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Association Between the Level of Reported Good Medication Adherence and the Geographic Location of a Patient's Residence and Presence of a Glucometer Among Adult Patients with Diabetes in Ethiopia: A Systematic and Meta-Analysis

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ABSTRACT

Background: Diabetes mellitus (DM) is a major public health problem worldwide that was estimated to have affected the lives of 425 million people globally in 2017. The prevalence and mortality rates of DM have increased rapidly in low- and middle-income countries with an estimated 2.6 million cases of DM occurring in Ethiopia alone in 2015.

Objective: Considering that Ethiopia is undergoing an epidemiological transition, it is increasingly important to understand the significant influence DM has on Ethiopians annually. A systematic review and meta-analysis of the existing studies were conducted to better understand the factors that are associated with DM medication adherence across Ethiopia and to elucidate areas for further studies.

Methods: Studies were retrieved through search engines in Cumulative Index to Nursing and Allied Health Literature, Embase, Medline, PubMed, Google Scholar, Web of Science, Science Direct, and Scopus. The Newcastle–Ottawa Scale for cross-sectional studies was used to assess the critical appraisal of the included studies. Random effects model was used to estimate the association between the level of medication adherence and the geographic location of a patient's residence and presence of a glucometer at 95% CI with its respective odds ratio. Meta-regression was also used to identify the potential source of heterogeneity. Beggs and Egger tests were performed to determine publication bias. Subgroup analyses, based on the study area, were also performed.

Results: A total of 1046 articles were identified through searching, of which 19 articles representing 7756 participants were included for the final analysis stage. Reported good medication adherence among patients with diabetes in Ethiopia was 68.59% (95% CI, 62.00%–75.18%). Subgroup analysis was performed, and the pooled estimate of reported good medication adherence among these patients in regions outside Addis Ababa was 67.81% (95% CI, 59.96%–75.65%), whereas in Addis Ababa it was 70.37% (95% CI, 57.51%–83.23%). Patients who used a glucometer at home had an odds ratio of 2.12 (95% CI, 1.42–3.16) and thus reported good adherence. We found no statistically significant association between the geographic loca-

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tion of a patient's residence and a good level of reported medication adherence (odds ratio, 1.81; 95% CI, 0.78–4.21).

Conclusions: Most adult patients with diabetes in these studies had a good level of reported DM medication adherence. Having a glucometer was significantly associated with reported increased medication adherence. Our findings suggest the need for interventions to improve diabetes medication adherence.

Introduction

Diabetes mellitus (DM) is a major public health problem that was estimated to have impacted 425 million people globally in 2017.[1] According to the World Health Organization, "in 2016, an estimated 1.6 million deaths were directly caused by diabetes."[2] Although world leaders have targeted DM as a noncommunicable disease of priority, the prevalence of diabetes has steadily increased over the past few decades.[1–3] The global prevalence (age standardized) of diabetes specifically has nearly doubled since 1980, increasing from 4.7% to 8.5% in the adult population in 2014.[1]

The prevalence and mortality rates of DM are higher in low- and middle-income countries than those in high-income countries.[1] Sub-Saharan Africa has been particularly affected by this trend. Within sub-Saharan Africa, an estimated 2.6 million cases of DM occurred in Ethiopia alone in 2015.[2]

Ethiopia is currently undergoing a major epidemiological transition.[4] As described by other authors,[5,6] an epidemiological transition occurs when the disease burden of a population changes from infectious to noncommunicable. Epidemiological transitions have been largely observed over the past centuries in high- and middle-income countries. Thus, the adequacy of existing frameworks for describing the transitions now occurring in low-income countries is being debated. In sub-Saharan Africa, among the largest barriers preventing confidence in these models is the lack of data and evidence-based written sources documenting the changes in epidemiology and demographic characteristics.[7] In Ethiopia, a complete in-country vital registration system is lacking, leaving researchers only the ability to estimate the mortality burden from communicable and noncommunicable diseases.[4] Some work has been performed to try to fill in data gaps, but their results may not be representative of all of Ethiopia.[8,9] Although past resources and policy have focused on reducing the influence of communicable diseases, it is only recently that noncommunicable diseases have been prioritized.[4,10]

The efforts that have been made to quantify the prevalence of overweight and obese Ethiopians[11,12] have found that a significant proportion of Ethiopians in certain regions are overweight, but still, additional studies are required to adequately understand the scope of the problem. Obesity has been associated with the consumption of a more Western-style diet high in processed and fatty foods for wealthier Ethiopians.[12–14] The incidence rates of diagnosed diabetes were also found to be 5 times higher in urban regions than in rural regions.[15]

In summary, Ethiopia is facing a double disease burden from common infectious and noncommunicable diseases, which include DM. Little work has been performed to map the epidemiology and management of DM in Ethiopia. This is problematic considering that complications associated with uncontrolled blood glucose level also disparately influence sub-Saharan Africa.[3] For example, the prevalence of retinopathy, a common complication in DM patients, was 3% in Central Africa, 3.4% in Southern Africa, and 3.1% in West Africa, all of which exceed the global rate of diabetes-related retinopathy at 2.6%.[1,16,17]

In addition to the influence on morbidity and mortality, DM also places a financial burden on countries with high DM prevalence. In total, the global health care expenditure on people with diabetes was estimated to be $850 billion in 2017.[1,18]

Little is known about managing DM in Ethiopia; however, a systematic review conducted by Nigatu[18] found that access to services, provision of care, glycemic control, and diabetes education were crucial components of well-managed DM. Previous studies have also shown that patients with chronic noncommunicable diseases such as diabetes have difficulty adhering to their recommended treatment regimens, resulting in poor control of the illness and a higher risk of morbidity and mortality.[19,20] Several factors identified in these studies were found to have positive and negative associations with medication adherence. The geographic location of a patient's residence and the presence of a glucometer in the home were identified as positive factors in medication adherence.[21–27]

Despite the significant influence of DM on Ethiopians, studies assessing DM, specifically in the area of medication adherence, in Ethiopia are insufficient. A systematic review and meta-analysis of the existing studies are required to better understand the factors that are associated with DM medication adherence across Ethiopia and to elucidate areas for further studies.

Methods

Search strategy

The systematic review and meta-analysis was conducted by adhering to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines.[28] The primary literature for this review was retrieved through electronic, Web-based searches, local journals, and university thesis databases using the indexed and free-text terms *medication adherence, therapy adherence, treatment adherence, medication intake adherence, medication compliance, patient compliance, diabetes mellitus, diabetes*, *Patients, individuals, clients, and Ethiopia* in various combinations, as described in **Supplemental Table 1** in the online version at doi:10.1016/j.curtheres.2020.100585. The databases Cumulative Index to Nursing and Allied Health Literature, Embase, Medline, PubMed, Web of Science, Science Direct, and Scopus were searched from May 2018 to February 2020. Unpublished studies were also considered from local journals and university thesis databases and Google scholar considering the lack of Ethiopian specific studies on glucometer adherence in several of the main scholarly databases. Endnote reference manager software (version 7.1) was used to collect and organize search outcomes and to remove duplicate articles.

Inclusion criteria

All studies that evaluated the association between DM medication adherence and the geographic location of a patient's residence and presence of a glucometer in patients' home were included.

Studies were included in the systematic review and meta-analysis if they reported either good or poor DM medication adherence with a defined cutoff point and used validated measures. Studies with cross-sectional study design were included. Only studies written in the English language were included. Only studies conducted in Ethiopia were included. Only studies published between 2013 and 2019 were included.

Exclusion criteria

Articles were excluded if they were not available in full text. Studies were also excluded if they did not report specific outcomes for medication adherence.

Outcome variable

The main aim of this review was to determine the pooled prevalence of medication adherence among adult patients with diabetes in Ethiopia. Considering the purposes of this study, "good adherence" was determined by each individual study. Most studies used the Morisky Medication Adherence Scale. Descriptions of each study's measurement of good adherence are presented in Table 1. Prevalence was measured as the number of adults with above the cutoff point for good medication adherence divided by the total number of adult patients with diabetes in a study multiplied by 100. For the analysis of the secondary outcomes (factors associated with adherence), we extracted data on factors that had been found to be associated with medication adherence in the literature, such as the presence of a glucometer at home and the geographic location of a patient's residence. Another criterion used when selecting variables was the frequency of reporting DM in studies included in the meta-analysis. In examining factors associated with medication adherence, data were extracted from the primary studies using 2 $\times$2 tables, and a crude odds ratio (OR) was calculated to determine the association between each of the independent variables and the independent variable.

Data extraction and quality assessment

Data were extracted following a standard format, which included first author, year of publication, regions, study design, types of DM and medication, and sample size. The prevalence of medication adherence was also extracted from each included study. Full texts of potentially eligible studies were assessed using the inclusion criteria described previously. The relevance of the reviewed studies was checked based on the topic, objectives, and methodology. When it was unclear from an abstract whether or not a study was relevant, it was excluded from full-text retrieval. A preliminary assessment was performed, and some articles were excluded from the first step based on the topic. After reviewing the full article, a score was given based on the Newcastle–Ottawa Scale.[29] We also evaluated the risk of bias in the studies that were selected using the 10-item rating scale developed by Hoy et al[30] for prevalence studies (see **Supplemental Table 2** in the online version at doi.10.1016/j.curtheres.2020.100585).

Articles were assessed for quality, with only high-quality studies included in the analysis. Two authors (GD and FW) independently assessed the quality of each article. The reviewers compared their quality appraisal scores and collaborated before calculating the final appraisal score. Disagreements were settled by a third reviewer (AN), whenever appropriate. The studies met the Newcastle–Ottawa Scale criteria in terms of adequate sample size, clarity of research aims, and appropriateness of design, recruitment, data collection, analysis, and reporting of findings.[29]

Data analysis

Data were extracted from each study using Microsoft Excel (Redmond, Washington) and were subsequently transferred to Stata software version 14 (StataCorp, College Station, Texas) for analysis. Heterogeneity was checked using the Cochran Q and the I^2 test statistic.[31] Funnel plot asymmetry and Egger test of the intercept were used to check publication bias.[32] If the results of the test suggested the presence of a significant publication bias with $P < 0.05$ in Egger test and Begg test, trim and fill analysis was used.[33–35] To confirm the results, 2 researchers independently performed the statistical analysis to check for consistency. The effect size estimates were reported in the form of pooled prevalence and ORs.

Results

Explanation of original studies

The results of the search strategy yielded a total of 1046 unique citations found in Cochrane Library, EBSCO, Embase, Google Scholar, Web of Science, PubMed, Science Direct, Scopus, Hinari, and local journals and university thesis databases.[36] A total of 1041 articles were excluded at initial assessment as their title was not related to the study scope. For the remaining 36 studies, their abstract and full text was accessed. Ten articles were excluded based on their lack of clarity in terms of the outcome variable. The remaining 26 studies[37–60] met the inclusion criteria and were included in the final analysis (Figure 1).

Characteristics of the included studies

Twenty-six studies representing 7756 patients with diabetes were included in the final analysis. From the included studies, eight observational studies (27%) were conducted in Oromia region,[38,47,48,52,53,55] 8 articles (30.8%) were from Addis Ababa,[39,41,43,45,46,49,50] 5 articles (19.2%) were from Amhara region,[40,44,54,56,60] and 2 articles were from the Southern Nations, Nationalities, and People's Region[51,59] and Tigray regions.[37,57] The remaining 1 article was from Harari region.[42] All of the studies were cross-sectional in nature. Levels of good medication adherence were reported as high as in Addis Ababa[41] and low as in Oromia region[52] (Table 1). Regarding risk bias, all studies has low risk bias score.

Pooled estimate of reported good diabetes medication adherence

A DerSimonian and Laird random effects model was fitted to determine the pooled effect size[61,62] because the I^2 test for heterogeneity showed a significant difference between studies ($I^2 = 94.1\%$; $P < 0.05$). Even after a subgroup analysis was performed, the results continued to show the presence of heterogeneity across the studies. Therefore, we performed a meta-regression analysis on publication years and sample size. However, these variables were insignificantly associated with heterogeneity in these models (Table 2).

The average pooled estimate of reported good medication adherence among patients with diabetes in Ethiopia was found to be 68.59 (95% CI, 62.00–75.18). A subgroup analysis also showed that the pooled estimate of reported good medication adherence among patients in Ethiopia's regional states was 67.81% (95% CI, 59.96–75.65), while in Addis Ababa, it was 70.37% (95% CI, 57.5–83.23) (Figure 2).

Funnel plot of precision asymmetry and Egger test of the intercept were used to detect publication bias. On visual examination, the funnel plot was found to be asymmetric, and Egger test of the

Table 1
Characteristics of the included studies for meta-analysis (2013–2018, Ethiopia).

Study No.	Author name	Year of publication	Type of DM	Region	Type(s) of medication	Study design	Sample size	How good adherence was measured	Proportion of good adherence (%)	NOS score
1	Teklay, et al[53]	2013	Type 2	Oromia	Oral hypoglycemic agent and insulin	Cross-sectional	267	MMAS	75.7	6
2	Gelaw, et al[47]	2014	Type 1, 2	Oromia	Oral hypoglycemic agent and insulin	Cross-sectional	270	4-point adherence survey	72.2	6.5
3	Gelaw, et al[48]	2014	Type 1, 2	Oromia	Oral and insulin	Cross-sectional	275	4-point adherence survey	78.2	7
4	Abebe, et al[44]	2015	Type 1, 2	Amhara	Oral hypoglycemic agent and insulin	Cross-sectional	407	MMAS	45.9	7
5	Mamo, et al[50]	2016	Type 1, 2	Addis Ababa	Oral hypoglycemic agent and insulin	Cross-sectional	660	Adherence survey	91.7	6.5
6	Kassahun, et al[23,38]	2016	Type 1, 2	Oromia	Oral hypoglycemic agent and insulin	Cross-sectional	285	Self-reported non-adherence survey	68.8	7
7	Girma Bizu, et al[39,46]	2016	Type 2	Addis Ababa	Oral hypoglycemic agent	Cross-sectional	155	MMAS	49	7
8	Abebaw, et al[40]	2016	Type 2	Amhara	Oral hypoglycemic agent and insulin	Cross-sectional	288	5-point MMAS	85.1	7
9	Sorato, et al[51]	2016	Type 2	SNNP	Oral hypoglycemic agent and insulin	Cross-sectional	194	8-point MMAS	84	7
10	Tsehay, et al[39]	2016	Type 2	Addis Ababa	Oral hypoglycemic agent and insulin	Cross-sectional	322	4-point MMAS	66.8	7
11	Jemal, et al[42]	2017	Type 2	Harar	Oral hypoglycemic agent and insulin	Cross-sectional	200	4-point MMAS	70.4	7
12	Ali, et al[45]	2017	Type 1, 2	Addis Ababa	Oral hypoglycemic agent and insulin	Cross-sectional	146	8-point MMAS	54.8	6
13	Tadele, et al[52]	2017	Type 1	Oromia	Insulin	Cross-sectional	256	Self-reported adherence survey	30.9	7
14	Mesfin, et al[43]	2017	Type 2	Addis Ababa	Oral hypoglycemic agent and insulin	Cross-sectional	275	MMAS	51.3	6.5
15	Gerada, et al[49]	2017	Type 1, 2	Addis Ababa	Insulin	Cross-sectional	378	Non-adherence described as taking <80% of prescribed insulin injection	66.9	7
16	Berhe, et al[37]	2017	Type 2	Tigray	Oral hypoglycemic agent and insulin	Cross-sectional	343	Adherence = taking >80% of prescribed treatment	83.7	7
17	Tewabe, et al[54]	2018	Type 1	Amhara	Insulin	Cross-sectional	182	Adherence = taking >80% of prescribed treatment	59.9	7
18	Wabe, et al[55]	2018	Type 2	Oromia	Oral hypoglycemic agent and insulin	Cross-sectional	384	Adequate glycemic control was defined as patients with fasting plasma glucose level between 90 mg/dL and 100 mg/dL	61.9	6.5
19	Bonger, et al[41]	2018	Type 2	Addis Ababa	Oral hypoglycemic agent and insulin	Cross-sectional	422	Self-reported adherence survey	95.7	6

(*continued on next page*)

Table 1 (*continued*)

Study No.	Author name	Year of publication	Type of DM	Region	Type(s) of medication	Study design	Sample size	How good adherence was measured	Proportion of good adherence (%)	NOS score
20	Abate TW[60]	2019	Type 1, 2	Amhara	Insulin	Cross-sectional	416	MMAS[7]	68.8	6
21	Ayele AA, et al[56]	2019	Type 2	Amhara	Insulin	Cross-sectional	275	Adherence = taking >50% of prescribed treatment during past 3 d	70.5	7
22	Wabe NT, et al[55]	2011	Type 2	Oromia	Oral hypoglycemic agent and insulin	Cross-sectional	384	MMAS[7]	41.8	6.5
23	Gelaw, BK et al[47]	2014	Type 2	Oromia	Oral hypoglycemic agent and insulin	Cross-sectional	113	Self-reported adherence survey	72	6
24	Yohannes Tekalegn, et al[58]	2017	Type 2	Addis Ababa	Oral hypoglycemic agent and insulin	Cross-sectional	412	**SDSCA**	87.6	6
25	Fseha B, et al[57]	2017	Type 2	Tigray	Oral hypoglycemic agent and insulin	Cross-sectional	200	Adherence = taking >50% of prescribed treatment during past 3 d	61	6
26	Tesfaye DK, et al[59]	2015	Type 1, 2	SNNP	Oral hypoglycemic agent and insulin	Cross-sectional	247	SDSCA	91.9	6.5

DM = diabetes mellitus; NOS = Newcastle-Ottawa scale; MMAS = Morisky Medication Adherence Scale; SDSCA = Summary Diabetes Self-Care Activity.

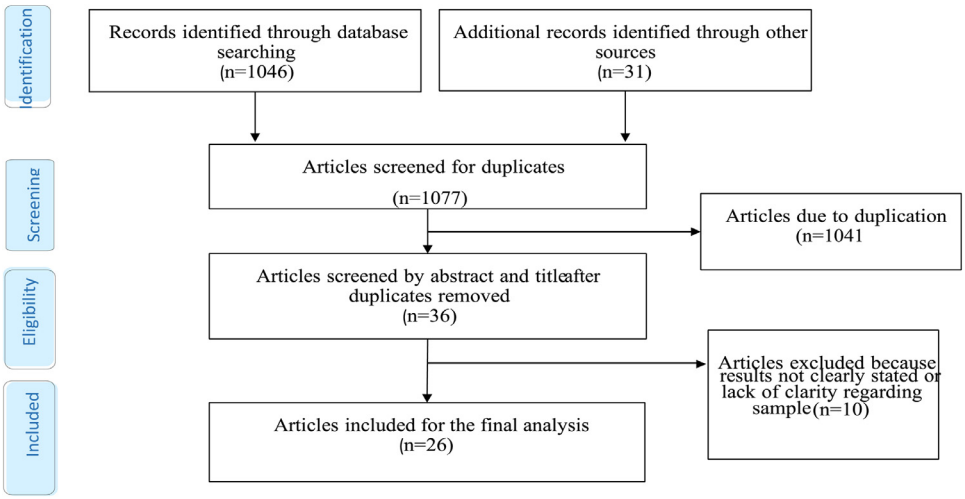

Figure 1. Flow diagram showing the procedure of selecting studies for meta-analysis in Ethiopia 2013–2019.

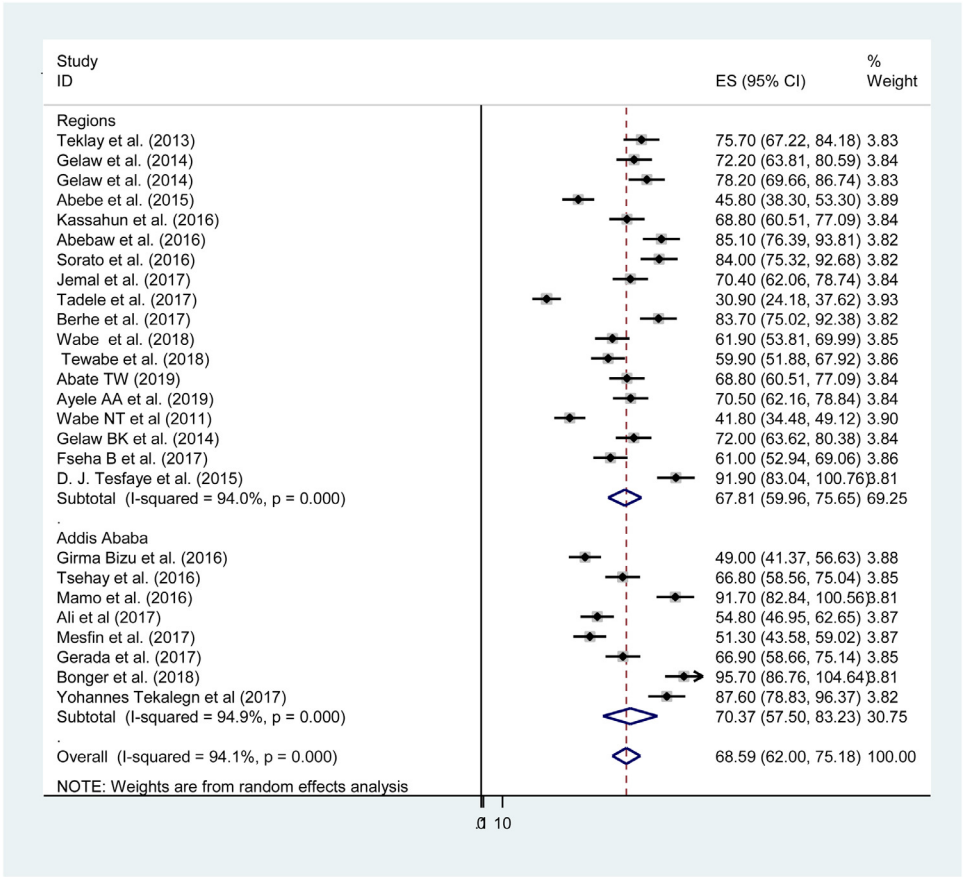

Figure 2. Forest plot showing the proportion of reported medication adherence among diabetic patients in Ethiopia (2013–2019).

intercept (B0) was found to be –0.22 (95% CI, –0.31 to -–0.13; $P < 0.05$). Furthermore, publication bias was also indicated using the Begg test with a P value < 0.05. Hence, the final effect size was determined by performing trim and fill analysis using the random effects model. However, relatively different results were obtained using the model.

Association between reported good medication adherence and the presence of a glucometer

Three studies[37–39] were included in the analysis assessing the association between the presence of a glucometer and reported medication adherence (Figure 3). A statistically significant association was observed between a good level of reported medication adherence and the presence of a glucometer in the home of patients with diabetes. The pooled effect size OR of reported good medication adherence among patients with diabetes who have glucometer at home was 2.12 (95% CI, 1.42–3.16).

Association between reported good medication adherence and geographic location of a patient's residence

Four studies were included in this subanalysis assessing the effect of the geographic location of a patient's residence on reported

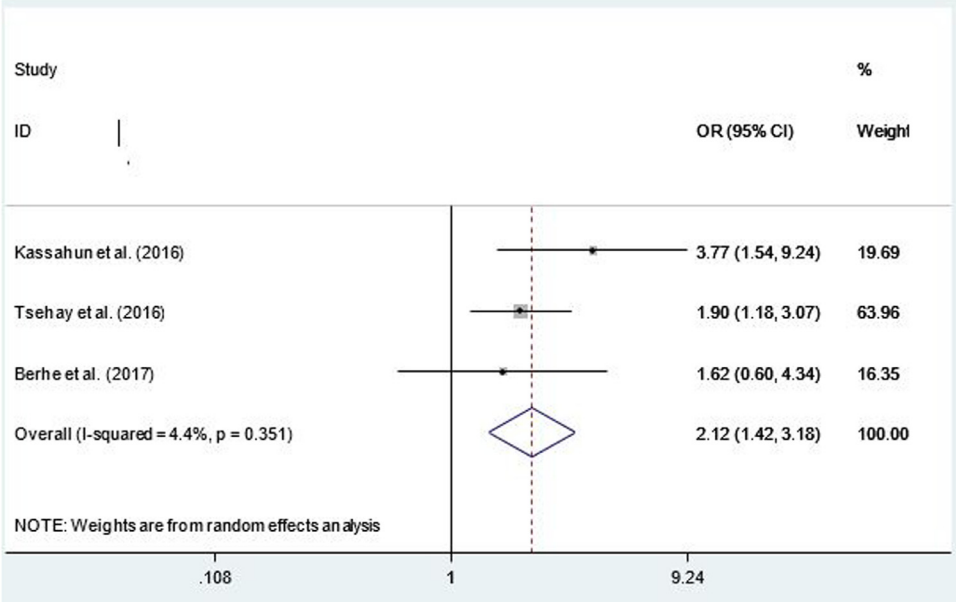

Figure 3. Forest plot showing the association between good diabetic medication adherence and the presence of a glucometer among diabetic patients in Ethiopia from 2013 to 2019.

Table 2
Meta-regression results on selected variables in studies conducted from 2013 to 2019 in Ethiopia.

Variable	Coefficient	*P* value
Publication year	−3.5	0.762
Sample size	0.052	0.712
Region		
Addis Ababa	−23.1	0.795
Amhara	−27.43	0.766
Harar	−13.3	0.905
Oromia	−33.5	0.705
SNNP	0.3	0.998
Tigray	83.7	0.336

medication adherence (Figure 4). A statistically significant association was not observed between the geographic location of a patient's residence and a good level of reported medication adherence (OR = 1.81; 95% CI, 0.78–4.21).

Discussion

The systematic review and meta-analysis were conducted to estimate the proportion of reported good medication adherence among DM patients in Ethiopia and its associated factors. During a time of epidemiological transition in Ethiopia, when obesity prevalence and rates of noncommunicable diseases are increasing, it is important to better understand the influence that DM has on Ethiopians and how Ethiopians are managing their disease.

We found that, on average, more than two-thirds (68.59%) of patients with diabetes in Ethiopia had good reported medication adherence. Regardless of the region in which they lived, levels of reported good adherence improved when patients had access to a glucometer in their home to self-check their glucose levels. Our prevalence of reported good DM medication adherence is almost identical to that found in a previous systematic review and meta-analysis conducted by Iglay et al[63] at the global level, which found that 67.9% of patients were considered adherent to their DM medication. These results were also consistent with the results of Odegard and Capoccia[66] and studies published by Cramer et al.[64]

Ethiopians face universal challenges in adherence and also challenges that are unique to Ethiopia when trying to adhere to their DM medication. Similar medication adherence levels in Ethiopia and high-income countries may be due in part to the similarities in the difficulty of maintaining medication adherence with chronic diseases. For example, challenges such as forgetfulness have been observed across several countries with a wide range of health care resources.[65] Other common challenges such as cost of medication, accessibility of health care facilities, lack of patient education, and poor patient-provider relationships may be more severe in Ethiopia compared with the other countries.[26] Considering these challenges, it is heartening that Ethiopia is able to maintain a similar medication adherence level as that of higher-income countries.

Subgroup analysis performed on regions in which patients lived found no significant difference in reported adherence by region. This consistency could be explained by Ethiopia's centralized national health system, which standardizes health education and services. Although there might have been differences in the accessibility of health care and health care providers by region, the patients with diabetes in the included studies probably had similar levels of short-term health education based on the national medication adherence guidelines. Whether a patient lives in the capital or outside of the capital, in a predominantly rural or urban region, the type of health education would be fairly consistent.

An additional aim of this study was to determine associated factors for good antidiabetic medication adherence. We found that there was a significant association between the presence of a glucometer and reported good medication adherence. DM patients who measured their own blood glucose level using a glucometer at home were more than three times more likely to have had good level of reported medication adherence compared with patients who did not measure their own blood glucose levels using a glucometer at home. This is probably because the presence of a glucometer allows patients to measure blood glucose on a regular basis and to prevent hyperglycemia or hypoglycemia. However, it may also be the result of the presence of confounding factors with income or education as higher-income and more educated patients may be more likely to both have glucometers and also more likely to be adherent.

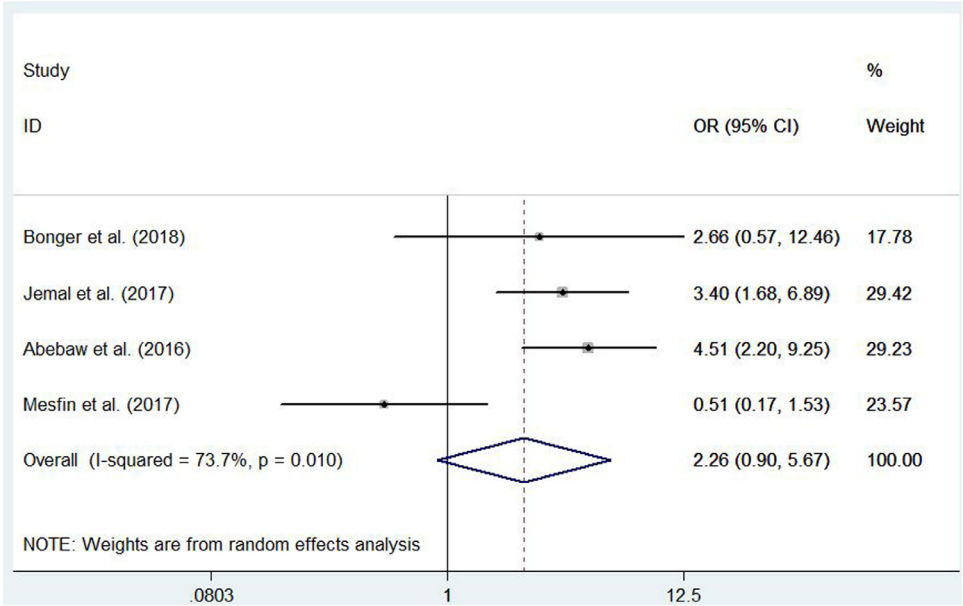

Figure 4. Forest plot showing the association between a good level of diabetic medication adherence and geographic location of a diabetic patient's residence in Ethiopia from 2013 to 2019.

Although both our study and the previous global meta-analysis[66] found that more than two-thirds of the study population maintain a good level of DM medication adherence, it must be emphasized that almost one-third of these study populations had low level of DM medication adherence. Patients who do not adhere to DM medication regimens are at a higher risk for later disease complications and higher costs to health care systems and patients personally than patients who adhere to DM medication regimes. Our findings indicate that medication adherence among DM patients is a significant issue in Ethiopia and suggest that the disease could be paid careful attention to by global and local authorities. We hope that in addition to highlighting this potential oversight and emphasizing the need to strengthen glucometer availability program, our findings could also be used as a reference or baseline for Ethiopian policy makers in creating guidelines for future levels of good medication adherence.

Limitations

The findings of this review need to be considered in the context of several important limitations. The protocol is not registered. More importantly, there was a lack of uniformity in defining good medication adherence across the studies included in the review. It was, therefore, defined on a study-by-study basis, which may bias the results of our meta-analysis. Additionally, due to the absence of data, crude ORs were used to estimate factors associated with the outcome variable; this means that we were not able to control the potential confounding factors.

Conclusions

A significant proportion of adult patients with diabetes in Ethiopia had good reported medication adherence. Reported medication adherence was improved with the presence of a glucometer in the patient's home. The geographic location of a patient's residence was not found to be associated with DM reported medication adherence. Because of the potential reduction in morbidity and mortality of DM due to the presence of a glucometer, future studies should continue to investigate this association and other potential interventions to increase DM medication adherence.

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G. Dessie developed the protocol and was involved in the design, selection of study, data extraction, statistical analysis, and development of the initial drafts of the manuscript. G. Dessie, F. Wagnew, H. Mulugeta, A. Negesse, and G. Kassa were involved in data extraction, quality assessment, and statistical analysis. T. D. Habtewold, A. Belachew, F. Wagnew, H. Mulugeta, A. Negesse, K. Parchinski, and G. Dessie prepared and revised the subsequent drafts. G. Dessie and K. Parchinski prepared the final draft of the manuscript. All authors read and approved the final draft of the manuscript.

Conflicts of Interest

The authors have indicated that they have no conflicts of interest regarding the content of this article.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.curtheres.2020.100585.

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