

Prevalence of anemia and its associated factors among children in Ethiopia: a protocol for systematic review and meta-analysis

Zegeye Abebe^{1,*}, Wubet Worku Takele², Degefaye Zelalem Anlay²,
Daniale Tekelia Ekubagewargies², Zegeye Getaneh³, Molla Abebe⁴,
Mulugeta Melku^{3,*}

¹ Department of Human Nutrition, Institute of Public Health, College of Medicine and Health Sciences, University of Gondar, Ethiopia

² School of Nursing, College of Medicine and Health Sciences, University of Gondar, Ethiopia

³ Department of Hematology and Immunohematology, School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar, Ethiopia

⁴ Department of Clinical Chemistry, School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar, Ethiopia

*Contributed equally to this protocol for sytematic review and meta-analysis

ARTICLE INFO

Corresponding author:

Mulugeta Melku
Department of Hematology
and Immunohematology
School of Biomedical and Laboratory Sciences
College of Medicine and Health Sciences
University of Gondar
P.O. Box 196, Gondar
Ethiopia
E-mail: mulugeta.melku@gmail.com

Key words:

anemia, children, Ethiopia, meta-analysis,
protocol, systematic review

ABSTRACT

Background

Anemia is one of the global public health problems that affect more than one third of the world population. It has been strongly associated with poor growth and development, limited psychomotor development, and poor long-term performance in cognitive, social, and emotional functioning in children. There is not a single national figure about childhood anemia in Ethiopia. There is also inconclusive evidence about factors associated with anemia. Moreover, the present meta-analysis will generate concrete evidence in which the result may urge policy makers and program managers to design appropriate intervention to control childhood anemia. Thus, the aim of this review is to estimate the pooled prevalence and to identify associated factors of anemia among children in Ethiopia.

Method

Published relevant cross-sectional studies will be searched using comprehensive search strings through PubMed/Medline, SCOPUS, HINARI, EMBASE, Web of Science databases. In addition, Google Scholar and Google will be searched for grey literature.

Reference lists and communication with content experts will be used to get additional relevant studies. Two groups of review authors will independently appraise the studies for scientific quality and extract the data using the Joanna Briggs Institute (JBI) tools. The pooled estimate will be determined using random effect model. Heterogeneity between the studies will be assessed using the I² statistics. Sensitivity and subgroup analysis will be employed in the case of heterogeneity. Publication bias will be assessed by visual inspection of the funnel plot, and using Egger's and Begg's statistical tests.

Discussion

Childhood anemia is known to have negative consequences on mental, physical and social development of children. The burden and its associated factors are greatly varied as to the social, economic, and geographical differences of the target population.

Therefore, the proposed systematic review will generate evidence about the pooled prevalence of anemia and its associated factors among children in Ethiopia.

Protocol registration

The protocol was registered at PROSPERO International Prospective Register of Systematic Reviews.

(Registration number: CRD42018088223).



BACKGROUND

Anemia is recognized as a major public health problem globally, mostly affecting children, women of childbearing age and pregnant women [1]. In developing countries, anemia can be a result of a number of causes; but nutritional anemia, particularly iron deficiency, is the most common cause. It is primarily caused by insufficient dietary intake and/or insufficient absorption, and suboptimal utilization of micronutrients like vitamin or mineral and/or due to frequent infections [1, 2].

The health implication of anemia is numerous. It is associated with impaired mental, physical, motor and language development; and poor coordination, scholastic achievement and immune function [3-5]. In addition, the outcomes of anemia can be considered from a variety of perspectives, including detrimental impacts on economic and social development [6].

According to World Health organization (WHO) 2015 report, about 43% of under five children were anemic, with regional variations of 62.3% in African, 53.8% in South-East Asia and 21.9% in Western Pacific Region [7].

In Ethiopia, though the prevalence of severe to moderate anemia in the last fifteen years has significantly declined, children and pregnant women are still suffering from the consequences of anemia due to high iron requirements, low intake of iron from foods, and frequent episodes of infection [8, 9]. As many as six in ten under five children in Ethiopia are anemic. Moreover, according to the local conditions, the proportion varies across the regions of the country due to feeding, wealth and cultural differences. As an illustration, the highest level of childhood anemia was found in Somali Region (83%), followed by Affar (75%) and Dire Dawa (72%), but the lowest was found in the Amhara Region (42%) [10].

The government of Ethiopia has been working to reduce childhood anemia. Accordingly, it endorsed the national nutrition program, bimanual school deworming, developed micronutrient deficiency prevention and control guideline and implemented micronutrient fortification. But studies from different corners of the country have shown that childhood anemia is still a major public health problem. In addition, there is not a single national figure about childhood anemia and also inconclusive evidence about factors associated with it. Systematic review and meta-analysis generates concrete evidence in which the evidence may urge policy makers and program managers to design appropriate intervention to control and minimize the negative consequences of childhood anemia. As far as the authors are aware, there is no published systematic review and meta-analysis that generated the pooled estimated prevalence of anemia and the pooled effect size of factors associated with childhood anemia in Ethiopia. Therefore, the aim of this systematic review and meta-analysis is to estimate the pooled prevalence of childhood anemia and its associated factors among children in Ethiopia.

OBJECTIVES

The objectives of this systematic review and meta-analysis are:

- To estimate the pooled prevalence of anemia among children in Ethiopia;
- To identify factors associated with childhood anemia in Ethiopia.

METHODOLOGY

Design and protocol registration

This protocol is designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P 2015 Guidelines) [11].

The protocol of this systematic Review and Meta-analysis has been registered in the PROSPERO, international prospective register of systematic reviews, with registration number of CRD42018088223.

Search strategy

Relevant published articles will be searched in PubMed/Medline, HINARI, SCOPUS, EMBASE and Web of Sciences electronic databases. Google scholar, and Google will be searched for grey literature. In addition, conference paper and thesis or research final report will be accessed, professional annual research conference log book, and research and publication directorate from each University in Ethiopia upon request.

The search terms will be developed in accordance with the Medical Subject Headings (MeSH) thesaurus using a combination of key terms. Hand searching of articles published in Ethiopian journal of health sciences, Ethiopian Medical journal, Ethiopian journal of Health and Development, and Ethiopian Journal of Health and Biomedical Sciences will be conducted.

Reference lists of retrieved articles will be probed to identify any studies that are not retrieved from electronic databases. Content experts will be contacted to get additional studies that are not retrieved by electronic database searching and reference list scrutinizing. Two author groups: group one (MM, ZA) and group two (DTE, WWT), will independently search the articles. In the case of lack of necessary data from studies, we will contact the corresponding author through email.

Search Strategy:

- anemia OR iron deficiency anemia OR nutritional anemia OR hemoglobin OR nutritional status OR hematological parameters OR determinant factors of anemia OR associated factors of anemia AND children OR adolescent OR preschool AND Ethiopia

Study selection and quality appraisal

All articles retrieved through search strategy will be imported to EndNote X7 (Thomson Reuters, New York, USA). After excluding the duplicate articles, titles and abstracts will be independently screened for inclusion in full text appraisal by two groups of review authors: group one (MM, ZA) and group two (DTE, WWT). Differences between two groups will be resolved through thorough discussion. In case of disagreement between the two groups of review authors' reports, the decision will be determined by third group of review authors (ZG, MA, DZA).

For articles deemed to appear relevant, the full text will be appraised for inclusion in systematic review and meta-analysis.

The quality of articles will be assessed using Joana Brigg's Institute (JBI) critical appraisal checklist for simple prevalence [12] and analytical cross-sectional studies [13] having nine and eight checklist items, respectively. Studies with an overall quality assessment score greater than 50% will be included. The discrepancies during critical appraisal will be solved as similar manner for title/abstract screening phase.

Participants

Studies reporting the prevalence and/or factors associated of anemia among children in Ethiopia.

Eligibly criteria

Inclusion criteria

Studies will be included in this systematic review if they met all the below inclusion criteria:

- Studies reporting the outcome of interest among children (up to 18 years old) in Ethiopia
- Observational studies like cross-sectional, prospective cohort studies and repeated cross-sectional studies. For prospective cohort and repeated cross-sectional studies

that reported the outcomes of interest, the baseline data will be used for our systematic review and meta-analysis.

Exclusion Criteria

Studies will be excluded if they have met at least one of the exclusion criteria below:

- Studies conducted in healthcare facilities
- Studies that used Visual comparative method (Sahli-hellige method, and MBS hemoglobinometer color scale) and Copper Sulphate densitometer to ascertain the outcome (anemia)
- Studies conducted in children living with HIV/AIDS

Outcomes of the study

The primary outcome of this systematic review is to determine the prevalence of anemia among children in Ethiopia. It will also identify factors associated with the burden of anemia among children in Ethiopia. Anemia is defined as hemoglobin value below the established reference interval for the sex and age of the population.

Data extraction

The JBI tool will be adopted for data extraction. Two groups of review authors, group one (MM, ZA) and group two (DTE, WWT), will extract the data independently. In case where there are differences between the two authors' groups with regard to the extracted data, the difference will be solved via discussion.

Unless resolved via discussion, the decision will rely on the third review authors' group (ZG, MA, DZA) report. Information such as name of first author, year of publication, age group of children, study year, study area/region, study design, total number of children, number of anemic children, and number of anemic cases and non-anemic cases for the reported associated factors will be extracted.

The data will be recorded in a Microsoft excel spreadsheet. When authors find multiple publications from the same dataset, the article reported the prevalence and factors associated of anemia in extractable form will be used.

Moreover, for prospective cohort and repeated cross-sectional studies that reported the outcomes of interest, the baseline data will be used for our systematic review and meta-analysis to facilitate comparability of results across studies and to reduce loss to follow-up bias.

Data analysis

The data extracted from primary eligible studies will be entered into Microsoft excel, and then will be exported to STATA version 14 (StataCorp LLC, Texas, USA) for analysis.

The magnitude of heterogeneity between included studies will be quantitatively measured by index of heterogeneity (I^2 statistics) [14]. I^2 values of 25%, 50% and 75% are assumed to represent low, medium and high heterogeneity, respectively.

The significance of heterogeneity will be determined by p-value of I^2 statistics; and a p-value of <0.05 will be an evidence of heterogeneity. If I^2 value is greater than 50%, we will use Dersimonian and Liard random effect model to determine the pooled estimates [15].

Sensitivity analysis will be carried out if there is heterogeneity between studies. Subgroup analysis will be done considering age group, region and study design as grouping variables.

Small-study effects and publication bias will be evaluated using the visual funnel plot test, and Egger's and Begg's statistics in the random effect model. In the evidence of small-study effect, trim and fill methods (Duval and Tweedie's) will be used to estimate the pooled prevalence anemia and to estimate effect size of factors associated with childhood anemia, as the method

is robustness for estimation due to publication bias [16]. Odds ratio with its 95% confidence will be used to estimate the measure of association between anemia and associated factors. The results will be presented both in text and Forest plot.

Ethical statement and dissemination

As this systematic review will be based on published data, ethical approval is not required. The final report will be disseminated through publication in a peer-reviewed scientific journal and will also be presented at Local, regional, national and international conferences.

DISCUSSION

Anemia has been shown to be a public health problem affecting low, middle and high-income countries. It has also been significantly associated with negative consequences on health, social and economic development [17, 18]. Globally, it is a moderate to severe public health problem in children.

As to the WHO 2015 estimate, the highest prevalence of anemia is found in children, 42.6% (95% CI: 37- 47%) of children were suffering from anemia [19]. The consequence of anemia is worse, as it limits the physical growth [20], mental [21], social [22] as well as the behavioral development of children [23].

Anemia prevalence data remains an important indicator of public health as anemia is related to morbidity and mortality, particularly in vulnerable segments of the population such as in children [10].

In Ethiopia, the magnitude of anemia is expected to be higher among children who are malnourished and economically disadvantaged; and among children who are living in areas where infectious diseases are highly prevalent and drought is common.

Previous studies highlighted that the prevalence of anemia among children in Ethiopia ranged from 5.83% [24] to 83% [10].

At a global level, anemia prevalence data is a useful indicator to assess the impact of widespread or highly effective interventions and to track the progress made towards the goal of reducing anemia in children [25].

In order to design more adaptable intervention and control strategies to the local context, national estimate of anemia and its associated factors needs to be generated. Given the importance of such data, there is no published meta-analysis estimate on the prevalence of anemia and its associated factors among children in Ethiopia.

Therefore, the authors believe that, this systematic review and meta-analysis will generate concrete evidence on the national burden of anemia and its associated factors among children. The review will provide substantial evidence for the government and other stakeholders working on child health; and it will help them in designing intervention and control strategies to reduce anemia in a better adaptable and more effective manner.

STRENGTH AND LIMITATION OF THIS SYSTEMATIC REVIEW

Strengths

- This will be the first published systematic review and meta-analysis that comprehensively estimate the burden of anemia, and its associated factors among children in Ethiopia.
- The involvement of experts from public health, biomedical and clinical fields during searching, screening, appraisal, and data extraction processes will help to make the evidence generated more comprehensive.
- The data reporting will adhere as to the guideline outlined in the Preferred Reporting Items

for Systematic reviews and Meta-Analyses protocol (PRISMA-P 2015 Statement).

Limitations

- A potential limitation of this systematic will be the heterogeneity between published studies that can be raised from differences in study design, study period and geographic areas. Besides, studies reported in other than English language may not be included.

Amendments of the protocol

- In case there is a need to amend this protocol, the reasons for the amendment and the date when it has been amended will be explicitly described.



Conflicts of Interest

The authors declared that they have no competing interests.

Availability of data and materials

Not applicable.

Authors' contributions

MM, ZA, ZG and WWT: have been developing the search strategy;

MM, ZA, ZG, DTE, WWT, DZA and MA: will search, screen and appraise the studies, and will extract the data;

MM, ZA, DZA, MA and WWT: will analyze the data;

ZA, MM, ZG, WWT and MA: involved during the drafting of the protocol.

All authors read and approved the final protocol for publication.

Funding Statement

No funding was secured for this review.



REFERENCES

1. Harika R, Faber M, Samuel F, Mulugeta A, Kimiyew J, Eilander A. Are Low Intakes and Deficiencies in Iron, Vitamin A, Zinc, and Iodine of Public Health Concern in Ethiopian, Kenyan, Nigerian, and South African Children and Adolescents? *Food and Nutrition Bulletin* 2017; 38:405-427.
2. Herrador Z, Sordo L, Gadisa E, Buño A, Gómez-Rioja R, Iturzaeta JM, de Armas LF, Benito A, Aseffa A, Moreno J, Cañavate C. Micronutrient Deficiencies and Related Factors in School-Aged Children in Ethiopia: A Cross-Sectional Study in Libo Kemkem and Fogera Districts, Amhara Regional State. *PLoS ONE* 2014; 9:e112858.
3. Walter T. Effect of iron-deficiency anemia on cognitive skills and neuromaturation in infancy and childhood. *Food and Nutrition Bulletin* 2003; 24:S104-110.
4. WHO. Worldwide prevalence of anaemia 1993–2005. Geneva: World Health Organization; 2008. Accessed at: http://apps.who.int/iris/bitstream/10665/43894/1/9789241596657_eng.pdf; accessed date: January 20, 2018.
5. Santos JN, Rates SPM, Lemos SMA, Lamounier JA. Consequences of anemia on language development of children from a public day care center. *Rev Paul Pediatr* 2009; 27:67-73.
6. Plessow R, Arora NK, Brunner B, Tzogiou C, Eichler K, Brügger U, Wieser S. Social costs of iron deficiency anemia in 6–59-month-old children in India. *PLoS One* 2015; 10:e0136581.
7. WHO. The global prevalence of anaemia in 2011. Geneva: World Health Organization; 2015. Accessed at: http://www.who.int/nutrition/publications/micronutrients/global_prevalence_anaemia_2011/en/; Accessed date: January 20, 2018.
8. Getaneh Z, Enawgaw B, Engidaye G, Seyoum M, Berhane M, Abebe Z, Asrie F, Melku M. Prevalence of anemia and associated factors among school children in Gondar town public primary schools, northwest Ethiopia: A school based cross-sectional study. *PLoS ONE* 2017; 12:e0190151.
9. Deribew A, Alemseged F, Tessema F, Sena L, Birhanu Z, Zeynudin A, Sudhakar M, Abdo N, Deribe K, Biadgilign S. Malaria and Under-Nutrition: A Community Based Study Among Under-Five Children at Risk of Malaria, SouthWest Ethiopia. *PLoS ONE* 2010; 5:e10775.
10. Central Statistical Agency [Ethiopia] and ICF International. Ethiopia Demographic and Health Survey 2011. Addis Ababa, Ethiopia and Calverton, Maryland, USA: Central Statistical Agency and ICF International. 2016.
11. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015; 350:g7647.
12. Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and incidence data. *International journal of evidence-based healthcare* 2015; 13:147–153.
13. JBI. The Joanna Briggs Institute Critical Appraisal tools for use in JBI Systematic Reviews: Checklist for Analytical Cross Sectional Studies. 2016. Accessed at: <http://joannabriggs.org/research/critical-appraisal-tools.html>; accessed date: January 21, 2018.
14. Higgins J, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine* 2002; 21:1539-1558.
15. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled clinical trials* 1986; 7:177-188.
16. Tweedie R, Duval S. A Nonparametric “Trim and Fill” Method of Accounting for Publication Bias in Meta-Analysis. *Journal of the American Statistical Association* 2000; 95:89-98.
17. Smith RE Jr. The Clinical and Economic Burden of Anemia. *Am J Manag Care* 2010; 16:S59-S66.
18. Alcázar L. The economic impact of anaemia in Peru. Lima: Group for the Analysis of Development and Action Against Hunger; 2013. Accessed at: http://www.grade.org.pe/upload/publicaciones/archivo/download/pubs/LIBROGRADE_ANEMIAENG.pdf; accessed on: February 11, 2018.
19. WHO. The global prevalence of anaemia in 2011. WHO, Geneva, Switzerland, 2015. Accessed at: http://www.who.int/nutrition/publications/micronutrients/global_prevalence_anaemia_2011/en/; Accessed date: February 11, 2018.
20. Soliman AT, De Sanctis V, Kalra S. Anemia and growth. *Indian J Endocrinol Metab* 2014; 18:S1-S5.
21. Hurtado EK, Claussen AH, Scott KG. Early childhood anemia and mild or moderate mental retardation. *Am J Clin Nutr* 1999; 69:115-119.
22. Chang S, Wang L, Wang Y, Brouwer ID, Kok FJ, Lozoff B, Chen C. Iron-Deficiency Anemia in Infancy and Social Emotional Development in Preschool-Aged Chinese Children. *Pediatrics* 2011; 127:e927–e933.
23. Lozoff B, Corapci F, Burden MJ, Kaciroti N, Angulo-Barroso R, Sazawal S, Black M. Preschool-Aged Children with Iron Deficiency Anemia Show Altered Affect and Behavior *The Journal of Nutrition* 2007; 137:683–689.

24. Gashu D, Stoecker BJ, Adish A, Haki GD, Bougma K, Marquis GS. Ethiopian pre-school children consuming a predominantly unrefined plant-based diet have low prevalence of iron-deficiency anaemia. *Public Health Nutrition* 2016; 19:1834–1841.

25. Kraemer K, Zimmermann MB. *Nutritional Anaemia*. Basel, Switzerland: Sigh and Life Press; 2007. Available at: http://ernaehrungsdenkwerkstatt.de/fileadmin/user_upload/ED-WText/TextElemente/Ernaehrungswissenschaft/Naehrstoffe/nutritional_anemia_book.pdf; accessed on: Feb. 12, 2018.