

The Heterogeneity of Measles Epidemiology in India: Implications for Improving Control Measures

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Background. Measles vaccination coverage varies in India. Trainees of the Field Epidemiology Training Programme (FETP) investigated 8 outbreaks from 2004 through 2006 in Himachal Pradesh, Uttaranchal, Tamil Nadu, and West Bengal. We reviewed these outbreaks to contribute to the description of the epidemiology of measles and propose recommendations for control.

Methods. FETP trainees searched for measles cases through stimulated passive surveillance or door-to-door case search; estimated attack rates, case fatality, and the median age of case patients; interviewed mothers about vaccination status of their children; and collected serum samples for immunoglobulin M serological testing whenever possible. For 3 outbreaks, the trainees estimated the vaccine efficacy for children >12 months of age through cohort studies.

Results. Six of the 8 outbreaks were serologically confirmed. Compared with outbreaks in other states, outbreaks in states with vaccination coverage of >90% had a higher median age among case patients and a lower median attack rate. Six deaths (case fatality rate, 1.5%) occurred during the 5 outbreaks for which vitamin A was not used. The vaccine efficacy was 84% (95% confidence interval [CI], 74%–91%) in Himachal Pradesh. In West Bengal, it was 66% (95% CI, 44%–80%) in 2005 and 81% (95% CI, 67%–89%) in 2006.

Conclusions. In states with higher coverage, attack rates were lower and case patients were older. Although states with coverage of <90% should increase 1-dose coverage and address coverage in pockets that are poorly reached, a second opportunity for measles vaccination could be considered in states such as Himachal Pradesh and Tamil Nadu. Use of vitamin A for case management needs to be generalized.

In 2001, the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) adopted a strategy for measles mortality reduction and regional elimination [1]. The goal of this strategy was to reduce measles mortality by 50% in 2005 relative to 1999 estimates, and its 4 components were (1) achieving at least 90% routine vaccination coverage with at least 1 dose of

measles vaccine, (2) provision of a second opportunity for measles vaccination for all children, (3) measles surveillance, and (4) improved management of complicated cases. Measles surveillance emphasizes (1) regular reporting of cases, (2) investigating outbreaks, and (3) monitoring vaccination coverage. Investigations of outbreaks provide information that allows prevention of future ones. This includes identification of high-risk groups, description of changes in measles epidemiology, and detection of weaknesses in routine immunization. In addition, outbreak investigation is followed by administration to case patients of vitamin A, an intervention that is effective in reducing the case fatality [2]. In 2005, WHO considered that from 1999 through 2005, measles deaths had been reduced by 60% globally [3]. However, India accounted for a substantial part of the remaining burden.

All countries in the WHO South-East Asia region introduced measles vaccine in their immunization

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programs during the 1980s. Subsequent to the global measles elimination initiative, the reported immunization coverage increased in the region from <59% in 1999 to 65% in 2005 [3, 4]. As a consequence, the estimated number of cases decreased by 27% from 1999 to 2005 [3]. During 2005 and 2006, 321 and 357 measles outbreaks were reported from the region, respectively [5, 6]. Four countries in the region have already initiated surveillance for measles elimination. However, India, Bangladesh, Myanmar, Timor Leste, and Nepal still face challenges in measles control. In 2005, in these countries, the reported coverage ranged between 48%–81% and the annual incidence was .15–2.7 cases per million people, respectively [4].

In India, measles vaccination was introduced in 1985 [7]. The country is setting up surveillance for outbreak prevention while continuing to address the challenges of measles control. In 2005, a national strategic plan was formulated to reduce measles mortality by two-thirds by the year 2010 as compared with the 2000 estimates [8]. One of the elements of the plan emphasized achieving at least 90% vaccination coverage in 80% of the districts by 2009. Little information is available about measles epidemiology in India. Reliable surveillance data are missing and few outbreaks are investigated. In 2001, the National Institute of Epidemiology of the Indian Council of Medical Research initiated a 2-year, competency-based Field Epidemiology Training Programme (FETP) that assigned epidemiologists in training to various states of the country [9]. We reviewed the results of the measles outbreak investigations conducted by the FETP in India from 2004–2006 to contribute to the description of the epidemiology of measles and to propose recommendations for the measles control.

METHODS

Descriptive Epidemiology

In our investigations of measles outbreaks, we defined measles cases according to the WHO criteria [10] or as the combination of fever and rash. We searched for cases actively (ie, door-to-door) or through stimulated passive surveillance and calculated attack rates and case-fatality ratios.

Vaccination Coverage

We obtained administrative measles vaccination coverage estimates from public health officials. We also estimated vaccination coverage in the population by means of interviews with mothers, vaccination cards, and health care facility records.

Vaccine Efficacy

For selected outbreaks, we conducted cohort studies among the affected age groups to estimate vaccine efficacy. We defined a case of measles according to WHO criteria [10] and ascertained the vaccination status by use of 1 or more of the following 3 criteria: immunization cards, health care facility records, and

mothers' history. We calculated the relative risk associated with measles vaccination and estimated the vaccine efficacy by means of the relative-risk formula [11].

Laboratory Investigations

We organized laboratory investigations where logistically feasible. Serum samples were tested for immunoglobulin M antibodies against measles at either the National Institute of Virology in Pune or the King Institute in Chennai.

Abstraction of Information About Outbreaks

We reviewed our measles outbreak investigation reports during the period from 2004 through 2006. Using a standardized abstraction form, we abstracted information about attack rates and case-fatality ratios to estimate overall medians. We reviewed the distribution of cases over time to estimate the duration of the outbreaks and identify the months of occurrence. We identified the settings (rural or urban) of each outbreak and states where they occurred. We noted the median age of case patients, the median proportion of male case patients, and the median proportions of case patients who were vaccinated. We compared data from states that had reached the national 90% coverage target with those from other states. We compared the vaccination coverage estimated through mothers' interviews with the coverage estimated by the Reproductive and Child Health–District Level Household Survey 2 (RCH-DLHS 2) for the corresponding district from 2002 through 2004 [12]. We merged the 2 cohort studies conducted in 2006 in Purulia district of West Bengal to increase the precision of the vaccine efficacy estimate. We reviewed the data available regarding the use of vitamin A for management.

RESULTS

Descriptive Epidemiology

We investigated 8 measles outbreaks from 2004 through 2006 (3 outbreaks in 2004, 2 outbreaks in 2005, and 3 outbreaks in 2006) (Table 1). All outbreaks were in rural areas of 4 states: 2 outbreaks in Uttaranchal [13, 14]; 3 outbreaks in West Bengal ([15, 16], 1 outbreak in Ahartore village of Purulia district, West Bengal [D. Maji, unpublished data, 2006]); 2 outbreaks in Tamil Nadu ([17], 1 outbreak in Paramkudi village, Ramanathapuram district, Tamilnadu [A. Mohan, unpublished data, 2004]); and 1 outbreak in Himachal Pradesh [18]. We used the WHO case definition in 7 outbreaks. For 1 outbreak in Nainital district, Uttaranchal, we defined measles as fever and rash. We actively searched for cases in 7 outbreaks because these had occurred in a specific village. In 1 outbreak that involved many villages in Cuddalore district, Tamilnadu, we used stimulated passive surveillance [17].

We identified 432 measles cases (median no. of cases per outbreak, 48; range, 22–101). The overall median attack rate

Table 1. Selected Characteristics of the Measles Outbreaks Investigated by the Indian Field Epidemiology Training Programme of India, 2003–2006

Characteristic	Himalayan states			Other states				
	Uttaranchal	Himachal Pradesh		West Bengal			Tamil Nadu	
Location								
District	Nainital	Nainital	Kangra	Purulia	Purulia	Purulia	Ramnathapuram	Cuddalore
Setting	Rural	Rural	Rural	Rural	Rural	Rural	Rural	Rural
Year	2004	2004	2006	2005	2006	2006	2004	2005
Diagnosis								
Case definition used	Fever and rash	WHO	WHO	WHO	WHO	WHO	WHO	WHO
Serological test result	Negative	IgM	IgM	Negative	IgM	IgM	IgM	IgM
Virus isolation	No	No	Yes	No	Yes	No	No	Yes
Magnitude								
No. of cases	37	87	51	68	22	44	22	101
Attack rate, %	33 ^a	46 ^a	9.8 ^b	57 ^c	11 ^a	9 ^a	5.3 ^a	.01 ^a
Severity								
No. of deaths (case fatality rate, %)	0 (0)	1 (2)	0 (0)	3 (4)	0 (0)	2 (5)	0 (0)	0 (0)
Vitamin A treatment	No	No	Yes	No	95% coverage	Delayed	No	No
Demographic characteristics								
Median age, years	7	7	9	2	5	4	4	5
Proportion of male case patients, %	54	45	65	53	46	50	32	45
Proportion of case patients vaccinated, % ^d	2	19	69	22	68	32	50	97
Measles vaccination coverage, %								
Administrative data	99	99	113	75	84	75	100	100
Survey data								
Interviews with mothers	93	44	88	72
Vaccination cards	NA	35	37
Health care facility records	42	57	46
Coverage in the district as per RCH-DLHS 2 ^e	78	78	95	70	70	70	98	94
Method used to determine vaccine efficacy	Cohort study	Cohort study	Cohort study	Cohort study
Vaccine efficacy, % (95% CI)								
Interviews with mothers	82 (70–90)	...	81 (67–89)	81 (67–89)
Vaccination cards
Health care facility records	66 (44–80) ^f

NOTE. CI, confidence interval; IgM, immunoglobulin M; RCH-DLHS 2, Reproductive and Child Health–District Level Household Survey 2; Government of India.

^a Among patients ≤ 14 years of age.

^b Among patients 6–14 years of age.

^c Among patients ≤ 10 years of age.

^d According to mothers.

^e According to the Reproductive and Child Health–District Level Household Survey 2002–2004.

^f According to health care facility data (for children <5 years old) and mothers' history (for children >5 years old).

among children 0–14 years of age was 10% (range, .01%–57%). It was >10% in most outbreaks in Uttaranchal and West Bengal, where the vaccination coverage, as assessed by the survey conducted by the trainees or by RCH-DLHS 2, was below the 90% target. The attack rate was lower (median, 5%; range, .01%–6%) in Tamilnadu and Himachal Pradesh, where

coverage was >90%. There were 6 deaths during 3 of the outbreaks (overall case fatality, 1.4%; range, 0%–5%). In 2 of these 3 outbreaks, vitamin A was not used, whereas in the third outbreak, it was used at a later stage of the outbreak. The median duration of the outbreaks was 45 days (range, 30–93 days). The outbreaks occurred throughout the year, in January ($n = 1$),

March ($n = 1$), April ($n = 2$), September ($n = 1$), October ($n = 1$), and December ($n = 2$).

The overall median age of case patients was 5 years (range, 2–9 years). In the Himalayan states, it was higher in Himachal Pradesh (9 years) than in Uttaranchal (7 years). In the non-Himalayan states, the median age was 5 years in Tamil Nadu and 4 years in West Bengal. The median proportion of male patients among case patients was 48% (range, 32%–65%). The proportion of the case patients whom their mothers said had been vaccinated was 2%–97% (median, 41%).

Vaccination Coverage

The administrative measles vaccination coverage among children aged 12–23 months was 75%–113% (median, 99%). Four investigations estimated vaccination coverage through surveys (Table 1). Coverage according to surveys was generally lower than that according to administrative estimates. Coverage according to mothers' interviews was 44%–93%. In 3 of the 4 surveys, the vaccination coverage was comparable to that estimated by the RCH-DLHS 2.

Vaccine Efficacy

We conducted cohort studies in 3 outbreaks. In Himachal Pradesh, vaccine efficacy was 82% (95% confidence interval [CI], 70%–90%). In Purulia district, West Bengal, vaccine efficacy was 66% (95% CI, 44%–80%) in 2005 and 81% (95% CI, 67%–89%) in 2006 (pooled analysis of the 2 outbreaks that occurred in the district that year).

Laboratory Investigations

We sent 45 serum samples for serological testing during 6 of the 8 outbreaks. Serological testing detected measles immunoglobulin M antibodies in 35 (78%) of the samples.

DISCUSSION

Three outbreaks were investigated in the Himalayan states of Uttaranchal and Himachal Pradesh, which have a scarce population living in remote villages. In Himachal Pradesh, where vaccination coverage reached the 90% national target, the attack rate was lower and the median age of the case patients was older (9 years). In Uttaranchal, where vaccination coverage was <90% [18], the attack rates were >4 times higher than in Himachal Pradesh and the median age of the case patients was younger (7 years). Epidemiological features of the outbreaks also differed in non-Himalayan states. In Tamil Nadu, where vaccination coverage was 100%, attack rates were lower than in West Bengal, where the coverage did not reach the 90% target. The median age of case patients was also slightly higher in Tamil Nadu than in West Bengal, although the difference was less marked than that between Himachal Pradesh and Uttaranchal: the median age of patients with measles was higher in West Bengal (5 years) than in Tamil Nadu (3 years) in the prevaccination era [19].

These differences between states with high coverage and those with low coverage suggested that the higher 1-dose coverage reduced the attack rates during outbreaks and delayed the age at which children were exposed to the virus.

In Uttaranchal and West Bengal, the 1-dose coverage was substantially lower than the national target. Furthermore, the 2005 measles outbreak in Purulia district, West Bengal, occurred among members of a religious minority for whom the coverage was lower than the mean coverage of the district. Pockets of lower coverage may exist in spite of high overall coverage [20] and have led to outbreaks in slums [21]. Thus, in Uttaranchal and West Bengal, priorities should be to increase 1-dose coverage and to target potential pockets of lower vaccination coverage. In contrast, for outbreaks in Himachal Pradesh and Tamil Nadu, 1-dose coverage was high, exceeding the 90% target. However, a small number of susceptible children may have accumulated in the community until a threshold was reached that allowed transmission. Such accumulations are typically caused by the combination of the expected measles vaccine efficacy (around 85%) and the children left unimmunized each year [22]. They can be addressed through a second measles immunization opportunity. Two of the studies conducted during these outbreaks generated evidence sufficient to suggest that the efficacy of the vaccine was consistent with the 85% efficacy expected in India [23]. The vaccine efficacy suggested by the third study [15] was lower than expected, although the upper limit of the CI was still compatible with a normal efficacy, all the more because the poor documentation of vaccination status could have led to an underestimation of the vaccine efficacy.

The estimated 1-dose measles vaccination coverage in India was 56% in 2005 [5]. Thus, a large number of measles outbreaks would be expected to occur. Of these, the surveillance system would detect only a subset. Three studies indicated that the surveillance system captured <5% of the measles cases that happen in India [23–25]. Of those outbreaks detected, only a proportion lead to a detailed epidemiological investigation. Of those investigated, only a proportion lead to a report made publicly available that could be used to make decisions. From 2000 through 2006, 6 reports of measles outbreaks in India were published in the indexed literature, for a mean of 1 study per year [17, 21, 26–29]. Over 3 years, FETP epidemiologists in training investigated 8 outbreaks that occurred in 5 districts of 4 states where the trainees were assigned. This number exceeded the national level of outbreak detection and investigation, suggesting that assignment of FETP trainees in the district improved outbreak detection and investigation. However, FETP trainees cannot capture all outbreaks. All of the outbreaks that they investigated were in rural areas, but outbreaks would be occurring in urban areas as well.

WHO and UNICEF recommend laboratory confirmation for outbreaks as a part of enhancement of measles surveillance [1]. Laboratory confirmation was available for 6 of the 8 outbreaks.

FETP trainees accessed reference laboratory facilities through special means in the absence of a routine system for specimen collection, transportation, and analysis. Such special means may not be available to most rapid response teams in the country. Thus, laboratory confirmation of a suspected measles outbreak remains difficult.

In India, where the prevalence of undernutrition among children <3 years of age during 2005 was 46% [30], the measles case-fatality ratio can be high. The case fatality rate was >20% in a remote rural area of India where access to quality health care was not possible for the treatment of complications [31]. A review of measles outbreaks in India suggested that the mean case fatality rate was 2.5% in the country [32]. Overall case fatality during our outbreaks was somewhat lower (1.4%).

Our report suffers from 2 limitations. First, trainees used different methods for different aspects of their investigations. This limited our capacity to compare specific parameters or to aggregate data. To address this limitation, starting in 2006, we developed a training module that included an applied problem-solving-based exercise (now available online at <http://searo.who.int/phi>). This led to better standardization of the latest investigations, conducted in 2006 [16, 18]. Second, this set of investigations was performed in districts where an epidemiologist in training was assigned. As a result, the states with lower vaccination coverage (eg, Uttar Pradesh, Bihar, and Madhya Pradesh) that do not have a large participation in the FETP were not represented. Although this set of investigations captured key determinants of measles outbreaks in India, it underrepresented epidemiological evidence pointing to the importance of increasing the 1-dose coverage in states where it is the lowest. In the future, wider use of field epidemiology methods through engagement of additional states in the FETP should provide a more comprehensive picture of measles epidemiology in India.

In India, use of measles vaccine increased the age of individuals with measles virus infection and decreased the attack rates during outbreaks. Mechanisms involved in measles outbreaks include (1) low 1-dose coverage in some states and (2) a progressive accumulation of susceptible individuals despite high 1-dose coverage in other states. Outbreak detection, investigation, and reporting remain insufficient, particularly in urban areas. Laboratory confirmation remains a challenge. Vitamin A is underused. On the basis of these conclusions, we can formulate recommendations. First, higher 1-dose coverage is needed in the 32 of the 35 states that have not reached the 90% national coverage target, through strengthening of the routine system and in a way that addresses pockets of lower vaccination coverage [8]. Outreach methods may be required [1]. Measles vaccination coverage requires better documentation, including through measures to increase card retention and regular validations. Second, provision could be made for introduction of a second vaccination opportunity in states with 1-dose coverage exceeding the national target. Third, enhanced surveillance

through the Integrated Disease Surveillance Project (IDSP) should provide better documentation of measles outbreaks and response. Fourth, IDSP must organize the availability of laboratory confirmation for measles outbreaks through routine mechanisms at the state level. Fourth, universal use of vitamin A needs to be ensured and documented to further decrease the case-fatality ratio.

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