CLINICAL OUTCOME OF MEASLES AND RUBELLA WITH MACULOPAPULAR RASH AT CHILDREN'S HOSPITAL, PIMS, ISLAMABAD

Jai Kirshin[1], Sameena Afghan[2], Aqeela Ayub[3], Kishor Shah[4] and Maqbool Hussain[5]

[1]Professor of Paedatrics, children's hospital, Pakistan Institute of Medical Sciences (PIMS), SZABMU, Islamabad, Pakistan. [2] Senior Lecturer Public health Departement, children's hospital, Pakistan Institute of Medical Sciences (PIMS), SZABMU, Islamabad, Pakistan. [3]Assistant Professor of Paedatrics, children's hospital, Pakistan Institute of Medical Sciences (PIMS), SZABMU, Islamabad, Pakistan. [4]Posgraduate Student, children's hospital, Pakistan Institute of Medical Sciences (PIMS), SZABMU, Islamabad, Pakistan. [5]Associate Professor of Paedatrics, children's hospital, Pakistan Institute of Medical Sciences (PIMS), SZABMU, Islamabad, Pakistan. Corresponding Author: Dr Jai Kirshin, Professor of Paedatrics, children's hospital, Pakistan Institute of Medical Sciences (PIMS), SZABMU, Islamabad, Pakistan, Email: jaik_1961@hotmail.com, Cell #: +923335094933

Abstract

Background: Measles is highly endemic disease in Pakistan that can be prevented by vaccinating the child. Patients with rash and fever are the major syptoms of this infection. The aim of this study was to find the association of clinical and serological outcome of measles and rubella with demographic profiles in patients hospitalised with clinical suspicion of these conditions.

Methods: A descriptive cross sectional study was conducted in children hospital of PIMS Islamabad where all children presenting with maculopapular rash in outdoor patient, indoor patient and accident and emergency department were enrolled. The study duration was one year or the completion of required sample size. A total of 73 children who fulfilled the inclusion criteria were enrolled in this study. A purposive sampling technique was used to select cases. Data was collected through a structured proforma especially designed for this study. Permission was taken from the Hospital Ethical Committee before the commencement of the study. A written consent was also taken from the parents of children prior to conduct the study.

Results: All the children in this study was 46.5 (± 40.1) months of age, the mean (SD) age was 4 years and 10 months (± 3 years and 4 months). The median age of all children was 24 months (2 years). The youngest child was 7 months old while the eldest child was 12 years (144 months) of age. Out of 73 children enrolled in the current study who presented with maculopapular rash and their serological outcome was assessed, 50 (68.5 percent) were boys whereas 23 (31.5 percent) were girls. Koplik's spots were present among 56 (76.7 percent) children whereas 17 (23.3 percent) did not have Koplik's spots at the time of enrolment. lymphadenopathy was assessed in 35 (47.9 percent) children while 38 (52.1 percent) did not have lymphadenopathy at the time of enrolment.

Conclusion: Study concluded that a higher proportion of children presenting with maculopapular rash were diagnosed to have measles on the basis of serology.

Key words: Measles infection, rubella, children, vaccination and maculopapular rash.

Introduction

Introduction: High population immunization coverage is the mainstay of measles control, reducing ongoing transmission of virus and the risk of outbreaks. At least 95 percent of the population needs to be immune to avoid ongoing outbreaks. To achieve this goal, the immunization coverage must be more than 90 percent. The WHO also recommends that a second opportunity for immunization should be available for all children (1). In Pakistan, the estimated measles deaths are 81,000 annually among children under 5 year old (2). An effective vaccine is available for measles under Extended Programme for Immunization (EPI) in Pakistan. Vaccine is given subcutaneously at the age of 9-15 months, as recommended by WHO. Antibodies develop in 95 percent of children vaccinated at the age of 12 months of age and 98 percent of children vaccinated at 15 months of age. In Pakistan, vaccine is given at the age of 9 and 12 months. However, the measles vaccine coverage is quite low in Pakistan. The recent Pakistan Demography and Health Survey (2006-07) reports a country-wide coverage of 50 to 60 percent for measles immunization (3). This reflects a possible gap in herd immunity.

Maculopapular rashes are small confluent bumps are usually divided into three major groups; classic rashes, non-specific rashes and paraviral eruptions (4). Measles, rubella, scarlet fever, exanthem subitum, erythema infectiosum and varicella are classic rashes. Study which was carried out between 1994 and 1998,

immediately after a mass vaccination programme carried out in 1992 in children aged 9 months to 14 years, the researchers found that the most common causes of morbilliform rash were dengue fever 33 %, rubella 20%, parvovirus 9%, measles 7% and HHV-6 2% (5). It is recommended that the differential diagnosis of measles and rubella should be made with other infectious exanthematic diseases, drug reactions and Kawasaki disease. Often, clinicians confused between the Kawasaki disease and the measles at the time of presentation. Kawasaki disease usually presents in children < 5 years of age and the condition is often diagnosed on the basis of high fever for > 5 days with a poor response to antipyretic agents and the presence of four important signs. These signs are polymorphous maculopapular rash, involvement of the hands and feet (early oedema and reddening or late desquamation), exanthema (cracked lips, pharyngitis or strawberry tongue), bulbar conjunctivitis not associated with exudates and unilateral cervical lymphadenopathy > 1 cm. It is important to highlight here that the diagnosis should always rule out other aetiologies of rashes. However, the rash present in Kawasaki disease may be practically indistinguishable from measles. Nevertheless, it is found that few characteristics, which clearly differentiate Kawasaki disease from measles, are absence of coryza and the onset of rash in the extensor surfaces of the limbs with later propagation to the trunk (4). It is reported that rubella cannot be confirmed based on clinical signs and laboratory confirmation is highly recommended. The rubella case is confirmed at the laboratory by the presence of the rubella specific IgM. It is suggested that the blood sample for laboratory confirmation of rubella should be taken within a week of rash onset. Mostly rubella is a contagious when the rash is erupting. However, the condition is communicable from a week before to 5 – 7 days or more after the rash onset. However, research has shown that about half of rubella infections are subclinical and may not be detected clinically but the condition can be confirmed by laboratory methods (6).It is observed that there is an increase in the admitted patients with rash and fever and there is misdiagnosis of measles. This observation led us to do the current study.The aim of this study was to find the association of clinical and serological outcome of measles and rubella with demographic profiles in patients hospitalised with clinical suspicion of these conditions.

Methodology:

A descriptive cross sectional study design was chosen in order to achieve the study objective. All children presenting with maculopapular rash and sign and symptoms suggestive of either measles or rubella in outdoor patient, indoor patient and accident and emergency department of the Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad were screened for enrolment. Those who fulfilled the below mentioned inclusion criteria were enrolled in this study. The total duration of the study was one year or the completion of required sample size. The enrolment of patients was started in June 2012, and data collection was completed by May 2013. A total of 73 children presenting with maculopapular rash and were suspected cases of either measles or rubella, who fulfilled the inclusion criteria were enrolled in this study. The sample size was estimated by using the WHO sample size calculations on confidence interval level (Z) was considered at 95 percent and participating population (P) was taken as 95 percent (7). A purposive (non-probability) sampling technique was used to select cases. Children Age > 6 months and < 13 years with maculopapular rash having Fever >104oF were included in this study. However, children with pruritic rash, allergic condition and drug induced rash were excluded from the study.

Data was collected through a structured Proforma especially designed for this study. Permission was taken from the Hospital Ethical Committee before the commencement of the study. Patients who presented with maculopapular rash and were suspected cases of either measles or rubella were prospectively enrolled either from Isolation Ward or from the outpatient department and accident and emergency department of the Children Hospital, PIMS, Islamabad. A written informed consent was taken from those who fulfil inclusion and exclusion criteria and enrolled in the study. The demographic characteristics of each patient were collected and noted on the Proforma. Data regarding clinical presentation like fever, rash, lymphadenopathy, eye and/or mouth complications, pneumonia, diarrhoea and vomiting were noted. Samples of the clinically confirmed cases of measles and rubella were taken and sent to the virology department of the National Institute of Health (NIH), Islamabad for analysis. The serological results were in the form of measles and rubella IgM. The isolation of the virus was done using sensitive ELISA technique. The details of investigations in terms of type of sample and results were noted in the proforma. To control any bias, all the study procedures including patient selection, examination, monitoring and investigations were done by the researcher himself. The study outcome was the serological outcome and its association of suspected cases presenting with maculopapular rash with measles and rubella.

Data was analysed by using software SPSS version 18. The descriptive analysis was carried out and reported as mean with standard deviation and median for continuous variables such as age. For categorical variables such as gender, presence of fever, positive or negative IgM, lymphadenopathy, eye complications including ocular, pneumonia, diarrhoea, vomiting etc, frequencies and percentages were calculated and reported. As this is a descriptive study, therefore, no statistical test was used. Findings are presented as tables and figures in the result section.

Results:

The age distribution of all the enrolled children is shown in Table I. The mean (standard deviation) age of all the children in this study was 46.5 (± 40.1) months, i.e. in terms of years, the mean (SD) age was 4 years and 10 months (± 3 years and 4 months). The median age of all children was 24 months (2 years). The youngest child was 7 months old while the eldest child was 12 years (144 months) of age. Seven (9.6 percent) children were less than 9 months of age while 17 (23.3 percent) were aged between 9 months and 12 months. Hence, about one third of the children [24 (32.9 percent)] were infants in our study. Twenty eight (38.4 percent) children were aged between 1 year and 5 years whereas 21 (28.8 percent) were older than 5 years of age.

Out of 73 children enrolled in the current study who presented with maculopapular rash and their serological outcome was assessed, 50 (68.5 percent) were boys whereas 23 (31.5 percent) were girls. Out of 73 enrolled children, fever was present in substantial majority [68 (93.2 percent)] of children while only 5 (6.8 percent) did not have fever at the time of enrolment. Out of 73 enrolled children, on examination at the time of enrolment, Koplik's spots were present among 56 (76.7 percent) children whereas 17 (23.3 percent) did not have Koplik's spots at the time of enrolment. Out of 73 enrolled children, on examination at the time of enrolment, lymphadenopathy was assessed in 35 (47.9 percent) children while 38 (52.1 percent) did not have lymphadenopathy at the time of enrolment. Out of 73 enrolled children, eye disorders (complications) were present in 48 (65.8 percent) children while 25 (34.2 percent) did not have any eye disorder or any eye complication at the time of enrolment. Out of 73 enrolled children, 28 (38.4 percent) children were diagnosed to have pneumonia at the time of enrolment whereas 45 (61.6 percent) did not have pneumonia at the time of enrolment. Out of 73 enrolled children, 28 (38.4 percent) children had vomiting at the time of enrolment whereas 45 (61.6 percent) did not have vomiting at the time of enrolment. Out of 73 enrolled children, 15 (20.5 percent) children had diarrhoea at the time of enrolment whereas 58 (79.5 percent) did not have diarrhoea at the time of enrolment. Out of 73 children enrolled in the current study, 35 (47.9 percent) were unvaccinated while, 38 (52.1 percent) were vaccinated (for measles and/or rubella). Out of 73 children enrolled in the current study, IgM was positive for measles in 61 (83.6 percent) children and IgM was positive for rubella in 2 (2.7 percent) children presenting with maculopapular rash. However, in 10 (13.7 percent) children serology was negative for both measles and rubella.

Table I: Age distribution of all the enrolled children (n=73)

Age	No. of children	Percentage (%)
Mean	46.5	
Standard deviation	± 40.1	
Median	24.0	
Range (min - max)	7.0 - 144.0	
Age categories		
Less than 9 months	7	9.6%
9-12 months	17	23.3%
1 year to 5 years	28	38.4%
More than 5 years	21	28.8%

Table II present the findings of serology with demographic features (age and gender respectively) of all the children enrolled in the current study. Among children less than 9 months of age, out of 7, IgM was positive for measles in 6 (85.7 percent) children while one (14.3 percent) child had IgM negative for both measles and rubella. None of the child had IgM positive for rubella in this age group. Among children aged between 9 and 12 months, out of 17 children, IgM was positive for measles in 14 (82.4 percent) children while 2 (11.8 percent) children had IgM negative for both measles and rubella. One (5.8 percent) child had IgM positive for rubella in this age group. Among children aged between 1 year and 5 years, out of 28 children, IgM was positive for measles in 22 (78.6 percent) children while 6 (21.4 percent) children had IgM negative for both measles and rubella. Among children more than 5 years of age, out of 21 children, IgM was positive for measles in 19 (90.5 percent) children while one (4.7 percent) child had IgM negative for both measles and rubella and another one (4.7 percent) child had IgM positive for rubella in this age group. Among male children, out of 50, IgM was positive for measles in 45 (90.0 percent) male children while five (10.0 percent) male children had IgM negative for both measles and rubella. None male child had IgM positive for rubella. Among female children, out of 23, IgM was positive for measles in 16 (69.6 percent) female children while 5 (21.7 percent) female children had IgM negative for both measles and rubella. Two (8.7 percent) female children had IgM positive for rubella.

Table II: Distribution of findings of serological test for measles and rubella with various age categories among all the enrolled children (n=73)

Age categories	No. of children with			Total
	Positive serology for measles (%)	Positive serology for rubella (%)	Negative serology (%)	
Less than 9 months	6 (85.7%)	0 (0.0%)	1 (14.3%)	7
9 to 12 months	14 (82.4%)	1 (5.8%)	2 (11.8%)	17
1 year to 5 years	22 (78.6%)	0 (0.0%)	6 (21.4%)	28
More than 5 years	19 (90.5%)	1 (4.7%)	1 (4.7%)	21
Total	61 (83.6%)	2 (2.7%)	10 (13.7%)	73

Discussion:

Most infants are protected during the first months of life via maternally derived antibodies. However, when immunity is lacking, measles can be severe (8). Our study findings show measles is common in infants (younger than 1year of age) also. Out of 73 children presenting with maculopapular rash, about one third of the children (32.9 percent) are infants in our study. Our findings are comparable with other studies conducted previously in Pakistan and other regions of the world. A study conducted by Aurangzeb and co-workers in the same hospital few years ago enrolled 205 hospitalized children with complicated measles. In their study they found 20.5 percent of the complicated measles children were infants (9). A study conducted in a tertiary care hospital in Rawalpindi enrolled 68 children admitted to hospital due to complicated measles. The author found that out of 68 children with complicated measles, 22 (32 percent) were infants (10). Recently, a study was carried out in a teaching hospital in Larkana and enrolled 73 children with complicated measles. In their study, they found that out of 73, 9 (12.3 percent) children were infants (11). In Peshawar, a study was conducted by Khan and co-workers at one of the major teaching hospital. They enrolled 310 children who were hospitalized due to complications of measles. They found that out of 310 children with measles, 75 (24.2 percent) were infants (12). In Bangkok, Thailand researchers conducted a study in one of the tertiary care hospital and enrolled 156 cases of measles admitted to the hospital. They found that out of 156 children, 63 (40.4 percent) were infants. Reason for slightly higher proportion of infants in their study could be due to the fact that a great majority of infants were unvaccinated (92 percent)in their study (13). All the above mentioned studies reported a higher proportion of boys with measles compared to girls, even in children admitted to hospital with complicated measles.

An effective vaccine is available against measles and it is a part of Pakistan's EPI. However, the coverage is quite low as only 50-60 percent of the children are vaccinated against measles according to latest survey (3). Findings from our study show that 47.9 percent of the children are unvaccinated. Our findings are comparable to other studies in this region. Aurangzeb and colleagues in their study population of 205 hospitalized children with complicated measles, found that 88 (45 percent) were unvaccinated (9). In Rawalpindi, out of 68 children with complicated measles, the author found 34 (50 percent) children were unvaccinated. However, a study from Larkana enrolled 73 children with complicated measles, reported a substantial majority of children [67 (91.8 percent)] were vaccinated. Only 7 (8.2 percent) children were unvaccinated. However, reasons for this high coverage of vaccination in Larkana are unknown (11).

The success of measles elimination requires continued high-quality surveillance and high vaccination coverage. Case investigation and identification of contacts are now recommended for all suspected cases of measles. In order to trigger further investigation and laboratory or epidemiologic confirmation, the current definition of a suspected measles case that has been adopted in many countries (including by Pakistan's Ministry of Health) relies on the presence of a generalized maculopapular rash of ≥ 3 days' duration, fever, and at least one of the following - cough, coryza, or conjunctivitis (14). However, the performance of the definition of a suspected case is affected by the occurrence and distribution of measles and of other maculopapular febrile rashes that may be misdiagnosed as measles.

Therefore, the above mentioned studies assessed the value of clinical diagnosis of

measles compared to the serological outcome. Research has revealed that although serological confirmation is essential to ensure an accurate diagnosis of measles when the disease is rare, the use of a clinical definition of measles might be useful in measles surveillance when serum samples are not available (15). Furthermore, it would be easy to diagnosed clinically in countries like Pakistan where only few laboratory facilities are available.

Conclusion:

Study concluded that a higher proportion of children presenting with maculopapular rash were diagnosed to have measles on the basis of serology. Complicated measles cases are common in our clinical settings and the most common complication is eye disorders followed by pneumonia and gastroenteritis. However, there is need to conduct large sample size, multicentre clinical trials in Pakistan to validate the results of the current study.

References:

1. Senn N, Riddell M, Omena M, Siba P, Reeder JC, Clements CJ, et al. Measles in Papua New Guinea: An age-specific serological survey. Vaccine. 2010; 28: 1819-23.

2. Gaffar T, Mohsin E, Lievano F. The challenge of achieving measles elimination in the eastern Mediterranean region by 2010. J Inf Dis. 2003; 187: 164-71.

3. National Institute of Population Studies (NIPS)[Pakistan], Macro International Inc. Pakistan Demographic and Health Survey 2006-07. Islamabad, Pakistan: National Institute of Population Studies and Macro International Inc; 2008.

4. Garcia JJG. Differential Diagnosis of Viral Exanthemas. The Open Vaccine Journal. 2010; 3: 65-8.

5. Oliveira SA, Siquiera MM, Camacho LAB, Nogueira M, Spinetti CCJ, Cubel RCN, et al. The aetiology of maculopapular rash diseases in Niteroi, State of Rio de Janeiro, Brazil: implications for measles surveillance. Epidemiol Infect. 2001; 127: 509-16.

6. Drago F, Rampini P, Rampini E, Rebora A. A typical exanthems: morphology and laboratory investigations may lead to an aetiological diagnosis in about 70% of cases. Br J Dermatol. 2002; 147: 255-60.

7. Murhekar MV, Hutin YJ, Ramakrishnan R, Ramachandran V, Biswas AK, Das PK, et al. The heterogeneity of measles epidemiology in India: Implications for improving control measures. JID. 2011; 204: S421-2.

8. Perry RT, Halsey NA. The clinical significance of measles: A review. JID. 2004; 189: S4-16.

9. Aurangzeb B, Nisar YB, Hazir T, Burki F, Hassan M. Clinical outcome in children hospitalized with complicated measles. J Coll Physicians Surg Pak. 2005; 15: 547-51.

10. Tariq P. Assessment of coverage levels of single dose measles vaccine. J Coll Physicians Surg Pak. 2003; 13: 507-10.

11. Junejo AA, Abbasi KA, Shiakh AH. Complications of measles in hospitalized children. MC. 2011; 17: 41-4.

12. Khan A, Aqeel M, Khattak AA. Measles is still a severe problem in North West Frontier Province of pakistan: Study of hospitalized patients. MC. 2009; 15: 140-3.

13. Ariyasriwatana C, Kalayanarooj S. Severity of measles: a study at the Queen Sirikit National Institute of Child Health. J Med Assoc Thai. 2004; 87: 581-8.

14. De Oliveira SA, Camacho LAB, Pereira ACDM, Setúbal S, Maria R, Nogueira R, et al. Assessment of the performance of a definition of a suspected measles case: implications for measles surveillance. Pan Am J Public Health. 2006; 19: 229-35.

15. Ciccone FH, Carvalhanas TRMP, Afonso AMS, Flannery B, Waldman EA. Investigation of measles IgM-seropositive cases of febrile rash illnesses in the absence of documented measles virus transmission, State of São Paulo, Brazil, 2000-2004. Rev Soc Bras Med Trop. 2010; 43: 234-9.