quality and hypertension in patients with type 2 diabetes. J Neyshabur Univ Med Sci 2015;2(5):35–41 [In Persian)].
[25] Ghofraniha L, Amini M, Davoudi Y, Eslami S, Layegh P, Lotfi Z, et al. The relation of carotid arteries' intima-media thickness with snoring and obstructive sleep apnea in type 2 diabetes patients. Acta Med Iran 2017:765–71.
[26] Yazdi MS, Samadi A, Akrami R. Prevalence of obesity and risk of obstructive sleep apnea among people with type II diabetes mellitus. J Sleep Sci 2018;3(1–2):10–6.
[27] Einhorn D, Stewart D, Erman M, Gordon N, Philis-Tsimikas A, Casal E. Prevalence of sleep apnea in a population of adults with type 2 diabetes mellitus. Endocr Pract 2007;13(4):355–62. https://doi.org/10.4158/EP.13.4.355.
[28] Shim ULH, Oh JY, Sung YA. Sleep disorder and cardiovascular risk factors among patients with type 2 diabetes mellitus. Korean J Intern Med 2011;26(3):277–84. https://doi.org/10.3904/kjim.2011.26.3.277.
[29] Saad AM, Hiyasat D, Jaddou H, Obeidat N. The prevalence of high risk obstructive sleep apnoea among patients with type 2 diabetes in Jordan. Diabetes Res Clin Pract 2019;152:16–22. https://doi.org/10.1016/j.diabres.2019.04.035.
[30] Reutrakul S, Mokhlesi B. Obstructive sleep apnea and diabetes: a state of the art review. Chest 2017;152(5):1070–86. https://doi.org/10.1016/j.chest.2017.05.009.
[31] Redline S, Storfer-Isser A, Rosen CL, Johnson NL, Kirchner HL, Emancipator J, et al. Association between metabolic syndrome and sleep-disordered breathing in adolescents. Am J Respir Crit Care Med 2007;176(4):401–8. https://doi.org/10.1164/rccm.200703-375OC.
[32] Sulit L, Storfer-Isser A, Kirchner HL, Redline S. Differences in polysomnography predictors for hypertension and impaired glucose tolerance. Sleep 2006;29(6):777–83. https://doi.org/10.1093/sleep/29.6.777.
[33] Foster GD, Sanders MH, Millman R, Zammit G, Borradaile KE, Newman AB, et al. Obstructive sleep apnea among obese patients with type 2 diabetes. Diabetes Care 2009;32(6):1017–9. https://doi.org/10.2337/dc08-1776.
[34] Ye L, Pien GW, Weaver TE. Gender differences in the clinical manifestation of obstructive sleep apnea. Sleep Med 2009;10(10):1075–84. https://doi.org/10.1016/j.sleep.2009.02.006.
[35] Franklin KA, Lindberg E. Obstructive sleep apnea is a common disorder in the population—a review on the epidemiology of sleep apnea. J Thorac Dis 2015;7(8):1311–22. https://doi.org/10.3978/j.issn.2072-1439.2015.06.11.
[36] Amin A, Ali A, Altaf QA, Piya MK, Barnett AH, Raymond NT, et al. Prevalence and associations of obstructive sleep apnea in South Asians and white Europeans with type 2 diabetes: a cross-sectional study. J Clin Sleep Med 2017;13(04):583–9. https://doi.org/10.5664/jcsm.6548.
[37] Eikermann MJA, Chamberlin NL, Gautam S, Wellman A, Lo YL, White DP, Malhotra A. The influence of aging on pharyngeal collapsibility during sleep. Chest 2007;131(6):1702–9. https://doi.org/10.1378/chest.06-2653.
[38] Lam JCSS, Lam B. Obstructive sleep apnoea: definitions, epidemiology & natural history. Indian J Med Res 2010;131:165–70.