

Clinical spectrum of measles related diseases in children admitted in PICU of public-sector hospital of Pakistan

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ABSTRACT

Background: Measles is a highly contagious, grave viral disease that can cause severe complications and death. Despite the availability of a safe and cost-effective vaccine, measles remains a major health problem in many developing countries, including Pakistan. To evaluate the clinical spectrum of measles related diseases (MRD) including risk factors, complications and outcomes in children admitted with complicated measles in pediatric intensive care unit (PICU).

Materials and Methods: The aim of this retrospective observational study was conducted at the Sindh Institute of Child Health and Neonatology (SICHN), Karachi, Pakistan. Medical records of children younger than 12 years admitted with clinically diagnosed complicated measles to the PICU between January 2023 to June 2023 were reviewed. Demographic characteristics, vaccination status, nutritional status, clinical manifestations, complications, treatment modalities, and outcomes were analyzed.

Results: The study included 228 (13.8%) patients of all admissions, who were admitted to PICU with MRD. The median age was 11 months (IQR 8–24), and 89 (39%) were younger than 9 months. Malnutrition was present in 150 (66%) patients. A total of 143 (63%) had not received the first dose of vaccination and 192 (84%) had not received the second dose. Case-specific mortality was 23/228 (10%). Mortality was significantly associated with post-measles status, pneumonia (61.4%), encephalitis (12.7%), the need for mechanical ventilation, and inotropic support ($p < 0.001$).

Conclusion: Complicated measles continues to cause substantial morbidity and mortality among critically ill children, particularly in those who are young, unvaccinated or malnourished. Measles elimination can be achieved through high vaccination coverage to decrease the spread of disease contacts.

Key Words: Child, Measles, Mortality, Risk factors, Vaccination.

BACKGROUND

Measles is a highly contagious viral disease that can cause serious complications and mortality, particularly among children younger than five years.¹ Despite the availability of vaccine, measles remains a major public health problem in many countries, including Pakistan.^{2–4}

According to the World Health Organization (WHO) The COVID-19 pandemic was associated with a historic 65% reduction in immunization activities in Pakistan, accompanied by an estimated 21.3% rise in mortality in 2020.⁵ Another report says there were an estimated 136,000 measles deaths globally in 2022, most of them

were unvaccinated.^{6–7} Following the COVID-19 pandemic in Pakistan, measles vaccination coverage dropped to 81% in 2021, which meant that more than 24.7 million children missed their first dose of the vaccine while 14.7 million children did not receive their second dose of the vaccine.^{8–11} Reported cases of measles in Pakistan continue to rise after COVID pandemic.¹² To combat this issue world's largest measles-rubella campaign was conducted countrywide in November 2021 and 90 million children were vaccinated. This was not the first time, previously four supplementary immunization activities were conducted, that showed very successful results in reducing cases over the next few years but in 2022 even after mass supplementary immunization measles cases continue to increase.¹³

Karachi, the largest metropolitan city of Pakistan, has a high burden of measles. Measles can cause serious complications in children under five years of age with more serious and life-threatening complications include gastroenteritis, pneumonia, encephalitis, and cardiogenic shock. About 30–40% of patients with

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measles develop one or more complications. Measles can affect multiple organ systems of the body because it causes damage to mucous membranes and transient but profound immunosuppression. One in twenty children develops pneumonia which causes 56-86% of measles related deaths.¹⁴⁻¹⁶ Mortality due to encephalitis as a complication can also leave permanent damage to the CNS among survivors.¹⁷⁻¹⁸

Due to high influx of patients with measles and high mortality, 14 bedded pediatric intensive care unit was designated as isolation room measles PICU in public-sector hospital in slum area of Korangi, Karachi. The study was designed to identify the risk factors and complications of measles. Also, to understand the different clinical presentations of measles complications which may or may not lead to mortality, this may help us plan better treatments by understanding the burden of the most common complications in the area. This study will help us recognize and plan future research in order to eliminate those risk factors.

MATERIAL AND METHODS

A retrospective observational study was conducted using medical records of children younger than 12 years admitted with complicated measles to the Pediatric Intensive Care Unit (PICU) of Sindh Institute of Child Health and Neonatology, Karachi, between January 2023 and June 2023. To ensure the ethical conduct of the study, approval from the Sindh Institute of Child Health and Neonatology (SICHN) Institutional Review Board (IRB) was obtained (SICHN/Ex-002/2023) on 5th April 2023. The 28-bedded Pediatric Intensive Care Unit (PICU) at SICHN is a specialized unit that provides critical care services to children with life-threatening illnesses or injuries. The PICU is equipped with state-of-the-art medical equipment with a patient centric vision. SICHN is a public-sector tertiary care hospital that is focused on catering patients with a broad spectrum of rural and urban populations.

The diagnosis of measles was based on WHO clinical criteria Measles Surveillance Guidelines with the following symptoms; high-grade fever preceding the appearance of rash by 2-4 days, generalized erythematous maculopapular, non-vesicular rash and one or more of the following: cough, conjunctivitis or coryza, or as laboratory confirmation by IgM antibody testing or polymerase chain reaction (PCR).¹⁹ Cases were categorized as active measles when children presented during the acute febrile rash illness and as post-measles when admitted after resolution of the rash

with documented complications considered related to recent measles infection. Death was declared as measles related if it is 15 days after the presentation of the characteristic rash unless proven due to some other disease or unrelated cause.

Patients younger than 12 years of age with clinical diagnosis of complicated measles requiring therapy admitted in isolation room pediatric intensive care unit of SICHN. Children with suspected but undocumented measles, uncomplicated measles not requiring PICU admission, or alternative diagnoses associated with rash were excluded. Patient records were identified through the Medical Records Department using admission and discharge diagnoses of measles and its complications. Relevant demographic and clinical information were initially extracted from the hospital electronic medical record (EMR) system and subsequently verified through review of paper-based medical records, where detailed clinical documentation was available. Data were collected as demographic data and clinical data to identify risk factors, complications and treatment modalities given on Microsoft Excel spreadsheet.

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 26. Frequencies and percentages were reported for categorical variables. Continuous variables were summarized using median and interquartile range (IQR). Data distribution was assessed using the Shapiro-wilk test. Associations between outcome and categorical variables were assessed using Pearson's chi-square test or Fisher's exact test, as appropriate. Fisher's exact test was applied when expected cell frequencies were less than 5. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 228 children with measles-related disease requiring PICU admission were included during the study period, accounting for 13.8% of all PICU admissions. Most patients were younger than 24 months of age, with approximately one-third being younger than 9 months. The majority of children were either unvaccinated or had incomplete vaccination status. Malnutrition was common, affecting nearly two-thirds of the cohort. Most patients had a documented history of contact with a measles case, with healthcare facilities being the most frequently reported site of exposure. Baseline demographic and clinical characteristics are presented in Table-I.

No significant association was observed between mortality and age, sex, nutritional status, vaccination status, or history of contact. However, mortality was significantly higher among children classified as post-

measles cases compared with those admitted during the acute phase of illness (Table-I).

The clinical spectrum of disease ranged from mucocutaneous manifestations to severe systemic complications. Oral ulcers and conjunctivitis were the most frequently observed clinical manifestations. Among major complications, pneumonia was the most common, followed by encephalitis. Less frequent complications included otitis media and pneumothorax. Mortality was significantly associated with pneumonia and encephalitis, whereas no significant association was observed for other manifestations or complications (Table-II).

Treatment requirements reflected the severity of illness in the study population. A substantial proportion of patients required supplemental oxygen, while smaller proportions required high-flow nasal cannula support, invasive mechanical ventilation, or inotropic therapy. Children requiring mechanical ventilation or inotropic support experienced significantly higher mortality than those who did not require these interventions ($p < 0.001$ for both comparisons). Treatment modalities and their association with outcomes are summarized in Table-III.

Table-I: Characteristics of participants and association with survival.

	Outcome			P value
	Alive n(%)	Expired n(%)	Total n(%)	
Age				
≤9 months	81(39.5)	8(34.8)	89(39)	0.659 ^f
>9 months	124(60.5)	15(65.2)	139(61)	
Total	205(100)	23(100)	228(100)	
Gender				
Male	119(58)	12(52.2)	131(57.5)	0.589 ^f
Female	86(42)	11(47.8)	97(42.5)	
Malnutrition status	136(66.3)	14(60.9)	150(65.8)	0.600 ^f
MR Vaccine at 9 Months	76(37.1)	9(39.1)	85(37.3)	0.847 ^f
MR vaccinated at 15 months	34(16.6)	2(8.7)	36(15.8)	0.545 [†]
History of Contact	179(87.3)	22(95.7)	201(88.2)	0.326 [†]
Specify History of Contact				
Clinic	28(15.6)	4(18.2)	32(15.9)	0.208 ^f
Home	57(31.8)	3(13.6)	60(29.9)	
Hospital	94(52.5)	15(68.2)	109(54.2)	
Measles Status				
Active	146(71.2)	7(30.4)	153(67.1)	<0.001 ^{**f}
Post	59(28.8)	16(69.6)	75(32.9)	

**p value<0.001, *p value<0.05, ^f Pearson Chi square, [†] Fisher's Exact Test

Table-II: Clinical spectrum of MRD and association with survival.

Complications	Outcome			P value
	Alive n(%)	Expired n(%)	Total	
Pneumonia	120(58.5)	20(87)	140(61.4)	0.008* ^f
Encephalitis	18(8.8)	11(47.8)	29(12.7)	<0.001 ^{**†}
Otitis Media	2(1)	-	2(0.9)	-
Pneumothorax	1(0.5)	1(4.3)	2(0.9)	-

**p value<0.001, *p value<0.05, ^f Pearson Chi square, [†] Fisher's Exact Test

Table-III: Treatment modalities and association with survival.

	Outcome			p value
	Alive n (%)	Expired n(%)	Total n (%)	
Mechanical Ventilation	16(7.8)	19(82.6)	35(15.4)	<0.001 ^{**†}
Inotropes	21(10.2)	18(78.3)	39(17.1)	<0.001 ^{**†}
Oxygen	140(68.3)	10(43.5)	150(65.8)	0.017 ^{*f}
HFNC	50(24.4)	9(39.1)	59(25.9)	0.126 ^f

**p value<0.001, *p value<0.05, ^f Pearson Chi square, [†] Fisher's Exact Test

DISCUSSION

This study describes the clinical spectrum, complications, treatment requirements, and outcomes of children admitted to a PICU with measles-related

disease in Karachi, Pakistan. The majority of patients were under 1 year of age and almost one-third (39%) of patients were less than 9 months, which is the age at which the first dose of vaccination is administered in

Pakistan, similar findings were observed in other studies from Pakistan.^{17-18,21} Leuridan *et al* found that maternal antibodies provide protection for only 2.6 months after birth, suggesting that infants may remain susceptible for many months before vaccination.²⁰ Ain *et al* also highlighted the vulnerability of infants younger than 9 months during measles outbreaks and emphasized the need to evaluate preventive strategies for this age group.²¹ During outbreaks, inadequate community vaccination coverage increases the likelihood of exposure among vulnerable infants who are not yet eligible for routine immunization. The high proportion of young infants requiring PICU admission in our cohort highlights the need for strengthening population-level immunity and evaluating outbreak-control strategies aimed at protecting this age group.

We found that most children were either unvaccinated or incompletely vaccinated that is evident in previous studies.^{3-4,8-9} However, 36 (16%) children who received both doses and 82 (38%) who received the first dose were also admitted with complicated measles, similar findings have been reported in local studies.¹⁷⁻¹⁸ Although some vaccinated children developed severe disease, the present study was not designed to evaluate vaccine effectiveness or causes of vaccine failure. Nevertheless, the predominance of unvaccinated children among severe cases underscores the importance of maintaining high routine immunization coverage and supports that the vaccine is effective.¹

Malnutrition was present in nearly two-thirds (66%) of patients, indicating a substantial burden of undernutrition among children admitted with complicated measles. However, no significant association was observed between malnutrition and mortality ($p=0.600$). This finding differs from some previous studies that identified undernutrition as a predictor of poor outcomes.¹⁸ In our study, there was significantly higher mortality in post measles patients (p value <0.001). High mortality rate may have been caused by the fact that many of the children were already malnourished and evidence suggests that measles-associated immune suppression may persist beyond the acute phase of illness and increase susceptibility to secondary infections and other complications. Aarushi *et al* also describes post-measles complications, despite recovery from the acute phase, can lead to significant morbidity and mortality.²²

Pneumonia was the most frequent major complication, followed by encephalitis. Both conditions were significantly associated with mortality.^{17-18,23} Many previous studies published have reported respiratory illnesses being the commonest complication and cause of mortality in measles. Piastra *et al* presented a case series of children with measles-induced respiratory distress, air leak and acute respiratory distress syndrome.¹⁶ Recent study from another public hospital of Karachi found similar findings, Shazia *et al* describes bronchopneumonia being the leading cause of hospitalization and death (13.5%), which further strengthen our findings.¹⁷ Aurangzeb *et al* reported that encephalitis, non-vaccination and under-nutrition were significantly associated with mortality (17%) in measles.¹⁸

These findings are consistent with previous reports identifying young age, malnutrition and missed vaccination as key risk factors for complicated measles and poor outcomes, particularly in low- and middle-income countries.¹⁷⁻¹⁸ The substantial burden of respiratory and neurological complications among critically ill children highlights the importance of timely diagnosis, appropriate supportive care, and early recognition of severe disease. Further multicenter prospective studies are needed to understand the risk factors for these complications and to develop strategies to prevent them as well as prevention of measles under 9 months of age.²⁴⁻²⁶

LIMITATIONS

Due to retrospective nature of the study, there was missed data and information. Another limitation of this study is its single-center design which restricts generalizability, further studies are needed that covers multiple centers to recognize districts with high burden of measles and to understand the reasons for low vaccination rates and to develop strategies to improve vaccination coverage in these areas.

CONCLUSION

Complicated measles continues to cause substantial morbidity and mortality among critically ill children, particularly in those who are young, unvaccinated or malnourished. Strengthening routine immunization coverage and ensuring early recognition and management of severe complications may help reduce measles-related morbidity and mortality.

DISCLOSURES

The abstract of this study was presented as an oral presentation in Critical Care Congress January 21-24, 2024 at Phoenix, AZ, USA [Abstract # 274]. Critical Care Medicine 52(1):p S112, January 2024. <https://doi.org/10.1097/01.ccm.0000999284.37743.a6>

CONFLICT OF INTEREST

None

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AUTHOR CONTRIBUTION

Urooj Faisal: Substantial contributions to methodology, investigation, validation, analysis, acquisition of data, manuscript writing, critical review, final approval, accountable for all aspects of publication

Anwarul Haque: Substantial contributions to methodology, data curation, investigation, data analysis, manuscript writing, critical revisions, final approval, accountable for all aspects of publication

Aimen Zafar: Contributed to conceptualization, data analysis, review and editing, final approval, accountable for all aspects of publication

Aqsa Majeed: Contributed to conceptualization, data analysis, supervision, manuscript review, resource provision, final approval, accountable for all aspects of publication

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