

## Measles in Children Younger Than 9 Months in Pakistan

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Pakistan has one of the highest burden of measles and measles-related deaths in the world. We compared the clinical course and outcomes of measles in infants aged  $\leq 9$  months with those  $>9$  month old amongst children admitted to a tertiary care hospital. Data were collected by a retrospective chart review, and compared between age  $\leq 9$  months (Group A) and age  $>9$  months (Group B). Severe malnutrition ( $P=0.039$ , adjusted odds ratio=3.02), anemia ( $P=0.017$ ), leukocytosis ( $P<0.001$ , adjusted odds ratio 4.1), and conjunctivitis ( $P=0.021$ ) were higher in Group A children. All four deaths occurred in Group B.

**Key words:** Epidemic, Immunization, Measles, Pakistan.

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Measles is the most prevalent cause of vaccine-preventable childhood deaths, with greatest mortality seen in regions where access to primary health care is limited(1). Despite the availability of an effective vaccine and a single causative serotype, measles continues to cause approximately about one million deaths annually among infants and children throughout the world(1-2). According to the Expanded Program for Immunization (EPI) schedule for Pakistan; Measles immunization is recommended at 9 months of age, which may be why mortality is higher amongst infants younger than 9 months, who are too young to have the vaccine(1-3). In 2004, an estimated 454,000 deaths were caused by measles; most of these concentrated in developing countries like Pakistan(4), with younger children being more frequently affected(5). Mortality from measles is highest in children aged less than 12 months(6).

Pakistan Demography and Health Survey (2006-2007) reports a country-wide coverage of 50-60% for measles immunization(7). This reflects a possible gap in herd immunity. We compared the clinical features and outcome of measles in infants younger

than 9 months with those older than 9 months to highlight the importance of age (infancy vs. older) and vaccine status in determining clinical outcome in children.

### METHODS

We retrospectively reviewed the charts of children aged 0-15 years who were discharged with the diagnosis of measles during a period of six years (January 2001 till December 2006). We identified 225 children using coded discharge records for terms "measles", "measles with pneumonia", and "complicated measles"; of these, 205 were included in the final analysis. Chronically ill, immunocompromized, and patients with any malignancy were excluded. Information was extracted on age, gender, weight, co-morbidity, date of admission, vaccination status, history of exposure, laboratory parameters (hemoglobin, WBC count), length of stay, and complications. These parameters were compared between the two groups [(Group A, age  $\leq 9$  months) and (Group B, age  $>9$  months)]. Data analysis was conducted with SPSS 16 (version 16.0, SPSS Inc. Chicago, IL).  $P<0.05$  was considered significant. Variables found significant (cut off 0.25) at univariate analysis were entered into multivariate

logistic regression analysis for calculating adjusted odds ratios (AOR). The study was approved by the hospital ethics review committee of the Aga Khan University Hospital, Karachi, Pakistan.

## RESULTS

The highest number of cases occurred in 2006 (68, 33.2%) and 2003 (44, 21.5%). Majority of cases were seen during the winter and spring seasons. Males accounted for 59% of cases. Overall, 59% of total patients were not vaccinated for measles. History of prior exposure to measles cases was found in 8.2% cases and 29% of patients developed two or more complications simultaneously.

Group A ( $\leq 9$  mo) comprised of 48 children (23.4%); of these 9 (4.4%) cases were below 6

months of age. Both groups had similar presenting complaints *viz.*, fever, cough, rash, diarrhea and vomiting. A significantly greater proportion of hospitalized measles cases below 9 months of age were anemic (43.8%) and severely malnourished (20%), as compared to children in Group B. There was no significant difference in the length of hospitalization between the two groups. More than half of Group A developed pneumonia (53%), followed by gastroenteritis (33%), conjunctivitis (23%) and encephalitis (2%). Four patients of group B died during the hospitalization (**Table I**).

## DISCUSSION

Measles is endemic to Pakistan, with periodic epidemics occurring every 2-3 years. **Figure 1** shows the periodic epidemics and months of peak

**TABLE I** DEMOGRAPHY AND GROUP FEATURES

	Group A (age $\leq 9$ mo)	Group B (age $> 9$ mo)	P value	OR (CI)	AOR (CI)*
Number of patients	48 (23.4%)	157 (76.6%)			
Males	29 (60.4%)	92 (58.5%)	0.48	1.10 (0.6-2.05)	
Severe malnutrition	9 (20%)	53 (34%)	0.039	2.2 (0.9- 4.8)	3.0 (1.2- 7.5)
Weight (Mean, SD)	8.01 $\pm$ 2.5	16.3 $\pm$ 10.9			
History of exposure	6 (12%)	16 (10%)			
Presenting complaint					
Fever	51 (100%)	154 (100%)			
Cough	35 (67%)	104 (68%)			
Diarrhea	20 (39%)	49 (32%)			
Vomiting	17 (33%)	44 (29%)			
Rash	32 (63%)	102 (66%)			
Anemia (Hb $< 10$ g/dL)	21 (44%)	41 (26%)	0.017	0.4 (0.2- 0.9)	0.5 (0.2 - 1.2)
Leukocytosis (WBC $> 10^4$ )	23 (48%)	31 (20%)	$< 0.001$	4.0 (1.9 - 8.0)	4.1 (1.9 - 8.6)
Length of hospital stay					
mean ( $\pm$ SD)	3.3 $\pm$ 2.1	3.6 $\pm$ 4.2	–	–	–
$\geq 5$ days	27 (17%)	9 (19%)	0.478	1.1 (0.9-1.6)	
Complications					
Pneumonia	25 (53%)	65 (41%)	0.128	1.5 (0.8- 3.0)	1.6 (0.8- 3.4)
Gastroenteritis	16 (33%)	39 (25%)	0.164	1.5 (0.7- 0.9)	1.7 (0.7- 3.7)
Conjunctivitis	11 (23%)	63 (40%)	0.021	0.4 (0.2- 0.9)	0.4 (0.2- 0.1)
Encephalitis	1 (2%)	6 (4%)	0.483	0.5 (0.1- 4.)	
Died	--	4 (2.5%)			

\*AOR: Adjusted odds ratio. Variables that were found significant at univariate analysis level ( $P < 0.25$ ) were then taken into account for logistic regression analysis and calculating AOR.

**WHAT THIS STUDY ADDS?**

- Measles is rare in younger infants where routine immunization coverage is high, but periodic epidemics in younger infants are seen where routine coverage is not upto the mark.

hospital admissions. The disease is more common during the winter and spring seasons as corroborated by our study findings. Our data showed a high incidence of measles in infants <9months (33%) than that reported earlier (20-22% in infants aged 1 year) from Pakistan and SEARO region (3.9% - 11.5%)(5, 8-10). This may be due to lower levels of maternal antibody in our setting and poor baseline herd immunity.

The vaccination status for measles in group B was low and comparable with other Pakistani studies(5,8). Factors associated with increased incidence of measles in regional literature are lack of or incomplete vaccination, improper cold chain maintenance, and decreasing immunity with age (reflects need of booster doses)(8,11-12). Our study design and data allow us to corroborate the first and the third. Occurrence of measles in patients with

severe malnutrition is also well reported in other studies from Pakistan with prevalence between 9 – 53%(8-12).Three of our patients died because of pneumonia, bringing the pneumonia proportionate mortality rate to 75%, while it was 14-59% in previous studies(8,13).

Our study reflects data from a single center, and hence it may not be representative of the whole country. However, it does highlight a gap in herd immunity, made evident by the increasing number of measles patients in children <9 months. Due to the retrospective nature of our study, we could not assess all relevant variables and had to rely on the degree of completeness in documentation by the treating physicians. We have however tried to reduce confounders by logistic analysis.

We propose that poor routine coverage of

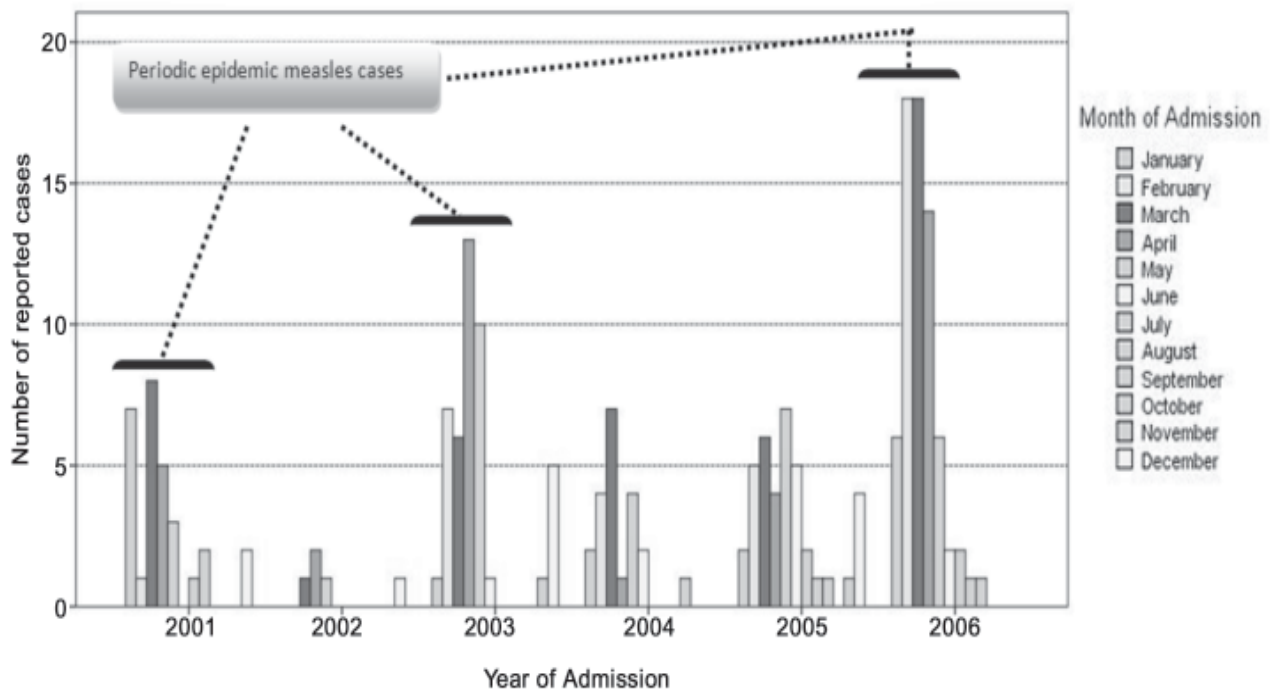


FIG.1 Periodic measles epidemics and months of admission.

measles vaccination in children >9 months and failure to catch unvaccinated children at a later stage during a health facility visit has caused a decrease in herd immunity in this region. This has led to periodic epidemics, and an associated rise in morbidity in children younger than 9 months and mortality in older children. An earlier age of vaccination should be considered in epidemic or higher endemic situations.

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