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ORIGINAL ARTICLE

# The spectrum of measles in COVID-19 pandemic; An observational study in children.

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**ABSTRACT… Objective:** To assess the spectrum of measles during COVID-19 era among children. **Study Design:** Cohort study. **Setting:** Department of Pediatric, Dr. Ziauddin University Hospital, Kemari Karachi. **Period:** February 2019 to February 2021. **Material & Methods:** Clinically diagnosed measles children of either gender aged between 3 months to 5 years admitted to our tertiary care center in the 2 years marked period of the study were analyzed. Measles was labeled as the presence of high grade fever (>104 $^0$F) and maculopapular rash. Medical history was noted and clinical examination was performed in all children. Necessary laboratory investigations like complete blood count and chest X-rays (CXR) were evaluated. All patients were treated as per standard institutional protocols. Outcomes were noted in terms of successful discharge or expiry. **Results:** In a total of 88 children, 55 (62.5%) were male. The mean age was 1.61±1.12 years while 49 (55.7%) children were aged ≤ 1 year. Twenty four (27.3%) children were fully vaccinated appropriate to their age. Fever and rash were found among all children (100%) while respiratory distress and coryza were reported by 82 (93.2%) and 51 (58.0%) children respectively. Overall duration of hospitalization was 7.02±2.32 days. Mortality was reported in 11 (12.5%) children while 76 (86.4%) children were successfully discharged. Development of acute respiratory distress (p=0.0011) and shock (p<0.0001) proved to have significant association with mortality. **Conclusion:** Mortality was relatively high among children with measles during the COVID-19 pandemic era. During hospitalization, most frequent complications were pneumonia, and eye and/or mouth related complications. Development of acute respiratory distress and shock proved to have significant association with mortality.

**Key words:** Coryza, COVID-19, Measles, Pneumonia, Respiratory Distress.

## INTRODUCTION

Measles is a highly contagious and infectious respiratory disease caused by Morbillivirus, a member of the Paramyxoviridae family.[1] Clinically measles is characterized by high fever, cough, rhinitis, conjunctivitis, Kolpik's spots, and maculopapular rash.[2] The infection is acquired via the respiratory tract and mostly affects infants and children under the age of five estimated at approximately 100,000 deaths in children aged less than five in 2008.[3] The measles virus has a reproduction number of 12 to 18 (expected number of cases directly generated by one case in a population where all individuals are susceptible to infection) as compared to COVID which has a reproduction number of 2.5 to 3.5 therefore measles is considered as the most infectious virus on the planet.[4] The virus incubation period is usually 2 weeks; individuals usually recover in 3 weeks if they do not develop any complications. Immune suppression caused by the virus can last even after recovery thereby increasing the susceptibility to secondary infections. Pneumonia is therefore the most common fatal complication of the disease with 50% of them being due to a bacterial superinfection.[5,6]

Measles continues to be a burden on the global health system despite the availability of a safe vaccine for the last 5 decades. The estimated total global measles death in 2016 were around 90,000 which drastically increased to approx. 207,000.[7-10] Between 2000 to 2018 there has been a 73% decrease in the mortality of measles

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worldwide through vaccination but it is still prevalent in the developing nations of Asia and Africa with poor health infrastructure.[11] Pakistan is amongst those countries where measles is still a common sight. In 2017, there were 6,494 confirmed measles cases in Pakistan, according to WHO; this figure accounted for more than 65% of the total number of cases reported in WHO's Eastern Mediterranean Region comprising 22 countries.[12] Dating back to 1974 WHO initiated the immunization program against vaccine-preventable diseases and Pakistan started it in 1978.[13] Two doses of the measles vaccine have been recommended by WHO; the first one conferring 85% immunity against the disease and the second dose making children 95% immune to the disease.[8] The Expanded Program of Immunization (EPI) schedule of Pakistan includes two shots of measles vaccine at 9 months and 15 months.[14] The global target of the Program is to immunize over 95% of infants.[6] A Survey conducted in Pakistan in 2017 and 2018 indicated the nationwide coverage of the first and second dose of measles vaccine at 73% and 67%, respectively which is well below the target mark of 95%.[15] During the COVID pandemic, we observed a rapid increase in hospitalized measles patients supported by preliminary data of 1550 cases of measles reported at the beginning of 2021 according to the National Institute of Health Islamabad Weekly Field Epidemiology report.

Given the recent pandemic of COVID-19 is over, a more objective understanding of its impact on measles as a disease in terms of prevalence is required. This study was aimed to assess the spectrum of measles during COVID-19 era among children.

## MATERIAL & METHODS

This cohort study was conducted in the Pediatric Department (Pediatric Ward, PICU) at Dr. Ziauddin University Hospital, Kemari Karachi from February 2019 to February 2021. Ethical approval was acquired by "Institutional Review Board and Ethical Committee" (4631221PBPED). Informed and written consents were acquired from parents/caregivers of all the children studied.

The sampling technique used was a non-probability convenient sampling technique. Clinically diagnosed measles children of either gender aged between 3 months to 5 years admitted to our tertiary care center in the 2 years marked period of the study were analyzed. Children whose parents/caregivers did not want to be part of this study or those who were having any chronic illness or underlying immunodeficiency syndrome were excluded. Measles was labeled as the presence of high grade fever (>104 $^0$F) and maculopapular rash.

Medical history was noted and clinical examination was performed in all children. Necessary laboratory investigations like complete blood count and chest X-rays (CXR) were evaluated. All the investigations were performed and reported by Ziauddin Hospital. Nutritional status was evaluated considering Weight to height Z –scores as severe acute malnutrition (SAM) with scores <-3Z while moderate acute malnutrition was labeled as weight to height Z-scores between -1Z up to -3Z. All patients were treated as per standard institutional protocols. Outcomes were noted in terms of successful discharge or expiry.

For statistical analysis, "Statistical Package for Social Sciences (SPSS)", version 26.0 was used. Qualitative data were expressed as numbers and percentages while numeric data were shown as mean and standard deviation. Chi-square test was used to compare outcomes between study variables considering $p<0.05$ as significant.

## RESULTS

In a total of 88 children, 55 (62.5%) were male and 33 (37.5%) female representing a male to female ratio of 1.7:1. The mean age was $1.61 \pm 1.12$ years while 49 (55.7%) children were aged $\leq$ 1 year. History revealed that 36 (40.9%) children were exclusively breastfed while complementary feeding was reported in 46 (52.3%) children. Evaluation of the nutritional status revealed that severe acute malnutrition and moderate acute malnutrition were present in 3 (3.4%) and 30 (34.1%) children respectively. Twenty four (27.3%) children were fully vaccinated appropriate to their age. Table-I is showing details about the

demographic and clinical characteristics of children studied.

| Characteristics | | Number (%) |
|---|---|---|
| Gender | Male | 55 (62.5%) |
| | Female | 33 (37.5%) |
| Age (years) | ≤1 | 49 (55.7%) |
| | 2-5 | 39 (46.3%) |
| Exclusive breastfeeding | | 36 (40.9%) |
| Complementary feeding | | 46 (52.3%) |
| Nutritional Status | Normal | 55 (62.5%) |
| | Moderate acute malnutrition | 30 (34.1%) |
| | Severe acute malnutrition | 3 (3.4%) |
| Fully vaccinated appropriate to age | | 24 (27.3%) |
| Place of admission | Emergency room | 59 (67.0%) |
| | Outpatient department | 29 (33.0%) |

**Table-I. Demographic and clinical characteristics (n=88)**

Fever and rash were found among all children (100%) while respiratory distress and coryza were reported by 82 (93.2%) and 51 (58.0%) children respectively. Figure-1 is showing details about the presenting signs and symptoms.

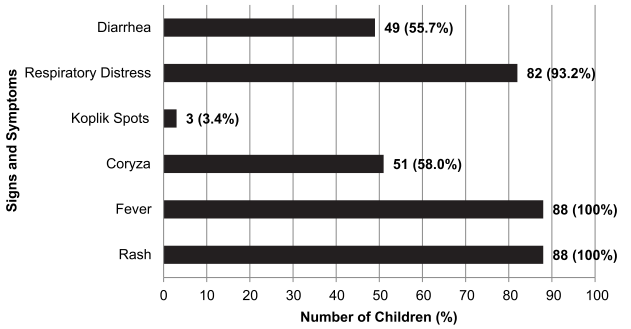


**Figure-1**

The complications reported were pneumonia, acute respiratory distress syndrome (ARDS), eye and/or mouth complications, shock, otitis media, subacute sclerosing panencephalitis (SSPE), and myocarditis in 86 (97.7%), 13 (14.8%), 85 (96.6%), 37 (42.0%), 23 (26.1%), 1 (1.1%), 1 (1.1%) and 15 (17.0%) children respectively. Descriptive statistics about the biochemical analysis of children with measles are shown in Table-II.

There were 33 (37.5%) children who were not responsive to first line antibiotic treatment and were shifted to 2nd line antibiotic treatment later on. Overall duration of hospitalization was 7.02±2.32 days. Mortality was reported in 11 (12.5%) children while 76 (86.4%) children were successfully discharged. One (1.1%) child left against medical advice. Outcome in terms of children successfully discharged or expired was compared with respective to study variables and the details are shown in table-3. Development of acute respiratory distress (p=0.0011) and shock (p<0.0001) proved to have significant association with mortality.

| Laboratory Parameter | Mean±SD |
|---|---|
| Hb (g/dl) | 9.62±1.70 |
| TLC ($x10^9$/l) | 12.46±10.69 |
| Neutrophils (%) | 61.34±12.57 |
| Lymphocytes (%) | 34.30±13.15 |
| Platelets ($x10^3$/ul) | 429.69±203.7 |

**Table-II. Laboratory parameters (n=88)**

## DISCUSSION

The present study shows that measles continues to be an important public health problem especially during pandemic and caused significant morbidity and complications. In the present study, 62.5% measles children were male and 55.7% were aged ≤1 year. Based on the meta-analysis by Green et al, it was found that the incidence rates of clinical measles were 7%, 10%, 3%, and 5% significantly higher in males in infancy, aged 1–4, 5–9 and 10–14, respectively.[16] According to Wang et al, it was reported from China that measles had a significantly higher incidence in males (57.6%) which is quite close to what were found.[17] Sex differences in measles incidence rates may be related to the imbalance in the expression of genes encoded on the X and Y-chromosomes of a host. The phenomenon of X chromosome inheritance and expression is a cause of the immune disadvantage of males and the enhanced survival of females following immunological challenges.[18,19]

In the present study, all (100%) children were having fever and rash. Hisada et Al from Indonesia reported that 100% of measles patients were found to have fever as a symptom.[20]

| Study Variables | | Discharged (n=76) | Expired (n=11) | P-Value |
|---|---|---|---|---|
| Gender | Male | 49 (64.5%) | 6 (54.5%) | 0.5233 |
| | Female | 27 (35.5%) | 5 (45.5%) | |
| Age (years) | ≤1 | 39 (51.3%) | 9 (81.8%) | 0.0573 |
| | 2-5 | 37 (48.7%) | 2 (18.2%) | |
| Exclusive breastfeeding | | 28 (36.8%) | 7 (63.6%) | 0.0903 |
| Complementary feeding | | 41 (53.9%) | 5 (45.5%) | 0.5979 |
| Nutritional Status | Normal | 47 (61.8%) | 7 (63.6%) | 0.5032 |
| | Moderate acute malnutrition | 27 (35.5%) | 3 (27.3%) | |
| | Severe acute malnutrition | 2 (2.6%) | 1 (9.1%) | |
| Fully vaccinated appropriate to age | | 21 (27.6%) | 3 (27.3%) | 0.9801 |
| Place of admission | Emergency room | 49 (64.5%) | 10 (90.9%) | 0.0794 |
| | Outpatient department | 27 (35.5%) | 1 (9.1%) | |
| Presenting Signs and Symptoms | Coryza | 43 (56.6%) | 8 (72.7%) | 0.3095 |
| | Koplik spots | 2 (2.6%) | 1 (9.1%) | 0.2725 |
| | Respiratory distress | 71 (93.4%) | 10 (90.9%) | 0.7586 |
| | Diarrhea | 42 (55.3%) | 7 (63.6%) | 0.6008 |
| Complications During Hospitalization | Pneumonia | 74 (97.4%) | 11 (100%) | 0.5862 |
| | Acute respiratory distress syndrome | 7 (9.2%) | 5 (45.5%) | 0.0011 |
| | Eye and/or mouth related complications | 74 (97.4%) | 10 (90.9%) | 0.2725 |
| | Diarrhea | 35 (46.1%) | 2 (18.2%) | 0.0805 |
| | Shock | 14 (18.4%) | 9 (81.8%) | <0.0001 |
| | Otitis media | 1 (1.3%) | - | 0.7020 |
| | Subacute sclerosing panencephalitis | 1 (1.3%) | - | 0.7020 |
| | Myocarditis | 11 (14.5%) | 3 (27.3%) | 0.2803 |

**Table-III. Comparison of outcomes with respect to study variables**

Cherry et al studied patients in California and reported that 95.3% of measles patients presented with fever.[21] Data from Serbia reported that 84.1% measles children had fever.[22] Measles patients from Serbia, in a study by Jelena et Al, reported 89.7% measles patients to have cough.[22] Cherry et al reported that 86.6% of measles patients presented with cough.[21] In our study population, 93.2% had respiratory distress. Data reported from Israel reported that 87.2% measles patients were having cough.[23]

The present study found that development of acute respiratory distress syndrome (p=0.0011) was significantly linked with mortality. This could be explained by the fact that during Covid-19 pandemic era, COVID infection could have been a major concern in the studied children. We were unable to rule to COVID-19 infection in the present set of cases but it was reported that 97.7% children with measles developed pneumonia during hospitalization. One of the most commonly reported complications in the existing literature among patients of measles is pneumonia and our findings were consistent with what has been reported previously.[24-28] A study from Pakistan reported that 63% measles patients had pneumonia.[29] We found relatively higher rates of complications development among current set of children with measles. This could have been due to the fact that during COVID pandemic, people were hesitant to head to hospitals and that could have caused a delay in management of measles, allowing more patients to develop complications before heading to a healthcare facility. Moreover, strict vigilance of lung related problems was being done during the pandemic which should have created a reporting bias.

The present study noted a mortality rate of 12.5% among admitted children with measles. Mortality due to measles is reported to be nearly negligible in most of the studies.[30] Relatively high rates of morality among children with measles marks that there was a delay in the management of measles due to closure of outpatient department and

hesitancy in reporting to hospital. Most patients only reported to hospital when the case became too complicated to be managed, eventually causing greater mortality.

We unable to verify the presence of COVID-19 infection in the studied children which was one of the limitations of this study. Being a single center study, our findings cannot be generalized but the current study documented very important insights about the clinical presentation and spectrum of complication development among children with measles which adds to the worth of this study.

## CONCLUSION

Mortality was relatively high among children with measles during the COVID-19 pandemic era. During hospitalization, most frequent complications were pneumonia, and eye and/or mouth related complications. Development of acute respiratory distress and shock proved to have significant association with mortality.



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| 2 | Muhammad Salik | Data analysis, Literature review. | |
| 3 | Heena Rais | Concept and Designing, Critical revisions. | |
| 4 | Bina Fawad | Proof reading, Literature review. | |
| 5 | Saba Sadar | Critical revisions. | |
| 6 | Muhammad Saad | Data collection. | |