Factors precipitating outbreaks of measles in district Kangra of North India: A case-control study

Surender Nikhil Gupta, Ramachandran Vidya1, Naveen Gupta2, Mohan D Gupte1
MAE-FETP Graduate from National Institute of Epidemiology (NIE), Chennai; presently at Regional Health and Family Welfare Training Centre, Chheb, Kangra, Himachal Pradesh, 1FETP Faculty at NIE, Chennai, 2Freelance Researcher in Epidemiology, Kangra, India

Abstract

Background: Globally, measles is the fifth killer disease among children under five years of age. Despite high immunization coverage in Himachal, outbreaks are occurring. Upon two outbreaks in a hilly district in North India, a case control study was conducted to identify factors contributing to outbreaks and to recommend remedial measures to prevent further outbreaks. Materials and Methods: Factors were reviewed under three heads: program related, health care providers, and beneficiaries related. Cold chain maintenance was determined and responses were compared between workers from study Shahpur and control Nagrota Bagwan blocks. All 69 mothers of age and sex matched children with measles were enrolled. A pre-designed pre-tested data collection instrument was used. For statistical analysis, the odds ratio (OR) and adjusted odds ratio with 95% confidence interval (C.I.) among women of children exposed and unexposed to selected characteristics were calculated. Results: Poor cold chain maintenance and gaps in knowledge of health workers supplemented with beneficiary-related issues precipitated outbreaks in case area. Univariate analysis yielded strong statistical significance to 17 variables. Important statistically significant variables are educational status; OR 27.63 (C.I. 9.46-85.16); occupation; OR 0.35 (C.I. 0.16-0.75); income; OR 5.49 (C.I. 2.36-13.00); mode of transport to health care facility; OR 8.74 (C.I. 2.90-28.23); spread of illness from one person to another; OR 5.60 (95% C.I. 1.40-25.97); first help for sick child OR 2.12 (C.I. 1.00-4.50), and place of visit after recovery; OR 3.92 (C.I. 1.80-8.63). Multiple logistic regression yielded significant association with educational status, drinking water sources, and time taken to reach the nearest health facility. Conclusion: Measles outbreaks were confirmed in high immunization coverage areas. We recommend 2nd dose opportunity for measles (MR) between 5 and 17 years; refresher trainings to workers; mobile access to health care facility, and Information Education Communication activities for social behavioral change in affected areas.

Key words: Beliefs and barriers, immunization, measles, outbreaks

Introduction

Measles is the fifth killer disease among children under five years of age in the world.1-3 Sri Lanka, Latin America,4 Romania5, and South Korea6 experienced outbreaks of measles in spite of sustained high coverage with single-dose vaccination strategy. Thus, the 2001–2005 WHO/UNICEF strategic plan for measles mortality reduction and regional elimination recommended achieving high routine vaccination coverage (>90%) in every district and ensuring that all children receive a second opportunity for measles immunization.6 The three phases of the strategy are measles control, outbreak prevention, and measles elimination.7

Measles immunization coverage in India ranging from 42.2% to 58.8%8-10 suggests that there is gradual rise over the years while it satisfactorily increased from 71.8%11 to 89.1%12 to 86.3%13 in Himachal Pradesh. Generally, measles outbreaks follow a cyclic pattern and occur every 3–4 years as a result of build up of the susceptible. As the coverage increases, inter epidemic interval increases as well as focus
shifts towards older age groups as observed in Thailand and Sri Lanka. This is on account of high measles immunization (>95%) in Himachal Pradesh that the incidence of the measles cases have gone down from 19 to 8/lac from 2001–2003.

Despite high immunization rate, outbreaks of measles were reported in hilly areas of Himachal Pradesh in 2006. Two reported outbreaks of measles in highly immunized hilly areas were investigated under two sub centers, namely, Sailli and Sarah. In the same year, an outbreak of rubella was also detected and investigated in the Shahpur-Samote blocks of Kangra district. The last reported outbreak of measles in the block was 8-9 years ago. These blocks are situated at an altitude of 2600 feet to 3500 feet above the sea level with over 50% of the population belonging to the poor socio-economic strata. During the same period, no such outbreaks were reported from any other blocks within the district. Hence, a study was undertaken with the following objectives; to identify factors associated with outbreaks of measles in Shahpur block and to recommend appropriate remedial measures to prevent further outbreaks.

Materials and Methods

Many factors are reported to be associated with measles such as geographically difficult hilly areas, poor socio-economic strata with unemployment, illiteracy, overcrowding, traditional beliefs of people seeking help from the local Chellla/quacks, irregular cold chain maintenance, lack of training of the health workers etc. An in-depth review of the literature on the factors associated with measles outbreaks enabled selection of specific issues/factors for the study; namely, “Program-related issues”-vaccine coverage, vaccine efficacy, cold chain maintenance, and availability of vaccine and supplies; “Health care providers’ issues”-training of health workers under sub centers, knowledge of measles and measles prevention; “Beneficiary-related issues”-help seeking behavior of mothers and the factors associated with it. The study design was the case-control study conducted between 1st September 2006 to 15th November 2007, after obtaining clearance from Institutional Ethical Committee. The study area selected were two sub-centers Sailli and Sarah from Shahpur block (measles outbreak exposed) and two sub-centers Mallan and Samloti of Nagrota Bagwan (measles non-exposed) block of district Kangra. The study population included four health-workers from measles exposed-Shahpur block from two sub-centers and equal numbers of institutions and health-workers from unexposed-Nagrota Bagwan block, and all mothers of total 69 cases with exposure to measles (5 to 17 years with median age of 9 years) in study area. For each case, two age and sex matched, one from measles area (control-1) and second one from non measles area (control-2) were recruited.

Measles was case defined as per WHO standard: (i) Any person with generalized maculopapular rash (non-vascular) and history of fever of 38°C (101°F) or more, (if not measured, “hot” to touch) and at least one of the following: cough, coryza (runny nose), conjunctivitis (red eyes), or any person in whom a health professional suspects measles or (ii) clinical case definition of suspected measles; any person in whom a clinician suspects measles or any person with fever and generalized maculopapular rash and cough, coryza or conjunctivitis. (iii) Laboratory criteria for diagnosis: presence of measles-specific IgM antibodies.

A case of measles was defined as per WHO standard for the residents of the villages under sub centres Sailli and Sarah of Shahpur block (Kangra) between 1st September 2006 and 30th November 2006 (period of outbreak) while control-1 was defined as the resident living in the same areas but without developing any symptoms of fever and rash and control-2 from the adjacent non measles area (Nagrota Bagwan block) who have not developed the febrile rash but the population characteristics are the same.

Multiple methods were used to generate data on the three factors viz.: a. Program-related issues: (i) Vaccine coverage reported by health system was compared for Shahpur and Nagrota Bagwan blocks; (ii) Vaccine efficacy was calculated for Shahpur block by door to door search by retrospective cohort study. The formula used was: Attack Rate among unvaccinated – Attack Rate among vaccinated/Attack rate among unvaccinated: 100 (ARU-ARV/ARU*100). (iii) Cold chain maintenance was checked in both case and control areas through observational visits using a check list and (iv) availability of vaccines and supplies were ensured again through observational visits using a check list.

b. Health care providers-related issues: Several factors such as training of the health personnel, knowledge about measles prevention and vaccination, and practices with respect to measles vaccination were assessed in Shahpur and Nagrota Bagwan blocks through interview technique and observational visits using interview schedules and check lists.

c. Beneficiary-related issues: An assessment of several factors (like socio-economic status, knowledge, attitude and practice variables, traditional beliefs, vitamin A supplementation, distance from health care facility etc.) associated with help seeking behavior of mothers of cases and mothers of age and sex matched controls was carried out using in-depth interviews. The pre-tested pre-designed standardized questionnaires in local language for women were administered by trained field workers.
**Data entry and statistical analysis**

The odds ratio among women of children exposed and unexposed to selected characteristics was estimated. Data collected was analyzed using univariate analysis after making a variable directory. Univariate analysis was then performed by converting all continuous variables and categorical variables into dichotomous variables by selecting appropriate coding of 1 for presence of risk factors and 0 for absence of risk factors. Crude odds ratio (OR) and 95% confidence intervals (CI) were calculated. Multiple logistic regression analysis was done to determine the factors associated with measles. Multivariate analysis was performed to identify risk factors. Adjusted odds ratio (AOR) and 95% confidence intervals (CI) were calculated by logistic regression analysis using Epi info Version 3.3.2.

**RESULTS**

Topographically and demographically, both blocks are more or less similarly placed, e.g., in both blocks, 25-30% of total population are Scheduled Castes (SC), 4-5% are Scheduled Tribes (ST) and 30% are of Other Backward Classes (OBC) categories, while rest of the population is constituted by general category. In case block, there are 36 sub-centers, five primary health centers, one community health centre with 90% of the man power in position; while in control block, there are 38 sub-centres, five primary health centres and two community health centres with 95% of human resource in position.

The median age of the case and control children was 9 years (range 5–17 years). Thirty-five (51%) cases and controls were ≤9 years. The proportion of the males in study areas were high (43, 62.3%) as compared to females (26, 37.7%). Forty-five cases (65.2%) had the nuclear families.

**Program-related issues**

The reported measles vaccine coverage by health system authorities for 2006 in Shahpur block was 95% and Nagrota Bagwan block was 94%. Vaccine efficacy was calculated for two affected sub centres, viz., Sailli and Sarah. In Sailli, the total number of cases were 51 with overall attack rate (AR) of 6%; (sex specific AR-male 12%, female 7%); and in Sarah there were 18 cases with overall AR of 4.2%; (sex specific AR-male 6.94%, female 7.2%). All cases were over five years, ranging from September to November, 2006. A retrospective cohort study was carried out by door to door search for the children in the age group of 10 months to 17 years in the case block only. Data on children vaccination status were collected by interviewing the mothers, reviewing health records, and verifying with vaccination cards. In sub centre Sailli, attack rates of measles by age and vaccination status indicated 16 case patients of 56 non-immunized (28.6%) compared to 35 case patients of 790 immunized (4.4%) children and it was statistically significant. (Relative risk (RR): 6.44%; 95% C.I.: 3.81–10.91 P < 0.001). The proportion of the children vaccinated was 93.3%. The calculation of vaccine efficacy among those exposed to the vaccine yielded an estimate of 84.4% [Table 1].

In sub centre Sarah, attack rates of measles by age and vaccination status indicated four cases out of 22 non-immunized (18.18%) compared to 14 cases out of 408 immunized (3.43%) children and it was statistically significant. (RR: 5.3; 95% C.I.: 1.90 – 14.77; P < 0.001). The calculation of vaccine efficacy yielded an estimate of 81.13% when children under 10 months of age and the previous history of measles were excluded [Table 2]. The vaccine efficacy for Nagrota Bagwan block could not be calculated, as there was no outbreak in the area.

Cold chain maintenance and its equipments were assessed by checking availability of refrigerator, ice liner, deep freezer, vaccine carriers in both case and control areas. Ice Liner Refrigerator (ILR), deep freezers, and vaccine carriers were physically present in sufficient numbers and were in the working conditions in both study areas. On observation in the case area, the practice of maintaining the temperature record on ILR and deep freezers was not carried out in twice a day schedule as per

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**Table 1: Attack rates of measles by age and vaccination status in villages of Shahpur block, district Kangra, Himachal Pradesh, India, 2006**

| 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 % |
| Sailli               | 0-5   | 0    | 0             | 0     | 0    | 0             |
| Kanol               | 0-5   | 0    | 0             | 0     | 0    | 0             |
| Kutharna            | 0-5   | 0    | 0             | 0     | 0    | 0             |
| Nauli               | 0-5   | 0    | 0             | 0     | 0    | 0             |
| Sailli               | 6-15  | 3    | 123 (2.4)     | 6     | 16   | 38            |
| Kanol               | 6-15  | 3    | 169 (2)       | 2     | 15   | 13            |
| Kutharna            | 6-15  | 27   | 129 (21)      | 4     | 15   | 27            |
| Nauli               | 6-15  | 2    | 42 (5)        | 4     | 10   | 40            |

(Proportion of the children vaccinated: 93.3% with the calculated vaccine efficacy: 84.4%)
program recommendations while the control area was noticed to be normal. Thermometers and the temperature registers were available in both case and control areas. Both case and control areas have adequate supply of pressure cookers, stoves, sterilizers, kerosene, vaccine carrier boxes, and icepacks.

**Health care provider-related issues**

All eight workers in both blocks could correctly list the six vaccine preventable diseases (VPDs) and could also correctly state the national immunization schedule for children 0–59 months old. Six out of eight of the workers could correctly calculate vaccine requirement and had the correct knowledge of storage of different vaccines and packing them in the vaccine carriers in case area, but in the control area, all workers were able to give the correct information for all the above issues.

**Beneficiaries-related issues**

The cultural epidemiology and help seeking behavior of mothers of children in Shahpur and Nagrota Bagwan blocks were assessed with in-depth interviews [Tables 3 and 4].

**Analytical epidemiology**

Univariate analysis to determine the strength of association of potential risk factors for measles cases as compared to

| Table 2: Attack rates of measles by age and vaccination status in villages of Shahpur block, district Kangra, Himachal Pradesh, India, 2006 |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| 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 % |
| Jathrear | 0-5 | 0 | 80 | 0 | 0 | 0 |
| Bathrear | 0-5 | 0 | 63 | 0 | 0 | 0 |
| Gujrear | 0-5 | 0 | 32 | 0 | 0 | 0 |
| Jathrear | 6-10 | 4 | 40 | 10.0 | 1 | 3 | 33.33 |
| Bathrear | 6-10 | 1 | 54 | 1.90 | 0 | 2 | 0 |
| Gujrear | 6-10 | 1 | 41 | 2.40 | 0 | 3 | 0 |
| Jathrear | 11-17 | 6 | 45 | 13.33 | 2 | 7 | 29 |
| Bathrear | 11-17 | 1 | 26 | 3.84 | 1 | 4 | 25 |
| Gujrear | 11-17 | 1 | 27 | 3.70 | 0 | 3 | 0 |
| Grand total | 0-17 | 14 | 408 | 3.43 | 4 | 22 | 18.18 |

(Relative risk: 5.3; 95% confidence interval: 1.90 – 14.77; P < 0.001); (proportion of the children vaccinated: 94.9% with the calculated vaccine efficacy: 81.13%)

| Table 3: Univariate analysis of Socio-cultural, economic and personal characteristics among measles cases and two controls |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Variables | Cases (n=69) | Control-1 (n=69) | Odds ratio (95% CI) | \( \chi^2 \) (Yates corrected) (P value) | Control-2 (n=69) | Odds Ratio (95% CI) | \( \chi^2 \) (Yates corrected) (P value) |
| Educational Stat us | ≤Primary (1) | 50 (72.4%) | 47 (68.1%) | 1.23 (0.56-2.73) | 0.14 (0.70) | 6 (8.2%) | 26.73 (9.46-85.16) | 55.57 (<0.001) |
| | >Primary (0) | 19 (27.6%) | 22 (31.9%) | 63 (91.8%) | |
| Occupation | Unemployed (1) | 33 (47.9%) | 44 (73.7%) | 0.52 (0.25-1.09) | 2.94 (0.08) | 50 (72.5%) | 0.35 (0.16-0.75) | 7.74 (0.005) |
| | Employed (0) | 36 (52.1%) | 25 (36.3%) | 19 (27.5%) | |
| Income PM | ≤1500 (1) | 37 (53.6%) | 32 (46.4%) | 1.34 (0.65-2.76) | 0.46 (0.49) | 12 (17.3%) | 5.49 (2.36-13.00) | 18.23 (<0.001) |
| | >1500 (0) | 32 (46.4%) | 37 (53.6%) | 57 (82.7%) | |
| Type up of house: | Katchcha/Thatched (1) | 55 (79.7%) | 44 (63.8%) | 2.23 (0.97-5.16) | 3.57 (0.058) | 27 (39.1%) | 6.11 (2.68-14.11) | 21.91 (<0.001) |
| | Pucca (0) | 14 (20.3%) | 25 (36.2%) | 42 (60.9%) | |
| Cooking/fuel in house: | Firewood (1) | 56 (88.9%) | 56 (81.2%) | 1.00 (0.39-2.55) | 0.05 (0.82) | 30 (43.5%) | 5.60 (2.44-13.05) | 19.29 (<0.001) |
| | Kerosene/Gas (0) | 13 (11.1%) | 13 (18.8%) | 39 (54.5%) | |
| Toilet facilities | Open defecation (1) | 55 (79.7%) | 39 (56.5%) | 3.02 (1.33-6.91) | 7.51 (0.006) | 27 (39.1%) | 6.11 (2.68-14.11) | 21.91 (<0.001) |
| | In-house (0) | 14 (20.3%) | 30 (43.5%) | 42 (60.9%) | |
| Drinking water sources | Natural springs/Wells. (1) | 16 (23.2%) | 20 (29%) | 0.74 (0.32-1.70) | 0.34 (0.56) | 39 (56.6%) | 0.23 (0.10-0.51) | 14.63 (<0.001) |
| | Govt. Tap/Hand pump (0) | 53 (76.8%) | 49 (71%) | 30 (43.4%) | |
| Number of rooms in the house | One room (1) | 51 (73.9%) | 46 (66.6%) | 1.42 (0.64-3.15) | 0.56 (0.45) | 23 (33.3%) | 5.67 (2.56-12.69) | 21.24 (<0.001) |
| | > two rooms (0) | 18 (26.1%) | 23 (33.4%) | 46 (67.7%) | |
controls was performed and 16 statistically significant variables were found to be associated with measles as listed below: illiteracy, OR 27.63, (C.I. 9.46–85.16); low income group 5.49 (C.I. 2.36–13.00); unemployed, OR 0.35 (0.16–0.75); drinking water 0.23 (0.10–0.51); type of house 6.11 (2.68–14.11); fuel 5.60 (2.44–13.05); toilet facilities 6.11 (2.68–14.11); and number of the rooms in the house 5.61 (2.44–13.05); spread of illness from one person to other person, 5.60 (1.40–25.97); contact-person for treatment, 2.85 (1.27–6.46); mode of transport to the health care facility 8.74 (2.90–28.23); time taken to reach the nearest health facility 9.04 (1.55–52.50) [Table 5].

**Discussion**

The results of the present study need to be interpreted in context of three major factors, namely program-related issues, healthcare provider issues, and beneficiaries-related issues. The study areas did not differ with respect to vaccine coverage. Vaccine coverage was above 90%. Cold chain maintenance and availability of vaccine and other supplies were almost satisfactory in both blocks except the prescribed maintenance of the cold chain of the case area. It is erratic was compared to the control area, indicating the possibility of the failure of the vaccine potency. A similar result had been seen in highly vaccinated population by Lamb WH in 1989.[17] Vaccination efficacy as per mothers’ interviews in Shahpur block ranged from 81%–84%, which was close to the expected norms [Tables 1 and 2]. As the vaccine efficacy is only 85% for first dose of measles at nine completed months, there is progressive
accumulation of a small number of susceptible children in the community over the years. Such accumulations are typically caused by the combination of the measles vaccine efficacy that does not reach 100% and children left un-immunized each year. As the coverage increases, inter-epidemic interval increases as well as a shift towards older age groups may be observed as in Thailand and Sri Lanka.\[18\]

Although awareness and practice regarding measles were satisfactory among healthcare providers in both settings yet in the Shahpur block workers, there were observable gaps not only in the knowledge part but also in the scientific usage of the vaccine carriers, while conducting the immunization sessions in the fields which might lead towards the mechanism of cold chain failure. Yeung et al. recorded the findings of the cold chain failure despite 95% vaccination as one of the factors for the measles outbreak.\[19\]

With respect to beneficiaries related issues, results in two areas suggest difference with respect to knowledge regarding cause of measles, treatment and follow-up practices. Measles is locally known as Dharrssali. Illiteracy and knowledge are complimentary. Added with beliefs and barriers, many statistically significant factors like geographically difficult hilly areas, poor socio-economic status, poverty with over-crowding in the muddy thatched houses and illiterate mothers were found to be more inclined towards traditional unscientific lines in terms of cause and effect. Earlier studies had also shown that cases hypothesize the genesis of measles as curse of goddess.\[20-23\] Despite high immunization coverage in the areas, majorities of respondents opted for traditional faith healing treatment and with diet rich in Seul—a medicinal plant employed to facilitate eruption of measles during illness. For the vaccination of the children, they had to travel a distance of 6–10 kms on hilly terrain on foot consuming 3/4th hour to 2 and ½ hour for nearest available health care facility [Table 4]. The attack rates even among highly vaccinated children aged 11–17 years in Jathrear and 6–15 years in Kutharna villages were higher. This suggests waning of immunity with age (secondary vaccine failure), which can be due to the use of poorly stored vaccine. However, effect of exposure to ultra violet radiation to wane immunity as observed by Mary cannot be ruled out.\[24\] There was no measles cases in the age group of 0–5 years, and it is possible that there is 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 Jathrear had their measles vaccine. Further, there is the risk of misclassification of cases, because the outbreak of Rubella, that is one of measles-like syndrome with fever and rash occurred in the implicated area at the same time.

On the other hand, population in Nagrota Bagwan block were aware of measles as a disease caused by close contact with infected person, resorted to treatment and follow-up by qualified doctors at healthcare facility unlike seeking blessings from goddess Sheetla. From in-depth interviews it was evident that socio-cultural and economic factors were more favorable among control mothers. Mothers in the control area had better access to healthcare facilities as compared to the case area. The studies by Murray and Rasmussen,\[25\] Grais et al.\[26\] and Sharma et al.\[27\] support the observations of the present study.

Limitations
Recall bias could have occurred with respect to recollection of immunization of the children of the both study areas. However, the bias could apply to both study areas. So the bias would be non differential.

In conclusion, the present study shows that measles outbreaks in Shahpur block typify outbreaks in high immunization coverage settings. (a) Program-related issues such as erratic charting of temperature log book leading to chances of failure of cold chain and (b) healthcare provider related issues like gaps in the knowledge of workers may be associated with measles outbreak in Shahpur block. (c) Beneficiary-related issues may also be related with outbreaks such as...
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