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Measles Outbreak among Nomadic Population with Low Herd Immunity in an Eastern District of Bhutan, 2016

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Abstract

During September-November 2016, a number of measles cases were reported from Trashigang District, Bhutan. The outbreak was investigated to determine epidemiological characteristics and risk factors, and recommend control measures. Hospital records of measles cases were reviewed. An active case finding was conducted in the affected communities and schools. Vaccination records were also reviewed. A case-control study was conducted to determine risk factors for measles infection. Tests for measles and rubella immunoglobulin M (IgM) antibodies, viral identification in throat swabs by polymerase chain reaction, and viral genotyping were performed. Total 62 suspected cases were identified, with no reported deaths. The first case developed symptoms on 15 Sep 2016 and 72.2% of the cases occurred in October 2016. The majority (85.0%) were 14 years old and younger (median 8.2 years, interquartile range 6.5-12.0). Cases were from Sakteng (87.1%) and Merak (12.9%) Subdistricts, the latter being a common place where nomads lived. Among 40 cases tested for measles IgM and viral identification, 33 (82.5%) were found to have measles IgM antibodies. All positive samples were genotyped and 11 (33%) were identified as D8 strains which circulated in India during 2016. The measles vaccine efficacy was 82.0%. Significant risk factors were having previous contact with a measles case (OR = 8.46, 95% CI = 2.08-34.41) and not receiving measles vaccination (OR = 6.61, 95% CI = 2.60-16.82). Immunization for outbreak response, case-based investigation and supplementary immunization activities were recommended.

Keywords: measles, outbreak, nomad, vaccine, coverage, Bhutan

Introduction

Measles is an acute and highly communicable viral disease characterized by fever with maculopapular rashes, cough, coryza, conjunctivitis and Koplik's spots. The disease is transmitted by respiratory droplets or direct contact. Normally, infected persons are contagious from four days before eruption of the rash until four days after eruption. The incubation period varies from 8-15 days.

Measles can be prevented readily with immunization. However, 95% of a community needs to be immunized in order to develop herd immunity. Measles remains a significant cause of morbidity and mortality worldwide. In 2012, 43% of global measles deaths occurred in the South-East Asia region. Of which 14% were from India.[1,2]

In Bhutan, measles monovalent vaccinations were introduced into the routine immunization program during 1979. The measles-rubella (MR) containing vaccine was replaced in 2006, and two doses of measles vaccination was added in the routine immunization program in 2010, with the first dose of measles vaccine given at nine months of age and the second dose of MR at 24 months. Hence, the incidence of measles per 100,000 population declined from 254 in 1980 to 24 in 1990, which could also attribute to high measles vaccination coverage (95%) in Bhutan during recent years.[3]

In line with the measles elimination goal of the World Health Organization (WHO) South-East Asia Regional Office, a measles elimination strategy was developed in Bhutan to achieve zero indigenous measles cases by April 2017. Measles elimination is defined as an interruption of indigenous measles virus transmission in a geographical area for at least 12 months in the presence of a well-performing surveillance system.[4]

In Bhutan, measles is an immediately notifiable disease, which implies that a single suspected measles case has to be reported to the National Early Warning Alert and Response Surveillance (NEWARS) within 12 hours of detection. The last endemic measles case was detected in 2012, and no measles cases were detected in 2013 and 2014. However, sporadic cases of measles (12 laboratory confirmed) were reported from some districts in the last quarter of 2015. These cases were classified as being imported or travel-related since the source of infection was epidemiologically linked to an Indian border town.

During September to November 2016, a number of measles cases were reported in Sakteng Subdistrict, Trashigang District, Bhutan. Following a preliminary investigation conducted by the district rapid response team in early November 2016, a team from the Royal Center for Disease Control (RCDC) joined the investigation on 15 Nov 2016.

The objectives of this report are to confirm the outbreak, determine epidemiological characteristics, identify risk factors of the outbreak, assess the measles vaccine coverage and efficacy, and recommend preventive and control measures.

(a)

(b)

Figure 1. Maps showing (a) Bhutan and (b) Sakteng Subdistrict in Trashigang District

Methods

Trashigang District is located in the eastern part of Bhutan. A population of 3,152 resided in Sakteng Subdistrict which is located at an altitude of about 3,000 meter above the sea level. It borders with the Indian state of Arunachal Pradesh to the northeast and Tibet of China to the north (Figure 1). The majority of the people of Sakteng were nomads whose livelihoods were contingent on their yak herds. They frequently migrat with their yak herds to many areas.

Epidemiological Investigation

Retrospective case finding was carried out by reviewing patient records at local and district hospitals from 15 Sep to 25 Nov 2016 to identify suspected measles cases. Active case finding in the communities and schools was also conducted using a standard measles case-based investigation form.

A suspected case was defined as an individual who lived in Sakteng Subdistrict and had fever with maculopapular (non-vesicular) rash between 15 Sep and 25 Nov 2016. A confirmed case was defined as a suspected case with positive measles IgM antibody or viral identification by real time polymerase chain reaction (RT-PCR).

Cases or their guardians were interviewed to obtain information on vaccination status, history of contact with other cases, travel history, and illness among family members.

Mother and child health records in health centers were reviewed to determine the measles vaccination coverage for the period of 2011-2015 as well. In addition, a community survey was conducted to ascertain the immunization coverage for measles and each individual was asked about the vaccination status.

Laboratory Investigation

Specimens of blood serum and throat swabs were collected in cryovials and viral transport mediums from the outbreak areas, and transferred to the national measles reference laboratory at RCDC for laboratory testing[5]. A cold chain transportation system, with temperatures maintained at 2-8°C, was used for the sample shipment. Enzyme-linked immunosorbent assay was performed on serum samples for detecting anti-measles immunoglobulin M (IgM) antibody using Enzygnost® Anti-Measles-Virus/IgM (Siemens). Using the manufacturer's instructions, viral RNA was extracted from the throat swabs (Qiagen extraction kit) and RT-PCR was performed (invitrogen®).

Positive samples were referred to the National Institute of Health (NIH), the WHO measles regional reference laboratory in Thailand, for genotyping under cold chain. All samples were tested for anti-rubella IgM antibody as well.

Analytic Study

A case-control study was conducted using four controls for each case to identify possible risk factors associated with the outbreak. Cases (either suspected or confirmed) were recruited from the descriptive study. Controls were those who did not contract measles during the outbreak and had no history of previous measles infection.

Frequencies, proportions and attack rates were computed to describe the epidemiological characteristics of the outbreak. Odds ratios (OR) and 95% confidence intervals (CI) were used to assess the strength of association of risk factors for measles infection. Multiple logistic regression was used to adjust for potential confounders. Vaccine efficacy was calculated using the standard formula: [ARU-ARV]/ARU, where ARU is attack rate among unvaccinated and ARV is attack rate among vaccinated. All statistical analyses were performed using Epi Info version 7[6].

Results

To confirm the outbreak, we reviewed monthly reported number of measles cases during 2016 in Bhutan and compared to 5-year monthly median. A steep increase in the number of cases in October 2016 was evidenced. Compared to 5-year median, there was a measles outbreak during October and November 2016 (Figure 2).

From 15 Sep to 25 Nov 2016, a total of 62 suspected measles cases were identified in Trashigang District. The majority (61.3%) were males. Out of 40 cases tested, 33 (82.5%) were laboratory confirmed by anti-measles IgM antibody and RT-PCR while the rest were epidemiologically linked and clinically compatible with measles infection.

The first case of this outbreak was a 36-year-old male from Merak Block who had an onset of fever and rash on 15 Sep 2016. A 3-month old child who visited the first case on 16 Sep 2016 was the first laboratory confirmed measles case during the outbreak. A school teacher who was probably infected while in a hospital could have transmitted the disease among the students of Sakteng Lower Secondary School. Onset of the last case was 19 Nov 2016 and the curve also suggested as a propagated outbreak (Figure 3).

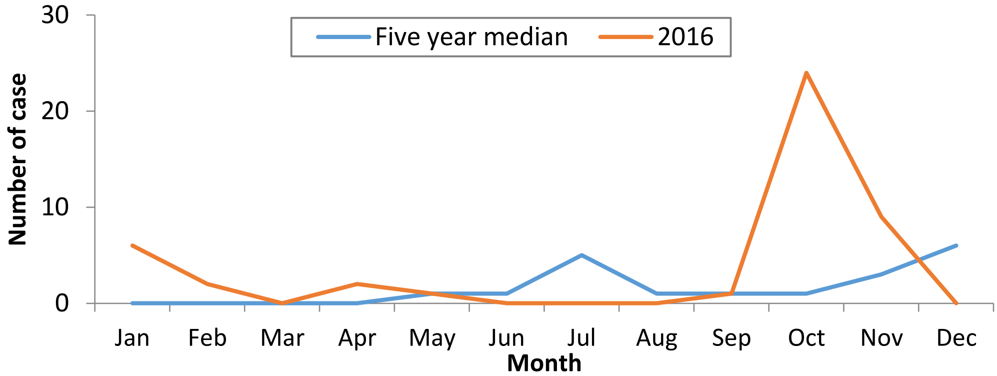

Figure 2. Number of confirmed measles cases in 2016 by month and past 5-year monthly medians (2011-2015), Bhutan

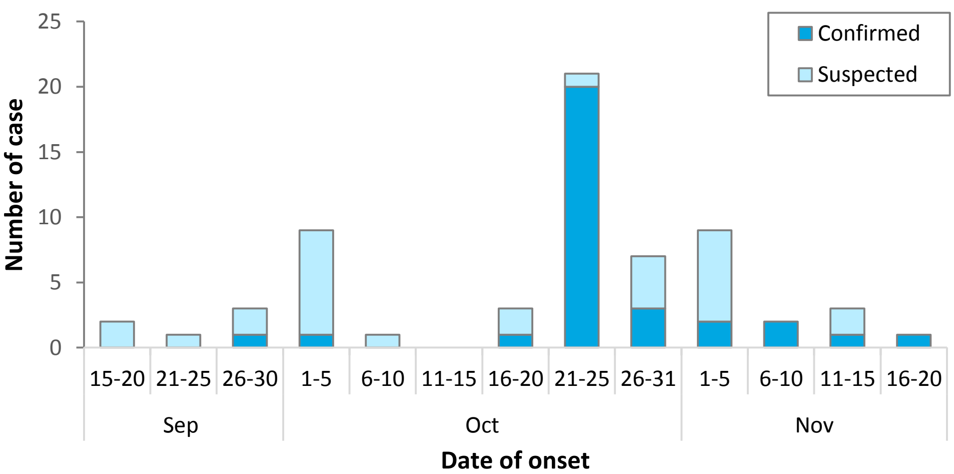

Figure 3. Number of measles cases by date of onset in Sakteng Subdistrict Trashigang District, Bhutan, September-November 2016 (n = 62)

The majority (85.0%) of the 62 cases were 14 years old and younger. The highest attack rate (50.0%) occurred in 5-9 years old (Table 1). The median age was 8.2 years (interquartile range: 6.5-12.0). The youngest was aged three months while the oldest was a 48-year old male. While the majority of cases (71.0%) were students, 9.7% were pre-school children, and the rest were six farmers, five monks or a teacher. Measles cases were only reported from Sakteng and Merak Blocks in Sakteng Subdistrict, and the highest number of cases (87.1%) was observed in Sakteng Block.

All cases had fever with maculopapular rash. Other common symptoms included cough (71.0%), coryza (66.1%), and conjunctivitis (32.3%). Twenty-one (34.0%) cases were admitted at the district hospital in Trashigang for further management. No complications or deaths was identified in this outbreak.

Laboratory Findings

Of 40 cases tested, 33 (82.5%) were positive for measles by IgM antibody and RT-PCR. Molecular sequencing and phylogenetic analysis of all positive specimens isolated the measles virus in 11 (33%) samples as D8 genotype which was similar to the strain reported from India during 2016 (Figure 4). All samples were negative for rubella IgM antibody.

Vaccination Status

Of total 3,152 population in Trashigang District, 388 people from highly affected communities were contacted and interviewed for vaccination status. Among 62 cases, six (10.0%) had documented evidence of measles vaccination, 44 (71.0%) had never been vaccinated, and 12 (19.4%) could not confirm their vaccination status. Age group that had the highest complete proportion of vaccination was among 1-4 years old (64.3%) (Figure 5).

There was a significant difference between the overall MR immunization coverage achieved at the district level (95%) and that achieved in Sakteng Subdistrict (48%) (p-value <0.001). The overall attack rate was found to be 15.0% and the measles vaccine efficacy was 82.0%.

Case-control Study

A total of 388 individuals living in Sakteng Subdistrict were interviewed, regarding vaccination status, contact with measles cases, and whether they lived in the same house with a measles case. Those who did not receive the measles vaccine were 4.78 (95% CI = 1.97-11.60) times more likely to have measles infection compared to those who received the vaccination. Those who had contact with another measles case were 7.90 times more likely to be a case (95% CI = 4.25-14.68), and those who lived in the same household with a case were 5.28 (95% CI = 2.96-9.43) times more likely to be a case (Table 2).

Two factors remained significant in the multivariate analysis were having contact with a measles case (OR = 8.46, 95% CI = 2.08-34.41) and not received measles vaccination (OR = 6.61, 95% CI = 2.60-16.82) (Table 3).

Discussion

The recent measles outbreak in Sakteng Subdistrict posed a great setback to the Department of Public Health for the national goal to achieve measles elimination by April 2017.

Since the last case of measles reported in 2012, there were no measles cases identified in 2013 and 2014. However, the country experienced a resurgence of measles with sporadic cases reported across the country in 2015. However, all measles cases detected in 2015 were classified as imported or travel-related since the sources of infection for all cases were epidemiologically linked to a measles outbreak in an Indian border town. In 2016, sporadic measles cases were reported from most of the districts, including Trashigang District, which was followed by the outbreak notification in Sakteng Subdistrict.

Table 1. Attack rates by age groups and blocks in Sakteng Subdistrict, Trashigang District, Bhutan, September-November 2016

Age group (year)	Total population		Number of case		Attack rate (%)	
	Sakteng	Merak	Sakteng	Merak	Sakteng	Merak
1-4	240	166	4	2	1.7	1.2
5-9	332	148	27	4	8.1	2.7
10-14	259	144	14	1	5.4	0.7
15-19	252	162	3	0	1.2	0.0
≥ 20	959	492	6	1	0.7	0.2
Total	2042	1112	54	8	2.7	0.7

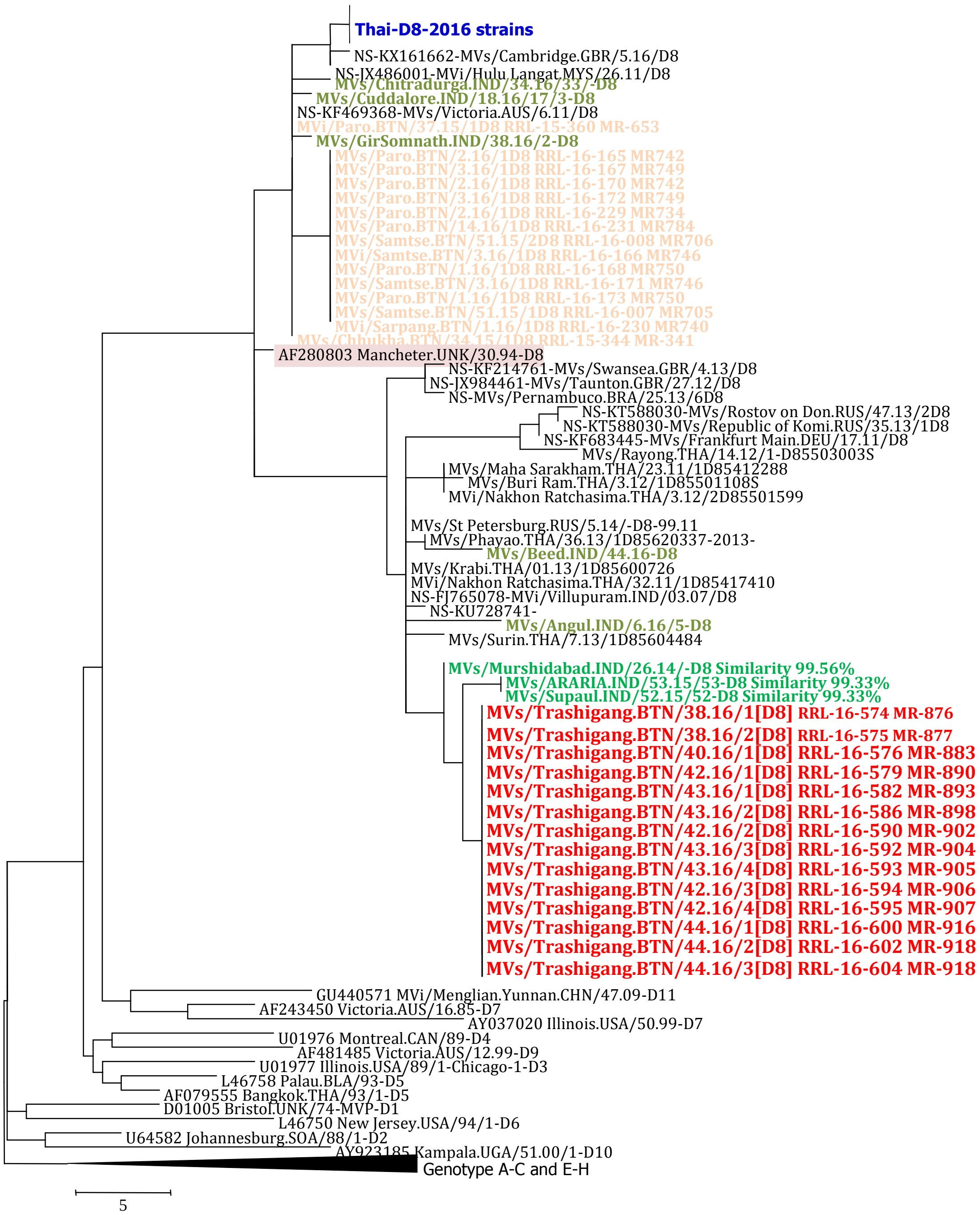

Figure 4. Phylogenetic analysis of measles virus isolated from samples during the outbreak (red color) in Sakteng Subdistrict, Trashigang District, Bhutan, 2016

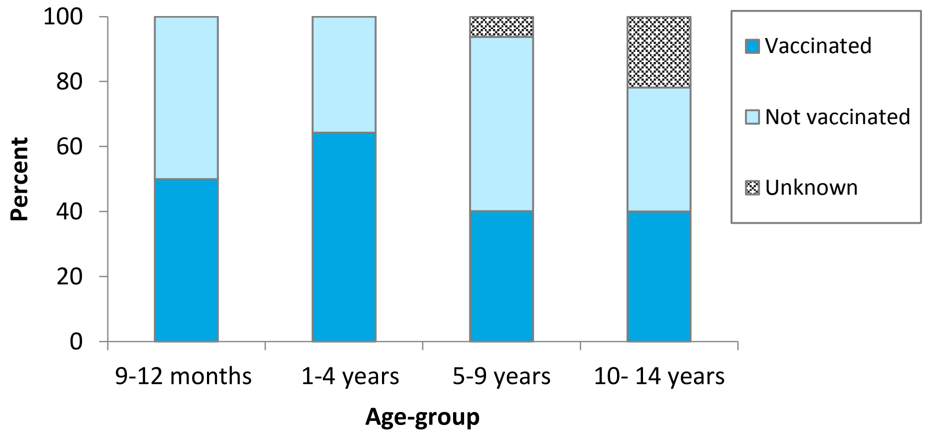

Figure 5. Measles vaccination coverage among children 9 months to 14 years, community survey, Sakteng Subdistrict, Trashigang District, Bhutan, September-November 2016 (n = 266)

Table 2. Potential risk factors for measles infection, Sakteng Subdistrict, Trashigang District, Bhutan, September-November 2016

Risk factor	Case (n=62)		Control (n=326)		Odds ratio	95% CI
	Yes	No	Yes	No		
Contact with a measles case	46	16	87	239	7.90	4.25 - 14.68
Being a boarding school student	41	21	88	238	5.28	2.96-9.43
No previous vaccination*	41	6	176	123	4.78	1.97-11.60
Pre-school children	6	56	134	192	0.15	0.06-0.37

*Excluding those with no data.

Table 3. Association between potential risk factors and measles infection by multiple logistic regression analysis, Sakteng Subdistrict, Trashigang District, Bhutan, September-November 2016

Risk factor	Adjusted odds ratio	95% CI
Sex (male vs female)	1.45	0.73-2.89
Age (years)	0.95	0.92-0.99
Contact with a measles case	8.46	2.08-34.41
Being a boarding school student	0.67	0.17-2.69
No previous vaccination	6.61	2.60-16.82

The measles vaccine coverage of 48% among those aged under 14 years in Sakteng was found to be low compared to the national coverage of 95% and much lower than the minimum vaccination coverage required to protect the population from a measles outbreak[1]. Our study showed that having previous contact with a measles case and being unvaccinated against measles were independent risk factors for contracting measles. The low vaccine coverage could have increased the susceptibility of children and adults for measles infection. Similar findings of low vaccine coverage being associated with measles outbreaks were observed in different parts of India[7,8], Nepal[9], Bangladesh[10,11], Sri Lanka[12,13], Thailand[14] and Lao PDR[14].

The most affected age group was 5-9 years, with 85% of cases being aged 14 years or less. Analysis of our data showed that there was a cohort of susceptible individuals who had perhaps never received measles immunization nor been exposed to natural infection. The migratory habit of residents and low literacy rate of nomadic populations might have further contributed to poor uptake of vaccination programs by the communities living in Sakteng. They might have migrated to temporary posts at the time of vaccination campaigns and might not visit health centers once they returned to the communities. This highlighted the challenge of achieving herd immunity among migrant populations.

Additionally, higher number of cases and delay in public health response could be due to late diagnosis due to low suspicion of measles by clinicians. Our investigation revealed that a substantial number of initial cases were misdiagnosed by the attending physicians, which indicated that health care providers or clinicians in hospitals were no longer familiar with the clinical presentation of measles cases, probably due to high measles vaccine coverage and low incidence of measles in the community. Late diagnosis and confirmation of the primary cases resulted in delayed contact tracing and follow-up. Early action in notifying public health authorities and timely provision of MR vaccination to those at risk are crucial steps in minimizing the risk of secondary cases.

This outbreak also highlighted the importance of molecular epidemiology. The phylogenetic analysis of the measles virus isolated from the outbreak samples revealed D8, a genotype which has a high similarity with the strains reported in India during 2015. This further suggested that acquisition of the infection could have been from across the border in India. The D8 genotype had been reported to be circulating in most regional and neighboring countries such as India, Nepal, Bangladesh and Sri Lanka[5,15-17]. Genetic analysis of measles isolates can aid in identifying the geographic and personal source of the outbreak, confirm possible relationship among cases, and identify routes of transmission. The measles outbreak among this particular nomadic population in Bhutan during 2016 served as a reminder that imported measles cases could lead to large outbreaks, particularly among unvaccinated populations. If the infection is introduced into areas with pockets of unvaccinated migrants, the population could remain at risk for acquiring and transmitting the disease. The countries that had achieved measles elimination goal such as Australia, United Kingdom and USA had experienced measles outbreaks imported from other endemic countries as well.[18-20]

Conclusions

This reported measles outbreak was predominantly localized in the nomad populations with low vaccine coverage. The consistently low immunization coverage over the past few years had created a large immunity gap among populations in the community and could have increased the susceptibility for measles infection. The introduction of a single measles case, whether from within the country or across the border, consequently triggered the outbreak. The majority of cases were children aged 14 years or less and reflected a significant percentage of non-immune young population. This outbreak caused a setback to the national measles elimination program of the country. As D8 measles genotype had commonly been reported from India, the outbreak could be considered as imported based on findings from epidemiological investigation and molecular characterization. However, whether the D8 genotype was indigenous among the Bhutanese people or imported from another country needed further confirmation.

Public Health Interventions and Recommendations

As an outbreak response, the mop-up MR vaccination were provided to those aged nine months to 40 years within two days after detecting the outbreak. Active case finding was conducted by visiting the communities and school. Isolation of cases and onsite case management, including provision of vitamin A supplement to all cases, were performed. Health education on importance of immunization in preventing diseases, isolation of cases to prevent further spread, and seeking health care during sickness was delivered to the public.

Constant health education campaigns should be provided to raise awareness in the communities about benefits of vaccination and increase acceptance of the vaccine. The district health authorities should assess the vaccination coverage, particularly in hard-to-reach populations. At the same time, a mechanism should be developed to obtain an accurate estimate of the vaccine coverage across the nation. When merely a single laboratory confirmed case was detected, immunization for outbreak response and investigation should be recommended as a policy guidance. Supplementary immunization activities among hard-to-reach and high risk populations were recommended as well. Policy makers should take all possible measures to maintain high level of measles vaccination coverage for disease elimination in the near future. Training courses on clinical management of measles cases for clinicians was also recommended.

Limitations

The incidence of measles in this study might have been under-estimated as people with mild symptoms might not seek medical care at a health facility. Data interpretation might be hampered by recall bias as some subjects could not remember their vaccination or disease history. Finally, the sample size for the genotype study might be small to make concrete conclusions.

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