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Epidemiological investigation of mixed outbreaks of measles/varicella in hilly villages of district Kangra, Himachal Pradesh, India

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ABSTRACT

Background **On 26th September 2006, a local health worker informed us about sudden increased number of cases of fever and rash in three villages of district Kangra. We investigated the suspected outbreak to confirm diagnosis and recommendation to prevent and control.**

Methods **A case of measles was defined as occurrence of fever with rash in a child between six months to 17 years of age, from 26th September to 2nd week of January, 2007. The information on age, sex, symptoms, signs, date of onset, residence, traveling history treatment taken and assessment of cold chain system was collected. The outbreak was described by place, time and person characteristics. We also conducted a retrospective cohort study among children between 10 months and 15 years of age to estimate the vaccine efficacy. We confirmed diagnosis clinically, epidemiologically and serologically.**

Results **We identified 29/35 measles and 6/35 were confirmed as epidemiologically linked unvaccinated chickenpox case patients. The overall attack rate (AR) was 8.13%; maximally in the age group of 11-17 years ranging in between 17-35%. Sex specific AR was more (17%) in females. There was neither any death nor any serious complications. The proportion of the children vaccinated was 95% for measles but nil for varicella. Of 35 case-patients, 27 (78%) were vaccinated for measles only with no vitamin A supplementation (relative risk: 5.3; 95% confidence interval: 1.90 – 14.77). The measles vaccine efficacy was estimated to be 82%. 3/3 case-patients for measles IgM antibodies and 2/3 nasopharyngeal swabs were tested positive by PCR and D4 measles strain genotyped.**

Conclusion **Measles/varicella outbreaks were confirmed. We recommended varicella vaccination, second dose opportunity for measles and vitamin A supplementation to all cases in affected areas.**

Keywords: **D**ouble infection, measles, varicella, outbreak, IgM antibodies

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INTRODUCTION

Three WHO regions–the Americas, the Eastern Mediterranean and Europein recent years, have had remarkable success in eliminating measles by means of various kinds of vaccination strategies. United States, Hungary and Finland have eliminated indigenous measles transmission with a routine two-dose schedule by reaching coverage exceeding 95%. Canada, United Kingdom and Oman have also got the similar results by following a catch-up campaign

with a routine two-dose schedule[1]. WHO and UNICEF adopted a three-phase strategy for global measles elimination. The three phases of the strategy are (1) Measles control (2) Outbreak prevention and (3) Measles elimination[2].

In developing countries like Pakistan, Africa and India, the pediatric mortality and morbidity due to the lack of the first dose of measles immunization constitutes the major cause[3]. However, South Korea[4], Romania[5] and Sri Lanka[6] in spite of sustained high coverage with single dose vaccination strategy, continue to experience outbreaks of measles. Due to local festivals in the villages and the population movement in the hilly areas, transmission of the measles virus is facilitated. The outbreaks are quite common in school children[7] and simultaneous outbreak of varicella and measles has also been recorded[8]. In such cases of double infection, the notable finding is that first infection diminishes the severity of rash of the second infection[9,10]. During emergencies WHO and UNICEF recommend vaccinating all children from six months to 14 years of age along with vitamin A supplementation[11]. We investigated the outbreak with the objectives of confirming the existence of the outbreak anddiagnosis through laboratory investigation; initiate preventive measures and formulate recommendations on the basis of the results of present outbreak investigation.

MATERIALS AND METHODS

A multi-purpose worker reported an outbreak of rubeola in the remote hilly villages of Jathrair, Bathrair and Gujrair under sub centre Serah of Shahpur block of Kangra district on September 26th, 2006. Having lodged the first hand information report (FIR), we commenced investigating the outbreak on September 28th, 2006 after the call from the district health authority Kangra. A review of the number of cases reported and a comparison with retrospective data indicated that there was an increase of more than 10% in the number of case patients, exceeding two standard deviations, thereby suggesting an outbreak. As there was no population migration and no change in surveillance practices, we decided to investigate.

By WHO criteria, a case of measles was defined clinically as the occurrence of a febrile rash with or without cough, coryza and conjunctivitis in a resident of the three villages of Shahpur block since September 26th until the 2nd week of January, 2007. Case classification includes *clinically confirmed*-a case that meets the clinical case definition; 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[9]. Laboratory criteria for diagnosis employed was at least a fourfold increase in antibody titre or isolation of measles virus or presence of measles specific IgM antibodies. Complications and deaths due to measles were considered if these occurred within 30 days of onset. Active case search was initiated by visiting house to house to identify the cases that meet the case definition or stimulated passive surveillance in forenamed three villages with the population of 430. We interviewed the mother of the every case patient with the semi-structured questionnaire in Hindi language for twenty (20) minutes or alternatively, the next elder available member of the family.

The case patients were line listed and described in terms of person, place and time characteristics. We also collected information about age, sex, symptomatology, date of onset of illness, place of residence, immunization status of case patients and the susceptible population, assessment of cold chain system and taken treatment of modern/conventional medicine. The villages by location of households were mapped to show the distribution of the cases by residence. The attack rates of cases by age group, sex groups using population data obtained from the district health authorities were calculated and the dynamics of the outbreaks through the construction of an epidemic curve was examined. The use of vitamin A for case management was also reviewed during the outbreak.

Administrative measles vaccine coverage estimates were collected and during field visit, the vaccine coverage in the population using *health care facility records reviews, mothers' interviews and immunization cards reviews* was estimated. Retrospective cohort design was employed to estimate the vaccine efficacy

by using the formula; (attack rate among non-vaccinated – attack rate among vaccinated) / attack rate among non-vaccinated for cohort study. (Formula used was ARU-ARV/ARU*100; Table 2, see Results)

Detailed information was disseminated to the population of study areas for the purpose and processing of the samples. The written informed consent was taken. In the fourth week of the ongoing outbreak, observing universal safety precautions, we collected (i) 3 random samples of 5ml of blood for each specimenfrom different places. We crystallized, separated the sera and refrigerated under +4 to +8*C for testing specimens for IgM/IgG antibodies using ELISA. (ii) 3 samples of nasopharyngeal swabs in Virus Transport Media (VTM) for virus isolation and genotyping of the strain by Polymerase Chain Reaction (PCR) and (iii) 3 samples of 50 ml each of urine for culture/sensitivity using sterile equipment in Virus Transport Media were stored. International identification numbers were assigned and other epidemiological details on all the samples were labeled. In reverse cold chain separately, the specimen were transported to the accredited laboratory, Pune. The samples were taken from those only who were willing while seven reluctant/refusing populations were dropped.Ethical committee review was not indicated, since this investigation was conducted in the context of a public health response to an outbreak and therefore. We entered dataset by double data entry technique and analyzed using Epi info version 3.3.2.

RESULTS

Our study identified a total of 35confirmed case patients (24/35 measles and 6/35 chicken pox-epidemiologically linked with maculopapulovesicular rash and 05/35 laboratory confirmed) from a study population of 430. Attack Rate (AR) ranged from 5% to 13%; with overall attack rate 8.13% from three villages. (Median age-11 years with range as 6 years to 17 years) The sex-wise AR constituted more (17%) for females (Table 1).

Table 1 Age and sex specific attack rates of mixed outbreaks of measles/chickenpox cases in Jathrair, Bathrair and Gujrair villages, Kangra district, Himachal Pradesh, India, 2007

Name of village	Age group	No. of cases	Total population	Attack Rate %age
Jathrair	0-5years	02	80	**2.5**
	6-10years	02	43	**4.7**
	11-17years	18	52	**35**
	Total	**22**	**175**	**13**
Bathrair	0-5years	00	63	**00**
	6-10years	01	56	**2.0**
	11-17years	06	30	**20**
	Total	**07**	**149**	**5.0**
Gujrair	0-5years	00	32	**00**
	6-10years	01	44	**2.2**
	11-17years	05	30	**17**
	Total	**06**	**106**	**6.0**
	Grand total (3 villages)	***35***	***430***	***8.13***
Sex				
Male	0-5 years	0	99	**0**
Female	0-5 years	0	76	**0**
Male	6-17 years	16	144	**11.0**
Female	6-17 years	19	111	**17.0**

There were 02/06 cases of varicella in the age group of 0-5 years while the rest of the cases fell in the age group of 6-17 years. The attack rate was maximal in the highest age group of 11-17 years which fluctuated in between 17% to 35%. There were minimal complications in the form of diarrhea (9%) but no measles/varicella related death reported.

There is a history of the measles outbreak in the area nine years ago. In all case patients the history of the febrile rash was 100% (Figure 1). The severity of the symptoms was more (23/35) towards the older ones particularly in the lower socio-economic strata, especially in illiterates Vs literates (p >0.00); Other Backward (OBC) Classes (66%) vs. Others (p <0.00). According to the mothers' statements, 27/35 cases (78%) were immunized against measles only. All the case patients were unvaccinated for varicella. Neither supplemental ring immunization for measles nor for varicella case patients nor vitamin A was administered to the children under sub centre Serah.

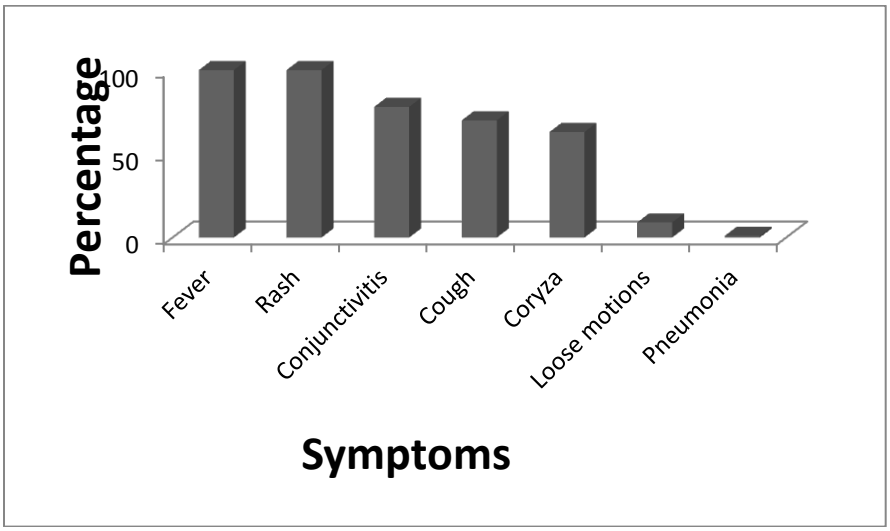

Figure 1 Symptomatology (n=35) in measles/varicella outbreak in villages under sub centre Sarah of Shahpur block, Kangra district, Himachal Pradesh, India, 2007

The case patients took the treatment from the nearby Military Hospital and Dr. Rajinder Prasad Govt. Medical College Hospital, Dharamshala.The cold chain was observed maintained during the vaccination sessions, but the defective practice of frequent opening and closing of the vaccine carriers continued.6/35(18%) of the cases opted for the traditional treatment of *Vannan bushes* (medicinal herbal plant) movements from nearby local chelas/faith healers (Traditional healers Vs. modern medicine, p <0.05) and diet rich in *seul*, more so in Gujrair areas (Restricted diet Vs. Nutritious diet, p <0.005) while 14/35 (41%) had their treatment of choice to the modern system of medicine. Still majorities of the case patients, i.e., 15/35 (42%) believed the treatment in both ways.

The index case was identified on 26th September, 2006 from Jathrair village due to cross infection from local festival *Sayar*in 25 kms approximately far away from infected Kutharna village. It spread to other villages one incubation period after the local festival Sayar on September 16th, 2006. The festival attracted the people and their relatives and they exchanged food preparations. Sporadic distribution of the cases by households, with maximum 22/35 number of the case patients (63%) was observed in Jathrair. The dynamic of the outbreak in epidemic curve (Figure 2)

indicated that this propagated outbreak had a number of generations of cases peaking around November 11th, 2006. The number of cases declined during second fortnight of December, 2006 and the outbreak ceased in second week of January, 2007 with two weeks free of any new case patients up to 4th week of January, 2007.

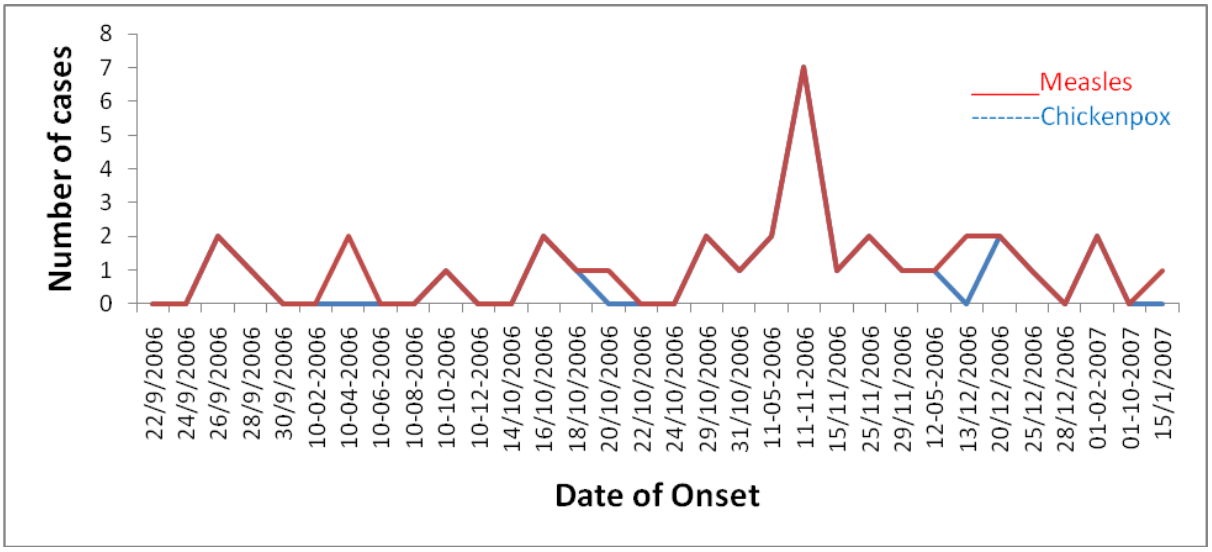

Figure 2 Epidemic curve of measles/varicella case patients (n=35) by date of onset in three villages under sub centre Sarah of Kangra district, Himachal Pradesh, India, 2007

Attack rates of measles by age and vaccination status indicated 08 case patients of 22 non-immunized (36.36%) compared to 27 case patients of 408 immunized (6.61%) children and it was statistically significant. (Relative risk: 5.49; 95% confidence interval: 2.03-14.55; P <0.001) The vaccine efficaciesas per mothers' interview and vaccination cards were calculated to be 82% and 64% (Table 2). The vaccination coverage as per mothers' interview is 93%–the least specific criteria while according to vaccination cards, the most specific criteria- it is 64%.

Serologically, (i) 3/3 samples for measles IgM antibodies with four fold rise of IgM antibodies (ii) 2/3 nasopharyngeal (NP) swabs were positive. No result for chicken pox cases was available from laboratory. One NP swab and all the urine samples leaked out while in transportation and mismanagement and hence, there was nil result available for these samples. Two NP swabs were genotyped for measles D4 strain. It suggested that D4 virus strains are circulating in district Kangra of Himachal Pradesh.

Table 2 Attack rates of measles (n=35) by age and vaccination status, in Jathrair, Bathrair and Gujrair villages of Shahpur block, district Kangra, Himachal Pradesh, India, 2007

		Children immunized against measles (By Mothers' Interview)			Children not immunized against measles (By Mothers' Interview)		
Name of the village	Age group in years	No. of Cases	Total	Attack rate %	No. of Cases	Total	Attack rate %
Jathrair	0-5	0	80	0	0	0	0
Bathrair	0-5	0	63	0	0	0	0
Gujrair	0-5	0	32	0	0	0	0
Jathrair	6-10	4	40	10	1	3	33
Bathrair	6-10	1	54	2	0	2	0
Gujrair	6-10	1	41	2	0	3	0
Jathrair	11-17	13	45	29	4	7	57
Bathrair	11-17	4	26	15	2	4	50
Gujrair	11-17	4	27	15	1	3	33
Grand Total	0-17	27	408	7	8	22	36
		Children immunized against measles (By vaccination cards)			Children not immunized against measles (By vaccination cards)		
		16	292	05	19	138	14

Proportion of the children vaccinated: 95% with the calculated vaccine efficacy: 81% as per mothers' interview (Relative risk: 5.49; 95% confidence interval: 2.83-10.65; P <0.001) and vaccine efficacy as per vaccination cards: 64% (Relative risk: 2.51; 95% confidence interval: 1.33-4.73; P <0.006)

DISCUSSION

Double outbreaks of measles and chickenpox struck three hilly villages under Sarah sub centre from 26th September to first week of January, 2007. Initially, we investigated this propagated outbreak on the suspicion of measles but the epidemiologically linked sporadic confirmed case patients of varicella were also examined concurrently on the symptoms of maculopapulovesicular rash. The rash was atypical in appearance (maculopapular with few or no vesicles) in 3/6 cases and severity of symptoms was mild in nature[8,9 10], fewer than 50 skin lesions and shorter duration of illness. Although the casepatients in the outbreak were sporadic, belonging to the lower socio-economic strata and were malnourished[12], yet the duration of illness coupled with severity of the symptoms were more especially in the older generation. Symptoms frequency also supported the laboratory diagnosis. The serology proved IgM positive for measles and D4 measles strain was genotyped. Majority of the case patients identified belonged to the older age group, meaning thereby, there was an obvious shift to the higher age group (6 years to 17 years) with no fatality or minimal complications thereof.On account of better awareness and availability of health services, there were low attack rates, fewer complications and no mortality which reflected the mild nature of the two in one outbreak. Similar findings have also been reported by others workers[13-14]. The attack rates were higher in aged 11-17 years in Jathrair village. This suggests waning of immunity with age (secondary vaccine failure) which can be due to the use of poorly stored vaccine at the place of these children's vaccination. There are no measles cases in the age group of 0-5 years, it is possible there is the higher risk of the occurrence of secondary vaccine failure that reduce the immunity to measles over time than the primary vaccine failure that did not develop the immunity. Also there is the possibility of the failure of the cold chain maintenance in the area with the lower vaccine efficacy at the time when the older children aged 11-16 years in Jathrair had had measles vaccine before. However, South Korea [4], Romania [5] and Sri Lanka[6]suffered outbreaks of measles in spite of consistent high coverage with single-dose vaccination strategy warranting for second dose opportunity for measles.

Despite over 95% high coverage in Shahpur block (104% to 113%) and those of the affected villages under sub centre Sarah, (80% to 100%), inter epidemic interval was more & the number of the cases are sporadic[15-16]. The outbreak burst out due to the steadily increasing accumulation of a small number of susceptible children over the years in the community. Such accumulated pools are typically caused by 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 (82%) was within the anticipated level thereby warranting the requirement of the 2nd dose opportunity for the measles to develop the herd immunity[17]. One of the limitations of coverage surveys was that in the affected villages of district Kangra, the low proportion of parents retained the card of their child.

It is critical to recognize that no supplementary immunization activities during double infection were done, nor the vitamin A supplementation was instituted as the affected areas are not far away from the block health authorities. The cold chain was observed maintained but there were few shortcomings like poorly maintained temperature log book at primary health centre, Charri.

Traditional beliefs about measles do not foster healthy behaviors in the population like measles occurs due to curse of goddess and VANNAN bushes movement on the patient's body as part of the traditional treatment before or with modern medicines forms the mainstay[18]. That is why a less number of the patients have reported to sub centre Sarah.

Limitations

Recall bias may have occurred with respect to recollection of immunization of the children of the area.

CONCLUSION

Double outbreaks measles/varicellawas confirmed clinically, epidemiologically and serologically in highly measles immunized area.There was absenceof

Supplemental Immunization Activities (SIA) for measles as well as varicella and Vitamin A supplementation.The mainstay of the treatment part constituted the traditional beliefs and barriers mainly in marginalized families. Mal practices of the cold chain system could influence the effectiveness of the vaccine.

Recommendations

1. We need to proceed for the 2nd dose opportunity of the measles vaccination in highly immunized areas and varicella vaccination to the affected areas.
2. Provide vitamin A supplementation to the cases and SIA to the susceptible.
3. Information, Education and Communication (IEC) activities should be targeted to modify the help seeking behavior of mothers in the district, especially in the measles affected areas. 4. The workers of the affected areas needs to be imparted the refresher trainings for proper cold chain maintenance.

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