Systematic Review / Meta-analysis

# The magnitude of mortality and its determinants in Ethiopian adult intensive care units: A systematic review and meta-analysis

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ABSTRACT

*Introduction:* Despite mortality in intensive care units being a global burden, it is higher in low-resource countries, including Ethiopia. A sufficient number of evidence is not yet established regarding mortality in the intensive care unit and its determinants. This study intended to determine the prevalence of ICU mortality and its determinants in Ethiopia.
*Methods:* PubMed, Google Scholar, The Cochrane Library, HINARI, and African Journals Online (AJOL) databases were systematically explored for potentially eligible studies on mortality prevalence and determinants reported by studies done in Ethiopia. Using a Microsoft Excel spreadsheet, two reviewers independently screen, select, review, and extract data for further analysis using STATA/MP version 17. A meta-analysis using a random-effects model was performed to calculate the pooled prevalence and odds ratio with a 95% confidence interval. In addition, using study region and sample size, subgroup analysis was also performed.
*Results:* 9799 potential articles were found after removing duplicates and screening for eligibility, 14 were reviewed. Ethiopia's pooled national prevalence of adult intensive care unit mortality was 39.70% (95% CI: 33.66, 45.74). Mechanical ventilation, length of staying more than two weeks, GCS below 9, and acute respiratory distress syndrome were major predictors of mortality in intensive care units of Ethiopia.
*Conclusion:* Mortality in adult ICU is high in Ethiopia. We strongly recommend that all health care professionals and other stakeholders should act to decrease the high mortality among critically ill patients in Ethiopia.

## 1. Introduction

The intensive care unit (ICU) is a sophisticated, expensive, interdisciplinary hospital unit designed to monitor and treat patients with critical illnesses. Critically ill patients can be admitted to ICU from their homes or various corners of the hospital unit, including the emergency room, operation room, recovery room, and inpatient wards. Mechanical ventilation, invasive monitoring, vasopressor/inotrope medication, dialysis, and nutritional rehabilitation are among the medical interventions provided to critical patients to improve clinical outcomes [1–3].

Recently, higher admission rates to ICU, up to 54%, were reported despite admission rates lower as 1%, also shown in studies conducted worldwide [4–9]. Traumatic injury, respiratory failure, myocardial infarction, heart failure, sepsis and septic shock, renal failure, routine postoperative care, and chemical poisoning are among the plethora of reasons for ICU admission [10–24].

Even though medical care has significantly improved over the last century, mortality in intensive care units remains a global public health issue [9]. In addition to death in ICU, other metrics of intensive care outcome include morbidity and functional disability [25]. Despite a rise in admission rates, there has been a decline in the general incidence of intensive care unit mortality in affluent nations. On the other hand, mortality rates in underdeveloped countries continue to be significantly higher [1,9,26,27].

The mortality rate in critical care units across the world range from 9 to 61% [28]. In comparison to the rest of the globe, the ICU mortality rate in North America, Oceania, and Europe is comparatively low at 9.3%, 10.3%, and 18.7%, respectively; however, in South America and the Middle East, it is 21.7% and 26.2% respectively [9,29]. In Africa, the ICU mortality rate is high, ranging from 32.9 to 54%, compared to the other developed continents [6,30–32].

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Establishing ICUs in impoverished nations, including Ethiopia, is extremely difficult due to the limited resources. Ethiopia had 114 million people and 51 intensive care units with only 324 intensive care unit beds, resulting in a national ICU bed-to-population ratio of 0.3 per 100,000 people [33]. According to various studies conducted in Ethiopia, the mortality rate following ICU admission was high, ranging between 18.3 and 67.4% [11,34–46]. Among factors related to the resources of a hospital that contribute to the mortality of patients in ICU include training and skills of medical staff, nurse-to-patient ratio, infrastructure, and shortage of essential drugs and equipment [47]. Age, Duration of ICU stay, presence of comorbidities, complications at ICU, traumatic injury, sepsis, need for mechanical ventilation, need for vasopressors/inotrope, and low GCS score as potential factors affecting the survival of patients in ICU [34,35,40,41,46].

Multiple studies have reported the prevalence and factors associated with mortality in ICUs in Ethiopia; however, there is no systematic review and meta-analysis regarding ICU mortality and its determinants. The objective of this study was to gather all available national data about the prevalence of death in critical care units in Ethiopia and its determinants. First, combining these findings may assist in filling a research gap. Second, this study provides an overview of the intensive care outcome in Ethiopia. The findings of this study will aid policymakers and program planners in critical care in making decisions.

## 2. Methods

### 2.1. Study registration and reporting protocol

This systematic review and meta-analysis are registered on Researchregistry.com under the unique identification number (UIN): reviewregistry1364. This systematic review has been reported in line with the Preferred Reporting Item for Systematic Review and Meta-analysis (PRISMA) guideline [48] and Assessing the methodological quality of systematic reviews (AMSTAR 2) criteria [49].

### 2.2. Search strategies

Following the PRISMA guideline, studies were searched using PubMed, Google Scholar, The Cochrane Library, HINARI, and African Journals Online (AJOL) without language and publication type restrictions. Search terms used to access studies using PECO (population, exposure, context, outcome) strategy are the following: "prevalence," "incidence," "predictors," "mortality," "morbidity," "outcome," "survival," "intensive care unit," "ICU," "critical care unit," and "Ethiopia." In addition to search terms, the Boolean operators "AND" and "OR" were also used. After identifying the included articles, cross-references were examined to discover any additional relevant studies.

### 2.3. Inclusion/exclusion criteria

All selected studies fulfilled the following criteria: interventional and observational studies (cross-sectional, case-control, and cohort) that report the prevalence/incidence of mortality and factors contributing to mortality in ICU among adults (age≥ 16) patients in Ethiopia.

Excluded are studies that did not provide the outcome (mortality in ICU) and articles for which the full text was unavailable. Two attempts were made to contact the associated author for publications without full text to access the full-text articles. Case reports, case series, and systematic reviews were also omitted.

### 2.4. Outcome

The prevalence of ICU mortality in Ethiopia was the primary outcome of interest., expressed as percentage and frequency in articles. PECO: The study population was adult patients aged≥16 who were admitted to ICU and the occurrence of death during ICU stay.

### 2.5. Determinant factors for ICU mortality

Possible risk factors that affect mortality in ICU were screened and identified, including male gender, comorbidities, length of stay, mechanical ventilation, vasopressor support, low arterial oxygen saturation level (SpO2 < 90%), cardiac arrest in ICU, septic shock, ARDS, infection, trauma, GCS score below 9, requiring antibiotics in ICU, hyperthermia during admission to ICU, and aspiration during ICU stay. Nevertheless, to increase the accuracy of this meta-analysis, factors reported in at least two studies were considered for further analysis.

### 2.6. Data extraction and study quality assessment

Microsoft Excel 2019 was used to construct a data extraction checklist encompassing the first author, publication year, region, study type, sample size, prevalence/incidence of death, and reported mortality determinants. Studies were evaluated using the Joanna Briggs Institute Prevalence Critical Appraisal Tool for systematic reviews of prevalence studies [50]. Two independent reviewers evaluated each article that was selected for retrieval before inclusion in the review based on its methodological and other quality characteristics using the Newcastle-Ottawa appraisal Scale(NOS) based on a modified version of the Newcastle-Ottawa Scale for non-randomized studies. The tool is validated for observational studies, quick and easy to use. Studies will be evaluated and scored from 0 to 7 (7 indicates high quality). Studies with a score of ≥5 meet the adequate methodological quality, so they are included for further analysis [51,52]. Firstly, two independent reviewers (SB and HT) screened the title and abstracts against the inclusion criteria. Secondly, two reviewers conducted the full-text article's independent assessment in accordance with the inclusion and exclusion criteria. Lastly, the discrepancies raised were addressed by the senior researcher (FT), and all investigators reached a discussion for a common consensus. In order to avoid mistakes, two authors (AS and BC) extracted the data from the included studies.

### 2.7. Statistical analysis

STATA/MP version 17 (StataCorp, College Station, Texas 77845 USA) was used for further statistical analysis. The pooled prevalence with a 95% CI of adult ICU mortality in Ethiopia was determined using DerSimonian-Laird random-effects model. The $I^2$ statistic was used to assess study heterogeneity, and values of 75, 50, and 25% correspond to high, moderate, and low levels of heterogeneity [53]. The publication bias was investigated using a funnel plot as well as the Begg's and Egger's tests [54]. In addition, subgroup analyses were conducted based on sample sizes, study regions. and. study design The relationship between adult ICU mortality and the predictive factors was examined using odds ratios.

## 3. Results

### 3.1. Literature search and study quality assessment

As the selection and exclusion procedure shown in Fig. 1 with PRISMA flow diagram, a total of 9799 potentially eligible studies were identified from PubMed (n = 265), Cochrane Library (n = 12), Google Scholar (n = 8260), HINARI (n = 237), and AJOL (n = 1000) databases. After removing 9500 duplicates and 250 records excluded, 24 reports were sought for retrieval. Finally, based on the predetermined exclusion criteria (studies conducted in pediatrics, age below 16, case reports/case series, studies without full text, and conference abstracts), ten studies were excluded, then 14 studies were included for the final review and analysis.
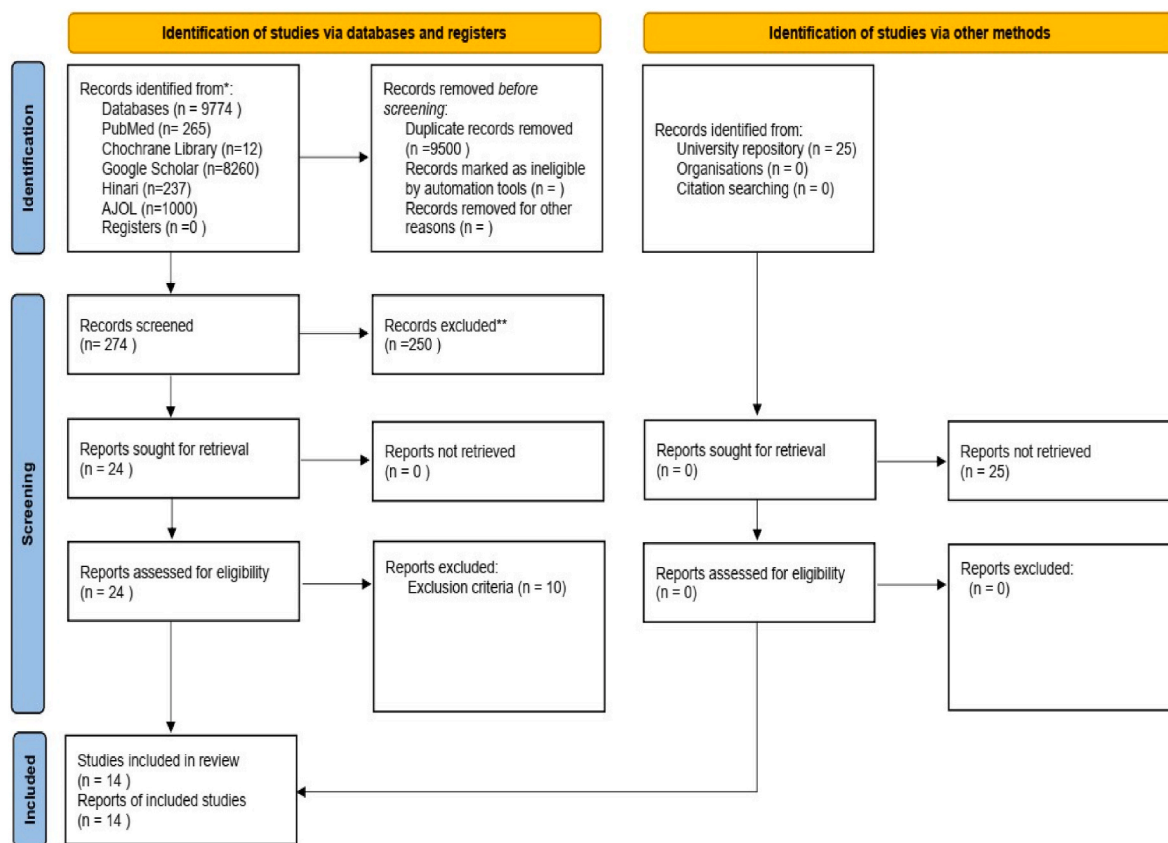
**Fig. 1.** PRISMA flow diagram showing screening and selection procedure of studies.

### 3.2. Study characteristics

We extracted and summarized information from the selected articles about the authors, publication year, study area, study region, number of events (mortality), sample size, and key findings (Table 1). Studies included were conducted in Ethiopia and published in journals that are indexed. Based on the region, three studies were conducted in Addis Ababa [34,38,40], three studies in Amhara [37,44,46], four studies in Oromia [11,36,42,45],.two studies in Southern Nations, Nationalities, and Peoples (SNNP) [35,41], and two studies in Tigray [39,43]. Seven studies were cross-sectional, four studies were cohort (retrospective and prospective), two studies were longitudinal, and one study was prospective observational. The sample size ranged from 69 to 2789, making the total sample size of all studies 8915.

### 3.3. Prevalence of mortality in adult ICU

In this systematic review and meta-analysis using a forest plot (Fig. 2), the pooled prevalence of ICU mortality estimated by a random-effects method was found to be 39.70% (95% CI: 33.66, 45.74).

### 3.4. Subgroup analysis

The subgroup analysis revealed that the region of SNNP had the highest prevalence of adult ICU mortality. (46.67%; 95% CI; 43.21, 50.14), followed by Amhara (45.18%; 95% CI; 23.81, 66.55) and Oromia (41.10%; 95% CI; 29.56, 52.64) regions (Table 2). Based on the sample size, mortality was higher in studies having a sample size <500 [41.65%, (95% CI; 30.85, 52.46)] compared to those having ≥ 500 sample size [36.20%, (95% CI; 29.97, 42.42)] (Table 2).

**Table 1**
Study characteristics.

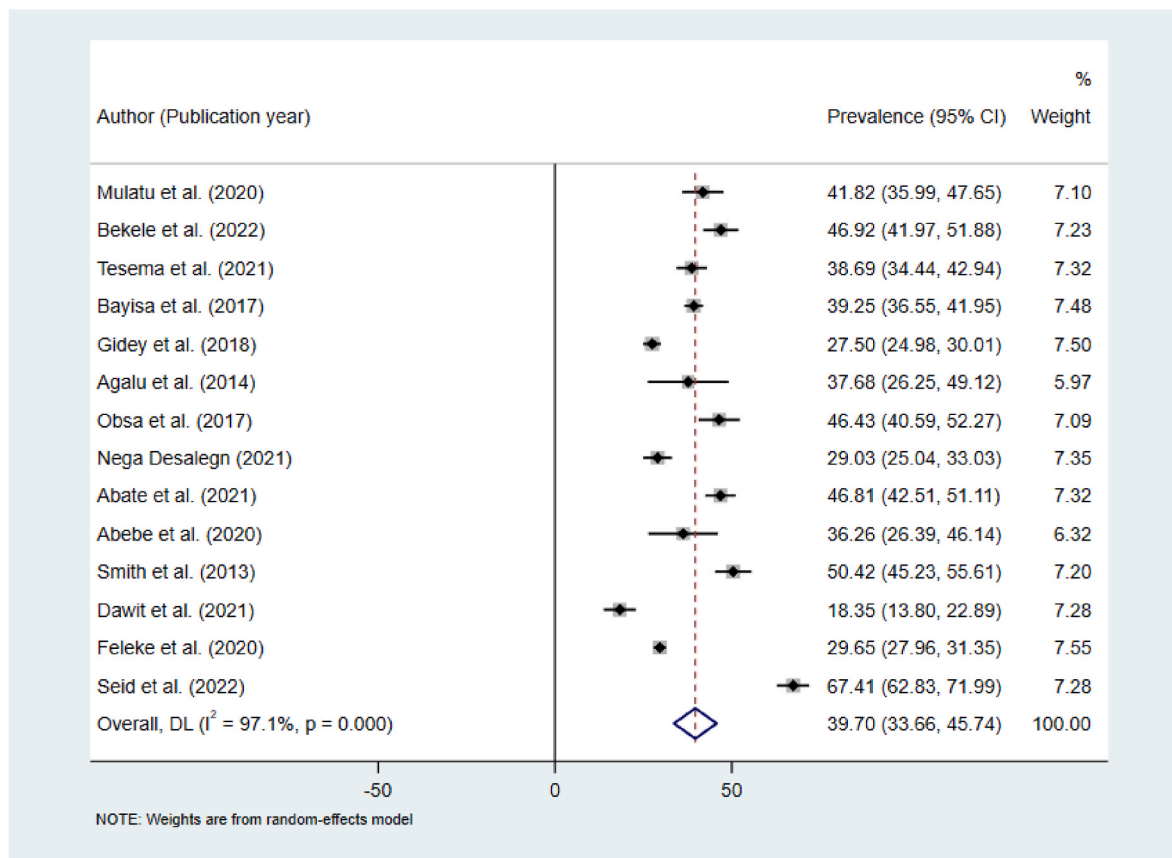| Author | Publication Year | Study region | Study design | Sample size | Event | Prevalence (%) |
|---|---|---|---|---|---|---|
| Mulatu et al. [34] | 2020 | Addis Ababa | Prospective observational | 275 | 115 | 41.81 |
| Bekele et al. [36] | 2022 | Oromia | Retrospective cohort | 390 | 183 | 46.92 |
| Tesema et al. [37] | 2021 | Amhara | Cross-sectional | 504 | 195 | 38.69 |
| Bayisa et al. [38] | 2017 | Addis Ababa | Cross-sectional | 1256 | 493 | 39.25 |
| Gidey et al. [39] | 2018 | Tigray | Cross-sectional | 1211 | 333 | 27.49 |
| Agalu et al. [11] | 2014 | Oromia | Longitudinal | 69 | 26 | 37.68 |
| Obsa et al. [41] | 2017 | SNNP | Cross-sectional | 280 | 130 | 46.42 |
| Desalegn [42] | 2021 | Oromia | Cross sectional | 496 | 144 | 29.03 |
| Abate et al. [35] | 2021 | SNNP | Retrospective cohort | 517 | 242 | 46.80 |
| Abebe et al. [40] | 2020 | Addis Ababa | Cross-sectional | 91 | 33 | 36.26 |
| Smith et al. [45] | 2013 | Oromia | Cross-sectional | 357 | 180 | 50.42 |
| Dawit et al. [43] | 2021 | Tigray | Longitudinal | 278 | 51 | 18.34 |
| Feleke et al. [44] | 2020 | Amhara | Prospective cohort | 2789 | 827 | 29.65 |
| Seid et al. [46] | 2022 | Amhara | Cross-sectional | 402 | 271 | 67.41 |

**Fig. 2.** The pooled prevalence of adult ICU mortality in Ethiopia shown by the forest plot.

**Table 2**
The prevalence of mortality in adult ICU by sample size and study region.

| Variables | Characteristics | Included studies | Sample size | Prevalence (95% CI) |
|---|---|---|---|---|
| Regions | Addis Ababa | 3 | 1622 | 39.51 (37.13, 41.88) |
| | Amhara | 3 | 3695 | 45.18 (23.81, 66.55) |
| | Oromia | 4 | 1312 | 41.10 (29.56, 52.64) |
| | Tigray | 2 | 1489 | 23.13 (14.17, 32.09) |
| | SNNP | 2 | 797 | 46.67 (43.21, 50.14) |
| Sample size | <500 | 9 | 3142 | 41.65 (30.85, 52.46) |
| | ≥500 | 5 | 5773 | 36.20 (29.97, 42.42) |
| Overall | | 14 | 8915 | 39.70 (33.66, 45.74) |

### 3.5. Publication bias evaluation

Despite the asymmetrical funnel plot (Fig. 3), the Egger's (p = 0.5563) and Begg's (p = 0.2736) tests did not show a significant publication bias.

### 3.6. Investigation of heterogeneity

A meta-regression analysis using the sample size and publication year was performed to observe the possible cause of differences between the studies. However, the result did not demonstrate significant heterogeneity (Table 3).

### 3.7. Determinant factors for mortality in adult ICU

#### 3.7.1. Mechanical ventilation

Four studies reported the association between mechanical ventilation and mortality in ICU. This meta-analysis revealed that patients who needed mechanical ventilation were nearly five times more likely to die in ICU than those who did not. The pooled odds ratio was 4.86 (95% CI: 3.43, 6.88). There was no significant heterogeneity, $I^2 = 10.4\%$, and publication bias in Begg's (p = 1.19) and Egger's (p= 0.08) tests (Fig. 4).

#### 3.7.2. Length of stay

Three studies examined the association between length of stay in the ICU and mortality. The pooled effect shows that the length of stay in ICU of more than two weeks has a 5.5 times higher risk of mortality than the length of stay of less than two weeks. The pooled odds ratio was 5.54 (95% CI: 3.00, 10.24), with no significant heterogeneity $I^2 = 3.3\%$ and publication bias (Begg's (p = 1.70) and Egger's (p = 0.26)) (Fig. 5).

#### 3.7.3. GCS level at admission

Two studies were involved in this meta-analysis to show the sscoi = ciation between GCS level at admission and ICU mortality. Using this meta-analysis's random effect model, patients with a GCS level below 9 have 4.72 more likely to die in ICU than those with a GCS score of 9 or above [OR = 4.72 (95% CI; 2.30, 9.69), $I^2 = 35.2\%$, p = 0.214] (Fig. 6).

#### 3.7.4. Oxygen saturation level at admission

Two studies were involved in this meta-analysis to show the association between arterial oxygen saturation levels at admission and ICU mortality. The included studies reported that a low level of arterial oxygen saturation ($SpO_2 < 90\%$) upon admission to ICU is significantly associated with mortality in ICU. However, this meta-analysis using random-effect model implied that having $SpO_2 < 90\%$ was not
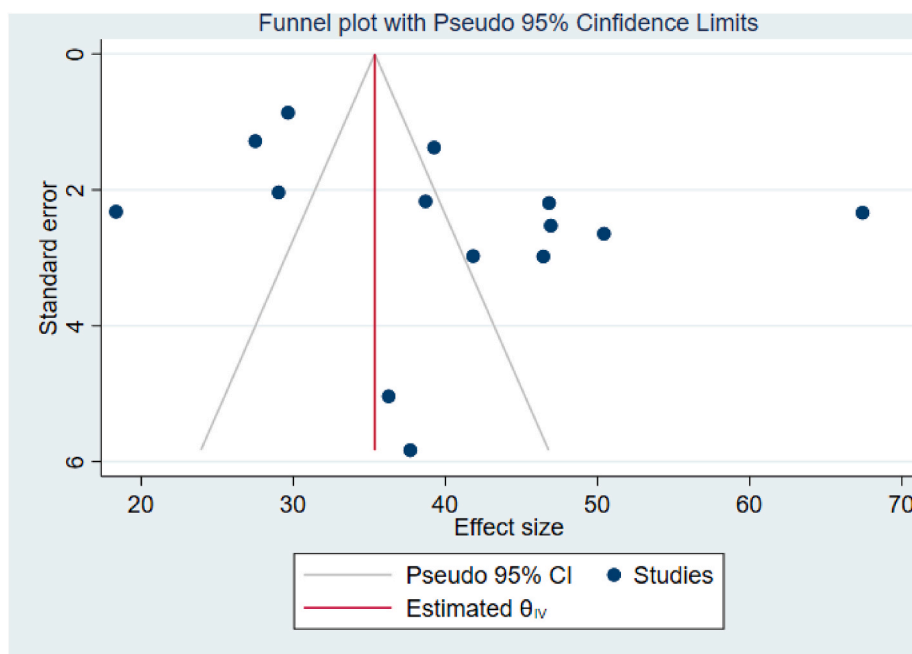
**Fig. 3.** Illustration of the distribution of 14 studies using a funnel plot.

**Table 3**

Meta-regression of adult ICU mortality with publication year and sample size to detect heterogenicity.

| Heterogenicity source | Coefficients | Standard error | p-value |
|---|---|---|---|
| Publication year | .0049437 - | .0047838 | 1.03 |
| Sample size | .0700934 - | 1.22054 | 0.06 |

significantly associated with mortality in ICU [OR = 0.65 (95% CI; 0.06, 6.52), $I^2$ = 86.2%, p = 0.007] (Fig. 7).

### 3.7.5. ARDS

Meta-analysis of two studies using the random effect model showed that among the reasons for ICU, patients diagnosed with ARDS have a 21.05 times greater risk of dying in ICU than their counterparts. The pooled OR = 21.05 (95% CI; 5.70, 77.77), $I^2$ = 34.4 p = 0.217 (Fig. 8).

### 3.8. Sensitivity analysis

A sensitivity analysis using the random effect model showed that a single study did not alter ICU mortality prevalence (Fig. 9).

### 4. Discussion

This systematic review and meta-analysis offered a comprehensive synthesis of evidence about mortality in adult ICU and the main contributing factors in Ethiopia. According to the results of our study, 39.70% of adults in Ethiopian ICUs died. Our study result was comparable with study findings of Tanzania [7], Uganda [30], Nigeria [32], and Pakistan [55]. However, our findings were higher than reports from the United States of America, Ireland, Denmark, Scotland, China, and Thailand [9,29,56–60]. This notable disparity could be attributable to differences in the availability of resources in the ICU, including
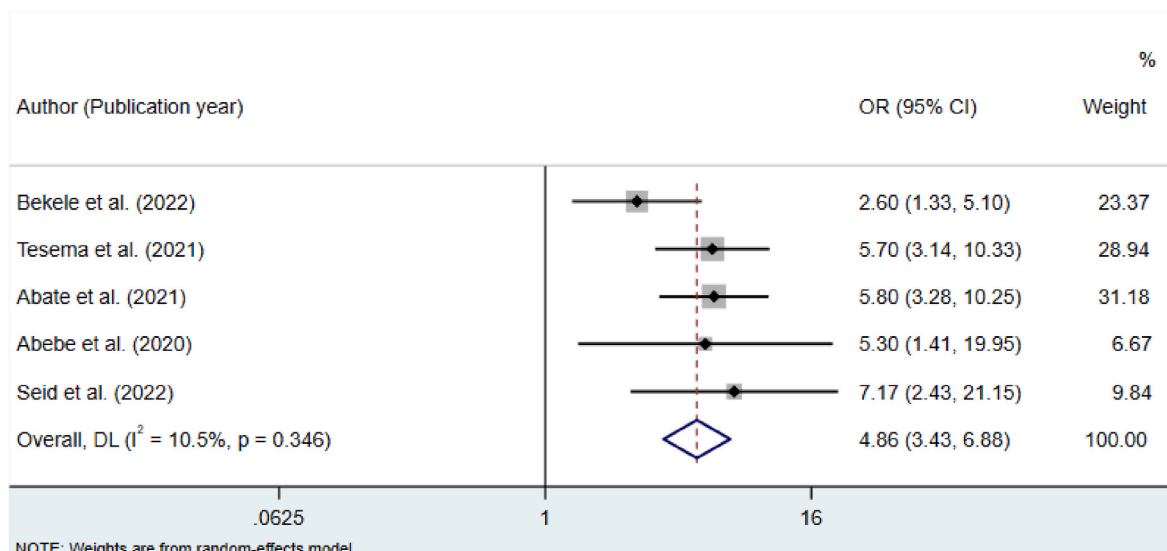


**Fig. 4.** The relationship between mechanical ventilation and ICU mortality (estimated with the pooled odds ratio).
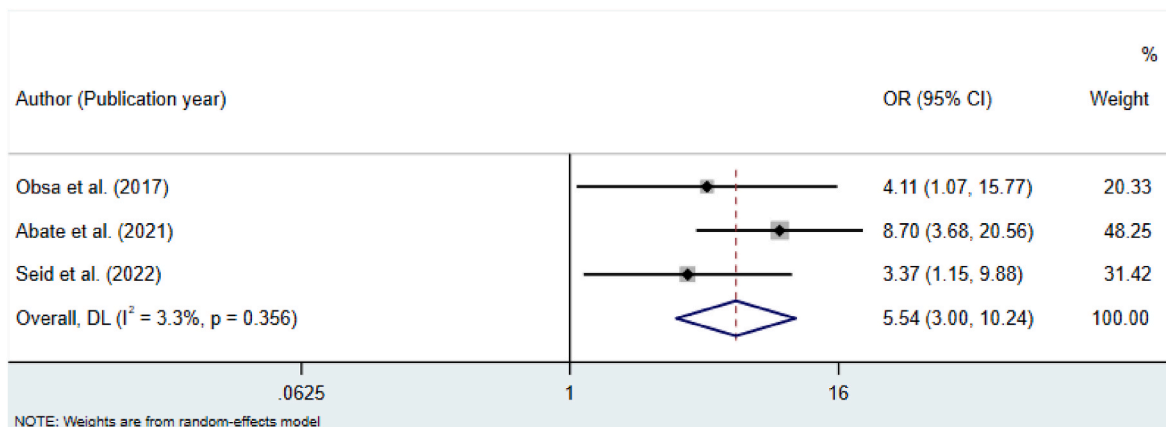
**Fig. 5.** The relationship between the length of stay of more than two weeks and ICU mortality (estimated with the pooled odds ratio).
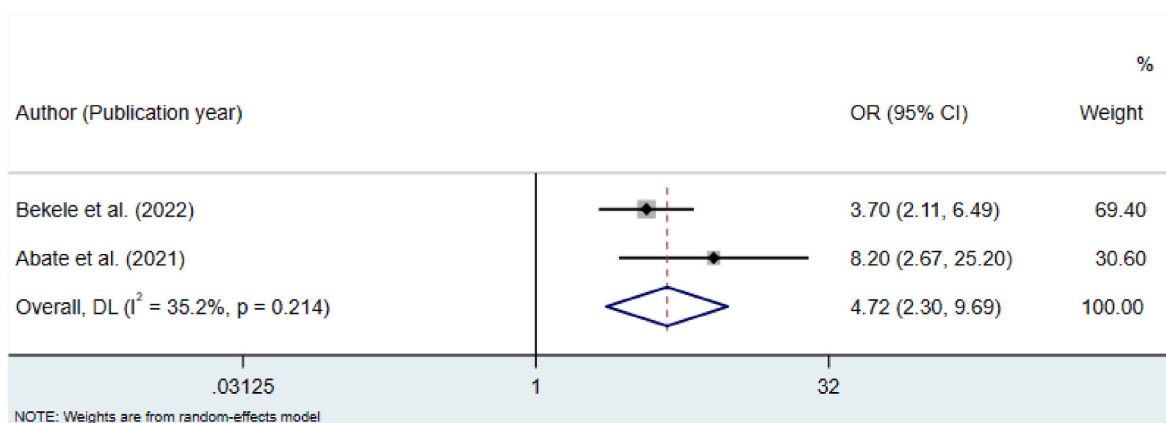


**Fig. 6.** The relationship between a GCS score below 9 and ICU mortality (estimated with the pooled odds ratio).
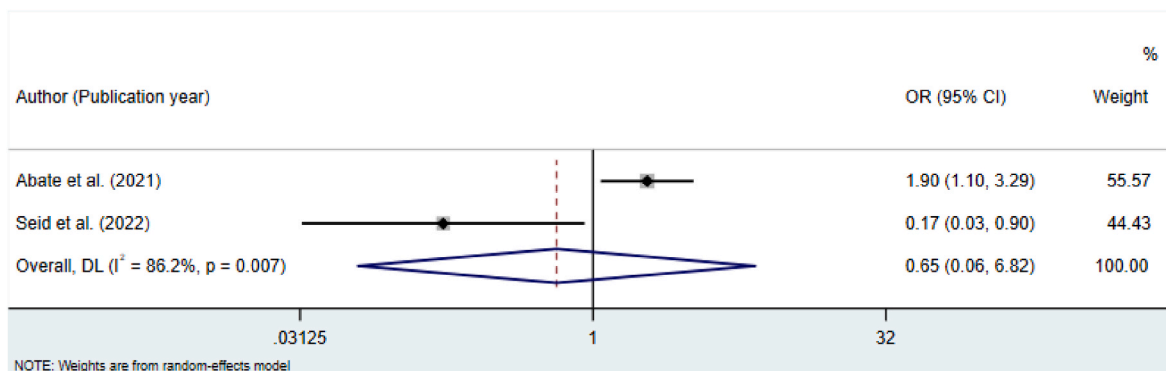


**Fig. 7.** The relationship between SpO2 below 90% and ICU mortality (estimated with the pooled odds ratio).

medications and medical equipment [61]. On the other hand, the result of this study is lower than studies conducted in Burkina Faso (60%) [62] and the National Hospital of Abuja, Nigeria (68.4%) [63]. The discrepancy might contribute to methodological aspects, including study design and patient population.

The SNNP region had the greatest prevalence of mortality in adult ICU (46.67%), whereas Tigray(23.13%) had the lowest, according to the subgroup study. The possible reason might be that in the SNNP region, there is a high prevalence of trauma related to motor vehicle accidents [64]. Additionally, the studies included in the SNNP region are multi-centered compared with other regions.

We also sought the need for mechanical ventilation in the ICU to

significantly predicted mortality in the adult ICU. Requiring mechanical ventilation in ICU significantly increased the mortality risk. Mechanically ventilated patients had a mortality risk of about five times greater than non-mechanically ventilated patients. Results in Brazil [65] and Kenya [7] support this finding. The possible reason for this link could be that mechanical ventilation is instituted for patients who have respiratory failure, can not protect their airways, and have unstable hemodynamics. In addition, critically ill patients requiring a mechanical ventilator are at a greater risk of developing ventilator-associated pneumonia and other hospital-acquired infections, further decreasing survival [36,40,66,67].

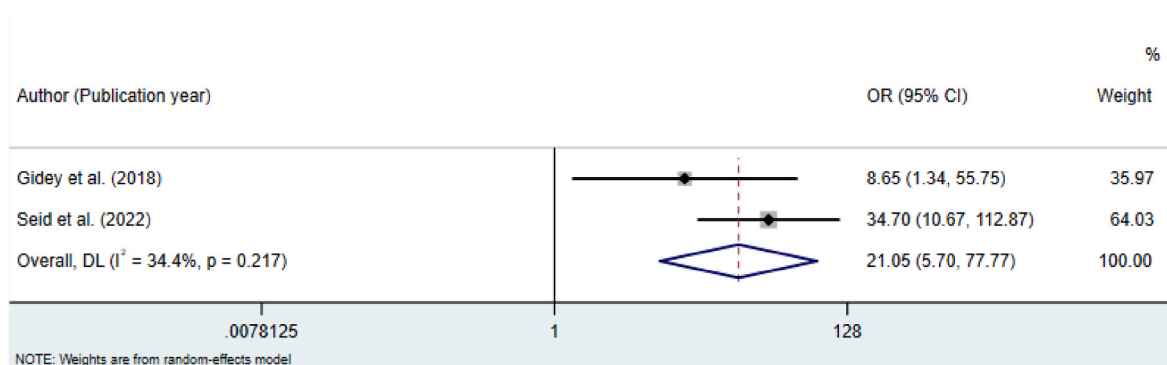Our systematic review and meta-analysis findings revealed that

**Fig. 8.** The relationship between ARDS and ICU mortality (estimated with the pooled odds ratio).
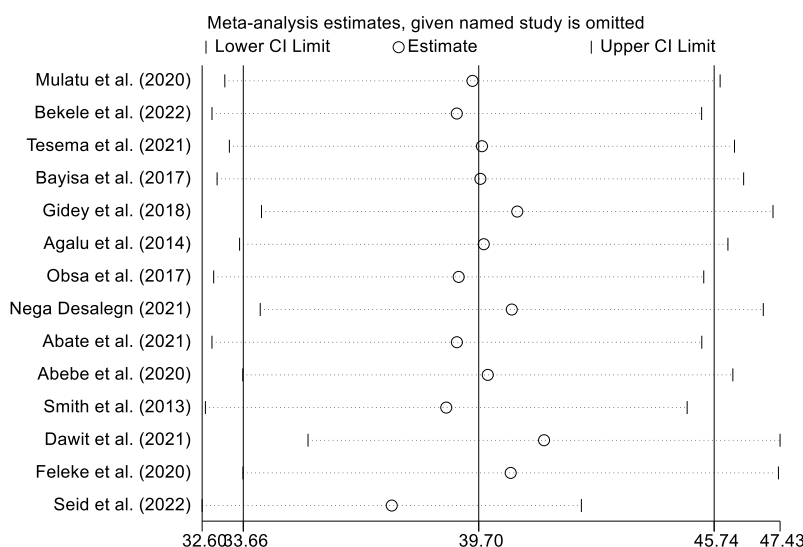


**Fig. 9.** Result of sensitivity analysis of 14 studies.

patients who were admitted to ICU and had a more extended stay than two weeks had a 5.54 times higher risk of ICU mortality than other patients who stayed less than two weeks in the ICU. This result was consistent with a review by Awad et al. [68]. The link between staying in the ICU for more than two weeks and death in the ICU could be due to the risk of developing adverse events, like arrhythmias, deep vein thrombosis, and infections, which all increase the risk of mortality in the ICU [22,69,70].

In addition, we looked for ARDS and GCS scores below nine, which strongly predict mortality in the ICU but not SpO2 below 90%. Our meta-analysis found that patients admitted to ICU with a GCS level below nine have a 4.72 times greater risk of dying in ICU than their counterparts, which is in line with a study done in Denmark [71]. This could be due to patients with low GCS scores who might have prior blood loss and need mechanical ventilation in the ICU [72]. Patients admitted to ICU with an ARDS diagnosis have a greater risk of mortality when compared to non-ARDS patients. The high mortality among patients with ARDS can be explained by their exposure to a prolonged duration on a mechanical ventilator that might lead to systemic inflammatory response syndrome (SIRS), severe sepsis, or septic shock [73,74]. Our study's odds of death for patients with ARDS are very high (22.06); this might be due to studies including Covid-19 positive patients [46].

This systematic review and meta-analysis will be used as input for policymakers, governmental organizations, and non-governmental organizations working in critical care to better understand ICU mortality and quality of care. In addition, this study can be used as a standpoint for further research in Ethiopia's intensive care domain. Although this study provided valued evidence of ICU mortality and its determinants, some limitations must be mentioned. To begin with, most of the study designs included in the analysis are cross-sectional, which can not demonstrate a causal relationship between adult ICU mortality and predictors. Furthermore, the studies included in the analysis are conducted in only five regions of Ethiopia, which might affect the generalizability to the whole country of Ethiopia. In addition, this meta-analysis did not use predictive scores for critical care patients as the Acute Physiology and Chronic Health Evaluation (APACHE), SOFA (The Sequential Organ Failure Assessment Score), or MODS (The Multiple Organ Dysfunction Score). Because the included studies were heterogeneous, further randomized and non-randomized studies should be conducted for a specific group of patients admitted to the ICU to determine the independent risk factors of mortality.

## 5. Conclusion

Overall, adult ICU mortality is high, putting a significant health care burden in Ethiopia, which needs collaboration between all stakeholders to improve critically ill patients' outcomes. The demand for mechanical

ventilation, prolonged stay in ICU for more than two weeks, GCS below nine, and ARDS were major predictors in adult ICU. Furthermore, clinicians working in the intensive care unit of Ethiopia should give attention to patients needing mechanical ventilators, who stay more than two weeks in the intensive care unit, have a low Glasgow coma scale, and have a diagnosis of acute respiratory distress syndrome.

## Please state any conflicts of interest

None.

## Please state any sources of funding for your research

We did not receive funding from any source.

## Ethical approval

Because it is a systematic review and meta-analysis, ethical approval is not applicable.

## Consent

Not applicable.

## Author contribution

A.S. Endeshaw and BC Gete: involved in developing the protocol and study design, study selection, data extraction, statistical analysis, and editing of the final manuscript draft. F.T.: involved in quality assessment, statistical analysis, and manuscript revision. S.B. Ayalew and H.T. Bayu: study selection and extraction. All authors read and approved the final draft of the manuscript.

## Registration of research studies

Name of the registry: researchregistry.com
Unique Identifying number or registration ID: reviewregistry1364
Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/browse -the-registry

## Guarantor

Amanuel Sisay Endeshaw: Corresponding author.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi. org/10.1016/j.amsu.2022.104810.

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## Abbreviation and acronyms

*CI:* Confidence Interval
*OR:* Odds Ratio
*ICU:* Intensive Care Unit
*SpO2:* arterial oxygen saturation
*GCS:* Glasgow Coma Scale
*ARDS:* Acute Respiratory Syndrome