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Diabetes Mellitus and Its Association with Hypertension in Ethiopia: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Diabetes mellitus (DM) is a growing public health concern globally, including Ethiopia. Although numerous studies have been published from different parts of Ethiopia, no attempt is made so far to estimate the burden of DM at the national level. This study aims to estimate the pooled prevalence of DM and its association with hypertension in Ethiopia.
Methods: A systematic search was conducted in major databases. Two authors extracted the necessary data and analysis was conducted using STATA version 14. Heterogeneity across the studies was evaluated by Cochran's Q test and I^2 statistics.
Results: Eighteen studies with a total of 45,284 participants were included in this review. The pooled prevalence of DM was 4.99% (95% CI: 3.86%, 6.11%). Hypertension was significantly associated with DM (OR: 8.32; 95% CI: 3.05, 22.71).
Conclusion: The burden of DM in Ethiopia is considerable, and the association between diabetes and hypertension is significant. Based on the evidence, this review recommends establishing the coordinated national programs that counteract the increasing burden of DM in the country is very essential. In addition, Early hypertension screening should be done in diabetic patients to control co-morbidity and further complications.

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1. Introduction

Diabetes mellitus (DM) is a growing public health concern that affected more than 285 million people worldwide [1–3]. The burden of DM has significantly increased by 12-fold between 1985 and 2011 [4,5]. According to the International Diabetes Federation, the number of adults with DM will increase to 50.7% globally by 2030 [4]. DM also annually claims the lives of more than 4 million people with high proportion in developing countries [6]. Evidence also indicated that the number of people with DM would reach 592 million by 2030 [7]. Complications related to DM are a major cause of morbidity, mortality and reduced quality of life. For instance, globally an estimated five million people aged 20–79 years old prematurely die each year due to DM [7]. Developing countries will share the burden of DM to the magnitude of 77% of the global burden in the 21st century [8]. This possibility is due to population growth, aging, unhealthy diets, obesity and sedentary life styles [9]. The burden of diabetes is high in Sub-Saharan Africa countries following Asian countries [10]. In Ethiopia, a recent survey conducted in Gilgel Gibe Field Research Center indicated that the prevalence of DM is 6.5% [11]. Furthermore, patient attendance rates and medical admissions in hospitals are currently rising in Ethiopia [12]. Small-scale studies with highly variable results have been reported. However, no national data on the prevalence of diabetes are available [13]. Therefore, the present systematic review and *meta*-analysis is designed to consolidate available data for determining the current magnitude of DM and associated factors among the Ethiopian population.

2. Methods

Studies published and unpublished on prevalence of DM and associated factors in Ethiopia till 17 April 2019 were retrieved using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

2.1. Protocol and registration

The review protocol was not registered since it is optional.

2.2. Eligibility criteria and review process

2.2.1. Inclusion criteria

Population: This review included studies conducted in different regions of Ethiopia to determine the prevalence of DM and its associated factors, on all age groups, any occupation and both sexes were included. Studies conducted among Ethiopian populations residing outside Ethiopia were also included.

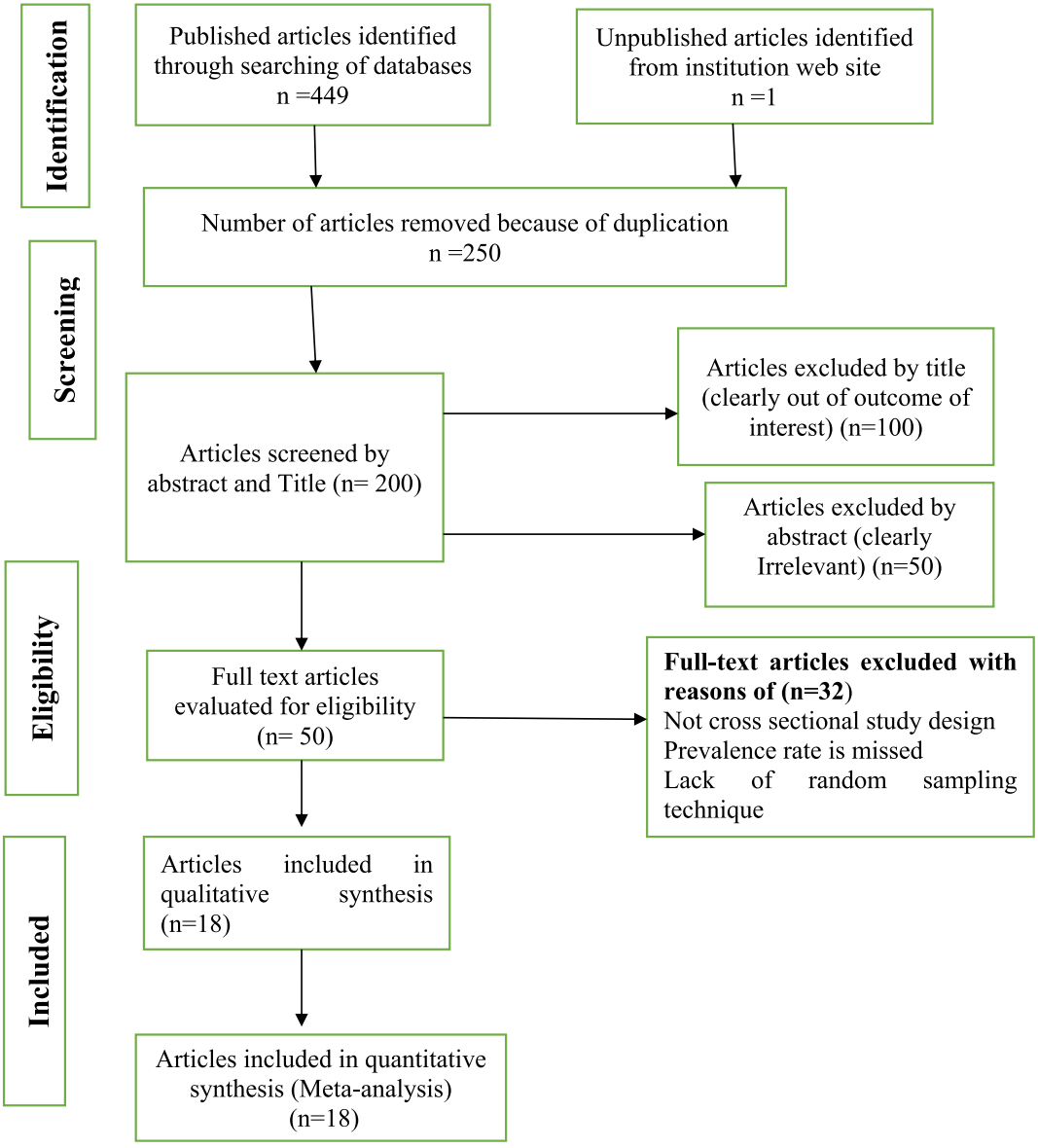

Fig. 1 – Process of identification and selection of studies for inclusion in the review.

Study setting: Studies conducted at community or institutional level were included.

Study design: All types of observational studies were included.

Publication type: Published and unpublished studies written in English were included. For studies published in more than one report, most comprehensive and up-to-date versions were considered.

2.2.2. *Exclusion criteria*

Letters to editors, case series and case–control studies were excluded from the analysis because of their insufficient data. Title, abstract and full text of studies were evaluated and assessed before being included in the final review and *meta*-analysis. Moreover, studies that were partially accessed after at least two email contacts of the primary authors were excluded for the difficulty encounters during assessing the methodological quality in the absence of the full text. Studies that appeared under more than one search term, reported by another language other than English, studies that are self-identified as pilot/feasibility work, follow-up work with no new outcome measures and research with multiple publications were excluded.

2.2.3. *Study selection*

Studies were identified through electronic database search and reference lists. Another study was identified from the online digital library of Addis Ababa University. Following the search, all identified citations were collected and uploaded into EndNote version 7.0 and duplicates removed. Titles and abstracts were then be screened by two independent reviewers for assessment against the inclusion criteria for the review. The Cochrane acronym PICO or PICOC, which stands for population, intervention, comparison and outcomes (and context), was used to decide on all key components prior to starting the review. The identified studies

were filtered to select the relevant ones from the searches. The first step is pre-screening, that is, to decide which studies will be retrieved fully. The second step includes selecting the studies that need to be re-examined and deciding on the ones that will be included in the review. The next step is selecting eligible studies based on similar study design, publication year, language, choice among multiple studies, sample size or follow-up issues, similarity of exposure and completeness of information. All relevant studies, including unpublished ones (desk drawer problem), those that came with negative conclusions or thesis, reports and studies with small sample sizes, were included. The full text of selected citations was assessed in detail against the inclusion criteria by two independent reviewers. Reasons for exclusion of full text studies that did not meet the inclusion criteria were recorded and reported in the systematic review. In this review, a total of 450 studies were retrieved through electronic database and manual searches. From the retrieved studies, 100 were excluded by their titles, 50 by abstract review and the remaining ones due to exclusion criteria (Fig. 1). Finally, 18 studies were included in the systematic review and *meta*-analysis (Fig. 1).

2.2.4. *Information source and search strategy*

The following main databases were systematically searched to identify possible studies for inclusion in this review: MEDLINE, EMBASE, PsychINFO, Web of Science, CINAHL, SocINDEX, Academic Search Premier, Family and Society Studies Worldwide, Women's Studies International, Africa-Wide Information and Google Scholar. The official electronic database of Addis Ababa was also searched [14]. Unpublished studies undisclosed in mainstream databases were sourced from Addis Ababa University registries/digital library. Studies were searched using the following key words separately or in combination with Boolean operators: ('epidemiology'[Subheading] OR 'epidemiology'[All Fields] OR 'prevalence'[All Fields] OR 'prevalence'[MeSH Terms]) AND ('diabetes mellitus'[MeSH Terms] OR ('diabetes'[All Fields] AND 'mellitus'[All Fields]) OR 'diabetes mellitus'[All Fields]) AND associated [All Fields] AND factors [All Fields] AND ('Ethiopia'[MeSH Terms] OR 'Ethiopia'[ll Fields]). The literature search strategy was adapted to suit each database. The main search strategy conducted in searching in PubMed/MEDLINE was reported in Additional file 1. The searching language was limited to English, and the study category was limited to human research. The searching of studies was carried out from March 2019 to April 2019. The present systematic review and *meta*-analysis was reported using the guideline of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [15].

2.2.5. *Data extraction*

Two investigators (BT and AA) extracted all the necessary data by using pretested data extraction format. Extracted data included first author, publication year, study design, study setting (population-based or institution-based), sample size, age group of study participants, response rate, study region, type of DM, prevalence of DM and study quality. Disagreements between the two investigators on the study inclusion was resolved through discussion with the third reviewer (AG). The studies retrieved from different databases were exported into Endnote X7 to identify and delete duplicate records.

2.2.6. *Types of outcomes*

This review revealed two main outcomes. The primary outcome was the pooled prevalence of DM in Ethiopia, while the second outcome was the association between DM and hypertension. Individuals who present symptoms (polyuria, polydipsia and unexplained weight loss with glucosuria and ketonuria); fasting blood glucose concentration > 126 mg/dl, random blood glucose > 200 mg/dl, two-hour blood glucose > 200 mg/dl during oral glucose tolerance test and/or gestational DM 2-hour post glucose load greater than 140 mg/dl; or self-history/report of antidiabetes medications were considered to have DM based on the definition of the included studies. The prevalence of DM was determined by dividing the number of participants with fasting blood sugar $\geq$ 126 mg/dl and/or random blood sugar > 200 mg/dl by the total study sample size. The association between DM and hypertension was assessed in terms of odds ratio.

2.2.7. *Quality assessment*

The quality of the included studies was separately assessed by two reviewers, and disagreements between them were resolved through discussion with the third reviewer. The Newcastle–Ottawa Scale for cross-sectional studies was used to assess the quality of the included studies [16]. This method was developed to assess the methodological quality of non-randomised studies. The scale assesses three main perspectives, namely, participant selection, comparability between groups and outcome ascertainment [16]. A study was awarded with a maximum of one star for each numbered item within the selection and exposure categories. A maximum of two stars were given for the comparability. High-quality studies were determined if the total score was six or above out of 10.

2.2.8. *Qualitative synthesis of systematic review*

An adapted version of the risk of bias tool for prevalence studies developed by Hoy and colleagues was used to assess the quality of the included studies for the outcomes of interest [17]. A score of 0–4, 5–7 or 8–10 rated the risk of bias as high, moderate or low, respectively. Two investigators (CT and AF) independently assessed the quality of the included studies. The disagreements between the two authors were resolved through consensus or arbitration involving the third reviewer (KA).

2.2.9. *Data analysis*

Data were extracted from each study by using a format prepared in Microsoft Excel spreadsheet and imported to STATA version 14 statistical software for analysis. Statistical heterogeneity was evaluated by Cochran's Q statistics and I^2 test. The I^2 test provides an estimate of the percentage of the variability in effect estimates as a result of heterogeneity rather than sampling error or chance differences. The existence of heterogeneity was verified using Cochran's Q test. The I^2 test values of 25%, 50% and 75% were regarded as the availability of low, medium and high heterogeneity, respectively [18]. A random effects *meta*-analysis model was used to estimate the Der Simonian and Laird's pooled effect to show heterogeneity. Similarly, a funnel plot was used to asses publication

Table 1 – Summary characteristic of studies in the *meta*-analysis to show the prevalence diabetes mellitus in Ethiopia.

Author	Publication year	Study type	Region	Type of DM	Age group	Sample size	Response rate (%)	Prevalence	Quality score
Tinsae et al.	2017	community based	Addis Ababa	NS	7–12	1067	100	0.3	7
Tesfa et al.	2015	Institution-based	Amhara	NS	NS	385	95.3	0.3	7
Ambachew et al.	2015	Institution-based	Tigray	NS	>=15	20,939	100	1.3	6
Uhomoibhi	2003	Institution-based	Addis Ababa	NS	>= 16	533	89	3.4	7
Abebe et al.	2014	community-based	Amhara	NS	>= 35	1100	97.3	3.6	6
Seyoum et al.	1999	community based	Tigray	GDM	15–50	890	100	3.7	5
Seifu et al.	2015	community based	Oromia	NS	15–64	4371	96.7	5.0	3
Tesfaye et al.	2016	Institution-based	Addis Ababa	NS	18–55	1003	93.3	5.0	7
Muluken G. et al.	2015	Institution-based	Addis Ababa	NS	NS	8048	100	5.2	5
Belachew et al.	2007	Community based	Oromia	Type 2	>=40	576	91.3	5.3	4
Mohammed et al.	2015	Institution-based	Oromia	NS	21–75	403	100	6.4	7
Nshisso et al.	2012	Institution-based	Addis Ababa	NS	NS	2153	100	6.5	7
Ayana et al.	2015	Institution based	Harai	Type2	NS	787	91	7.0	7
Sachithananthan et al.	2013	Institution based	SNNR	NS	18–50	176	100	8.0	6
Abebe et al.	2016	Institution based	Amhara	Type 2	>=15	483	95.6	8.0	6
Workneh et al.	2016	Institution based	Amhara	NS	>=15	1353	97	8.3	7
Assefa G,et al.	2013	Institution based	Amhara	NS	>=15	199	100	8.5	6
Emeshaw et al.	2014	Institution based	Addis Ababa	NS	>=25	120	100	15.8	5

NB:
NS = Not Specified.
GDM = Gestational Diabetes Mellitus.

bias. Moreover, presence of heterogeneity was also assessed by subgroup analysis and metaregression. The effect size in this review is to mean pooled prevalence and odds ratio. Duval and Tweedie's non parametric'trim and fill' method was used to estimate the number of missing studies from the *meta*-analysis as a source of publication bias [19].

2.2.10. *Sensitivity analysis*

Sensitivity analysis was employed to check uncertainty of one or more variables included in the model or to determine whether the conclusions of the analysis are robust when a range of estimates is used. I.e to evaluate the effect of single study on the overall estimation and to explore the impact of excluding or including studies in meta analysis based on sample size, regions and other important variables. Moreover, the values at the extremes of the 95% confidence intervals for effect estimates of key variables or areas with the most uncertainty can be included in additional modeling to determine the stability of the conclusions. For example, each study was left out to see how much changes occurred. If results remain consistent across the different analyses, the results can be considered robust and if it differ, this is an indication that the result may need to be interpreted with caution. Point prevalence with 95% confidence interval was presented in the forest plot. The Egger's weighted regression and Begg's rank correlation test methods were used to assess publication bias ($p < 0.05$ was considered suggestive of statistically significant publication bias). Moreover, publication bias was also assessed by funnel plot using the logit of the prevalence of DM.

3. Results

A total of 18 unique studies were included to estimate the prevalence of DM in Ethiopia and its association with hypertension. The process of identification and assortment of studies for inclusion and exclusion in the review are depicted in (Fig. 1).

3.1. *Characteristics of included studies*

The included 18 studies were cross-sectional in their study design. The age of studies range from 1999 to 2017. Among them, four were community [20] based studies [21–24] and 14 were institution-based studies [25–39]. One included study was unpublished [30], and the rest were published on peer-reviewed journals. The minimum and maximum sample sizes of the included studies were 120 [27] and 20,939 participants [25], respectively. Data on 45,284 participants were pooled. Among the nine regional states and two city administrations under Ethiopian justification, five studies were reported from Amhara regional states [23,26,32,38,39], three from Oromia [22,24,35], one from Southern Nation and Nationality [29], one from Harari [33], two from Tigray [21,25] and six from Addis Ababa City administration [27,28,30,34,36,37] (see Table 1).

3.2. *Quality of studies included in the systematic review*

The quality
of the studies ranged from three to seven out of ten. The majority of the studies scored medium on statistical analysis and data presentation. These studies used a binary logistic regression model to assess factors associated with DM and Chi-squared test to compare among groups [21–39]. Only three studies reported the association of DM with hypertension [32,35,37]. One study used Student's *t* test to compare means of fasting blood sugar among groups and assess their association [38].

One study evaluated the goodness of fit to a normal distribution using the Kolmogorov–Smirnov test [29], and the other studies used Hosmer and Lemeshow goodness of fit test [35]. None of the studies checked for multi-collinearity through Variance Inflation Factor/tolerance and the standard errors of regression coefficients. The outcome variable (DM) was

diagnosed or measured through different methods (see Table 1), such as; symptoms (polyuria, polydipsia and unexplained weight loss with glucosuria and ketonuria) and fasting blood glucose concentration > 126 mg/dl [23–27,29,30,32,33,35–37], random blood glucose > 200 mg/dl [28,38] and two-hour blood glucose > 200 mg/dl during an oral glucose tolerance test [22]. One study used a2 hour post glucose load greater than 140 mg/dl [21], and only one work used medical files [34].

3.3. *Heterogeneity and publication bias*

A significant heterogeneity was observed among the studies in terms of the prevalence of DM (i.e.I^2 = 97.8%, p = 0.00). To address this, random effects *meta*-analysis model was used to estimate the Der Simonian and Laird's pooled effect. Meta-regression was implemented to identify possible sources of heterogeneity using sample size, however, the finding was not statistically significant (p > 0.05). The Egger's weighted regression (i.e. p = 0.02) and Begg's rank correlation test (i.e.p = 0.03) methods were used to assess publication bias and it shows significant publication bias (p < 0.05). Duval and Tweedie's 'trim and fill' method was used to estimate the number of missing studies from the *meta*-analysis as a source of publication bias[19], but the finding was not significantly varied since the newly estimated pooled prevalence is 4.95 as compared to previous 4.99 (Fig. 2).

3.4. *Sensitivity analysis*

The result of sensitivity analysis using random effects model suggested that no single study unduly influenced the overall prevalence estimate of DM (Fig. 3).

3.5. *Meta-analysis*

3.5.1. *Pooled prevalence of DM in Ethiopia*

The highest prevalence of DM was reported in a study among patients with active pulmonary tuberculosis at St. Peter Specialised Hospital, Addis Ababa, Ethiopia [27]. The lowest prevalence was detected in 7–12-year-old school children presented to the Department of Paediatrics and Child Health, Tikur Anbessa Specialised Teaching Hospital, Addis Ababa [28]. As illustrated in Fig. 2, the I^2test result showed high heterogeneity (I^2 = 97.8%) across the included studies, thereby justifying the use of the random effects model to assess the association. The overall pooled prevalence of DM in Ethiopia was 4.99% (95% CI:3.86%, 6.11%) (Fig. 4). The sub-group analysis by regional state indicated that the highest prevalence of DM was reported from Amhara regional state (5.54%; 95% CI: 2.34, 8.74), and the lowest was from Tigray regional state (2.40%; 95%CI:1.01, 4.80) (Fig. 5). Ethiopia has nine regions and two city administrations. The major six regions have been included that represents approximately 94.6% of the whole population according to 2015 Population Census. However, five smallest regions namely, Afar, Somalia, Benishangul Gumez, Dire Dawa, and Gambela were not included due to unavailability of published studies for these regions.

Moreover, the pooled prevalence of diabetes was not separately analyzed for type 1 and 2 DM due to the fact that included studies did not specifically report the type of DM. Similarly, studies that reported the prevalence of DM in pediatric populations and pregnant women were included with the assumption that the review can be benefited from a broader focus without specific population and our research question was also any type of DM in general population (prevalence of DM in Ethiopia) regardless of the type of population.

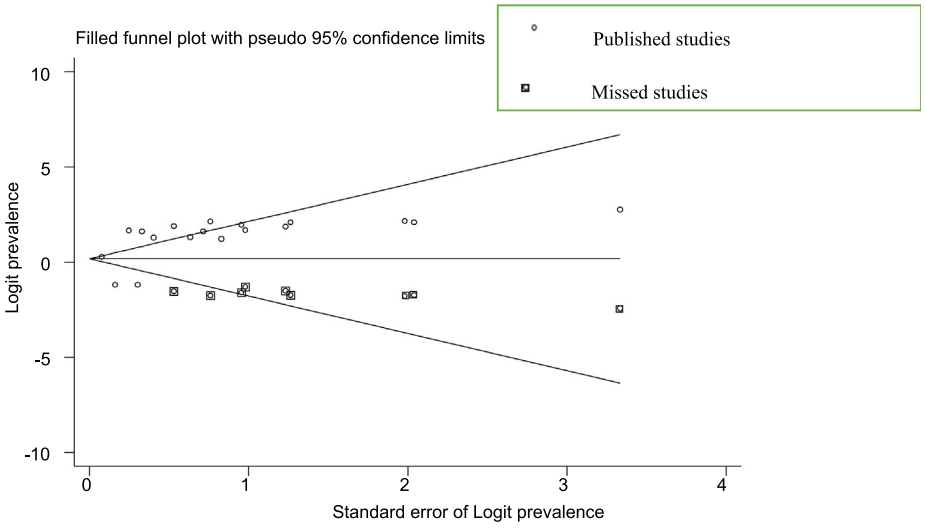

Fig. 2 – The funnel plot of a simulated *meta*-analysis containing 27 studies. The 9 studies with the most negative effect sizes were suppressed due to publication bias, and the remaining 18 studies were "published". NB -The small data points represent the identified studies included in the *meta*-analysis, and the large data points represent the imputed missing studies after adjustment for publication bias. The publication bias is confirmed by the results of the Egger's test (p = 0.02).

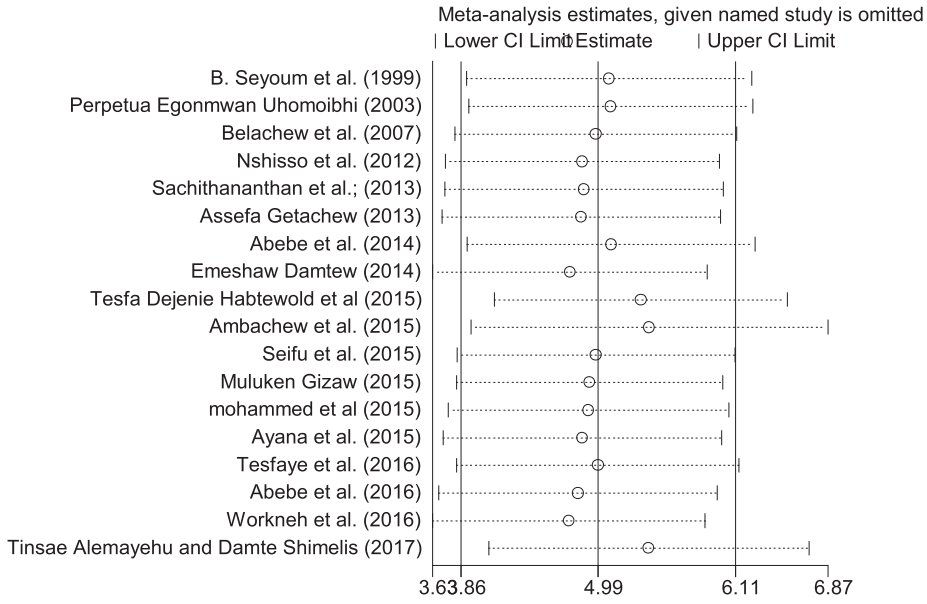

Fig. 3 – Result of Sensitivity analysis of the 18 studies.

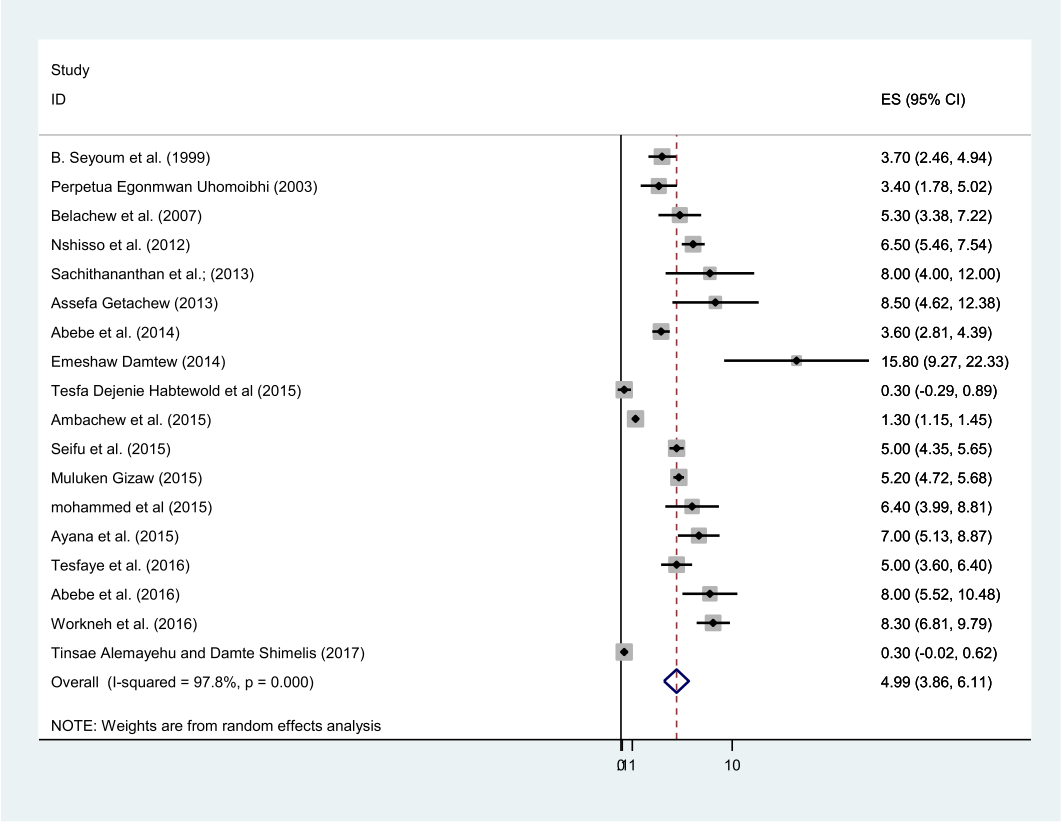

Fig. 4 – Forest plot of the 18 studies that quantitatively assessed prevalence of diabetes mellitus in the Ethiopian by settings (study area), 2019.

We used the following assumptions for the meta analysis like, there is, as yet, no unanimously accepted strategy for performing a *meta*-analysis but researchers agree that each *meta*-analysis should be conducted like a scientific experiment and begin with a protocol, which clearly states its aim and methodology, *meta*-analysis is powerful but also controversial because several conditions are critical to sound it, and there is no golden rule.

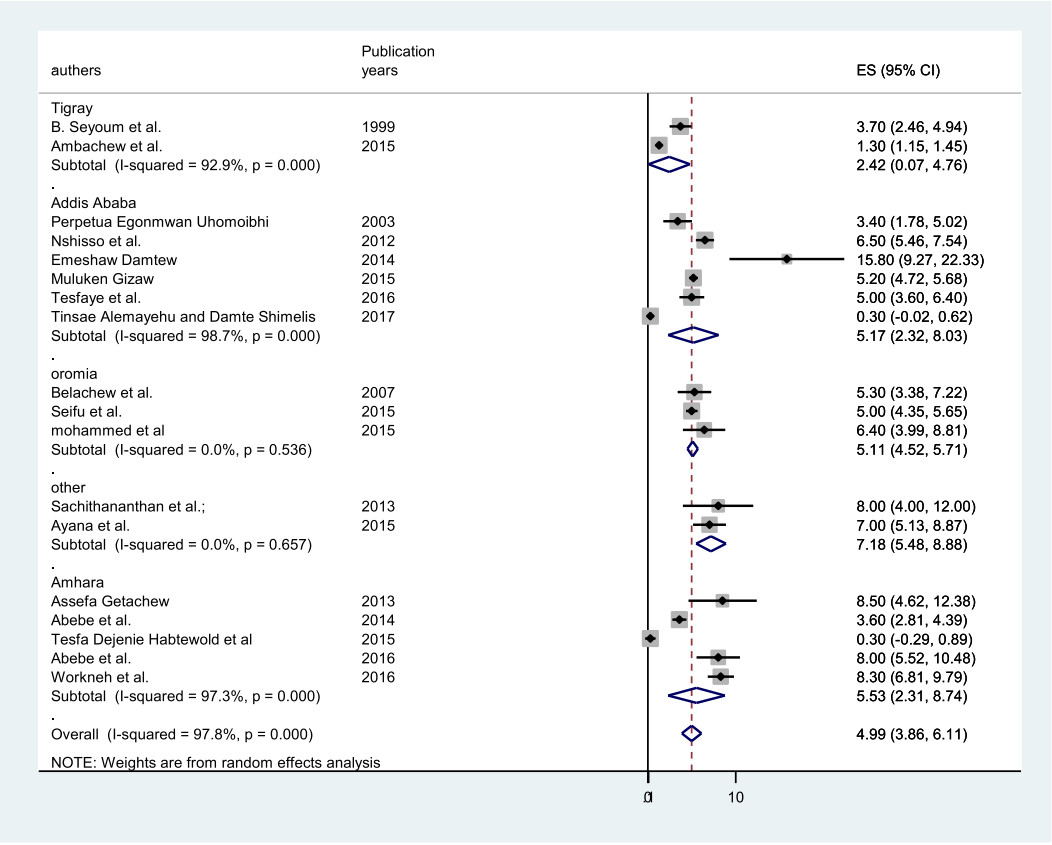

Fig. 5 – Pooled prevalence of diabetes mellitus among different regions in Ethiopia.

3.5.2. *Association between hypertension and DM*

Three studies with 1889 participants were included to identify the association between hypertension and DM [32,35,37]. Hypertensive patients were 8.32-fold more likely to have DM than non-hypertensive diabetic individuals (OR: 8.32, 95% CI: 3.05, 22.71) (Fig. 6).

4. Discussion

This review is first in kind to evaluate literature and conduct a *meta*-analysis on the prevalence of DM and its association with hypertension in Ethiopia. The findings provide insights to the recent magnitude and topographical distribution of diabetes in Ethiopia.

The current findings are similar to the systematic review and *meta*-analysis of DM conducted in Ghana [40], Ireland [41], Nigeria [42] and Zimbabwe [43]. However, these findings varied slightly compared to the *meta*-analytical finding of low and middle-income countries (5.6%) [44] and Sub-Saharan Africa countries (e.g. South Africa:3.6%, Ivory Coast: 5.7%, rural Uganda:1%, urban Kenya:12% [45] and Zimbabwe [46]) [Hall et al. Diabetes in Sub Saharan Africa 1999–2011: Epidemiology and public health implications. a systematic review. BMC Public Health2011, #59]. This variation might be due to the higher burden of DM in developing countries than comparatively more industrialised countries [47] as well as due to several factors, such as; increased life expectancy of population [48], rapid urbanisation [20], consumption of processed foods [49,50], shift from cultural foods towards fat and refined carbohydrate-based diets [51], high fat and energy foods [52,53], epidemiological shift from communicable to non-communicable diseases [54,55] and lifestyle changes [52,56,57]. The current finding is also varied with study conducted in Asian countries, such as 4.5% in Maldives [58] and 4.3% in India [59], 2012 international diabetes federation estimation to Ethiopia [60], South Asian region [61], rural Uganda [62], urban Kenya, Cameroon, Ghana, Guinea, Kenya, Nigeria, South Africa and Uganda [16]. This variation could be due to increased life expectancy, expansion of urbanisation [63] and epidemiological disease transition in African countries [64].

The review finding is lower than that of Pakistan (8.7%) [65], Sri Lanka (10.3%) [66], India (9.2% rural and 18.6% urban) [14] and Maldives [61,66]. The discrepancy could be due to the differences in methodology, diagnostic criteria, age variation, socioeconomic difference, sensitivity of screening methods and un-standardised diagnostic criteria [67].

This review revealed a significant regional variation across the country, that is, from the lowest in the Tigray region to the highest in other regions (Southern Nation and Nationalities and Harari). The variation across regions might be due to the fact that Ethiopia is a country with multi-lingualism, diverse culture and different topographical areas with 80 and above nation and nationalities who practice distinct lifestyle habits. Significantly, hypertension co-morbidity is found to be the most significantly associated factor with the DM. Patients with hypertension are eightfold more likely to develop diabetes

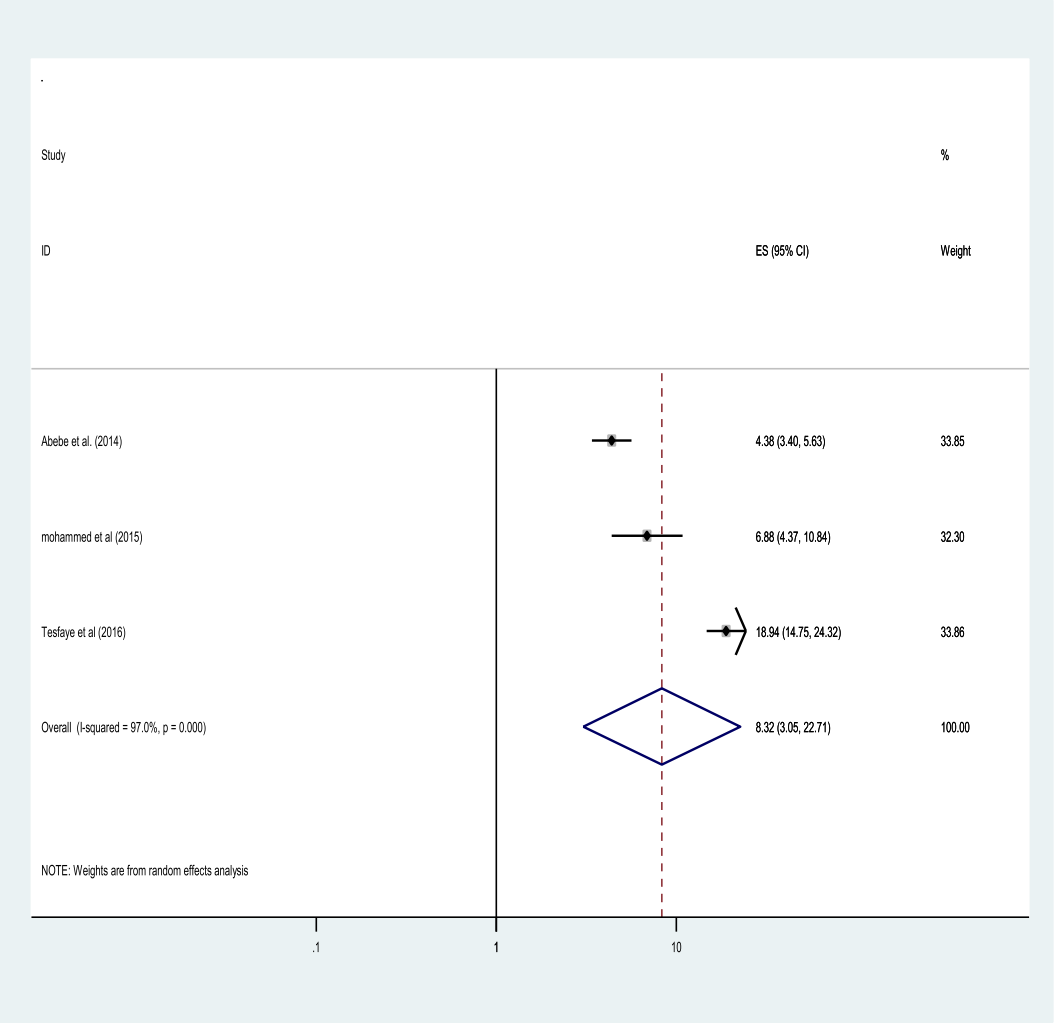

Fig. 6 – Hypertension co morbidity and diabetes mellitus in Ethiopia.

than those without hypertension. This finding is in line with South Asian pooled studies [61,68], India [69], France [70] and American Diabetes Association studies [71]. The reasons for the association and causal dimensions are unclear, but a postulated hypothesis states that diabetes increases plasma fluid and vascular resistance by hardening arteries, thereby increasing the blood pressure [72]. This association is more likely happen specifically in type 2 DM and hypertension.

5. Strengths and limitations

The strength of this review lies with the exhaustive search used on published and unpublished studies and utilisation of many minds to digest the study. The main limitation of this review was the low number of included studies from the rural areas of Ethiopia, which might had the limited generalisability of the study to the rural setting since very few studies conducted in rural areas. Regions with small population was not included in this review since there is no published studies in the area. Moreover, the pooled prevalence of diabetes was not separately estimated for type 1 and 2 diabetes due to the fact that included studies did not specifically reported the type of DM. Separate analysis for each specific DM types could be more informative for scientific community and other beneficiaries. In addition, the primary interests of articles might be general DM without distinguishing the types of diabetes. Another limitation of this review was analyzing the pediatric populations with DM and populations with gestational DM in the assumption that the review can be benefited from a broader focus regardless of the type of population and results in slight variation from adult population. So, this review used any type of DM in general population (prevalence of DM in Ethiopia) regardless of the type of population. In addition, only three studies were used to estimate the effect of hypertension on the burden of DM, which could lead to high heterogeneity on the estimated effect size. Moreover, the measure used to assess the correlation between hypertension and DM was unadjusted for other confounders, which might cause biased estimate.

6. Conclusion

The prevalence of DM in Ethiopia was considerably high. A strong association was observed between diabetes and hypertension.

7. Recommendation

Based on the evidence, this review recommends establishing the coordinated national programs that counteract the increasing burden of DM in the country is very essential. In addition, Early Hypertension screening should be done in diabetic patients to control co-morbidity and further complications. Moreover, large-scale study must be conducted to assess risk factors associated with DM other than hypertension to ascertain the reasons of the rising burden of DM in Ethiopia.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

Relevant data will be available upon request from the corresponding author.

Authors' contribution

Conceptualisation- Bekele Tesfaye, Animut Alebel, Cheru Tesema and Habtamu Abera.
Datacuration:-Alemu Gebrie and Habtamu Abera.
Formal analysis-Bekele Tesfaye.
Investigation- Bekele Tesfaye, Alemu Gebrie, Abriham Zegeye and Khorshed Alam.
Methodology- Bekele Tesfaye.
Resources- Abriham Zegeye.
Software-Aster Ferede.
Validation- Khorshed Alam.
Writing original draft- Bekele Tesfaye and Aster Ferede.
Writing review and editing-Bekele Tesfaye, Khorshed Alam and Habtamu Abera.

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Declaration of Competing Interest

The authors declare no competing interest.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2019.107838.

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