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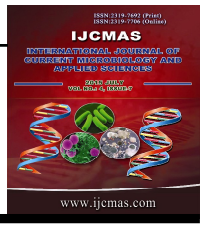


**Original Research Article**

# A Retrospective Study of Measles Outbreak Investigation in North East India

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**A B S T R A C T**

Measles is a highly contagious outbreak-prone acute viral disease characterized by fever and maculopapular rash. Measles virus is highly contagious, with >90% secondary attack rates among susceptible individuals. Infected persons shed virus and are contagious shortly before the onset of clinical symptoms and several days afterwards. (1) To study the epidemiological pattern and attack rate of measles in the study population. (2) To assess the extent of measles immunization and its vaccine efficacy in the study population. A total of 206 serum samples from 37 outbreak cases of fever and maculopapular rash from various areas over Northeast India were included in the study. Among the 37 outbreaks, 25 (67.57%) outbreaks were positive for Measles IgM antibody, 10 (27.02%) outbreaks were positive for Rubella IgM antibody and 1 (2.70%) outbreak with both Measles and Rubella IgM positive. Of the total samples that were received in our laboratory, 61.16% were positive, 36.89% were negative and 1.94% were equivocal for Measles IgM antibody. The highest number of cases inducted into our study as well as the highest number of positive cases was in the 1–5 years age group. From the study it has been seen that there is high prevalence of Measles amongst the pediatric population of northeast India. Presence of positive cases amidst even the vaccinated population may point towards failure of cold chain maintenance as well as accumulation of susceptible population.

**Keywords**

Measles, Outbreak, Northeast

## Introduction

Measles is a highly contagious outbreak-prone acute viral disease characterized by fever and maculopapular rash. The virus is transmitted via the respiratory route (aerosolized respiratory droplets) or by direct or indirect contact with nasal and throat secretions of infected persons. Measles virus is highly contagious, with >90% secondary attack rates among susceptible individuals. Infected persons shed virus and are contagious shortly before the onset of clinical symptoms and several days afterwards (www.euro.who.int). Approximately 30% of reported measles cases have one or more complications. Complications of measles are more common among children less than 5 years and adults over 20 years of age. Relatively common complications of measles include otitis media, laryngo-tracheobronchitis,

pneumonia, transient suppression of cellular immunity. In developing countries, persistent diarrhoea with protein losing enteropathy may ensue, particularly in young infants. Subacute sclerosing panencephalitis (SSPE) is also seen (Measles Surveillance & Outbreak Investigation, November 2005). Measles is extremely prone to epidemics. In settings with endemic transmission, it is characterized by winter–spring seasonality and periodic epidemics every few years, followed by inter-epidemic intervals with lower incidence. As disease incidence declines, the inter-epidemic periods become longer with eventual disappearance of a cyclical pattern. Also, the infections tend to occur at a later time in life and the average age of cases increases because of reduced opportunities for exposure due to less widespread transmission. In elimination settings, where most cases result from importations, the infections can occur any time during the year and, therefore, the seasonal pattern of measles is no longer present (www.euro.who.int).

Measles transmission with subsequent outbreaks can occur in communities and congregate settings such as households, workplaces, the military, schools and universities. The setting, extent of spread and size of the outbreak will determine the magnitude of the response. Because measles virus is highly contagious and the infection is normally accompanied by an evident rash, measles outbreaks may be more easily identifiable than outbreaks of rubella, which is less contagious and often asymptomatic (www.euro.who.int).

Urban slums occupied by migrant population are at high risk for measles epidemic. Many migrant families experience crowded and unsanitary living conditions and maintain a stressful and inconsistent lifestyle. They are exposed to significant health problems especially the risk of focal outbreak of infectious diseases, yet their access to health care is limited and fragmented.

Generally measles cases do not report to health facilities, and only some of the cases with complications reach the public sector hospitals. This leads to incomplete reporting. The reported cases are underestimates of the actual incidence of measles cases and deaths. Pockets of low immunization and population movement ensure its continued transmission resulting in numerous unnecessary epidemics in India (Singh *et al.,* 1996). Maximum numbers of measles cases in India are reported among children less than five years of age (Singh and Datta, 1997a). Unfortunately, in our country, we have a very poor surveillance system which reports less than 5% of the cases (Singh and Datta, 1997b).

**Definitions for measles (www.euro.who.int)**

The clinical criteria for measles are:

- Fever
- Maculopapular rash (i.e. non-vesicular rash)
- Cough or Coryza (runny nose) *or* conjunctivitis (red eyes).

The laboratory criteria for measles surveillance case confirmation are:

- Measles immunoglobulin M (IgM) antibody detection or
- Measles virus isolation or
- Measles viral ribonucleic acid (RNA) detection by reverse transcription-(RT)-PCR or
- A significant rise in measles immunoglobulin G (IgG) antibody in paired sera.

The main objectives of this study include that studying the epidemiological pattern and attacking rate of measles in the study population and also to assess the extent of measles immunization and its vaccine efficacy in the study population.

## Materials and Methods

The present study concentrates on the focal outbreaks of suspected measles in 13 (thirteen) districts of Assam, 6 (six) districts in Manipur, 3 (three) districts in Tripura, 4 (four) districts in Mizoram and 1 (one) district each in Arunachal Pradesh and Meghalaya during the time period from April 2014 to May 2015. The study is based on the serum samples sent to the Virology Laboratory, Department of Microbiology, Gauhati Medical College & Hospital from the various pockets of outbreak. A total of 206 serum samples from 37 outbreak cases were tested.

### Study area

The study was carried out at Virology Laboratory, Department of Microbiology, Gauhati Medical College & Hospital.

### Inclusion criteria

All outbreaks with fever and rash which fall under the case definition of measles as stated above were investigated. 5 (Five) cases selected randomly of each outbreak were investigated. All serum samples of suspected cases sent to the laboratory were inducted into the study

### Period of study

From April 2014 to May 2015

### Sampling procedure

The blood samples were allowed to clot, and then centrifuged at 3000 rpm for 5 minutes. The sera were then separated harvested into clean sterile bottles and were then frozen at -20°C until needed for assay.

### The test

The test was carried out using Enzyme Linked Immunosorbent Assay (ELISA). ELISA has been shown to be a sensitive and reliable procedure for detection of antibodies to measles with diagnostic sensitivity of 98% and diagnostic specificity of ≥ 98%. The ELISA kit used was Enzygnost® Anti-Measles–Virus IgM assay prepared and manufactured by SIEMENS. The protocol and manufacturer's instructions were strictly followed. Circulating IgM antibodies to Measles in the patient's serum were tested.

### Calculation of result

The results were calculated as indicated by the prospectus. The microtitration plate is coated with inactivated measles virus antigen. The wells in the left row of each strip are coated with antigen derived from permanent simian kidney cells infected with measles virus, and the wells on the right row are coated with antigens from non infected cells (Control antigen)

For all evaluations, the absorbance values obtained from measurement with measles virus antigen minus the absorbance value of the same sample obtained with measles virus control antigen must be used. This is referred to as A.

Each A value must be within the lot-dependent lower and upper margin listed in the respective barcode table of values: lower margin ≤ $A_{\text{Reference P/P}}$ ≤ upper margin. [Where Reference P/P means the OD value difference of P in Ag well and Control well]

For achieving an optimal reproducibility of results, the measurements require correction. The correction factor (CF) is calculated as CF = Nominal value / $A_{Reference\ P/P.}$ The difference in absorbance i.e. A is multiplied with the CF to get the final OD value.

**Statistical analysis**

The data obtained were analysed using EPI INFO 7 software program. p value < 0.05 between two variables was taken to be statistically significant.

**Results and Discussion**

A total number of 37 outbreaks were reported in the said period of which 25 (67.57%) outbreaks were positive for Measles IgM antibody, 10 (27.02%) outbreaks were positive for Rubella IgM antibody and 1 (2.70%) outbreak with both Measles and Rubella IgM positive. 206 samples were received in total in our laboratory, of which 126 (61.16%) were positive, 76 (36.89%) were negative and 4 (1.94%) were equivocal for Measles IgM antibody. The highest no. of cases inducted into our study as well as the highest number of positive cases was in the 1–5 years age group (Table 1, Fig. 1).

However, no statistical significance was observed (p=0.4563) between age and the incidence of measles.

The highest number of cases inducted in our study hailed from the 13 districts of Assam. However, positivity rate was observed to be maximum in the cases hailing from Tripura followed by Manipur (Table 2, Fig. 2). However, no significant statistical correlation was observed between Measles prevalence and geographical distribution of study cases (p=0.1837) which indicates that the disease is equally prevalent all over the Northeast region.

Of the 206 cases, 48 (23.30%) were vaccinated while 158 (76.70%) were either not vaccinated or were not documented. Among the Vaccinated cases, 14 (29.17%) were positive and33 (68.75%) were negative for Measles IgM. While amongst the rest 158 cases, 112 (70.89%) were positive and 43 (27.21%) were negative for Measles IgM. However, no statistical correlation was observed between vaccine status and Measles seropositivity (p=0.276504) (Table 3).

**Table.1** Age Distribution of total inducted cases and Measles positive cases in our study

| Age Group | Total cases | Positive for Measles IgM | | | % Positive for Measles IgM |
|---|---|---|---|---|---|
| | | Vaccinated | Non-vaccinated | Total | |
| < 1 Year | 11 | 0 | 6 | 6 | 54.54% |
| 1–5 Years | 98 | 7 | 67 | 74 | 75.51% |
| 5–10 Years | 57 | 3 | 30 | 33 | 57.89% |
| 10–15 Years | 31 | 2 | 9 | 11 | 35.48% |
| >15 Years | 9 | 2 | 0 | 2 | 22.22% |

**Table.2** State specific distribution of study cases

| State | Total cases | Measles Positive | % Measles Positive | Measles Negative | Equivocal cases |
|---|---|---|---|---|---|
| Assam | 121 | 66 | 54.54% | 54 | 1 |
| Manipur | 30 | 25 | 83.33% | 4 | 1 |
| Mizoram | 20 | 15 | 75.0% | 5 | 0 |
| Meghalaya | 5 | 0 | 0% | 5 | 0 |
| Tripura | 25 | 20 | 80.0% | 3 | 2 |
| Arunachal Pradesh | 5 | 0 | 0% | 5 | 0 |

**Fig.1** Age Distribution of total inducted cases and Measles positive cases in our study

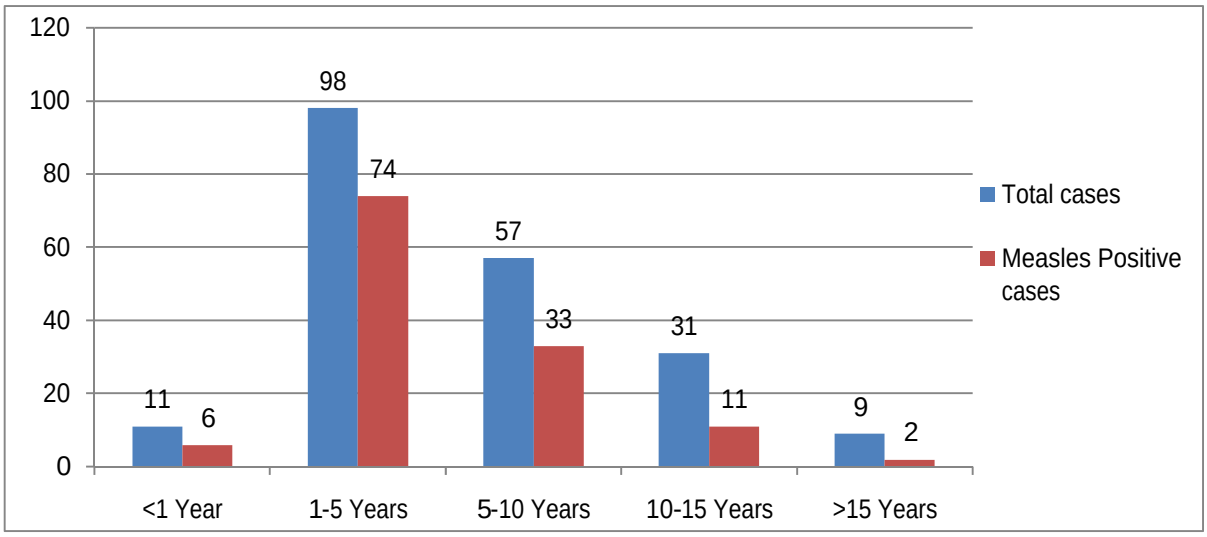
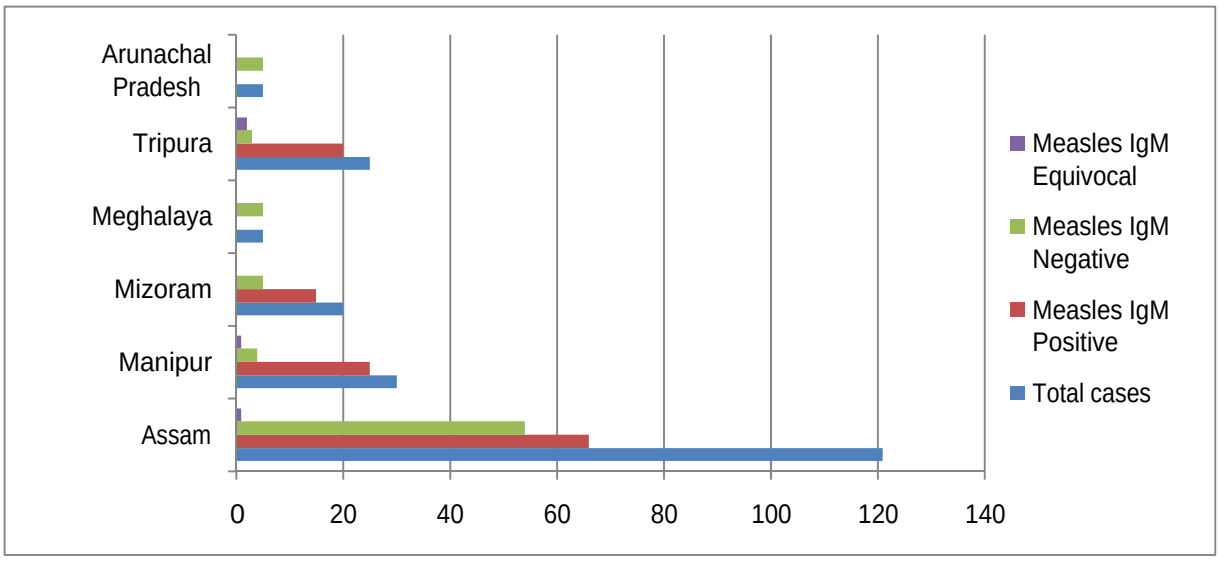



**Fig.2** State wise distribution of study cases



The 80 samples (76 Negative and 4 Equivocal for Measles IgM) were further subjected to Rubella IgM ELISA assay. Of these, 39 (48.75%) were positive and 41 (51.25%) negative for Rubella IgM antibody. All the 4 samples showing equivocal results for Measles IgM antibody were found to be negative for Rubella IgM antibody. 35 (17.85%) samples were negative for both Measles and Rubella IgM.

Measles is rightly called as captain of killer team, especially in developing countries (Gupta *et al.,* 2013). More than one-third of all measles deaths worldwide (around 56000 in 2011) are among children in India (http://www.who.int/features/2013/india_measles/en). Median age of the cases was 6 years, which was comparable to the previous outbreaks reported in India (Risbud *et al.,* 1994; Sharma *et al.,* 1984; Jajoo *et al.,* 1984; Bhuniya *et al.,* 2013). In the present study, 91.25% of positive cases below 5 years of age had not received measles immunization, which is indicative of the accumulation of susceptible population. Partially protected as well as unprotected human beings serve as the reservoir of measles virus and this could be the reason for the outbreak. Hence, one catch up measles immunization campaign is required to prevent future outbreak and there is also need of sero-surveillance for measles in the Northeastern region. Males were affected more often than females 74 (58.73%) vs. 52 (41.27%) but this difference was not statistically significant like other studies (Gupta *et al.,* 2013; Bhuniya *et al.,* 2013). About 15% of vaccinated children fail to develop immunity with the first dose, meaning that if only 80% are fully immunized, an outbreak is likely (Gupta *et al.,* 2013). In our study, it was noticed that 15.22% (7/46) of positive cases above 5 years had received primary immunization of measles, which may be an indication of vaccine failure or short lasting immune response as also reported by Vitek *et al.* (1999). Defective practices of the cold chain system could affect the efficacy of the vaccine. The recognition of early warning signals, timely investigation and application of specific control measures can contain an outbreak. There is further need of strengthening of existing routine immunization. Cold chain monitoring needs special attention.

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