Two in One Outbreak of Rubeola-Rubella in Tobacco Affected Maan Vajreshwari Nagarkot Dham-District Kangra of Northern Himanchal

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Abstract **Background:** A local community leader informed us about sudden increase in number of cases of fever and rash in five villages of district Kangra on 14th September 2006,. We investigated the suspected outbreak to confirm diagnosis and recommend for prevention and control. **Methods:** A case of rubeola was defined as occurrence of fever with rash in a child between from 3rd September to13th January, 2007. We collected information on age, sex, date of onset, residence, signs, symptoms, vaccination and cold chain and smoking status. We described the outbreak by place, time and person characteristics. We conducted a retrospective cohort study to estimate vaccine efficacy. We ascertained the measles immunization status by interviewing the mothers and reviewing immunization cards. We confirmed diagnosis clinically, epidemiologically and serologically. **Results: S**ixty case patients were identified in five villages (41/60 rubeola and 11/60 confirmed epidemiologically linked unvaccinated rubella). The overall attack rate (AR) was 9%. Sex specific AR was 11% for male. Majorities of cases were >5years of age. No death/minimal complications occurred. Of 60 case-patients, 42 (70%) were vaccinated for rubeola. The AR of rubeola among unvaccinated children was 25.8% as compared to AR among vaccinated of 4.5% (Relative risk: 5.75%; 95% confidence interval: 3.48–9.51 P <0.001). We estimated general vaccine efficacy (VE) to be 83% while gender based VE for male was 84%. Eight case-patients were confirmed serologically for measles IgM antibodies, two nasopharyngeal swabs positive by PCR. Rubeola virus was genotyped D4. Only 30% (18/60) of the cases took the treatment from modern system of medicine. **Conclusion:** A mixed outbreak of rubeola/rubella was confirmed clinically, epidemiologically and serologically. We recommend MR vaccination at the age of 18-24 months and aggressive IEC activities to modify help seeking behavior of community, especially in the measles affected areas. **Key Message:** In the outbreak setting, two viruses'- rubeola and rubella were investigated simultaneously in the district Kangra of Northern India in highly immunized mountainous area for rubeola but unvaccinated for rubella. The single virus of rubella has been investigated in 2006 and officially documented in the state of Himachal Pradesh. The attack rate was highest in older age group warranting the need for MR vaccination.

***Keywords:** twin outbreak, IgM antibodies, highly immunized villages, D4- genotype, Kangra*

1. Introduction

In developing countries, measles (rubeola) is rightly called as captain of killer team especially, it killed 770,000 children worldwide in 2000, accounting for nearly half of vaccine preventable deaths [1]. Deprivation of at least one dose of measles vaccine to all infants contributes the principle reason for high measles mortality and morbidity in developing countries like India, Africa, and Pakistan [2]. However, in spite of sustained high coverage with single-dose vaccination strategy, there were outbreaks of rubeola in Latin America [3], Romania [4], Sri Lanka [5], and South Korea [6].

In developing countries like India, Delhi state has higher vaccine coverage since it has taken the initiative and lead of the two dose schedule of (i) measles at 9 months and (ii) measles, mumps, rubella (MMR) at 15 months respectively [7]. Nowadays there is distinct change in the measles and mumps disease pattern due to

measles and MMR vaccination [8] More and more case patients of measles and rubella are being examined in higher age group adolescent children [9,10]. The more vaccination coverage, the more is the time in between the outbreaks and a shift towards older age groups may be seen as in Thailand and Sri Lanka [11,12].

2. Materials and Methods

We investigated the outbreak on the suspicion of measles with the objectives of confirming existence of the outbreak; estimate measles immunization coverage among cases and vaccine efficacy; initiate appropriate measures to reduce morbidity and mortality and formulate recommendations on the basis of the results of present outbreak investigation.

2.1. Descriptive Epidemiology

On 13th September, 2006, a local community leader of sub centre Seilli circulated information regarding the cluster of cases of fever and rash in the remote hilly villages of Kuthaarna, Kanoul Nouli, Lahri and Seilli. We visited area on 23rd September, 2006 and observed that number of cases exceeded two standard deviations as compared to retrospective data thereby suggesting an outbreak. No ethical committee review was indicated, as this epidemiological investigation was conducted purely in the context of a public health response to an outbreak.

We case defined clinically by WHO criteria as the occurrence of a febrile rash with or without cough, coryza, conjunctivitis and lymphadenopathy in a resident of the five villages of Shahpur block since 1st September to second week of January, 2007. Laboratory criteria for diagnosis employed was at least a fourfold increase in antibody titre or isolation of virus or presence of measles specific IgM antibodies. Case classification includes *clinically confirmed*-a case that meets the clinical case definition; *Probable* is not applicable and *Laboratory confirmed* indicates a case patient that meets the clinical definition and that is laboratory-confirmed, or linked epidemiologically to a laboratory-confirmed case.

We initiated house to house search to identify the cases that meet the case definition or stimulated passive surveillance in affected villages with the target population of 1026 children. We interviewed the mother of every case patient or the next elder available member of the family with the semi structured questionnaire in Hindi language for 20 minutes. We employed coding for the participants to maintain confidentiality while analysis. We analyzed the data by MS-excel sheet using Epi info version 3.3.2.

Prior to sampling, the purpose and processing of the samples were explained. We took their written informed consent. In the fourth week and 7th week, we used sterile equipment to collect 2 samples of nasopharyngeal swabs for virus isolation and genotyping of the strain circulating in Himachal Pradesh; five samples of urine for culture/sensitivity and 13 randomly collected samples of blood (9 unpaired and 4 paired) at random from afflicted population. The sera were separated out; the international identification numbers with other epidemiological details were labeled on all the samples to transport the specimen to National Institute of Virology (NIV), Pune and reference laboratory in New Delhi in reverse cold chain separately. We sampled those who were willing while four reluctant/refusing populations were dropped. The cases meeting the case definition were line listed and detailed out in terms of place, person and time characteristics. The pieces of information about age, sex, symptomatology and date of onset of illness, treatment taken like modern medicine/traditional treatment, assessment of cold chain system, travel history; immunization status and smoking status of case patients and the susceptible population were also collected.

The villages by location of households were mapped to show the distribution of the cases by residence. The attack rate of cases by age group, sex groups using population data obtained from health care facilities and local authorities were calculated. We constructed an epidemic curve to examine the dynamic of the outbreak. Use of vitamin A for case management during the outbreak was reviewed. We also estimated the vaccine coverage in the population using mothers' interviews, immunization cards reviews and health care facility records reviews during field visit.

2.2. Vaccine Efficacy Using Analytical Epidemiology

We adopted retrospective cohort design to estimate the general as well as gender based vaccine efficacy. We selected the affected age groups from 10 months to 15 years as study populations. We ascertained the vaccination status by using one or more of three criteria: immunization cards, health care facility records and mothers' history. They used (attack rate among non-vaccinated – attack rate among vaccinated) / attack rate among non-vaccinated for cohort study. (Formula used was ARU-ARV/ARU*100).

3. Results

Our study results identified a total of sixty confirmed case patients (41/60 clinically, 8/60 laboratory confirmed case patients of rubeola and 11/60 epidemiologically linked rubella cases with lymphadenopathy and upper respiratory catarrh preceding the light maculopapulovesicular rash) from the study population of 1026. There were 02/11 cases of rubella in the age group of 0-5 years while majorities of rubeola and rubella case patients belonged to the age group of 6-15 years. The overall attack rate (AR) was 9% with median age of the cases as ten years (range 6-15 years) (Table 1). The sex specific AR constituted more (11%) for males. No rubeola/rubella related death was reported while the complications in the form of arthralgia (10%) and diarrhea (5%) were minimal. There was a history of the rubeola outbreak in the area eight to ten years ago. The history of the maculopapular rash (Figure 1) was 100% in the all cases with fever case patients as 95% (Figure 2). The severity of the symptoms of the outbreak was less among the younger cases and more towards the older ones particularly in the lower socio-economic strata, especially in Scheduled castes (62%) Vs Others (p <0.001) and illiterates Vs literates (p >0.000). According to their mothers' statements among 60 cases in the five villages, 42/60 (70%) cases were immunized against measles while nil vaccination for rubella. Supplemental measles

immunization in the form of ring immunization to the children in the affected villages and in the adjoining villages was instituted by district authorities but nil immunization for rubella.

Table 1. Age and sex specific attack rates in two in one outbreak of rubeola-rubella in Maan Vajreshwari Nagarkot Dham

S. No.	Name of the Village	Total Houses	Total Population	Age group 0-5yrs	No. of cases	Attack rate%	Age group 6yrs-15yrs	No. of cases	Attack rate%
1	**Kuthaarna**	110	761	91	0	0	144	31	21.5
2	**Kanoul**	161	973	116	0	0	184	5	2.7
3	**Lahri**	70	413	56	2	3.6	124	7	5.6
4	**Nouli**	36	274	32	0	0	52	6	11.5
5	**Seilli**	132	735	88	0	0	139	9	6.4
Grand Total	**Five villages**	509	3156	383	2	0.5	643	58	9.0
	Sex			Male	193	2	1.0	335	38	11.34
				Female	190	0	0	308	20	7.2

Proportion of male cases = 51%

Figure 1. Maculopapular rash (n=60) in two in one outbreak of rubeola-rubella in Maan Vajreshwari Nagarkot Dham (Light maculopapular skin rash on the back and chest in rubella)
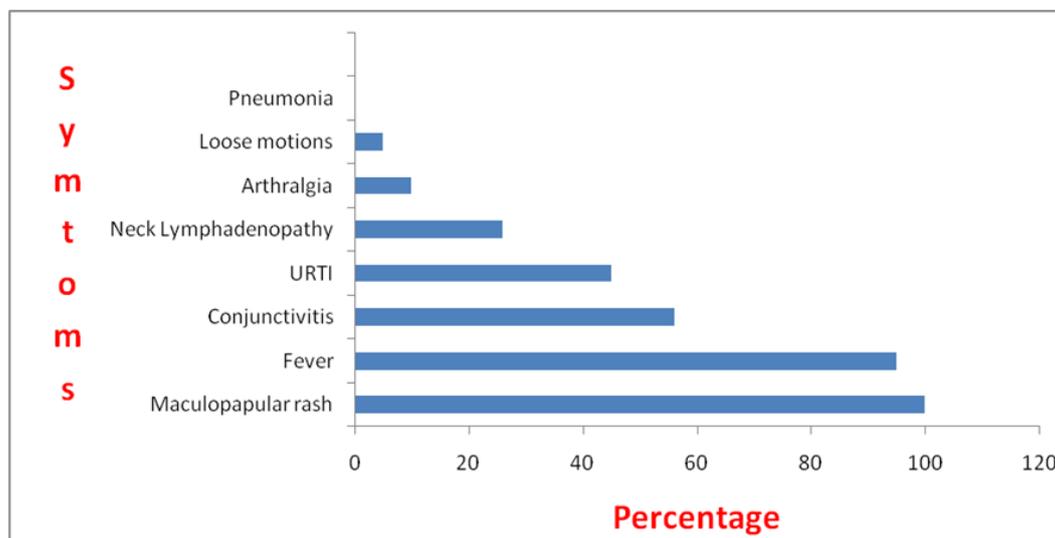

Figure 2. Symptomatology (n=60) in two in one outbreak of rubeola-rubella in Maan Vajreshwari Nagarkot Dham

We identified the index case in the area which was reported by the community leader on 1st September 2006 from Kuthaarna village and maximum numbers of cases were reported on 12th September 2006 one incubation period after the inter school game competition at Harchakiyan village. The outbreak encompassed to the other villages; Kanoul, Nouli, Seilli after the local festival Sayar on 16th September, 2006. In the festival the people visited the relatives and exchanged food preparations. Sporadic distribution of the cases by households was observed, with maximum number of the cases observed in Kuthaarna. This village has three houses with more than two cases while the village Kanoul has one house exceeding one case. The epidemic curve (Figure 3) indicated the dynamic of the outbreak that there were number of generations of cases with the propagated outbreak which peaked around 12th September, 2006. The number of cases declined during 2nd week of January, 2007.
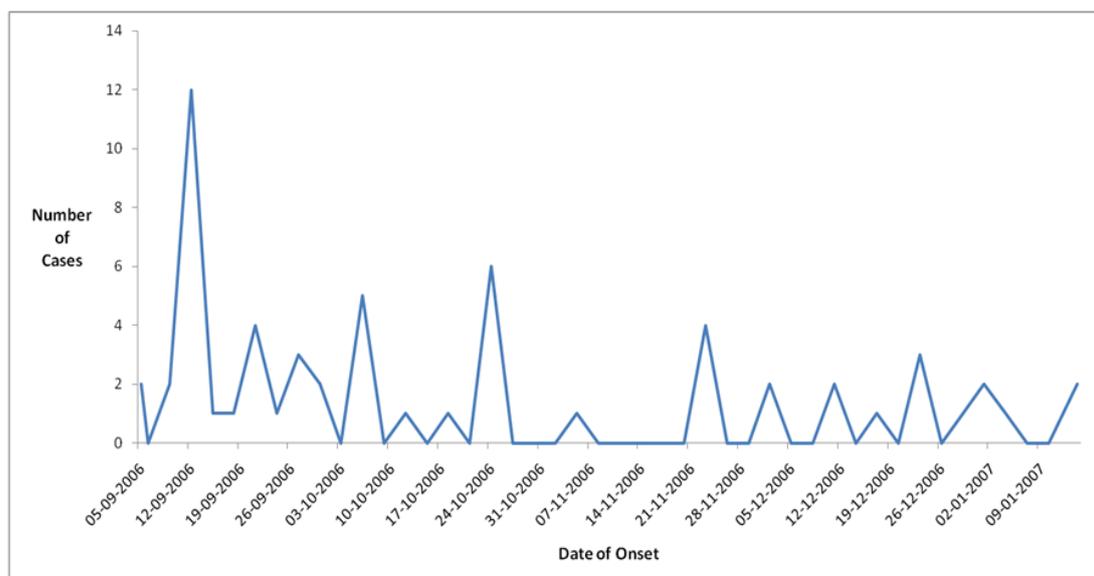
Figure 3. Symptomatology (n=60) in two in one outbreak of rubeola-rubella in Maan Vajreshwari Nagarkot Dham

The cases were managed symptomatically, vitamin A was supplemented and antibiotics in case of need whereas the supplemental measles vaccination was done among the susceptible in ring fashion. The cold chain was observed maintained during the vaccination sessions. The temperature log book was not regularly maintained at primary health centre Darini. 20% (12/60) of the cases went for the traditional treatment of ***Vannan bushes*** (medicinal herbal plant) movements for the nearby local chelas/faith healers (Traditional healers Vs modern medicine, p <0.05) and diet rich in ***seul***, more so in Kuthaarna and Nouli areas while 30% (18/60) had their treatment of choice to the modern system of medicine. Still majorities of the case patients, i.e., 50% (30/60) believed the treatment in both ways. The smoking habits (75%) are quite prevalent in early adolescents (10-20 years) and youth.

2/5 nasopharyngeal swabs for Polymerase Chain Reaction (PCR) test and 8/13 samples for measles IgM antibodies were positive serologically. Three blood samples and three nasopharyngeal and all the eight urine samples leaked out while in transportation and hence, they were result less. Measles genotype D4 was detected in the two swabs suggesting that D4 virus strains are circulating in district Kangra.

3.1. Coverage Assessment and Vaccine Efficacy Using the Screening Method

The immunization coverage of whole of Shahpur block as per health record is in between 104% to 113% and that of the sub centre Seilli lies in between 78% to 127% between 2001 to 2006 for <5 years children[13]. The vaccination coverage as per mothers' interview (the least specific criteria) was 94% (960/1026) whereas according to vaccination cards (the most specific criteria)-it is 37%. (380/1026).

Table 2. Attack rates of two in one outbreak of rubeola-rubella in Maan Vajreshwari Nagarkot Dham_Cases by age and vaccination status (Retrospective Cohort Study)

Name of the village	Age group in years	Children immunized against measles			Children not immunized against measles		
		Cases	Total	Attack rate %	Cases	Total	Attack rate %
Kuthaarna	0-5	0	91	0	0	0	0
Kanoul	0-5	0	116	0	0	0	0
Nouli	0-5	0	32	0	0	0	0
Lahri	0-5	2	56	3.6	0	0	0
Seilli	0-5	0	88	0	0	0	0
Total	**0-5**	**2**	**383**	**0.5**	**0**	**0**	**0**
Kuthaarna	6-15	27	129	21	4	15	27
Kanoul	6-15	3	169	2	2	15	13
Nouli	6-15	2	42	5	4	10	40
Lahri	6-15	6	114	5	1	10	10
Seilli	6-15	3	123	2.4	4	16	38
Total	**6-15**	**41**	**587**	**7.0**	**15**	**56**	**26.7**
Grand Total	*0-15*	*45*	*960*	*4.6*	*15*	*66*	*22.7*

15 case patients of 66 non immunized (22.7%) children compared to 45 case patients of 960 immunized (4.6%) and it was statistically significant. RR*: 4.85; 95% CI†: (2.86–8.22) P <0.001); VE‡ = 83%.

Gender based VE-Male	84%	26	488	5.3	13	40	32.5

13 case patients of 40 non immunized (32.5%) children compared to 26 case patients of 488 immunized (5.3%) and it was statistically significant. (RR: 6.10%; 95% CI (3.41–10.92) P <0.001); VE=84%.

Gender based VE-Female	76%	17	472	3.6	4	26	15

4 case patients of 26 non immunized (15%) children compared to 17 case patients of 472 immunized (3.6%) and it was statistically significant. RR: 4.27%; 95%: CI (1.55–11.79) P <0.001); VE=76%

*RR-(Relative risk)

‡VE (Vaccine efficacy)

†CI (Confidence Interval)

3.2. Vaccine Efficacy Using Analytical Epidemiology

General vaccine efficacy (VE) = 83% while the vaccine efficacies for the gender based for (i) male, VE is 84% while that of female, it is 76% (Table 2).

4. Discussion

A combined outbreak of rubeola/rubella struck in the remote mountainous five villages under sub centre Seilli of Shahpur block in the month of September to January, 2007. The present outbreak was first reported by the local community leader of Kuthaarna Panchayat and was not detected by existing surveillance system. In the beginning, we investigated this propagated outbreak on the provisional diagnosis of measles, as there were two more laboratory confirmed outbreaks of measles and german measles in adjoining different blocks of district. Rubeola is a notifiable disease in this country, but not rubella; hence, cases with maculopapular rash are often although in the present double infection, the clinical presentation of fleeting nature of symptomatology is more suggestive of epidemiologically linked sporadic confirmed case patients of rubella [14]. However, the 'misdiagnosis' that led to 'misnotification' as seen in this outbreak setting was not surprising, as rubella is a mild disease and often 30-50% of infected people may not notice any symptoms at all. The serology proved IgM positive for rubeola and D4 rubeola strain was genotyped.

Though the case patients in the outbreak were sparsely distributed principally belonging to the lower socio-economic strata and were malnourished [15], yet the younger generation was less afflicted. The older aged group identified in between 6 years to 15 years were the main sufferers meaning thereby, there was an obvious shift to the higher age group. Availability of health services and better awareness resulted into low attack rates, fewer complications and no mortality which demonstrated the mild nature of the two in one outbreak. The others workers [16, 17] have also reported similar findings. There are a few rubeola/rubella cases in the age group of 0-5 years, possibility is that there is the higher risk of the occurrence of secondary vaccine failure that reduce the immunity to rubeola over time than the primary vaccine failure that did not develop the immunity. The attack rates were higher in aged 06-15 years in Nouli and Seilli villages. This suggests waning of immunity with age (secondary vaccine failure) which can be on account of use of poorly stored vaccine at the place of the children's vaccination. Also there is the possibility of the failure of the cold chain maintenance in the area with the reduced vaccine efficacy at the time when the older children aged 06-15 years in Nouli and Seilli villages were vaccinated against measles before. The cold chain was observed maintained from district head quarter to sub-centers. However, there were few drawba cks like ill maintained temperature log book at primary health centre and repeated opening and closing of the vaccine carriers during the sessions warranted attention. There are odds of failure of the vaccine potency. A likewise result has been seen in highly vaccinated population by Lamb WH [18] Many developed countries like United States, Canada, Finland, Hungry, Oman and United Kingdom had eliminated rubeola by 2 doses schedule.

Despite > 95% high coverage in Shahpur block and those of the affected villages under sub centre Sarah, inter epidemic interval became more & the number of the cases are sporadic [19]. The epidemic appeared out due to the gradual accumulation of a small number of susceptible children over the years in the community. Such accumulations typically resulted owing to the combination of (1) 85% measles vaccine efficacy and (2) subsequently, children left un-immunized each year. Retrospective cohort study conducted during these outbreaks proved that the efficacy of the vaccine (83%) was within the anticipated level thereby warranting the requirement of the 2nd dose opportunity for rubeola to develop the herd immunity.

Traditional beliefs and barriers about measles do not foster healthy behaviors in the population like the intake of the medicines suppresses the disease and VANNAN bush movement on the patient's body as part of the traditional treatment before or with modern medicines forms the mainstay. That is why, very less number of the patients have reported to sub centre Seilli.

It is critical to recognize that supplementary immunization activities during double infection were done only for rubeola and all the case patients remained unvaccinated for rubella. Although rubella is a relatively innocuous illness for the non pregnant patient, yet in contrast, rubeola infection during pregnancy has not been associated with congenital malformations [20]. But under affected sub centre Seilli there were four pregnant ladies in five villages at the time of investigation of outbreak and no pregnant female was affected by double infection and the outcome of the pregnancies were normal. The smoking habits are quite prevalent in early adolescents (10-20 years) and youth. Eighty percent of the youth start their first smoking before they reach age of 20 years. This study corroborates the findings [21]. Rubella case patients are more in the higher age group in adolescents, especially in those ones who are smokers. Here lies the role of ensuring Information, Education Communication (IEC) activities aggressively.

4.1. Limitations

Recall bias could have surfaced with respect to recollection of immunization of the children of the area.

A mixed outbreak of rubeola/rubella was confirmed epidemiologically, clinically and serologically in highly immunized mountainous area for rubeola but unvaccinated for rubella. Surveillance system in place was weak. Defective practices of the cold chain system could affect the efficacy of the vaccine. Besides above, traditional beliefs and barriers mainly in poor families formed the mainstay of the treatment part. Prevalence of more tobacco smoking in adolescent patients was observed.

On the basis of investigation we proposed a number of recommendations:

1. Go for the MR vaccination at the age of 18-24 months with first booster of DPT/Polio. **2.** Strengthen measles surveillance through the upcoming Integrated Disease Surveillance Programme (IDSP). **3.** Refresher trainings to the workers of the affected areas for proper cold chain maintenance; **4.** Information, Education and

Communication (IEC) activities should be targeted towards (i) modifying the help seeking behavior of mother in the district, especially in the measles affected areas and (ii) also avoidance of tobacco smoking in adolescent patients.

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