Original Article

A Mixed Outbreak of Rubeola-rubella in District Kangra of Northern India

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Abstract

Background: On 14th September 2006, a local community leader informed us about the sudden increase in number of cases of fever and rash in five villages of district Kangra. We investigated the suspected outbreak to confirm the diagnosis and recommend for prevention and control. **Materials and Methods:** We defined a case of rubeola as the occurrence of fever with rash in children from 3rd September to 13th January, 2007. We collected information on age, sex, date of onset, residence, signs, symptoms, vaccination and cold chain status. We described the outbreak by place, time and person characteristics. We conducted a retrospective cohort study to estimate vaccine efficacy (VE). We ascertained the measles immunization status by interviewing the mothers and reviewing immunization cards. We confirmed diagnosis clinically, epidemiologically and serologically. **Results:** We identified 60 case patients 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 >5 years of age. No death/minimal complications have 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 VE to be 83% while gender based VE for male was 84%. Eight case-patients were confirmed serologically for measles immunoglobin M antibodies, two nasopharyngeal swabs positive by polymerase chain reaction. 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 measles and rubella (MR) vaccination at the age of 18-24 months and aggressive Information, Education and Communication (IEC) activities to modify help seeking behavior of the community, especially in the measles affected areas.

Keywords: D4-genotype, highly immunized villages, immunoglobin M (IgM) antibodies, Kangra, rubeola-rubella outbreak

Introduction

Measles is rightly called as captain of killer team especially in developing countries. In 2000, measles killed 770,000 children world-wide, accounting for nearly half of the 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, despite 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]

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In developing countries like India, Delhi state has higher vaccine coverage since it has taken the initiative and lead to the two dose schedule of measles mumps and rubella (MMR) at 9 months and at 15 months respectively.[7] Now a days there is a 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 (MR) are being examined in higher age group adolescent children[9,10] and multiple concurrent outbreaks of measles, rubella, varicella and herpes zoster have been observed in the higher age groups; 6-25 years; with increased attack rate (AR) more in 10-25 years group and it is important for the clinical practitioners of primary care physicians about the role of administration of triple vaccine, MMR or measles, mumps, rubella vaccine (MMRV).[11,12] The more vaccination coverage, the more is the time in between the outbreaks and a shift toward older age groups may be seen as in Thailand and Sri Lanka.[13,14]

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

Materials and Methods

Descriptive epidemiology

Information regarding the cluster of cases of fever and rash in the remote hilly villages of Kuthaarna, Kanoul Nouli, Lahri and Seilli was communicated to us on 13th September, 2006 by a local community leader of sub center Seilli. A visit to that area on 23rd September, 2006 revealed 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 World Health Organization 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 2nd week of January, 2007. Laboratory criteria for diagnosis employed was at least a four-fold increase in antibody titer or isolation of virus or the presence of measles specific immunoglobin M (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.

House to house search was initiated 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 the 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.

(Epi Info is a free software package developed by the US Centers for Disease Control)

Prior to sampling, the purpose and processing of the samples were explained. We took their written informed consent. In the 4th week and 7th week, we used sterile equipment to collect two 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 (nine unpaired and four 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 of case patients and the susceptible population were also collected.

We mapped out the villages by location of households to show the distribution of the cases by residence. The AR 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 mother's interviews, immunization cards reviews and health-care facility records reviews during field visit.

VE using analytical epidemiology

We adopted retrospective cohort design to estimate the general as well as gender based VE. 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 (AR among non-vaccinated — AR among vaccinated)/AR among non-vaccinated for a cohort study (formula used was ARU — ARV/ARU*100).

Results

Our study identified a total of six 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 maculopapular vesicular rash) from the population of 1026. There were 2/11 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 AR was 9% with the median age of the cases as 10 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 8-10 years ago. The history of the maculopapular rash [Figure 1] was 100% in 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%) versus others ($P < 0.001$) and illiterates versus 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

Table 1: Age and sex specific attack rates of mixed outbreak of rubeola-rubella cases in five villages, Kangra district, Himachal Pradesh, 2006

Name of the village	Total houses	Total population	Age group 0-5 years	No. of cases	Attack rate %	Age group 6-15 years	No. of cases	Attack rate %
Kuthaarna	110	761	91	0	0	144	31	13
Kanoul	161	973	116	0	0	184	5	1.7
Lahri	70	413	56	2	3.6	124	7	5.6
Nouli	36	274	32	0	0	52	6	7
Seilli	132	735	88	0	0	139	9	4
Five villages (Grand total)	509	3156	383	2	1.0	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 mixed outbreak of rubeola-rubella cases in five villages of Kangra district, Himachal Pradesh, 2007. Light maculopapular skin rash on the back and chest in rubella

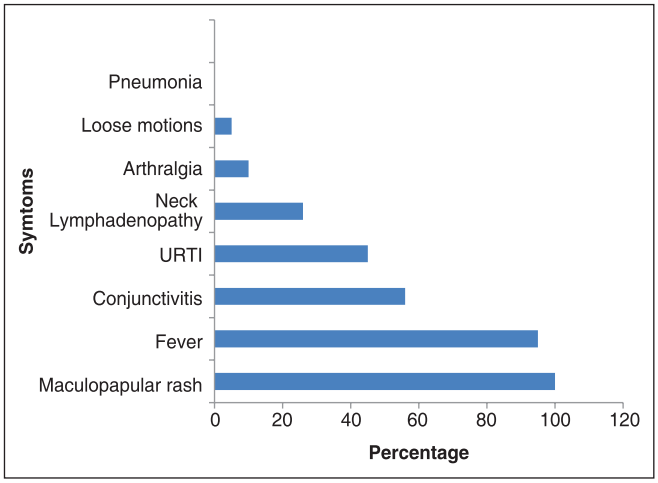

Figure 2: Symptomatology (n = 60) in mixed outbreak of rubeola-rubella cases in five villages of Kangra district, Himachal Pradesh, 2007

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

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 that festival the people visited the relatives and exchanged food preparations. Sporadic distribution of the cases by households was observed, with the 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 outbreak that there were a 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.

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 center 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.

Out of 5, 2 nasopharyngeal swabs for polymerase chain reaction 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.

Coverage assessment and VE using the screening method

The immunization coverage of whole of Shahpur block as per health record is in between 104% and 113% and that of the sub center Seilli lies in between 78% and 127% between 2001 and 2006 for <5 years children.[15] 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).

VE using analytical epidemiology

General 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].

Discussion

A mixed outbreak of rubeola/rubella struck in the remote mountainous five villages under sub center 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.[16] 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.[17] 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%

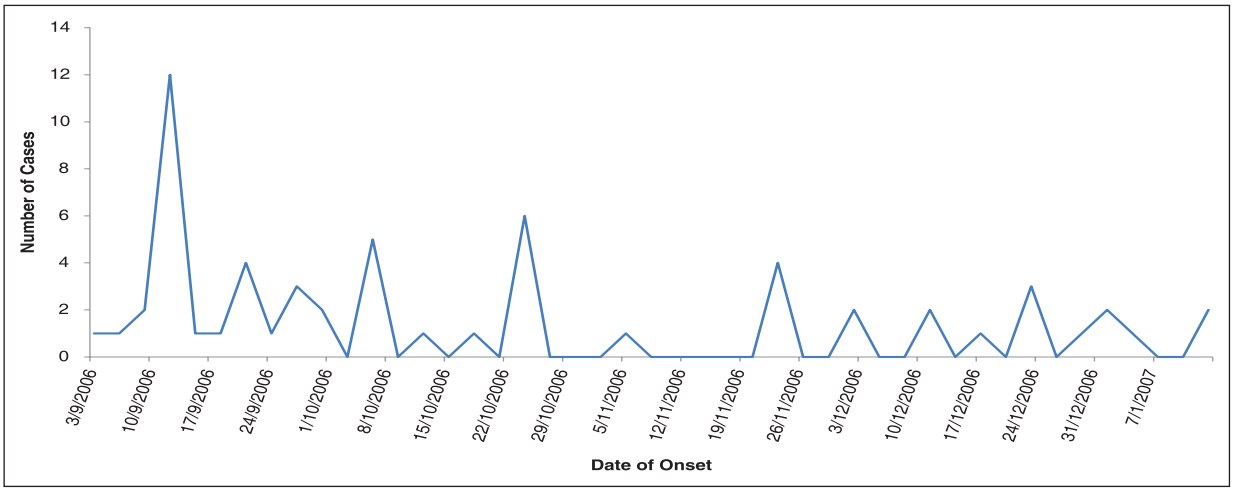

Figure 3: Symptomatology (*n* = 60) in mixed outbreak of rubeola-rubella cases in five villages of Kangra district, Himachal Pradesh, 2007

Table 2: Attack rates of mixed outbreak of rubeola-rubella cases by age and vaccination status in five villages of Shahpur block, district Kangra, Himachal Pradesh, India, 2007 (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	0	383	0	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	6	16	38
Total	6-15	41	587	7.0	16	56	28.6
Grand total	0-15	43	960	4.5	17	66	25.8
17 case patients of 66 non-immunized (25.8%) children compared to 43 case patients of 960 immunized (4.5%) and it was statistically significant. RR: 5.75%; 95% CI: 3.48-9.51 *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

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,[17,18] yet the younger generation was less afflicted. The older aged group identified in between 6 and 15 years were the main sufferers meaning thereby, there was an obvious shift to the higher age group. It is an important point to add here that in the light of recent development of outbreaks in the plus five age category, diphtheria tetanus pertussis (DPT) vaccination has been introduced in Universal Immunization Program by Government of India at the age of 5 years, but the case patients of mumps and rubella have also been observed in the higher age groups and so is measles troubling our adolescents.[11,12,14,16] Hence, introduction of MMR or MMRV is very useful for the clinical practitioners of primary care physicians. The immunity from MMR lasts for 10-15 years of age. Therefore, why not give booster dose of MMR say by 10 years of age? A booster dose at this age will give a lifelong immunity.[12]

Availability of health services and better awareness resulted into low ARs, fewer complications and no mortality, which demonstrated the mild nature of the two in one outbreak. The other workers[19,20] 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 ARs 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. Furthermore, there is the possibility of the failure of the cold chain maintenance in the area with the reduced VE 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 a few drawbacks like ill-maintained temperature log book at primary health center 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.[21] Many developed countries such as United States, Canada, Finland, Hungary, Oman and United Kingdom had eliminated rubeola by two doses schedule.

Despite >95% of this high coverage in Shahpur block and those of the affected villages under sub center Seilli, inter epidemic interval became more and the number of the cases are sporadic.[14,16,22] 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 VE 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 the modern medicines forms the mainstay. That is why, very less number of the patients have reported to sub center 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.[12,23] But under affected sub center Seilli there were four pregnant ladies in five villages at the time of investigation of the outbreak and no pregnant female was affected by double infection and the outcome of the pregnancies were normal.

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.

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 Program.
3. Refresher trainings to the workers of the affected areas for proper cold chain maintenance.
4. Information, education and communication activities should be targeted towards modifying the help seeking behavior of mother, education and communication in the district, especially in the measles affected areas.

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