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Poor treatment outcome and associated factors of hyperglycemic emergencies among diabetic patients in Ethiopia: A systematic review and meta-analysis

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ABSTRACT

Background: Despite the fact that hyperglycemic crisis poses a significant threat to the health care systems of developing countries like Ethiopia, there is a dearth of reliable data regarding the poor treatment outcome and associated factors among hyperglycemic emergencies in Ethiopia. Therefore, this review aimed to assess poor treatment outcome and associated factors of hyperglycemic emergencies among diabetic patients in Ethiopia.
Methods: Published articles regarding poor treatment outcome and associated factors of hyperglycemic emergencies among diabetic patients in Ethiopia were extensively searched from PubMed, Google Scholar, Cochrane library, and African journal online. After extraction, data were exported to Stata software version 11 (Stata Corp LLC, TX, USA) for analysis. Statistically, the Cochrane Q-test and I^2 statistics were used to determine the presence or absence of heterogeneity.
Results: 3650 duplicates were eliminated from the 4291 papers (PubMed [18], Google scholar (1170), African journal online [21], and Cochrane library (3082)). The pooled estimate of poor treatment outcome among hyperglycemic emergencies in Ethiopia is found to be 16.21% (95% CI: 11.01, 21.41, $P < 0.001$). Creatinine level >1.2 mg/dl, stroke, sepsis and comorbidity were associated factors of poor treatment outcome.
Conclusion: Poor treatment outcome from hyperglycemic emergencies among diabetic patients was found to be high. Poor treatment outcome was predicted for those patients who had creatinine level >1.2 mg/dl, stroke, sepsis and comorbidity. As a result, we recommend healthcare providers to monitor thoroughly and have close follow-ups for patients with the identified predictors to improve poor treatment outcome from hyperglycemic crises

Introduction

Approximately 5 million people have died from diabetes mellitus (DM) worldwide in the previous ten years due to the disease's sharp increase in prevalence [1]. Diabetes mellitus is a chronic metabolic condition described by elevated blood glucose level results from abnormality of insulin secretion, insulin action, or both [2]. World Health Organization (WHO) 2016 report stated that 1.6 million fatalities were occurred as a result of diabetes related complications. Hyperglycemic emergencies (HGEs) are becoming the main life-threatening metabolic complications leads to significant diabetes-related morbidity, mortality, and medical expenses [3,4]. Untreated DM can lead to potentially fatal acute complications such as diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) requiring intensive treatment and hospitalization [5]. Diabetic ketoacidosis occurs in type 1 and HHS most often occurs in type 2 diabetes; however, each type of diabetes may be associated with DKA or HHS [6]. These complications typically result in impairment, shortened life expectancy, and high health expenses [7]. According to Center of Disease Control and Prevention (CDC) report, the annual hospitalization rate of adults with diabetes in the United States

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has been continuously rising, with 9.7 hospitalizations per 1000 persons as a result of HGEs [8].

Hyperglycemic emergencies represent almost 12% of diabetes-related hospitalizations in Africa [9]. Many research conducted across the world have revealed that the mortality rates of hyperglycemic hyperosmolar syndrome (HHS) and diabetic ketoacidosis (DKA) ranges from 10 to 20% and 2–5%, respectively, with the highest premature death reported in Ethiopia and other countries in Sub-Saharan Africa [10–12]. The hyperglycemic crisis in Africa was the primary cause of hospital admissions for diabetic patients, which ranged from roughly 26% in South Africa to 40% in Nigeria. Death rates also varied, from 7.5% in South Africa to 34% in Nigeria [13–15]. According to studies conducted in Ethiopia, 14.6% of patients with a history of diabetes had a hyperglycemic crisis, whereas 23.6–43% of patients had newly developed diabetes at the time of admission with a 30-day case fatality rate of 4.1% [11,16,17].

Lack of funding for non-communicable illnesses control, poor public healthcare service, inadequate health education, poor self-glycemic control, and a dearth of population-specific research and guidelines all contribute significantly to the rising burden of HGEs in sub-Saharan Africa [12,18]. Many nations have implemented various methods and preventive steps to improve poor treatment outcome, such as diabetes self-management education, raising awareness on the pathophysiology of hyperglycemic emergencies, and adopting hyperglycemic emergency treatment standard [19]. These methods, meanwhile, have not been applied well in Ethiopia. The prevention and management of hyperglycemic emergencies in Ethiopia are further complicated by the high cost and scarcity of treatment supplies, the existence of comorbid illnesses, improper insulin storage, medication non-adherence, electrolyte imbalance, and smoking habits [20,21].

According to many research conducted in different countries admission serum creatinine >1.2 mg/dl, co-morbidity, rural residents, medical history of stroke, shock on presentation, hypokalemia, severity, type 2 diabetes and sepsis were independent predictors of poor treatment outcome of HEs among diabetic patients [11,22–25].

Despite the fact that hyperglycemic crisis poses a significant threat to the health care systems of developing countries like Ethiopia, there is a dearth of reliable data regarding the poor treatment outcome and associated factors of hyperglycemic emergencies in Ethiopia. The results of the review will be helpful to provide evidence based information to manage hyperglycemic crisis better, minimizing in-hospital mortality, and shortening hospital stays for hyperglycemic patients. Therefore, this review aimed to assess poor treatment outcome and associated factors of hyperglycemic emergencies among diabetic patients in Ethiopia.

2. Methods

2.1. Search strategy and database

The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guideline was used to report this systematic review and meta-analysis [26] (Supplementary file). Published articles regarding poor treatment outcome and associated factors of hyperglycemic emergencies among diabetic patients in Ethiopia were extensively searched from the following databases: PubMed, Google Scholar, Cochrane library, and African journal online from November 20/2023 to January 16/2024 by two Authors (A.M. and W.C). To include many pertinent studies as possible, reference lists of eligible studies were also searched. The following Medical Science Heading (MeSH) terms were used to search studies from the aforementioned database: "treatment outcome" OR "mortality" OR "poor treatment outcome" AND "determinants" OR "predictors" OR "associated factors" OR "risk factors" AND "diabetic ketoacidosis" OR "hyperglycemic emergencies" OR "hyperglycemic hyperosmolar non-ketotic syndrome" and "Ethiopia". EndNote X7 was utilized to handle article duplication.

2.2. Outcome of review

The review's outcome variable is the poor treatment outcome of hyperglycemic emergencies and its associated factors among diabetic patients. The following operational definition was considered for the current review purpose. Good treatment outcome: those patients who showed improvement after treatment at discharge. Poor treatment outcome: those patients who left against medical advice, develop treatment complications, have long hospital stay or died in the hospital [20].

2.3. Inclusion and exclusion criteria

Any quantitative studies that reported the prevalence of treatment outcome of hyperglycemic emergencies among patients with diabetes in Ethiopia, freely accessible articles and articles published in English language were the main focus of the inclusion criteria for this review. Studies carried out outside of Ethiopia, qualitative research, articles with restricted access, abstracts, case reports, and studies published in languages other than English were among the exclusion criteria.

2.4. Data extraction

Two authors (WCT, and AMZ) independently extracted the data using a standardized data extraction checklist on a Microsoft Excel spreadsheet. The discrepancies between the two authors during data extraction were raised and managed by discussion. Standardized Microsoft Excel sheet template was used to extract the following data; corresponding authors name with publication year, study design, study population, study area/region, sample size, sampling technique, participants, prevalence of poor treatment outcome, and associated factors of poor treatment outcome. The extracted associated factors are selected based on the following criteria: 1) have similar operational definition in the primary studies 2) reported with similar measure of association 3) have similar direction of associated and reported in two and above studies. Critical analysis was done on the extracted data, and the results were narratively described.

2.5. Quality assessment

Three authors (YAF, GWA and GMB) evaluated the quality of the included studies using the Newcastle-Ottawa Scale, which allows evaluation of each article based on methodological quality, caliber of comparability, and excellence of outcome divided across eight specific items. Each item on the scale is scored from one point, except for comparability, which can be adapted to the specific topic of interest to score up to two points. Thus, the maximum score for each study is 9, with range of overall scores 0–3, 4–6, and 7–9, indicating low, moderate, and high risk of bias, respectively [27].

2.6. Statistical analysis

After extraction, data were exported to Stata software version 11 (Stata Corp LLC, TX, USA) for analysis. To visualize the heterogeneity between the studies, a forest plot was used, which reported the prevalence of poor treatment outcome at 95% confidence interval for each study, as well as the pooled prevalence of the combined studies. Statistically, the Cochrane Q-test and I^2 statistics were used to determine the presence or absence of heterogeneity, based on the values of 0–40, 40–60, 60–90 and 90–100% indicated low, medium, substantial and high heterogeneity respectively [28]). A sensitivity analysis was conducted to determine the influence of single studies on pooled estimates. Publication bias (small study effect) was checked graphically using a funnel plot and statistically using Egger's regression test at the significance level of $P < 0.05$.

3. Results

3.1. Study selection and identification

3650 duplicates were eliminated from the total record of 4291 papers (PubMed [18], Google scholar (1170), African journal online [21], and Cochrane library (3082)). Additional 540 items were eliminated based on a review of the title and abstract. Lastly, 93 were eliminated because they were conducted out of Ethiopia, not conducted among diabetic patients and didn't report the outcome of interest i.e. prevalence of poor treatment outcome. Finally, the meta-analysis included 8 published articles (Fig. 1).

3.2. Characteristics of included studies

Four of the included studies were institutional based cross-sectional and the remaining were retrospective studies. The highest prevalence of poor treatment outcome is reported from Oromia region (26.2%) [20] and the least is from Addis Ababa (3.9 %) [22]. The included studies were conducted from different regions of the country; 2 from Addis Ababa [22,24], 3 from Oromia region [11,20,29], 1 from Eastern Ethiopia [25], 1 from Amhara region [23] and 1 from Tigray region [30]. Detailed characteristics of the included studies are presented in (Table 1).

3.3. Quality of the included studies

From the total included studies, the quality assessment showed that about six (n = 75%) of the studies had high quality, and the remaining two (n = 25%) of studies had medium quality (Supplementary file).

3.4. Publication bias

Egger's regression intercept tests were also carried out to determine publication bias. Egger's test results, the absence of significant publication bias was declared objectively (P = 0.146) and using symmetrical observation of Funnel plot subjectively (Fig. 2).

3.5. Meta-analysis

The pooled estimate of poor treatment outcome among hyperglycemic emergencies in Ethiopia is found to be 16.21% (95% CI: 11.01, 21.41). The meta-analysis showed high heterogeneity across the included studies with $I^2 = 100\%$, $P < 0.001$). As a result, random effect model was used to compute the pooled estimate of poor treatment outcome among hyperglycemic emergencies among diabetic patients in Ethiopia (Fig. 3).

3.6. Associated factors of poor treatment outcome

A total of four common factors were identified to predict poor treatment outcome among hyperglycemic emergencies. They include creatinine level >1.2 mg/dl, stroke, sepsis and comorbidity. This meta-analysis found that creatinine level >1.2 mg/dl is associated with poor treatment outcome. The odds of poor treatment outcome from hyperglycemic crises were 3.04 times higher in patients with serum creatinine >1.2 mg/dl compared to those with serum creatinine ≤1.2 mg/dl (POR = 3.04; 95% CI: 1.66–5.54). There was no heterogeneity between studies. Therefore we used fixed effects model ($I^2 = 0.00\%$, P-value <0.001) (Fig. 4). Patients with comorbidity had 2.83 times higher risk of poor treatment outcome from hyperglycemic crises as compared to those without comorbidity (POR = 2.83; 95% CI: 0.10–77.54). There was heterogeneity between studies in the random effects model ($I^2 = 94\%$, P-value <0.001) (Fig. 5). In this review patients who had sepsis were 4.04 times more likely to poor treatment outcome from hyperglycemic crises as compared to those who had no sepsis (POR = 4.04; 95% CI: 1.66–9.81). There was substantial heterogeneity between studies in the random effects model ($I^2 = 68.4\%$, P-value = 0.002) (Fig. 6). The likelihood of poor treatment outcome from hyperglycemic crises was 4.16 times higher in patients with stroke as compared to those without stroke (POR = 4.16; 95% CI: 2.51–6.87). There was no heterogeneity between studies. Therefore fixed effect model was utilized ($I^2 = 0.0\%$, P-value<0.001) (Fig. 7).

4. Discussion

In this review, we have reported the prevalence of poor treatment outcomes of patients for hyperglycemic emergencies in Ethiopia among

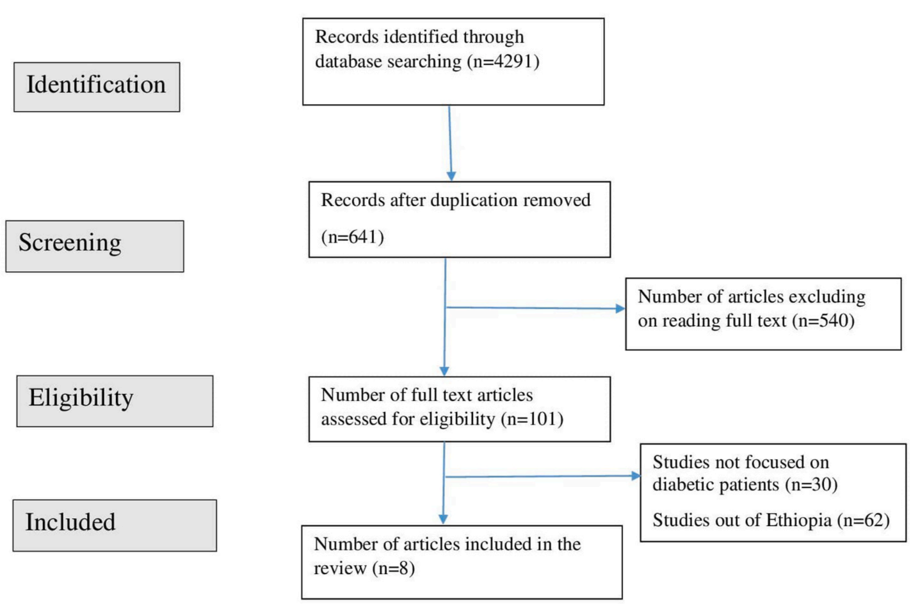

Fig. 1. PRISMA flow diagram of article selection for a systematic review and meta-analysis of poor treatment outcome and associated factors of hyperglycemic emergencies among diabetic patients in Ethiopia (N = 8).

Table 1
Baseline Characteristics of included studies in the review of poor treatment outcome and associated factors of hyperglycemic emergencies among diabetic patients in Ethiopia.

Author	Pub Year	Region	Study Design	Study Population	Sample size	Prevalence of poor treatment outcome	Quality score
Desse et al. [11]	2015	Oromia	Retrospective	DM patients	421	9.8%	Medium
Gebremedhin et al. [30]	2021	Tigray	Retrospective	DM patients	589	15.5%	High
Mekonnen et al. [23]	2022	Amhara	Retrospective	DM patients	388	4.4%	High
Dagim et al. [29]	2019	Oromia	Institutional based cross-sectional study	DM patients	358	15.1%	Medium
Bacha et al. [24]	2022	Addis Ababa	Institutional based cross-sectional study	DM patients	270	14.7%	High
Taye et al. [20]	2021	Oromia	Retrospective	DM patients	236	12%	High
Tekeste et al. [25]	2021	Eastern Ethiopia	Institutional based cross-sectional study	DM patients	352	17.8%	High
Derse et al. [22]	2023	Addis Ababa	Institutional based cross-sectional study	DM patients	358	3.9%	High

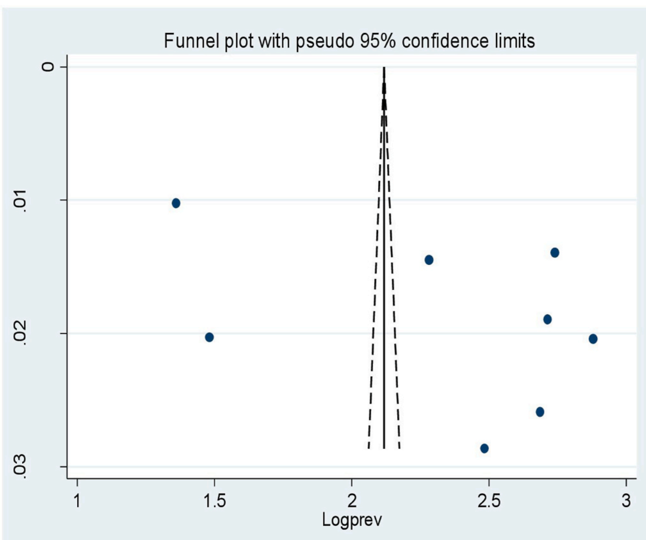

Fig. 2. Funnel plot assessed for publication bias in the review of poor treatment outcome and associated factors of hyperglycemic emergencies among diabetic patients in Ethiopia (N = 8).

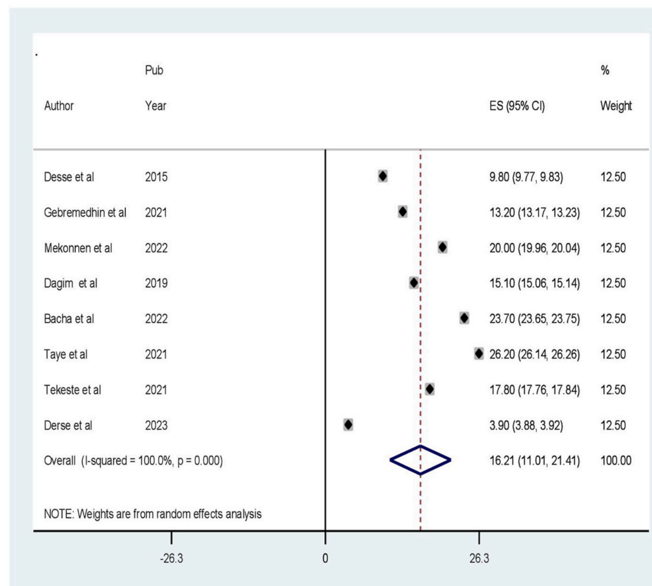

Fig. 3. Forest plot indicating pooled prevalence of poor treatment outcome hyperglycemic emergencies among diabetic patients in Ethiopia (N = 8).

diabetic patients. The pooled estimate of poor treatment outcome of hyperglycemic emergencies among diabetic patients in Ethiopia is found to be 16.21% (95% CI: 11.01, 21.41, $P < 0.001$), which is consistent with the finding of Nigeria 16% [31]. But the finding is lower than a studies conducted in Nigeria 34% [13] and Cameroon 21.7% [32]. The discrepancies may be due to setting variations in the clinical presentation of patients and efficient detection and management of hyperglycemic crises, precipitating factors, and complications. In contrast in is higher in studies done in South Africa 7.5% [14], Nigeria 4.8% [33], Colombia 2.3% [34] and Thailand 8.5% [35], in Colombia, China, and Taiwan, that reported poor treatment outcome ranging from 2.27 to 10.6% [36–38]. This disparity might be due to a delayed diagnosis of DM and then present for medical attention after developing diabetes complications. And also it might be due to the absence of inpatient management protocol, and insufficient laboratory monitoring during treatment to monitor patient response in the primary study settings due to the relatively high number of medical personnel deployed in the management of these patients. The other justification for the higher prevalence of poor treatment outcome in our review might be due to in developing countries like Ethiopia patients have less access to diabetes screening and preventive services, low health care services, and increased treatment gaps. Likewise, patients are unaware of their glycemic state and then present for medical attention after developing diabetes complications and worsening of the conditions.

The odds of poor treatment outcome from hyperglycemic crises were higher in patients with serum creatinine >1.2 mg/dl compared to those with serum creatinine ≤1.2 mg/dl. Similar finding is found from China and Taiwan [39,40]. Diabetes is recognized to negatively impact renal function, although the underlying pathophysiology is still unclear. It's uncertain if the damage is the result of end organ damage from atherosclerosis or the continuous hyperglycemia effect. There are theories that hyperglycemia might cause increment of oxidant levels, TGF-β, and NF-kappa B activation to rise, which can cause kidney damage and ultimately poor treatment outcome [41].

Patients with comorbidity had higher risk of poor treatment outcome from hyperglycemic crises as compared to those without comorbidity. The finding is similar with the study done in Jordan and United Kingdom [42,43]. By impacting numerous body systems, co-morbidities can weaken the body's natural defense mechanism against diseases, complicate the clinical course of disease, and raise the severity of the disease.

In this review patients who had sepsis were more likely to poor treatment outcome from hyperglycemic crises as compared to those who had no sepsis, which is consistent with the finding of China and United States [40,44]. This could be because sepsis is a potentially the cause for

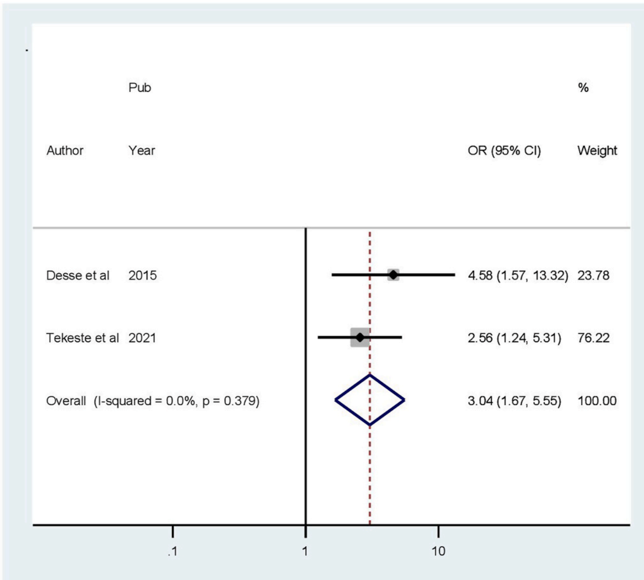

Fig. 4. Pooled association between serum creatinine >1.2 mg/dl and poor treatment outcome of hyperglycemic emergencies among diabetic patients in Ethiopia (N = 8).

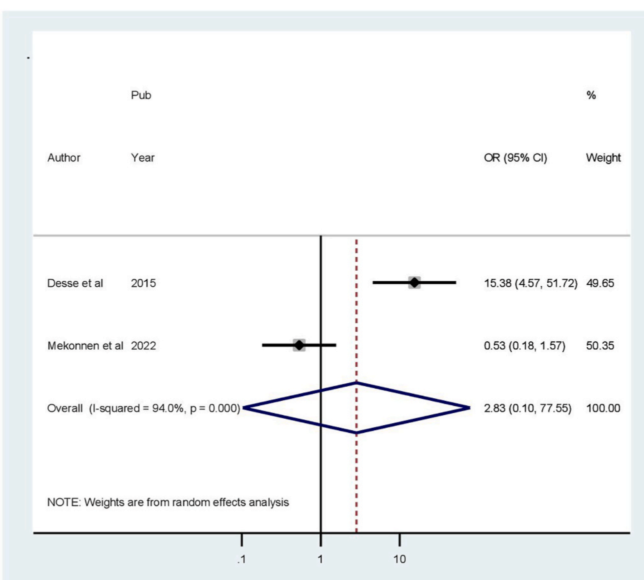

Fig. 5. Pooled association between comorbidity and poor treatment outcome of hyperglycemic emergencies among diabetic patients in Ethiopia (N = 8).

fatal organ failure brought on by an uncontrolled host reaction to an infection. Preclinical research shows that diabetes inhibits the adaptive immune system and affects a number of innate immune system components. Increased blood glucose levels and changes in the glycaemia-dependent immune response are present in both type 1 and type 2 diabetes, and these factors may have an impact on the pathophysiology and worse prognosis of sepsis in diabetic patients [45,46].

The likelihood of poor treatment outcome from hyperglycemic crises was higher in patients with stroke as compared to those without stroke. The result is consistent with the study done in Jordan, China and United States [42,44,47]. This is justified by diabetes is a well-established risk factor for stroke. It can result in pathologic alterations in blood vessels in different parts of the bodies and, if cerebral vessels are directly damaged, can induce stroke. Additionally, stroke patients with

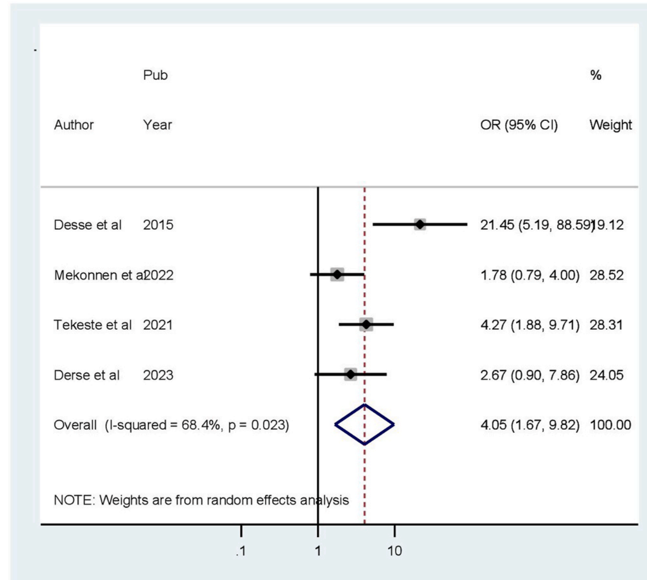

Fig. 6. Pooled association between sepsis and poor treatment outcome of hyperglycemic emergencies among diabetic patients in Ethiopia (N = 8).

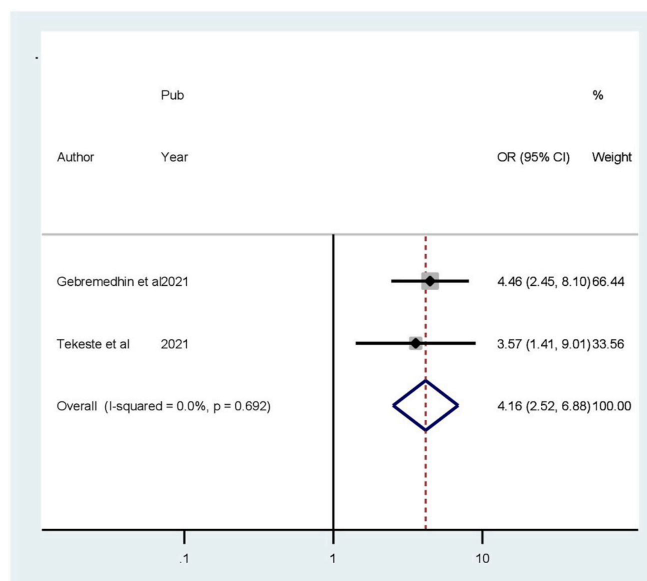

Fig. 7. Pooled association between stroke and poor treatment outcome of hyperglycemic emergencies among diabetic patients in Ethiopia (N = 8).

uncontrolled glucose levels had worse post-stroke outcomes and in turn leads to poor treatment outcome in such patients [48].

4.1. Limitations

Selection bias in the estimation of prevalence may be introduced as many of the studies included in the meta-analysis recruited participants from hospitals. Moreover, this meta-analysis represented only studies reported from some regions of Ethiopia, which could affect the estimated prevalence reported. In addition, the majority of the research that were chosen for the final analysis were limited to a few parts of Ethiopia, meaning that they do not accurately represent the remaining regions. Finally, only English language articles were reviewed, potentially overlooking valuable publications in other languages.

5. Conclusion

Poor treatment outcome from HGEs among diabetic patients was found to be high. Poor treatment outcome was predicted for those patients who had creatinine level >1.2 mg/dl, stroke, sepsis and comorbidity. To improve poor treatment outcome from hyperglycemic crises, we advise healthcare personnel to closely monitor and evaluate on patients who have the above identified predictors. Additionally, we advise including diabetes screening in health extension packaging initiatives and extending diabetes care services to basic healthcare facilities. Physicians should also detect and manage precipitants of HGEs and comorbidities early at initial patient presentation. Furthermore, improving the inpatient management protocol of hyperglycemic crisis and equipped advanced laboratory investigations is mandatory.

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Not applicable since the study is systematic review and meta-analysis.

Ethics approval and consent to participate

Ethical approval not applicable for this systematic review and meta-analysis study.

Informed consent not applicable.

Availability of data and materials

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

CRediT authorship contribution statement

Gashaw Melkie Bayeh: Data curation, Visualization, Review of final draft. **Yeshiwas Ayale Ferede:** Data curation, Visualization, Review of final draft. **Agerie Mengistie Zeleke:** Data curation, Visualization, Review of final draft.

Declaration of competing interest

We, the authors of this article declare that we have no any competing interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.metop.2024.100275.

Abbreviations

CI	Confidence interval
DM	Diabetes mellitus
DKA	Diabetic Keto-Acidosis
HHNS	Hyperglycemic Hyperosmolar Non-ketotic Syndrome
HGEs	Hyperglycemic Emergencies
POR	Pooled Odds Ratio

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