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Uncontrolled asthma in Ethiopia: a systematic review and meta-analysis

Abstract

Introduction: Despite significant improvement in the diagnosis and management of this disorder, asthma in the majority of Ethiopians remains poorly controlled. Although the prevalence of uncontrolled asthma is a public health problem in Ethiopia, its reported prevalence varies from study to study. Hence, this review aims to determine the true prevalence of uncontrolled asthma among asthmatic patients in Ethiopia.

Material and methods: Different database searching engines were used including PubMed, Scopus, Google Scholar, Africa journal online, World Health Organization (WHO) afro library, and Cochrane review. They were systematically searched for published studies on uncontrolled asthma in Ethiopia from 2014 to 2019. Primary search terms were "asthma", "uncontrolled asthma", "uncontrolled wheezing", and "Ethiopia". The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guideline was followed. Publication bias was examined by the funnel plot. The random-effect model was fitted to estimate the pooled prevalence of uncontrolled asthma among asthmatic patients. All statistical analysis was done using R version 3.5.3 and the RStudio version 1.2.5033 software for Windows.

Results: The overall pooled prevalence of uncontrolled asthma was found to be 71.67% [95% CI (0.6772; 0.7562)].

Potential associated factors were: unscheduled visits, frequency of short-acting beta2-agonist (SABA) use, type of treatment and perceived rate of asthma control, low monthly income, age group, presence of comorbidity, moderate persistent asthma, severe persistent asthma and use of SABA alone as anti-asthmatic medication, use of biomass fuel for cooking, longer duration of asthma (> 30 years), incorrect inhalation technique, and asthma exacerbation in the last 12 months. Self-perceived poor asthma control was associated with any activity limitation due to asthma, inconsistent inhaled corticosteroid use, and lack of health education on metered-dose inhaler technique [AOR =4.96; 95% CI (1.08–22.89)].

Conclusions: Nearly two-thirds of patients were determined to have uncontrolled asthma. Thus, this evidence suggests that attention should be given to asthma patients and health care providers.

Key words: uncontrolled asthma, asthmatic patient, determinants, Ethiopia

Introduction

Approximately 300 million people worldwide have asthma and recent projections indicate that an additional 100 million people will be living with asthma by 2025 [1, 2]. The World Health Organization (WHO) reports that there are approximately 250,000 asthma deaths per year, primarily in low-and middle-income countries (LMICs) [3, 4]. As with many other chronic diseases in Ethiopia, rapid urbanization rates have been related to a rise in the burden of asthma and other allergic diseases [3–6]. The incidence of these conditions can, in principle, have the

potential to reach higher rates than those seen in high-income countries (HICs) due to the primary effects of parasitic helminthic infections on the immune system, as these infections are widespread in Ethiopian settings [5]. The International Study of Asthma and Allergy in Childhood (ISAAC) stated that the burden of asthma among adults in Africa, including Ethiopia, has risen and has contributed most to the burden of disease through its effects on quality of life [3]. In-patient admissions and sales of medications account for much of the direct government expenses, while the lack of employment due to absenteeism from work and decreased education is responsible for many of the indirect costs [7, 8].

In Ethiopia, challenges, including those resulting from overuse of health facilities, lack of qualified personnel and testing equipment, and lack of access to and availability of inhaled medicines have hampered efforts to improve the management of asthma [8, 9]. The lack of coordinated health promotion initiatives, such as effective control strategies for environmental causes, air pollutants, and occupational dust, has also led to an increasing burden of disease [10]. The WHO has indicated that the rate of regulation of asthma and health responses combatting the diease on the continent have been below the required requirements and have led to the large size of the disease burden [3, 4]. Besides, while many African countries have national guidelines on the treatment of asthma and other CRDs, these guidelines have not been enforced in most rural areas [11, 12]. Economic analyses (Placeholder2) in many African settings have shown that the direct costs of asthma are typically higher than indirect costs. Nonetheless, indirect costs reflect a relatively higher proportion of overall costs for pediatric patients compared to adult patients [8]. Moreover, the broader economic strain on individuals, households, employers, and the community, owing to the lack of future potential sources of livelihood, has also been devastating in many resource-poor environments [7]. It is assumed that many children with asthma in Africa may fail to reach their full potential unless appropriate treatment and control measures are put in place [1]. It has been proposed that awareness by health care professionals and the public is a critical element in reacting to the challenge raised by asthma in Africa [3, 13].

By 2015, the urban population of the world is projected to rise from 45% to 59%, with more than half of this happening in Africa, including Ethiopia [8]. The prevalence of asthma and other chronic diseases in Africa is also projected to increase due to this increasing population growth, impact of subsequent urbanization, and adoption of western lifestyles [14].

Because of reasons that include these changes, the low output of research, and limited quality of health services data on the burden of asthma in Africa, it is important to evaluate the available data through a systematic review of literature to attempt to measure the burden, direct the setting of health priorities, and inform the formulation of effective health policy responses. Understanding the determinants of uncontrolled asthma will also help to manage premature death from non-communicable diseases (NCD) in general, as well as asthma in particular.

This result will also allow the Ministry of Health and Clinical Services, facility managers, and governmental and non-governmental organizations to be informed of the determinants of uncontrolled asthma and to commit to taking action. Besides, this analysis should be used as a model for prospective researchers and other stakeholders.

Therefore, this study will be trying to assess the prevalence and determinants of uncontrolled asthma among asthma patients in Ethiopian hospitals.

Methods and materials

Setting

Ethiopia is an east African country and is divided into 9 regions named Tigray, Afar, Amhara, Oromia, Somali, Benishangul-Gumuz, Southern Nations Nationalities and People Region (SNN-PR), Gambella, and Harari, as well as two administrative states (Addis Ababa city administration and Dire Dawa city administration).

Search strategy

The search strategy has been applied using Online Databases (PubMed/MEDLINE, Google Scholar, Web of Science, Cochran Library, Africa Wide Knowledge, and Africa Index Medicus) from 2014 to January 2020. Only articles written in English and full-texts published from peer-reviewed journals were eligible for inclusion. Primary search terms were "asthma", "uncontrolled asthma", and "Ethiopia". Studies that reported associated factors or determinants or predictors of uncontrolled asthma only, or did not report the magnitude or prevalence of uncontrolled asthma were excluded.

The literature search technique was developed using the headings of the medical subject headings (Mesh), BOOLEAN (AND/OR) operator was used.

The last electronic search was run on 30 January 2019. Although no complete study protocol was written before starting this review, we developed and piloted a screening guide to make sure that the inclusion criteria were adhered to and consistently applied by all review authors. Two reviewers (DBT and KGK) independently screened the titles, abstracts of all citations retrieved, and full-text search results to identify potentially eligible studies. The agreement between review authors was measured using Cohen's κ statistic. Disagreements were resolved by discussion after mutual consensus and third-party independent review (AH).

Inclusion and exclusion criteria

The following factors were a part of the inclusion criteria for our analysis: studies presented as original articles; studies that assessed uncontrolled asthma among patients; studies conducted among Ethiopian asthmatic patients living in Ethiopia and aged 18 and above; studies conducted and published from 2014 to 30 January 2019; and studies written in English. Studies that did not explain the criteria for the level of asthma control and studies that didn't state the number of patients with uncontrolled asthma were excluded.

The types of studies included were all published and unpublished observational studies (cross-sectional, prospective/retrospective cohort studies, or case-control studies). Baseline data from randomized controlled trials conducted in Ethiopia reporting on the prevalence of uncontrolled asthma were also included. Experimental studies, letters, reviews, commentaries, editorials, case reports, or case series were not included. In the case of duplicate reports, the most comprehensive and up-to-date version was taken into account.

The participants of the study included adult populations with known asthma on any form of anti-asthmatic medication. Study participants should be at least 18 years of age.
Intervention(s)/exposure(s): On any form of anti-asthmatic medications.
Outcome: Prevalence of uncontrolled asthma among people who report taking antihypertensive drugs
Settings: Hospital-based studies.
Publication date: 2014, to January 30, 2019.
Language: No language restriction.

Exclusion criteria

Studies not performed on humans, qualitative studies, studies that lack relevant data needed to compute the prevalence of uncontrolled asthma, studies among children and adolescents < 18 years of age, and studies that did not use the disease control criteria through the ACQ, C-ACT, ACT, or GINA were excluded.

Data extraction and quality assessment

Data extraction used a preconceived and standardized data collection form and was performed by two independent authors (DBT and KGK). Any discrepancies between these authors were reconciled through discussion. Data extracted comprised information about the year of publication, country, objective and design of the study, diagnostic criteria of uncontrolled asthma, mean age, sex (male proportion), duration of asthma, signs and symptoms, anti-asthmatic medications, complications, prevalence and/or incidence, and risk factors for uncontrolled asthma.

Quality assessment of included studies

The methodological quality of the included studies was evaluated using the Newcastle-Ottawa Scale. The Newcastle-Ottawa Scale was designed to assess the quality of non-randomized studies in meta-analyses. This scale is primarily formulated by a star allocation system, assigning a maximum of 10 stars for the risk of bias in three areas: a selection of study groups (4 or 5 stars), comparability of groups (2 stars), and ascertainment of the outcome of interest or exposure (3 stars). No validation study provides a cut-off score for rating low-quality studies. A priori, we arbitrarily established that 0–3, 4–6, and 7–10 stars would be considered as a high, moderate, and low risk of bias, respectively.

Data analysis and presentation of results

Data were analyzed using the R software V.3.5.3. Data were summarized using ranges, means ± SDs, and frequencies (percentages) where appropriate. Forest plots were drawn to visualize the combined prevalence of uncontrolled asthma and the extent of statistical heterogeneity between studies. Statistical heterogeneity was assessed using the $\chi 2$ test on Cochrane's Q statistic [20] and quantified by calculating the I^2 statistic (with values of 25%, 50%, and 75% representative of low, medium, and high heterogeneity, respectively) [21]. There was a clinical heterogeneity between studies included in this study. The defi-

nition of uncontrolled asthma was different across studies. Consequently, we used a random-effects meta-analysis to estimate the overall pooled prevalence of uncontrolled asthma. To assess possible publication bias, Egger weighted regression methods were used. A p-value < 0.05 was considered indicative of statistically significant publication bias. Moreover, other relevant findings were summarized in a narrative format.

Data management

Based on the inclusion and exclusion criteria, a tool has been developed a priori to guide the screening and selection process. The tool was be piloted and revised before data extraction begins. The search results were first be uploaded to EndNote software first to remove duplicates.

Selection process

Once data are obtained, two investigators will independently screened the titles and abstracts of articles retrieved from the literature search against the inclusion criteria. Full texts for the eligible titles and/or abstracts including those where there is uncertainty were obtained for further assessment on whether to include in the study or not. Where necessary, authors were contacted for additional information to confirm the eligibility of studies. Disagreements were resolved through discussion and, when needed, there was arbitration by a third reviewer. Reasons for excluding articles were recorded.

Data collection process

Data were extracted using a standardized data extraction form. From the studies included, two assessors were independently extracted data using the predefined standardized extraction form. Disagreements were resolved through discussion and, when needed, there was arbitration by a third reviewer.

Where there is missing information, the corresponding author of the study was contacted to request the missing information. A maximum of three emails will be sent to the corresponding author to request for additional information before excluding the study. For studies appearing in more than one published article, we considered the one that is most recent, comprehensive, and with the largest sample size. For surveys appearing in one article with multiple surveys conducted at different time points, we shall treat each survey as a separate study. For multi-national studies, data were separated to show the estimate by country level.

Data items

Data on general information, authors, year, country, region, type of publication, study characteristics (study design, setting, sample size, response rate, mean or median age, or age range), data on the diagnosis of asthma, information on the use of anti-asthmatic medication/therapy, and prevalence estimates of uncontrolled asthma among those on treatment were extracted. Where anti-asthmatic treatment or prevalence information relevant for estimating uncontrolled asthma among those on treatment are not available, we contacted the corresponding author of the study to request the missing information. The prevalence of uncontrolled asthma were estimated as a percentage of all the participants on treatment with an anti-asthmatic.

Outcomes and prioritization

The primary outcome is the prevalence of uncontrolled asthma among people who report taking anti-asthmatic treatment in Ethiopia.

Risk of bias in individual studies

To assess the risk of bias and quality of studies included in this review, a tool developed by Hoy *et al.* for prevalence studies was used [15]. The tool contains 11 items; items 1–4 assess the external validity, 5–10 assess the internal validity, and item 11 is a summary of the overall risk by the reviewer based on the responses of the above 10 items which are scored 1 if yes and 0 if no. Studies were classified as having either a low (> 8), moderate, or high (≤ 5) risk of bias. This exercise was done by two reviewers and disagreements were solved by discussion and, where necessary, by arbitration involving a third reviewer/author.

For each included study, we estimated the precision (C) or margin of error considering the sample size (SS) and the observed prevalence (p) of uncontrolled asthma from the formula:

$$SS = \frac{z^2 \times p \times (1-p)}{d^2}$$

where z was the value fixed at 1.96 across studies (corresponding to 95% confidence interval). The desirable margin of error is 5% (0.05) or lower.

Data synthesis

Crude numerators and denominators from the individual studies were used to recalculate the study-specific prevalence. Prevalence estimates
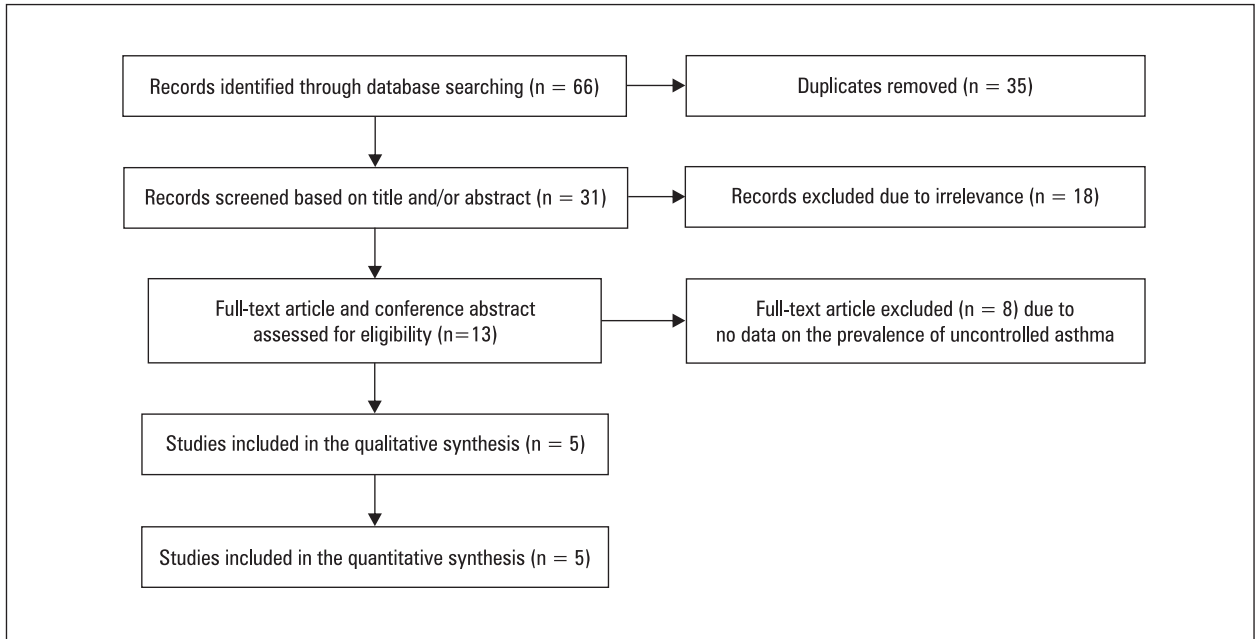
Figure 1. Process of the identification and selection of studies for inclusion in the review (PRISMA flow diagram)

will be summarized by geographic regions and by comorbidities.

A meta-analysis were performed on variables that are similar across the included studies. Proportions were stabilized using the double arcsine transformation, and then, a random-effects meta-analysis was performed to determine the pooled estimate of the prevalence of uncontrolled asthma among patients on anti-asthmatic treatment across studies in Ethiopia.

Heterogeneity was be explored using Cochrane's Q and quantified by I^2 statistics [16]. Subgroup analyses were performed based on the following: Regions (Eastern, Western, Central, and Southern of Ethopia) to identify the possible sources of heterogeneity. The definitions of the comorbidities of interest were collected, and those with the same definitions were analyzed together.

The presence of publication bias was assessed using Egger's test and funnel plots [17]. A p-value of < 0.10 on the Egger's test was considered statistically significant for publication bias. Inter-rater agreements between the researchers involved in study selection and those involved in the identification of risk of bias were assessed using Cohen's κ coefficient.

All analyses were performed using a "metaprop" routine using R version 3.5.3 for Windows [18]. Results were reported as proportions with corresponding 95% confidence intervals (CIs).

Results

Screening flow

Figure 1 is a flow diagram outlining the process of identification and selection of included studies. We identified 66 records through a comprehensive search among which 35 duplicates were identified and removed. Subsequently, we screened 26 titles and abstracts and excluded 18 irrelevant papers. Then, the abstracts of thirteen full-text articles were reviewed for eligibility, among which eight publications were excluded for not reporting the prevalence of uncontrolled asthma. At the end of the process, only five studies met the inclusion criteria and were thus retained for qualitative and quantitative analyses (Figure 2).

Prevalence of uncontrolled asthma

All included studies were observationally conducted from 2014 to 2019 in different regions. Five studies were included with a total of the sample being 1001. The sample sizes for each study were as follows: 243 in Oromia [19], 197 in Oromia [20], 182 in Addis Ababa [21], 182 in Addis Ababa [22], 206 in Amhara [23]. The prevalence for each study was as follows: Jimma University Specialized and Teaching Hospital(JUSH) (71.3%), JUSH (64.4%), Addis Ababa (75.8%), Addis Ababa (75.8%), and University of Gondar (70%) [19–23]. The overall mean pooled prevalence was 71.7% (Figure 2).
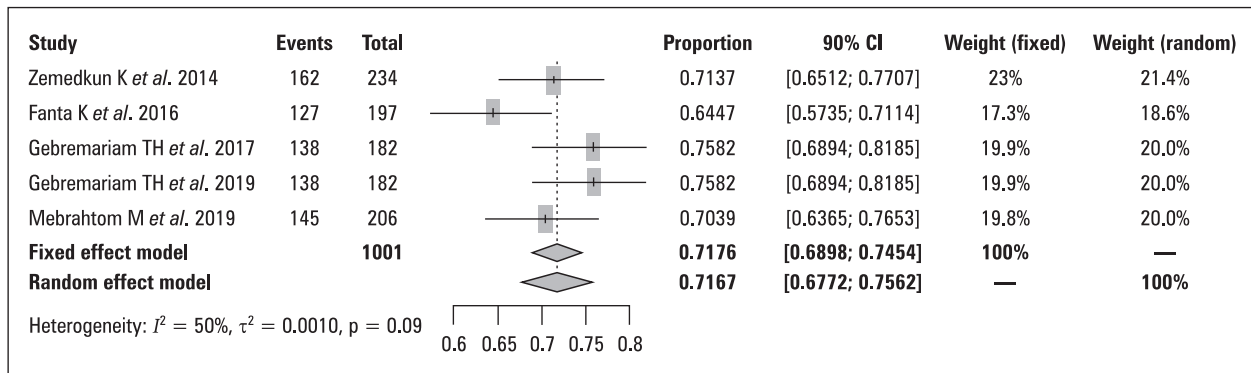
Study	Events	Total		Proportion	90% CI	Weight (fixed)	Weight (random)
Zemedkun K *et al*. 2014	162	234		0.7137	[0.6512; 0.7707]	23%	21.4%
Fanta K *et al*. 2016	127	197		0.6447	[0.5735; 0.7114]	17.3%	18.6%
Gebremariam TH *et al*. 2017	138	182		0.7582	[0.6894; 0.8185]	19.9%	20.0%
Gebremariam TH *et al*. 2019	138	182		0.7582	[0.6894; 0.8185]	19.9%	20.0%
Mebrahtom M *et al*. 2019	145	206		0.7039	[0.6365; 0.7653]	19.8%	20.0%
Fixed effect model		1001		0.7176	[0.6898; 0.7454]	100%	—
Random effect model				0.7167	[0.6772; 0.7562]	—	100%

Heterogeneity: $I^2 = 50\%$, $\tau^2 = 0.0010$, p = 0.09

0.6 0.65 0.7 0.75 0.8

Figure 2. Forest plot for the pooled prevalence of uncontrolled asthma from 5 observational studies

Associated factors of uncontrolled asthma

The first and second studies were conducted in Jimma Specialized Hospital (Southeast Ethiopia) from June 1, 2012 to July 31, 2012 and in 2016, respectively. The third and fourth studies were conducted in Addis Ababa (Central Ethiopia) in 2017 and 2019, respectively. The fifth study was conducted in Gondar (Northwest Ethiopia) in 2019 (Table 1).

Discussion

The present systematic review with meta-analysis was performed to produce pooled estimates of nationwide results of uncontrolled asthma in Ethiopia among patients with asthma. This review emphasizes the burden of uncontrolled asthma among patients with asthma in Ethiopia for a better understanding of the medical condition which will help in mitigating the problem of uncontrolled asthma throughout the country. In addition, this review points out a critical lack of a high level of evidence regarding the burden of uncontrolled asthma in Ethiopia. Indeed, we have recorded only five studies that have assessed the prevalence and/or risk factors for uncontrolled asthma in Ethiopia. That being said, this review highlights the crucial and urgent need to focus on the epidemiology of uncontrolled asthma in Ethiopia to better understand the condition and address specific action plans that will surely result in mitigating the morbidity and mortality due to asthma and its related complications throughout the country.

This meta-analysis showed that the pooled estimated of uncontrolled asthma in Ethiopia was found to be 71.7% with a 95% CI between 67.72% and 75.62%. Individually, the prevalence of uncontrolled asthma in the studies included in our work was varied and ranged from 64.4% reported by Fenta *et al.* [20] to 75.8.2% reported by Gebremariam [22]. The reason for these variations could be due to the types of diagnostic tools and assessment methods.

Our meta-analysis study result was higher than the studies conducted in Ethiopia [20, 24], Canada [25], Zimbabwe [25], and Morocco [26]. This might be due to differences in sample size and study design. This study result is lower than the studies conducted in Ethiopia [27] and Israel [28]. This difference might be due to a difference in setting since our hospital is the largest hospital in the country and the most complicated patients are treated here.

Age, unscheduled visits, frequency of SABA use, types of treatment, and perceived rate of asthma control [20]. Low monthly income, presence of comorbidities, moderate persistent asthma, severe persistent asthma, and use of SABA alone as anti-asthmatic medication [21]. Use of biomass fuel for cooking, longer duration of asthma (>30 years), incorrect inhalation technique, and asthma exacerbation in the last 12 months [22]. Self-perceived poor asthma control was associated with any activity limitation due to asthma and inconsistent inhaled corticosteroid use [23]. Lack of health education on metered-dose inhaler technique [AOR = 4.96; 95% CI (1.08–22.89)] [29].

Nonetheless, we conducted this review following the rigor and standards of the industry. Besides, and to the best of our knowledge, this is the first systematic review and meta-analysis drawing a clear picture of the prevalence and risk factors for uncontrolled asthma in Ethiopia.

Our findings from the meta-analysis have implications in clinical practice because they contribute to giving attention to the prevention and care of patients with asthma. This pooled point of estimates for uncontrolled asthma in patients with asthma provides updated evidence

Table 1. Characteristics of studies included in the systematic review and meta-analysis of the prevalence of uncontrolled asthma among adult asthmatic patients in Ethiopia, 2020

| Author, year	Study area	Study Design	Sample size	Cases	Prevalence of uncontrolled asthma (%)	Associated factors	Diagnostic criteria
Zemedkun K, Woldemichael K, Tefera G 2014	JUSH	CS	234	167	71.3	Age, unscheduled visit, frequency of SABA use, type of treatment and perceived rate of asthma control [19]	Asthma Control Questionnaire (ACQ), Global Initiative for Asthma (GINA) and the Asthma Control Test (C-ACT/ACT)
Fanta K, Daba FB 2016	JUSH	CS	197	127	64.4	Low monthly income, presence of comorbidity, moderate persistent asthma, severe persistent asthma and use of SABA (short-acting beta2 agonist) alone as anti-asthmatic medication [20]	Asthma Control Questionnaire (ACQ), Global Initiative for Asthma (GINA) and the Asthma Control Test (C-ACT/ACT)
Gebremariam TH, Binegdie AB, Mitiku AS, Ashagrie AW, Gebrehiwot KG, Huluka DK, Sherman CB, Schluger NW 2017	Addis Ababa	CS	182	138	75.8	Use of biomass fuel for cooking, longer duration of asthma (> 30 years), incorrect inhalation technique, and asthma exacerbation in the last 12 month [21]	Asthma Control Questionnaire (ACQ), Global Initiative for Asthma (GINA) and the Asthma Control Test (C-ACT/ACT)
Gebremariam TH, Sherman CB, Schluger NW 2019	Addis Ababa	CS	182	138	75.8	Self-perceived poor asthma control was associated with any activity limitation due to asthma and inconsistent inhaled corticosteroid use [22]	Asthma Control Questionnaire (ACQ), Global Initiative for Asthma (GINA) and the Asthma Control Test (C-ACT/ACT)
Mebrahtom M, Mesfin N, Gebreyesus H, Teweldemedhin M 2019	Gondar	CS	206	145	70	Lack of health education on metered-dose inhaler technique [AOR = 4.96; 95% CI (1.08–22.89)] [23]	Asthma Control Questionnaire (ACQ), Global Initiative for Asthma (GINA) and the Asthma Control Test (C-ACT/ACT)
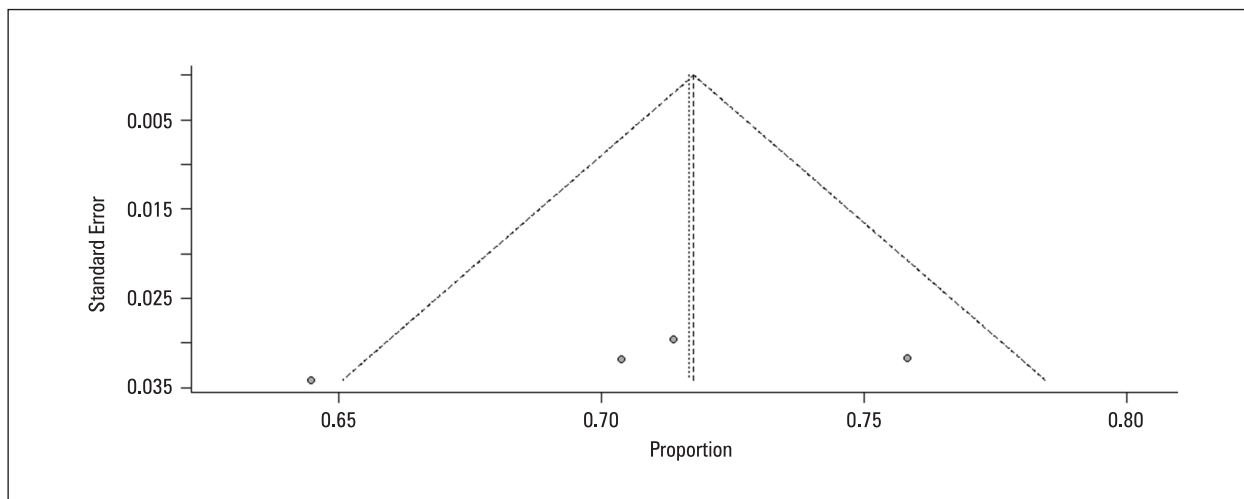
Figure 3. Funnel plot showing evidence of no publication bias across studies

to advance prevention strategies, to serve as a key indicator of patient safety, to reflect the quality of healthcare service, and to further advance potential and appropriate treatment strategies for uncontrolled asthma in patients with asthma. Finding the accurate prevalence of uncontrolled asthma will help to improve the use of adherence interventions such as patient education and counseling on how to self- monitor, as well as lifestyle modification interventions such as exercise, weight reduction, and healthy diet. Therefore, the asthma treatment strategy should keep in mind that in addition to prescribing appropriate anti-asthmatic medications and asthma care practice, they need to include resources that help patients overcome individual challenges to reduce the development of chronic complications using self-care practice. The implication of this study, particularly the pronounced variation between studies (64.4% to 75.8%), reflects that patients with asthma require developed standards for management and implemented endorsed guidelines in clinical practice.

Conclusion

In this study, the prevalence of uncontrolled asthma among asthmatic patients was considerably high. Potential associated factors were: unscheduled visits, frequency of SABA use, type of treatment and perceived rate of asthma control, low monthly income, age, presence of comorbidities, moderate persistent asthma, severe persistent asthma, use of SABA alone as anti-asthmatic medication, use of biomass fuel for cooking, longer duration of asthma (>30 years),

an incorrect inhalation technique, and asthma exacerbation in the last 12 months. Self-perceived poor asthma control was associated with any activity limitation due to asthma, inconsistent inhaled corticosteroid use, and lack of education on metered-dose inhaler technique. In response to this finding, future interventions that target the prevalence and resolution of associated factors is required.

Strengths and limitations of this study

To the best of our knowledge, this is the first and only systematic review and meta-analysis that has focused on uncontrolled asthma in Ethiopia.

Strong and reliable methodological and statistical procedures were used in this review.

Only nine studies were found eligible for inclusion in the qualitative and quantitative analyses.

The definition of uncontrolled asthma was different from one study to another, with a consequential high clinical heterogeneity across studies.

Different studies use different variables and this results in variation in the significant variables.

Most of the studies did have not separate.

Authors contribution

DBT, KGK, and AH conceived and designed the study, conducted the research for literature, and extracted and analyzed the data. AH, GTD, MA, EA, MN, and KGK drafted the manuscript. DBT, KGK, and AH critically revised the manuscript. All authors approved the final manuscript.

Conflict of interest

The authors declare that they have no competing interests.

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