

INVESTIGATION REPORT

Measles outbreak in Sakteng Lower Secondary School and Joenkhar community under Trashigang District in October and November 2016

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1. Background

Suspected Measles is one of the immediately notifiable diseases where every health center in Bhutan has to notify it to Royal Centre for Disease Control (RCDC) under National Early Warning Alert and Response Surveillance (NEWARS) through web based online Information System (NEWARSIS) As per the Measles and Rubella surveillance, the last single measles case was reported in 2012 and no measles was detected in 2013 and 2014. However, sporadic cases of (12 laboratory confirmed) Measles were reported from different district during the last quarter of 2015 which were all classified as imported or imported related case since source of infection was epidemiological linked to Indian boarder town; Jaigon under West Bengal. Around the same time, Trashigang district also reported a measles case which was also epidemiological link to Jaigon. Since then 24 Measles were reported sporadically from most districts till date.

On 24 October 2016, Sakten BHU under Trashigang district notified event (cluster of suspected measles cases) in Sakten Lower Secondary School in NEWARSIS. RCDC and VPDP immediately instructed Trashigang District Health Authority to dispatch District Rapid Response Team (DRRT) to investigate an event and submit the report. On 14 November 2016, Joenkhar BHU under Trashigang district also notified similar event (cluster of suspected measles cases). Following the two measles event notification, the RCDC dispatched the team on 15th November to investigate measles outbreaks in Merak and Sakteng gewog with DRRT. The main objectives of the investigation were to verify measles outbreaks reported by Sakteng and Joenkhar BHU, determine the possible source of infection and epidemiological characteristics of the outbreak, describe the vaccine coverage in the outbreak locality, describe risk factors and implement the control measure.

2. Methods

Sakten, Joengkhar and Merak communities are part of Sakteng Dungkha (sub-Dzongkhag) which is situated at an altitude of about 3000m above sea level under Trashigang dzongkhag (Figure 1). It shares border with Indian state of Arunachal Pradesh in North-East and China in

North. There are three BHUs which provide health services to approximately 3,154 people of Sakteng, Merak and Joenkhar. Majority of the people were nomads whose livelihoods are contingent on their yaks.



Figure 1: Merak and Sakteng gewog (Sakteng Dungkha)

2.1 Epidemiological investigation

2.1.1 Case Definition of outbreak

Suspected case was defined as an individual who lived in Sakteng, Joenkhar and Merak BHU catchment area and developed fever with maculopapular rash, cough, coryza or conjunctivitis between 1st September and 30th November, 2016 or whom a clinicians and health workers suspected as measles during the period.

Confirmed case was a suspected measles case confirmed by serology and molecular tests in National Measles Laboratory, RCDC.

2.1.2 Case finding:

Retrospective case finding was done by reviewing patient's admission records in the Trashigang Hospital, and Ranjung BHU-1 from 1st September 2016 to November 23 2016 to identify suspected measles cases. Those two hospitals are the immediately referral point for Joenkhar, Merak and Sakteng BHUs. Monthly OPD and in-patient registers of Joenkhar, Merak and Sakteng BHUs were reviewed for aforesaid period. Active case search was conducted in communities and schools under Joenkhar, Merak and Sakteng BHUs. All individuals were interviewed using questionnaire of measles case-based investigation form.

2.1.3 Risk factors

The cohort study was conducted from September to November 24, 2016 to identify possible risk factors for outbreak. The Sakteng gewog which had the highest attack rate was included the study. Merak geog was excluded from the analytical study as no active case was detected since 2nd October. Non-cases were selected where those who did not report fever with rashes during the same time in same area.

2.2 Clinical investigation

Clinical features for all cases were collected through interview with individual and admission record for admitted cases using case-based investigation form.

2.3 Laboratory investigation

From total 62 suspected cases, 36 blood samples and throat swabs in viral transport media were collected (Sakteng – 27, Joenkhar - 5 and Merak - 4). Samples were shipped to RCDC in cold chain for laboratory testing. Serology test was performed using anti-measles antibody (IgM) using ELISA (Siemens Health Care diagnostic product) and Real time PCR using CDC test kit. Furthermore, conventional PCR was performed on all the positive samples, and the amplicons were referred to WHO Measles Regional Reference Laboratory, National Institute of Health under Department of Medical Sciences, Thailand for genotyping. All samples were also tested for Rubella.

2.4 Immunization

Annual immunization coverage submitted by Dzongkhag to Ministry and BHUs to Dzongkhag for the last 5 years (2011-2015) was collected from the Dzongkhag Health Office. Immunization records maintained on Mother and Child Health (MCH) registers of Joenkhar, Merak and Sakteng BHUs were also reviewed for MRCV1 and MRCV2 coverage from 2011-2015.

2.5 Statistical analysis

Percentage, median and range were used for descriptive statistics. The chi-square test was used for comparison of proportions. Risk Ratio, Odds Ratios and their 95% confidence intervals were calculated to indicate the strength of association. All statistical analyses were performed using *EpiInfo* version 7.5.3.

3 RESULTS

3.1 Epidemiological findings

3.1.1 Source of infection

The first suspected measles case was 36 year-old male from Merak and as per the medical record and interview conducted, the case suffered from high fever on September 14, 2016 and developed rashes on all part of the body on third day with cough and general body-ache. The case visited Tashigang hospital to seek medical care and was hospitalized on September 15 till

19, as suspected scrub typhus case for the treatment. The case had no travel history beyond the Trashigang town prior to onset of illness and no history of visitor visiting the family members from other places prior to illness (7-21 days). This case was the primary measles case.

On September 25, 2016, three months old child and a seven year girl in Merak developed fever and macupapular rashes. Two suspected measles cases visited the primary case in Tashigang hospital on September 16, 2016 during the time of hospitalization. They were neighbor of the primary cases. The three-month-old child was the first laboratory confirmed measles case in reported by Merak BHU and therefore the baby and seven years girl which was not reported but epidemiologically linked to baby were index cases in Merak. A total of six suspected measles cases were detected in Merak including index cases. The last case of measles from Merak had onset of illness on October 2, 2016.

On September 29, 2016, 41 years old man from Dakh village under Sakten developed fever and rashes. This suspected case also visited the primary case in Tashigang hospital on September 19, 2016. This case was the first case in Sakteng Gewog. The case lives in Dakh village and epidemiologically linked to the index case (lab confirmed case) in Merak.

On October 10, 2016, a women and school teacher from Sakten Lower Secondary School (SLSS) developed similar illness and investigation revealed that those two cases had contact with the first case of Sakten and epidemiologically linked to the Merak index case. Both visited Trashigang hospital to seek medical care and were hospitalized for observation.

The first suspected measles case from SLSS was notified to RCDC through NEWARS on October 24, 2016 after cluster of cases having similar signs and symptoms like school teacher was observed in the SLSS. The date of onset of illness of the first suspected measles case from school was on September 21, 2016. The teacher was the index case for measles outbreak in SLSS. Most cases had date on onset of illness from October 21 to 25, 2016.

3.1.2 Descriptive analysis

The total of 1035 people were contacted and interviewed during the active case search to detect the suspected measles cases. From the total, 62 cases met outbreak case definition as suspected measles cases. Based on case classification definition in the surveillance guideline, **31 were lab confirmed cases and 21 epidemiologically link cases.** The epi-curve (Figure 2) shows the course of measles transmission and case classification among cases.

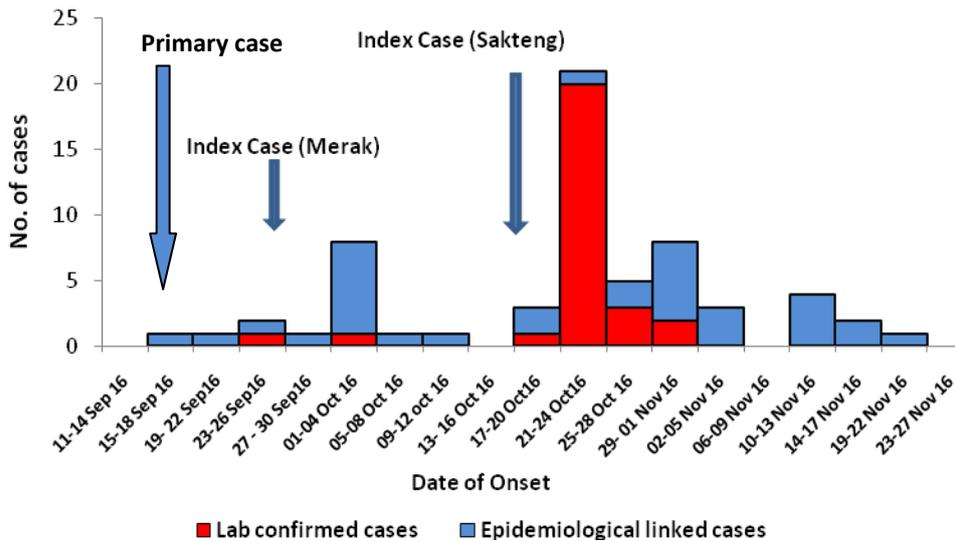


Figure 2: Epi-curve of cases (n=62) from Sakteng school and other adjacent area linked to outbreak

The median age among cases was 8.2 years with the IQR 5.59 years (6.5 - 12.08). The age range was from 0.3 – 48 years. A majority of cases were students from SLSS (58%) followed by Joenkhar Primary School (10%). The most affected age group was among 5-10 years (50%) and the same age group also had highest attack (42% in Sakteng, 20% in Joenkhar and 7% in Merak (Figure 3). Among cases 10% had vaccination history, 61% had no vaccination history and 29% case vaccination status was unknown. Figure 4 shows vaccination status by age group.

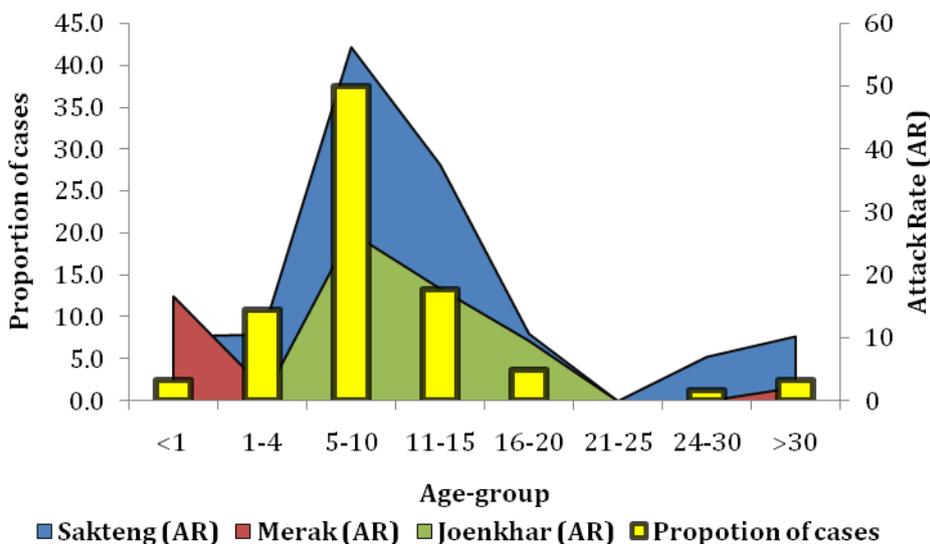


Figure 3: Proportion of case and attack rate by age group and BHU (n=62)

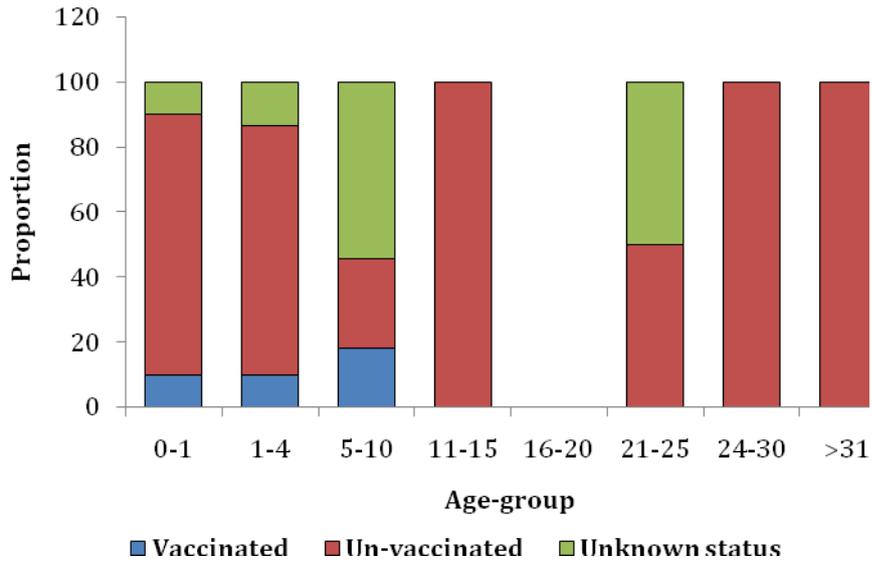


Figure 4: Proportion of immunization status among cases by age group (n=62)

3.1.3 Analytical analysis

A total of 368 inhabitants living under Sakteng Geog during the investigation period were included for risk factor analysis. From the uni-variate analysis, the risk of contracting the measles infection among population that did not receive MRCV1 vaccination was 4.1 (95% CI, 1.8 - 9.4) times high compare to those received vaccination. Risk of contracting measles as student was 3.9 (95% CI; 2.4-6.3) times high compare to other occupation and the risk of contracting measles among close contact with measles case was 3.9 (95% CI; 2.0-7.1) times high than those without contact (Table 1).

Table 1: Risk factors analysis

Risk factors	Exposed		Not-exposed		RR	OR
	Total	Cases	Total	Cases	(95 % CL)	(95 % CL)
Having no vaccination	216	41	130	6	4.1 (1.8- 9.4)	4.8 (1.9-11.0)
Having no vaccination including ≤ 9 months	216	38	130	9	2.7 (1.4- 5.4)	3.1 (1.4-6.7.0)
Contact with cases	113	24	255	14	3.9 (2.0-7.1)	4.6 (2.9-9.4)
Student	129	41	259	21	3.9 (2.4-6.3)	5.8 (3.2-10.6)
Pre-school	254	15	134	47	0.7 (0.09-0.28)	0.1 (0.06-0.2)

3.2 Clinical features

All cases including those admitted in hospital had 100% fever, 97% maculopapular rashes, 92% cough, 66% coryza and 55% conjunctivitis (Fig 5). About 34% cases were admitted in hospital.

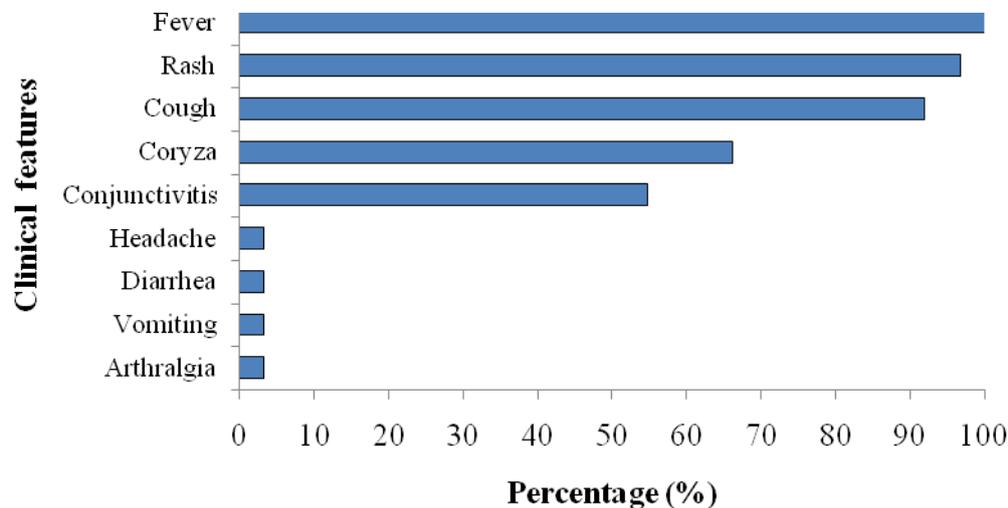


Figure 5: Clinical profile among cases (n=62)

3.3 Laboratory result

Of 36 serum samples tested, 86% (31) were tested positive for anti-measles antibody (IgM) by ELISA and positive for measles antigen by Real Time PCR. From the total positive samples, 75% was from Sakteng, 5.5% from Merak and 8.3% (3) positive from Joenkhar.

3.4 Immunization coverage

MRCV1 immunization coverage of the Dzongkhag Health Office records was consistently above 95 % from 2011-2015 similar to national MRCV1 coverage. The median of three BHU's MRCV1 coverage reported to Dzongkhag Health Office ranges from 58.8% to 146.9%. However, the median MRCV1 coverage found from data available in MCH records in BHU's ranges from 57.1% to 67.1% in 2011 to 2015 (Figure 6). There was significant difference in MRCV1 coverage reported by BHUs' to the Dzongkhag Health Office and what was available in MCH register maintained BHU's. MRCV2 immunization data collected from MCH register was not analyzed.

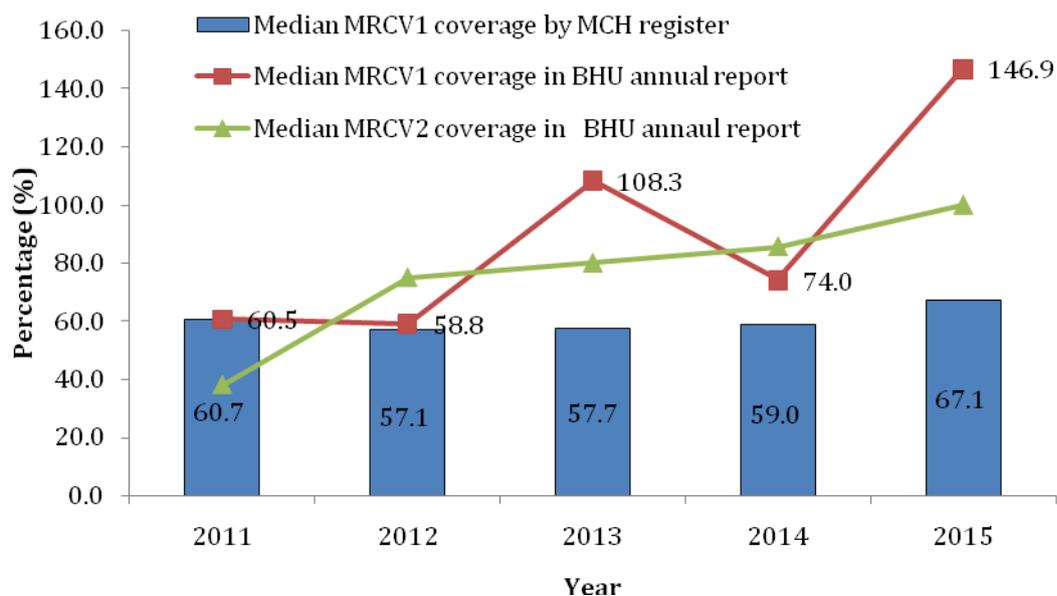


Figure 6: Median MRCV1 and MRCV2 coverage reported by three BHU annually and comparison of MRCV1 coverage data verified from MCH register record available in BHUs for 2011-2015

4. DISCUSSION

The Sakteng measles outbreak is the first documented measles outbreak in the country after a very long time. This outbreak could be a setback for country's plan to achieve measles elimination in April 2017.

After the last single measles case detected in 2012, there was no case in 2013 and 2014. However, Bhutan experienced resurgence of measles in 2015 with sporadic cases reported across the country. Based on case investigation report submitted by respective district health authority to programme, all measles cases of 2015 were classified either imported or imported related as the source of infection for all cases were epidemiologically linked to measles outbreak in Indian border town Jaigon. After the measles resurgence in 2015, sporadic measles cases were also reported in 2016 from most districts across the country in 2016. Prior to measles outbreak in Sakteng Lower Secondary School in Sakteng, surveillance record shows 11 laboratory confirmed measles were reported including one case from Merak (one of sub-districts) under Trashigang district.

The measles case reported from Merak under Trashigang district in September 2016 was three months old baby (laboratory confirmed). Our investigation revealed that the source of infection for three months old baby laboratory was 36 year-old male from Merak. We believed this 36 year male was the primary case because we could find circumstantial evidences for other case during the time of investigation. The primary case visited Tashigang hospital to seek medical care and was hospitalized for the treatment of suspected scrub typhus and it was during that time the three months baby with mother along with seven years old girl visited the primary case in Tashigang hospital. Therefore, the primary can be epidemiologically linked to lab confirmed three months baby because there was geographically and temporally correlation in disease transmission. The primary case was a local leader of Merak community and engages with many social activities with people in the community and beyond. However, the primary case had no travel history beyond Trashigang district town or history of any visitors visiting his family members from other place prior to onset of illness (7-21 days). Therefore, the primary case was likely an endemic/indigenous case. We also believe that the source of infection for the primary case could be indigenous and probably not detected because clinicians from Trashigang hospital had failed to suspect the primary case as suspected measles case despite presenting with high fever, macupapular rashes and cough. This indicates that clinicians and health workers would misdiagnose suspected measles case among patient visiting hospitals or health centers with fever and rashes for other common tropical disease particularly among adults. This degree of low suspicious for measles among patient with fever and rashes is also attributed by very low incidence of measles cases in the country for very long time.

The index case for outbreak in Sakteng School was a school teacher from the same school. The index case visited 41 years of male from Dakh village under Sakteng who in turn had visited the primary case from Merak in Tashigang hospital. The first and index case for outbreak can be epidemiologically linked also to three months baby from Merak. The source to Joenkhar outbreak was from Sakteng School as some students studying in SLSS were from Joenkhar. Since the primary case was likely an endemic/indigenous case, all cases of Sakteng School, Joenkha community and Merak could also be classified as indigenous cases. We could not establish the link between measles case reported by Trashigang district in October 2015 which was from Bikhari village. The epidemiological findings can be complemented when genotyping result is available.

The most affected age group was 5-10 year (median age was 8.2 years) with 85% cases below 14 years of age. This suggests that there was high proportion of susceptible population among children in Merak and Sakteng over the years. This could be attributed either because of low immunization coverage or accumulation of sero-conversion failure cases among children in the locality. In Meraka and Sakteng, we believe susceptible population among children was built up over the years due to low immunization coverage because only 10% cases had vaccination history. The attack rate was also found high in the same age group (5-10 years) in all three places and the same trend is also observed other countries measles outbreak that have similar setting to Bhutan. We have also looked into risk factors for outbreak in Sakteng school and found the risk of contracting measles infection among population who did not receive vaccination was 3.8 (95% CI; 1.7- 8.9) times high than those received vaccination. Student was found 3.9 (95% CI; 2.4-6.3) times higher in risk of contracting measles compare to other occupation and 3.9 (95% CI; 2.0-7.1) times high risk for close contact with case than those without contact.

All cases had fever (100%), maculopapular rashes, (97%); cough (92%), coryza (66%) and conjunctivitis (55%) which is common signs and symptoms observed in measles cases. All case had mild sickness however 34% cases were found hospitalized. From the experience of this outbreak, we strong feel that Bhutan should adopt fever with rash as MR surveillance case definition to improve sensitivity of MR surveillance as recommended by WHO although most measles cases would present with high fever, maculopapular rashes, cough, coryza and conjunctivitis. We found admission was done for precautionary measure only and none of the case required hospitalization related to measles complication.

Bhutan has consistently reported very high coverage of measles vaccination >95% for MRCV1 since 2007 and >90% for MRCV2 from 2011. The last SIA was conducted in 2006 with MR vaccine for age group (9 months-14 years male and 15-44 years female). While immunization coverage was reported very high at the national level for both MRCV1 and MRCV2, the coverage at district and sub-district level was not monitored and assessed. During the investigation, we observed massive discrepancy in immunization coverage report maintained at District Health Office and report submitted by respective BHU annually. We also found major discrepancy in immunization report submitted by BHU's compare to immunization data maintained in MCH register for MRCV1. We believe there could be same degree of discrepancy

for MRCV2 coverage report also although we have not analyzed MRCV2 data. We also believe that the same problem could be in other BHU's and hospitals across the country. Our findings was corroborated with community survey done by district rapid response team during immunization response conducted in Merak and Sakteng where MR immunization coverage in Merak was 62.6% and Sakteng 38.3%. This highlights existence of low immunization coverage in Merak and Sakteng gewog over the years. Geographically, Merak and Sakteng were among the hard to reach areas in the country and with migratory habits of residents in those two areas, achieving high immunization was always a challenge but the district health authority should have given due attention and priority for immunization service in those areas in light of Bhutan's target to eliminate measles by 2018.

This measles outbreak is a wake-up call for the country to urgently introspect measles immunization coverage at all level and plan for appropriate intervention at the earliest to achieve measles elimination verification as planned in line with measles elimination goal in SEA region by 2020.

5. Conclusion

The measles outbreak in Sakteng and Joekhar community was caused due to consistently low immunization coverage that has built up large immunity gap among population in the community.

6. Control measures Implemented

1. Mass MR vaccine was provided to all people whose age ranged from 9 months to 40 year in Merak, Joenkhar and Sakteng BHU catchment areas. The occurrence of new cases had subsequently stopped after five days of completing mass vaccination.
2. Conservative treatments were given to the cases.
3. Health education was also provided on the transmission and adverse health effect of measles.

7. Recommendations

1. Immunization coverage (MRCV1 and MRCV2) data need to be reviewed at BHU's and district health office.
2. Immunization coverage (MRCV1 and MRCV2) status need to be monitored at sub-district level based on BHU's catchment area

3. Strengthen MR case based surveillance and outbreak investigation capability of DRRT
4. Train health workers on calculation of immunization coverage.
5. Conduct immunity gap assessment using WHO tool in BHU's catchment areas if feasible.

Limitations of the Investigation

Poor memory of the people on their own history of vaccination for measles hampered effective data interpretation could have led to recall bias. The population of the analytic study was limited to only those people the investigation team contacted.

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