## Research Article

# Risk Factors and Complications in Measles Mortalities 

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#### Abstract

To determine the risk factors and complications in patients expired due to measles. Background: Measles is one of the vaccine-preventable diseases. Mortality and morbidity due to it has been decreased in many countries with preventive measures. However, epidemics occur off and on in some communities. Pakistan has faced an epidemic in 2012-13. Started from one province and affected others. Due to some risk factors, Pakistani children suffered from many complications.


Place \& Duration: Measles ward, the Children`s Hospital, Lahore form February to June 2013.
Methodology: All patients who were admitted and expired in measles ward were included in the study. A Performa was filled for each patient to document the risk factors and complications in affected patients.

Results: 1075 patients were admitted. 44 expired. 27 were males. Minimum age of patients who expired was 3 months and maximum was 7 years. Maximum deaths were in group 4: $27 \%$ (12/44), followed by group $2: 23 \%$ (10/44). $30(68 \%)$ were malnourished having weight less than $5^{\text {th }}$ centile. $70 \%$ of the patients died within 24 hours (31/44) because of severity of illness. $82 \%$ (36/44) patients had contacts in families or society. $86 \%(38 / 44)$ patients were unvaccinated and only one patient received two doses ( $2 \%$ ). 17 patients had co-morbid conditions. These were; cystic fibrosis, dilated cardiomyopathy, complex cyanotic heart disease, Gaucher`s disease, hypothyroidism, chronic renal failure, hepatitis (3), seizures disorders, pulmonary tuberculosis, hydrocephalus, Aplastic anemia and severe nutritional anemia (3). Complications documented were; pneumonia (measles pneumonia with superadded bacterial infection) $100 \%$ ( $n=44$ ), Encephalitis $47 \%$ ( $n=21$ ), Enteritis $9 \%$ $(\mathrm{n}=4)$ and respiratory failure $4.5 \%(\mathrm{n}=2)$.

Conclusion: Lack of vaccination is the most important risk factor for mortality, followed by malnutrition and co-morbid illness.
Keywords: Measles, Vaccination, Measles Encephalitis, Mortality, Morbidity.

## INTRODUCTION

Globally, a number of diseases are responsible for childhood mortality and morbidity. The major preventable diseases are; respiratory infections, diarrhea, measles, malnutrition and malaria.

Measles is a contagious disease. It is also known as Rubeola. Depending upon these factors, any one the following complications can occur. Complications are; Otitis Media, Diarrhoea, Bronchitis, Croup, Pneumonia, Encephalitis and Subacute Sclerosing Panencephalitis (SSPE) and many others.
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It spreads by droplets. It's estimated that an infected person usually infects 9 out of 10 persons who come in contact, provided, they are non-immunized or not infected previously.

Measles is diagnosed, mainly on clinical features, especially the cough, coryza and conjunctivitis along with typical maculopapular rashes. However, immunological test or virus detection can confirm the case. The only medication, which has significant effect upon disease morbidity and mortality, is vitamin- A supplementation.

## METHODS

The study was conducted in The Children`s Hospital, Lahore. In the first week of February, when the number of measles patients increased rapidly, a separate ward for measles
patients was established under the supervision of staff of emergency department.

Any suspected patient seen by medical officers of outpatient departments or casualty medical officer was referred to measles ward for further evaluation. Duty medical officers were advised to follow these protocol/screening criteria for measles cases.

Any person with generalized maculo- papular rash \& fever and at least one of the following:

- Cough and or coryza (running nose) or
- Conjunctivitis, or
- Any person in whom expert clinician suspects measles.

The study conducted from $4^{\text {th }}$ February up to $30^{\text {th }}$ June 2013. All the deaths that occurred in measles ward were included. A Performa was designed. All the relevant data filled to identify the risk factors and complications in the patients died of measles. Complications observed in patients were also documented. The aim of this study was identify the risk factors responsible for mortalities of measles patients in our setting. We also planned to determine the complications that occurred in these patients. Co-morbid conditions were also documented.

## RESULTS

During this duration, 1052 patients were admitted in measles ward of The Children`s Hospital, Lahore (up till, July, total admissions were 1075). Maximum admissions were in month April (384) and in month of July, total admissions were just 23 (Table 1).
Table 1. Measles Admission (Month wise).

| Sr. No. | Month | No. | \% Age |
| :---: | :---: | :---: | :---: |
| 1 | February | 104 | 10 |
| 2 | March | 261 | 24 |
| 3 | April | 384 | 36 |
| 4 | May | 268 | 25 |
| 5 | June | 35 | 3 |
| 6 | July | 23 | 2 |
|  | Total | 1075 |  |

Patients of all groups were admitted. Minimum age was 3 months and maximum age among admitted patients was 7 years. Patients were divided into 3 groups according to age. There were 13 patients in group 1 ( 3 months -6 months), 21 patients in group 2 ( 6 months -9 months) and 10 patients in group 3 ( $2 \mathrm{yrs}-5 \mathrm{yrs}$ ). Total patients under five years of age were 42 (Table 2). Males predominate in our data, i.e., 27/44 (Table 3).

Table 2. Age Groups.

| Sr. No. | Group | Age Range | Number | Percentage |
| :---: | :--- | :---: | :---: | :---: |
| 1 | Group 1 | $<9 \mathrm{mo}$ | 13 | $29.5 \%$ |
| 2 | Group 2 | $9 \mathrm{~m}-36 \mathrm{mo}$ | 21 | $47.7 \%$ |
| 3 | Group 3 | $>36 \mathrm{mo}$ | 10 | $22.7 \%$ |

Table 3. Gender.

| Sr. No. | Sex | No. | Percentage |
| :---: | :---: | :---: | :---: |
| 1 | Male | 27 | 61 |
| 2 | Female | 17 | 39 |

We determined nutritional status according to WHO growth charts. Weight for age was drawn on those growth charts and percentiles were calculated. Patients were divided into 5 groups. Group 1: $<5^{\text {th }}$ centile, Group 2: $5^{\text {th }}-10^{\text {th }}$ centile, Group 3: $10^{\text {th }}-25^{\text {th }}$ centile Group 4: $25^{\text {th }}-50^{\text {th }}$ centile and Group $5:>$ $50^{\text {th }}$ centile. Maximum patients were less than $5^{\text {th }}$ centile; $30(\%)$ and only 2 patients were more than $50^{\text {th }}$ centile (Table 4).

Table 4. Nutritional Status ( $\mathrm{n}=44$ ).

| Groups | Percentiles | No. | \%Age |
| :---: | :---: | :---: | :---: |
| 1 | $<5^{\text {th }}$ Centile | 30 | 68 |
| 2 | $5^{\text {th }}-10^{\text {th }}$ centile | 5 | 11 |
| 3 | $10^{\text {th }}-25^{\text {th }}$ centile | 4 | 9 |
| 4 | $25^{\text {th }}-50^{\text {th }}$ centile | 3 | 7 |
| 5 | $>50^{\text {th }}$ | 2 | 5 |

Patients were also categorized depending upon duration of hospital stay. Group 1: less than 24 hours, Group 2: 24-48 hours, Group 3: 2 days to 5 days and Group 4: more than 5 days. Maximum patients were in Group 1: 31(70\%) (Table 5).

Table 5. Hospital Stay.

| Groups | Hospital Stay | No. | \%Age |
| :---: | :---: | :---: | :---: |
| 1 | Less than 24 hours | 31 | 70 |
| 2 | 24 hrs -48 hrs | 7 | 16 |
| 3 | 2 day- 5 days | 3 | 7 |
| 4 | $>5$ days | 3 | 7 |

Most of the patients had acquired infection from contacts in their families or communities (Table 6), however; patients acquired it while visiting hospital / clinics for checkup of

Table 6. Source of Infection.

| Groups | Source | No. | \%Age |
| :---: | :---: | :---: | :---: |
| 1 | Community Acquired | 36 | 82 |
| 2 | Hospital / Clinic | 8 | 18 |

some disease inquired about their vaccination status. 38 ( $86 \%$ ) patients were unvaccinated for measles vaccine, 5 got one dose of vaccine at 9 months of age and only one got two doses from EPI Centre (Table 7).

Table 7. Vaccination Status of Measles.

| Groups | Source | No. | \%Age |
| :---: | :---: | :---: | :---: |
| 1 | Unvaccinated | 38 | 86 |
| 2 | One dose of measles | 5 | 11 |
| 3 | Two dose of Measles | 1 | 2 |

17 patients had other diseases, which affected the survival of measles patients (Table 8).

Table 8. Co-Morbid Conditions.

| Sr. No | Co-Morbid Condition | Number |
| :---: | :---: | :---: |
| 1 | Cystic Fibrosis | 1 |
| 2 | Dilated Cardiomyopathy | 1 |
| 3 | Complex Cyanotic Heart Disease | 1 |
| 4 | Gaucher`s Disease | 1 |
| 5 | Hypothyroidism | 1 |
| 6 | Chronic Renal Failure | 1 |
| 7 | Hepatitis | 2 |
| 8 | Seizure Disorder | 1 |
| 9 | Pulmonary Tuberculosis | 3 |
| 10 | Hydrocephalus | 1 |
| 11 | Aplastic Anemia | 1 |
| 12 | Severe Nutritional Anemia | 3 |
|  | Total | 17 |

All the patients who expired suffered from some complication. Pneumonia was present in $44(100 \%)$ patients and encephalitis in $21(47 \%)$ patients (Table 9).

Table 9. Complications.

| Sr. No | Complication | No. | \%Age |
| :---: | :---: | :---: | :---: |
| 1 | Pneumonia | 44 | 100 |
| 2 | Encephalitis | 21 | 47 |
| 3 | Enteritis | 4 | 9 |
| 4 | Respiratory failure | 2 | 4.5 |

## DISCUSSION

Measles is one of very important communicable disease. It has high mortality and morbidity. With the introduction of vaccines, the mortality has decreased significantly and with the addition of second dose of measles or MMR (Mumps, Measles, and Rubella) at 12-15 months of age has further reduced its incidence. Some of important infectious diseases are; diarrhea, viral hepatitis, cholera, measles, dengue fever and tetanus etc. [1].

In fact, we do not know exactly the immune status of children against these diseases as it occurred in measles epidemic of Lahore in 2013. Here comes the role of public health practitioners [2].

EPI in Pakistan has introduced 2nd dose of measles vaccine, but most of the parents have not inoculated their children for
$2^{\text {nd }}$ dose and in fact in our study of mortalities, only one patient was given 2nd dose. Two doses of measles vaccines at appropriate ages are very important for protection of children and prevention of outbreaks in the community, as it occurred in Denmark in 2011 [3].

One of the causes of low coverage of vaccines is refusal to immunization by parents or guardians. It has been observed that parents of children who are not vaccinated suffer from a lack of reliable information [4].

An outbreak of measles occurred in a boarding school of USA. 9 students got laboratory-confirmed measles out of 663 students. Vaccine effectiveness among students who had received 2 doses of MCV was $98.8 \%$. This shows that if more than $90 \%$ of subjects in a community are immunized, than the cases are not transformed into epidemic. Unfortunately prior to Lahore epidemic, almost $50 \%$ of the population had not received even a single dose of MCV and most of the children who got Vaccination, received just a single dose. At the same time, we do not have any reliable data that what percentage of population is immunized (sero-conversion), who got one or two doses of MCV [5].

Age presentation is variable in different areas and different epidemics. In our study, although all age groups are affected but more mortality occurred in less than 5 years of age. Where as in another study it is somewhat different ; like, in a report about outbreak of measles in France, they have observed that among 407 cases, children of less than one year of age were highest i.e., $32 \%$ followed by individuals between 17 and 29 years old (31\%). They had observed complications in $18 \%$ of cases [6].

One of the important risk factor identified in our study is malnutrition. $68 \%$ children in our study had weight of less than 5th percentile. This is also documented in another study in which they have observed that infants in sub-Saharan Africa, non-stunted and nutritionally better children had better zero-conversion rate as compared to stunted or malnourished population [7].

In Pakistan epidemic started in Sind Province in Nov/Dec 2012. Whenever an outbreak occur, quick response is required to vaccinate the community, as it has been observed that reaction within 2 to 4 weeks avoids large outbreaks and reacting within 40 to 50 days reduces the outbreak size [8].

The mortality rate from measles has been decreasing rapidly in Eastern Mediterranean Region (EMR) in 1997; the member countries passed a resolution for measles elimination from their region by the year 2010. The strategies to achieve this goal were four. 1. Routine coverage more than $95 \%$ in children under 1 year of age. 2. A one time, mass immunization campaign targeting children from 9 months to 15 years of age. 3. Follow-up campaigns after 3-5 years. 4. To strengthen detection of suspected cases through surveillance
and laboratory confirmation [9].
Global efforts should be done to restrict the spread of measles. Otherwise, there is always chance of importation of cases in measles-free region from any endemic country as it occurred in Rhode Island [10].

In our study, we have found a significant increase in numbers of deaths in un-immunized patients. This is evident from our data as well as in another study [11].

Some parents are afraid of drug reactions with vaccinations, especially in rural areas of Pakistan. However, hypersensitivity reactions are rare after vaccination and especially; major side-effects are even rarer. In Brazil, they have reported drug hypersensitivity reaction for MMR varying from 1 to 15 cases per 100,000 doses [12].

Age of patients varies in different outbreaks. In our study, majority of cases are below 5 years of age. Whereas, in an outbreak in Geneva, Switzerland in 2011, most of the cases were young adults with median age of 18 years. In that outbreak vast majority were unvaccinated (81\%) or incompletely vaccinated (8\%) [13].

Facilities provided by state with sponsorship of WHO/UNICEF are not properly delivered at the doorsteps of the population in remote areas [14].

Although, outbreaks do not occur after high coverage of measles vaccination. But, it occurred in Malawi in 2010. Reason may be the accumulation of susceptible person during the last decade [15].

In an epidemic occurred in India, measles killed over 100,000 children. Majority of deaths occurred in highly populous districts and mortality was $70 \%$ in girls [16].

In an epidemic that occurred in Netherlands, they had observed that in a school, 25 children were vaccinated against measles and all of them were protected during epidemic [17].
Complications of measles are very common. In our study, all the patients who died had pneumonias, followed by encephalitis. It is somewhat different from other studies. France was also close to eliminate the disease, when an outbreak erupted in 2008-2011, affected more than 20,000 people. More than half to the patients were adolescents and young adults. 5000 patients hospitalized, 1023 had pneumonia, and 27 had encephalitis and 10 deaths. $80 \%$ of the cases occurred in unvaccinated persons [18].

In our study, minimum age of patient died of measles was 3 months old. Whereas, $7 \%$ babies were in age range of 3 months to 6 months and $23 \%$ from 6 months to 9 months.

In a review article [19] data of 53 papers showed that percentage of measles cases in young infants ranged from $0.25 \%$ to $83 \%$.

When we started mass immunization in Lahore, deaths started declining. Mass immunization is helpful in reducing the cases of measles in the community [20].
Most of the hospitals are not well-prepared to receive the cases during such epidemics. When a large number of cases visit the emergency departments, it causes undue stress on emergency staff, both in terms of workload and financial [21].
Measles was decreasing in countries of European Union until 2009 but has re-emerged in 2010-2011 due to unvaccinated population of about 5 million in the age group of 2-12 years [22].

Mass immunization after 3-4 years is a good strategy to achieve high immunization rates in the communities. As routine immunization may not cover the susceptible group, as shown in study conducted in Western Cape [23].

In some of the day care centers and boarding schools, vaccination coverage is low. It may be due to their lack of awareness. The low coverage in a group of individuals in any community is a threat of epidemic at any time in that community [24].

Many of our patients had contact in community or family, however, a significant number of patients had acquired infection from different hospital settings or clinics. Many of our patients who died during illness had other co-morbid conditions. In fact, if any patient is suffering from some other chronic illness the rate of complications increase in those patients and there are increased chances of mortality and morbidity in such cases.

## CONCLUSION

1. Lack of vaccination is the most important risk factor for mortality, followed by malnutrition and co-morbid illnesses.
2. The most frequent complication found is pneumonia followed by encephalitis.

## RECOMMENDATIONS

- Increase immunization coverage for measles.
- Two doses must be given.
- Nutritional status of children should be improved.


## CONFLICT OF INTEREST

Declared none.

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## REFERENCES

[1] Yao KH. Common pediatric infectious diseases following natural disasters. Zhongguo Dang Dai Er Ke Za Zhi 2013; 15(6): 435-9.
[2] Nielly H, Bauer C, Ramon F, Castel F, Houzé B. Practical limitations of recommendations for managing a cluster of measles cases in a professional setting. Sante Publique 2012; 24(2): 157-63. DOI:10.3917/spub.122.0157
[3] Toft KMA. Primary failure of measles vaccine in a ten-year-old boy. Ugeskr Laeger 2013; 175(9): 567-8.
[4] Bégué P. Vaccine refusal and implications or public health in 2012. Bull Acad Natl Med 2012; 196(3): 603-17.
[5] Yeung LF, Lurie P, Dayan G, et al. A limited measles outbreak in a highly vaccinated US boarding school. Pediatrics 2005; 116(6): 1287-91. DOI:10.1542/peds.2004-2718
[6] Huoi C, Casalegno JS, Bénet T, et al. A report on the large measles outbreak in Lyon, France, 2010 to 2011. Euro Surveill 2012; 17(36): 20264.
[7] Sudfeld CR, Duggan C, Histed A, et al. Effect of multivitamin supplementation on measles vaccine response among HIV-exposed uninfected Tanzanian infants. Clin Vaccine Immunol 2013; 28(8): 1123-32. DOI:10.1128/CVI.00183-13
[8] Marinović AAB, Swaan C, Wichmann O, van Steenbergen J, Kretzschmar M. Effectiveness and timing of vaccination during school measles outbreak. Emerg Infect Dis 2012; 18(9): 1405-13. DOI:10.3201/eid1809.111578
[9] Hamed RA, Alireza AB, Moshki M. Elimination phase of measles: An epidemiological survey in Gonabad (Iran) during 2006-2010. Iran J Pediatr 2012; 22(2): 277-8.
[10] Bandyopadhyay AS, Bandy U. Emerging global epidemiology of measles and public health response to confirmed case in Rhode Island. R I Med J 2013; 96(2): 41-4.
[11] Wolfson LJ, Grais RF, Luquero FJ, Birmingham ME, Strebel PM. Estimates of measles case fatality ratios: A comprehensive review of community-based studies. Int J Epidemiol 2009; 38(1): 192-205. DOI:10.1093/ije/dyn224
[12] Freitas DR, Moura E, Araújo G, et al. Investigation of an outbreak of hypersensitivity-type reactions during the 2004 national measles-mumps-rubella vaccination campaign in Brazil. Vaccine 2013; 31(6): 950-4. DOI:10.1016/j.vaccine.2012.11.095
[13] Delaporte E, Wyler CA, Iten A, Sudre P. Large measles outbreak in Geneva, Switzerland, January to August 2011: Descriptive epidemiology and demonstration of quarantine effectiveness. Euro Surveill 2013; 18(6); 18(6). pii: 20395.
[14] Pradhan NA, Narjis Rizvi N, Sami N, Gul X. Insight into implementation of facility-based integrated management of childhood illness strategy in a rural district of Sindh, Pakistan. Glob Health Action 2013; 6: 10.
[15] Minetti A, Kagoli M, Katsulukuta A, et al. Lessons and challenges for measles control from unexpected large outbreak, Malawi. Emerg Infect Dis 2013; 19(2): 202-9. DOI:10.3201/eid1902.120301
[16] Morris SK, Awasthi S, Kumar R, et al. Measles mortality in high and low burden districts of India: Estimates from a nationally representative study of over 12,000 child deaths. Vaccine 2013; 19: 12. DOI:10.1016/j.vaccine.2013.07.012
[17] van den Hof S, Meffre CM, Conyn-van Spaendonck MA, Woonink F, de Melker HE, van Binnendijk RS. Measles outbreak in a community with very low vaccine coverage, the Netherlands. Emerg Infect Dis 2001; 7(3 Suppl): 593-7. DOI: 10.3201/eid0707.017743
[18] Antona D, Lévy-Bruhl D, Baudon C, et al. Measles elimination efforts and 2008-2011 outbreak, France. Emerg Infect Dis 2013; 19(3): 357-64. DOI:10.3201/eid1903.121360
[19] Leuridan E, Sabbe M, Van Damme P. Measles outbreak in Europe: Susceptibility of infants too young to be immunized. Vaccine 2012; 30(41): 5905-13. DOI:10.1016/j.vaccine.2012.07.035
[20] Ntshoe GM, McAnerney JM, Archer BN, et al. Measles outbreak in South Africa: Epidemiology of laboratory-confirmed measles cases and assessment of intervention, 2009-2011. PLoS One 2013; 8(2): e55682. DOI:10.1371/journal.pone. 0055682
[21] Pezzotti P, Valle S, Perrelli F, et al. Measles outbreak in the Lazio region of Italy: Surveillance and impact on emergency departments and hospitalizations. Ann IG 2013; 25(4): 299-309.
[22] Carrillo-Santisteve P, Lopalco PL. Measles still spreads in Europe: Who is responsible for the failure to vaccinate? Clin Microbiol Infect 2012; 18(Suppl 5): 50-6. DOI:10.1111/j.1469-0691.2012.03982.x
[23] Bernhardt GL, Cameron NA, Willems B, Boulle A, Coetzee D. Measles vaccination coverage in high-incidence areas of the Western Cape, following the mass vaccination campaign. S Afr Med J 2013; 103(3): 181-6. DOI:10.7196/SAMJ. 6196
[24] Braeye T, Sabbe M, Hutse V, Flipse W, Godderis L, Top G. Obstacles in measles elimination: An in-depth description of a measles outbreak in Ghent, Belgium, spring 2011. Arch Public Health 2013; 71(1): 17. DOI:10.1186/0778-7367-71-17

