Clinical and laboratory profile of children admitted with measles in a tertiary care teaching hospital

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ABSTRACT

Background: Measles is a vaccine-preventable viral illness associated with substantial childhood morbidity and mortality. Recently, changing trends in the occurrence of measles are noted like incidence in younger infants and in those who have received measles vaccine. **Objectives:** The objective was to study the clinical profile of children with measles and to study the usefulness of polymerase chain reaction (PCR) in diagnosing measles and to study the measles-specific immunoglobulin M (IgM) response in children with measles. **Materials and Methods:** This study was done in the Pediatrics Department of a Tertiary Care Center, and the study population was children up to 12 years of age admitted in the setting with a clinical diagnosis of measles during the study period and who were laboratory confirmed by PCR/IgM ELISA or both. **Results:** Of 173 clinically diagnosed cases, 149 laboratory confirmed cases were taken for analysis and studied. Of these, 47% of cases were below 9 months. Newborns constituted 2.01% of the total cases. The mean age was 13 months and the male:female ratio was 1.13:1. A total of 24.8% children were unimmunized, 16.77% had a single dose, and 8.72% had 2 doses of measles vaccine. Overall mortality was 0.67% and bronchopneumonia was the major complication (76.5%). Among immunized children with measles confirmed by PCR, measles-specific IgM response was reactive in 36.4% of cases. In the early phase of measles (within 3 days) confirmed by PCR, IgM response was inconclusive in 60% of cases. **Conclusion:** In our study, 47% of the cases of measles were below 9 months; therefore, the age of measles vaccination may be reconsidered. Among eligible cases (>9 months), 24.83% were not immunized for measles which indicates that measles immunization coverage should be increased. Among the measles cases, 25% had measles vaccination which highlights the need to check for the determinants of vaccine failure. In our study, the RT-PCR was found to be useful for early diagnosis of measles and for diagnosis in immunized children.

Key words: *Measles-specific IgM response, Measles, Reverse transcription-polymerase chain reaction*

Measles is a highly contagious vaccine-preventable disease that results from infection with measles virus and is still responsible for >100,000 deaths every year, down from >2 million deaths annually before the introduction and widespread use of measles vaccine. Every year in India, nearly 2.7 million children get measles. Those, who survive, suffer from serious complications including diarrhea, pneumonia, and malnutrition. To ensure protection against the vaccine-preventable diseases, the health ministry has initiated a Measles-Rubella (MR) vaccination campaign in the nation. However, only 63% of the member states of the World Health Organization (WHO) have met the target of immunizing at least 90% of children with measles first dose, while <50% of the world's children have been immunized with the globally recommended second dose of the vaccine [1-6].

Recently, changing trends in the occurrence measles are noted like incidence in younger infants and in those who have received measles vaccine. Furthermore, measles infection of immunocompromised individuals may not result in typical measles symptoms. Therefore, the current measles elimination goals in all the WHO regions necessitate case-based surveillance including laboratory confirmation of suspect cases. With coordination from the WHO, the Global MR Laboratory Network performs case-based laboratory surveillance using standardized methods. The WHO case definition for measles requires the presence of acute febrile disease (≥38.3°C) featuring a generalized maculopapular rash lasting 3 days or longer, and coryza, cough, or conjunctivitis. A suspected case meets the case definition with attendant suspicion of measles by the examining clinician. A laboratory-confirmed case meets these clinical criteria, along with the laboratory confirmation of infection, typically by detection of MeV-specific immunoglobulin M (IgM) antibodies in serum or by detection of viral RNA by reverse transcription-polymerase chain reaction (RT-PCR). In addition, serological techniques play an important role in the evaluation of population immunity [7-15].

The measles vaccine coverage was just 56% in 2000 and increased to 87% in 2015. The National Family Health

Survey-4 (2015–2016) has assessed it to be 81.1%. This is low compared to the 95% coverage level required for elimination. In addition, the coverage is unevenly distributed in different states in India. India still accounts for a significant proportion (estimated to be over 36%) of measles-related deaths in children [8]. India achieved an estimated 51% reduction in mortality (2000–2015) as compared to that achieved in African (85%), Western Pacific (80%), and European (79%) regions and in South-East Asian region excluding India (91%). However, the pace of this progress will have to be greatly enhanced, if our country has to eliminate measles by 2020 [16-20].

Measles continues to remain a significant public health challenge in India [21-22]. India accounts for maximum measles-related mortality worldwide. Hence, this study regarding the clinical and laboratory profile of children with measles is relevant.

MATERIALS AND METHODS

This study was done in the Department of Pediatrics, SAT Hospital, Govt. Medical College, Thiruvananthapuram, over a period of 2 years. Ethics clearance for the study was obtained from the Institutional Ethics Committee, and informed consent was obtained from the parents of each participant. Consecutive cases of clinically diagnosed measles in children up to 12 years were recruited for the study. Detailed history and physical examination were done. From each study participant, 4 ml blood was collected for routine investigations and serological tests for diagnosis of measles. Throat/nasopharyngeal sample was obtained as soon as possible after admission for PCR and measles-specific IgM ELISA assays.

Measles IgM ELISA was carried using a commercially available measles IgM ELISA kit (IBL International, Germany). Test results were interpreted as IgM ELISA reactive, non-reactive, or borderline. Measles RT-PCR assay was performed on RNA isolated from throat/nasopharyngeal samples by an in-house measles N-gene based RT-PCR assay which amplifies a 600 nucleotide length region of measles genome. Amplicons were run on agarose gel and read on a Gel Doc instrument. Results were reported as either measles virus RNA detected or not detected. Measles IgM ELISA and measles RT-PCR assay were carried out at Rajiv Gandhi Center for Biotechnology, Thiruvananthapuram, Kerala, India. Laboratory proven (PCR/IgM ELISA Positive or both) cases of measles were taken for analysis. Data were entered in Microsoft Excel sheet. Completeness was checked. The analysis was done using statistical software SPSS.

RESULTS

Of 173 clinically diagnosed cases, 149 laboratory confirmed cases by RT-PCR, ELISA, or both were taken for analysis. Considering the age distribution, the mean age was 13 months. High incidence was noted in infants (62%), and 70 (47%) of cases were <9 months of age. 3 (2%) of the total cases were <28 days of age. 36 (24.16%) of cases were aged between 9 months and 5 years, 24 (16.1%) were aged 5–10 years, and 19 (12.75%) were >10 years of age. Regarding gender distribution, 53% were male children and 47% were female with male:female ratio of 1.13:1.

Regarding the immunization status of the study participants, 47% of cases were <9 months of age and were not eligible for measles vaccine according to the National Immunization Schedule. Among children eligible for immunization (>9 months), 24.8% were unimmunized, 16.77% were immunized with single dose, and 8.72% had 2 doses of measles vaccine. Among the cases with measles, 25% had measles vaccine.

Regarding the nutritional status, 38.9% of cases were undernourished and 35.6% of cases had contact with measles. Following complications were seen in cases: bronchopneumonia (76.5%), diarrhea (24.16%), laryngotracheobronchitis (11.4%), and otitis media (2.68%). As per the Kuppuswamy's scale of socioeconomic status (SES), 59.7% were from SES 4, 35.6% from SES 3, and 4.7% belonged to SES 2. Of 149 cases, 53% (n=79) needed hospital stay <5 days and 47% (n=70) had hospital stay >5 days. More frequency of prolonged hospital stay due to complications was noted among unimmunized children. Statistically significant difference was noted regarding the duration of hospital stay among immunized and non-immunized children (p=0.006).

Mortality was 0.67% (n=1) due to sepsis, myocarditis, and shock in a young infant with measles. Regarding the laboratory profile, mean Hb was 10.5 g/dl and mean leukocyte count was 7993/mm^3. Among immunized children with measles confirmed by PCR, measles-specific IgM response was reactive in 36.4% cases, borderline in 39.4%, and non-reactive in 24.2% cases. In the early phase of measles (within 3 days of onset of rashes) that were confirmed by PCR, IgM response was found to be inconclusive or non-reactive in 60% cases. Seasonal pattern was noted in the incidence of measles, and high incidence was noted during the month of January to May and August to September.

DISCUSSION

Measles continues to be a major public health challenge despite the availability of a safe and effective vaccine. There are no animal or environmental reservoirs for measles [1]. In line with the WHO goal for accelerated measles control, it is important to have accurate data on epidemiology of measles in different geographic regions of the country. In the present study, we studied the clinical and laboratory profile of children admitted with measles over a period of 2 years in our hospital. Furthermore, the usefulness of RT-PCR is evaluated and measles-specific IgM response is noted. Of 173 clinically diagnosed cases of measles, 149 laboratory confirmed cases by RT-PCR or ELISA or both were included for analysis and studied.

In this study, high incidence of measles was noted in infants (62%). Another important finding was that 47% of the cases were below 9 months of age including newborns (2.01%). Incidence noted in infants in this study is high compared to the previous reports [1-4]. After the introduction of measles vaccine, the increasing incidence in younger age group is reported in many studies [5,6]. High incidence of measles in infants is also

reported in the study done by Indwar *et al*. at West Bengal [9]. High incidence in children <9 months of age noted in this study should be given due consideration and measures should be taken to protect these children from the measles infection and the age of administration of measles vaccine may be reconsidered. Furthermore, maternal health, immune status, and maternally transmitted antibody levels should be given due consideration.

Among eligible children for immunization, 24.8% were unimmunized, 16.77% were immunized with single dose, and 8.72% had 2 doses of measles vaccine. Similarly, in a study by Lawrence *et al*., 54.3% of cases of measles were unimmunized [5]. Therefore, it is essential to stress on the measles immunization coverage. Among the cases, 25% had received the measles vaccine and this is in accordance with the study by Lawrence *et al*. where the incidence of measles was noted in 28.6% of the immunized children [5]. This indicates that the factors affecting vaccine efficacy should be given due consideration. The NFHS-4 (2015–2016) has reported that the measles vaccine coverage in India was 81.1% [7]. This is low compared to the 95% coverage level required for elimination of measles [8].

The mortality noted in our study was 0.67%. It was an infant with measles complicated by sepsis, myocarditis, and shock. In the study done by Indwar *et al*. at Kolkatta, West Bengal, age-specific case fatality rate of children admitted with measles in a tertiary care center was found to be 17% in children <5 months, 7% in 6–8 months, 5% in 9 months to 1 year, 3% in children of 2–5 years, 0.7% in 6–10 years, and 0 in children of >10 years of age. The most common cause of death was very severe pneumonia and respiratory failure [9].

Regarding gender distribution, 53% were male children and 47% were female with slight male dominance. The same results were observed in other studies also. 59.7% of the cases were from SES 4 and 35.6% were from SES 3 which are supported by the previous evidence suggesting higher incidence of measles in children of low-socioeconomic background [10-14]. The seasonal pattern in measles incidence is noted in our study. Same finding was noted in other studies also [13,14]. In our study, 38.9% of cases were undernourished. Undernutrition is reported as a risk factor for measles virus infection and complications in other studies also [6,16,17]. Pneumonia was the major complication (76.5%). Same observation was noted in other studies also [17].

Considering the laboratory tests for confirmation in this study, RT-PCR was found to be particularly useful for early diagnosis of measles and for diagnosis of measles in children who have received the measles vaccine. Depending on geography and seasonality, the clinical presentation of measles may mimic those of other viral diseases. Furthermore, measles infection of immunocompromised individuals may not result in typical measles symptoms. Therefore, the current measles elimination goals in all the WHO regions necessitate case-based surveillance including laboratory confirmation of suspect cases [18]. Molecular surveillance in combination with standard epidemiologic information can be used to trace pathways of transmission and to provide evidence for verification of measles elimination. Although detection of viral RNA by RT-PCR is playing an increasing role in case confirmation, IgM detection by enzyme immunoassay is still the most commonly used diagnostic method. In addition, serological techniques play an important role in the evaluation of population immunity. Despite the genotypic diversity, measles virus has only one serotype. Genetic stability of measles virus is exceptionally good. Because of the availability of a highly effective and relatively inexpensive vaccine, the monotypic nature of the virus and the lack of an animal reservoir, measles is considered eradicable [18-20,23-25]. Our study has certain limitations and results may vary from the actual community data as this study was done in a tertiary care setting.

CONCLUSION

The incidence of measles in fairly good number of children (47%) below 9 months including the newborns is highlighted in this study. This finding indicates the need for considering immunization in children <9 months of age. About 24.83% of children were not immunized with measles vaccine; therefore, measles vaccine coverage should be stressed. Among cases, 25% had prior measles vaccination, so factors affecting vaccine efficacy should be given due consideration. RT-PCR was found to be particularly useful for early diagnosis of measles and in immunized children.

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