

Glycemic control among Iranian people with type 2 diabetes: a systematic review and meta-analysis

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Abstract

Background Glycemic control reduces the risk of cardiovascular complications among people with diabetes. However, the current status of glycemic control is uncertain among Iranian people with diabetes. This study aims to systematically review the studies on the status of glycemic control among people with type 2 diabetes in Iran.

Methods A systematic literature search was conducted in international databases including Medline database (PubMed), Web of Science, Google Scholar, and Scopus, as well as domestic databases such as Iran Medex, SID, Magiran, Irandoc, and Medlib, up to end of 2020. All observational studies (cross-sectional, case-control, and cohort) were included. Studies that reported the status of glycemic control among people with type 2 diabetes in Iran were selected. Good glycemic control was defined as glycated hemoglobin A1c (HbA1c) less than 7%.

Results A total of 23 eligible studies (15,358 patients) were included in the quantitative analysis. Of 15,358 patients, 5882 had good glycemic control. The pooled prevalence of good glycemic control was 33.1% (95% CI, 25.6–41.1%). Meta-regression showed no significant improvement in glycemic control rate by year.

Conclusion Despite the importance of good glycemic control in the prevention of micro- and macrovascular diabetic complications, the high proportion of Iranian people with type 2 diabetes remains poorly controlled. The result of this meta-analysis indicates the need for better approaches to diabetes management in Iran.

Keywords Glycemic control · Diabetes mellitus, type 2 · Glycated hemoglobin A · Iran

Introduction

Type 2 diabetes mellitus is one of the global health problems that increase micro- and macrovascular problems in patients. Lifestyle factors and genetics can lead to type 2 diabetes. Obesity is the most important factor associated with type 2

diabetes. The core defects are insulin resistance and impaired insulin secretion [1, 2].

Diabetes increases morbidity, mortality, and economic costs. It affects an estimated 425 million adults globally among which 75% of whom live in low- and middle-income countries [3]. People with diabetes are at increased risk for vascular events, including macrovascular complications (e.g., peripheral arterial disease, stroke, and coronary artery disease), microvascular complications (e.g., retinopathy, neuropathy, and nephropathy), and lower extremity amputations [4].

Iran is one of the developing countries that have more than 4 million adults (11.3%) suffering from diabetes [5]. The prevalence of diabetes and its complications are increasing [5]. The age-standardized mortality rate of diabetes increased from 8.7 in 2000 to 11.3 in 2015 in Iran [6]. In addition, diabetes has enormous economic implications in the country. The average treatment cost for Iranian people with type 2 diabetes was estimated to be equal to \$2209 in 2017. This amount was \$2557 and \$1861 per treated patient in the private and public sectors, respectively. Also, the average cost of complications management was \$9529 [7].

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Improved glycemic control is correlated with the reduction of microvascular complications and associated with reduced risk of macrovascular complications [8]. Additionally, several studies suggested that a good glycemic control was associated with healthcare cost saving in health system or lower use of healthcare services by individuals [9, 10]. Glycosylated hemoglobin (HbA1C) is recognized as the primary target of glycemic control. In this regard, the American Diabetes Association (ADA) has suggested the goal of achieving HbA1c level of less than 7% (< 53 mmol/mol) for majority of people with diabetes [11].

Several studies investigated the status of glycemic control among Iranian people with type 2 diabetes [12, 13]. However, most of them had a single-centered design with relatively small sample sizes, making it difficult for healthcare policymakers to make decisions based on such reports. Thus, a systematic assessment of the current status of this clinical indicator is important to provide a holistic overview of healthcare quality in people with diabetes in the country. Therefore, this systematic review and meta-analysis aimed to examine the status of glycemic control among Iranian people with type 2 diabetes.

Materials and methods

Search strategy

This systemic review was conducted according to the PRISMA 2020 guidelines [14]. A systematic literature search was conducted in Medline (PubMed), Scopus, and Web of Knowledge, Iran Medex, SID, Magiran, Irandoc, and Medlib databases up to end of 30 September 2020. The following search terms were used: (diabetes OR diabetes mellitus OR T2DM OR hyperglycemia OR hyperglycaemia OR glucose OR HbA1c OR glycated hemoglobin OR insulin resistance OR glucose homeostasis OR glycemic control OR glycemic control OR glucose tolerance OR glucose metabolism) AND “Iran”. Two reviewers (MM and MHB) reviewed and screened the suitable articles independently. Also, the reference lists of related review articles were checked to find undetected desirable studies. The reviewers resolved any disagreements by discussion with a third investigator (RK).

Eligibility criteria

Those papers with the following criteria were selected: (a) investigate people with type 2 diabetes, regardless of age and sex, (b) assess glycemic control by measure of glycohemoglobin and report glycemic control status according to ADA criteria, i.e., HbA1c<7 indicating good glycemic control and HbA1C≥7% indicating poor

glycemic control [11], and (d) English or Persian language articles. Studies that investigated people with gestational diabetes or type 1 diabetes mellitus and those reported glycemic control status in terms of other categories or guidelines were excluded. If there were multiple published papers from the same study, we included only one of them with the most detailed information.

Quality appraisal and data extraction

The following information was extracted from eligible studies: first author, study design, study location/setting, target population, sample size, patient characteristics, and glycemic control frequency. The most recent data was considered in case of multi-times measurement.

We assessed the quality of studies and risk of bias applying a modified form of STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement [15]. The items of this tool are five main components including sample population, sample selection, participation/response rate, outcome assessment, and analytical methods to control for bias. In brief, the item is evaluated by scoring (low risk = 2, moderate risk = 1, high risk and unclear = 0) of each bias type for each included study and the total score is provided as the summary assessment of risk of bias. This phase of the study was performed by two investigators independently and a final decision was reached by the third author when there were discrepancies.

Statistical analysis

We combined the proportion of individuals with good glycemic control in each study, using a random-effects model, to give a pooled prevalence of good glycemic control for all studies with 95% confidence intervals (CI). Before pooling the results, estimated prevalence was transformed via the Freeman-Tukey double arcsine method [16]. This method is an effective way to stabilize the variance of estimated proportion and to minimize the effect of extreme results on the overall estimates [17]. Statistical tests of heterogeneity were used to assess whether studies are consistent. The potential heterogeneity across studies was investigated by the Cochran's Q -test and was expressed by the I^2 index [18]. We produced forest plots of pooled prevalence and pooled prevalence rate with 95% confidence intervals (CIs). Publication bias was examined by generating funnel plot and quantitatively by Egger's test [19]. Subgroup analysis (for qualitative variables: capital/non-capital province; study design) and meta-regression (for quantitative variables: publication year; mean age; diabetes duration) were applied to explore potential sources of heterogeneity regarding the proportion of people achieving glycemic control target. In this regard, we produced a bubble plot to explore the relationship between year of the

study publication and prevalence of good HbA1C control. All analysis was performed using meta package in R open-source statistical software (R Foundation for Statistical Computing) [20].

Results

The initial search recognized 919 articles. One hundred sixty-seven articles remained after removing duplicate and irrelevant articles. The full texts of the remaining studies were reviewed carefully by three researchers and 23 articles [21–43] were included in the meta-analyses (Fig. 1).

Characteristics of included studies

According to the quality assessment tool, two studies received a score of 9 [39, 43], four received a score of 8 [22, 25, 27, 28, 37], eleven received a score of 7 [23, 24, 26, 30, 33, 35, 36, 38, 40–42], and five received a score of 6 [21, 29, 31, 32, 34]. All of the studies had acceptable quality.

The detailed characteristics of the included studies are presented in Table 1. All of the included studies were published from 2009 to 2020, reporting on 15,358 people with type 2 diabetes. One of the studies was conducted at a national level [27], one study was conducted in two neighboring provinces (East Azerbaijan and Ardebil) [40], and other studies were

conducted in 11 provinces including Tehran [23, 31, 34–36, 39], Kerman [29, 41, 43], Fars [30, 32], Khuzestan [21, 42], Yazd [26, 33], East Azerbaijan [22], Khorasan-e-Razavi [25], Kurdistan [28], Mazandaran [37], Qazvin [24], and Qom [38].

All of the 23 studies were cross-sectional analytical, and 21 studies were conducted in clinical settings and two studies [27, 43] had a community-based design. The included studies had sample sizes ranging from 103 [31] to 4582 [35] people with type 2 diabetes.

From 13,181 patients of 20 studies that reported the gender distribution of participants, 8159 were female (61.8%). Twenty-one studies reported the mean age of the participants and the pooled mean age of studies was 56.4 years (95% CI, 54.7–58.1). Among 14 studies that reported mean HbA1C level ($n = 10,757$), the pooled mean HbA1C level was 7.8% (95% CI, 7.4–8.1%). Only nine studies [23, 25, 28, 30, 33, 34, 39, 41, 42] reported the mean duration of diabetes that a pooled mean duration of diabetes was 9.4 years (95% CI, 8.2–10.6).

Glycemic control

Glycemic control was reported in terms of HbA1C (%/mmol/mol). The mean HbA1C was 6.7 to 13.0%. Of the 15,358 patients included in this meta-analysis, 5882 patients achieved the desired glycemic control. Proportion of good glycemic control ranged from 14.2% [42] to 77.7% [36].

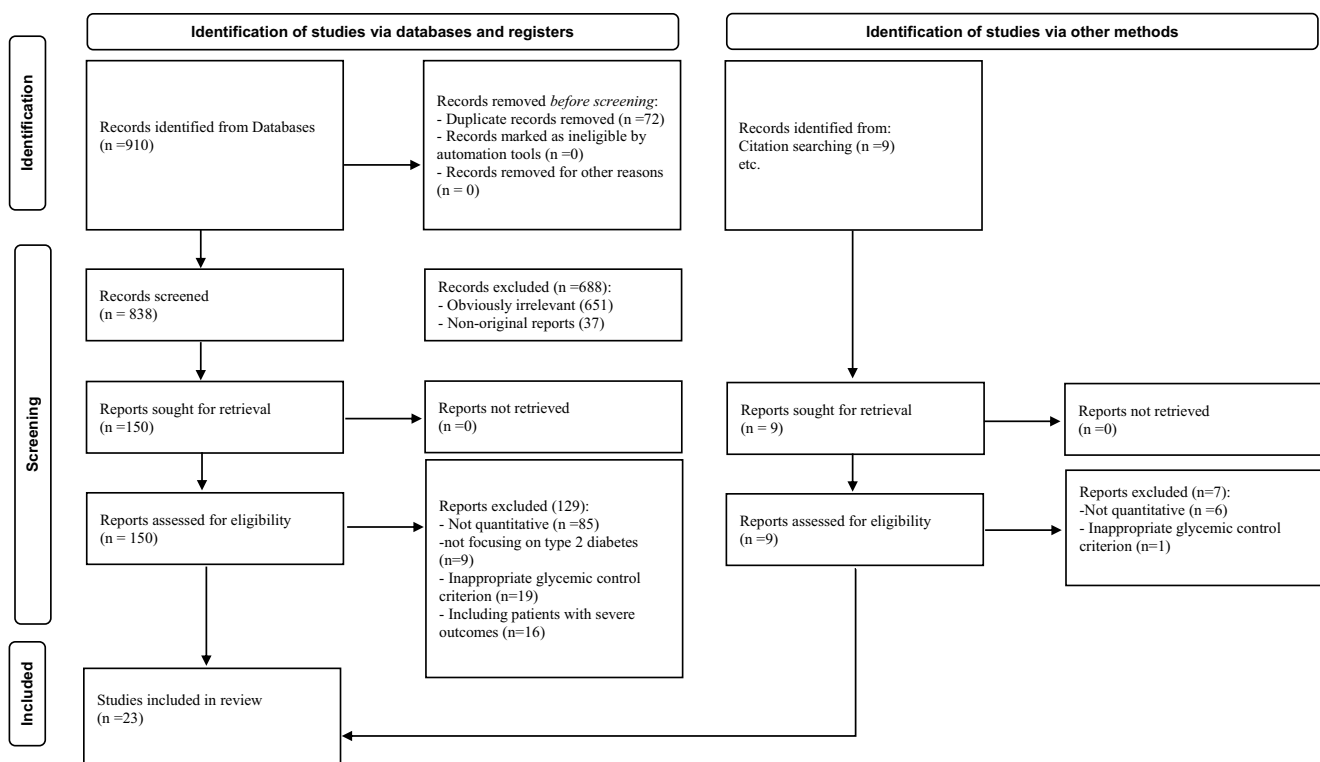


Fig. 1 Study selection flow diagram

Table 1 Characteristics of studies included in the meta-analysis

Study	Recruitment year	Province	Setting	Population	Mean age, years	DM duration, years	Exclusion criteria	Sample, n	n female	Mean BMI	Good control, n
Anari, 2016	NR	Khuzestan	Diabetes clinic	≥ 20-year-old patients with diabetes	54.5±9.4	NR	Patients with insulin treatment	157	104	29.3±5	57
Azadi, 2020	2016	East Azerbaijan	Diabetes clinic	Over 65-year-old people with type II diabetes	71±5.4	NR	Having major health condition	290	134	NR	141
Babaniamansour, 2020	2017–2018	Tehran	Diabetes clinic	≥ 18-year-old patients with diabetes	56.1±10.4	8.9±7.1	Pregnancy, history of type 1 DM, gestational diabetes mellitus, malignancy, participation in an interventional study or hospitalization in past 3 months	562	362	28.1±4.6	130
Barikani, 2020	2017	Qazvin	Diabetes clinic	Age above 18 years old, having type 2 DM	53.6±8.5	NR	Having major health condition	347	256	27.9±4.2	157
Bonakdaran, 2011	2006–2008	Khorasan-e Razavi	Diabetes clinic	Type 2 diabetes patients aged ≥ 40 years	52.7±10.5	7.9±6.4	NR	752	397	28±4.1	188
Dehghani, 2016	NR	Yazd	Diabetes clinic	Patients with type 2 diabetes	55.6±9.5	NR	Positive history of mental disorders and non-local patients	240	140	NR	54
Delavari, 2009	2005	National	Community	Patients with type 2 diabetes	NR	NR	NR	169	N/A	NR	30
Esmailnasab, 2013	2010	Kurdistan	Diabetes clinic	Patients with type 2 diabetes	57.2±11.5	6.7±4.5	Died patients	411	306	NR	193
Fadayevatan, 2020	2017	Kerman	Diabetes clinic	≥ 60-year-old patients with diabetes	69.3±9.6	NR	NR	177	98	NR	61
Ghaem, 2018	2015–2016	Fars	Diabetes clinic	People with diabetes routinely checked by an expert physician	56.6±12.4	11.4±9	NR	478	291	NR	223
Ghazanfari, 2010	2008–2009	Tehran	Diabetes clinic	Women with type 2 diabetes	46.4±11.4	NR	History of diabetes complications, and mental and disabling disorders	103	103	NR	45
Hedayati, 2016	NR	Fars	Diabetes clinic	30 to 70-year-old patients with type 2 diabetes	52.9±8.8	NR	Having major health condition	112	45	NR	67
Heidari, 2015	2014	Yazd	Diabetes clinic	People with diabetes visiting the clinic	58.2±9.6	10.8±6.0	History of diagnosed mental illness	150	97	NR	28
Jafarian-Amirkhizi, 2018	2015	Tehran	Paraclinic center	People with type 2 diabetes attending a community pharmacy and pathobiology laboratory	55.8±12.7	9.4±7.8	Cases of dementia, cognitive impairment, or schizophrenia, having a hospital admission and/or serious illness in the past month	348	127	NR	62
Janghorbani, 2012	2010	Tehran	Diabetes clinic	Patients with type 2 diabetes	56.2±2.0	NR	NR	4582	2857	NR	1631
Larry, 2020	2012–2017	Tehran	Diabetes clinic	Patients with type 2 diabetes attending a diabetes clinic	N/A	NR	Heart failure, infectious diseases, using glucocorticoids, drug addiction, and a history of gestational diabetes	2008	NR	NR	1562
Maddah, 2016	2012–2013	Mazandaran	Nutrition and diet therapy clinic	18 years of age or older, with a diagnosis of type 2 diabetes	52.9±11.6	NR	Pregnant women or those being too ill or cognitively impaired	367	235	NR	98

Table 1 (continued)

Study	Recruitment year	Province	Setting	Population	Mean age, years	DM duration, years	Exclusion criteria	Sample, <i>n</i>	Mean BMI female	Good control, <i>n</i>
Parham, 2013	2012	Qom	Nutrition and diet therapy clinic	Patients with type 2 diabetes attending a diabetes clinic	51.1±1.0	NR	Pregnant women, with chronic kidney and liver diseases, and insulin treatment	116	NR	20
Rabizadeh, 2019	NR	Tehran	Diabetes clinic	Patients with type 2 diabetes attending a diabetes clinic	55.7±11.4	8.1±7.1	Age < 30, type 1 diabetes, history of malignancy, GFR < 30 cc/min, and dialysis	2029	28.3±4.8	594
Shamshirgaran, 2017	2014–2015	Ardabil & East Azerbaijan	Diabetes clinic	> 25-year-old patients with type 2 diabetes attending a diabetes clinic	55.7±9.0	NR	Unwillingness to participate in the study and having other types of diabetes	649	NR	274
Valizadeh, 2016	2015	Kerman	Diabetes clinic	Patients with type 2 diabetes attending a diabetes clinic	60.4±8.3	13	Having type 1 diabetes and incomplete information related to retinopathy and HbA1c	206	NR	40
Yazdampannah, 2018	2014	Khuzestan	Diabetes clinic	Patients aged over 18 years with diabetes attending a diabetes clinic	53.8±10.7	9.2±7.1	Disabling diseases or psychological disorders	605	28.6±4.4	86
Yousefzadeh, 2015	2009–2011	Kerman	Community	> 18-year-old patients having FBS > 126 mg/dl and had been through treatment for their diagnosed diabetes	59.3±10.3	NR	Those with malignant disease, severe renal insufficiency, cirrhosis, active liver disease attributable to viral infection, and/or other acute infectious or inflammatory disorders	500	NR	141

NR, not reported

Results of the random-effects meta-analysis showed that the pooled prevalence of desired glyceamic control is 33.1% (95% CI, 25.6–41.1%). The forest plot for the overall estimates is shown in Fig. 2.

The current meta-analysis demonstrated a high degree of heterogeneity ($I^2 = 99%$, [18]). Egger’s test and funnel plot (Figs. 3 and 4) did not show asymmetry in the published studies for pooled analysis ($p = 0.48$). Moderator analysis did not detect any significant influence of available covariates on the prevalence of good glyceamic control ($p = 0.114$) (e.g., publication year: Fig. 3).

Discussion

To the best of our knowledge, this is the first meta-analysis on the status of glyceamic control in people with type 2 diabetes in Iran. Our results indicated that the pooled overall prevalence of good glyceamic control (i.e., HbA1c: < 7%) among Iranian people with type 2 diabetes is 33.1% (95% CI, 25.6–41.1%). This suggests that a large proportion of Iranian people with type 2 diabetes (66.9%) are not able to achieve good glyceamic control.

According to our meta-analysis, the prevalence of good glyceamic control (HbA1c < 7%) in developed countries such as Japan (45%), the USA (52.1%) [44], Germany (48.6%) [45], and Sweden (56.5%) [45] was higher than that in Iranian people with type 2 diabetes. However, the prevalence

of good glyceamic control was higher in Iranian people with type 2 diabetes compared with some low- and middle-income countries such as the Philippines (15.0%) [46] and Bangladesh (23.1%) [47].

One concern is the low prevalence of people with type 2 diabetes with good glyceamic control. The prevalence of diabetes is increasing and failure to achieve good glyceamic control means a significant number of people with diabetes are exposed to excess risks of diabetes-related complications. Improved glyceamic outcome requires complex interactions among patient level (e.g., self-care and motivation), healthcare provider level (e.g., therapy intensification), and health system level (e.g., healthcare organization and patient access to quality health services). A systematic review of qualitative studies reported multifaceted challenges regarding the management of diabetes in Iran including holistic understanding of patients, service delivery, workforce, financing, and research [48]. Key stakeholders in diabetes care expressed ineffective diabetes care coordination [49], inadequate access to diabetes care [50], and shortage of diabetes-specific facilities [51] were the main problems in diabetic care. They also stated that inadequate treatment guidelines and challenges regarding self-care management affected the diabetes management in the country [48].

Many strategies have been suggested to improve guideline targets for people with type 2 diabetes. One systematic review was conducted to establish the effectiveness of clinical guideline implementation strategies [52]. This study assessed the

Fig. 2 Forest plot of meta-analysis of good glyceamic control among Iranian patients with type 2 diabetes

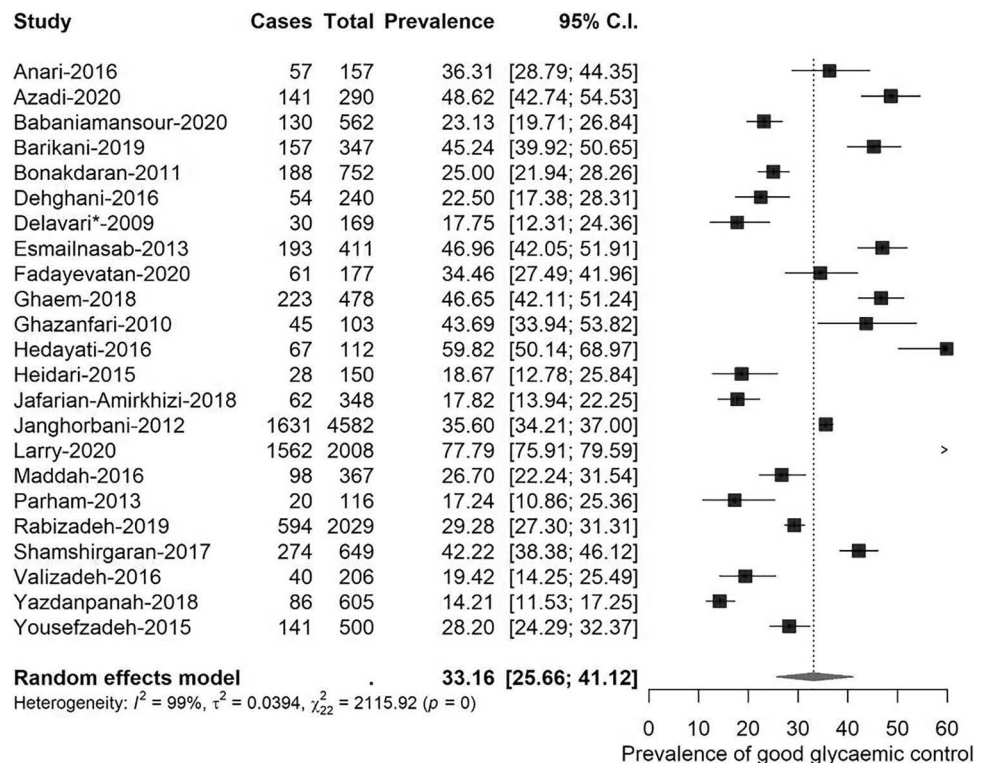
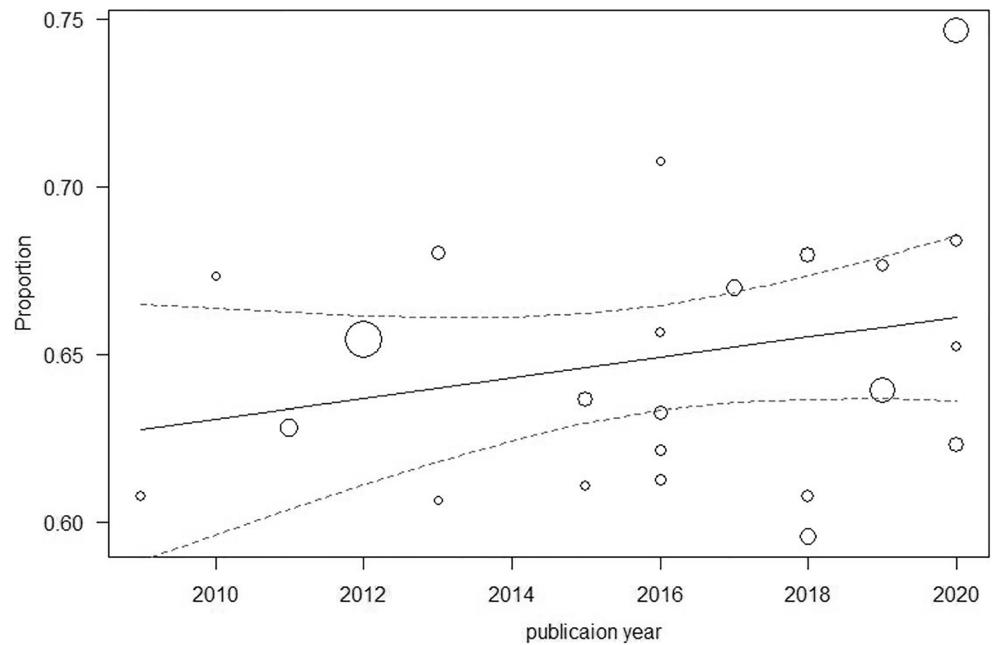


Fig. 3 Random-effects meta-regression of prevalence of good glycemic control against publication year as a covariate. Circles are proportional precision of study estimates

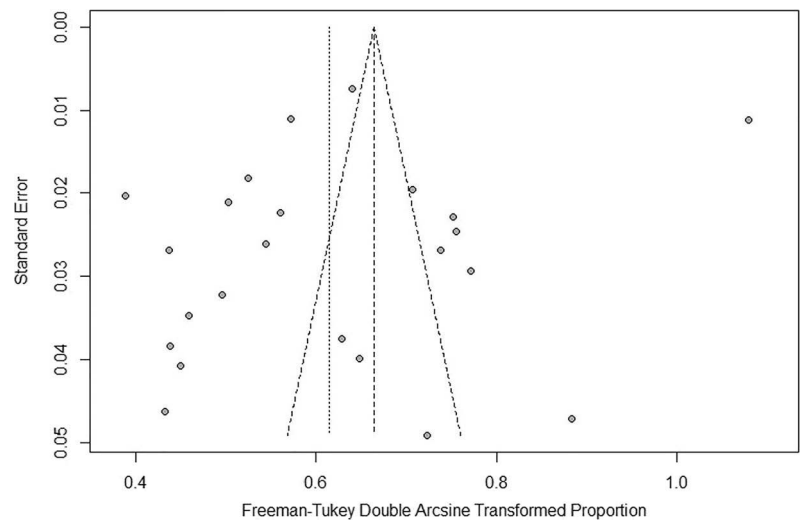


results of 714 primary studies in a wide range of healthcare settings. It suggested that multifaceted interventions, interactive education, and clinical reminder systems were effective implementation strategies.

The primary strength of this systematic review and meta-analysis is the assessment of the status of glycemic control in terms of the international ADA criteria. This meta-analysis was able to obtain data regarding the glycemic control of a large number of Iranian people with type 2 diabetes ($N = 15,358$). This data provides deep and wide information that can be used by healthcare providers and policymakers in decision-making and holding effective interventions to prevent and control of diabetes.

However, this study has limitations that should be considered when interpreting the results. Most of the reports that were used in the present study were against the fixed ADA target (i.e., $HbA1C < 7\%$) rather than personalized targets as recommended in many recent guidelines [53]. In addition, we were unable to provide the pooled analysis for determining factors associated with uncontrolled glycaemia because the included studies classify the variables in various methods. Finally, meta-regression and subgroup analyses did not indicate enough factors to explain the observed heterogeneity. We propose future studies are necessary to better understand differences in glycemic control among different populations.

Fig. 4 Funnel plot of studies reporting achievement of HbA1c target



Conclusion

Only 33.1% of people with type 2 diabetes had good glycemic control according to HbA1C. The results of this meta-analysis imply the need to mobilize public health resources to enhance empowerment of people with diabetes to increase appropriate self-care practice and to identify effective strategies to improve patient-physician partnerships. Further large-scale nationally representative studies are needed to assess current practice against individualized glycemic control targets. In this regard, population-based databases and registries are recommended.

Author contribution MM, MHB, and RK contributed to the conception and design of the research. MM, MHB, and RK reviewed the literature and drafted the manuscript. MM and MHB contributed to the analysis of data. All authors contributed to the interpretation of the data and revision. All authors read and approved the final manuscript.

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Declarations

Conflict of interest The authors declare no competing interests.

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