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Original Article

Case-control Study for Measles Outbreak in a Tertiary Care Hospital

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Abstract

Objectives: To compare the profile of measles patients (cases) with non-measles (controls) admitted in Pediatric units of Civil Hospital, Karachi during the measles epidemic.
Study type, settings and duration: Retrospective, case control, hospital record analysis of children admitted in pediatric units of Civil Hospital, Karachi from October 2012-March 2013.
Subjects and Methods: From the list provided by the ward authorities, case records of children (cases) admitted in pediatric units of Civil Hospital, Karachi with the clinical diagnosis of measles were selected using convenient sampling. From the same wards, age and gender matched non-measles cases (controls) were also selected. The signs, symptoms, mortality and hospital stay of cases and controls were taken from the hospital record, while some information like socio-economic status, vaccination status, symptoms, number of days ill before presenting to health facility, health status of the child, history of similar illness in the family, neighbors, relatives and history of calamity in the area in recent past was taken from the parents or care givers telephonically. Sample size of 300 children (150 cases, 150 controls) was calculated.
Results: Out of 150 children having measles, 84 (56%) were females. Most cases reported to health facility after a median of 8 days of onset of symptoms. Almost 98 (65%) children were vaccinated for measles and 52 (35%) were not vaccinated Median age of cases, vaccinated for measles was 30 months while median age of cases not vaccinated for measles was 21 months. All cases had history of fever and maculo-papular rash. Death occurred in 10 (7%) cases due to pneumonia. There was history of measles in their family in 90 (60%) cases, 54 (36%) had measles in neighbors and 30 (20%) in relatives. Out of 150 controls, 76 (51%) were vaccinated for measles and 74 (49%) were not vaccinated. The main reason for admission was pneumonia in 78 (52%) and bronchial asthma in 45 (30%). The risk of measles was 0.83 times higher for cases who were vaccinated for measles as compared to controls who were vaccinated for measles. Using univariate analysis, symptoms of breathlessness and lower respiratory tract infection at the time of admission were significantly associated with measles disease. Using multivariate analysis, children between 9 to 60 months of age, presenting with breathlessness and lower respiratory tract infection had a significantly high chance of suffering from measles disease.
Conclusion: Almost 65% who had received measles vaccination as per their mothers statement suffered from measles.
Policy message: Measles outbreak occurring in many children despite getting measles vaccine needs further workup both for the timing of vaccination, actual verification of vaccination and its efficacy.
Key words: Measles disease, Schedule EPI vaccination, presenting symptoms.

Introduction

Measles is the most common cause of vaccine preventable childhood deaths, with highest mortality in regions where access to primary health care is limited[1]. Despite the availability of an effective vaccine and a single causative serotype, approximately one million deaths occur annually among infants and children throughout the world due to measles[2]. For a successful measles immunization, there should be absence of maternal antibodies in the child at the time of vaccination. Passive maternal antibodies are transferred through placenta during the first trimester of pregnancy and they gradually wane off in the first year of life[3]. The optimal age for measles vaccination varies from country to country and there is no standardized vaccination schedule. In developing countries, WHO recommends measles vaccination at nine months[4].

In Pakistan majority of children are immunized at the age of nine months with a single dose of measles vaccine and only those who report to EPI clinics at the age of 15 months are given the second dose of measles vaccine. According to EPI, the measles vaccine coverage is less than 80% in Pakistan, leading to a gap in herd immunity[5]. Over 95% coverage is required to interrupt measles transmission[6].

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Measles vaccine efficacy is 85% after the first dose given at 9 months. There is progressive accumulation of a small number of susceptible children in the community due to a combination of deficient measles vaccine efficacy that does not reach 100% and due to children who are not immunized each year[7]. A community based study conducted in school children in Pakistan reported measles antibodies in 78% children only[8]. It is therefore important to understand the role of primary vaccine failure (failure of seroconversion after vaccination) and secondary vaccine failure (waning of immunity after seroconversion) while evaluating measles control program in developing countries[9].

The case definition of measles according to WHO, is generalized maculo-papular rash (non-vesicular), history of fever ≥ 101ºF and at least one of the following: cough, coryza, conjunctivitis or clinical case definition of suspected measles or laboratory criteria of diagnosis: presence of measles specific IgM antibodies[10]. According to WHO African Region (WHO AFRO), measles outbreak is defined as five or more reported suspected cases of measles in a health facility or local government area in one month with a plausible means of transmission[11].

In 2012, measles outbreak occurred in Sindh Province of Pakistan, where 14000 cases were reported with 300 deaths. These figures for the year 2011, were 4000 cases and 64 deaths. A paper published in Lancet on this outbreak reported that community demands for childhood vaccines was not fulfilled in most areas of Sindh and this was compounded by other contributing factors like devolution of health to the Provinces with weak transition of health services including EPI program without adequate preparation and existing malnutrition, the population resulting in reduced immunity and adverse consequences of measles[12].

Subjects and Methods

This was retrospective, case record analysis of age and gender matched measles and non-measles cases who were admitted in pediatric units of Civil Hospital, Karachi during the measles epidemic i.e. October 2012-March 2013.

Sample size was calculated using 24% [13] prevalence of malnutrition in children, (factor for high measles epidemic/morbidity) and a case to control ratio of 1:1 and a confidence interval of 95% came out as 284 [14] which was rounded off to 300 i.e. 150 cases and 150 controls. The WHO's clinical definition of measles comprising of generalized maculo-papular rash (non-vesicular), history of fever ≥ 101ºF and at least one of the following: cough, coryza, conjunctivitis was used. Cases and controls were selected from the list provided by the hospital authorities. Convenient sampling was used to select cases and controls. Apart from the information gathered from the files of these patients (measles and non measles) on signs, symptoms, morbidity and mortality, some data was also collected from respondents/mother on telephone. Information collected telephonically included age, gender, place of residence, socio-economic status of the family, EPI vaccination including measles vaccine, symptoms of the disease, number of days child was ill before presenting to health facility, history of intercurrent illness, health status of the child, number of children under 5 in the family, history of measles in the family, neighbors or relatives and history of calamity in the area in recent past. The information was collected on questionnaire.

The study was approved by Institutional Review Board of Dow University of Health Sciences, Karachi. Permission was also obtained from Heads of the respective departments.

Data was analyzed on computer package SPSS version 15; Odds ratio (OR) at 95% Confidence Interval for estimating risk among cases vs. controls, univariate and multi-variate analysis for association of the variables and chi-square for statistical significance at alpha level 0.05 was used.

Ethical clearance was obtained from the Institutional Review Board (IRB) of the Dow University of Health Sciences, Karachi.

Results

Out of 300 children, 150 had measles and 150 had no measles. Out of 150 cases, 144 (96%) were residents of Karachi and 114 (76%) belonged to low socio-economic group (labourer, daily wager and factory workers).

Majority of the measles cases 84 (56%) were females with male to female ratio of 1:1.3. Median age was 30 months (mode 24 months) and age ranged from 6-144 months. Age distribution showed that 16 (11%) were less than 9 months of age (Table-1).

Table 1: Age and gender of measles cases.

Age Groups (Months)	*Male*	*Female*	*Total n (%)*
≤ 9	6	10	16 (11)
10-12	6	10	16 (11)
13-24	20	16	36 (24)
25-36	12	16	28 (19)
37-48	4	6	10 (6)
49-60	6	12	18 (12)
61 and above	12	14	26 (17)
Total	66 (44%)	84 (56%)	150 (100)

After the onset of symptoms, 89 (59%) measles cases reported to health facility after a median of 8 days (range 3-14 days), Vaccination status showed that 98 (65%) cases had been vaccinated for measles in the past. Median age of vaccinated cases for measles was 30 months, while the median age of cases not vaccinated for measles was 21 months. All measles cases had history of

fever and maculo-papular rash (non-vesicular), 12 (8%) had coryza, 10 (7%) conjunctivitis, 18 (12%) diarrhea/vomiting, 32 (21%) breathlessness and 40 (27%) had lower respiratory tract infection. It was found that 32 (21%) measles cases were malnourished. Death occurred in 10 (7%) cases and the cause of death was pneumonia. Family size showed that 52 (35%) families had one child less than 5 years old in their family. History of measles in the family was present in 90 (60%) cases while 54 (36%) reported measles in neighbors and 30 (20%) in relatives.

Out of 150 controls, 76 (51%) were vaccinated for measles. Reason for admission of non measles cases was pneumonia in 78 (52%), bronchial asthma in 40 (30%) tuberculosis in 12 (8%) and other illness in 15 (10%). Commonest symptoms were fever 114 (76%) and breathlessness 116 (77%).

The number of children immunized through routine EPI were more among cases than controls ($p < 0.007$) and this number was 98/150 (65%) in measles cases and 76/150 (51%) among controls (Table-2).

Table 2: Number of children vaccinated through schedule EPI immunization in cases and controls. (n = 150)

Vaccination	*Cases n (%)*	*Controls n (%)*	*95% C.I*	*p value*
BCG given	136 (91)	112(75)	2.02-1.77	0.000
BCG not given	14 (9)	38(25)	2.71-2.21	
OPV given	136 (91)	125(83)	2.07-1.83	0.043
OPV not given	14 (9)	25(17)	2.59-1.96	
Pentavalent 1 given	106 (71)	98(65)	2.09-1.82	0.193
Pentavalent 1 not given	44 (29)	52(35)	2.28-1.88	
Pentavalent 2 given	98 (65)	90(60)	2.10-1.81	0.202
Pentavalent 2 not given	52 (35)	60(40)	2.25-1.88	
Pentavalent 3 given	94 (63)	89(59)	2.11-1.82	0.318
Pentavalent 3 not given	56 (37)	61(41)	2.22-1.85	
Measles given	98 (65)	76(51)	2.02-1.72	0.007
Measles not given	52 (35)	74(49)	2.34-2.00	

Using univariate analysis, children having symptoms of breathlessness and lower respiratory tract infection at the time of admission were more likely to be suffer from measles (Table-3).

Table 3: Univariate logistic regression analysis for measles cases on selected indicators.

Indicator	*Odds ratio*	*95% C.I*	*p value*
Presenting symptom at admission			
Breathlessness			
Breathless not present(reference)			
Breathlessness present	12.581	21.73-7.28	0.000
Lower respiratory tract infection			
Lower respiratory tract infection not present (reference)			
Lower respiratory tract infection present	4.750	7.76-2.90	0.000

Using multivariate analysis children above 9 to 60 months of age having symptoms of breathlessness and lower respiratory tract infection had more chances of suffering from measles (Table-4).

Table 4: Multivariate logistic regression analysis for measles cases on selected indicators.

Indicator	*Odds ratio*	*95% C.I*	*Sign*
Age groups.			
61 months and above (reference)			
≤ 9 months	0.925	2.57-0.33	0.882
10-12 months	4.124	4.61-1.24	0.020
13-24 months	1.208	4.01-0.36	0.758
25-36 months	2.400	6.77-0.85	0.098
37-48 months	1.230	3.66-0.41	0.710
49-60 months	1.364	5.75-0.32	0.672
Presenting symptom at admission			
Breathlessness			
Breathless not present(reference)			
Breathlessness present	16.76	32.06-8.76	0.000
Lower respiratory tract infection			
Lower respiratory tract infection not present (reference)			
Lower respiratory tract infection present	6.002	11.22-3.20	0.000

Discussion

In our study, measles outbreak occurred in both groups of children i.e. those who were vaccinated against measles and those who were not vaccinated. Measles vaccination did not protect our children as 65% children vaccinated for measles had developed the disease. Faulty cold chain could be one of the main reasons as other study reported failure in cold chain in reducing vaccine efficacy[15]. Though measles occurs mostly in winters and early spring (January - April), the present outbreak occurred between October - March which supports the view that virus can spread in any season[16]. In our study, median age of measles vaccinated cases was 30 months where as it was 21 months in measles non-vaccinated cases which shows an age shift in occurrence of measles cases among those who had received measles vaccine. This could be due to waning of immunity of the first dose or inadequate efficacy of the first dose[16]. It has been found that if second opportunity is given it can slow the increase in the number of susceptible children by vaccinating those who had missed the first dose and providing protection to those who did not develop an immune response after a single dose of measles vaccine[17]. About 17% vaccinated children developed measles after the age of 60 months which suggests secondary vaccine failure or it could be due to poorly stored vaccine or exposure to ultra violet radiation which wanes immunity[18]. Finding of 17% measles cases in our study among children more than 5 to11 years old shows

age shift of measles and is a warning for physicians to include measles in the differential diagnosis of older children with febrile illness and rash as found in other studies[19,20].

Our study reflects data from one tertiary care hospital hence may not be representative of the whole Province of Sindh. Due to retrospective nature of the study, some important information were not found in the hospital case records.

Authors Contribution

SH conceived idea, data collected and analysed as well as wrote manuscript. JA did overall supervision and proof reading of manuscript. MSAM supported in data collection.

Conflict of interest: None declared.

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