

Pertussis outbreak in Southern Ethiopia: challenges of detection, management and response

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Abstract

Background: Despite the availability of effective vaccines, pertussis remains endemic with high fatality rates in low and middle-income countries (LMIC). This study aims to describe an outbreak of pertussis in a health district of Ethiopia. The study highlights the challenges faced by the health system in identifying pertussis cases and appropriately responding to the outbreak at the district level.

Methods: a descriptive cross-sectional study was conducted using data sourced from the District Public Health Emergency and Management (PHEM) surveillance service and outbreak management field reports. Stratified attack rates and fatality rates for pertussis are described. Systemic problems leading to the outbreak are explored and narrated. A modified CDC pertussis case definition was employed with a polymerase chain reaction used to confirm cases.

Results: From September 2018 to January 2019, 1840 suspected, probable, and confirmed pertussis cases and six deaths were identified. Pertussis cases ranged from 1 month to 51 years in age and an outbreak occurred in 14 out of the 24 villages of Dara Malo district. The overall attack rate was 1708 per 100,000 population with a fatality rate of 3.3 per 1,000 pertussis cases. The highest attack rate of 12,689/100,000 was seen in infants. Among confirmed, probable and suspected pertussis cases, only 41.1% had completed the three-dose pertussis vaccine's primary schedule. The household survey revealed the population coverage of 73.4% and 40.8% for Pentavalent vaccine dose one and three respectively. Investigations suggested the existence of a poor cold chain management system in the study area.

Conclusions: There is an urgent need to build capacity to strengthen routine vaccination services and improving the maintenance of the vaccine cold chain. Other Low-and Middle -Income Countries (LMICs), are urged to take lessons learned from this outbreak and strengthen their own vaccination programs and capacitate health workers to manage local outbreaks.

Background

Pertussis is an extremely infectious vaccine-preventable disease caused by the gram-negative coccobacillus, *Bordetella pertussis*, and less commonly by *Bordetella parapertussis* [1]. Pertussis remains endemic and has reemerged as a public health problem in many countries despite decades of high vaccination coverage in infants [2]. Pertussis is widely distributed in many countries throughout the world. Globally, around 24.1 million pertussis cases and 160,700 deaths from pertussis were reported in children younger than five years in 2014. The African region contributed the largest proportion with 7.8 million (33%) cases and 92,500 (58%) deaths. Infants and young children have remained most susceptible to pertussis-related morbidity and mortality. Around 5.1 million (21%) estimated pertussis cases and 85,900 (53%) estimated deaths were in infants younger than one year [3, 4].

In children, pertussis presents classically with paroxysms of cough ending with the characteristic whoop and post-tussive vomiting. However, in young infants, pertussis can initially present as apneic or cyanotic episodes prior to the development of cough [5]. The mode of transmission is person-to-person via aerosolized respiratory droplets or by direct contact with respiratory secretions. In its early catarrhal stage, pertussis is highly contagious, with a secondary attack rate of up to 90% among non-immune household contacts. Untreated patients may transmit infection for up to three weeks or more following the onset of typical coughing attacks, although communicability diminishes rapidly after the catarrhal stage [6].

The most common complication and the cause of most pertussis-related death is secondary bacterial pneumonia. Young infants are at the highest risk of acquiring pertussis-associated complications [7]. Adolescents and adults are an important reservoir for *B. pertussis* and are often the source of infection for children [8, 9].

Vaccination is the best way to prevent pertussis in all age groups [10]. Evidence suggests that high coverage with highly efficacious vaccines leads to high levels of protection in children under five years of age. In contrast, even minor reductions in overall coverage can lead to an increase in cases [11]. Completion of a three-dose pertussis-containing vaccine schedule prevents 80% of cases and 95% deaths. Incomplete immunization has been shown to prevent severe morbidity with one dose and two doses decreasing mortality by 50% and 80%, respectively [12, 13].

In Ethiopia, a pertussis whole-cell vaccine (wP) has been in use since 1980 [14]. From 2007 this has been in the form of a pentavalent that in addition to pertussis whole-cell vaccine, also contains Diphtheria, Tetanus, Hepatitis B, and *Haemophilus influenzae* type B (DTP-HepB1-Hib1) vaccines. The pentavalent vaccine is given three doses scheduled at 6, 10, and 14 weeks of birth [14, 15].

Based on World Health Organization (WHO) estimates the Ethiopian national coverage of one dose of pertussis-containing vaccines in 2018 was 85% while that of three doses was 72% which is less than the average coverage for Sub Saharan countries [10]. This

immunization coverage differs greatly between districts and regions of Ethiopia with coverages of 3 doses of pentavalent ranging from 20.1% in Afar to 81.4% in Tigray. The difference in vaccine coverage is partly due to geographical inaccessibility and other social determinants [16]. However, according to the routine health management information system (RHMIS) report, the Dara Malo district health officials reported a higher vaccine coverage for the third pentavalent dose to be 103.0% in 2016/2017 and 94.8% in 2017/2018. The pentavalent vaccine dropout rates were 3.0% and 3.4% respectively over the same period [17].

Uncoordinated and poor epidemic response mechanism is a challenge in containing epidemics, reducing morbidity, mortality, and economic loss in different countries. Diagnosis of pertussis, which is largely based on the clinical picture, may be modified by age, history of previous immunization or infection, antibiotic exposure, and concurrent infection with other pathogens [18]. According to the WHO vaccine-preventable diseases 2019 global summary report there were no reported pertussis cases from 2000 to 2017 in Ethiopia. In 2018, however, there were 2423 cases of pertussis reported in Ethiopia [15]. WHO data is further corroborated by independent data sources that indicated the occurrence of cases of pertussis in Ethiopia [19, 20].

This study aimed to describe an outbreak of pertussis in the Dara Malo district of Gamo Administrative Zone, Southern Ethiopia, and to investigate possible factors that may have led to the outbreak. In addition, the study explores and highlights the challenges faced by a low and middle-income country's (LMIC) health care system in case identification and management in response to a pertussis outbreak.

Methods

Study area and population

Dara Malo is one of 160 districts administered under Southern Nations, Nationalities and Peoples Region (SNNPR), Ethiopia. The district has 24 administrative structures consisting of one urban and 23 rural villages [17]. Based on the 2007 Ethiopian national census, the projected population of Dara Malo district in 2018 was 107,715 with 16,814 under five and 3,436 under one year of age [17].

Study design and sampling methods

The study employed a cross-sectional descriptive study design. Data were sourced from the Public Health Emergency and Management (PHEM) database that includes surveillance data on pertussis. Available data included information on age, sex, geographical location, immunization status, dates of onset and health facility visits, treatment received, and outcomes of reported pertussis cases. In addition, the study reviews availability data to explore the cause of the outbreak in terms of a functional cold chain, vaccines, and supplies system at the targeted health facilities and district health office.

All surveillance records collected from 1st September 2018 to 9th January 2019 were reviewed to identify all documented suspected, probable, and confirmed pertussis cases during the period. Health records were reviewed for each of these cases.

The sample size (n) for household survey was calculated using single population formula:(see Formula 1 in the Supplementary Files)

Where n is sample size, P is the proportion of third dose pentavalent vaccination coverage [22], and d is the margin of error.

The following assumption was used: since P is 0.53% ($p=0.53$, $q=0.47$), allowing 5% for expected margin of error (d) with 95% confidence level ($Z_{\alpha/2}=1.96$), considering a design effect of 1.5 and 10% for non-response rate the required sample size n is **631**. After allocating the required sample size for each village using probability populational to size sampling method, primary data were collected from households selected using systematic random sampling technique.

Data collection

In the pertussis case review component of the study, socio-demographic variables, immunization related information of the children, dates of onset and health facility visits, treatment received, and its outcome were addressed from the line list. In addition, to verify the reported immunization coverage household survey was conducted to collect primary data on vaccination status of children 5 to 23 months.

The data were collected by four trained health professionals, each with a master's degree in public health (MPH) and had the experience of reviewing documents. In addition, project advisors and program officers from Transform: Primary Health Care (TPHC), a USAID program, oversaw the quality of collected data.

The quality of data was assured first by providing training to the data collectors and their supervisors. At the end of every data collection day, a meeting was held between the data collectors and a supervisor to discuss practical problems and issues of major concern. The investigators rechecked the completeness of the collected data on a daily bases.

Case definition

To confirm pertussis nasopharyngeal samples were taken from suspected cases by experienced laboratory professionals from the Ethiopian Public Health Institutes and tested using polymerase chain reaction (PCR) for *Bordetella pertussis* and *Bordetella parapertussis* (RealStar® Bordetella PCR Kit 1.0. Altona Diagnostics). Suspected cases with paroxysmal cough illness for more than 2 weeks were assessed for possible epidemiological links to cases confirmed by a positive PCR for *Bordetella pertussis*. Pertussis cases reported to the district health office PHEM department were classified by the outbreak investigation team as laboratory-confirmed, probable, or suspected pertussis using modified Center for Diseases Prevention and Control (CDC) criteria [23].

Confirmed: A confirmed pertussis case is defined as acute cough illness of any duration with a positive PCR for *B. pertussis*, or a case that meets the clinical case definition and is epidemiologically linked directly to a lab-confirmed case [23-24]. In this study, the confirmed pertussis case is an acute cough illness of any duration with a positive PCR for *B. pertussis*.

Probable: A probable case is defined as a cough lasting ≥ 2 weeks AND paroxysms of coughing, inspiratory “whoop” or post-tussive vomiting AND No laboratory confirmation AND No epidemiologic linkage to a lab-confirmed case. In this study, probable pertussis case is a case Cough lasting ≥ 2 weeks AND Paroxysms of coughing, inspiratory “whoop” or post-tussive vomiting, AND No laboratory confirmation [23-24].

Suspected: A suspected case is defined as a non-improving cough of 14 days or more or cough of any duration with paroxysms, or cough of any duration with a whoop.

An epidemic of pertussis: According to the CDC pertussis epidemic is defined as a situation when two or more cases clustered in time.

- ≥ 2 PCR confirmed cases clustered in time (within 42 days of each other) and space (e.g. in one building) where transmission is suspected to have occurred in that setting (e.g. nosocomial transmission in a hospital) OR
- 1 PCR confirmed case AND 1 epi-linked case with cough illness lasting ≥ 2 weeks with one of the following: paroxysms of cough, inspiratory whoop, or post-tussive vomiting [23-24].

Data management and analysis

The data were collected in a spreadsheet, cleaned, summarized, and analyzed using Microsoft Excel® and Statistical Packaged for Social Sciences Research (SPSS IBM V 20) [25].

Proportions of cases have been presented as percentages. All continuous data were summarized using medians and ranges. The frequency of cases was reported as a case attack per 100,000 population using the 2018 population for Dara Malo as the denominator, while deaths were reported as fatality rates per 1000 cases. Epidemic curves were depicted using the date of onset of paroxysmal cough and date cases were identified by health workers. This analysis shows the propagated nature of the outbreak. Data were reported stratified by age groups and geographical locations and described in terms of time, place, and person.

The data of household survey were used to determine population immunization coverage and to verify the accuracy of routine EPI reports. The first and third doses of pentavalent vaccination were recounted from the register, tally sheet, and compared against caretakers' report. To characterize the report consistency, national recommended categories were used i.e. consistent if the ratio reported was ≥ 90.0 and $<110.0\%$; overreported if it was $<90.0\%$; and underreported if the ratio was $\geq 110.0\%$ [26].

The result of the quantitative analysis is presented in frequency tables and graphs. In addition, the findings of filed reports and observations were thematically analyzed to explain possible factors for the reported pertussis outbreak.

In addition, using ArcView GIS (Ver 10) a spatial analysis was made to show most affected villages using attack rates and case-fatality rates.

Ethical clearance

Ethical clearance was obtained from both JSI Research & Training Institute, Inc., and the SNNPR Health Bureau, Ethiopia, Institute Review Boards (IRBs). Permission to conduct the study was obtained from facility managers.

Results

Rumor investigation

On 31st August 2018, a community member reported the death of a 72 months old girl with a history of prolonged paroxysmal cough, post-tussive vomiting, and respiratory whoops. Three more children had died earlier in the month in the same village where a similar illness had been observed in August 2018 affecting almost all children in the village.

On September 1st, 2018, the Dara Malo district Health Office revitalized the rapid response multi-sectoral committee and reviewed its Risk and Emergency Management Plan. On the same date, the district health office request technical, and other resources support from Gamo Zone Health Departments, SNNP regional health bureau, Ethiopian Public Health Institute (EPHI), World Health Organization, USAID's Transform: PHC Activity and other development partners.

The PHEM core process established and deployed an epidemic investigation team which comprised a field epidemiologist, an integrated disease surveillance response officer, and health extension workers. The team members were oriented on the case definitions, diagnosis and treatment protocols, strengthening community-based surveillance, and enhancing community mobilization strategies.

Verifying the pertussis outbreak

The index case, a five-year-old child with unknown vaccination status was identified from Daro Dime village on 1st September 2018. Reported pertussis suspected case presented at Daro Dime Health Center with a complaint of paroxysmal cough, post-tussive vomiting, and respiratory whoop since 2nd August 2018. The source of infection for the index cases was not documented. The case was treated with trimethoprim-sulfamethoxazole (TMP- SMZ) with a dose of trimethoprim 8 mg/kg/day, sulfamethoxazole 40 mg/kg/day in two divided doses for 14 days. The outbreak investigation team regards this probable case as the index case of the current pertussis outbreak. The case had a cough of more than two weeks, with an inspiratory whoop and post-tussive vomiting. The district health office and Daro Dime Health Center instituted an active case search from 4th to 13th September 2018. Over the period, 471 suspected and probable pertussis cases were identified in five kebeles. The outbreak investigation team-oriented community leaders, health workers, and elders. The active case search was extended through 27th March 2019. Over the whole surveillance period, a total of 1840 suspected, probable, and confirmed pertussis cases including six deaths, were identified.

Descriptive analysis of Reported Pertussis Outbreak

The pertussis outbreak of the line-list is described in terms of time, place, and person.

Demographic distribution of the cases

From 1st September 2018 to 9th January 2019, there were a total of 1840 reported cases of pertussis. Of the reported cases 9 (0.5%) were confirmed (all due to *Bordetella pertussis*) while 454 (24.7%) were probable cases and the rest of 1377(74.8%) suspected cases. The socio-demographic characteristics of the study participants are shown in Table I. Dara Dime village reported 838 (45.5%) of the pertussis cases. The age of the cases ranged from 1 month to 50 years of age with a median of 36 months. Of the total cases, 230 (12.5%) were aged less than six months while 801 (42.5%) were 1 to 4 years old Table 1.

Table 1: Demographic characteristics of pertussis cases in Dara Malo District

Variable	Characteristics	n =1840(%)	Total population
Sex	Male	883 (48.0)	54935
	Female	957(52.0)	52780
Age groups	≤ 5 months	230 (12.5)	1615
	6 - 11 months	206 (11.2)	1821
	1 - 4 years	801 (43.5)	13378
	5- 9 years	457 (24.8)	14603
	10 -14 years	136 (7.4)	13388
	≥ 15 years	10 (0.5)	62910
	Mean ± SD= 45.4± 42.8 months; median = 36 months; and range = 599 months		

The overall attack rate was 1,708/100,000. The attack rates by age category were 12,689/100,000, 5,965/100,000, and 667/100,000 reported in under one-year infants, 1 to 4 years children, and 5 or more years of children and adults, respectively (Additional file 1).

A total of six deaths due to pertussis were reported to give a total case fatality rate of 3.3 deaths per 1000 cases. These include five deaths from Dara Dime and one death from Menena Aba kebele. Two deaths each were under 6 months, and between 6 to 12 months. One death each was from 1 to 4 years and 5 to 9 years. The highest case fatality rate was found among infants less than 5 months of age with a case fatality rate of 8.7/1000 cases, followed by infants aged 6 to 11 months with 4.85/1000 cases (Figure 1).

Clinical presentation

The most frequent presentation was paroxysmal cough which was a complaint in all 1840 (100.0%) cases. This was followed by post-tussive vomiting which was reported in 1579 (85.8%). Inspiratory whoop was reported in 454 (24.7%) while 136 (7.4%) had a low-grade fever. In addition, 37(2.0%) of the cases had additional signs and symptoms indicative of severe illness. The most frequently reported signs of severity were syncope and apnea in eight (21.6%) and six (16.2%) cases, respectively Figure 2.

Descriptive Analysis by Time

Figure 3 below presents the Epi-Curve which plots the frequency of pertussis cases over time by date of onset of paroxysmal cough and date cases identified by health workers, respectively. The epi-curve presented below clearly demonstrates the classic propagated or progressive source nature of pertussis outbreak, where three peaks observed over time. The mean delay to seek medical care by patients or caretakers was 9.4 days, with a median of 7 days ranged from one day up to 63 days.

Geographical distribution of the outbreak cases

The highest attack rate was reported from Dara Dime village while the highest case fatality rate was noted in *Menena Aba* village. Figure 4 depicts ArcView GIS spatial analysis pertussis case attack rates and case fatality rates by a village.

Vaccination status

The vaccination status of pertussis cases was collected from reviewed EPI registers at health posts and oral reports of family members or caretakers. The number of cases who had received a pertussis-containing vaccine was found to be 169 (9.2%), 321 (17.4%), and 761 (41.4%) for one dose, two doses, and three doses, respectively. Of the rest of the reported pertussis cases, 232 (12.6%) had not received any vaccine dose while 357 (19.4%) had unknown immunization status. For individuals who received three doses of the pentavalent, a median of 41 (Interquartile range 19 - 67) months had elapsed between the last dose and the current illness.

Management of the pertussis outbreak

There were delays in notification and lack of timely proper management of probable or suspected pertussis cases in the community. The health workers were treating cases as pneumonia, pertussis was never suspected until the death of four children occurred due to the outbreak.

The outbreak response team lobbied community leaders and elders to mobilize the community to report cough of 2 weeks or more to nearby health posts. Information leaflets were developed and distributed to all household members using the local language, Gamo.

Individual cases were treated with antibiotics to reduce the severity and duration of symptoms, and to prevent complications. From 1st September to 22nd December 2018, 1832 (99.5%) of the identified pertussis cases were treated with amoxicillin, cotrimoxazole, or erythromycin. The outbreak response was hindered by a lack of sufficient erythromycin syrup doses for children under five years of age.

In order to reduce the spread of infection, a Mass Drug Administration (MDA) program was initiated following a facilitated two days training for 110 health workers including 90 drug distributors, 17 supervisors, and three district coordinators. The MDA was conducted from 23- 27 December 2018 using Azithromycin with a dose of 10 mg/kg/24hr, P.O. once under the direct supervision of health workers on the first day followed by 5mg/kg/24hr, P.O. from 2nd to 5th day. This prophylactic mass campaign targeted 69,587 residents of the 14 pertussis-affected villages. Directly observed azithromycin therapy was received by 67236 (96.6%) people under the supervision of health care providers. Among these, 21,003 (31.2%) were under 10 years of age. The campaign required \$18325.00 USD of investment from the district health office and partners for its successful implementation.

Prevention of spread of infection

EPI register reviews and oral responses of patients or caretakers were counted and mapped for supplementary immunization campaigns. After completing prophylactic antibiotic treatment with azithromycin, the outbreak management team organized a pentavalent vaccination campaign from 24th – 28th January 2019. Three supplementary immunization campaigns were organized and children less than two years were vaccinated including 1697 who received their first dose, 2564-second dose, and 3287 the third dose of pertussis-containing vaccine.

All schools were closed for the period of mass preventive prophylaxis campaigns while community members were advised to avoid participating in local markets. In addition, community members were advised to implement strict personal hygiene including frequent hand washing and avoiding contact with pertussis suspected individual.

Following the last reported case, the District Health Office continued active case search for more than two months on a daily bases. The outreach investigation team continued to provide support for individual case management, mass health education for community members, and enhance the capacity of health workers on cold chain management, defaulter tracing, and use of data for decision making. After no further cases of pertussis were reported from 10th January to 27th March 2019, the investigation team was demobilized.

Formulate the hypothesis

The outbreak investigation team reviewed the surveillance reports filled by four health centers and fourteen health posts and six private health facilities and organized by Dara Malo District Health Office. Based on the routine surveillance report, the completeness rate was assessed as high with a completeness rate of 84.0% in 2016/17; 88.0% in 2017/2018; and 91.0% in 2018/2019. In addition, housing conditions, vaccine potency, and vaccination coverage status of affected community were identified as a major factor contributing to the pertussis outbreak occurrence.

Pentavalent vaccination coverage

Three hundred- and thirty-six facility months' data were extracted. In addition, 595 children aged 7 - 23 months, with a response rate of 94.3%, were assessed and compared for immunization status between register, tallies and immunization card or through caretakers' oral report on household surveys. The household survey revealed a 73.4% and 40.8% vaccination coverage for pentavalent one and three doses, respectively. At the district level, the proportion of the re-counted vaccination data on EPI registers for the first and third doses of pentavalent were 95.2%, and 104.2% respectively. The ratio of vaccination data compared using tallies against the reports had evidences of overreporting which were 50.8%, for pentavalent 1 and 45.1% for pentavalent 3 doses (Figure 5).

Environmental factors

The housing condition and family size per household were assessed. The average house in the affected community had 7 people and lacked air circulation. Community members were encouraged to open ventilate their homes.

Cold chain, immunization services management

Wacha Health Center has a high-tension electric power supply. Three out of four health centers have solar panels to get un-interrupted electric power for cold chain maintenance. All fourteen health posts were collecting vaccines on scheduled vaccination campaigns and outreach services. The investigation team did not find continuously recorded temperature monitoring tools. And the observed vaccine vial monitor (VVM) which is a thermochromic label on vials, revealed that the vaccines were kept at temperatures that do not preserve vaccine potency. Overall cold chain maintenance was generally found to be poor.

Discussion

This study confirms pertussis that occurred between September 2018 and March 2019, in Dara Malo, a district in Southern Ethiopia. Pertussis outbreak cases occurred in 14 of 24 villages in the district and involved 1840 cases with six deaths. Pertussis is one of the under-reported major causes of morbidity and mortality among children in many low-income countries [3]. This report confirms the importance of strengthening community-based active surveillance programs and the need to enhance the capacity of community health workers in identifying pertussis suspected cases as well as providing a prompt effective response to any outbreaks [27, 28].

The current outbreak could have been the result of poor vaccination coverage, a non-functional cold chain management system combined with a lack of standardized national pertussis responsiveness, and management guidelines. Although almost 90% of cases were older than 5 months, only 41% of them had received the three doses of a pertussis-containing vaccine as would have been appropriate for age. This

report was in line with the population coverage revealed through household survey. In addition, there had been a long interval between the third pertussis vaccine dose and acquiring infection (median of 41 months); hence, the outbreak might have occurred as a result of waning vaccine acquired immunity overtime [29 - 31].

Though the district health officials confirmed the presence of high rate of community-based surveillance weekly report on public health notifiable diseases for over one year, the health systems did not identify the unusual health condition occurred in Dara Malo district. This finding might be occurred due to the limited capacity of the health care system in identifying risks, developing emergency preparedness plans, diagnosis and treatment of individual cases, prompt response, and management capacity.

The signs and symptoms for both uncomplicated and severe cases were consistent with either of CDC or WHO pertussis case definitions, proposed to report for pertussis suspected cases. The cause of this outbreak was *Bordetella pertussis*, which was a laboratory-confirmed causative agent using PCR. The overall pertussis case attack rate of 1,708 per 100,000 inhabitants of Dara Malo district was much higher than previously documented pertussis attack rate of 130 per 100,000 population reported in South Wollo, North Eastern Ethiopia in 2017 [19] or the 400 per 100,000 population reported in Papua New Guinea in 2012 [32]. The high attack rate documented in this investigation could be due to the case definition which includes confirmed, probable, and suspected cases. Once laboratory confirmation of the outbreak was made, subsequent cases were clinically diagnosed, a practice that is different from other studies, in particular those from high-income countries, in which only laboratory-confirmed and epidemiologically linked cases are considered. The highly sensitive case definition used would also have led to a relatively low case fatality rate compared to that described for pertussis in other Sub Saharan settings [33, 34].

Our report shows that there was a delay in appropriate management to control the outbreak using a nationally recommended and effective antibiotic regimen for individual cases [35]. Contact tracing was largely incomplete and the intervention did not include prophylaxis antibiotics administration to susceptible community members until late in the outbreak. Failure to protect close contacts of both confirmed and probable pertussis cases might have encouraged the spread of infection over an extended period. By the time mass prophylaxis treatment started, the outbreak was already dying out naturally. This is indicative of the lack of health system capacity to respond and manage the outbreak timeously.

The low health-seeking behavior of the community (with more than two months of delays recorded to visit the health facility) most likely due to lack of knowledge on severity and risk of pertussis in the community would have served to exacerbate the situation. As expected, the highest attack rate was in infants followed by children aged one to four years. This finding was consistent with the report of Yeung et al's global estimates [3] and the report of the outbreak in the South Wollo area of Ethiopia [19].

The overall pertussis case fatality rate of 3.3 per 1000 pertussis cases was much lower than the 37 per 1,000 pertussis cases from Mekdela [19] and the 30 per 1,000 pertussis cases reported from Papua New Guinea (2012) [32]. Four of the six deaths were reported before outbreak control interventions were initiated. The early initiation of the responsive program may have averted further deaths. All cases identified during the outbreak were treated with antibiotics which consisted of amoxicillin, and cotrimoxazole, erythromycin, or azithromycin. The use of antibiotics would have reduced the possibility of severe pneumonia which can occur as a complication of pertussis infection [28].

The cause of this outbreak could be multifaceted. Even though, the RHMIS reported a high rate of vaccination coverage of over 95% with three doses of a pertussis-containing vaccine in 2016/17 for Dara Malo district., a large proportion of pertussis cases were not fully vaccinated. The inconsistency between routine RHMIS outbreak data and may be due to poor data recording. Maintaining high vaccine coverage is one of the most important interventions in reducing pertussis cases and consequently averting outbreaks [11] [36] [37]. The poor vaccine vial monitoring observed during the outbreak investigation and non-functional cold chain management system at primary health care units may have resulted in poor vaccine potency even in cases that received all doses [38, 39]

Limitations

The study was limited by a lack of resources to confirm the majority of suspected cases which would have affected the diagnostic accuracy of cases; however, in an outbreak, clinical criteria have been shown to have high sensitivity and specificity in the diagnosis of pertussis [40]. We also noted the atypical spikes in the epidemic curve that could be a result of either an artifact created by intermitted augmentation of surveillance practice or real individual clusters within the overall outbreak. In addition, this study did not capture the reason for the delayed health-seeking behavior of caretakers and the completeness, consistency, and reliability of immunization data. As immunization records were not always available, information on vaccination status could have been affected by recall bias.

Conclusions

There is an urgent need to build capacity to strengthen routine vaccination services including defaulter tracing to keep vaccine coverage at a high level to avert outbreaks. Vaccinating all children with appropriate doses for age must be supplemented with building and strengthening the capacity of health workers to timeously and properly manage outbreaks when these occur. In addition, static and outreach services, community-based surveillance activities, and maintaining the cold chain need to be prioritized. A review of data quality status and capacity to respond to outbreaks at the district level must be urgently undertaken. Other LMICs, especially those in Sub-Saharan Africa, should use the lessons from this outbreak to actively review their vaccination systems if they are contextually sustainable ways to avert similar outbreaks [41].

Abbreviations

AR: Attack Rate; BCC: Behavioral Change Communication; CDC: Centers for Diseases Control and Prevention; CFR: Case Fatality Rate; EPI: Expanded Programme on Immunization; FMOH: Federal Ministry of Health; HEW: Health Extension Workers; HMIS: Health Management Information System; HP: Health Post; IEC: Information Education and Communication; IRB: Institution Review Board; MDA: Mass Drug Administration; MDG: Millennium Development Goal; PCR: Polymerase Chain Reaction; PHCU: Primary Health Care Unit; PHEM: Public Health Emergency and Management; SNNPR: Southern Nations, Nationalities, and Peoples' Region; UNICEF: United Nations Children's Fund; USAID: United States Agency for International Development; VPD: Vaccine Preventable Disease; WHO: World Health Organization

Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from John Snow Inc. with certificate reference number: IRB # 19- 18 and from the Southern Nations, Nationalities and Peoples Regional Health Bureau with reference number: ZS/1-6/36/22. And permission to conduct the research was obtained from the local health office and primary health care units. To maintain the confidentiality of collected data, anonymity was maintained throughout the research process.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

The authors of this manuscript are ADM, MDA, BFD, ZTT, AAA, BBT, ET, DR, IA, AGA, DAA, DTA AGS and RM. ADM, MDA, BFD AAA and RM made a substantial contribution to conceiving and designing the study, and ADM, MDA and AAA was responsible for overseeing the field work, cleaning the data, analysing the data, interpreting the analysis and drafting the manuscript. All authors read the final document and approved it. MDA, the corresponding author, submitted the manuscript for publication.

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Figures

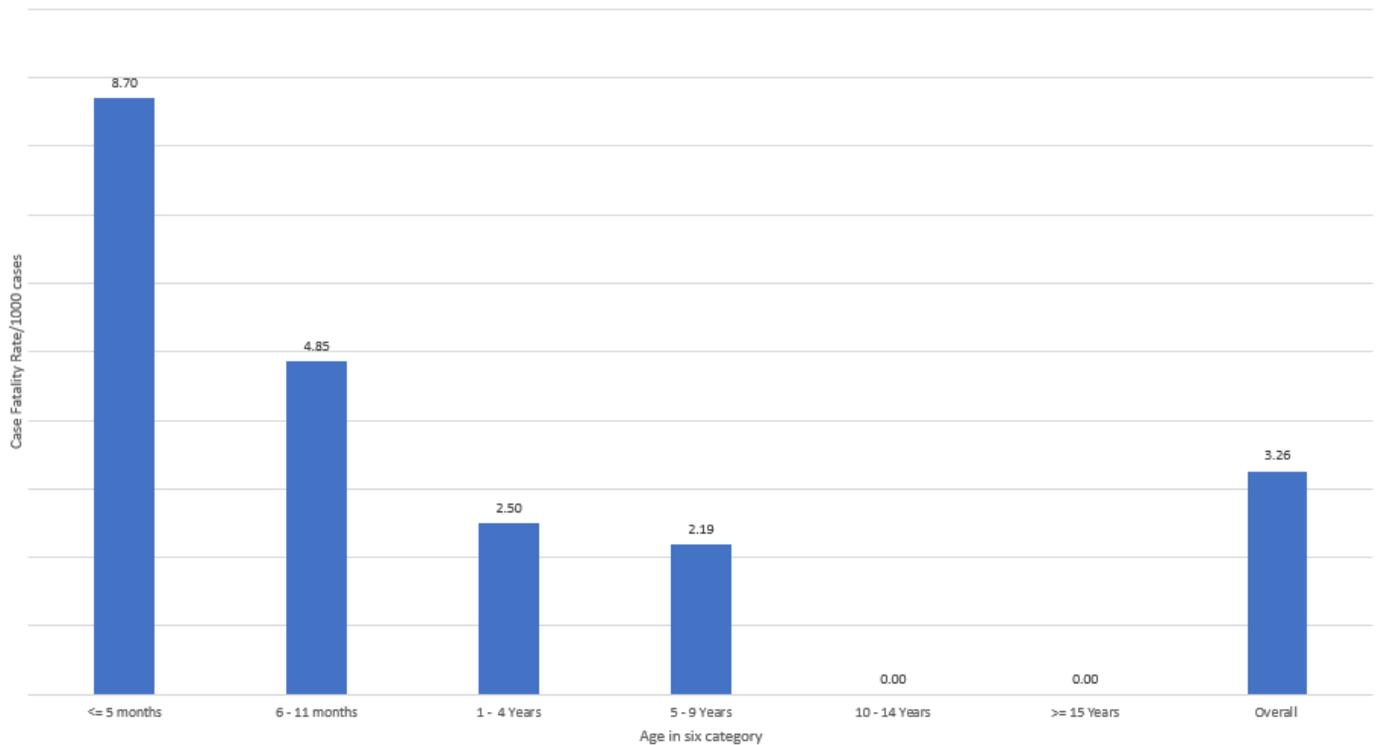


Figure 1

Pertussis cases fatality rate per 1000 cases by age group at Dara Malo district, Gamo Zone, SNNPR, Ethiopia, August 2018 - January 2019. The chart depicts the magnitude of death by age category. The highest CFR was reported among infant age less than 5 months.

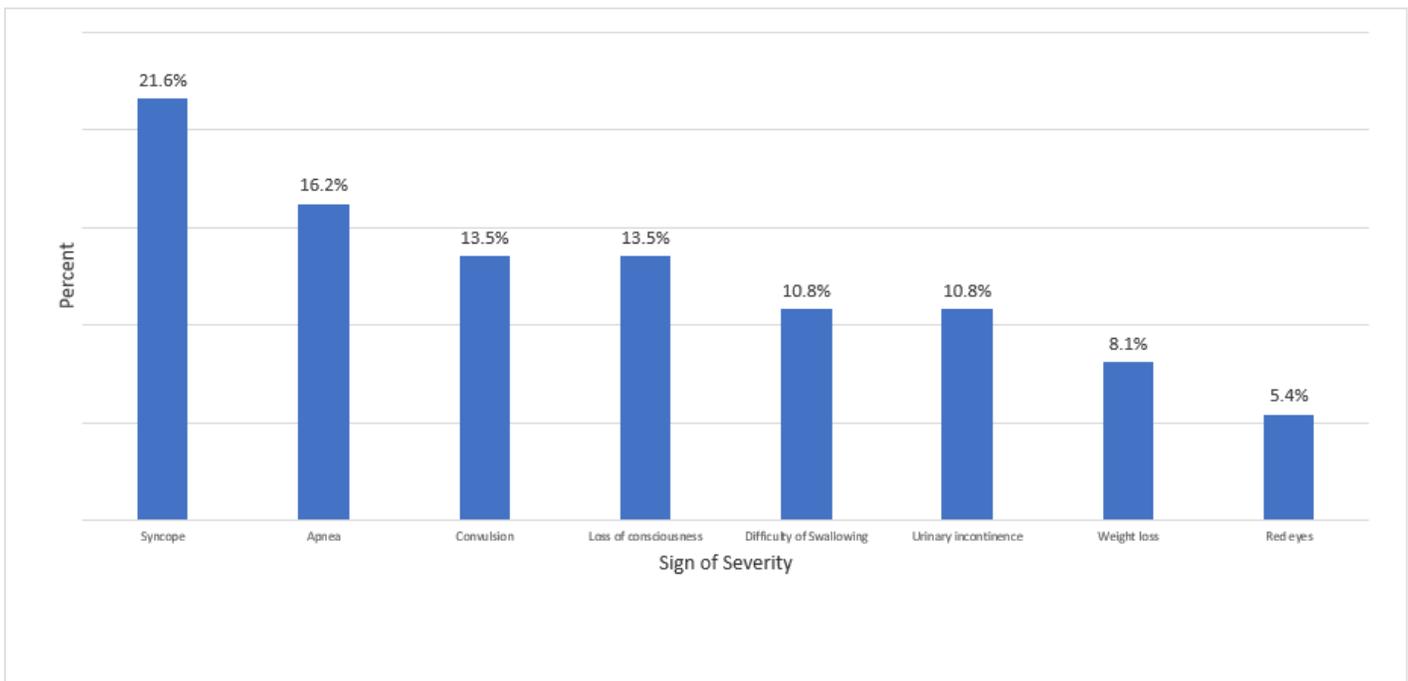


Figure 2

Bar chart presenting reported signs of severity among pertussis cases, cough in Dara Malo District, SNNP, August 2018 – January 2019. The figure clearly depicted the magnitude of reported signs and symptoms of severity among 43 pertussis cases. Syncope, apnoea and death the three top reported signs of severity.

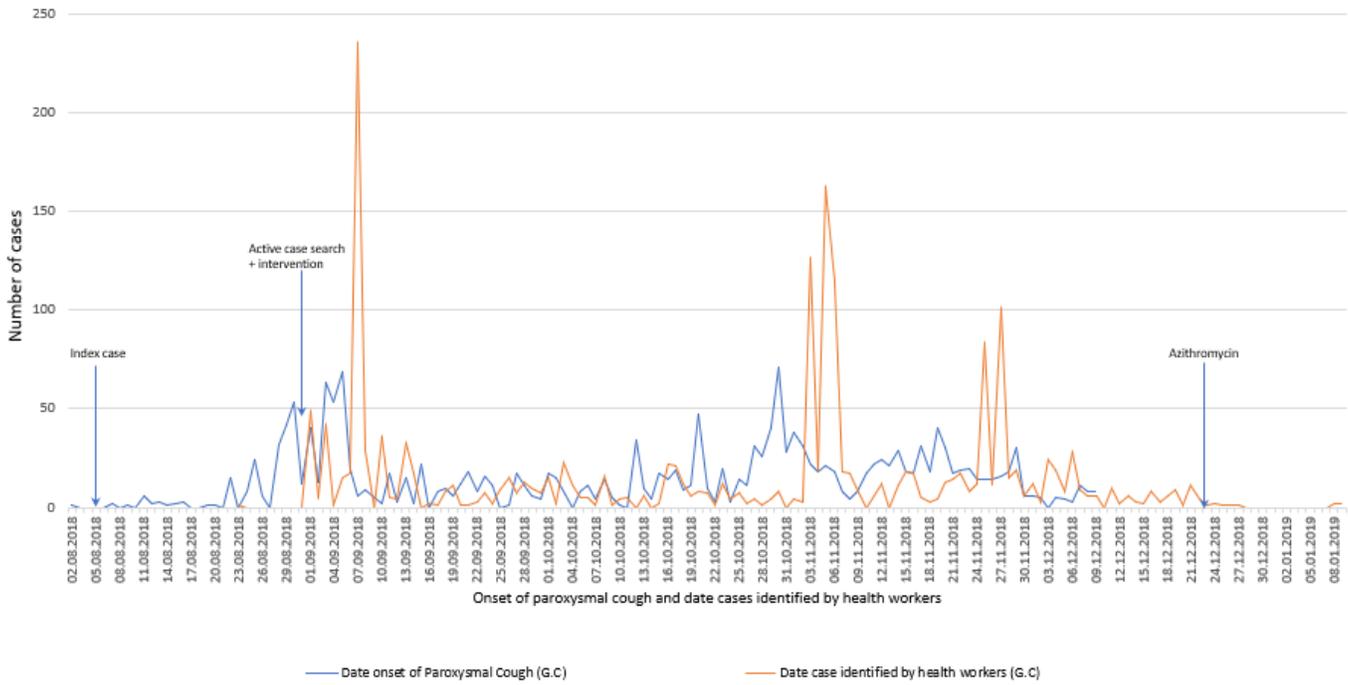


Figure 3

Epi Curve of Pertussis cases by date of onset of paroxysmal cough and identified by health workers in Dara Malo District, SNNP, August 2018 – January 2019. The epi-curve by date of onset of paroxysmal cough showed three peaks, which shows the propagative nature of the spread of pertussis infection. In addition, the epi-curve by date of pertussis case identified by health workers showed three peaks, which shows the long period taken to control the spread of infection.

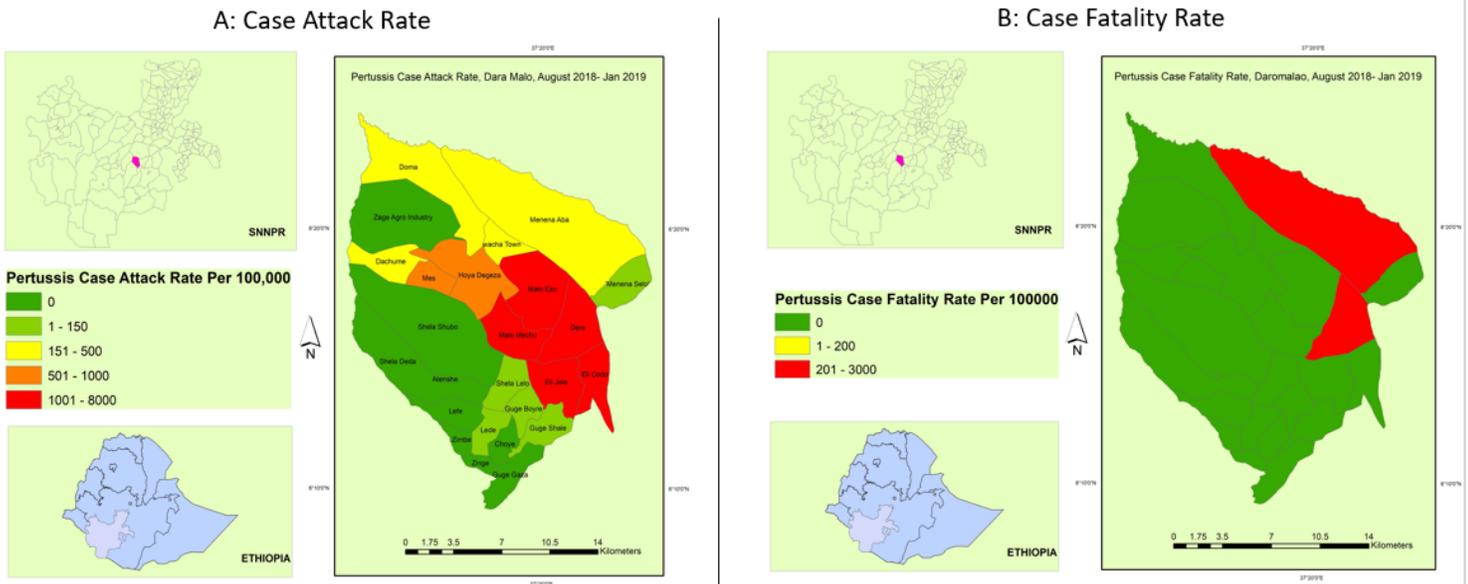


Figure 4

Pertussis Case Attack Rate (A) and Case Fatality Rate (B) by Village (Kebele), Dara Malo district, Gamo Zone, SNNP region, Ethiopia August 2018 - January 2019. The GIS ARCVIEW map presents the location of Ethiopia, SNNPR and Dara Malo district. In addition, the Pertussis Case Attack rate and Case Fatality rates were presented with spatial analysis by village (Kebele).

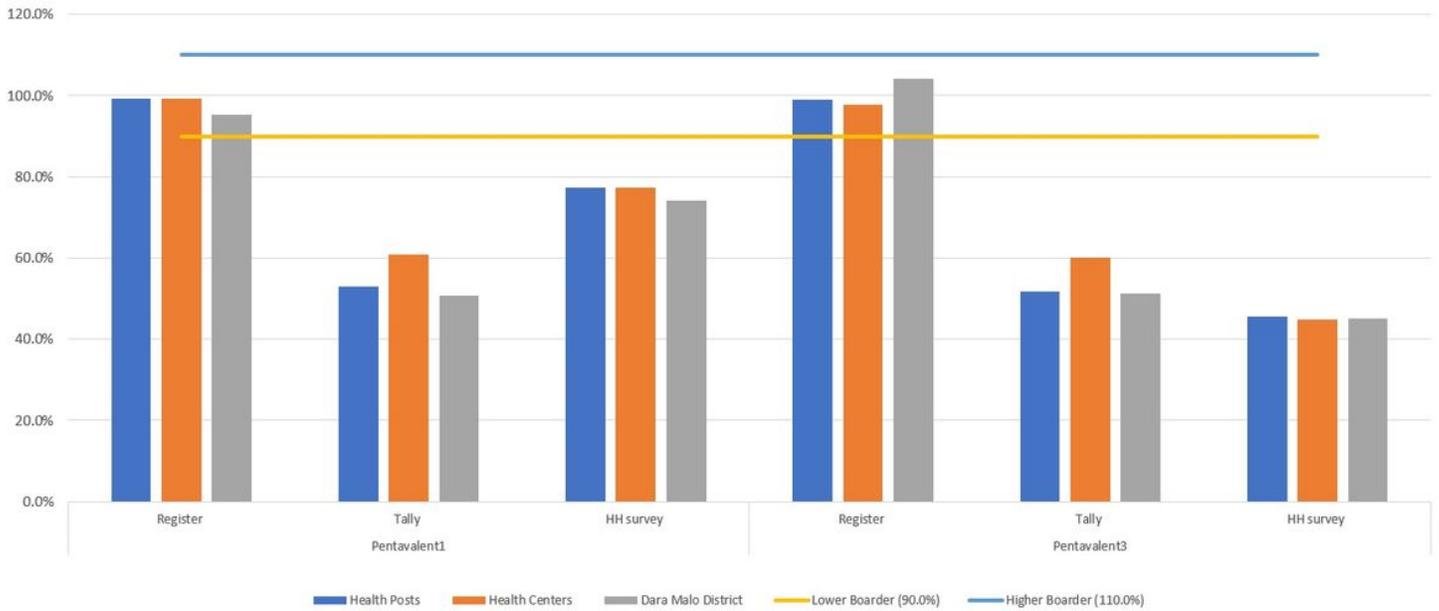


Figure 5

Verification of pentavalent one and three vaccination services report against household survey, July 2018 – June 2019. The bar chart shows the accuracy of routine EPI report against household survey data at health post, health center and district level.

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