

Frequency of Measles Vaccination and Its Complications among Children, A Single Centered Study

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Abstract

Background: The high incidence of measles remains a pressing concern in Pakistan, highlighting the critical need for enhanced vaccination efforts.

Objective: The study aimed to measure the complications associated with measles infection concerning vaccination status among Paediatrics patients in a tertiary care hospital.

Methods: This research adopts a cohort design, utilizing a consecutive sampling technique. The study was conducted from July 2023 to July 2024 in the Department of Paediatrics Medicine at Jinnah Hospital, Lahore. The participant cohort comprised 145 children, aged between 6 months and 12 years, diagnosed with measles based on the established operational definition *i.e.* acute, febrile illness characterized by cough, coryza, conjunctivitis, fever >990F and a characteristic maculopapular rash. The study included both male and female patients.

Results: 68.97% of the patients were admitted to the hospital and 37.24% of the patients were fully vaccinated. 49% of the children fall within the 1-5-year age group. Clinical presentation revealed nearly all patients (94.48%) experienced fever, and cough as the primary complaints. Complications developed in 66.89% of the patients with pneumonia being the most prevalent complication. Additionally, approximately two-thirds of the patients who experienced complications were unvaccinated.

Conclusion: The study underlines a significant finding: a substantial proportion of patients were not vaccinated. Complications associated with measles were notably more prevalent among unvaccinated individuals, emphasizing the critical role of vaccination in mitigating measles-related morbidity. These results highlight the urgent need for enhanced awareness and vaccination campaigns to address the concerning spread of measles.

Keywords: Measles, vaccination, complications, paediatrics, immunization.

INTRODUCTION

Measles is a highly transmittable airborne disease caused by an RNA virus that is single-stranded and belongs to the paramyxoviridae family. It is a common cause of mortality among young children especially in underdeveloped countries. It is highly prevalent among preschool and school-age children [1]. Fever, malaise, rash, cough, coryza, and conjunctivitis are major characteristic features of this disease. In developing countries like Pakistan, a large number of deaths are because of measles in different rural and urban areas [2, 3].

The measles vaccine is a live attenuated vaccine given by intramuscular or subcutaneous route. It is free of cost in Pakistan and given, in two scheduled doses by EPI at 9 and 14 months of age. Conversely, it can also be purchased from the private sector depending upon the affordability of the caregivers [4]. Owing to the COVID-19 breakout, routine vaccinations are tremendously affected globally and there is a possibility

that more than half of the world's population may acquire measles in the coming years [5, 6].

Measles is endemic throughout the world and epidemics usually occur during spring. The worldwide incidence of measles is about 39.9 million cases and here in Pakistan, about 81,000 deaths annually due to measles in children less than 5 years of age [7]. Unfortunately, vaccination coverage for measles in Pakistan is less than 60% even though it is freely available, quite safe, highly effective, and relatively inexpensive [8, 9].

The cases of measles are increasing even after using the vaccine for its prevention. It is important to understand different factors contributing to this like; the role of failure of primary vaccine, failure to produce antibodies after proper vaccination, failure of secondary vaccine, and decreasing immunity after seroconversion to evaluate the measles control programs in our country [1]. Previous epidemics were recorded in 2002 and 71.6% of children with measles were found to be vaccinated against this disease [10]. Another study in Lasbela district showed that the failure rate of measles vaccination was greater than 50% [11]. Many other studies are also in favour of the failure of the measles vaccine.

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Given the ongoing occurrence of measles outbreaks in Pakistan, even among vaccinated individuals, there is a clear need to re-evaluate the effectiveness of the current vaccination program and identify factors contributing to vaccine failure. The present study aims to address the frequency of measles vaccination and associated complications among paediatrics patients with measles in a tertiary care hospital. By analyzing the demographic and clinical characteristics of these cases, as well as the immunization status and outcomes, this study seeks to provide critical insights into the underlying causes of measles resurgence in Pakistan.

MATERIAL AND METHODS

This hospital-based cohort study was conducted to find the frequency and complications associated with measles infection concerning vaccination status among children aged from birth to 12 years, irrespective of gender. The study was carried out in the Department of Paediatrics at Jinnah Hospital, Lahore, from July 2023 to July 2024.

The study included a total of 145 diagnosed cases of measles presenting to both the outpatient and inpatient services of Jinnah Hospital, Lahore. The sample size of 145 was estimated with OpenEpi, Version 3, by 95% confidence level with Population size (for finite population correction factor or FPC)(N):10000, Population size(for finite population correction factor or FPC)(N): 40%+/-5, Confidence limits as % of 100(absolute +/- %)(d): 8%, and Design effect (for cluster surveys-DEFF): [4]. Jinnah Hospital is a tertiary care teaching hospital with a dedicated Paediatric ward providing comprehensive healthcare services to a large population in Lahore and its surrounding areas. Ethical approval for the study was obtained from the Institutional Ethical Review Committee (ERC approval no. 161/2/12-3-2024/S1 ERB). Informed consent was obtained from the parents or guardians of the children for the inclusion of their data in the study.

All consecutive children diagnosed with measles during the study period who met the inclusion criteria were enrolled. Children were included if they had a confirmed diagnosis of measles based on clinical examination, history, and review of their vaccination records. Those with complications were admitted and patients without complications were discharged after advising proper follow-up. Those who developed bronchopneumonia, excessive diarrhea with or without dehydration, purulent conjunctivitis, severe mouth ulcer, otitis media, laryngotracheobronchitis, and acute encephalomyelitis in the hospital or before were recognized as measles-complicated cases, while those who do not develop any of them were considered uncomplicated cases. The vaccination status was

confirmed by reviewing vaccination cards, and children who received measles vaccination within the last four weeks from the date of presentation were classified as unvaccinated. Vaccination status was considered to be valid if the vaccine was administered one month prior to the occurrence of the disease. Cases with incomplete records or unclear vaccination history were excluded. Children with other causes of rash like drug rash, roseola, rubella, chicken pox, Kawasaki disease and immunocompromised children were also excluded from the study.

A structured data collection form was used to gather detailed demographic information, clinical history, complications including diarrhoea, otitis media, pneumonia, encephalitis, and vaccination status of each patient. The clinical examination included an assessment of symptoms and signs consistent with measles, such as fever, cough, coryza, conjunctivitis, and rash. Vaccination status was classified into two categories: fully vaccinated and unvaccinated. Pneumonia as defined according to World Health Organization (WHO) criteria *i.e.* (respiratory rate > 50 breaths per minute for 2-11 months, or > 40 breaths per minute for 12- 59 months old children) or the presence of pulmonary infiltration in the chest radiograph. The central nervous system was considered to be involved if there was lethargy, headache or irritability, history of convulsions, disorientation, neck rigidity or any neurologic deficits. Diarrhoea was defined as the passage of three or more stools per day of consistency softer than usual. All the patients were given vitamin A orally at admission and the complications were managed according to the hospital protocol. Children admitted to the hospital were followed until discharge to monitor for any complications, while those treated on an outpatient basis were followed up after four weeks *via* scheduled clinic visits or telephone interviews to assess for complications.

Data were entered and analyzed using SPSS version 11. Descriptive statistics were used to summarize the data, with categorical variables presented as frequencies and percentages, and continuous variables presented as mean \pm standard deviation. A significance level of $P < 0.05$ was considered statistically significant. The results were tabulated to provide a clear overview of the gender distribution, vaccination status, age distribution, clinical presentations, and complications observed in the cohort.

RESULTS

A total of 145 paediatric measles cases were included in the study. The mean age was $22 \pm$ SD months. The gender distribution showed a slight male predominance. The vaccination status and age distribution were also presented.

Table 1 presents the gender distribution, vaccination status, age distribution of the patients and admissions. The majority of the cases were unvaccinated (62.75%), fell within the 1-5 years age group (49%) and (68.97%) got admitted.

Table 1: Gender distribution, vaccination status, and age distribution of measles cases.

Characteristic	Frequency (n)	Percentage (%)
Gender		
Male	79	54.44%
Female	66	45.51%
Vaccination Status among total cases		
Unvaccinated	91	62.76%
Fully Vaccinated	54	37.24%
Vaccination status among complicated cases		
Unvaccinated	91	62.76%
Vaccinated	54	37.24%
Age Distribution		
0 to 2 months	2	1.4%
2 to 6 months	14	10%
6 to 12 months	45	31%
1 to 5 years	71	49%
5 to 10 years	13	9%
Outpatient case	45	31.03%
Admissions	100	68.97%

Presenting Complaints

Table 2 outlines the clinical features presented by the patients. Fever was the most common complaint, reported in nearly all cases.

Complications

Table 3 presents the complications observed among the measles cases. Pneumonia was the most frequent complication, followed by gastroenteritis and encephalitis.

Binary logistic regression analysis was performed for the dependent variable measles vaccination status and complication. Cough, rash, and pneumonia show an odds ratio greater than 1. Gastroenteritis and mortality show a very high value of Exp(B) indicating that a unit change in the predictor variable results in an astronomical increase in the odds of an event occurring. This can happen if the unit change is much larger than what would ever be observed (Table 4).

DISCUSSION

Measles has been endemic in Pakistan for decades and accounts for 65% of the total disease burden in the Eastern Mediterranean region [12]. Measles containing vaccine-1 and 2 (MVC1 and MCV2) were introduced in the schedule of routine immunization in 1974 and 2009 in Pakistan, respectively [13].

Table 2: Presenting complaints among measles cases.

		Cough		Total	P-value
		Present	Not present		
Vaccination Status	Yes	34 (63%)	20 (37%)	54 (37%)	0.195
	No	67 (74%)	24 (26%)		
Total		101 (69%)	44 (31%)	145 (100%)	
		Fever		Total	P-value
		Present	Not present		
Vaccination Status	Yes	51 (94%)	3 (6%)	54 (37%)	1.00
	No	86 (95%)	5 (5%)		
Total		137 (94%)	8 (5%)	145 (100%)	
		Rash		Total	P-value
		Present	Not present		
Vaccination Status	Yes	29 (54%)	25 (46%)	54 (37%)	0.09
	No	60 (66%)	31 (34%)		
Total		89 (61%)	56 (39%)	145 (100%)	
		Triad (Cough, coryza and conjunctivitis)		Total	P-value
		Present	Not present		
Vaccination Status	Yes	11 (20%)	43 (80%)	54 (37%)	1.00
	No	20 (22%)	71 (78%)		
Total		31 (21%)	114 (79%)	145 (100%)	

Table 3: Complications among measles cases.

		Pneumonia		Total	P-value
		Present	Not present		
Vaccination Status	Yes	27 (50%)	27 (50%)	54 (38%)	0.005
	No	25 (27%)	66 (73%)	91 (62%)	
Total		52 (36%)	93 (64%)	145 (100%)	
		Encephalitis		Total	P-value
		Present	Not present		
Vaccination Status	Yes	5 (9%)	49 (91%)	54 (37%)	0.573
	No	8 (9%)	83 (91%)	91 (63%)	
Total		13 (9%)	132 (91%)	145 (100%)	
		Gastroenteritis		Total	P-value
		Present	Not present		
Vaccination Status	Yes	5 (9%)	49 (91%)	54 (37%)	0.335
	No	12 (13%)	79 (87%)	91 (63%)	
Total		17 (11%)	128 (88%)	145 (100%)	
		Pneumonia + Encephalitis		Total	P-value
		Present	Not present		
Vaccination Status	Yes	2 (4%)	52 (96%)	54 (37%)	0.556
	No	1 (1%)	90 (99%)	91 (63%)	
Total		3 (2%)	142 (98%)	145 (100%)	
		Pneumonia + Gastroenteritis		Total	P-value
		Present	Not present		
Vaccination Status	Yes	4 (7%)	50 (93%)	54 (37%)	0.340
	No	4 (4%)	87 (96%)	91 (63%)	
Total		8 (6%)	137 (94%)	145 (100%)	
		Encephalitis + Pneumonia + Gastroenteritis		Total	P-value
		Present	Not present		
Vaccination Status	Yes	2 (4%)	52 (96%)	54 (37%)	0.312
	No	1 (1%)	90 (99%)	91 (63%)	
Total		3 (2%)	142 (98%)	145 (100%)	
		Mortality		Total	P-value
		Present	Not present		
Vaccination Status	Yes	0 (%)	54 (100%)	54 (37%)	0.608
	No	2 (2%)	89 (98%)	91 (63%)	
Total		2 (1%)	143 (99%)	145 (100%)	

Surprisingly, and unfortunately, the coverage of routine vaccination was estimated to be below 50% in 2000 and still below 50% in 2019 [14].

Our study included 145 cases of measles, with the majority being unvaccinated (62.75%) and the remainder vaccinated (37.2%). The most commonly affected age group in our study was children aged 1-5 years, consistent with findings from studies by Muhammad and Albahadle [15, 16]. Additionally, we observed a slight male predominance in measles cases, a pattern also noted by Larson *et al.* [5]. The prevalence of measles in this age group is likely due to the waning

of maternal antibodies. The fact that 37.2% of children developed measles despite being vaccinated raises concerns about primary vaccine failure.

In past epidemics, notably in 2002, it was observed that 71.6% of children diagnosed with measles had a confirmed history of vaccination [10]. Similarly, research conducted in the Lasbela district revealed that the measles vaccination failure rate exceeded 50% [11]. Our findings align with previous research documenting elevated rates of measles vaccine failure, highlighting potential challenges to the vaccine's effectiveness. However, our study demonstrated a

Table 4: Binary logistic model for measles vaccination status and complications among measles cases.

Variables in the Equation								
A	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Upper
Cough (1)	0.240	0.563	0.181	1	0.670	1.271	0.421	3.835
Fever (1)	-0.064	0.844	0.006	1	0.940	0.938	0.179	4.911
Rash (1)	0.513	0.554	0.857	1	0.355	1.670	0.564	4.943
Triad (1)	-0.463	0.504	0.843	1	0.359	0.630	0.235	1.690
Pneumonia (1)	-1.081	0.424	6.496	1	0.011	0.339	0.148	0.779
Encephalitis (1)	-19.461	19995.590	0.000	1	0.999	0.000	0.000	-
Gastroenteritis (1)	20.268	19995.590	0.000	1	0.999	634431819.875	0.000	-
Pneumonia Encephalitis (1)	-0.261	1.780	0.021	1	0.883	0.770	0.024	25.219
Pneumonia Gastroenteritis (1)	0.399	0.994	0.161	1	0.688	1.491	0.212	10.464
Sepsis (1)	-41.463	56841.392	0.000	1	0.999	0.000	0.000	-
Mortality (1)	20.773	40192.933	0.000	1	1.000	1050927942.279	0.000	-
Constant	20.106	40192.933	0.000	1	1.000	539333635.822	-	-

A. Variable(s) entered on step 1: Cough, Fever, Rash, Triad, Pneumonia, Encephalitis, Gastroenteritis, Pneumonia Encephalitis, Pneumonia Gastroenteritis, Sepsis, Mortality.

noteworthy reduction in failure rates, suggesting room for improvement with enhanced practices. Our study included 54 fully vaccinated patients aged 1 to 10 years who developed measles, prompting questions about whether the cases were attributable to primary or secondary vaccine failure. While the precise cause of primary vaccine failure remains uncertain, they can be broadly attributed to two categories: vaccine-related factors, such as improper administration or cold chain disruptions, which are preventable, and host-related factors, including immune status, age, and genetic variability, which are more complex and less understood [17].

The measurement of IgG antibody avidity is an effective tool for differentiating primary and secondary immune responses; however, its use during measles outbreaks has been infrequently reported [18]. Helfand *et al.* used IgG avidity assays in Iran to differentiate primary measles infections from vaccine failure reinfections, finding that 18.4% of cases were reinfections and 24.2% of vaccinated individuals experienced secondary vaccine failure. The study emphasized the importance of a booster dose around age 10 to reduce reinfections [18]. Our study has a limitation in that it lacks immunological tests, which could have provided more precise insights into distinguishing primary vaccine failure from secondary vaccine failure or reinfection. This absence restricts our ability to draw definitive conclusions about the underlying immune mechanisms involved in the cases observed.

The actual coverage of routine vaccination against measles was already very low in Pakistan and the

COVID-19 pandemic made it worse [5]. Our study supports this theory by having 62% unvaccinated children. To combat the severe measles epidemic, Pakistan, with support from WHO, GAVI, and UNICEF, ran a nationwide Measles-Rubella (MR) vaccination campaign from November 15 to 27, 2021. Pakistan still requires such campaigns every 2 to 3 years to achieve the eradication of measles.

Among the 145 patients in our study, the vast majority presented with fever (94.4%). Cough was the second most common symptom, occurring in 69.6% of the cases, followed by maculopapular rash, which affected 61.37% of the patients. These findings underscore the typical presentation of measles, with fever being the most prevalent symptom. The study by Husada *et al.* also observed a similar pattern of clinical presentation in measles cases, further supporting our findings. Their research highlights the consistent nature of key symptoms such as fever, cough, and rash in measles across different patient populations [19].

Complications from measles have been observed in various organ systems, as the virus targets epithelial cells, reticuloendothelial cells, and white blood cells, leading to immunosuppression [20]. The Centres for Disease Control and Prevention report that about 30% of measles cases involve one or more complications. Our study revealed that out of total cases, Pneumonia was the most prevalent complication (36%), followed by gastroenteritis (11%) and encephalitis (9%). Xerri's study also found that most measles cases were complicated by pneumonia [21]. Out of the 145 children, 97 developed complications, with 62.75%

of these cases occurring in unvaccinated individuals. Tragically, two children died due to multi-organ system failure, highlighting the crucial role of vaccination in preventing measles-related complications and deaths.

LIMITATIONS

When interpreting the results of this study, it's important to acknowledge its limitations. The relatively small sample size may affect the generalizability of the findings to a larger population and thus may not fully capture the broader epidemiological patterns across different regions. Furthermore, the study was limited to patients from Jinnah Hospital in Lahore, which may not fully represent individuals from other regions or healthcare settings. Consequently, while the study provides valuable insights, the results should be interpreted with caution, and additional research is needed to confirm and expand upon these findings. Therefore, we suggest multi-centre studies to compare findings with data from other regions within Pakistan or similar countries.

CONCLUSION

In conclusion, our study reveals that most measles patients were unvaccinated, with a minor proportion experiencing vaccine failure. Complications were predominantly seen in unvaccinated children, underscoring the essential role of vaccination in mitigating measles-related morbidity and mortality. To address these concerns, it is crucial to implement more vaccination campaigns aimed at increasing coverage rates.

ETHICAL APPROVAL

Ethical approval was obtained from the Institutional Ethical Review Committee of Allama Iqbal Medical College, Lahore (REF letter No.: ERB161/2/12-3-2024/S1 ERB). All procedures performed in studies involving human participants followed the ethical standards of the institutional and/ or national research committee and the Helsinki Declaration.

CONSENT FOR PUBLICATION

Written informed consent was taken from the participants.

AVAILABILITY OF DATA

The data sets used and/or analyzed during the current study are available from the corresponding author on request.

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Declared none.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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AUTHORS' CONTRIBUTION

Jamal Ashraf is responsible for the conceptualization, planning, and writing of the manuscript. Faiqa Taj and Shafi-u-Zaman analyzed the data, Ayesha Sadia wrote the limitations and discussions, Urwa Afzal and Maheen Ijaz critically reviewed the manuscript and Asma Samee Malik revisited the whole article critically. All authors have read and approved the final manuscript.

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