Antihypertensive medications adherence and associated uncontrolled blood pressure among hypertensive patients in Ethiopia: Systematic review and meta-analysis

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ABSTRACT

Background: Despite remarkable progress in the reduction of communicable diseases, non-communicable diseases still pose a threat worldwide. One such non-communicable disease is hypertension which remains a major public health problem in Sub-Saharan Africa. Adherence to antihypertensive medication regimens is paramount in reducing its burden. Study findings in Ethiopia regarding adherence to antihypertensive medications and their impact on blood pressure control have been inconclusive and inconsistent. This systematic review and meta-analysis aimed to estimate the pooled adherence to antihypertensive medications and their association with uncontrolled blood pressure among hypertensive patients in Ethiopia.
Methods: International databases including PubMed, Web of Science, SCOPUS, CINAHL, PsycINFO, Google Scholar, Science Direct, and the Cochrane Library were systematically searched. All identified observational studies and/or predictors were included, and I^2 statistics were used to assess the heterogeneity of the studies. A random-effects model was computed to estimate the pooled adherence level and its association with uncontrolled blood pressure.
Results: The random-effect meta-analysis showed that a pooled national antihypertensive medication adherence among hypertensive patients was 65.1% (95% CI: 61.6%, 68.6%). The highest medications adherence was 83.5% (95% CI: 77.0%, 89.9%) occurring in the Somali Region with the lowest medication adherence being 58.5% (95% CI: 47.7%, 69.3%) in the Tigray Region. The meta-analysis suggested a significant increase in medication adherence among patients who had good knowledge of hypertension [POR = 4.26 (95% CI: 4.26 (2.70, 6.72)] and 2.54 times increase in the odds among patients who had co-morbidities [POR = 2.54 (95% CI: 1.06, 6.07)]. This meta-analysis also revealed a 51% reduction of uncontrolled blood pressure among patients who adhered to an antihypertensive medication regimen [POR = 0.49 (95% CI: 0.34, 0.69)].
Conclusions: Two of every three hypertensive patients have adhered to a medication regimen that was associated with reduced odds of uncontrolled blood pressure. Therefore, interventions of highest priority to increase antihypertensive medication adherence are aimed at improving knowledge of hypertension and identifying or screening hypertensive patients who have comorbidities. The Federal Ministry of Health and other relevant

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stakeholders should increase efforts in the prevention of uncontrolled blood pressure through education on adherence to medication regimens with a focus on modifiable risk factors.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide, accounting for 17.3 million deaths per year; this is expected to increase to > 23.6 million by 2030 (Merai et al., 2016). Hypertension is known to be the major risk factor for global CVD morbidity and mortality, with an estimated half of the CVD events attributed to it. Globally, hypertension has increased which estimates suggest that 1.39 billion (31.1%) of adults worldwide had hypertension. The prevalence of hypertension among adults was higher in low- and middle-income countries (LMICs) (31.5%) than in high-income countries (28.5%) (Mills, Stefanescu, & He, 2020). The prevalence of hypertension among the Ethiopian population is estimated to be 19.6 % which is considered high (Kibret & Mesfin, 2015). Thus, it is important to prevent, treat, and control hypertension to reduce the risk of CVD events and related healthcare burdens elsewhere in the world (Forouzanfar et al., 2017). The target systolic and diastolic pressure to be achieved via pharmacologic intervention varies depending on the comorbidities. In patients with no comorbidity, the goal is below 140/90, whereas for patients suffering from chronic kidney disease and Diabetic Mellitus, the target blood pressure is 130/90 (Cifu & Davis, 2017).

Untreated hypertensive adults or treated adults with uncontrolled blood pressure in the US were at increased risk of all-cause, CVD-specific, heart disease-specific, or cerebrovascular disease-specific mortality (Zhou, Xi, Zhao, Wang, & Veeranki, 2018). The treatment modality for hypertension is lifelong, and adherence plays a pivotal role in the effectiveness of the drug (Jeemon, Gupta, Onen, Adler, Gaziano, Prabhakaran, & Poulter, 2017). One of the main reasons stipulated for the failure of antihypertensive therapy is related to patient compliance and adherence. Non-adherence to medical treatment is a major public health concern, especially in patients with chronic conditions (Cheen, Tan, Oh, Wee, & Thumboo, 2019; Lemay, Waheedi, Al-Sharqawi, & Bayoud, 2018). Medication adherence, as defined by the World Health Organization (WHO), is 'the extent to which a person's behaviour taking medication, following a diet and/or executing lifestyle changes corresponds with agreed recommendations from a healthcare provider (Organization, 2016).' Adherence to antihypertensive medication is the proper use of antihypertensive prescribed medications to improve a patient's chance of maintaining a target blood pressure to control blood pressure and prevent complications (Hedna et al., 2015).

Varying research has been conducted in different areas regarding medication adherence and related factors (Ambaw, Alemie, & Mengesha, 2012a; Ambaw, Alemie, & Mengesha, 2012b; Chelkeba, 2013); however, the results obtained varied in different setups. Reports show there is variation in adherence level which ranges from 52% to 74% when adherence is defined as possession of medication at least 80% of the time (Sabaté & Sabaté, 2003; Seedat, 2000). A study done at the University of Gondar showed that almost one-third of patients had poor adherence (<80%) to their antihypertensive medication regimen (Gebreyohannes, Bhagavathula, Abebe, Tefera, & Abegaz, 2019). Moreover, a study conducted at the Addis Ababa Black Lion Hospital showed that the adherence level of hypertensive patients is 69.2% (Hareri & Abebe, 2013). Only 75.1% of patients adhered well to the study done at Debre Tabor Hospital (Teshome, Bekele, Habitu, & Gelagay, 2017). Different studies by different researchers on antihypertensive medication adherence conducted at Jimma University Hospital have obtained varying results ranging from 55.7% up to 61.8% (Girma, Emishaw, Alemseged, & Mekonnen, 2014a; Girma, Emishaw, Alemseged, and Mekonnen, 2014b; Asgedom, Atey, & Desse, 2018).

There were inconsistent and inconclusive findings on the area across the country that may not give a national adherence level of antihypertensive drugs in Ethiopia. Notwithstanding, the pooled results and comprehensive evidence on the adherence level of hypertensive patients may pave a way for policymakers to design strategies in combating adherence problems related to chronic diseases like hypertension. A recent meta-analysis showed that 48% of hypertension was uncontrolled in Ethiopia (Amare, Hagos, Sisay, & Molla, 2020). Studies supported that poor adherence to antihypertensive medication was associated with uncontrolled blood pressure (Abegaz, Tefera, & Abebe, 2017, Fekadu et al., 2020). However, there was inconsistent data on the association between adherence to medication regimens and uncontrolled blood pressure (Abegaz, Abdela, Bhagavathula, & Teni, 2018; Kebede, Chelkeba, & Dessie, 2021; Tesfaye et al., 2017). Therefore, estimating the pooled adherence using national-level data for evidence-based intervention is paramount. This study aims to systematically estimate the adherence level to antihypertensive medication regimens and the association with uncontrolled blood pressure in Ethiopia.

2. Methods

2.1. Study design, setting and search strategy

The findings of this systematic review and meta-analysis were reported following the recommendation of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (Moher, 2015) (Supplementary file 1). Ethiopia is found in Eastern Africa bordered by Djibouti and Somalia to the east, Sudan and South Sudan to the west, Eritrea to the north, and Kenya to the south. It is divided into 9 regions namely Amhara, Southern Nations Nationalities and People Region (SNNPR), Tigray, Somali, Oromia, Afar, Benishangul-Gumuz, Gambella, Harari, and two administrative cities -Addis Ababa and Dire Dewa. This systematic review and meta-analysis were designed to estimate the adherence to antihypertensive medications among hypertensive patients in Ethiopia. All published articles were searched for in major international databases: PubMed, Cochrane Library, PSYCHINFO, CINAHL, Web of Science, Science Direct, Google Scholar, and African Journals Online databases from January 15 to March 25, 2019. Google searching for unpublished studies was also done. In addition, searching the reference list of studies already identified to retrieve additional articles was completed. The PECO (Population, Exposure, Comparison, and Outcomes) search formula was used for this review.

The population in this study consisted of hypertensive patients in Ethiopia. The primary outcome of interest was adherence to antihypertensive medication regimens among hypertensive patients and the main included determinants were knowledge of hypertension, presence of co-morbidities and number of antihypertensive drugs. The secondary outcome of interest of this meta-analysis was to estimate the impact of medication adherence on uncontrolled blood pressure.

Comparisons were defined for each predictor with the reported reference group for each predictor for each respective variable reported like, adherence among those who have good knowledge versus those without good knowledge as well as adherence among patients who have comorbidities versus those without comorbidities.

The electronic databases were searched with keyword searching and used the medical subject heading [MeSH] terms for each selected PECO component. The keyword searching included adherence, medication, hypertensive patients, and Ethiopia. The Boolean operators "OR" and "AND" were used to combine the searching terms. The PubMed search was done for antihypertensive medication adherence in Ethiopia as follows: ("antihypertensive agents"[All Fields] OR "antihypertensive agents" [MeSH Terms] OR ("antihypertensive" [All Fields] AND "agents" [All Fields]) OR "antihypertensive agents" [All Fields] OR

("anti" [All Fields] AND "hypertensive" [All Fields]) OR "antihypertensive" [All Fields]) AND ("medication adherence" [MeSH Terms] OR ("medication" [All Fields] AND "adherence" [All Fields]) OR "medication adherence" [All Fields]) AND ("Ethiopia" [MeSH Terms] OR "Ethiopia" [All Fields]).

2.2. Outcome measurement

Antihypertensive medication adherence was assessed based on the Medication Adherence Report and Eight-Item Morisky Medication Adherence Scale. Adherence to antihypertensive medication was defined by WHO as a hypertensive patient who had taken antihypertensive medication. The Morisky–Green–Levine Adherence Scale, a four-item self-report measure of medication-taking behaviour, which has high reliability and validity, was used for assessing patient adherence. The results were scored for all questions of medication adherence with a score of ≥ 3 classified as "having good adherence." For respondents who scored above the mean for medication adherence questions (among the 9 questions with highest score 4 and minimum 1), the mean was executed from the distribution. Hence, individuals with a score below the mean of the distribution were non-adherent and those above or equal to the mean of the distribution were adherent. Adherence to antihypertensive medications was also considered if respondents score ≥ 6 or 80% and above on the revised Morisky 8-Item Medication Adherence Scale (MMAS-8) (Morisky, Ang, Krousel-Wood, & Ward, 2008).

Uncontrolled blood pressure was defined as the achievement of an average of three BP readings $\geq 140/90$ mmHg for age < 60 years and $\geq 150/90$ mmHg for age ≥ 60 years in individuals being treated for hypertension (Van der Sande et al., 2000).

2.3. Eligibility criteria and study selection

Studies were included based on reporting the adherence to antihypertensive medications, patients demonstrating knowledge of hypertension, or presence of comorbidities and the association of medication adherence with uncontrolled blood pressure among hypertensive patients Ethiopians. All studies conducted at the community or health institution level, and encompassing cross-sectional or cohort study designs published and unpublished in the English language without period restriction were included. Studies conducted within the study populations other than hypertensive patients, case reports, surveillance data (Demographic Health Survey), conference abstracts, and articles without full access after at least two email contacts of the principal investigator were excluded from the review.

First, the two authors (MD and TA) independently assessed the articles for inclusion through title, abstract and full paper review. Any disagreement was resolved by a consensus between the two reviewers, and if necessary, with the third reviewer (DY). Then, potentially eligible studies underwent full-text review including whether the predetermined set of criteria were met or not and to search for any duplicated records. Only the full-text article was retained when duplication was encountered.

2.4. Quality assessment and data collection

The quality of included studies was assessed using the Newcastle-Ottawa Scale quality assessment tool based on three components (Seidu et al., 2019). The primary component of the tool focused on the methodological quality of each study graded from five stars. The second component was concerned about the comparability of each primary included study and the tool was graded from two stars. The last component of the tool used to assess the outcomes and statistical analysis of each original study was graded from three stars. The risk of bias in the studies was evaluated using the 10-item rating scale developed by Hoy et al. (2012). The tool included sampling, data collection, reliability

and validity of study tools, case definition, and periods. The rating scale was categorized as low risk of bias (Yes) or high risk of bias (No) to domain questions for individual studies. Each study was assigned a score of 1 or 0 for each domain, and these scores were summed to provide an overall study quality score. Scores of 8–10 were considered as a "low risk of bias", 6–7 a "moderate risk", and 0–5 a "high risk.

Two authors independently assessed and extracted the articles for overall study quality using a standardized assessment tool and extraction format. The data extraction format included the name of the primary author, publication year, region of the study, sample size, adherence to antihypertensive medication and knowledge of antihypertensive medication, history of any comorbidities, and the proportion of uncontrolled blood pressure among adherent and non-adherent patients.

2.5. Publication bias and statistical analysis

The publication bias was assessed using Egger's tests (Egger, Davey Smith, Schneider, & Minder, 1997) with a *p-value*<0.05. I^2 test statistics were used to assess the heterogeneity among studies, and a *p-value*<0.05 was used to declare heterogeneity. For heterogenic test results, a random effect model was used as a method of analysis (Central Statistical Agency (CSA) [Ethiopia] and ICF 2016). Data were extracted in Microsoft Excel and then exported to STATA version 11 for analysis. Subgroup analysis was conducted by geographic region. A meta-regression model was done based on sample size and year of publication to identify the sources of random variations among included studies. The pooled adherence to antihypertensive medication and its association with knowledge of antihypertensive medication and comorbidities was estimated. The effect of antihypertensive medication adherence on uncontrolled blood pressure was analyzed using separate categories of meta-analysis. The findings of the meta-analysis were presented using forest plots and Odds Ratio (OR) with a 95% confidence interval (CI).

3. Results

3.1. Study identification and characteristics of the included studies

This systematic review and meta-analysis included published studies on adherence to antihypertensive medications among Ethiopians. The review found a total of 1736 articles and 1548 published articles. From those, 132 duplicated records were removed and 1582 articles were excluded through screening of the title and abstracts due to irrelevance and location outside of Ethiopia. After that, a total of 22 full-text papers were assessed for eligibility based on the inclusion and exclusion criteria. Three articles were excluded because the outcome of interest was not reported. Finally, 19 studies were included for the final meta-analysis (Fig. 1). All included studies were cross-sectional comprising of hypertensive patients to estimate the pooled adherence to antihypertensive medications. The studies were conducted with a maximum sample size of 7764 participants done at the national level and the minimum sample of 241 was conducted at Debre Tabor Hospital in the Amhara Region. The studies were conducted between 2015 and 2019 across the country with most studies conducted in the six regions. Of those studies conducted, 6 were from the Amhara Region (Demisew, Mahmud, & Kechalew, 2018 , Ambaw et al., 2012a; Ambaw et al., 2012b, Chelkeba, 2013, Mekonnen, Gebrie, Eyasu, & Gelagay, 2017, Teshome et al., 2017, Gebreyohannes et al., 2019), five from Oromia Region (Girma et al., 2014a; Girma et al., 2014b, Hareri, Gedefaw, & Simeng, 2014, Asgedom et al., 2018, Labata, Ahmed, Mekonen, & Daba, 2019), 3 from the Tigray Region (Ali, Bekele, & Teklay, 2014, Gebremichael, Berhe, Beyene, & Gebrekidan, 2019; Gebremichael, Berhe, & Zemichael, 2019, Niriayo et al., 2019), 2 from Addiss Ababa Region (Hareri & Abebe, 2013, Tibebu, Mengistu et al. 2017), 1 from Southern Nations, Nationalities and Peoples Representative (SNNPR) (Getenet, Tesfa, Ferede, & Molla, 2019), and 1 study from Somali Region (Bekele,
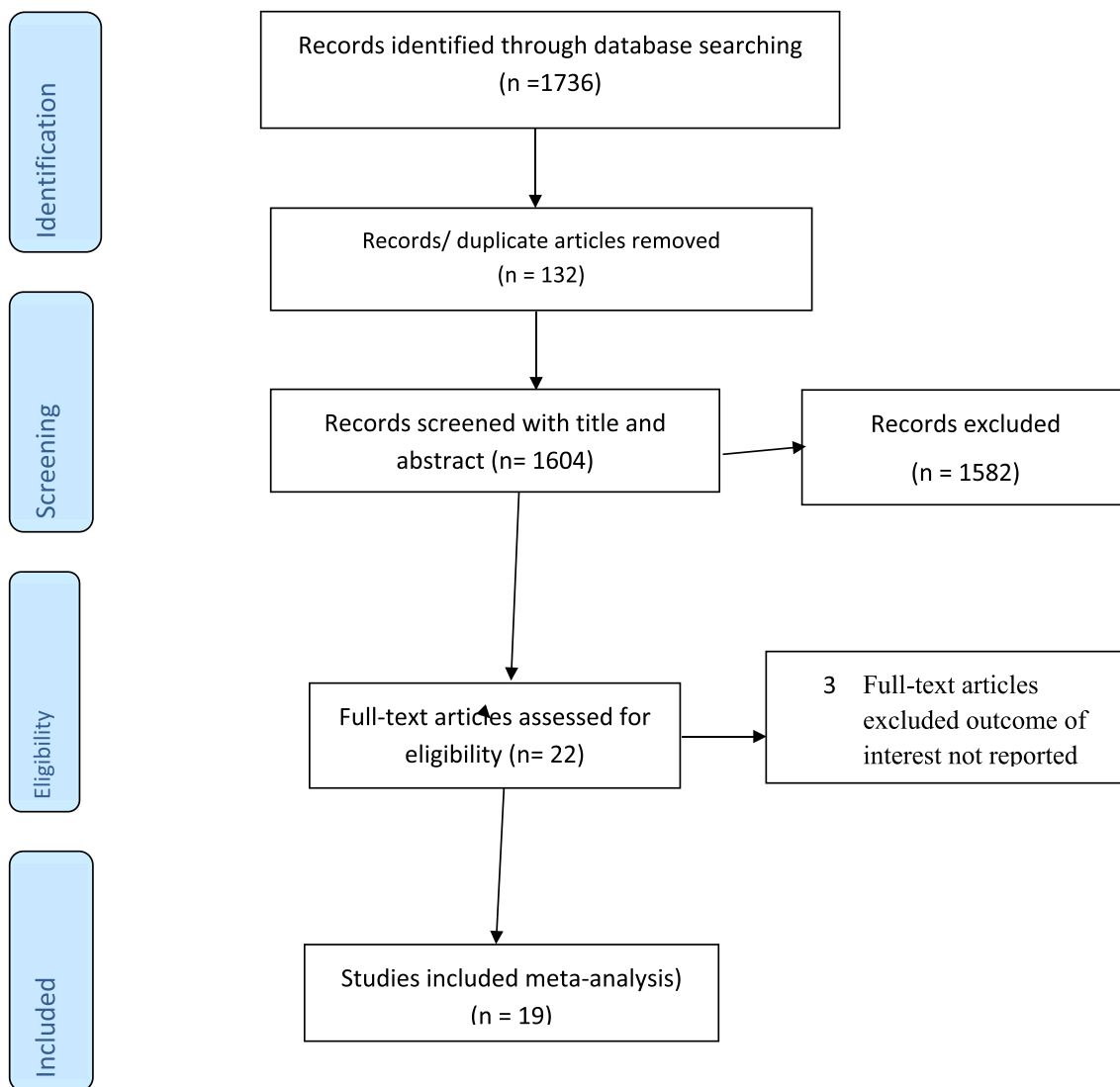
Fig. 1. PRISMA flow diagram to estimate antihypertensive medication adherence.

Table 1
Characteristics of the included studies in the meta -analysis, Ethiopia.

Author	Year	Region	Adherence	Sample	Tool	Medication Adherence
(Teshome et al., 2017)	2017	Amhara	75.1	337	MoriskyMAS-4	Morisky score ≥ 3
(Ambaw et al., 2012a; Ambaw et al., 2012b)	2012	Amhara	64.6	384	MoriskyMAS-4	Morisky score ≥ 3
(Mekonnen et al., 2017)	2017	Amhara	67.2	409	MoriskyMAS-8	MMAS-8 score ≥ 6
(Chelkeba, 2013)	2013	Amhara	84	100	MoriskyMAS-8	Morisky score ≥ 80%
(Gebreyohannes et al., 2019)	2019	Amhara	62.7	249	MoriskyMAS-8	Morisky score ≥ 80%
(Demisew et al., 2018)	2018	Amhara	63	270	MoriskyMAS-8	MMAS-8 score ≥ 8
(Tibebu, Mengistu, & Bulto, 2017)	2017	A/A	66.8	404	MoriskyMAS-4	Morisky score ≥ 3
(Hareri & Abebe, 2013)	2013	A/A	69.2	286	MoriskyMAS-4	Morisky score ≥ 3
(Hareri et al., 2014)	2014	Oromia	59.5	365	MoriskyMAS-8	≥ mean score
(Girma et al., 2014a; Girma et al., 2014b)	2014	Oromia	55.7	314	MoriskyMAS-8	Morisky score ≥ 80%
(Labata et al., 2019)	2019	Oromia	61.9	341	H-SCALE	Score ≥ 21
(Asgedom et al., 2018)	2018	Oromia	61.8	280	MoriskyMAS-8	MMAS-8 score ≥ 6
(Ali et al., 2014)	2014	Tigray	52.9	121	MoriskyMAS-4	Morisky score ≥ 6
(Niriayo et al., 2019)	2019	Tigray	48.2	276	H-SCALE	Score ≥ 21
(Gebremichael, Berhe, Beyene et al., 2019; Gebremichael, Berhe, & Zemichael, 2019)	2019	Tigray	74.1	320	H-SCALE	Score ≥ 21
(Bekele, 2019)	2019	Somalia	83.46	127	H-SCALE	Score ≥ 21
(Getenet et al., 2019)	2019	SNNPR	67	1600	MoriskyMAS-4	Morisky score ≥ 3
(Berhe et al., 2017)	2017	Tigray	58	925	MoriskyMAS-8	Morisky score ≥ 6
Gamachu B et al	Unpub	Oromia	61.9	341	H-SCALE	Score ≥ 21

2019). The quality of studies was high (Table 1). Most studies have a low risk of bias, and two studies have a moderate risk of bias (Appendix 1).

3.2. Adherence to antihypertensive medications

The lowest adherence rate to antihypertensive medications was 52.9% observed in a study conducted at the Tigray region, and the highest adherence rate was 84% observed in a study conducted in the Somalia Region (Gebremedhin, Samuel, Mamo, Moges, & Assefa, 2014). The pooled random-effect meta-analysis found that the pooled prevalence of adherence to antihypertensive medications among hypertensive patients in Ethiopia was 65.1% (95% CI: 61.6%, 68.6%). A random-effect model was used due to the presence of significant heterogeneity among studies (I^2 = 89.7% at the p-value < 0.05) (Fig. 2). Visual inspection of the funnel plot also showed the symmetrical distribution of included articles. The univariate meta-regression model was used to identify possible sources of heterogeneity based on year of publication, sample size, and region, but none of these variables was found to be statistically significant (p-value > 0.05). The sensitivity analyses used a random-effects model showed that three studies conducted by Chelkeba

and Dessie (Chelkeba, 2013), Niriayo et al. (2019), and Bekele, Fekadu, Dugassa, and Bekele (2019), unduly influenced the estimate of adherence to antihypertensive medications (S2 Figure). Thus, dropout sensitivity analysis of studies making the pooled prevalence of 64.1% (95% CI: 61.3%, 66.9%) which is under the overall pooled estimate of all 19 studies analyzed (S3 Figure). The funnel plot of observation showed that there was a symmetrical distribution (Fig. 3). There was no publication bias found using Egger's and Begg's tests (p-value of 0.99 and 0.65, respectively).

A subgroup analysis by geographic region was computed to compare the adherence to antihypertensive medications across different areas of the country. The highest antihypertensive medication adherence among hypertensive patients was observed in the Somali Region at 83.5% (95% CI: 77.0%, 89.9%) followed by the Amhara Region at 69.2% (95% CI: 63.4%, 75.1%) and the Addis Ababa Region at 67.8% (95% CI: 64.3%, 71.3%). Whereas, the lowest medication adherence at 58.5% (95% CI: 47.7%, 69.3%) was observed among patients in the Tigray Region (Table 2).
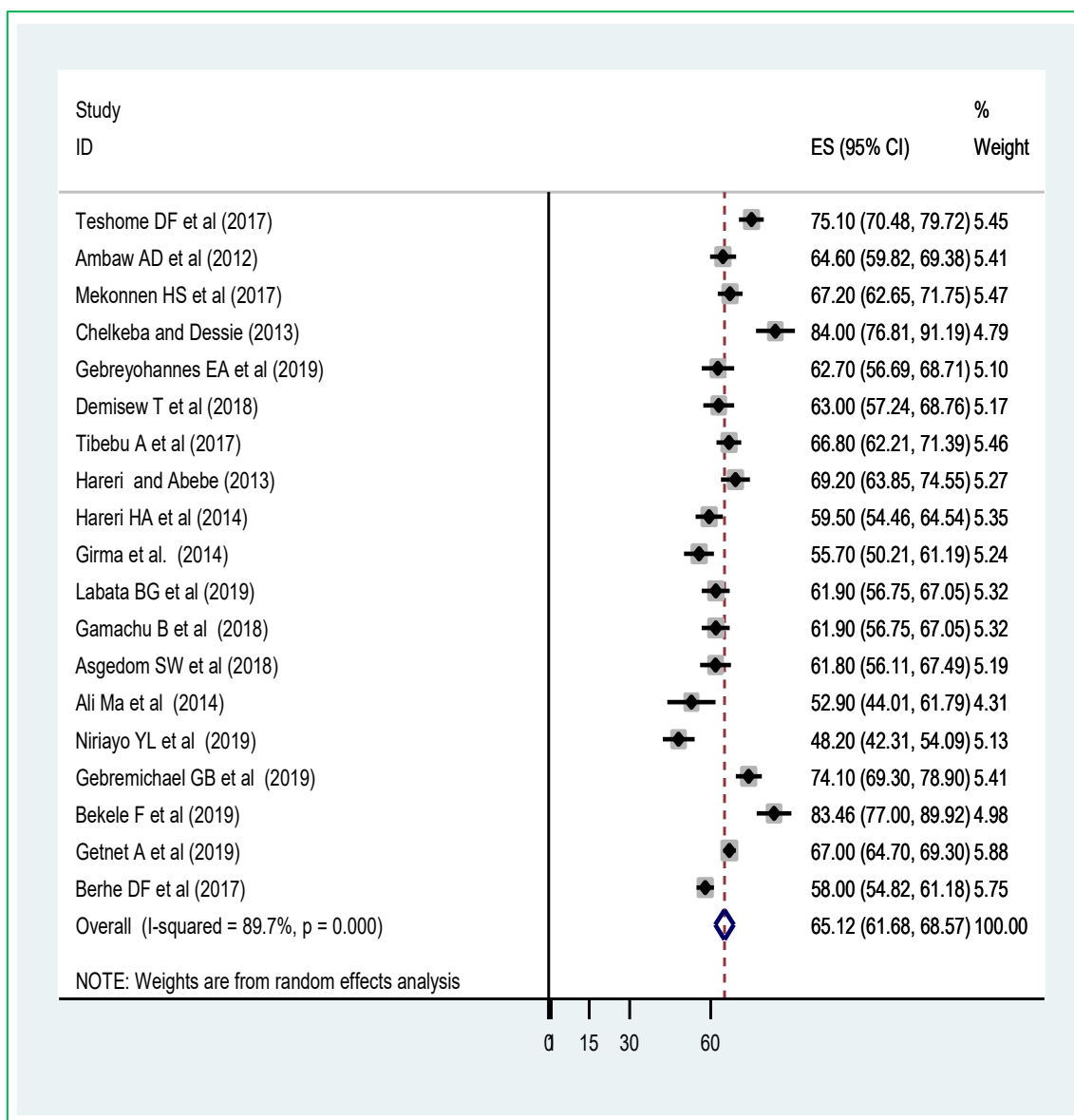

Fig. 2. Pooled prevalence of antihypertensive medication adherence in Ethiopia.
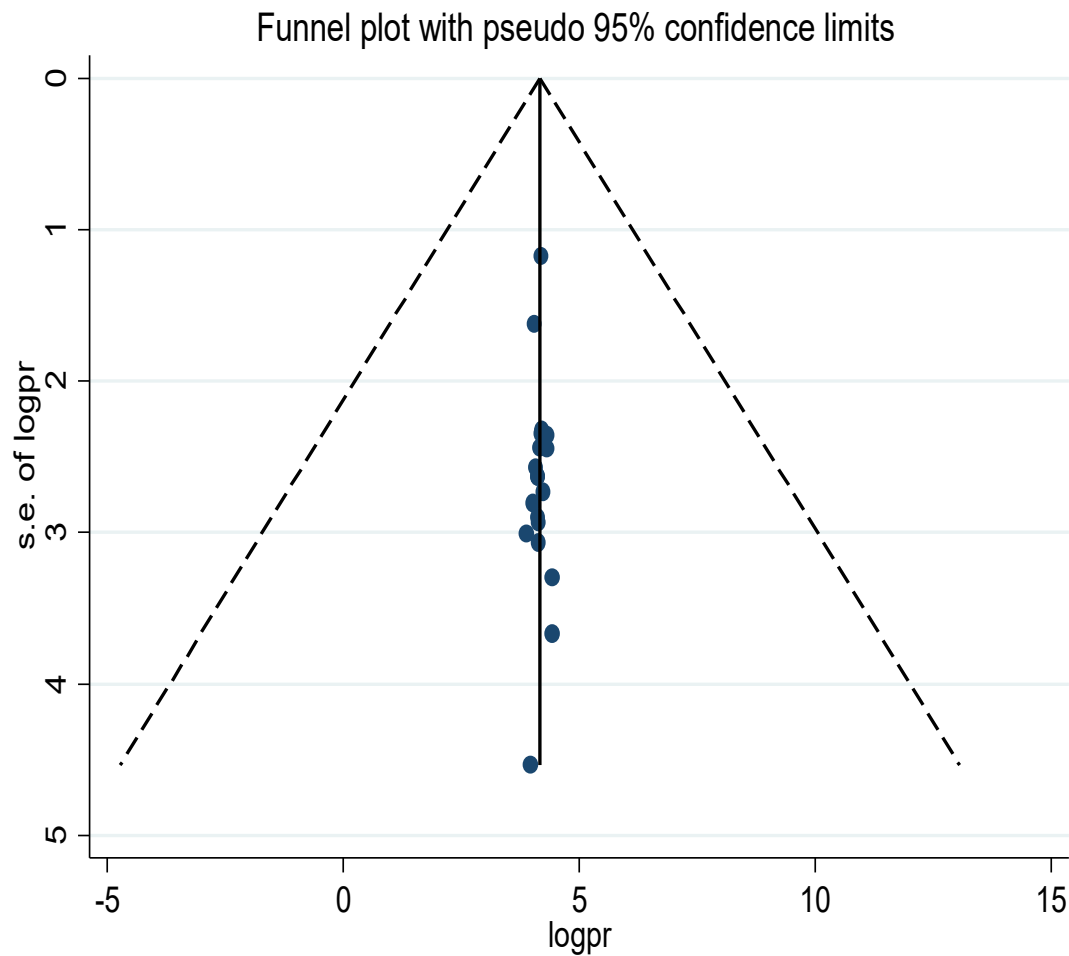
Funnel plot with pseudo 95% confidence limits

Fig. 3. Funnel plot to assess publication bias.

Table 2
Subgroup analysis of antihypertensive medication adherence by region.

Region	No. of included studies	Prevalence (95% CI)	*p*-value	I^2
Amhara	6	69.2 (63.4, 75.1)	<0.0001	86.0%
SNNPR	1	67.0 (64.7, 69.3)		
Tigray	4	58.5 (47.7, 69.3)	<0.0001	94.3%
Oromia	5	60.2 (57.8, 62.6)	<0.44	0%
Somalia	1	83.5 (77.0, 89.9)		
Addis Abeba	2	67.8 (64.3, 74.3)	0.51	0%

3.3. Association of knowledge of hypertension and adherence to medication

Five studies were included to assess the association between the knowledge of patients on hypertension and their adherence to antihypertensive medications. Therefore, the pooled effect meta-analysis showed that those hypertensive patients who had good knowledge of hypertension were 4.26 times (POR = 4.26, 95% CI: (2.70, 6.72)] more likely to have good adherence toward antihypertensive medication supplementation than those patients who had poor knowledge. The heterogeneity test showed there was statistical evidence of moderate heterogeneity ($I^2 = 76.1\%$ and $p = 0.002$) (Fig. 4). Egger's test showed no significant publication bias.

3.4. Association of comorbidities and antihypertensive medication adherence

This systematic review and meta-analysis considered five studies to evaluate the pooled effect of the presence of co-morbidities associated with hypertensive patients on the adherence to an antihypertensive medication regimen. The pooled odds ratio of the five included studies revealed that hypertensive patients who had associated comorbidities were 2.54 times [POR = 2.54 (95% CI: 1.06, 6.07)] more likely to adhere to medication regimens than those adults with no comorbidities. The random-effect model of the meta-analysis was used showings a significant source of heterogeneity with $I^2 = 90.1\%$ at *p*-value < 0.05 (Fig. 5). The Egger's and Begg's tests also showed that there was no publication bias.

3.5. Association of number of drugs and antihypertensive medication adherence

The number of drugs a person takes and its association with antihypertensive medication adherence was assessed based on four included studies. The random-effect meta-analysis showed that the number of drugs is not significantly associated with the adherence to medication [POR = 1.27 (95% CI: 0.58, 2.79)]. There was a significant source of heterogeneity ($I^2 = 86.5\%$ with a *p*-value at 0.0001), and a random-effect model of the meta-analysis was used (Fig. 6). There was no publication bias based on the Egger's and Begg's tests (*p*-values 0.54 and 0.73, respectively).
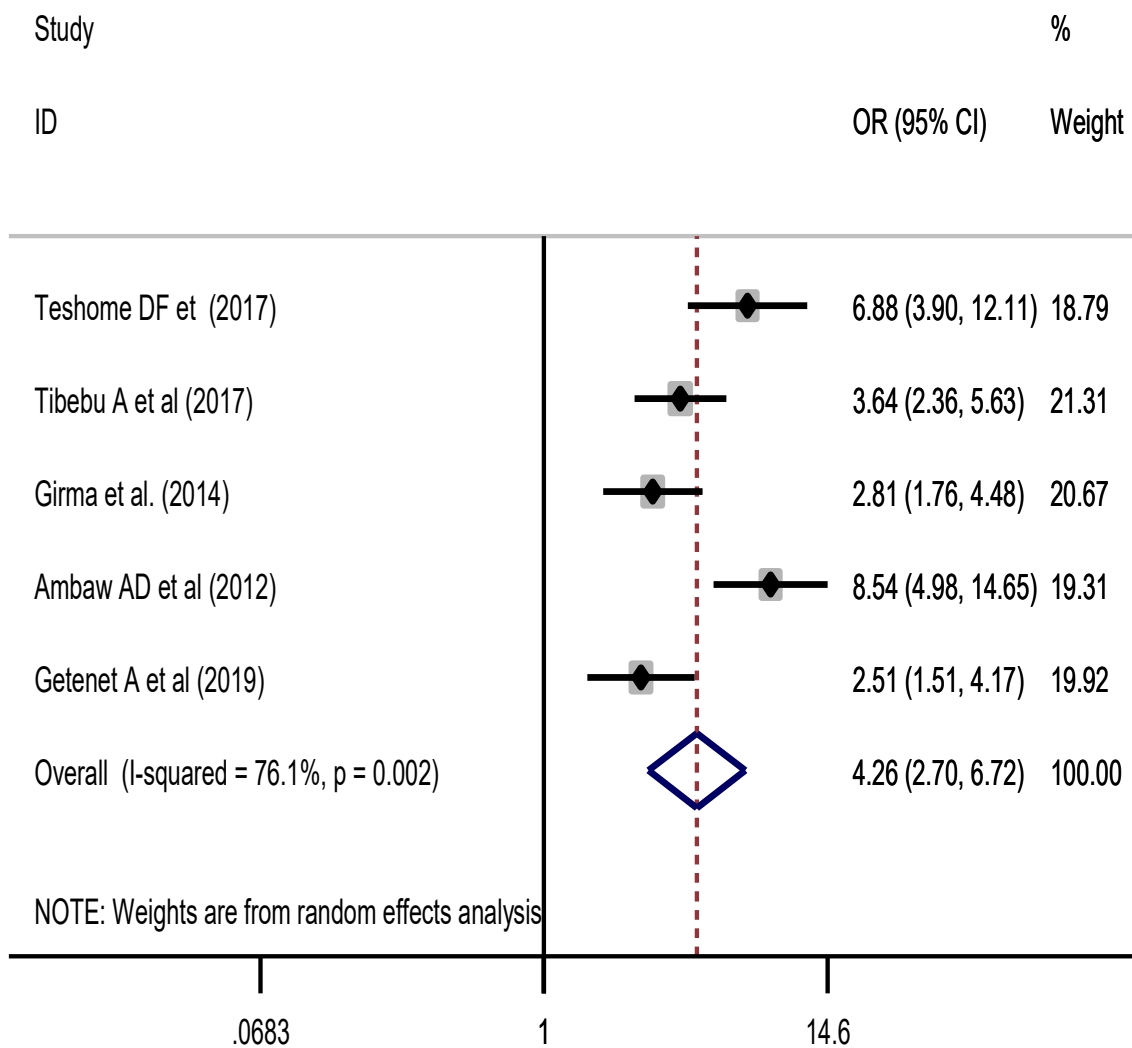
Study   %

ID   OR (95% CI)   Weight

Teshome DF et (2017)   6.88 (3.90, 12.11) 18.79

Tibebu A et al (2017)   3.64 (2.36, 5.63) 21.31

Girma et al. (2014)   2.81 (1.76, 4.48) 20.67

Ambaw AD et al (2012)   8.54 (4.98, 14.65) 19.31

Getenet A et al (2019)   2.51 (1.51, 4.17) 19.92

Overall (I-squared = 76.1%, p = 0.002)   4.26 (2.70, 6.72) 100.00

NOTE: Weights are from random effects analysis

.0683   1   14.6

Fig. 4. Association of knowledge of hypertension and medication adherence.

3.6. Association of antihypertensive medication adherence and uncontrolled blood pressure

The systematic review and meta-analysis also investigated the association between antihypertensive medication adherence with uncontrolled blood pressure. The pooled effect model of the meta-analysis of seven studies revealed that hypertensive patients who had adhered to antihypertensive medication regimens had a 51% [POR = 0.49 (95% CI: 0.34, 0.69) chance of reducing the odds of uncontrolled blood pressure. The random-effect model was used due to the presence of a significant source of heterogeneity (Fig. 7).

4. Discussion

This systematic review and meta -analysis showed that a pooled national antihypertensive medication adherence among hypertensive patients was 65.1% (95% CI: 61.6%, 68.6%). The pooled prevalence in the current meta -analysis was comparable with the estimated global adherence rate of reports from systematic review and meta -analysis (68.6%) (Uchmanowicz, Jankowska, Uchmanowicz, & Morisky, 2019). This pooled estimate was higher than when compared with the findings of meta -analyses conducted in low- and middle-income countries (LMICs): 36.65% (Nielsen, Shrestha, Neupane, & Kallestrup, 2017) to 54.8% (Abegaz, Shehab, Gebreyohannes, Bhagavathula, & Elnour, 2017), Iran (33%) (Jafari Oori, Mohammadi, Norouzi-Tabrizi, Fallahi-

Khoshknab, & Ebadi, 2019), Egypt (46.1%) (Hussein, Awad, & Mahmoud, 2020), the Middle East (55.9%) (Alhaddad, Hamoui, Hammoudeh, & Mallat, 2016), and Taiwan (Lee, Huang, Shih, & Huang, 2013) in which 52.9% of patients adhered to antihypertensive medication regimens. The reported higher adherence in our estimate might be explained by variations in the study, design, and definition of adherence among the studies. The Pill count ≥ 80% was used as the adherence measurement and the time gap with that of Taiwan the adherence rate from was from 2004 to 2007 was reported (Lee et al., 2013). The time variation of studies might be a possible variation to the adherence of medication. The meta -analysis conducted in LMICs and global reports included studies published before or during 2016 while our study included only four published studies before 2015. Despite this, the results of our meta -analysis were lower when compared with the adherence rates of the studies conducted in Korea (81.7%) (Choi et al., 2018), the Taiwan National Health Survey (82.7%) (Chou et al., 2020), and the Chinese National Cohort Study (Wong, Jiang, & Griffiths, 2010) which showed that 85.5% of patients had adhered to antihypertensive medications. This variation might be due to the differences in sociodemographic characteristics in addition to the fact that Ethiopia has a limited quality of healthcare systems that are not yet as committed and competitive regarding implementing different strategies and preventive modalities to increase adherence to antihypertensive medications due to limited access to care, economic scarcity or non-affordability of resources. The population of Taiwan have stable governments and well developed
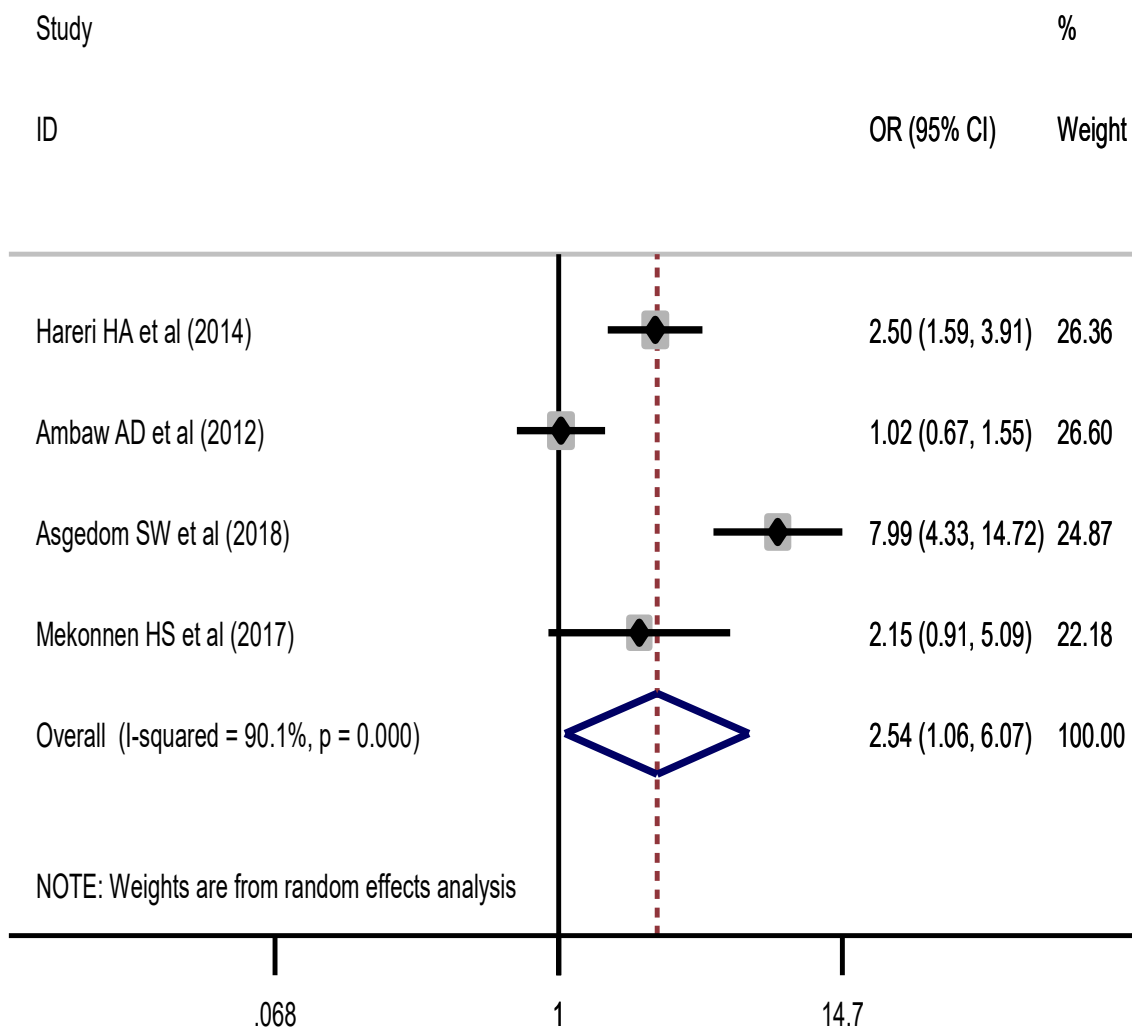
Fig. 5. Association of co-morbidities of hypertension and medication adherence.

national infrastructure, including functioning commercial and financial systems, embedded utility grids delivering clean water and energy; systems that facilitate communication and transportation; liveable national housing; a functioning judicial and educational system (McKee et al., 2009). Improving the quality of health services is vital to improving the level of health in Ethiopia and critically looking at the management of health organisations at all levels, proper quality healthcare planning, improvement and control is needed. Hence, delivering quality health services is a means of achieving global universal health coverage including improving healthcare service utilization of chronic illness screening (Organization, 2018).

The relatively lower adherence in this meta -analysis might be partly explained by the fact that the cost of medical care and medications may be a barrier to adherence to medications in Ethiopia. Thus, the government, in collaboration with other stakeholders and nongovernmental organizations, should enhance strategies to improve adherence to antihypertensive medications following the WHO targets. The highest medication adherence was 83.5% (95% CI: 77.0%, 89.9%) occurring in the Somali Region with the lowest medication adherence being 58.5% (95% CI: 47.7%, 69.3%) in the Tigray Region. The sociodemographic characteristics and the lifestyle activities in the regions are associated with self-care behaviour and practices that might also attribute to the differences in adherence to antihypertensive medication regimens. This suggests that other regions should commit to improve healthcare service utilization which might sustainably increase adherence to these medications.

This systematic review and meta -analysis found that hypertensive patients who had good knowledge of hypertension and its treatment were more likely to have increased medication adherence than patients who had poor knowledge of hypertension. This finding is supported by studies conducted in Indonesia (Titaley & Dibley, 2015) and South Africa (Mbhenyane & Cherane, 2017). A possible explanation could be that patients who have good knowledge of hypertensive medications might attain a higher level of education, might be more likely to receive information regarding medication or control of hypertension, and might have increased good awareness. Beyond this, knowledgeable patients might be more concerned about their health outcomes and more likely to utilize good self-care practices (Gebremichael, Berhe, Beyene et al., 2019; Gebremichael, Berhe, & Zemichael, 2019, Worku Kassahun et al., 2020) and healthcare services, which further improves antihypertensive medication adherence. Thus, improving the health literacy strategies used in educational material interventions to increase the adherence to medication regimens is recommended.

This systematic review and meta -analysis revealed that hypertensive patients who have associated comorbidities were 64% more likely to adhere to an antihypertensive medication regimen for hypertensive patients than those who did not have comorbidities. The findings of our meta -analysis were in line with the results of previous studies (Lee et al., 2013). These studies showed that hypertensive patients who had comorbid conditions were more likely to adhere to antihypertensive medications. This might be because patients who have comorbidities are more likely to be aware of being at a higher risk and perceive the benefit
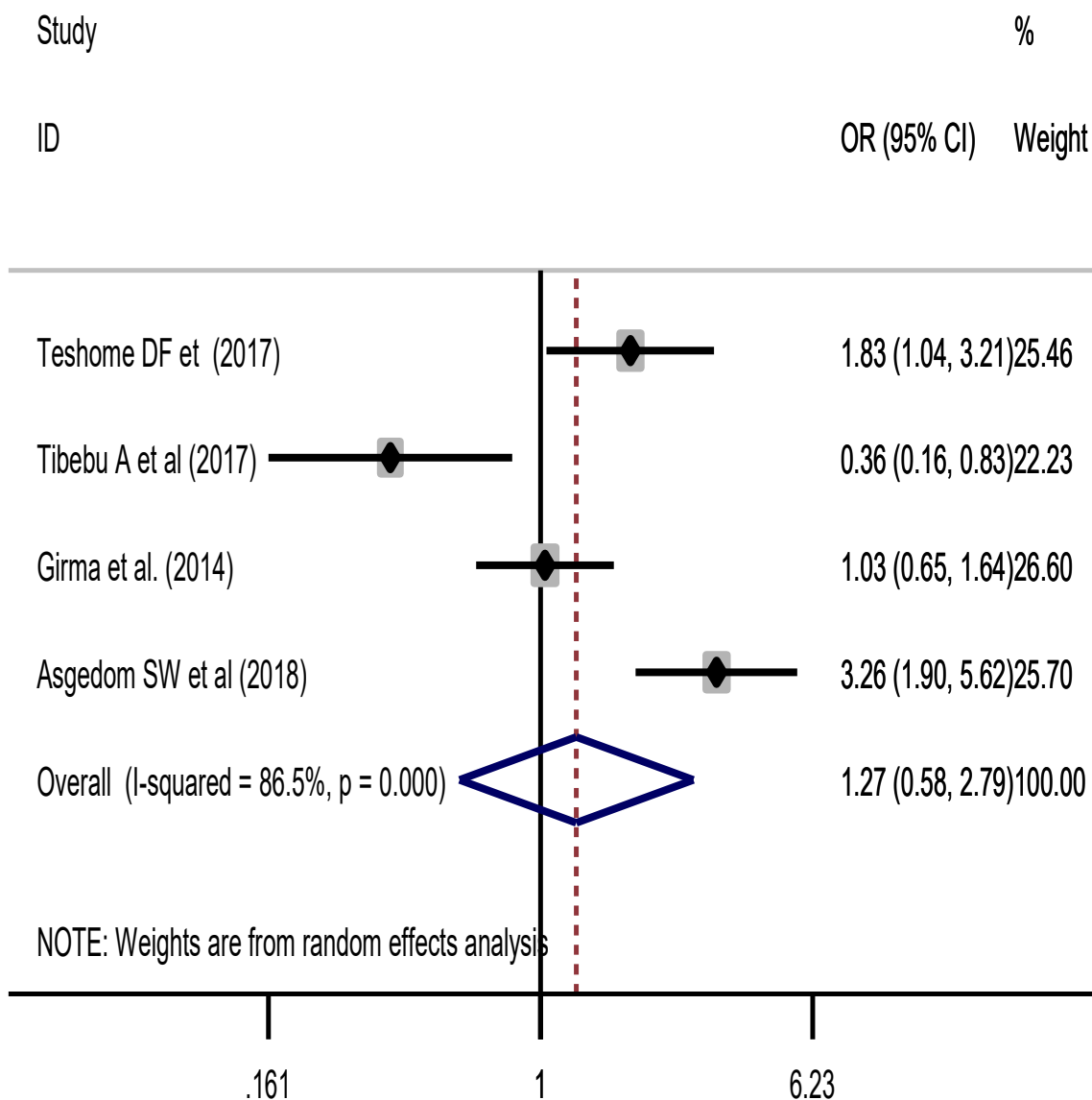
Fig. 6. Association of number of drugs on antihypertensive medication adherence.

of the medications versus the risk of the uncontrolled disease which resulted in an improvement of adherence to a therapeutic regimen. Studies support perceived susceptibility and severity increase the adherence to medication regimens (Larki, Tahmasebi, & Reisi, 2018). Unfortunately, our evidence was in contrast to the reports from Egypt (Hussein et al., 2020) and the Taiwan National Survey (Chou et al., 2020).

Furthermore, this systematic review and meta-analysis also showed that there was a significant reduction of uncontrolled blood pressure among hypertensive patients who had adhered to antihypertensive medication regimens better than their counterparts. This was in line with other studies (Elperin, Pelter, Deamer, & Burchette, 2014, Goverwa et al., 2014, Menanga et al., 2016, Sarfo et al., 2018, Gebremichael, Berhe, Beyene et al., 2019; Gebremichael, Berhe, & Zemichael, 2019). Antihypertensive medication adherence controls hypertension and reduces high blood pressure by increasing vasodilatation and decreasing vasoconstriction, increasing urine output, and blocking the sympathetic activation of the heart. Thus, the national burden of cardiovascular and cerebrovascular diseases, stroke, chronic renal diseases, and the associated morbidity and mortality are expected to decrease with controlled blood pressure to the optimal level through adherence to

antihypertensive medication regimens. Controlled blood pressure reduces the risk of all causes, CVD specific, heart disease-specific, or cerebrovascular disease-specific mortality.

Despite this systematic review and meta-analysis, only studies with a moderate to high-quality score based on the Newcastle quality scale were included, and there was a comprehensive literature search over multiple databases restricting the meta-analysis to the primary studies that used validated screening instruments with the recommended cutoff scores. This review has to be interpreted based on some of the following limitations. There was substantial heterogeneity in the estimates of included studies. Heterogeneity was not explained by the type of tool, geographic region variation, sample size, or year of publications. Some studies had a small sample size thus affecting the estimation. In addition, the studies were conducted in only 6 regions out of 9 regions and two administrative cities which might reduce representation for the country. In addition, self-reporting of treatment adherence could introduce recall bias by either overreporting or underreporting, depending on the patient's memory of the recent past.
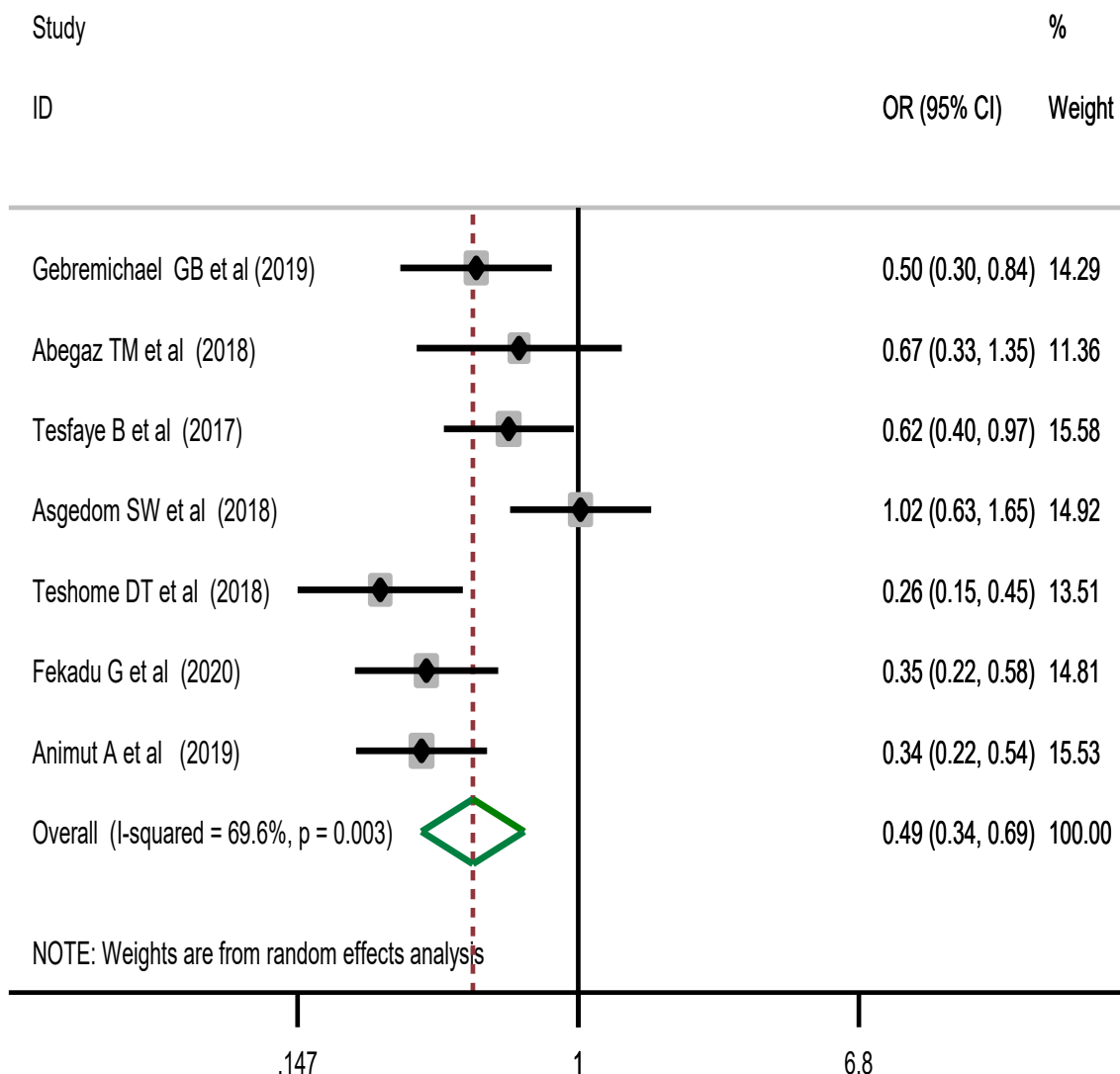
Fig. 7. Association of antihypertensive medication adherence with uncontrolled blood pressure.

5. Implications for Nursing practice

Weak health systems have been identified as a major obstacle in effectively responding to the rising burden of chronic conditions such as hypertension in developing countries. Improving knowledge of the patients on the treatment of hypertension has paramount clinical importance for the reduction of hypertension and glycaemic control. Hence, adherence with anti-hypertensive medications is significantly associated with glycaemic control (Chodosh et al., 2005). Thus, to improve the knowledge of the hypertensive patients, healthcare providers mainly nurses are expected to have a better level of counselling skill and knowledge on the area for the achievement of universal health coverage mainly provision of adequate and competent health care services important for reduction of cardiovascular disease. Knowledgeable patients are more concerned about their health outcomes and more likely to utilize good self-care practices. Moreover, belief-laden factors including confidence in the nurse's knowledge or ability, belief of control over one's health and illness perception were all found to be significantly related to medication adherence (Jankowska-Polańska, Uchmanowicz, Dudek, & Mazur, 2016). Thus, this study might be an input for the improvement of the nurses' clinical practice.

6. Conclusions

Two of every three hypertensive patients have adhered to antihypertensive medication regimens. This study revealed that hypertensive patients who had good knowledge of hypertension and associated comorbidities were more likely to adhere to antihypertensive medication regimens. Antihypertensive medication adherence was associated with reduced odds of uncontrolled blood pressure. Therefore, interventions of highest priority are aimed at improving knowledge of hypertension and identifying or screening those patients who have comorbidities. The Federal Ministry of Health and other relevant stakeholders should increase efforts in the prevention of uncontrolled blood pressure through education on adherence to medication with an emphasis on the identified modifiable risk factors.

7. Ethical approval and consent to participate

Not applicable

8. Consent to publication

Not applicable.

9. Availability of data and materials

Data will be available from the corresponding author upon reasonable request.

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Melaku Desta: Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Desalegn Yibeltal:** Visualization. **Peter Memiah:** Visualization. **Temesgen Ayenew:** Visualization. **Henok Mulugeta:** Investigation, Data curation, Supervision. **Mihretie Gedefaw:** . **Bekalu Bewket Kidanie:** Investigation, Data curation, Supervision. **Molla Yigzaw Birhanu:** Investigation, Data curation, Supervision. **Zenaw Tessema:** Investigation, Data curation, Supervision. **Belayneh Mengist:** Investigation, Data curation, Supervision. **Muluneh Alene:** Investigation, Data curation, Supervision. **Muluye Molla Simieneh:** Investigation, Data curation, Supervision. **Atsede Alle Ewunetie:** Investigation, Data curation, Supervision. **Wondimeneh Shibabaw Shiferaw:** Investigation, Data curation, Supervision. **Yordanos Gizachew Yeshitila:** Investigation, Data curation, Supervision.

Declaration of Competing Interest

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijans.2022.100404.

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