



Epidemiology of Laboratory Confirmed Measles and Rubella Outbreaks in Rajasthan

Pooja Choudhary¹, Sushil Kumar Singh², Manoj Verma³, Sunil Kumar⁴

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Author's Affiliation:

¹Senior Demonstrator, Dept of Microbiology, SP Medical college, Bikaner;

²Senior Professor, Dept of Microbiology, SMS Medical college, Jaipur;

³Senior Demonstrator, PSM, Dr. SN Medical college Jodhpur; ⁴Medical officer, Dept. of Health & FW Govt of Rajasthan

Correspondence

Dr. Manoj Kumar Verma
Manojverma300@gmail.com

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ABSTRACT

Introduction: Measles continues to be a major cause of childhood morbidity and mortality in India. The Measles & Rubella Initiative was launched in 2001 as a global partnership program to strengthen surveillance for measles elimination.

Objective: To determine the proportion of lab confirmed outbreaks by IgM ELISA and to describe the epidemiology of Measles and Rubella outbreak in Rajasthan.

Material and method: this observational study was conducted at WHO Sub National Measles and rubella laboratory at a tertiary centre in Rajasthan. Samples from 112 suspected measles outbreaks from April 2015 to August 2016 were tested for measles and rubella IgM antibodies using WHO approved ELISA kits.

Results: On lab confirmation, only 60% were found to be measles outbreak, 17% were Rubella outbreak and 18% were mixed outbreak. 5% outbreaks were neither measles nor Rubella. Most cases were seen in dry months of February and April. Measles cases were found in relatively younger age as compared to Rubella. Most outbreaks were reported from few selected districts.

Conclusion: Though most outbreaks are due to measles, Rubella alone or mixed outbreak are also common in Rajasthan, hence lab diagnosis is key for both Measles and Rubella is essential specially when targeting elimination and justifies inclusion of Rubella vaccine in National schedule.

Keywords: Measles, Rubella, Surveillance, Epidemiology

INTRODUCTION

Measles is a globally occurring, highly contagious viral disease, clinically manifesting as fever with rash, malaise, cough, coryza, and conjunctivitis ¹. Measles is endemic in the developing countries due to low immunization coverage. Humans being the only reservoir with no subclinical case and a highly effective vaccine make measles a potential candidate for eradication ², still elimination had been achieved in very few regions of the world, due to social and political factors and high transmissibility.^{3,4}

Rubella is a mild viral disease that presents with fever and rash. The public health importance of

rubella is because early pregnancy infection can lead to miscarriage, foetal death or the birth of infant with severe congenital anomalies. Congenital rubella syndrome manifests as blindness, deafness, congenital heart disease, and mental retardation.⁵

Morbidity and mortality from measles and rubella are completely preventable with safe and inexpensive vaccines and timely and accurate laboratory diagnosis and with this view, in 2001, a global partnership programme, The Measles & Rubella Initiative (M&R Initiative) was launched, led by the American Red Cross, United Nations Foundation, Center for Disease Control and Prevention, UNICEF and WHO.⁶

As clinical diagnosis can be unreliable, Laboratory confirmation of measles and rubella cases becomes a vital aspect of surveillance at all stages of control programmes.⁷ Detection of measles specific immunoglobulin M (IgM) antibodies in serum samples is the mainstay of laboratory confirmation^{8,9}. Measles specific IgM antibodies appear within the first few days of the rash and decline rapidly after about one month. Their presence provides strong evidence of current or recent measles infection.

Present study aimed to determine the IgM antibody positivity among clinically suspected Measles cases and Rubella IgM antibody positivity among measles IgM negative cases, and to describe the epidemiology of measles and Rubella outbreak in Rajasthan.

MATERIAL AND METHODS:

A Descriptive observational study was conducted at WHO Sub National Measles and rubella laboratory, Department of Microbiology in a tertiary centre of Rajasthan. Serum samples from 112 outbreaks of measles and rubella in Rajasthan which occurred from April 2015 to August 2016 were taken for study purpose. Sample from Patient fulfilling WHO measles case definition were included in study. "Any person with high grade fever (38°C or more) with a maculopapular rash and atleast one of the symptoms like conjunctivitis, cough & coryza"⁸ was considered as measles case. Sample received in poor conditions such as visibly lysed, inadequate collection, and cold chain not maintained during transport or contaminated sample were excluded.

The samples were tested for the presence of IgM antibodies against Measles & Rubella by using ELISA kits (Behring Enzygnost Anti-Measles Virus IgM Kit) as approved by WHO. The test was performed as per the directions given in the kit leaflet supplied along with the kits. Samples were first tested for Measles IgM antibodies and result Equivocal or negative of measles IgM testing was further tested for rubella IgM antibodies. Outbreak was confirmed when atleast two samples from an outbreak tested positive for IgM antibodies. If two samples each were positive for measles and rubella IgM, then it was considered as mixed infection. Ethical clearance was obtained from Institutional Research Review Board prior to initiation of study.

Statistical analysis: Categorical data was expressed as percentage and was compared using Chi square test. Significance level was kept at P value <0.05. All statistical analysis was done using statistical software 'Epi-info' version 7.2.1.0.

RESULTS

A total of 584 serum samples from 112 outbreaks of measles and rubella in Rajasthan were tested. Out of these 112 outbreaks, 67 (60%) were confirmed as measles outbreak and 20 (18%) were Mixed outbreak. Rubella outbreak was confirmed in 19 (17%) of outbreaks. Six outbreaks suspected clinically were negative for both measles and rubella. (Table 1).

Out of the 584 samples tested, Measles IgM was positive in 314 (53.5%) samples only. Rubella IgM antibodies were tested in the 270 samples negative for Measles IgM, out of these 270 samples, 104 (38.5%) were positive for Rubella IgM Antibodies. Most cases of measles and Rubella were seen in months of February to April with peak occurring in March (Figure 1). Measles cases were reported throughout the year with peak in March, where as Rubella cases were found only for three months i.e. February to April and though for most part of the study period, measles cases were more than Rubella, but in March 2016 Rubella cases in Rajasthan surpassed Measles cases (Figure 1).

Most of the measles cases were reported from districts of Jaipur (47 cases), Alwar (31 cases) and Kota (29 cases). Most of the Rubella cases were seen from Bharatpur and Kota. Rubella cases were proportionally more in districts bordering Haryana, Madhya Pradesh and Uttar Pradesh. These Districts include Alwar, Bharatpur, Karoli, Kota, Chittorgarh, Pratapgarh and Bhilwara. Few districts like Jalore and Sirohi reported zero cases.

Table 1: Laboratory confirmation of suspected outbreaks

Result	Cases (n=112) (%)
Measles IgM positive	67 (60)
Rubella IgM positive	19 (17)
Mixed infection (both Measles and Rubella IgM positive)	20 (18)
Both negative	6 (5)

Table 2: Age distribution of Measles and Rubella cases

Age group	Measles (%)	Rubella (%)	Total (%)
< 1 year	7 (2.5)	1 (1.1)	8 (2.1)
1 - 4 year	150 (53.4)	18 (20)	158 (42.6)
5 - 9 years	101 (35.9)	49 (54.4)	150 (40.4)
10 - 14 years	23 (8.2)	21 (23.3)	44 (11.9)
≥ 15 years	0 (0)	1 (1.1)	1 (0.3)
Total	281 (100)	90 (100)	371 (100)

Table includes only those cases where proper age and sex data was available

Chi-square = 38.005 with 3 df P < 0.001 (S) ; For Chi square test, ≥15 age group was combined with 10-14 years group

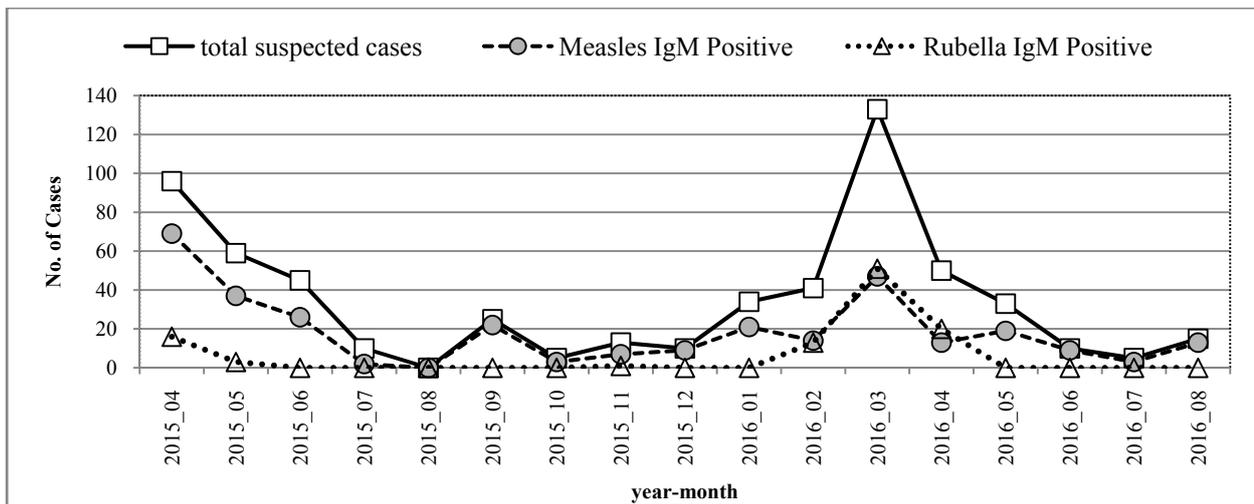


Figure 1: Time trend of Measles and Rubella cases

Measles cases were seen in relatively younger age group with most cases in 1-4 years age (53.4%) as compared to Rubella where most cases were seen in 5-9 years age group (54.4%) and this difference in age distribution of measles and rubella cases (Table 2) was found to be statistically significant ($p < 0.001$). Almost half of the measles (48%) and Rubella (51%) cases were male and sex Distribution of measles and rubella was not significantly different. The age distribution of was not significantly different in male and female cases.

Majority (90%) of the study subjects had not been vaccinated for measles. Out of the 314 measles positive cases, only 34 (10.8%) were vaccinated and those with Rubella IgM positive, only 5.8% were vaccinated for measles.

DISCUSSION

Measles is one of the major causes of death in children in India and most of these deaths occur in few high burden districts in a small number of states.¹⁰ Though immunization coverage have improved, but it is still low, especially in Rajasthan. According to NFHS-4 data (2015-16)¹¹, only 54.8% of children (12-23 months) are fully immunised in Rajasthan. Nearly 90% of the measles cases in present study had no history of vaccination and clearly there is a need to still improve the vaccination coverage with focus of high risk districts.

Clinical diagnosis of measles in many cases can be difficult and unreliable, especially in individuals with pigmented skin. Previous studies like EL Mubarak et al¹² have reported misdiagnosis of measles on clinical grounds. Other infectious agents like Parvovirus B19, HHV6, Dengue virus, Ebstein-Barr virus, *Mycoplasma pneumoniae* and *Rickettsia conorii* causes fever and rash similar to measles. Differentiation of Rubella from measles is

also difficult on clinical grounds. In present study, only 60% of suspected outbreaks were lab confirmed as measles outbreak, and 5% of clinically-suspected outbreaks were negative for both Measles and Rubella IgM antibodies. In a similar study by Sunil R Vaidya et al¹³ in Maharashtra, only 62% of suspected outbreaks were found to be positive for measles. In yet another study done by Syed Tanwir Alam et al¹⁴, 67.6% of suspected outbreaks were positive for measles. Tony Lawrence et al¹⁵ in Kerala found only 54% as measles outbreaks and Ramamurthy N et al¹⁶ found 75% positivity for measles on lab confirmation. Babita et al¹⁷ reported 53% measles positivity and Surendra Gupta et al¹⁸ found 68% positive for measles. This indicates the need for laboratory confirmation of measles cases and outbreaks for accurate diagnosis, especially when we are targeting Measles elimination.

In present study 17% of outbreaks were confirmed as rubella. Other studies by Babita et al¹⁹, Sunil R Vaidya et al¹³, Syed Tanwir Alam et al¹⁴ reported Rubella outbreaks to be 6.3%, 12%, 27% respectively. Also 18% outbreaks were found as mixed infection similar to findings of Vaidya et al (20%)¹³. These numbers seem enough to justify inclusion of Rubella in routine immunization and improved surveillance as measles in being targeted for elimination.

Most of the outbreak occurred in dry months of February to May as was similarly found by Satinath Bhuniya et al²⁰ and Simbarashe Chimhuya et al²¹ in their study. Nicholas C Grassly et al 2006²² in the study of seasonal infectious disease epidemiology, concluded that in the tropics, measles incidence peaks during the dry season and increased survival of the virus in the dryer air could be responsible for these dry season peaks. Most (54%) measles cases were seen in children 1-4 years age group as was similarly reported by Syed Tanwir Alam et al.¹⁴

In present study few districts like Jaipur and Alwar had maximum outbreak and Alwar, Barmer, Bundi, Dholpur, Jaipur, Jodhpur, Kaurali, Sawai madhopur and Tonk have been identified as high focus districts in Rajasthan. Six districts including Jalore and Sirohi reported zero cases which may be indicative of poor surveillance and reporting rather than high level of Immunity.

Proportionally higher number of Rubella cases in districts bordering Haryana, Uttar Pradesh and Madhya Pradesh would be indicative of transmission from these neighbouring states.

CONCLUSION

In present study sixty percent outbreaks are due to measles only and most remaining outbreaks were confirmed to be due to rubella or measles and rubella combined. This infers that Lab confirmation is essential for accurate diagnosis of outbreak because of clinical similarity of measles and Rubella cases. Few districts reporting maximum number of cases indicating good surveillance and need for vaccination coverage with both Measles and rubella and districts reporting zero or few cases may need better surveillance. Rubella cases were found to occur in relatively older children as compared to measles.

Recommendation - Early diagnosis and reporting of suspected measles outbreak is a key factor for controlling outbreaks and to prevent spread in susceptible community through immunization. For efforts toward measles elimination, lab confirmation of suspected outbreaks becomes important for accurate diagnosis. IgM antibody ELISA offers an accurate lab diagnosis method for measles and rubella surveillance. Strengthening of surveillance and reporting system is required especially in low reporting districts. Improvement in routine immunization coverage and inclusion of Rubella in routine immunization are required to achieve elimination.

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