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Review Article

Systematic Review and Meta-Analysis Estimating the Prevalence, Burden, and Trend of Diabetes Mellitus in Saudi Arabia

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Abstract

The aim of this study was to determine, using meta-analysis, the prevalence of diabetes mellitus (DM) and to explore the influence of method of diagnosis, DM types, and study year on the prevalence of DM with the view to evaluating the trend and the burden of DM in KSA. Prevalence estimates were derived using a random effect model on carefully selected population-based studies in KSA. The derived estimates were applied to the total populations in the country to give an estimated burden of DM. Twenty-one studies, with 376,998 participants out of whom 54,837 had DM, were selected. The prevalence of DM was 20.9%, 0.9%, and 12.6% for T2DM, T1DM, and combined T1/T2DM, respectively. Subgroup analysis using the method of DM diagnosis showed that the prevalence of DM was 14.2% (95% confidence interval [CI]: 9.3% to 19.0%) in the fasting plasma glucose group, 6.8% (95% CI: 2.6% to 11%) in oral glucose tolerance group, and 12.5% (6.2%–18.9%) in glycated hemoglobin group. Meta-regression revealed 4.6×10^{-3} increase in prevalence per year. The prevalence of DM in Saudi Arabia is high. There is a rising trend in the prevalence of DM in KSA and it is accompanied by a proportionate increase in the burden of DM.

Keywords: Burden, diabetes mellitus, prevalence, Saudi Arabia, trend

Introduction

The increasingly burgeoning prevalence of diabetes mellitus (DM) is a growing global health concern. In a recent report by the International Diabetes Federation (IDF), about 425 million persons are living with DM worldwide, with nearly 50% of them undiagnosed.[1]

DM is a metabolic disease of multiple etiologies. It occurs as a result of defects in insulin secretion, action, or both resulting in hyperglycemia.[2] The magnitude of DM in a community tends to change with the demography of that community. Populations that were hitherto considered minimally affected or entirely unaffected by DM are now reporting an increasing prevalence of the disease.[3] An increase in the prevalence of DM is often accompanied by a real challenge of health financing by governments and nongovernmental organizations.

The Middle East, due to rapid economic uptrend, has witnessed marked urbanization, a monumental lifestyle transformation, and a consequential rise in the prevalence and burden of diabetes.[1] The Kingdom of Saudi Arabia, like many other nations in the middle east, has seen a quantum leap in socio-economic status. Regrettably, accompanying this upswing in lifestyle was the lack of exercise, indulgence in unhealthful diet, obesity, and overweight. A corollary to this development was the inclusion of the kingdom in the global epidemic of DM.[4] DM has become the most challenging health problem facing KSA.[5] Saudi Arabia Ministry of Health estimated that about 0.9 million people were diagnosed with diabetes in 1992, but this figure rose to 2.5 million people in

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2010, representing a 2.7 times increase in the incidence rates in <2 decades.[6] In 2015 alone, almost 5000 people living with diabetes attended the family and medical clinics across the country.[6]

Many studies have evaluated the prevalence of DM in KSA, but the exact prevalence of DM has been difficult to obtain. Consequently, there are marked variations in the prevalence of DM figures in different in different regions or neighboring geographical settings of the same country.

Data on the prevalence of DM in KSA varied remarkably from one part of the country to another with figures obtained from population-based studies ranging from 4.08%[7] to 31.5%.[8] This marked variation in prevalence estimates of DM could be attributed to the wide variation in the study design, risk factors, population demographics, case definitions, or case ascertainment. The wide variation in the estimates of prevalence from KSA complicates the use of these data in estimating the number of people with DM who may benefit from treatment and in informing national public health policy. Furthermore, differences in prevalence figures could have implications for resource allocation in public health interventions.

Thus, a robust national prevalence rate of DM is needed to assess the burden of DM, and to develop programs and priorities to tackle problems associated with DM. Besides, knowledge of a national estimate of epilepsy would be useful in the design and implementation of a multisite nation-wide prevalence study on DM.

A systematic review and meta-analysis of observational studies in epidemiology (MOOSE) could help explain the variability in the existing literature, and through pooling of the available data, produce a more precise estimate of prevalence as the strength of a well-conducted meta-analysis is in its ability to pool the results from the existing small studies that are possibly underpowered to detect a desired robust effect size.

The current study, therefore, aimed to determine the prevalence of DM by pooling population-based data from studies conducted in various parts of KSA, explore the existing variations in the prevalence of DM in KSA along the method of diagnosis of DM, types of DM, and year of the study with the view to finding the trend of the disorder and evaluate the burden of DM in KSA.

Methods

Literature search

We conducted English-language literature search on PubMed, MEDLINE, EMBASE, and ISI databases. We also referenced the existing systematic reviews, specialty journals, several websites, and other search engines such as Google Scholar. Reference lists of identified articles were also searched for relevant titles, and these were, in turn, searched online. Conduct and reporting of this study were in accordance with the guidelines on MOOSE and Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) respectively.[9,10]

Search strategies

The database search was performed using the main search terms such as "DM," "hyperglycemia," "Diabetes," "Prevalence," "incidence," "epidemiology" "Kingdom of Saudi Arabia," and "Saudi Arabia" to identify relevant articles published anytime up to December 2018. We contacted the authors of articles in journals that were not available online. Combined text words and Medical Subject Headings (MeSH) terminologies were used where applicable. Boolean operators were used to combine the search terms as necessary, and the MeSH tree was used to increase the specificity of the search terms in MEDLINE, and EMBASE databases. We broke down the review question into search terms to develop a search strategy.

To make our search more effective, a combination of these keywords was also explored. Titles and abstracts of the search results were screened to determine the relevance of the studies. Full-texts of selected studies were also reviewed. We also manually searched the reference lists of all identified publications and recent systematic reviews. Book chapters and review articles on the subject were also perused independently by two investigators on-screen to select potentially relevant studies. To reduce potential publication bias conference proceedings, technical reports on DM and medical organizational websites were also searched. The last search was performed on December 8, 2018. Studies that evaluated the prevalence of DM were considered prima facie relevant.

Study selection

We included cross-sectional or prospective community-based or population-based studies measuring the prevalence of DM from any part of KSA. The prevalence estimate was obtained from papers that met the following criteria:

Inclusion criteria

A study was included if it reported the prevalence of DM or provided the denominator to allow recalculation of the presented or required estimates. Two independent authors (OLF and ODS) selected the studies based on our eligibility criteria. Disagreements were resolved Studies using a third author (BA). Studies included in the meta-analysis were those that utilized the oral glucose tolerance test (OGTT), the random plasma glucose (RPG) test, the fasting plasma glucose (FPG) test, and glycated hemoglobin (HbA1c) as well as studies that included already diagnosed diabetic patients on medications.

Exclusion criteria

A study was excluded if it provided inadequate or ambiguous information on the prevalence and mode of diagnosis of DM.

Data extraction

We extracted data using a form designed to capture the information of interest from the articles for this review. Three investigators (OLF, ODS, AII) extracted all the data independently. All the studies were re-checked against pre-determined inclusion and exclusion criteria. From each

included study, we obtained information on the author, year of study, year of publication, study setting, study type, study population, data collection and ascertainment method(s), and age of study participants. The data were coded based on the name of the first author of the study, and the year the article was published. Multiple coder agreements were assessed using Cohen's kappa.[11]

Operational definitions

Consideration was given to studies in which DM was diagnosed based on the 1999 WHO diagnostic criteria for DM or the ADA 2010 diagnostic criteria for DM.[2,12] Using 1999 WHO diagnostic criteria,[2] the cutoff considered for diagnosing DM in this study were plasma glucose values were FPG of 7.0 mmol/L, RPG of 11.1 mmol/L, and plasma glucose 2-h postglucose load (75 g) of 11.1 mmol/L. A study was also considered for this meta-analysis diagnostic of DM if conducted on the basis of HbA1c value of 6.5% in accordance with the 2010 ADA diagnostic criteria for DM.[2]

Quality assessment and reporting format

This meta-analysis was performed and reported in accordance with specific guidelines/checklist of the MOOSE[9] and PRISMA statements[10] [Figure 1]. A 12-point scoring system was used to rate the quality of the articles extracted. The scoring was based on the modified Downs and Black checklist.[13] The Modified checklist, which had been previously used and validated,[14] comprises a 12-point questions (if the objectives of the study were clearly described if the study design was clearly outlined, if the participants were representative of the population from which they were recruited if the participants were recruited during the same time period if used of modest sample size, if management of missing data, age, gender, and other characteristics were explored or reported. The other questions in the checklist included a report of confounders, report on potential biases and a clear statement on the outcome, i.e., prevalence. Also included in the assessment were other established items associated with study quality.

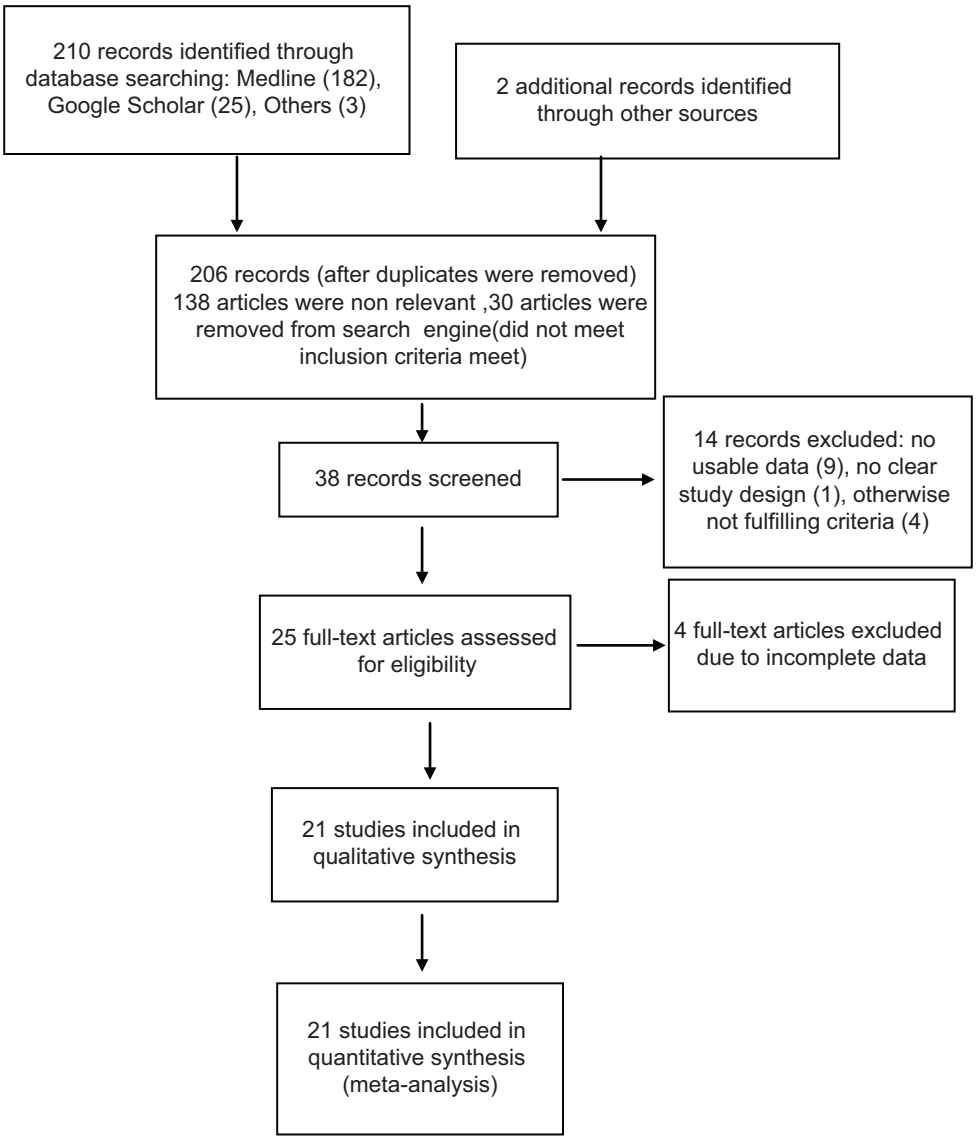

Figure 1: Flow diagram of the process of article selection for the systematic review and meta-analysis

Two of the investigators independently conducted the scoring of the articles. We graded the quality of the studies into three levels (C [1–4], B [5–8] and A [9–12]) in increasing order of quality from C to A.

Data synthesis including assessment of heterogeneity

The primary outcome measure was the prevalence of DM in KSA. The binomial probability distribution was used to determine the standard error of prevalence. The prevalence of DM, expressed in percentage and 95% confidence interval (95% CI), was calculated for each of the selected studies. The log of prevalence (logP) and the standard error of logP were computed for the respective studies. Meta-analyses were conducted for prevalence estimates. Because of the variability associated with observational studies, we used a random-effects model (REM) by DerSimonian and Laird for estimate summary and 95% CIs from included studies.[13] combined results and obtained meta-analysis estimates using.

Statistical heterogeneity was evaluated by conducting tests of between-study heterogeneity, and I square (I^2) statistics with $I^2 > 50\%$ denoting substantial heterogeneity. The impact of publications on the overall prevalence was examined using sensitivity analysis.

Restricted scenario or sub-group analyses were performed on data derived from studies with similar characteristics. Publication bias and small-study effect were assessed by visual inspection of funnel plots and by using Begg's adjusted rank correlation tests and Egger's regression asymmetry test.[15,16] Given the inconsistency and the insensitivity of the tests,[17] publication bias was considered to exist only if detected in both tests. We also performed univariate, weighted, least-squares meta-regressions to identify study-level characteristics (mean or median age of participants and years of study) associated with prevalence.

The trend of DM over time was determined for prevalence rates of DM using an absolute result of subgroup analysis over the years of publication classified into before 1989, between 1990 and 1999, between 2000 and 2009, and >2009. Further trend evaluation was also conducted using Meta-regression with prevalence as a dependent variable and study year as an independent variable. The burden of DM was calculated to reflect the total number of people living with DM in KSA.

The analysis was carried out using Stata version 12.0 (Stata Corp., College Station, TX, USA).

Results

Overview of selected studies and characteristics of participants in the studies

A total of 21 studies met the inclusion criteria for the meta-analysis. Table 1 shows the main characteristics of the studies included in the final analysis. They included studies from most of the regions of KSA and as such, can be considered to be fairly representative of KSA as a whole. The total number of participants was 376,998 in the 21 studies analyzed. Out of the study participants, 54,837 people were discovered to have diabetes. Random sampling technique was employed in the majority (13 out of 19) of the studies, whereas participants

Table 1: Characteristics of the studies included in prevalence of DM in Saudi Arabia

Author	Year	Total	Cases	Age (yrs)	Type of diabetes	Study design	Setting	Method of diagnosis	Quality grading
Al-Nozha *et al*	2000	16917	4004	30-70	T2DM	Cluster	Multi-region	FPG	A
Alqurashi *et al*	2011	6024	2279	≤70	T2DM	Convenience	Jeddah	SR*	C
Al- Rubeaan *et al*	2015	18034	4576	≥30	T2DM	Random sampling	Multi-region	FPG	A
Al- Rubeaan *et al*	2009	23523	2550	≤18	T2DM/T1DM	Multi-stage stratified	Multi-region	FPG	A
Al-Nuaim *et al*	1997	7495	970	≥15	T2DM	Random sampling	U	OGTT	A
Al-Nuaim *et al*	1997	5682	425	≥15	T2DM	Random sampling	R	OGTT	A
Abu-Zeid *et al*	1992	1233	57	≥10	T2DM/T1DM	Convenience	Abha	RBG	B
Fatani *et al*	1987	5222	224	>30	T2DM/T1DM	Convenience	Western region	RBG	B
Warsy *et al*	1999	14660	1224	>14	T2DM/T1DM	Multi-stage stratified	Multi-region	FPG	A
Altemani *et al*	2016	120	12	>20	T2DM/T1DM	Random sampling	Tabuk	FPG	A
Bacchus *et al*	1981	1385	34	All	T2DM/T1DM	Convenience	Al-Kharj	OGTT	A
Hussain *et al*	2014	4525	1408	All	T2DM/T1DM	Convenience	Hail	FPG	A
Al-Herbish *et al*	2007	45682	50	≤19	TIDM	Multi-stage stratified	Multi-region	SR	C
Karim *et al*	2000	3747	153	All	T2DM/T1DM	Retrospective	Riyadh	FPG	C
Al-Daghri *et al*	2011	9149	2114	≤80	T2DM	Cluster	Riyadh	FPG	B
Al-Daghri *et al*	2011	9149	161	≤80	T1DM	Cluster	Riyadh	FPG	B
El Hasmi *et al*	1988	3641	289	All	T2DM/T1DM	Convenience	Multi-region	FPG	C
Anokute *et al*	1990	3158	190	18-65	T2DM/T1DM	Convenience	Riyadh	FPG	C
Al Baghli *et al*	2010	195852	33859	>30	T2DM/T1DM	Convenience	Eastern province	FPG	A
Aldossari *et al*	2018	381	35	≥18	T2DM/T1DM	-	AlKharj	HBAic	A
Bahijiri *et al*	2016	1419	223	≥18	T2DM	Cluster	Jeddah	HBAic	A

*SR=Self report of previously diagnosed DM on medications

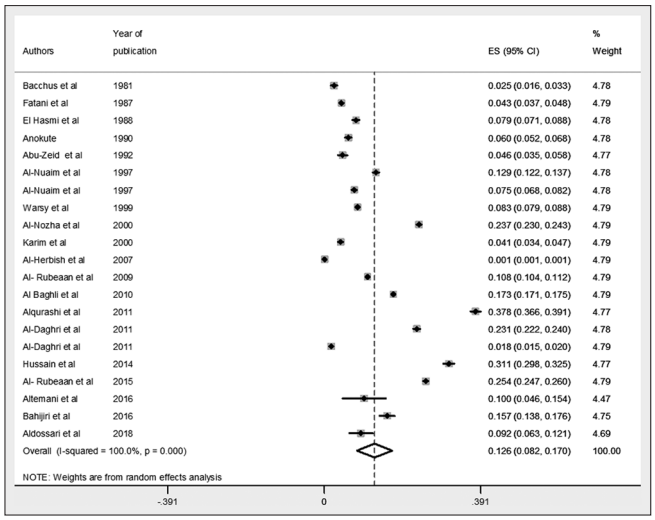

Figure 2: Forest plot of studies included in meta-analysis with pooled prevalence of DM

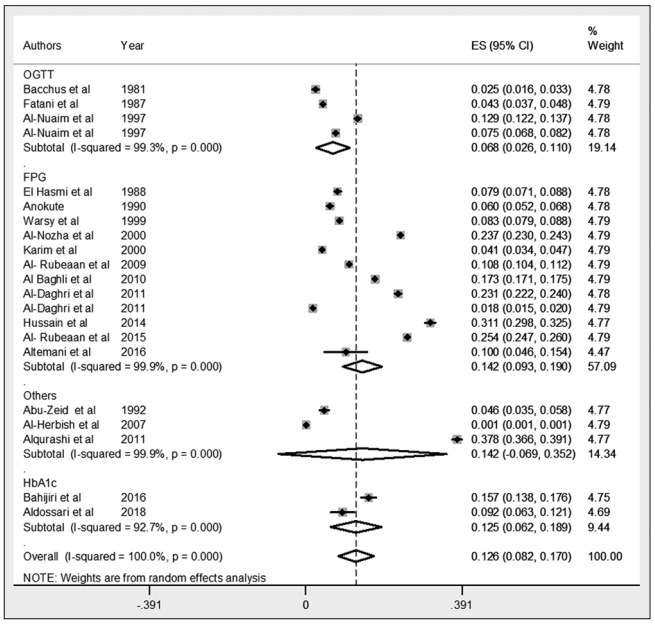

Figure 3: Forest plot of subgroup analysis of prevalence by method of diagnosis of DM

were selected by convenience sampling in the remaining six studies. Six of the studies covered multiple geopolitical regions of KSA [Table 1].[18-23] Twelve of the 21 studies used FPG as a means of diagnosis of DM, while two studies used HbA1c [Table 1] to diagnose DM. Only two studies[24,25] were conducted on <1000 participants. Eight of the studies were published before 2000,[21,22,26-29] 4 studies[8,18,19,23] were published between 2000 and 2009 (inclusive), and the remaining between 2010 and 2018 (inclusive).[7,20,24,25,30-32]

Overall prevalence in KSA

The overall prevalence estimate of DM (type 1 and type 2) in KSA was 12.6% (95% CI: 8.2-17.0%) [Figure 2]. Measure of heterogeneity showed significant heterogeneity (I^2 = 100%, P = 0.000).

Publication bias using Egger's test for small-study effects showed no small-study effect (P = 0.003). However, Begg's test showed significant publication bias (P = 0.753). This finding was also evident in an asymmetric funnel plot obtained during the analysis.

Sources of heterogeneity and Subgroup, sensitivity, and regression analyses

Sequel to the significant heterogeneity recorded in the overall meta-analysis which could be partly explained by the potential effect of the different estimate effect modifiers such as method of diagnosis of DM, types of diabetes DM studied, and year of the studies, we undertook subgroup analyses using the method of diagnosis, type of DM, and year of the studies. The subgroup analysis using method of DM diagnosis showed that the prevalence of DM was 14.2% (95% CI: 9.3%–19.0%) in the studies that used FPG, 6.8% (95% CI: 2.6%–11%) in OGTT group, 12.5% (6.2%–18.9%) in HbA1c group, and 14.2% (95% CI: 6.9%–35.2%) in other methods group (being a known diabetic on medications as at the time of the survey) [Figure 3]. Similarly, stratified analysis using the type of DM showed that the prevalence of T2DM was 20.9% (95% CI: 14.1%–27.6%), T1DM was 0.9% (95% CI: −0.7%–2.5%), and 9.7% (95% CI: 5.7%–13.7%) among studies that focused on both type 1 and type 2 DM [Figure 4].

To evaluate the trend of DM over time, subgroup analysis was also carried out over the years. The overall prevalence of DM was 4.9% (95% CI: 2.1%–7.6%) between 1980 and 1989, 7.9% (95% CI: 5.6%–10.3%) between 1990 and 1999, 9.7% (95% CI: 0.2%–19.2%) between 2000 and 2009, and 19.1% (95% CI: 11.9%–26.4%) after 2009 [Figure 5]. On sensitivity analysis, the study from Altemani *et al*. had the least influence on the pooled summary effect of the prevalence.

To further explore the heterogeneity observed in the study, we carried out meta-regression: Meta-regression of prevalence and year of the studies showed coefficient of −0.0046 (95% CI-0.00059–0.009, P = 0.030) with t = 2.47 and R^2 = 20.6% depicting that the prevalence of DM significantly increases by 4.6 × 10^{-3} per year. However, this relationship can only explain 20.6% (R^2 value) of the variance observed in the meta-analysis [Figure 6].

The burden of diabetes mellitus in KSA

Assuming KSA has an estimated population of 33,335,000 people (nationals and non-nationals) as of 2018,[33] the overall burden of DM, calculated based on the overall estimate of the prevalence (type 1 and type 2 DM) was 4, 200, 210 persons (95% CI: 2,733,470–5,666,950 persons). However, based on the prevalence of type 2 DM only, the burden was 6,967, 015 (95% CI: 4,666,900–9,200,460) people.

Discussion

The prevalence estimates of DM presented in the current study were based on a meta-analysis of the observational

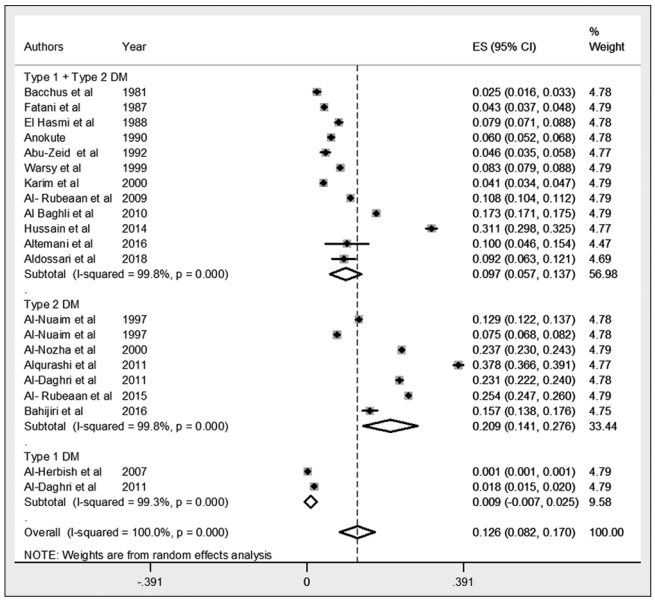

Figure 4: Forest plot of subgroup analysis of prevalence by type of DM

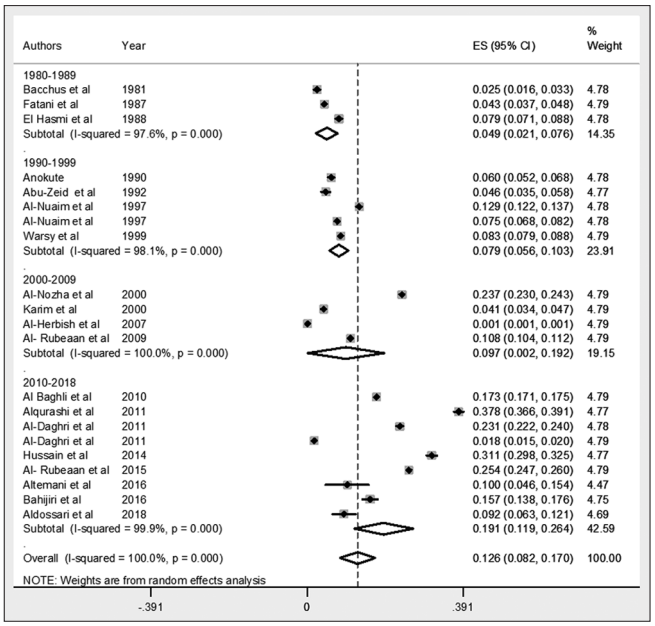

Figure 5: Forest plot of subgroup analysis of prevalence by year category

study technique showed that the overall prevalence of DM Kingdom of Saudi Arabia was 12.6%. However, the prevalence of T2DM was 20.9%. The marked difference between the overall and T2DM prevalence figures was possibly from the water-down-effect of T1DM studies that were included in determining the overall prevalence figure as the prevalence of T1DM is less than on (0.9%). That notwithstanding, these figures, which are similar to those reported for United Arab emirate[34] Tunisia,[35] OMAN,[36] is consistent with the IDF 2017 estimates of people living with diabetes in the Middle East and North Africa region.[4]

Of note is our finding on evaluation for the trend of DM, analysis of pooled data from studies carried out in Saudi Arabia before 1989, 1990–1999, 2000–2009, and after 2009 showed a remarkable steady increase over time, i.e., from 4.9% to 7.9% to 9.7% to 21%, respectively. This finding mirrors the demographic changes with increased life expectancy and lifestyle changes due to rapid urbanization and industrialization experienced in the kingdom.[37] Over the last forty years, there has been an increase in physical inactivity, unwholesome dietary habits, obesity, and increasing sedentary lifestyle in Saudi Arabia,[38] Al-Hazzaa *et al*. reported that a very high proportion (84% for males and 91.2% for females) of Saudi adolescents spent more than two hours on-screen time daily, and almost half of the males and three-quarters of the females did not meet daily physical activity guidelines.[38] Central to this phenomenon is the significant rapid socio-economic transformation as well as a change in dietary habit engendered by affluence and possibly spawned by an existing heredofamiliar susceptibility to DM.

In conformity to this trend, is our observation on meta-regression of prevalence over the years, which revealed that the prevalence of DM increases significantly by 4.6×10^{-3} per year.

The overall prevalence of DM obtained from a study that used OGTT for diagnosis was lower (6.8%) than the estimate from studies that used FPG (14.2%). This result implies that OGTT, being a more stringent method of diagnosis of DM, is less likely to over-diagnose the condition. Nevertheless, diagnosis of DM is easy when there are overt symptoms and thus, a glucose tolerance test is hardly ever necessary for clinical purposes. OGTT has, however, allowed more detailed epidemiological characterization based on the existence of separate glucose thresholds for a macrovascular and microvascular disease which correspond with the levels for the diagnosis of impaired glucose tolerance and diabetes as specified by the WHO criteria.[2] Although American Diabetes Association recommended the use of the glycosylated hemoglobin [HbA1c) test in the diagnosis of DM in 2010,[2] only two of the studies included in the current meta-analysis utilized the technique to diagnose DM in Saudi Arabia. HbA1C captures chronic hyperglycemia better than the two assessments of FPG or OGTT plasma glucose.[39] It is a biochemical parameter that describes the extent of a biological phenomenon over a long period, thereby providing a more robust indicator of glycemia than a parameter describing it in the short term or a given moment only. Thus, the use of HbA1c for diagnosing diabetes is fast becoming a reality in many Western countries.[39]

The reasons for the heterogeneity observed in this analysis may include the use of different survey methods, varying screening tools, and different case ascertainment standards. Nonetheless, several attempts were made to lessen the effect of possible methodological variation of the component studies in the course of this meta-analysis. We explored within and in-between studies variation by using a random-effect model for the analysis of the pooled data, by quantifying the

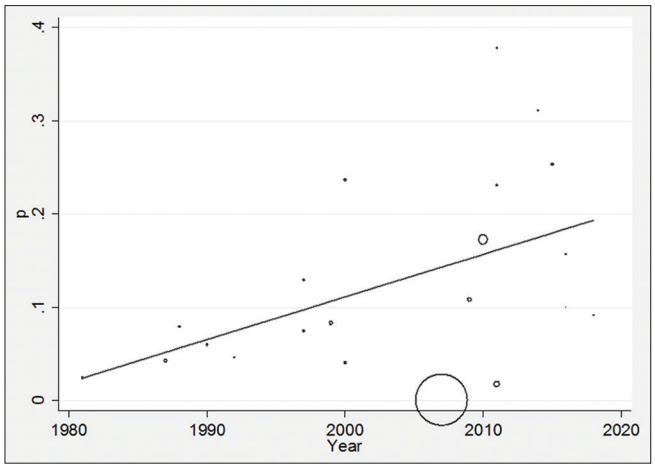

Figure 6: Meta-regression plot showing the trend in prevalence of DM over the years

magnitude of the heterogeneity, and by conducting sensitivity analysis and subgroup analysis.

Having noticed the potential burgeoning prevalence of diabetes in the middle east, the concerned experts from the region had an International Conference on Healthy Lifestyles and Non-communicable Diseases in the Middle East and Arab World and in Riyadh in Saudi Arabia in 2012 and came up with a communiqué (Riyadh Declaration) to have an annual screening for metabolic syndrome, and to refer individuals that are diagnosed through the screening package to adequate and accessible care. Moreover, the importance and recognition of schools as a major avenue for Non-Communicable Diseases prevention was also emphasized. Other essential points in the release included the imposition of nutritional labeling on all fast food items as well as the promotion of consumption of fresh fruits and vegetables as well as low-calorie diet were accorded attention in the communiqué. The governments, at all levels, were also charged to impose heavy taxation on items, such as energy drinks, tobacco products, and other food items with adverse health effects. They, among other things, advised that new residential developments should include environments that are exercise-friendly. In our opinion, if the Riyadh declaration can strictly adhere to Saudi Arabia will witness a tremendous reduction in the prevalence of DM in the country.

We, therefore, like previous authors,[39,40] recommend an intensive promotion of public health awareness in respect of DM, continued efforts geared towards a relentless community-based screening and an early intervention as part of the Saudi National diabetes care and prevention policy and program. An effort made along this line will be worthwhile to stem the skyrocketing prevalence of DM and its accompanying burden in the kingdom.

To the best of our knowledge, this meta-analysis is the first of its kind to quantitatively pool data from the existing studies; to generate estimates of the prevalence of DM, to evaluate the influence of subgroup variables on the prevalence estimate, and by using meta-regression model, to determine the trend of DM in Saudi Arabia.

Limitations of this meta-analysis include language restriction in our search to English giving room to the possibility of missing are not published in the English language. However, the official language of medical journals in Saudi is English, therefore, the chances of missing out work published in Arabic language is quite remote. Other limitations include the presence of methodological issues, such as the use of different screening or diagnostic tools and divergent study designs in the composite studies might have influenced the prevalence figures obtained in this analysis. Consequently, this raises questions about the possibility of under-estimation of DM in the areas where the studies were conducted. A number of the studies that we included in this analysis did not declare the focus of their studies as to whether their study was focused on type 1 or type 2 DM. Some of the authors did not explicitly state whether their studies were conducted in an urban or rural setting making subgroup analysis based on rural or urban dwelling difficult. Most of the studies included did not document gender or age-specific prevalence, thereby making it difficult to generate pooled gender or age-specific prevalence figures for the region. The burden of DM was calculated based on the total population of Saudi Arabia. It is, however, worthy of note that a significant percentage of the inhabitants of the kingdom are immigrants seeking economic opportunity. They constituted almost 40% of the total Saudi population.[41] As much as we would also have liked to calculate the burden of DM in the kingdom using daily adjusted life in years, the absence of adequate requisite data made this impossible.

It is, however, worthy of note that outcome of this study does not, in any way, underestimate the fact that only a large, representative, and rigorous national epidemiological survey, conducted at the same time using the same methodological approach with all the regions of Saudi Arabia represented, will deliver a more reliable overall prevalence of DM in Saudi Arabia. Nevertheless, in the absence of such a national survey, a meta-analysis of all the observational studies cutting across most of the geopolitical zones of the kingdom provides robust estimates of the magnitude of DM, and hence, could be of use in planning prevention and treatment of DM in Saudi Arabia.

Conclusion

The prevalence of DM in Saudi Arabia is high (20.9%, 0.9%, and 12.6% for T2DM, T1DM, and overall prevalence, respectively) and has been on the increase over the last four decades. This increase is accompanied by a proportionate increase in the burden of DM in the kingdom. Therefore, the need for improved national diabetes care and prevention policy and action cannot be overemphasized.

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Conflicts of interest

There are no conflicts of interest.

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