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Review

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Factors influencing recurrent measles outbreak in Ethiopia among under-five children: a systematic review

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Abstract

Measles is the primary cause of under-five morbidity and mortality in Ethiopia. Immunization has been judged to be the most cost-effective strategy for reducing childhood morbidity and mortality. It directly influences SDG3 targets and contributes to 14 out of the 17 Sustainable Development Goals (SDGs). Ethiopia implemented the African regional accelerated measles control strategies, focusing on reducing measles mortality through robust routine measles vaccination coverage (MCV1) and effective supplemental immunization activities (SIAs). Significant progress has been made in enhancing immunization efforts, particularly MCV1, which has contributed to the reduction of measles morbidity and mortality. However, measles outbreaks persist in many parts of the country, threatening the national elimination goals. This systematic review examines the measles outbreak situation in Ethiopia to understand the factors influencing the recurring outbreak in the country. A systematic review was conducted through a database search in five databases (Article, CAS, PubMed, PubMed Central, and Google Scholar). Twenty-two articles were included, and the Critical Appraisal Skills Programme checklists (CASP) were used to appraise the studies, and analysis was done using a narrative synthesis. The recurring measles outbreaks in Ethiopia hinder the country's progress toward the African measles elimination target. Key factors identified include low vaccination coverage, sub-optimal supplemental immunization activities (SIAs), poor nutrition, limited access to healthcare services, contact with infected individuals, seasonal weather patterns, inadequate surveillance, and inequalities. These factors contribute to the accumulation of susceptible, unvaccinated children, leading to frequent outbreaks. Enhancing routine measles vaccination coverage and conducting targeted SIAs in areas with weak systems, while addressing inequities in vaccine access for special populations (such as migrants, insecure regions, and conflict zones), would strengthen the healthcare system, halt recurring outbreaks, and help achieve measles elimination goals.

Introduction

The United Nations and its member states had in 2015 adopted the 2030 Agenda for Sustainable Development, which provides a shared pattern for peace and prosperity now and in the future catering to both people and the entire planet [1]. The General Assembly came up with the 2030 Agenda for Sustainable Development, with 17 goals as the main theme of the UN Sustainable Development Summit (SDS). The 17 SDGs goals with 169 targets call for urgent actions by all member countries (both developed and developing) in a systemic global partnership [2,3]. Out of the 17 goals of the SDG, the 3rd goal (SDG 3) seeks to ensure healthy lives and promote the well-being of people of all ages. One of the targets of SDG3 (3.2.1) is to end preventable deaths of newborns and children under the age of five years by 2030, by reducing neonatal and under-five mortality by 12 and 25 per 1,000 live births respectively [4]. Vaccine-preventable diseases (VPD) remain one of the major threats in sub-Saharan Africa, it has been estimated that over thirty million children under the age of five years are suffering from vaccine-preventable diseases (VPDs) yearly in the region (WHO Regional Office for Africa, 2019). Immunization has been a success story for global health and development, it saves millions of lives every year. An estimated 28 million Measles deaths were prevented between 2010 and 2018 with the measles vaccine alone [5].

Measles continues to be the leading cause of death among children. An estimated 136,216 measles deaths occurred at the global level in 2022, affecting mostly children under five years of age, with a 43% increase when compared to the mortality estimates for 2021 [6-8]. Measles is a serious disease that is highly contagious and caused by a virus that belongs to the paramyxovirus family, it is often passed through direct contact or the air, affecting the respiratory

tract and then spreading to the rest of the body. Its only known reservoir is the human [7]. The measles vaccine was first introduced in 1963, and its availability and utilization have had a significant impact on the global effort to eliminate measles [9], and several countries have succeeded in eliminating measles through the same approach [10]. The World Health Assembly (WHA) had in 2010 set aside three milestones for achieving measles control by 2015, through 90% and >80% routine coverage at national and district levels respectively, reducing the global incidence of measles annually to less than 5 cases per 1 million population, and the reduction of global mortality by 95% [11]. In the African region, the 46 Member countries adopted a goal of eliminating measles by the end of 2020 with five (5) targets that must be achieved at both national and district levels [12].

Several studies have demonstrated that children who are opportune to receive a dose of measles-containing vaccine, are less likely to come up with measles. Approximately 93% of people who receive the first dose develop immunity to measles, and 97% after the second dose become protected [13]. Therefore, having a strong routine immunization with the measles dose-1 coverage (CV1) of ≥90% and ≥80% at national and district levels will ensure life-long immunity to about 93% of the population, which can guarantee a reduction in measles outbreak and child mortality due to measles disease [14]. There are an estimated 24.7 million children who did not receive MCV1 in 2021, and the top (10) countries with the highest number of children are Nigeria, India, DRC, Ethiopia Indonesia, Pakistan, Philippines, Angola, Brazil, and Tanzania with (3.1, 2.5, 1.7, 1.7, 1.2, 1.2, 1.0, 0.8, 0.7 and 0.5 million) respectively, representing more than half of the global total (59%) [8]. Ethiopia, referred to as the Federal Democratic Republic of Ethiopia (FDRE), is a low-income landlocked country located in East Africa. It has a total land area of 1.13 million km^2, with a total population of 112,078 million, and a population growth rate of 2.6% in 2019 [15]. Ethiopia has an estimated Gross Domestic Product (GDP) of $81 billion and a GDP per capita of 862 USD in 2017, it is one of the poorest countries with a per capita income of $850 [16].

Ethiopia is accounting for approximately 6.9% of the total 24.7 million global estimated children who are not vaccinated with MCV1 in 2021. Measles accounts for more than 5% of childhood mortality in the country [17], and measles outbreaks continue to evolve in the country, which was linked to spatial heterogeneity of measles vaccination [18,19]. Measles vaccination coverage in Ethiopia has shown a mixed pattern between 2000 and 2022. Administrative coverage ranged from 37% in 2000 to a peak of 93.4% in 2020, with some fluctuations in between. The World Health Organization and UNICEF's WUENIC estimates also varied, ranging from 36% in 2000 to a high of 68% in 2011. Despite overall progress in improving measles vaccination coverage, there were occasional declines in certain years, highlighting ongoing challenges.[20].

Our research is intended to identify factors that are contributing to the frequent outbreaks in the country. The PICO approach was adopted for the research question (patients, intervention, comparison, and outcome). The P (patient or population)= Under five children, the I (intervention) is the children who receive MCV1, the C (comparison) is the children who did not receive MCV1, while the O (outcome) is the measles outbreak in children. This systematic review aims to determine the key factors contributing to recurring measles outbreaks; identify barriers to immunization and propose strategies to mitigate these barriers to reduce immunity gaps and prevent future outbreaks.

Methods

This research paper utilized the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to conduct a comprehensive literature review on the research

question. The PRISMA guidelines were employed to ensure a systematic and rigorous review process and to enhance the transparency and reproducibility of the study's findings [21]. The inclusion criteria for this literature review were journal articles published in English within the past 21 years (2000-2021), regardless of study design, that reported on the epidemiology, prevalence, and outbreaks of measles in Ethiopia. Articles reporting only on Rubella or isolated cases of measles without outbreaks, intervention studies, or studies not published in English or with unavailable full text were excluded from this review (Figure 1).

Search strategy/study selection: a comprehensive search was conducted across five electronic databases including Article, CAS, PubMed, PubMed Central, and Google Scholar. The search terms were selected based on the PICO format, with strict usage of words closely related to the background and existing literature. The selected terms were individually applied and then combined using the basic Boolean operators "OR" and "AND". The keywords used in the search were "vaccination", "immunization", "under-five children", "outbreaks", "measles", "elimination", "control", "VPDs", "prevalence", "epidemiology" and "Ethiopia". Additionally, relevant articles were identified through manual searching of the reference lists of included articles. In addition to the literature review, secondary data from the Ethiopian Demographic and Health Surveys (EDHS) conducted by the Ethiopia Institute of Public Health (EPHI) and the Federal Ministry of Health (FMOH) were also sourced and included in the analysis.

Data extraction and quality assessment: an Excel workbook was used to create a data extraction form, which was pilot-tested and refined to improve its validity. Specific article features reviewed included author, year, country of origin, study design, method used, results, factors/influencers, and study quality. The Critical Appraisal Skills Programme (CASP) checklists were used to appraise the studies. References were managed using Mendeley software.

Data analysis and synthesis: a descriptive synthesis was employed to provide an overview of the studies included in the analysis. This was followed by a thematic analysis of each individual study to determine the exhaustiveness of evidence and to identify relationships that exist between the selected studies. Through this process, the analysis aimed to provide a comprehensive understanding of the evidence base and to identify any knowledge gaps that may exist [21]. In addition, a narrative synthesis was conducted to summarize the findings from the included studies. This involved providing a corresponding explanation of the relationship between the studies to identify their strengths and weaknesses. The results of this synthesis were used to arrive at a conclusion that reflects the overall findings of the analysis and to identify areas for future research.

Results

Study selection: this study undertook a systematic review of the literature to examine the epidemiology and outbreaks of measles in Ethiopia, focusing on the impact of routine vaccination on morbidity and mortality among children under five. The search process initially identified 1,160 citations from four online databases. After the removal of 821 duplicates, the abstracts of 698 articles were screened, resulting in 123 articles considered for detailed assessment. Further evaluation reduced this number to 40 articles. Nine articles were excluded for the following reasons: six were focused on Rubella, one analyzed the cost-effectiveness of the measles vaccine, and two explored interventions. Additionally, five more studies were identified through reference tracking, culminating in a total of 22 studies included in the review. These studies utilized various methodologies to investigate the factors influencing recurring measles outbreaks in

Ethiopian children under five. The findings from this literature review are summarized in Annex 1.

Study characteristics: the included studies varied in design, with 73% cross-sectional and 27% descriptive or case-control. All the reviewed studies were conducted in Ethiopia, with some focusing on specific regions. Most studies (91%) targeted children under five eligible for measles vaccination. These studies identified factors contributing to recurring measles outbreaks, aiming to highlight gaps to help reduce or prevent future outbreaks.

Risk of bias: most of the studies (82%) included in the review achieved a score of 70% or higher, indicating high quality. However, a moderate risk of bias was identified in 4 out of the 22 studies, specifically in confounding and outcome assessment domains.

Results of individual studies: the reviewed studies identified several factors influencing recurring measles outbreaks in Ethiopia. Low or sub-optimal measles coverage, reported in 20 studies, led to a build-up of susceptible, unvaccinated children and inadequate performance of SIAs. Poor nutritional conditions were noted in 2 studies, while frequent outbreaks were documented in 6 studies and inequality in 3 studies. Other factors included seasonal patterns, contact with measles cases, population movement, inadequate maternal knowledge, traditional activities, travel history, and disparities in wealth and education.

Synthesis of results: the synthesis highlighted the recurring nature of measles outbreaks in Ethiopia, driven by low immunization rates, inadequate SIAs, and other socio-economic and environmental factors. The findings suggest a need for strengthened immunization programs and targeted interventions in vulnerable populations.

Discussion

The purpose of this systematic review was to identify factors contributing to the increased and continuous measles outbreaks in children under five in Ethiopia, looking at the measles situation (immunization coverage, surveillance, SIAs, etc.). Numerous factors have been identified that directly influence measles outbreaks, and these are categorized and summarized as follows. The studies revealed that low routine immunization, poor nutritional conditions, and seasonality were factors that contribute to measles outbreaks. Measles outbreaks were observed to occur seasonally [17,22]. These findings were consistent with other studies conducted in the country, which also identified low routine immunization as a major factor contributing to the accumulation of susceptible unvaccinated children [23-28]. Three cross-sectional studies focusing on under-five children have consistently identified low or sub-optimal measles immunization coverage (MCV1) as the primary factor contributing to susceptibility and ongoing outbreaks across much of Ethiopia [29-31].

A study conducted in Gondar, Ethiopia revealed that having a history of contact with a suspected or confirmed case of measles increases the likelihood of contracting the disease. When combined with low measles coverage resulting in susceptible unvaccinated children, it further increases the mortality rate of measles in children under five. The results showed that children immunized with measles vaccine had an 83% reduced risk of measles infection (AOR, 95%CI=0.17, 0.05-0.53), while those with a history of contact with suspected or confirmed measles cases had a 3.44 times increased risk of infection (AOR, 95%CI=3.44, 1.26-9.38) [32]. Additionally, the quality of data has been identified as a critical factor contributing to understanding the outbreak's magnitude. Delays in both surveillance and laboratory systems have impacted the scope and effectiveness of the response. The study specifically points out problems such as unknown vaccine doses in surveillance data, and delays in obtaining laboratory results to officially declare an outbreak, which hinder a prompt response [23]. Additionally, four descriptive/control studies using

multivariate analysis found that inadequate immunization coverage, accessibility to health services, history of contact with measles cases, and insecurity leading to service disruption as some of the major factors that contributed to the recurring measles outbreak in the country. The studies also highlight a lack of adequate maternal knowledge on measles prevention, with sex and age of the population as additional factors that tend to influence measles outbreak in the country [22,33-35].

A cross-sectional study conducted in Gondar found that MCV1 coverage in children under five varies spatially, with low coverage and other individual and community factors accounting for more than 82% of the variance in the odds of MCV1 vaccination [36]. In another study, inequality in education and wealth were found to be co-factors that lead to sub-optimal immunization coverage, with vaccination coverage being 33.3% in 2016 and 0.30 and 0.23 wealth and maternal education-related inequities. The study also showed that children in Addis Ababa and Dire Dawa regions were seven times more likely to be fully vaccinated than those in the Afar region, and 49% of children in female-headed households were less likely to be fully vaccinated [37]. In the context of the systematic review, it should be noted that not all the studies focused solely on children under five, as measles can affect individuals of all ages. Some of the studies that documented measles outbreak investigations found an increase in the number of measles cases up to 15 years of age [32,34].

The studies reviewed in this literature indicate that the country requires a combination of efforts for it to address the recurring outbreak of vaccine-preventable diseases including measles especially looking at the sub-optimal routine immunization coverage for most of the routine vaccines, which are expected to provide herd immunity against these diseases and reduce outbreak [26]. Measles routine vaccination coverage is still low at 67% (MCV1), and supplemental immunization activities do not adequately cover the increasing number of unvaccinated children, resulting in frequent outbreaks. This situation is further compounded by the COVID-19 pandemic, insecurity, and other factors that affect the country's health system [27].

It is important to acknowledge the limitations of the systematic review and the potential for selection bias. Additionally, while the studies included in the review provided insights into the factors influencing measles outbreaks in Ethiopia, they may not be generalizable to other countries or contexts. Further research is needed to better understand the complex interplay of factors contributing to low immunization rates and measles outbreaks in Ethiopia and other similar settings. The consistency of the findings across multiple studies indicates that the factors identified as contributing to the persistence of measles in Ethiopia are likely to be relevant and applicable to other countries in the African region that face similar challenges. This suggests that the interventions and strategies that are effective in addressing these challenges in Ethiopia may also be useful in other settings [38].

Strengthening routine immunization services and increasing MCV1 coverage to at least 90% at the national level and 80% at the district level can significantly reduce the burden of measles and contribute to achieving the regional measles pre-elimination targets. This will require a multi-sectoral approach that involves government agencies, non-governmental organizations, and community-based organizations to address the various factors that influence sub-optimal immunization coverage and improve access to immunization services. It is also important to maintain surveillance and outbreak response capacity to quickly detect and respond to any outbreaks that may occur.

To meet Ethiopia's measles elimination goals and mitigate recurring outbreaks, a multifaceted approach is necessary. This should include enhancing routine immunization coverage for both MCV1 and MCV2, addressing factors that

contribute to suboptimal coverage and frequent outbreaks, and bolstering the RED approach in regions with frail systems to overcome vaccine access disparities. Maintaining vaccine confidence, monitoring transboundary population movements, boosting local immunization funding, and enhancing data quality are crucial. Additionally, reducing delays in surveillance and laboratory reporting hastening outbreak confirmation is recommended. Furthermore, Ethiopia should undertake high-quality measles supplemental immunization activities (SIAs), driven by robust surveillance that utilizes epidemiological data to target the correct age demographics in areas with active measles transmission.

Conclusion

The increased number of measles cases and the resulting recurring measles outbreaks in under-five children of Ethiopia suggest that the country is not on track to achieve the measles elimination goal. This systematic review identified various factors influencing the increase in measles outbreaks, including low and suboptimal routine measles coverage, poor nutritional conditions, accumulation of susceptible children in densely populated areas, inequity, inequality in access to vaccines, accessibility to health care services, inadequate SIA quality, poor nutritional conditions, data quality and seasonal hot weather conditions among others. The factors identified in this review could guide program managers and researchers to develop necessary interventions to address the recurring outbreaks, focusing efforts on improving measles vaccination coverage, reducing missed opportunities for vaccination, integrating service delivery, among others.

What is known about this topic

- *Measles remains one of the leading causes of death and illness among children under five in Ethiopia, and measles outbreaks continue to occur throughout the country;*
- *Immunization, particularly through routine measles vaccination (MCV1) and supplemental immunization activities (SIAs), is the most effective method being used globally to reduce this burden;*
- *Several factors are influencing these recurrent outbreaks, which are fuelled by a higher number of susceptible, unvaccinated children.*

What this study adds

- *Comprehensive examination of the factors leading to recurring measles outbreaks in Ethiopia. Identification of specific challenges such as vaccination coverage, supplemental immunization strategies, and access issues etc;*
- *The study highlights the need for targeted strategies in vulnerable and underserved areas, which can guide policymakers and health practitioners to address the recurring outbreak in the country;*
- *It offers a blueprint for health authorities to follow to enhance the efficiency of measles programs and potentially be adapted for other similar public health challenges within Ethiopia or other countries with similar contexts.*

Competing interests

The authors declare no competing interests.

Authors' contributions

Isah Mohammed Bello initiated and proposed the conceptualization of the manuscripts, Isah Mohammed Bello, Godwin Ubong Akpan, Hailemariam Fasil Teshager, Lebo Emmaculate Jepkorir and Masresha Balcha Girma have participated in the interpretation of findings and

review of the manuscript. All authors read and approved the final version of this manuscript.

Figure

Figure 1: PRISMA flow diagram for the identification, screening, eligibility, and inclusion of studies

Annex

Annex 1: summary of a systematic review of selected publications on measles immunization and recurring measles outbreaks in Ethiopia (PDF-134KB)

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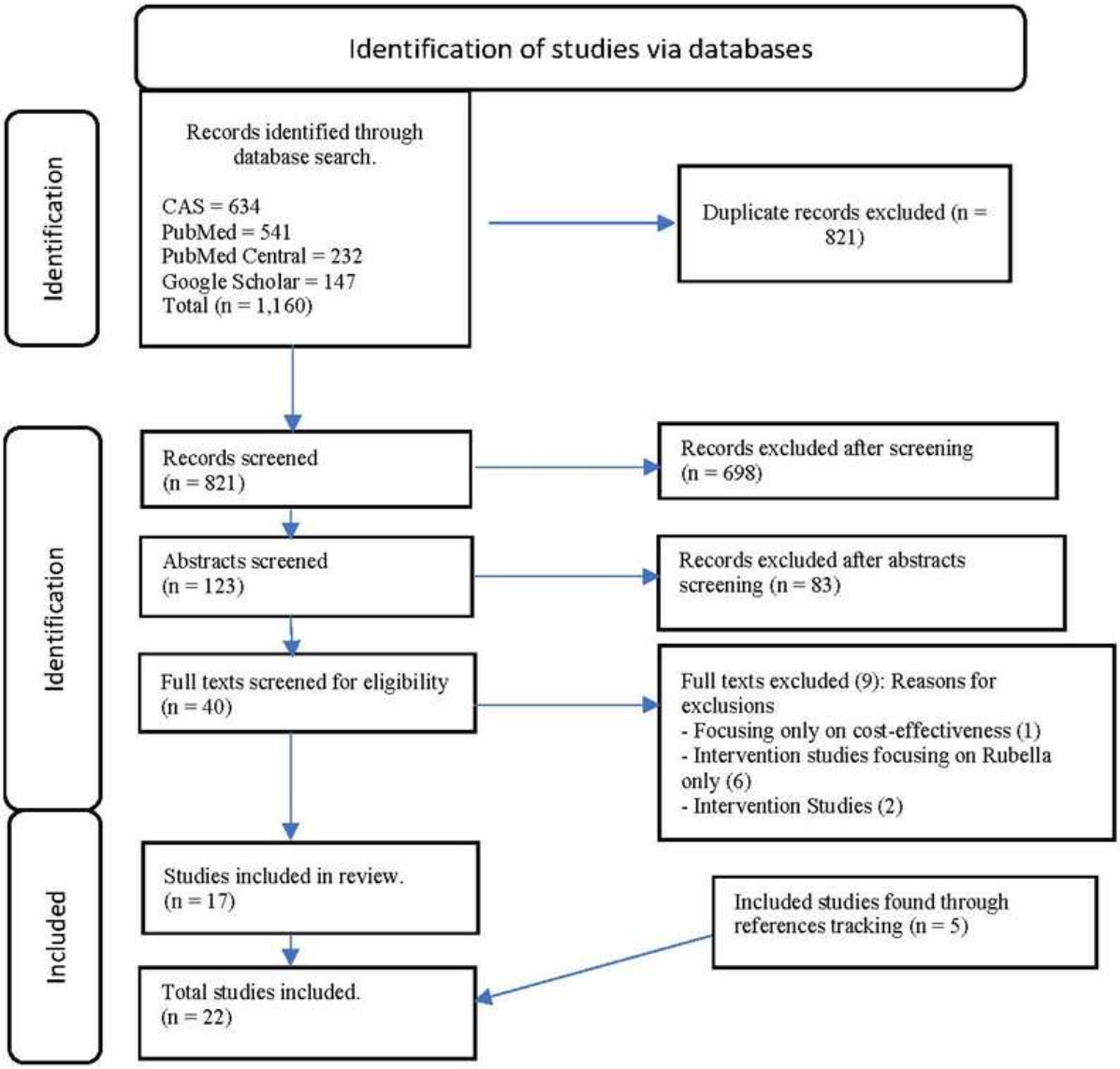

Figure 1: PRISMA flow diagram for the identification, screening, eligibility, and inclusion of studies