

# Frequency of Immunisation Status, Complications and Outcome in Children Admitted with Measles in Public and Private Sector Hospitals of Karachi

Musarrat Ameer<sup>1</sup>, Sina Aziz<sup>2</sup>, Shaista Ehsan<sup>3</sup>, Ume Kulsoom<sup>4</sup>

## Abstract

**Objective:** To assess the immunisation status, frequency of complications and the outcome in children admitted with measles in public and private sector hospitals of Karachi.

**Methods:** In this cross-sectional study a total of 382 patients admitted with measles, of either sex from 3 months to 13 years, who presented from March 2016 to March 2017 were included. A total of 265 (69.3%) children were from Ziauddin University Hospital (ZU) and 117 (30.6%) from Abbasi Shaheed Hospital (AS). Non-probability convenient sampling technique was used. Those with congenital anomalies and chronic medical illnesses were excluded from the study. Detailed history and physical examination was done, and findings entered in a Proforma. Immunisation status of the patients was recorded. All the patients were observed for complications like encephalitis, pneumonia, diarrhea, otitis media, epiglottitis, febrile fits and corneal ulcers. Statistical analysis was done using SPSS version 22. Categorical values were compared by chi-square test, p-value of <0.05 was considered significant.

**Results:** A total of 382 were patients admitted with measles, 265 (69.3%) from Ziauddin University hospital and 117 (30.6%) from Abbasi Shaheed Hospital. Overall, 57.4% were completely vaccinated in ZU vs. 32.5% in AS. Despite being completely vaccinated, children in ZU; 152/265 (80%) and in AS; 38/117 (30.6%) had complications with a statistically significant ( $p < 0.0001$ ) difference between private and government sector hospitals. Predominantly, in both hospitals pneumonia was common followed by gastroenteritis. Overall mortality was 13/382 (3.4%) in both hospitals combined.

**Conclusion:** A sizeable number of children admitted with measles in both private and government hospitals were unvaccinated. A significant number developed measles despite receiving two doses of vaccine. Frequency of complications was higher in private versus government hospitals. Mortality from measles was high (3.4%) especially in the unvaccinated.

**Keywords:** Measles, complications, age, nutritional status, vaccination status.

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## Introduction

Measles is a highly contagious viral exanthem. Before the introduction of the measles vaccine, it was responsible for millions of deaths

<sup>1,2,4</sup> Department of Paediatrics Unit-II, Abbasi Shaheed Hospital, Karachi

<sup>3</sup> Department of Paediatric Medicine, Ziauddin University Hospital, Karachi

**Correspondence:** Shaista Ehsan  
Department of Paediatric Medicine,  
Ziauddin University Hospital, Karachi  
**Email:** shaistaehsan@yahoo.com  
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annually worldwide. An estimated 164000 deaths were attributed to measles in the year 2008. Measles vaccine has helped in achieving remarkable progress in reducing the morbidity and mortality from this highly infectious disease. There are, however, major challenges for measles control and eventual eradication. These challenges need to be met in order to protect our future generations<sup>1</sup>.

Complications from measles can occur in almost every organ system. Pneumonia, croup and encephalitis are common causes of mortality. Encephalitis is the most common cause of long-term

sequelae, it occurs in 1 of every 1000 children with measles. Complication rates are higher in those less than 5 years old. Croup and otitis media are more common in those less than 2 years old and encephalitis in older children. In developing countries, measles case-fatality rates are 10 to 100-fold higher than in developed countries<sup>2</sup>.

Measles is an acute infectious disease of children, also known as Rubeola, caused by Paramyxovirus, which is a single stranded enveloped RNA virus. It is normally passed through direct contact and through the air. The virus infects the respiratory tract and then spreads throughout the body. The first sign of measles is usually a high fever, which begins about 10 to 12 days after exposure to the virus and lasts 4 to 7 days. A runny nose, a cough, red and watery eyes and small white spots inside the cheeks can develop in the initial stage. After several days, a rash erupts usually on the face and upper neck. It normally lasts 5 to 6 days and then fades. Unvaccinated young children are at the highest risk of developing measles and its complications. Populations with high level of malnutrition and lack of adequate health care are more susceptible. Therefore, measles is still common in many developing countries. In the year 2016 there were 89780 measles deaths globally, mostly in children under 5 years of age. Accelerated immunisation activities have had a major impact on reducing measles deaths. During 2000-2016 measles vaccination prevented an estimated 20.4 million deaths. In 2012, the Health Assembly endorsed Global Vaccine Action Plan, with an aim of eliminating measles in four World Health Organization (WHO) regions by 2015 and in five regions by 2020. All WHO regions have established goals to eliminate this preventable disease by or before 2020<sup>3</sup>. In 2015 also, there were 134200 measles deaths globally, about 267 deaths every day or 15 deaths every hour. Accelerated immunisation activities have had a major impact on reducing measles deaths. During 2000-2016 measles vaccine prevented an estimated 20.4 million deaths from occurring. Global measles deaths have decreased by 84% from an estimated 550100 in the year 2000 to 89780 in 2016. The measles vaccine has been in use for over 50 years.

It is safe effective and inexpensive. The measles vaccine is often incorporated with the rubella and/or mumps vaccines. It is equally effective in the single or combined form. Two doses of vaccine are recommended to ensure immunity and prevent outbreaks as about 15% of vaccinated children fail to develop immunity from the first dose. In 2016 about 85% of the worlds' children received one dose of the measles vaccine by their first birthday through routine health services as compared to 72% in the year 2000<sup>4</sup>.

Pakistan has one of the highest burdens of measles and measles-related deaths in the world. Measles is endemic to Pakistan, with periodic epidemics occurring every two to three years<sup>5</sup>. The proportion of incompletely immunised children in Pakistan varies from 37-58%, and this has recently resulted in outbreaks of measles<sup>6</sup>. In the year 2012, 14000 Pakistani children were reported with measles. The incidence of measles is increasing even after the use of vaccine for its prevention. It is important to understand the role of "failure to seroconversion" after vaccination and failure of secondary vaccine "waning immunity after seroconversion" for evaluation of measles control programmes in Pakistan<sup>7</sup>.

Countrywide measles outbreaks with over 15,000 cases and several hundred deaths in 2012-13 underscore sub-optimal Expanded Programme of Immunization (EPI) performance in delivering routine immunisations<sup>8</sup>. Pakistan as a member of Eastern Mediterranean Region (EMRO) adopted a resolution in 1997 to eliminate measles from Pakistan in 2010<sup>9</sup>.

Low coverage and poor vaccine efficiency is strongly associated with outbreaks of measles and its complications and hence high morbidity and mortality<sup>10</sup>. Measles Supplementary Immunisation Activities in 2015 achieved 97 per cent coverage, while 61.4% of one-year olds received their first measles immunisation, thus helping protect more Pakistani children against this potentially deadly but preventable disease<sup>11</sup>. However, despite extensive supplemental immunisation campaign, measles outbreaks continue to occur in Pakistan. It is there-

fore, important to determine the effectiveness of these measles Supplementary Immunisation Activities (SIA) by determining what proportion of children is still seronegative for measles and hence susceptible to this disease. If a significant proportion of children are found to be susceptible, then it would indicate that these SIA against measles need to be repeated and made more effective<sup>12</sup>. Adoption of WHO recommended strategies could lead to measles elimination within a short period of time as the experience in Korea<sup>13</sup> and the Americas has indicated<sup>14</sup>.

This multicentre hospital-based study in a private sector, Ziauddin University hospital (ZU) and government sector hospital, Abbasi Shaheed (AS) was carried out with the objective of evaluating the vaccination status of children hospitalised with measles both in public and private sector hospitals. Furthermore, the aim was also to determine the frequency of occurrence of measles and its complications in the children. As measles and its complications, still present as a fatal illness even among vaccinated children in our country and epidemics of the disease have been frequently occurring especially over the past few years therefore, keeping in view the magnitude of the problem this study was conducted.

### **Patients and Methods**

This was a cross sectional analytical study conducted in a public-sector hospital, Abbasi Shaheed Hospital (AS) and a private hospital Ziauddin University Group of Hospitals (ZU), from March 2016 to March 2017. A total of 382 patients of either sex from the ages of 3 months to 13 years who presented with measles or its complications were included with non-probability convenient sampling technique. Children less than 3 months of age and more than 13 years old, those with congenital anomalies and chronic medical illnesses were excluded from the study. The sample size estimation was done using the formula  $n = \frac{Z^2 P (1P)}{e^2}$  for an average measles prevalence of 71%, with margin of error 5%, on a 95% confidence interval (CI).

All children who were hospitalised because of measles and its complications were included in the study. As virtually every measles infection becomes clinically apparent, resulting in some combination of cough, coryza, conjunctivitis, high fever and erythematous maculopapular rash therefore measles was diagnosed in children with these signs and symptoms<sup>15</sup>. Pneumonia was diagnosed by using integrated management of childhood illness (IMCI)<sup>16</sup> criteria of increased respiratory rate or infiltrates on chest X-ray.

Central nervous system was considered involved if there was lethargy, unconsciousness, fits, and neurological deficit. Other problems of measles like diarrhea, stomatitis, eye complications, febrile fits and otitis media were also notified in case sheets. Informed consent was obtained from parents or caregivers of all eligible patients prior to data collection and confidentiality of all patients was ensured by a coding system. Detailed history and physical examination was done and findings entered in a proforma that had been prepared after thorough research of literature. Immunisation status of the patients was checked by examining the National Expanded Program on Immunisation (EPI) card where available or parental enquiry if EPI card was not available. All the relevant investigations like complete blood count, serum electrolytes and X-ray chest were carried out besides history and clinical examination. Cerebrospinal fluid examination was done where needed. All patients were managed according to the standard protocol of the hospital.

Malnutrition was assessed as per WHO charts and standard deviation was determined for weight for height. The patients were divided into well nourished, moderately malnourished (Weight for Height >3SD) and severely malnourished (Weight for Height <3 SD) or edematous malnutrition.

Data regarding age, sex, immunisation status, nutritional status, complications and outcome was entered on MS Excel sheet and analysed by using SPSS version 22 for windows. The results were expressed as frequencies and percentages for qualitative data and mean and standard deviation for quantitative data. Categorical values were compared

by chi-square test. To adjust for the large number of outcome variables, results were considered statistically significant at p-value of <0.05.

## Results

A total of 382 patients were admitted during the study period with measles and its complications in which 265/382 (69.3%) were from Ziauddin Hospital (private sector) and 117/382 (30.6%) were from Abbasi Shaheed Hospital (public sector).

Majority of the patients admitted in Ziauddin Hospital (ZU) were from Karachi South while in Abbasi Shaheed (AS) they were from Karachi central and west. Male were 145 (54.7%) and 120 (45.3%) female from ZU and 69 (59.0%) male, 48 (41.0%) female patients were from AS (Table 1).

Table 1 shows the age distribution of the measles cases. From ZU most of the patients were in the age group 1-3 years 108/265 (40.8%), 63/265 (23.8%) were between 7-11 months, 37/265 (14%) were between 4-6 years, 25/265 (9.4%) were between 3-6 months, 18/265 (6.8%) were between 7-9 years, 14/265 (5.3%) were between 10-13 years. From AS 59/117 (50.4%) were between 1-3 years, 27/117 (23.1%) were between 7-11 months, 21/117 (17.9%) were between 4-6 years, 5 (4.3%) each were between 3-6 months and 7-9 years respectively.

Complete vaccination against measles was present in 152 (57.4%) patients from ZU and 38 (32.5%) from AS. In both hospitals more than half patients presented with appearance of rash between 1-4 day of illness, 211 (79.6%), 73 (62.4%) from Ziauddin Hospital and Abbasi Shaheed Hospital, respectively (Table 1).

Table 1, shows that there was a significant difference in terms of measles case complications; in the vaccination status of children in ZU vs. AS  $p < 0.0001$  and in the appearance of rash ( $p < 0.0001$ ). Further analysis of the data in children with appearance of rash (in days) and its relation with vaccinated and unvaccinated status of the children in ZU versus AS hospitals, did not show a significant difference ( $p < 0.863$ )

Table 2, shows the complications seen in children with measles. As expected predominantly pneumonia 161/382 (42.1%) and gastroenteritis 91/382 (23.8%) were in the forefront overall in both ZU and AS hospitals. While 88/382 (23%), had no complications. There was no significant difference in the age of presentation in pneumonia and gastroenteritis in children with measles in ZU and AS.

294/382 (76%) had complications. In terms of outcome, of 382 patients, 13 patients expired, of which 8 were from Ziauddin Hospital and 5 were from Abbasi Shaheed Hospital with an overall mortality of 3.4%. Most of the expired patients (80%) were unvaccinated, male and malnourished. Pneumonia was the leading cause of mortality. Majority of patients, 254 (95.8%) and 97 (82.9%) were discharged from Ziauddin Hospital and Abbasi Shaheed Hospital respectively within a week.

## Discussion

Measles epidemics continue to occur time and again in Pakistan resulting in significant morbidity and mortality. In 2013, mortality from measles was nearly 0.14 million-worldwide<sup>17</sup>. Since the year 2012 an increasing number of outbreaks of measles have started occurring in Pakistan. A number of factors contribute to the resurgence of measles in the developing part of the world. These include improper vaccine storage, low vaccination coverage, malnutrition, lack of proper health infrastructure and failure to administer a second dose of measles vaccine<sup>18</sup>.

The results of this study are significant as it is a multicentre study unlike most local studies on measles that have been carried out in single tertiary care hospitals. In the present study, majority of measles cases (43.7%) were between 1-3 years of age, followed by 7-11 month age group (23.6%), while 15.2% of measles cases were between 4-6 years of age and 7.9% were below 6 months of age. These findings are similar to a local study from Karachi, which reported 11% measles cases to be less than 9 months<sup>19</sup>. Another study from Pakistan revealed a maximum number of children with measles to be between 6 months to 3 years of age<sup>20</sup>. Also, in a study conducted in Iran in 2015,

Table 1. Demographic and clinical characteristics of measles cases

Characteristics		Ziauddin Hospital (Private)		Abbasi Shaheed Hospital (Public)		Total		p-value
		N	%	N	%	N	%	
Gender	Male	145	54.7	69	59.0	214	56.0	<0.0001*
	Female	120	45.3	48	41.0	168	44.0	
	Total	265	100.0	117	100.0	382	100.0	
Age	3 to 6 months	25	9.4	5	4.3	30	7.9	
	7 to 11 months	63	23.8	27	23.1	90	23.6	
	1 year to 3 years	108	40.8	59	50.4	167	43.7	
	4 years to 6 years	37	14.0	21	17.9	58	15.2	
	7 years to 9 years	18	6.8	5	4.3	23	6.0	
	10 years to 13 years	14	5.3	0	0.0	14	3.7	
	Total	265	100.0	117	100.0	382	100.0	
Vaccination	Complete vaccinated	152	57.4	38	32.5	190	49.7	
	Unvaccinated	59	22.3	40	34.2	99	25.9	
	Partial vaccinated	54	20.4	39	33.3	93	24.3	
	Total	265	100.0	117	100.0	382	100.0	
Rash	Between 1-4 days	211	79.6	73	62.4	284	74.3	<0.0001*
	Between 5-12 days	54	20.4	44	37.6	98	25.1	
	Total	265	100.0	117	100.0	382	100.0	

Table 2. Clinical complications of measles cases in relation to public and private hospitals

Characteristics	Ziauddin Hospital (Private)		Abbasi Shaheed Hospital (Public)		Total	
	N	%	N	%	N	%
Pneumonia	93	24.3	68	17.8	161	42.1
Gastroenteritis	70	18.3	21	5.5	91	23.8
Febrile fits	0	0.0	6	1.6	6	1.6
Croup	0	0.0	2	0.5	2	0.5
Otitis media	5	1.3	0	0.0	5	1.3
Conjunctivitis	0	0.0	3	0.8	3	0.8
Encephalitis	0	0.0	7	1.8	7	1.8
PCM	0	0.0	1	0.3	1	0.3
Pneumothorax	0	0.0	2	0.5	2	0.5
Bronchiolitis	4	1.0	1	0.3	5	1.3
Gastroenteritis + pneumonia	4	1.0	5	1.3	9	2.4
Gastroenteritis+otitis media	2	0.5	0	0.0	2	0.5
No complications	87	22.8	1	0.3	88	23.0
Total	265	100.0	117	100.0	382	100.0

46% of the cases were observed to be under 1 year of age<sup>21</sup>. A similar study on measles conducted in Nigeria<sup>22</sup> revealed that the infection rate for measles increased across the age groups up to the age of 5 years after which there was a decline in the number of infected children. In the present study too, measles infection was observed to be common in children less than 5 years of age as compared to older children. This is explained by the fact that children in this age group have a high probability of being exposed to the virus due to the endemic na-

ture of the virus in developing countries. In children older than 5 years, life long immunity is conferred in most children thereby making those younger than 5 years old, the target population for measles infection. Furthermore, the increasing occurrence of measles in children less than 9 months of age can be explained by the fact that maternal antibodies against measles provide protection to the infant only up to the first 3 months of life while the first dose of the vaccine is administered at 9 months, thus increasing the susceptibility of the infant to

acquire the disease<sup>23</sup>. A study from Netherlands indicated that the duration of immunity in infants due to maternal antibodies against measles was until only 3.5-5.5 months after birth, thus making them vulnerable to contract the disease before 9 months of age<sup>24</sup>.

In the present study 214 (56%) of the patients with measles were male and 168 (44%) were female. The male to female ratio was 1.3:1. Similar observations have also been made by a few other local studies<sup>20</sup>. Male preponderance of measles cases can be explained by the fact that medical advice is sought earlier for males as our society gives the male child preferential treatment. Also, female children have a stronger immune system than males who are more susceptible to infections.

WHO recommends vaccination with two doses of measles vaccine and vaccination coverage up to and above 95% with both doses<sup>25</sup>. Despite the availability of free of cost vaccination facility by the EPI program, a large number of children in our country remain unvaccinated or partially vaccinated. This fact is reflected by the results of the present study, as it was observed that only 49.5% of the measles cases were completely vaccinated against measles with two doses of vaccine. It was also noted that 51.5% of the children admitted with measles were either unvaccinated or partially vaccinated with a single dose, thus making them quite vulnerable to contract the disease. This finding is consistent with the observations made by a study from Peshawar where only 52% of the children with measles were completely vaccinated<sup>26</sup>. Similarly, according to another local study<sup>19</sup>, a large majority (65.5%) of the children were unvaccinated the reason was primarily attributed to a lack of awareness, inaccessibility of health services, false beliefs like religious prohibitions and superstitions regarding vaccines as a cause of infertility in children. These findings therefore, highlight the significance of conducting mass media campaigns to create awareness among the masses regarding the importance of vaccination. The occurrence of measles in completely immunised children indicates vaccine failure. This could be due to improper vaccine storage or inability to maintain the cold chain. This observation is supported by a study from Lasbela where vaccine failure rate was reported to be over 50%<sup>27</sup>. A study

from Karachi by Sheikh et al. reported immunisation coverage for measles to be 90% but measles antibodies to be present in only 55% of the vaccinated children<sup>28</sup>, thus indicating inadequate seroconversion due to immunisation failure.

It was also noted in the present study that 80% of the measles cases that were admitted in a private hospital were vaccinated with two doses of measles vaccine while only 20% of cases admitted in a public-sector health facility were completely vaccinated. This finding indicates that the private sector is contributing significantly to immunisation service delivery in developing countries. Another local study<sup>29</sup> has made similar observations with a very large proportion of unvaccinated (60%) children admitted with measles in a public-sector hospital. This suggests that the health infrastructure of public sector especially the EPI needs to be strengthened.

In this study it was also observed that in patients with measles admitted in the private hospital the duration of skin rash was shorter i.e. between 1-4 days as compared to the public-sector hospital. This could be explained by a better immunisation and nutritional status of children with measles admitted in the private sector hospitals as they cater to a higher socioeconomic group. Pneumonia was reported to be the commonest complication amongst children of all age groups in both the private and public-sector hospitals occurring in 42.1% of the total cases of measles followed by acute gastroenteritis seen in 23.8% of cases. In 1.8% patients encephalitis developed, which is a fatal complication. More or less similar findings have been reported by a few other studies as well<sup>26</sup>. However, in a study from Lahore<sup>29</sup>, encephalitis was seen in a much higher percentage (34%) of children with measles and the same study also reported a higher mortality (16%) as compared to the present study in which the combined mortality from measles in both the public and private sector hospitals was 3.4% with no significant difference in mortality rate between them. Furthermore, another study from Peshawar<sup>30</sup>. Pakistan also reports a much higher mortality of 11% especially in those measles cases with encephalitis. These observations signify the importance of increasing vaccina-

tion coverage on an emergency basis in order to prevent epidemics of the disease in future.

There are however, certain important limitations of this study and the results of this study need to be interpreted in the light of these limitations. The study being cross-sectional is not truly representative of the entire population. Since the occurrence of measles in vaccinated children could be due to vaccine failure the results of this study, however, cannot establish whether the vaccine failure was primary or secondary, as serological testing was not undertaken. Also, being good indicators of the disease, the diagnosis of measles was made on the basis of clinical signs and symptoms only and not serological testing. The diagnosis can therefore be affected by the physician's experience and be confused with other diseases causing fever and skin rash. Another limitation was that only a few patients had a vaccination card with them therefore, in majority of the patients verbal parental reporting of vaccination status was done. Hence, further multicenter studies with measles antibody status need to be done.

In order to eradicate this highly contagious disease it is recommended that the EPI program be strengthened and made accessible to the masses especially in the rural areas. Also, mass campaigns to increase awareness among the masses about the importance of immunisation be launched more frequently. Apart from routine vaccination campaigns, supplementary immunisation activities should be carried out from time to time and should target all children regardless of their previous measles vaccination or disease status. Catch-up immunisation campaigns targeting children aged 8 months to 12 years be launched. Since measles in less than 6 months old infants has been frequently reported by local studies, therefore, it is necessary to administer the first dose of measles vaccine earlier than 9 months of age. Therefore, lowering the age at administration of the first dose of measles vaccine may be recommended.

It is important to create public awareness about the importance of double dose of measles vaccine and to achieve two-dose vaccination coverage to more than 95%. Furthermore, reaching and maintaining measles elimination will require strong political commitment and strengthening of

surveillance, so that all suspected cases are reported. There is also a need for stricter enforcement of rules requiring assessment of immunisation status at school entry. There is a need to conduct further research studies to identify factors leading to vaccine failure and to develop better next-generation vaccines which are more immunogenic and heat stable than the current vaccine.

## **Conclusion**

Results of this study indicate that a significant number of children are being admitted with measles in both the public and private hospitals of our country. A large number of patients developed the disease despite being vaccinated with two doses. Also, a large proportion were either unvaccinated or partially vaccinated. Pneumonia (42.1%) and gastroenteritis (23.8%) are common complications with a high mortality.

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## **Conflict of Interest**

Authors have no conflict of interests and no grant/funding from any organisation.

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