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# Rotavirus infections and their genotype distribution pre- and post-vaccine introduction in Ethiopia: a systemic review and meta-analysis

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## Abstract

**Background** Rotavirus infections are a significant cause of severe diarrhea and related illness and death in children under five worldwide. Despite the global introduction of vaccinations for rotavirus over a decade ago, rotavirus infections still result in high deaths annually, mainly in low-income countries, including Ethiopia, and need special attention. This system review and meta-analysis aimed to comprehensively explore the positive proportion of rotavirus at pre- and post-vaccine introduction periods and genotype distribution in children under five with diarrhea in Ethiopia.

**Methods** The review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. Database sources included PubMed, Scopus, EMBASE, and Epistemonikos, focusing on studies published before November 30, 2023. The search targeted rotavirus infection and genotype distribution in Ethiopia before and after the introduction of the Rota vaccine. Data was managed using EndNote 2020 software and stored in an Excel 2010 sheet. A random-effects model determined the pooled estimate of the rotavirus infection rate at 95% confidence intervals. The Q-and $I^2$ statistics were used to assess the study heterogeneity, and a funnel plot (Egger test) was used to determine the possibility of publication bias.

**Results** The analysis included data from nine studies conducted in different regions of Ethiopia. The overall prevalence of rotavirus infection was significant, with a prevalence rate of approximately 22.63% (1362/6039). The most common genotypes identified before the Rota vacation introduction were G1, G2, G3, G12, P [4], P [6], P [8], P [9], and P [10]. Meanwhile, G3 and P [8] genotypes were particularly prevalent after the Rota vaccine introduction. These findings highlight the importance of implementing preventive measures, such as vaccination, to reduce the burden of rotavirus infection in this population. The identified genotypes provide valuable insights for vaccine development and targeted interventions.

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**Conclusion** This study contributes to the evidence base for public health interventions and strategies to reduce the impact of rotavirus infection in children under five in Ethiopia. Despite the rollout of the Rota vaccination in Ethiopia, rotavirus heterogeneity is still high, and thus, enhancing vaccination and immunization is essential.

**Keywords** Rotavirus infection, Genotypes, Pre-vaccine, Post-vaccine, Ethiopia

## Introduction

Rotavirus infection detrimentally affects the childhood population, mostly in low-income counties, through the induction of severe diarrhea, leading to hospitalizations and fatalities [1, 2]. It constitutes a significant contributor to childhood morbidity and mortality on a global scale and still annually results in >500,000 deaths globally and >200,000 deaths in low-income countries [3]. The frequency of diarrhea diminishes with age [4, 5]. Several risk factors are associated with rotavirus infection, including the availability of contaminated water supplies, malnutrition, and the coexistence of individuals afflicted with gastroenteritis within the household [5]. Nevertheless, breastfeeding has been identified as a safe option against rotavirus-induced gastroenteritis. Children afflicted with rotavirus infection exhibit diminished levels of micronutrients such as ferritin and vitamin B12, rendering them more susceptible to allergic ailments [6]. Vaccination against rotavirus plays a pivotal role in preempting the onset of infection and its subsequent complications. Consequently, public health initiatives aimed at endorsing potable water consumption, adhering to effective personal hygiene practices, advocating for exclusive breastfeeding, and administering vaccinations are highly recommended to mitigate the impact of rotavirus infection within developing countries [7].

In Ethiopia, where infectious diseases pose a significant public health challenge, rotavirus infection has been a notable contributor to childhood illness and death [8]. Understanding the historical context of rotavirus infection in Ethiopia involves considering its impact on child health, healthcare infrastructure, and the burden it places on families and communities. Numerous studies in Ethiopia showed no seasonal variation in diarrhea associated with enterotoxigenic enterobacteria, rotavirus, and the two parasites *Giardia lamblia* and *Entamoeba histolytica*. The study isolated that rotavirus was present in 27.8% of the patients and 6.85% of the two parasites. The study also found that Rotavirus in 27.8% of the patients with diarrhea, most prevalent in the 7–12-month age group, and enterotoxigenic enterobacteria during the second year of life, while parasites continuously increased with age [9].

Rotaviruses are non-enveloped double-stranded RNA viruses with a complex genome of 11 segments of dsRNA and are classified into 32 G genotypes and 47 P genotypes. In Ethiopia, the distribution of rotavirus genotypes in children under five is diverse, with several dominant genotypes identified. The most common genotypes include G1, G2, G3, G12, P [4], P [6], P [8], P [9], and P [10]. The most prevalent combinations are G12P [8], G3P [6], G1P [8], and G3P [8]. These genotypes comprise a significant proportion of rotavirus strains in Ethiopia. The prevalence of rotavirus infection among children under five in Ethiopia is approximately 23%. The G3 genotype is prevalent, accounting for 27.1% of cases, followed by the P [8] genotype at 49%. The G8 genotype, which is more commonly found in cattle, has also been reported in Ethiopia, although at a lower frequency [10].

Without age restriction, the rotavirus vaccine was introduced in Ethiopia on November 13, 2013, according to the WHO/SAGE recommendation [11]. In Ethiopia, fully vaccinated children aged between 15 and 23 months took one dose of Bacille Calmette Guerin (BCG), three doses of PCV (pneumococcal conjugate vaccine), three doses of pentavalent, three doses of OPV, two doses of Rota, and two doses of measles vaccine by card plus mother history [12]. According to a study in Ethiopia, since no indication of the virus was isolated in children who had received the rotavirus vaccine, it suggests the vaccine shows a protective benefit [13].

The importance of examining rotavirus in Ethiopia resides in its implications for public health and the potential for well-informed interventions. The infection caused by the rotavirus disproportionately affects children in settings with limited resources, resulting in heightened costs for healthcare, economic burdens, and reduced productivity. Experts and policymakers can identify more susceptible populations, formulate targeted interventions, and enhance healthcare strategies by delving into the prevalence, impact, and risk factors associated with Rotavirus in Ethiopia. Furthermore, comprehending the distribution of genotypes can contribute to the development and effectiveness of vaccines.

Hence, this study aimed to comprehensively explore the positive proportion of rotavirus at pre- and post-vaccine introduction periods and genotype distribution in children under five years old with diarrhea in Ethiopia.

## Materials and methods

### Study protocol

The review was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [14]. Following the STROBE checklist and additional STROME-ID items, units were used to conduct systematic reviews to evaluate the

reported quality of records [15]. This systematic review and meta-analysis proposal was registered at the PROSPERO International Prospective Register of Systematic Reviews on November 24, 2023, as PROSPERO 2023 ID: = CRD42023481674.

### Searching strategies and information sources

We utilized the data from PubMed, Scopus, EMBASE, Epistemonikos database, and additional sources such as Google Scholar and Addis Ababa University Electronic Thesis and Dissertation for all published and unpublished articles before November 30, 2023. The search data from databases was done based on keywords, medical subject headings (MeSH) terms, and other terms such as epidemiology, risk factors, genotype distribution, and vaccination status of rotavirus infection in the pre-vaccine and post-vaccine introduction in Ethiopia, which are available in Annex S1 Supplementary Document (**Annex file 1**). The articles were searched and downloaded from databases on November 24–30, 2023, with language restricted to English.

However, for the search string of PubMed, Epistemonikos, EMBASE and Scopus, we used the terms; " rotavirus infection ‘’, “pre-vaccine,” " post-vaccine,‘’ “epidemiology,” " risk factors,” " genotypes,” vaccination status,” [MeSH], “Ethiopia” with the combination of Boolean logic (“AND,” OR”) based upon the given databases (**Annex file 2**).

### Study selection

**Inclusion criteria** The studies deal with the human population socio-demographics in Ethiopia under five years old (0–59 months) and original research, including cross-sectional, cohort, case-control, and randomized controlled trials (RCTs). Studies reporting epidemiological data on rotavirus infection in under-five children, including incidence and prevalence, and data on risk factors associated with rotavirus infection, specifically in the under-five age group, genotype distribution of rotavirus strains in under-five children, vaccination status of under-five children, and studies published in English or with an English translation available were included.

**Exclusion criteria** Studies focusing exclusively on populations above five, review articles, editorials, commentaries, letters, and conference abstracts without full-text availability, and studies with a high risk of bias or poor methodological quality were excluded. In addition, articles conducted after November 30, 2023, excluded studies without relevant epidemiological data on rotavirus infection, risk factors, genotypes, or vaccination status in the under-five age group.

### Quality assessment

The quality of the records was assessed according to the Joanna Briggs Institute's (JBI) 2017 checklist. The included records were critically appraised using the predetermined criteria or checklist. In addition, each article was appraised using the Joanna Bridges Institute (JBI) assessment tool for observational studies, particularly the analytical cross-sectional studies design. The study with a minimum of 5 scores was considered acceptable methodological quality and included in the review [16].

On the other hand, STROME-ID (Strengthening the Reporting of Molecular Epidemiology for Infectious Diseases) was also used to investigate the quality of each selected record. This statement is an extension of the 22-item STROBE statement with 20 additional elements aiming to promote transparency, clarity, and comparability of scientific reporting, specifically in Molecular Epidemiology for Infectious Diseases studies [15].

### Data extraction

Three reviewers (WT, BT, and DE) screened the titles and abstracts and independently evaluated the titles and abstracts of potentially eligible records. The full texts of selected records were assessed against inclusion criteria, and three reviewers extracted data separately using the prepared data extraction tool (Table 1). The extracted data included the first author's name and publication year, study area, population/sample, sample size, laboratory diagnostic methods, and total rotavirus-isolated genotypes. The extracted data was transferred to an Excel sheet. The results were then cross-checked, with a “checked” value of “1” for discrepancies. Any discrepancies that occurred between reviewers were discussed and resolved through consensus.

### Statistical analysis

The extracted data from the records was stored on the Excel version 2010 sheet. Descriptive statistics and bar graphs were prepared from extracted data in Excel 2010 and Jamovi 2.3.5. Comprehensive Meta-Analysis Version V3.ext software was installed, and a shortcut labeled on the personal computer with the Windows start menu was created. Next, the specific columns containing the study names, sample size, and outcome variables were transferred to the Comprehensive Meta-Analysis column for analysis.

A random-effect model determined the pooled rotavirus infection test to assess the possibility of publication bias by using Compressive Meta-analysis V3.exe software to analyze the data.

### Operational definition

**Epidemiology** Diagnosis of the prevalence and distribution of Rotavirus infection in pre- and post-vaccine intro-

**Table 1** Summary of the studies used in the systematic review and meta-analysis

| 1st Author name | Year of Publication | Study Area | Study Population | Study Design | Cases of RV Infection | Sample Size | vaccination status | Positivity Proportion | Lab Method Used | Genotype Distribution |
|---|---|---|---|---|---|---|---|---|---|---|
| Abebe A et al. | 2018 | Addis Ababa | Hospitalised children | Sentinel surveillance | 188 | 788 | Pre vaccine | 0.23857868 | EIA | G12P in 2011 (36%) & in 2012 (27%), G2P (35%) in 2013 |
| Abebe A et al. | 2018 | Addis Ababa | Hospitalised children | Sentinel surveillance | 161 | 815 | Post-vaccine | 0.197546 | EIA | G9P (19%) in 2014, G3P & G2P (19% each) in 2015, and G |
| Abebe A et al. | 2013 | Addis Ababa | Hospitalised children | Sentinel surveillance | 388 | 1841 | Pre-vaccine | 0.210755024 | EIA | G1p (20%), G12p (17%) & G3p (15%) |
| Stintzing G et al. | 1981 | Addis Ababa | Outpatient department | cross-sectional | 267 | 962 | Pre-vaccine | 0.277547 | IEO | NA |
| Getahun et al. | 2014 | Addis Ababa | Hospitalised children | Cross-sectional | 85 | 246 | Post vaccine | 0.345528 | EIA | NA |
| Abebe et al. | 1995 | Addis Ababa | Outpatient department | Cross-sectional | 65 | 358 | Pre-vaccine | 0.181564 | ELISA | NA |
| Bizuneh T et al. | 2004 | Jimma | Outpatient department | Cross-sectional | 41 | 154 | Pre vaccine | 0.266234 | ELISA | NA |
| Feleke H et al. | 2018 | Wegera | Community-based study | Cross-sectional | 10 | 225 | Post vaccine | 0.044444 | ELISA | NA |
| Gelaw A et al. | 2018 | Gondar & Bahir Dar | Outpatient department | Cross-sectional | 113 | 450 | Post vaccine | 0.251111 | RT-PCR | G3P[8], G2P[4], G9P[8], G12P[8], & G3P[6] |
| Yassin et al. | 2013 | Awassa | Hospitalised children & outpatients | Cross-sectional | 44 | 200 | Pre vaccine | 0.22 | RT-PCR | G3P[6] (48%), G1P[8] (27%) & G2P[4] (7%) |

Note: EIA=Enzyme Immunoassay, ELISA=Enzyme-Linked Immunosorbent Assay, IEO=Immunoelectro-osmophoresis, NA=Not applicable, RCR=Real-time Polymerase reaction, pre-vaccine period before June 13, 2013, post-vaccination period after 13, June 2013. The study by Abebe A. et al., published in 2018 and conducted in Addis Ababa, was a sentinel surveillance study that examined the cases of Rotavirus infection before introducing the vaccine. The study included a sample size of 788; the Rotavirus infection cases were 188. The lab method used in this study was EIA. The genotype distribution of Rotavirus was identified as G12P in 2011 (36%) and in 2012 (27%), and G2P (35%) in 2013

duction periods. It includes analyzing trends, affected age groups, and regional variations to provide a thorough understanding of the disease burden.

**Risk factors** Isolating the socio-economic characteristics, environmental, and topographic factors that contribute to the vulnerability of specific populations to Rotavirus infection. This analysis can guide targeted public health interventions to reduce risk and improve overall child health.

**Genotype distribution** Examining the genetic diversity of Rotavirus strains circulating in Ethiopia before and after vaccine introduction. Understanding genotype distribution is crucial for monitoring strain evolution, assessing vaccine efficacy, and adapting vaccination strategies if necessary.

**Vaccination status** Evaluating the impact and effectiveness of Rotavirus vaccination programs in Ethiopia. It involves assessing coverage rates, identifying challenges in vaccine distribution and administration, and determining the overall success in reducing the burden of Rotavirus-related morbidity and mortality among children.

By addressing these essential aspects, the literature aims to contribute valuable evidence that can inform evidence-based policies, improve healthcare practices, and ultimately reduce the impact of Rotavirus infection on child health in Ethiopia.

## Result

### Selection process and characterization of the included studies

A systematic review and meta-analysis were conducted to estimate the incidence of rotavirus infection

in Ethiopia pre- and post-vaccine introduction. A total of 479 research articles were accessed from PubMed, EMBASE, Scopus, and Epistemonikos. After excluding 52 articles due to duplication, 427 records remained. Among these, 233 were excluded for lacking laboratory diagnosis for rotavirus, and 46 were excluded for being review or systematic review articles, with 233 records considered irrelevant. After screening abstracts, titles, and full texts, 148 articles met the inclusion criteria for the systematic review and meta-analysis. Subsequently, these 148 articles were thoroughly evaluated, including only nine records in the final systematic review and meta-analysis (Fig. 1).

The introduction of rotavirus vaccines in Ethiopia in 2013 significantly reduced the incidence of rotavirus infections, a leading cause of severe diarrhea in children. A stratified data analysis from various study years reveals a substantial reduction in the positivity proportion of rotavirus cases after the vaccine's introduction. Before the vaccine's introduction, the positivity proportion was relatively high, with values ranging from 0.181 to 0.277. However, after the vaccine was introduced, there was a notable decline in the positivity proportion, particularly in 2018, where it dropped to as low as 0.044. This significant reduction indicates that the rotavirus vaccination program has profoundly impacted reducing the burden of rotavirus infections among children in Ethiopia, underscoring the need for continued monitoring and evaluation of the vaccination program.

The stratified analysis of rotavirus infections in Ethiopia provides valuable insights into the effectiveness of the rotavirus vaccine introduced in 2013. Before the vaccine rollout, data from various years of study indicated a concerning prevalence of rotavirus infections among

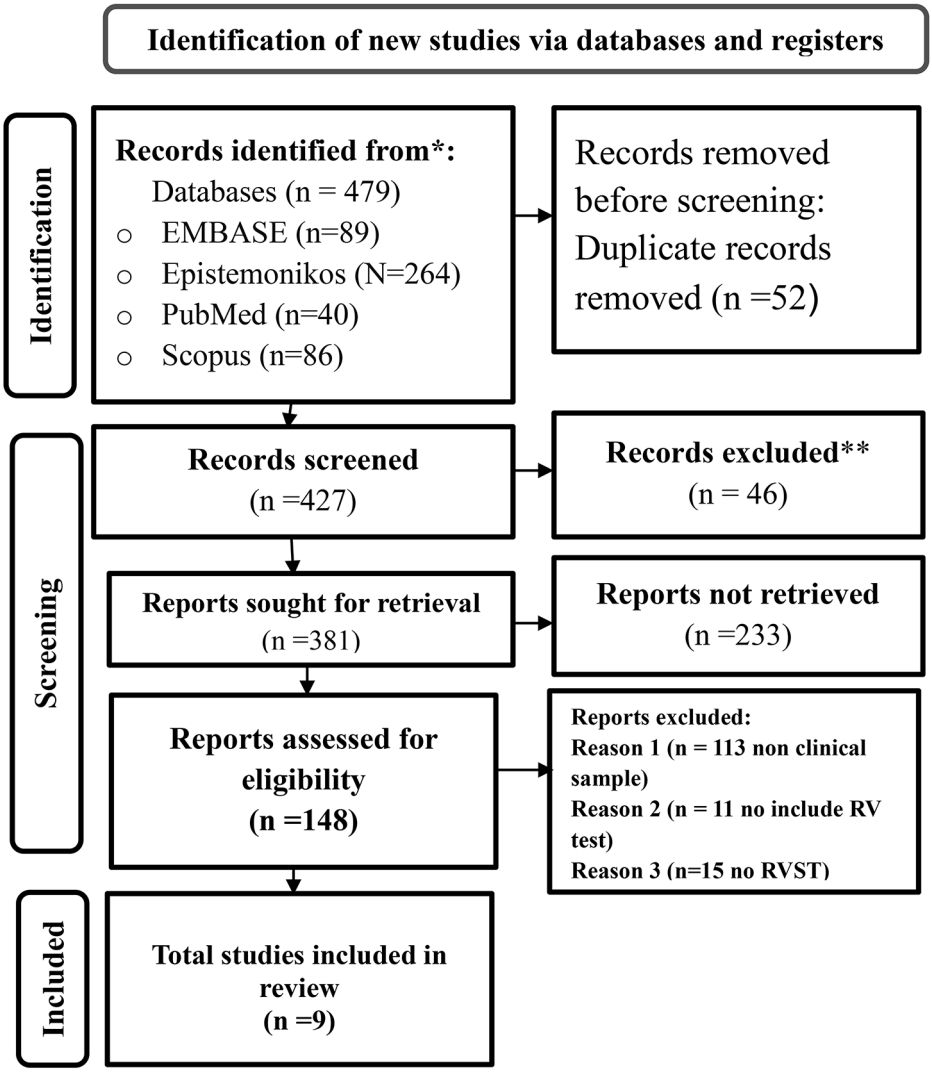


**Fig. 1** PRISMA 2020 flow diagram for updated systematic reviews, which included searches of database registers

children. For instance, in 1981, the positivity proportion was 0.277; in 2013, it was 0.210. These figures highlight the significant burden of rotavirus before vaccination efforts.

Following the vaccine's introduction, the data shows a marked decline in the positivity proportion of rotavirus infections. In 2018, the positivity proportion dropped to 0.197 in one study and decreased to 0.044 in another, indicating a substantial reduction in the number of positive cases relative to the sample size (Tables 1**and** Fig. 2). This decline suggests that the rotavirus vaccination program has effectively reduced the incidence of severe rotavirus infections among children, contributing to improved health outcomes.

However, it is essential to note that the data has fluctuations. There were instances of the positivity proportion in the post-vaccine years not following the expected trend. For example, in 2014, the positivity proportion was recorded at 0.345, higher than some pre-vaccine years. This variability may be attributed to changes in surveillance practices, the emergence of different rotavirus strains, or variations in vaccination coverage. These fluctuations remind us of the challenges and uncertainties we must navigate in public health.

The data extracted for the systematic review and meta-analysis studies provide valuable insights into the prevalence and characteristics of rotavirus infection with diarrhea in children under five in Ethiopia. As summarized in Table 1, the majority of the research articles were from Addis Ababa (6/10); cross-sectional studies by design (7/10), studies conducted before the introduction of the rotavirus vaccine in Ethiopia (6/10), and most studies (8/10) used the EIA/ELISA method for the determination of rotavirus infection and only two used RT-PCR.

A study by Abebe A et al. conducted in 2013 in Addis Ababa examined the positive proportion of rotavirus before the vaccine introduction. This pre-vaccine sentinel surveillance study included a larger sample size of 1841, and the positive proportion of rotavirus was 388 cases (21%) in 2013. The lab method used in this study was EIA. The genotype distribution of rotavirus was identified as G1p (20%), G12p (17%), and G3p (15%) (Table 1; Fig. 3).

Another study by Abebe A. et al., also published in 2018, focused on the post-vaccine period in Addis Ababa. This sentinel surveillance study included a sample size of 815, and the positive proportion of rotavirus was 161 cases. The genotype distribution in this study revealed

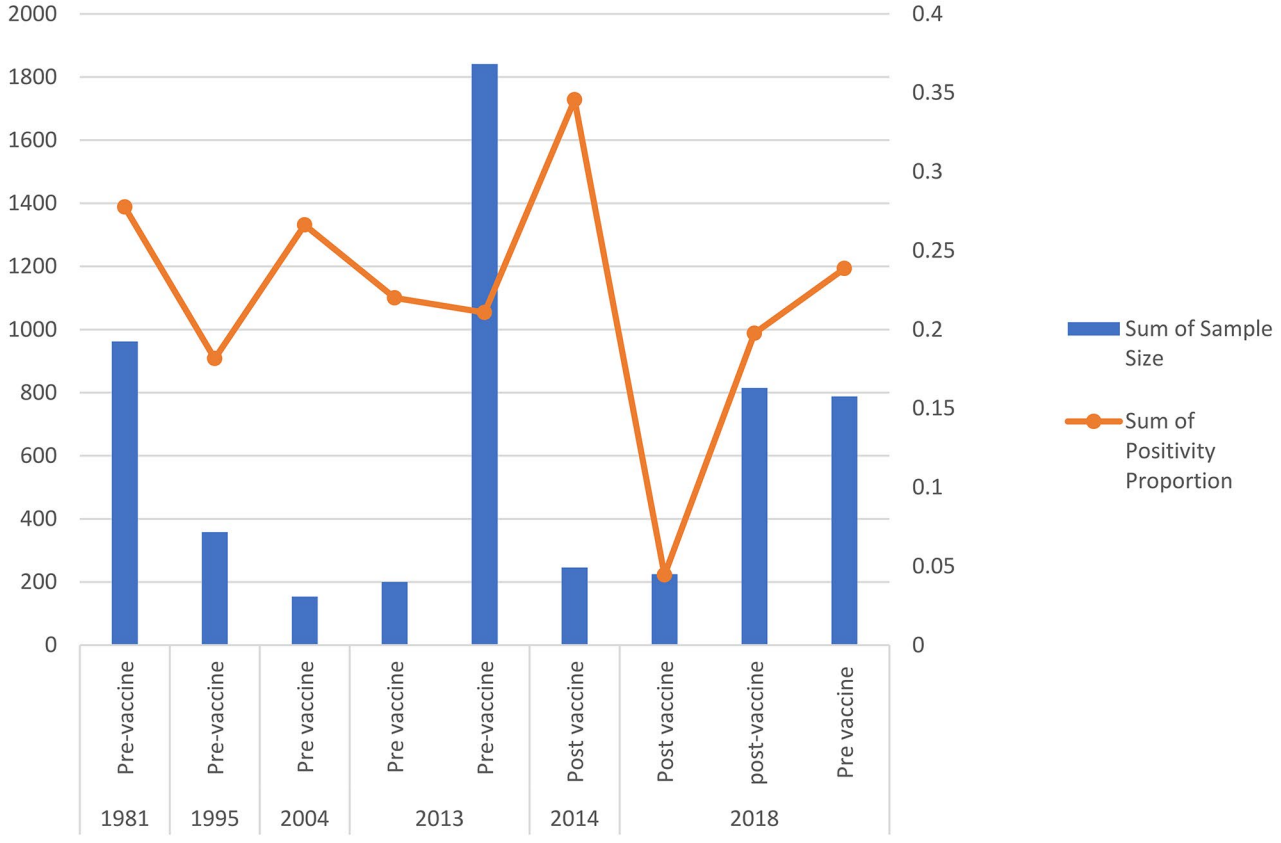


**Fig. 2** The positivity proportion of rotavirus cases at pre-vaccine and post-vaccine studies periods in Ethiopia

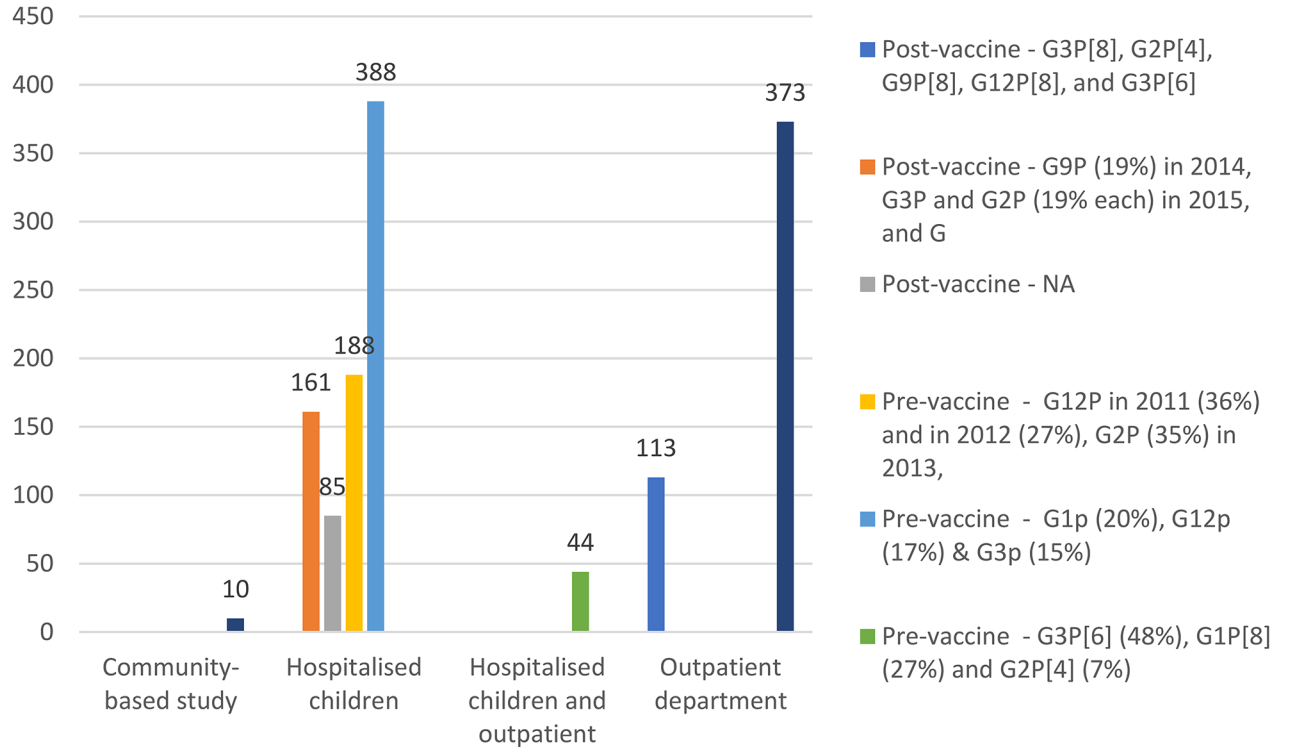


**Fig. 3** Genotype distribution by Rotavirus cases in the community, hospitalized and outpatient children during pre- and post-vaccine periods

G9P (19%) in 2014 and G3P and G2P (19% each) in 2015, which is a fluctuating trend in Rotavirus infections across different regions and years (Table 1).

The data is categorized by location: Addis Ababa, Awassa, Gondar and Bahir Dar, Jimma, and Wegera. Addis Ababa shows the highest number of cases, with peaks in 1981 (267 cases), 2013 (388 cases), and 2018 (349 cases). Awassa reported 44 cases in 2013. Gondar and Bahir Dar have significant cases in 2018 (113 cases). Jimma shows lower numbers, with 41 cases in 2004. Wegera presents minimal cases, with a notable report of 10 cases (Fig. 4).

The majority of studies used cross-sectional designs. Stintzing G. et al. conducted a survey in 1981 in Addis Ababa, which contained a sample size of 962. The number of rotavirus infections reported in this study was 267, and the lab method used was Immunoelectron microscopy (IEO). Getahun et al. conducted a survey in 2014 in Addis Ababa, with a sample size of 246, and found 85 Rotavirus infection cases. The lab method used in this study was EIA. Additional cross-sectional studies were conducted by Abebe et al. in 1995 and Bizuneh T et al. in 2004, both in Addis Ababa. Abebe et al.'s study included a sample size of 358, with a frequency of 65 rotavirus infection cases. The lab method used was ELISA. Bizuneh T et al.'s study included a smaller sample size of 154, with 41 rotavirus infection cases. The lab method used in this study was also ELISA.

Two more cross-sectional studies were conducted after the vaccine introduction. Feleke H et al. conducted a study in 2018 in Wegera woreda, Amhara region, with a sample size of 225, and reported a frequency of 10 rotavirus infection cases. The lab method used was ELISA. Similarly, Gelaw A et al. conducted a study in 2018 in the Amara region with a sample size of 450 and reported a frequency of 113 rotavirus infection cases. The lab method used in this study was reverse transcription polymerase chain reaction (RT-PCR), and the identified serotype distribution included G3P [8], G2P [4], G9P [8], 12P [8], and G3P [6].

Lastly, Yassin et al. conducted a cross-sectional study in Awassa in 2013, with a sample size of 200, and reported a frequency of 44 rotavirus infection cases. The lab method used in this study was RT-PCR, and the genotype distribution included G3P [6] (48%), G1P [8] (27%), and G2P [4] (7%).

This literature review examines the impact of rotavirus vaccination on the distribution of rotavirus genotypes in Ethiopia. The study findings indicate a notable shift in rotavirus genotype distribution in Ethiopia after introducing the vaccine in 2013. Pre-vaccine periods showed the prevalence of genotypes like G1p, G12p, G3p, and G2p, whereas post-vaccination samples displayed a shift

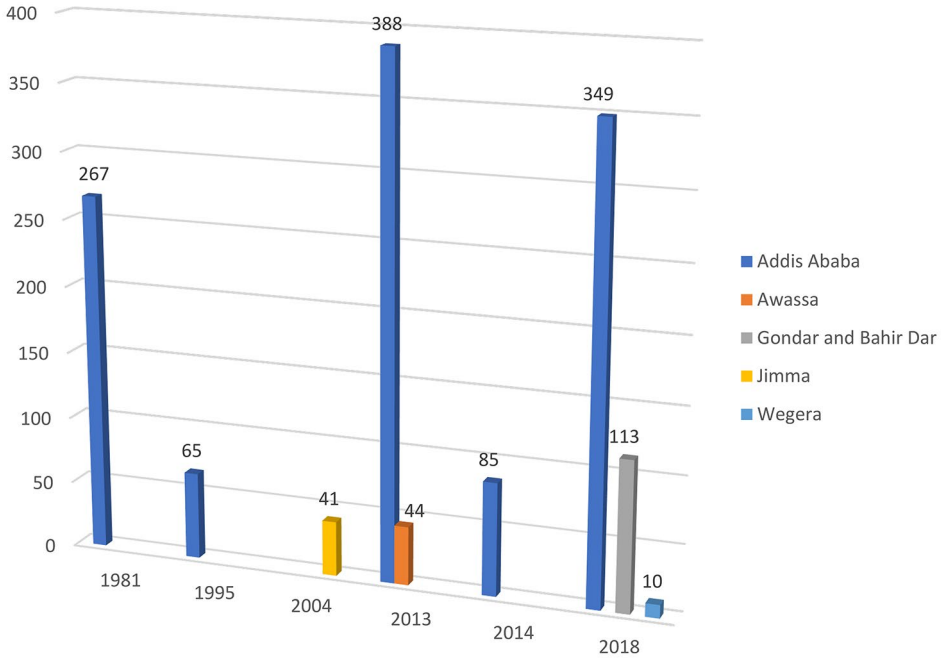


**Fig. 4** Illustrates the number of Rotavirus infection cases in different study areas during specific publication years from 1981 to 2018

to G9P, G3P, G2P, and G12P, with G3P [8] being the most common. This shift highlights the impact of vaccination on altering the predominant rotavirus genotypes.

The data we present here is a scientific observation and a call to action. It underscores the significant effect of vaccination on rotavirus infection patterns. The transition from pre-vaccine to post-vaccination periods demonstrates changes in the circulating genotypes, indicating the vaccine's effectiveness in influencing rotavirus genotype distribution in Ethiopia. These findings directly affect public health officials and researchers' efforts to combat the rotavirus.

The studies employed a rigorous methodology, utilizing various laboratory methods such as EIA, ELISA, and RT-PCR to identify rotavirus genotypes. This diverse approach in methods provides a comprehensive understanding of rotavirus epidemiology and genotype distribution in different regions of Ethiopia over time, ensuring the reliability and validity of our findings.

By analyzing data from 1981 to 2018, the study captures temporal trends in rotavirus genotype distribution, showcasing the evolution of prevalent genotypes before and after the vaccine's introduction. This longitudinal perspective offers valuable insights into Ethiopia's changing landscape of rotavirus infections.

Overall, the studies above provide essential data on the positive proportion of rotavirus, vaccination status, lab methods used, and genotype distribution in children under five years of age with diarrhea in various regions of Ethiopia. The findings contribute to our understanding of the epidemiology and characteristics of rotavirus infection in this population, which can inform public health interventions and strategies for prevention and control.

A summary review addressed a crucial understanding of the impact of rotavirus infection, assessing disease trends, and evaluating the effectiveness of interventions like vaccines in reducing the incidence of rotavirus-related illnesses in Ethiopia.

#### Meta-analysis

The systematic review and meta-analysis aimed to investigate the frequency, risk factors, genotype distribution by vaccination status, and age distribution of rotavirus infection with diarrhea in Ethiopia's children under five. The analysis included data from 9 studies, and both fixed and random effects models were used to estimate the effect size (Fig. 5).

In the fixed effects model, the overall effect size for Rotavirus infection in children under five with diarrhea was estimated to be 0.231 (95% CI: 0.221–0.242). This indicates a moderate prevalence of Rotavirus infection in this population. The null hypothesis test showed a significant association between Rotavirus infection and diarrhea in children under five (Z-value: -38.70, p-value: 2.18E-13).

Heterogeneity analysis revealed high heterogeneity among the included studies (Q-value: 79.35, df: 9, p-value: 8.16E-02, I-squared: 88.66%). This suggests that the variation in effect sizes across the studies is not solely due to chance. The estimated tau-squared value (0.286)

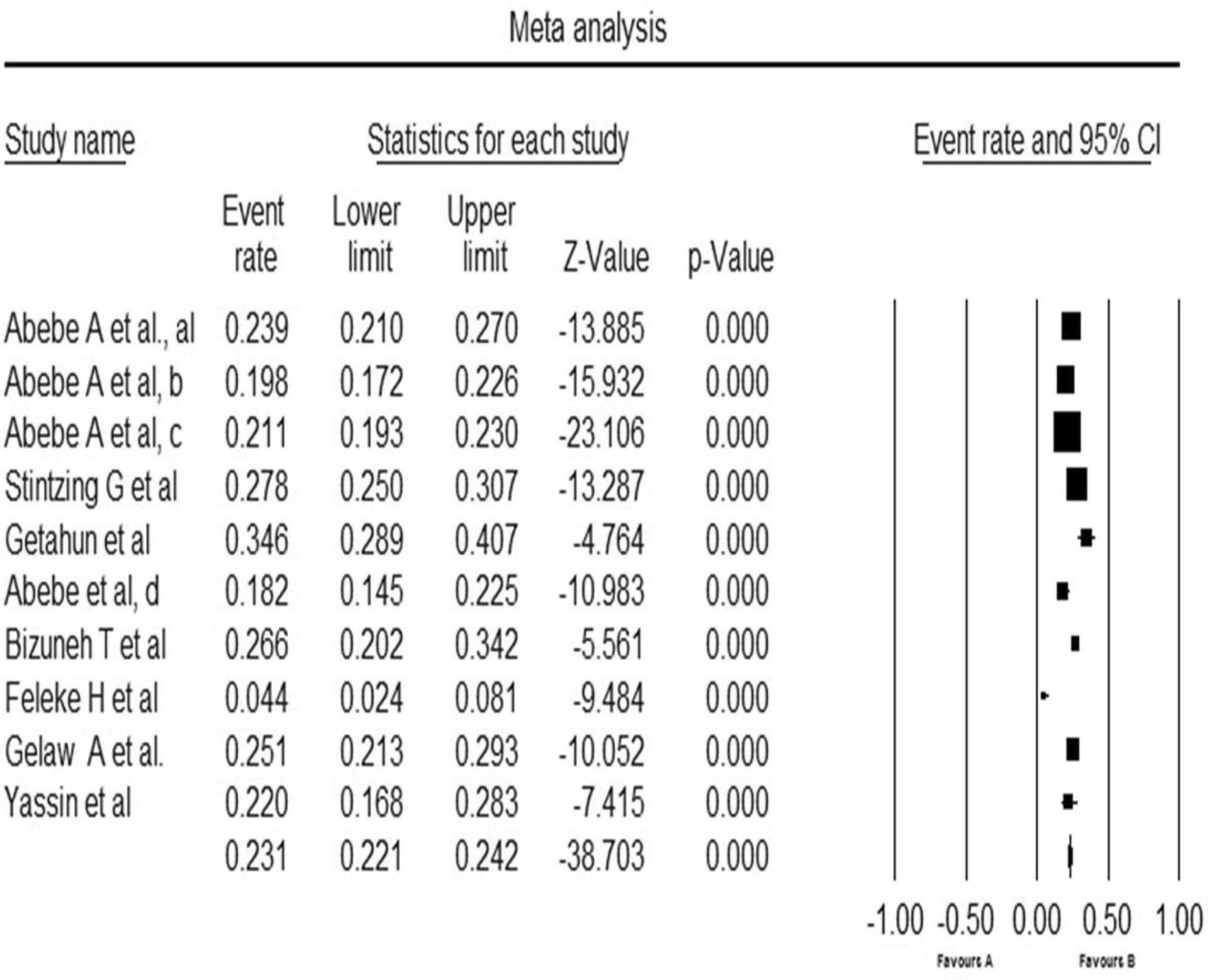


**Fig. 5** Rotavirus Infection in Pre- and Post-Vaccine Introduction in Ethiopia

indicates substantial heterogeneity beyond what would be expected by chance alone.

Given the high heterogeneity observed among the included studies in the analysis of Rotavirus infection in children under five, a fixed-effects model may not be appropriate. Fixed-effects models assume that the actual effect size is the same across all studies, which may need to be more accurate due to the substantial variation in effect sizes observed. In the presence of high heterogeneity, a random-effects model may be more suitable as it accounts for both within-study and between-study variability, providing a more robust estimate of the overall effect size. A random-effects model would better accommodate the observed heterogeneity and provide a more accurate representation of the actual underlying effect size across studies.

In the random effects model, the estimated effect size for rotavirus infection in children under five with diarrhea was slightly lower at 0.221 (95% CI: 0.189–0.257). Although the random effects model did not provide a p-value for the null hypothesis test, it can be inferred that there is still a significant association between rotavirus infection and diarrhea in this population (Fig. 5).

The findings suggest that rotavirus infection is a common cause of diarrhea in children under five in Ethiopia. The prevalence of rotavirus infection is moderate, indicating a need for preventive measures such as vaccination. The high heterogeneity observed among the studies highlights the need for further investigation into the factors contributing to the variation in effect sizes.

The results also indicate that the effect size estimates may vary depending on the model used. While the fixed effects model assumes a standard effect size across all studies, the random effects model accounts for both within-study and between-study variability. Therefore,

the random effects model may provide a more conservative estimate of the actual effect size.

Overall, this systematic review and meta-analysis provide valuable insights into the epidemiology of rotavirus infection in children under five with diarrhea in Ethiopia. The findings emphasize the importance of implementing effective vaccination strategies and identifying specific risk factors associated with rotavirus infection in this population. Further research is needed to understand the sources of heterogeneity better and to inform targeted interventions for preventing and controlling rotavirus infection in Ethiopia.

### Publication bias

The meta-analysis incorporated data from 9 studies categorized in 10 as pre-vaccine and post-vaccine studies, yielding a z-value of -36.19785 and a corresponding 2-tailed p-value of 0.00000. The Classic Fail-safe N for this meta-analysis is 3401, which means that 3401 additional 'null' studies would need to be located and included for the combined 2-tailed p-value to exceed 0.050. This indicates that for every observed study, there would need to be 340.1 missing studies for the effect to be nullified, suggesting the results are highly robust.

Egger's Test of the Intercept was also performed to assess publication bias. The intercept (B0) was found to be -1.61283, with a 95% confidence interval ranging from −7.10118 to 3.87552. The t-value was 0.67765 with 8 degrees of freedom. The 1-tailed p-value was 0.25855, and the 2-tailed p-value was 0.51711. These p-values are not statistically significant, indicating no significant evidence of publication bias according to Egger's test.

Furthermore, Duval and Tweedie's Trim and Fill method was applied. Under the fixed effect model, the combined studies' point estimate and 95% confidence interval were 0.23134 (0.22070, 0.24233). Using Trim and Fill, these values remained unchanged. Similarly, under the random effects model, the point estimate and 95% confidence interval were 0.22147 (0.18947, 0.25717), and these values also remained unchanged after applying Trim and Fill. This consistency suggests there is no significant publication bias affecting the results.

The funnel plot, which displays the standard error by logit event rate, is likely to show a symmetrical distribution given the results from Egger's Test and the Trim and Fill method (Fig. 6).

Overall, the meta-analysis demonstrates a robust effect with minimal evidence of publication bias. The high fail-safe N indicates the results are reliable and not easily nullified by potential missing studies.

## Discussion

Rotavirus infection poses a significant public health concern in low-income countries with poor socio-economic situations and a lack of appropriate sanitation, hygiene, and vaccination coverage. This systemic review and meta-analysis estimated the prevalence of rotavirus infection among children under five with diarrhea in

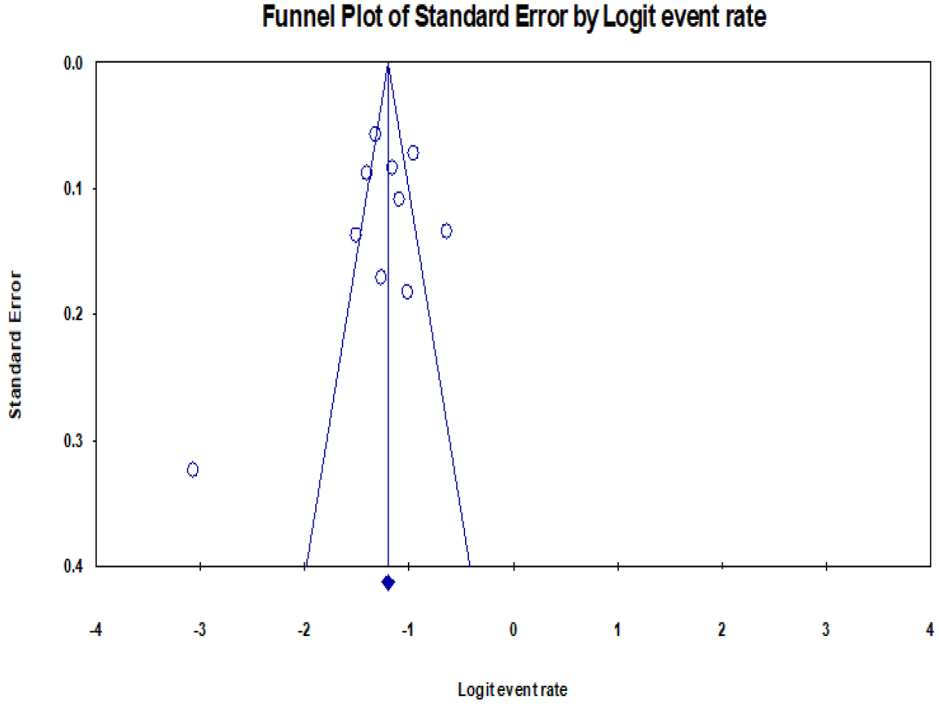


**Fig. 6** Forest plot

Ethiopia at 22.6%, highlighting the need for preventive measures such as vaccination. The obtained review data included cases from hospitalized children, community-based studies, and outpatient departments. However, data on mild cases (community-based study and outpatient department) are fewer, which suggests that the findings may only partially represent the broader spectrum of rotavirus infection severity in the population. This limitation may be considered when interpreting the results and their implications for public health strategies (Table 1; Fig. 3).

Hospitalized children from 2013 onwards were not exclusively vaccinated cohorts; the data includes pre- and post-vaccine cases. The data primarily focuses on rotavirus infection cases, sample sizes, vaccination statuses (pre- and post-vaccine), and genotype distributions without specific details on vaccination cohorts beyond 2013. The identified genotypes, including G1, G2, G3, G12, P [4], P [6], P [8], P [9], and P [10], provide insights into the circulating strains of Rotavirus in Ethiopia. Some surveillance studies also observed similar study results [17, 18].

#### Analysis of genotype variations in Rotavirus infections pre- and post-vaccination in Ethiopia

**Pre-vaccination Period** Before introducing the rotavirus vaccine on June 13, 2013, the predominant genotypes identified in various studies were G1, G12, G3, and G2. For instance, in Addis Ababa, sentinel surveillance data from 2013 showed the prevalence of G1P (20%), G12P (17%), and G3P (15%). In Awassa, the genotypes G3P[6] (48%), G1P[8] (27%), and G2P[4] (7%) were common.

**Post-vaccination Period** The most striking observation was the significant shift in genotype distribution following the introduction of the vaccine. The previously dominant genotypes G1, G12, G3, and G2 were replaced by G9P, G3P, G2P, and G12P. For instance, in Addis Ababa, the post-vaccination data from 2014 to 2015 revealed a dramatic change in the prevalence of genotypes. 2014 G9P emerged as the most common (19%), but in 2015, G3P and G2P (19% each) took the lead. Similarly, in Gondar and Bahir Dar, the genotypes G3P [8], G2P [4], G9P [8], G12P [8], and G3P [6] were prevalent in 2018.

**Year-by-year genotype distribution**:

- **2011–2013 (Pre-Vaccine)**: In Addis Ababa, G12P was prevalent in 2011 (36%) and 2012 (27%), while G2P was dominant in 2013 (35%).
- **2014–2015 (Post-Vaccine)**: The post-vaccination period in Addis Ababa saw a dynamic change in genotype prevalence. 2014, G9P was the most common (19%), but in 2015, G3P and G2P emerged as equally prevalent (19% each), marking a significant shift in just a year.
- **2018 (Post-Vaccine)**: In Gondar and Bahir Dar, the genotypes G3P[8], G2P[4], G9P[8], G12P[8], and G3P[6] were identified.

In summary, the introduction of the rotavirus vaccine in Ethiopia has had a profound impact on the genotype distribution of rotavirus infections. The pre-vaccination period was characterized by the dominance of genotypes G1, G12, G3, and G2, while the post-vaccination period witnessed a shift towards genotypes G9P, G3P, G2P, and G12P, with G3P[8] being notably common. This shift underscores the significant role of vaccination in shaping the epidemiology of rotavirus genotypes in the region (Fig. 3).

This systematic review and meta-analysis provide essential insights into the prevalence, genotype distribution, and risk factors of rotavirus infection in children under five in Ethiopia. The identified genotypes, including G1, G2, G3, G12, P [4], P [6], P [8], P [9], and P [10], highlight the diversity of rotavirus strains circulating in Ethiopia. Other studies in different regions have also reported these genotypes, emphasizing their global significance [17, 19].

The G3 genotype was particularly prevalent, accounting for 27.1% of cases, followed by the P [8] genotype at 49%. These findings are consistent with previous studies that have reported the predominance of G3 and P [8] genotypes in rotavirus infections [20, 21].

The prevalence of specific genotypes can have implications for vaccine development and effectiveness. For instance, the G12P [8] combination, identified as one of the most common genotypes in this study, has been associated with reduced vaccine effectiveness in some settings [22]. Therefore, monitoring the prevalence and distribution of genotypes is crucial for informing vaccine strategies and ensuring their optimal impact.

This systematic review and meta-analysis provide valuable insights into the prevalence, genotype distribution, and risk factors of rotavirus infection in children under five in Ethiopia. The findings underscore the importance of vaccination and ongoing surveillance to reduce this population's rotavirus-related morbidity and mortality burden [23, 24].

However, it is important to note that this study has some limitations. The high heterogeneity observed among the included studies suggests potential variations in study design, population characteristics, and diagnostic methods. Additionally, the limited number of studies available for inclusion may only partially represent part of the population of Ethiopia.

This systematic review and meta-analysis provide valuable insights into the prevalence, genotype distribution, and risk factors of rotavirus infection in children under five in Ethiopia. The findings underscore the importance

of vaccination and ongoing surveillance to reduce this population's rotavirus-related morbidity and mortality burden.

### Limitations

Among the limitations observed in this review is that there needs to be more sufficient data showing genotypes responsible for mechanisms of rotavirus infection in the included studies. In addition, these studies were limited to a few places, which didn't reveal the actual figure for the distribution of rotavirus infection in Ethiopia. The studies' limitations include focusing on specific regions like Addis Ababa and Awassa in Ethiopia, potentially limiting the findings' generalizability. Another limitation is the reliance on different laboratory methods, such as EIA, ELISA, and RT-PCR, across studies, which may introduce variability in the results. Additionally, the sample sizes varied between studies, which could impact the statistical power and precision of the results. A larger sample size generally leads to more robust and statistically significant results, providing greater confidence in the study's conclusions regarding rotavirus infection and vaccine efficacy.

### Conclusion and recommendations

In conclusion, the systematic review and meta-analysis of rotavirus infection in children under five in Ethiopia revealed a moderate prevalence of rotavirus infection in this population. Overall, the stratified analysis demonstrates that the introduction of rotavirus vaccines in Ethiopia has significantly reduced the positivity proportion of rotavirus infections, particularly in the years following the vaccine's implementation. However, this success should not lead to complacency. Continued monitoring and evaluation of the vaccination program are important to ensure its ongoing effectiveness and address any emerging challenges in controlling rotavirus infections in the future. This is a collective responsibility that we all share in the public health community, and it is crucial that we all actively participate in maintaining the success of the vaccination program. The genotype distribution was diverse, with G1, G2, G3, G12, P [4], P [6], P [8], P [9], and P [10] being the most common genotypes identified. The pooled prevalence of rotavirus infection was approximately 23%, with the G3 and P [8] genotypes being particularly prevalent. The findings underscore the importance of implementing preventive measures, such as vaccination, to reduce the burden of rotavirus infection in children under five years of age in Ethiopia. The identified genotypes provide valuable insights for vaccine development and targeted interventions. Water supply contamination, inadequate sanitation, and poor water quality can contribute to the spreading of rotavirus infection. Contaminated water sources can harbor the virus, leading to potential infections when children are consumed or used for hygiene. Proper water treatment and sanitation practices are essential to prevent rotavirus transmission and other waterborne diseases. Further studies are needed to address additional risk factors associated with rotavirus infection, better understand the observed heterogeneity among the included studies, and understand the burden of rotavirus infection, especially among children under five. Overall, this study contributes to the evidence base for public health interventions and strategies to reduce the impact of rotavirus infection in Ethiopia.

#### Abbreviations

| | |
|---|---|
| EIA | Enzyme Immunoassay |
| ELISA | Enzyme-Linked Immunosorbent Assay |
| IEO | Immunoelectro-osmophoresis |
| JBI | Joanna Briggs Institute |
| RT-PCR | Real-time Polymerase reaction |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-024-09754-7.

Supplementary Material 1

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#### Author contributions

WT outlined the review work, developed the protocol, oversaw the research process, and facilitated communication and manuscript submission; WT, BT, and DE worked on screening, extracting, data quality checking, analysis, and writing.

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#### Data availability

The datasets used and analyzed in the study are available from the corresponding author on reasonable request.

## Declarations

#### Ethics approval and consent to participate

Not applicable.

#### Consent for publication

Not applicable.

#### Competing interests

The authors affirm that they do not have any competing interests.

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## Publisher's note