Prevalence of Anemia Among COVID-19 Patients in Ethiopia: Systematic Review and Meta-Analysis

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Systematic Review

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Abstract

Background: Coronavirus disease-2019 is caused by the severe acute respiratory syndrome coronavirus-2 virus. Impacting various many systems in the human body including the hematological system. Consequently, anemia has become a significant public health concern in developing countries, such as Ethiopia.

Objective: This systematic review and meta-analysis aim to determine the overall prevalence of anemia among COVID-19 patients in Ethiopia.

Methods: Following PRISMA guidelines, literature search was conducted in PubMed/MEDLINE, Cochrane Library, Google Scholar, HINARI, and the Ethiopian Journal of Health Development for articles published before 2024, Manual searches were also performed to identify relevant studies. Authors independently selected studies, extracted data, and assessed study quality. The I^2 test statistics was used to assess heterogeneity among studies and overall prevalence was calculated using the random-effects restrict maximum likelihood model.

Results: Out of 590 obtained studies, 8 articles were included in the meta-analysis. The pooled prevalence of anemia among COVID-19 patients in Ethiopia was 26.09% (95% CI 16-36%). The prevalence of anemia in Addis Ababa and Amhara was 27.13% (95%CI: 14.59%-39.66%) and 23.41% (95%CI: 3.46%-43.36%) respectively.

Conclusions: This study indicates that anemia is a moderate public health issue among COVID-19 patients in Ethiopia. Therefore, preventive measures and control strategies for of anemia among COVID-19 patients in Ethiopia are crucial.

Introduction

Coronavirus disease 2019 (COVID-19) is a viral infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 has resulted 6 million deaths worldwide. The global the economic burden of COVID-19 was estimated to be between US $77 billion and US $2.7 trillion in 2019. It was first discovered in Wuhan, Hubei Province, China, following the initial cases of this primary respiratory viral illness. World Health Organization declared COVID-19 a global pandemic on March 11, 2020 (1, 2).

COVID-19 infection begins as a respiratory tract infection. It is considered a systemic disease that significantly impacts the hematopoietic system over time, leading to various hematological abnormalities (3, 4). Anemia is now recognized as an independent prognostic risk factor for COVID-19 and hemoglobin level can be used in laboratory diagnosis for risk stratification in patients care(5).

Anemia is a significant worldwide public health issue that impacts both developed and developing countries. Globally, it affects approximately 1.92 billion (24.3%) of the world 's population across all age

groups (6). Among patients with laboratory-confirmed COVID-19, the global prevalence of anemia was 61% (7).In Ethiopia COVID 19 has caused 7, 574 death (8). However there is limited data on the prevalence of anemia among COVID-19 patients in Ethiopia. Therefore, this review aims to demonstrate the national prevalence of anemia among COVID-19 patients.

Method

Search strategy

This review was conducted following the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (9). A literature search was performed on international scientific research databases such as Google Scholar, PubMed/MEDLINE, Cochrane Library, and the Ethiopian Journal of Health Development for studies published before 2024. The reference lists of published articles were also searched to identify relevant unpublished studies. The search utilized a combination of keywords and Medical Subject Headings (MeSH) terms including "Anemia" or "Hemoglobin", or "Hematocrit" "Hematological profile", or Hematologic abnormality" and "COVID-19", or SARS-CoV-2," and "Ethiopia". This systematic review and meta-analysis have been registered with PROSPERO under the number CRD42024508873.

Selection criteria and exclusion criteria

All types of population-based studies conducted in Ethiopia that reported the prevalence of anemia among COVID-19 patients in the country and were published in peer reviewed journals until 2022were included in this review. The study population consisted of Ethiopian covid-19 patients. Studies that only reported results as mean, median and interquartile range were excluded, as wells as studies based on secondary data and poster representation such as review articles, conference abstracts, case reports, and editorials.

Data extraction and quality assessment

The systematic review process involved importing articles to Endnote 20, screening titles and abstracts, appraising full texts, resolving discrepancies through discussion and consensus, summarizing data in an Excel spreadsheet, and assessing study quality using JBI critical appraisal tools. Study characteristics such as first author name, publication year, study year, setting, sample size, and number of COVID-19 patients with anemia were extracted. Descriptive statistics were used for data analysis, with any discrepancies resolved through author discussion. The results were presented in tables and figures for clear presentation. This review aims to provide a comprehensive summary of anemia prevalence in COVID-19 patients and may guide future research and clinical practice in this area.

Outcome of interest

The primary outcome of interest is the pooled prevalence of anemia according to the WHO definition hemoglobin value of less than 12g/dl for females and a hemoglobin value of less than 13 g/dl for males

(10).
Statistical analysis and synthesis

Overall, the study methodology involved presenting results in percentages with 95% confidence intervals, using narrative synthesis for included studies. A summary table was created to outline the characteristics of the studies, and a meta-analysis was conducted using a random-effects restricted maximum likelihood model in STATA version 17. Heterogeneity among studies was assessed using I^2 statistics, and publication bias was qualitatively analyzed through Funnel plots, Begg's, and Egger's tests. Subgroup analyses were also conducted to identify potential sources of heterogeneity.

Results

Identified studies

The literature search retrieved a total of 598 articles. Of these, eight were excluded due to duplication. From the remaining 590 articles 582 were excluded because they did not relate to the aim of this meta-analysis, and did not meet eligibility criteria. Eight articles were included in this meta-analysis (Fig. 1).

Description of included studies

The studies included in the meta-analysis varied in their design and location, with most of them conducted in Addis Ababa and two in the Amhara region. The studies were published between 2020 and 2024, and consisted of a mix of retrospective and prospective cohort studies, as well as cross-sectional studies. In total, 1877 COVID-19 patients were included in the meta-analysis. (Table 1).

Table: -1 Characteristics of included studies in systematic review and meta-analysis

Author name	Study year	Study Design	Sample size	Study area	Anemia	Prevalence (%)
Atinaf A *et al*, 2022(11)	2020	Prospective Cohort	136	Amhara	18	13.24
Araya S *et al*, 2021(12)	2020	Prospective cross-sectional	334	Addis Ababa	83	24.9
Alemayehu M *et al*, 2023(13)	2022	Retrospective cross-sectional	253	Amhara	85	33.6
Gize A *et al*, 2023(14)	2021	Comparative cross-sectional	319	Addis Ababa	135	42.3
Tufa A *et al*, 2022(15)	2022	Retrospective cohort	126	Addis Ababa	47	37.3
Tadesse Z et al, 2022(16)	2021	Retrospective cross-sectional	240	Addis Ababa	37	14.42
Yeshidenber A *et al*, 2022(17)	2021	Prospective cohort	40	Addis Ababa	17	42.5
Leulseged T *et al*, 2021(18)	2020	Retrospective cohort	429	Addis Ababa	23	5.36

Risk of bias and heterogeneity

According to the JBI critical appraisal tools, each study was evaluated for risk of bias and quality using ten different criteria. These criteria included case definition, method of data collection, non-response bias, representation, sampling, reliability and validity of study tools, prevalence period, numerator and denominator, random selection, and data collection methods. The risk of bias assessment showed that four studies had low risk, two studies had moderate risk, and two studies had high risk of bias. Furthermore, the included studies displayed high heterogeneity based on the I2 test (96.93%), which necessitated the use of a random-effects model (Supplementary file 1: Fig. 2).

However, we used a funnel plot to check for publication bias. It did not reveal any clear publication bias. Egger's regression and Begg test p-values were 0.02 and 0.38, respectively, indicating a lack of publication bias. In addition, the funnel plot showed no signs of publishing bias or asymmetry (Fig. 2). To reduce heterogeneity, subgroup analysis was conducted based on the study region (supplementary file 1: Fig. 1).

Prevalence of anemia

The prevalence of anemia in Ethiopia varies with rates of 5.63% among 429 COVID-19 patients in Addis Ababa to 42.5% among 40 COVID-19 patients in Addis Ababa. The overall prevalence of anemia from a meta-analysis of 8 studies, using the random-effects restricted maximum likelihood model was found to be 26.09% (95% CI: 16.15–36.03%) among COVID-19 patients in Ethiopia (Figure. 3).

Subgroup analysis was conducted by stratifying the data based on region. Prevalence of anemia among COVID-19 patients in Addis Ababa, and Amhara, was found to be 27.13% (95%CI: 14.59%-39.66%) and 23.41% (95%CI: 3.46%-43.36%) respectively. (see supplementary file: 1 Figure-1)

Discussion

The prevalence of anemia ranged from 5.63−42.5%. The highest prevalence of anemia was reported in Addis Ababa, Ethiopia in 2021 (17). The lowest prevalence was reported in Addis Ababa, Ethiopia in 2020 (18). In this study, we aimed to estimate the overall prevalence of anemia among COVID-19 patients in Ethiopia by reviewing available studies. The overall prevalence of anemia was found to be26.03%, which is similar to a study conducted Kenya where the prevalence was 25% (19). According to the WHO classification anemia is considered mild, moderate, or severe when its prevalence exceeds 5%, 20%, or 40%, respectively (20).

A scientific explanation for anemia among COVID-19 patients is that SARS-CoV-2 directly infects erythroid precursor cells, impairs hemoglobin homeostasis, and worsens the severity of COVID-19. This leads to impaired porphyrin metabolism and changes in the expression of key enzymes involved in iron and hemoglobin metabolism. And also SARS-CoV-2 inhibits heme metabolism and induces hemoglobin denaturation during erythrocyte development (21). SARS-CoV-2 interacts with protoporphyrin IX through spike protein 1 (SP1) causing the dissociation of iron from porphyrin. The interaction between the beta chains of hemoglobin, open reading frame 8, and the surface glycoproteins of the virus leads to a decline in hemoglobin levels during SARS-CoV-2 infection (22, 23). Another contributing factor toa anemia during SARS-CoV-2 infection is the presence of ACE 2 receptors in kidney cells such as podocytes and proximal tubular epithelial cells, which reduces erythropoietin synthesis (24). This results in a decrease in hemoglobin levels during SARS-CoV-2 infection and exacerbates COVID-19 disease(25, 26, 27).

Furthermore, the presence of SARS-CoV-2 such as transmembrane serine protease 2 (TMPRSS2), CD147, and CD26 in erythroid progenitor cells in bone marrow makes then a primary target for SARS-CoV-2 infection. This can result in cell lysis and the elimination of immature red blood cells by phagocytic cells (28, 29). The presence of viral receptors in these cells can lead to low hemoglobin levels in COVID-19 patients experiencing severe clinical manifestations of the disease (30).

In subgroup analysis based on the study area, the prevalence of anemia is higher Addis Ababa compared to the Amhara region. This difference may be attributes to the higher burden of non-communicable diseases in Addis Ababa (31). The presence of non-communicable diseases can exacerbate the severity of COVID-19 infection including anemia (32). Furthermore, the possible factors contributing to the difference in prevalence could include variations in sample size, geography, and research setting among the included studies.

Conclusion

This systematic review and meta-analysis reveal that the prevalence of anemia among COVID-19 patients in Ethiopia is moderate according to the World Health Organization classification of anemia. Addis Ababa shows higher prevalence of anemia compared to the Amhara region. Anemia was identified as major public health issue for all populations included in this study. Therefore, policymakers, healthcare professionals, and researchers should develop appropriate intervention to address this problem. Further research is needed to identify potential risk factors for the high prevalence of anemia.

Abbreviations

PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analysis; **WHO**: World Health Organization: **SARS-CoV-2**: Severe acute respiratory syndrome 2, **COVID-19**: Corona virus 2019, **ACE** 2: angiotensin-converting enzyme-2, **TMPRSS2**: Transmembrane serine protease 2, **CD**: Cluster of Differentiation.

Declarations

Availability of data and materials

All data supporting this document are found in the manuscript and supplementary files.

Authors' contributions

Abateneh Melkamu, and Yalew Muche: Design the systematic review, literature search and writing and editing manuscript.

Adane Adugna, and Aytenew Atnaf: Extract data equally, and edited manuscript.

Melaku Laikemariam, and Gashaw Azanaw Amare: Assess article quality assessment, and edited manuscript.

Zewudu Mulatie, Befikad Mandefro, Zigale Hibstu and Abebe Yensew: Editing the manuscript. All authors read and approved the final manuscript.

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Ethical Approval and Consent to Participate

Since the study did not use primary data, ethical approval is not applicable.

Consent for Publication

Not applicable.

Conflict of interests

The authors declare that there is no financial and non-financial conflict of interest.

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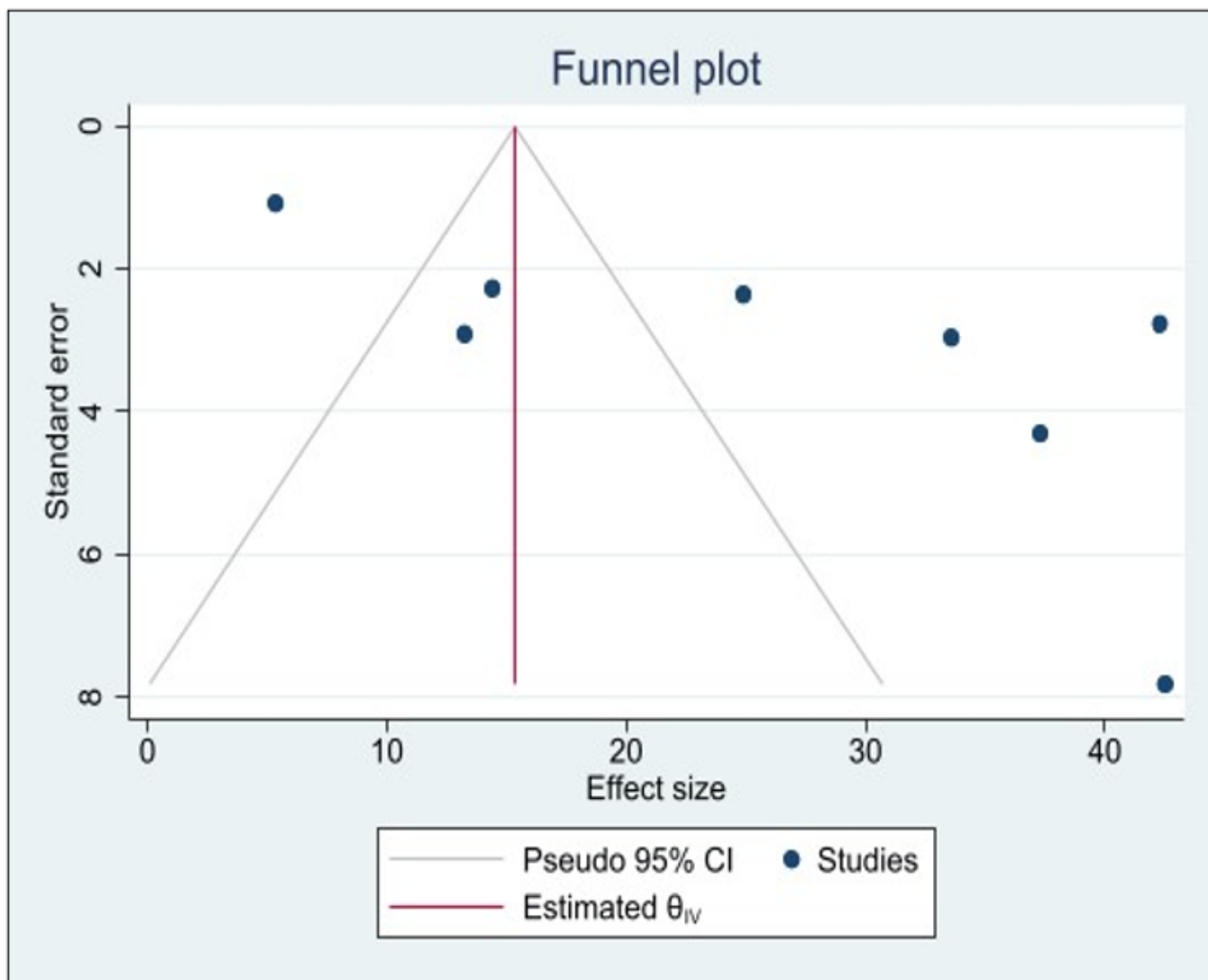
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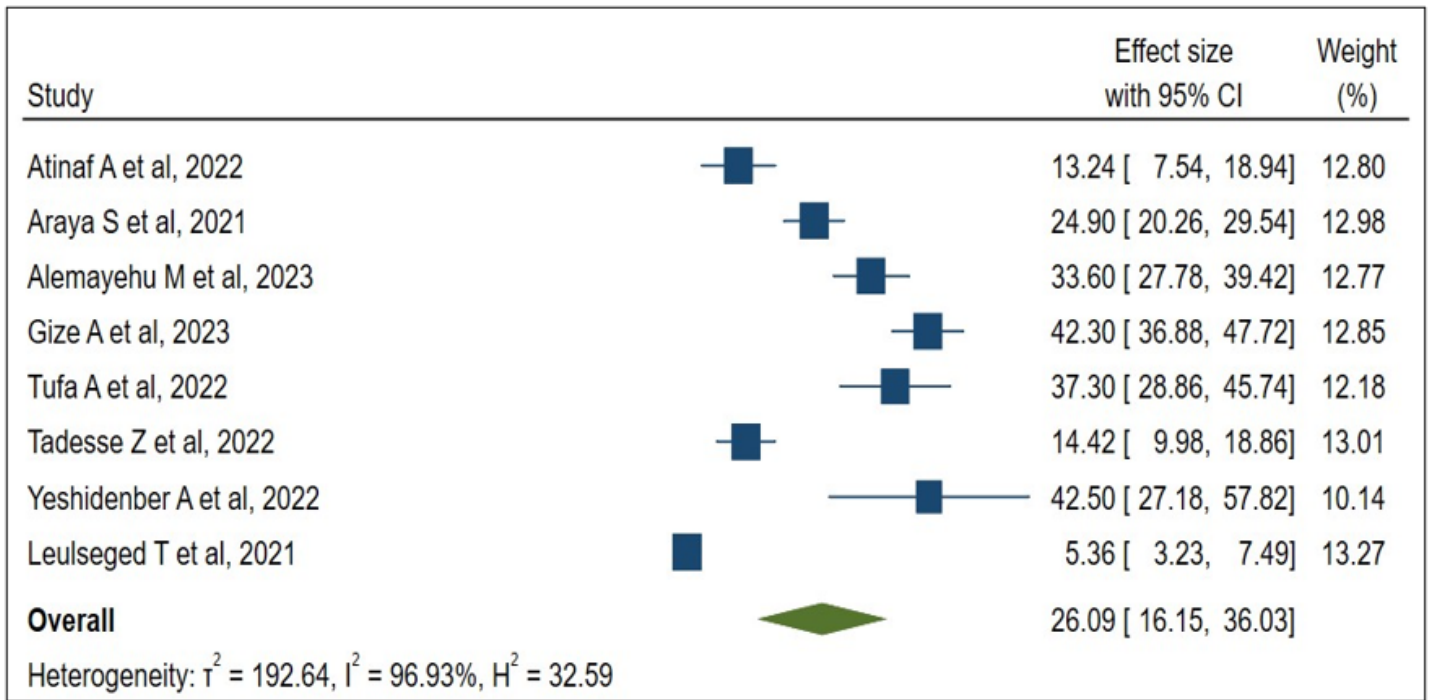Supplementary File 1 is not available with this version

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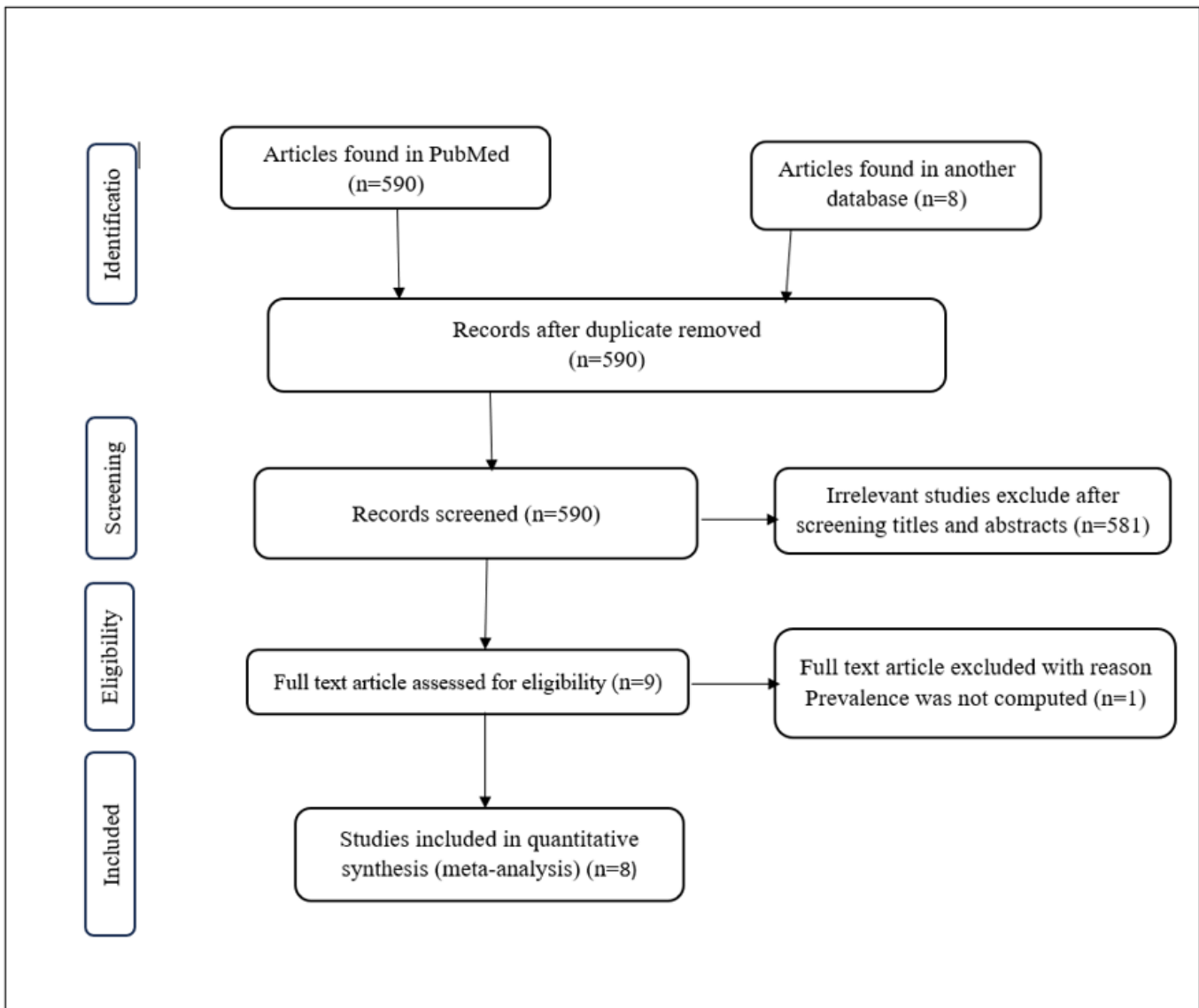
Figure 1

Flow chart for selection of studies for systematic review and meta-analysis on the prevalence of anemia among COVID-19 patients in Ethiopia

Figure 2

Publication bias analysis of the included study on the prevalence of anemia among COVID-19 patients in Ethiopia.

Figure 3

Forest plot of 8 studies on the prevalence of anemia among COVID-19 patients in Ethiopia.