

Etiology of a Suspected Measles Outbreak: Preceding Measles Reduction Activities in Pakistan

Adam L. Cohen², Abdul Salam¹, Altaf Bosan¹, Robert Perry², Syma Iqbal¹, Shaista Noor Qureshi¹, Lisa Cairns², Ondrej Mach², Frank Mahoney² and Rehan Hafiz¹

ABSTRACT

Objective: To characterize patients with suspected measles, determine the magnitude of the outbreak in selected areas, and perform laboratory testing on patients with suspected measles to confirm the etiology of the outbreak.

Study Design: Cross-sectional survey.

Place and Duration of Study: Islamabad and Rawalpindi in June 2006.

Methodology: Survey and specimen collection from households was carried out in areas affected by rash and fever during the outbreak. Teams asked if household members had rash and fever and administered a detailed questionnaire of clinical signs and symptoms for measles for each person who reported a rash and fever episode. A sample of cases with fever, rash, and either cough, conjunctivitis, or coryza was laboratory tested for measles and rubella.

Results: Of 2,225 households visited, 284 individuals met the rash and fever case definition. Laboratory testing of eleven blood specimens revealed that the rash and fever outbreak was caused by rubella in 6 and measles in 2 with three equivocal results.

Conclusion: Laboratory confirmation of suspected measles cases is essential during measles elimination activities in Pakistan and other countries with endemic rubella.

Key words: Disease outbreaks. Measles. Pakistan. Rubella.

INTRODUCTION

Despite a 60% decrease in global measles mortality between 1999 and 2005, measles still accounted for an estimated 345,000 deaths worldwide in 2005.¹ Pakistan is one of 47 priority countries targeted by the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) for accelerated sustainable measles mortality reduction activities and makes up a large proportion of measles deaths in the Eastern Mediterranean Region and worldwide.²⁻⁵ WHO estimates that approximately 1 million children less than 5 years of age acquire measles virus infection each year in Pakistan, including 20,000 children who die from this infection (WHO, unpublished data). In response, Pakistan conducted a nationwide measles vaccination campaign in 2007 and 2008, targeting over 60 million children.

Measles vaccination is given in Pakistan as a single dose at 9 months of age through routine immunization

services. Although reported measles vaccine coverage at 9 months has been > 60% nationwide from 2001 to 2005;⁶ some provinces, such as Sindh, have reported coverage as low as 20%; others, such as Punjab, have coverage as high as 82% (WHO, unpublished data). Since the measles vaccine is estimated to be 85% effective when delivered at 9 months of age, approximately 70% of children in the Punjab province are estimated to be protected from measles.^{7,8} Fewer children are protected in other provinces which have lower coverage rates. In contrast to measles, the rubella vaccine is not routinely given through the public vaccination system in Pakistan, and the burden of rubella in Pakistan is not well-described.

The Ministry of Health (MoH) in Pakistan currently collects measles surveillance data from three sources; two of the sources are passive systems i.e. line list data collected through the Expanded Program on Immunization (EPI) and aggregate data through a Health Management Information System. In the third system, surveillance officers make weekly visits to high volume health facilities to look through registers for patients aged less than 15 years with Acute Flaccid Paralysis (AFP) and actively count cases of patients with clinical measles. None of the surveillance systems routinely collects data on laboratory confirmation of the disease. From January to May 2006, 10,640 suspected clinical measles cases were reported in Pakistan through the AFP active surveillance system. This is

¹ National Institute of Health, Islamabad.

² Centers for Disease Control and Prevention, Atlanta, Georgia, USA.

Correspondence: Dr. Adam L. Cohen, Respiratory Diseases Branch, Division of Bacterial Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road NE, MS C-23, Atlanta, GA 30333, USA.

E-mail: alcohen1@cdc.gov

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much higher than the 2,981 and 3,479 cases for the comparable periods in 2005 and 2007, respectively. In response to the increase in suspected measles cases and concerns about vaccine effectiveness, the Pakistan National Institute of Health (NIH), WHO, and the United States Centers for Disease Control and Prevention (CDC) conducted the outbreak investigation of patients with rash and fever in Islamabad and Rawalpindi in June 2006.

The objectives of the study were to characterize patients with suspected measles, determine the magnitude of the outbreak in selected areas, and perform laboratory testing on patients with suspect measles to confirm the etiology of the outbreak.

METHODOLOGY

From hospital-based line lists and surveillance reports routinely collected from AFP active surveillance sites, suspected measles-affected areas in the capital city of Islamabad and in the neighbouring city of Rawalpindi in the Punjab province were identified using grassroots-level maps prepared for polio supplemental immunization activities. The G/6-2 sub-sector of Islamabad and the Sadiqabad/Muslim Town area of Rawalpindi were selected from these suspected measles-affected areas because they had the highest number of cases, corresponded to AFP surveillance sectors, and represented areas with a range of socioeconomic classes. On June 28-29, 2006, twenty-five field teams consisting of one AFP surveillance worker and one local nursing or university student approached every household in the selected areas and listed all household residents. The teams asked if any household members had rash and fever within 6 months prior to the interview and administered a detailed questionnaire of clinical signs and symptoms for measles for each person who reported a rash and fever episode. Cases were defined by the WHO-recommended standard case definition for suspected measles: fever, rash, and at least one of the following-cough, conjunctivitis, or coryza.⁹ For all cases, we calculated univariate descriptive statistics and report the age, sex, city, date of rash onset, date of last vacci-

nation, and laboratory results. All analyses were performed in Microsoft Excel.

WHO recommends that 5-10 clinical specimens should be collected for serologic testing at the beginning of an outbreak to confirm measles virus as the cause.¹⁰ To obtain blood samples for laboratory testing, teams attempted to re-visit the homes of 10 case-patients in each surveyed area within 2 days of administration of the survey instrument. These case-patients were chosen from among those whose rash onset occurred 4-28 days before the survey and who had no history of recent immunization.⁹ Every effort was made to take blood samples from case-patients living in different households. Laboratory testing for measles and rubella immunoglobulin (IgM) antibodies was performed by the NIH in Islamabad, with confirmation of all specimens at the WHO EMR Office in Cairo, Egypt. Both laboratories used ELISA tests by Dade Behring Holding GmbH, Eschborn, Germany. All samples were tested for measles IgM antibody; those with negative or equivocal results for measles IgM antibody were tested for rubella IgM antibody.

RESULTS

In the 1,307 households visited in Islamabad, 195 individuals were identified who had illness that met the WHO case definition of suspected measles. In the 918 households visited in Rawalpindi, 89 individuals were identified that met the case definition. Of the 284 total cases with suspected measles, 176 (62%) reported previous measles vaccination. Blood samples were taken for laboratory testing from 16 patients with ages ranging from 2-13 years; 3 did not meet the case definition because they did not have fever, and two had been vaccinated with measles vaccine within 28 days of testing. Results from the remaining 11 patients showed infections with both measles and rubella. Of those 11 patients, 7 were male, and the date of rash onset ranged from one to twenty one days prior to the date of survey. Laboratory testing confirmed rubella in 6 patients and measles in 2; the results from 3 were equivocal (Table I).

Table I: Results of laboratory testing of blood specimens for measles and rubella of confirmed cases during rash and fever outbreak in Islamabad and Rawalpindi, 2006.

Case	City	Age in years	Gender	Date of rash onset	Date of last vaccination	Date of specimen collected	Measles IgM results	Rubella IgM results
1	Islamabad	3	Male	27/6/2006	Reported yes, date unknown	29/6/2006	Equivocal	Positive
2	Islamabad	6	Male	20/6/2006	Reported yes, date unknown	29/6/2006	Negative	Positive
3	Islamabad	13	Female	12/6/2006	None reported	29/6/2006	Equivocal	Positive
4	Islamabad	6	Male	18/6/2006	None reported	29/6/2006	Negative	Positive
5	Islamabad	8	Female	15/6/2006	None reported	29/6/2006	Positive	Not performed
6	Islamabad	9	Male	20/6/2006	Reported yes, date unknown	29/6/2006	Equivocal	Negative
7	Rawalpindi	6	Male	24/6/2006	None reported	30/6/2006	Negative	Positive
8	Rawalpindi	7	Female	19/6/2006	Reported yes, date unknown	30/6/2006	Negative	Positive
9	Rawalpindi	2	Male	21/6/2006	None reported	30/6/2006	Equivocal	Equivocal
10	Rawalpindi	8	Female	20/6/2006	Reported yes, date unknown	30/6/2006	Negative	Equivocal
11	Rawalpindi	6	Male	6/6/2006	None reported	30/6/2006	Positive	Not performed

* Case definition is rash, fever, and either cough, coryza, or conjunctivitis.

In the 6 months preceding the outbreak investigation (January-June 2006), 176 blood samples from patients with rash and fever from the six provinces and territories of Pakistan were submitted to the NIH in Pakistan for evaluation. These included samples from the outbreak investigation in Islamabad and Rawalpindi. Between 7-10% of tested cases from Islamabad and Punjab province which includes Rawalpindi, were positive for measles; this positive proportion is lower than the percentage that were positive in other provinces (Table II). At this time, not all samples that were negative for measles IgM antibody were tested for rubella IgM antibody, and the only patients positive for the rubella IgM antibody were those identified in Islamabad and Rawalpindi.

Table II: Laboratory testing results from 176 rash and fever cases from January to June 2006 evaluated at the National Institute of Health, Pakistan.

Province	Measles number tested	Number (%) positive	Rubella number tested	Number (%) positive
Azad Jammu Kashmir	60	37 (62)	5	0
Federally Administrated Tribal Areas	13	5 (38)	7	0
Islamabad	68	7 (10)	45	8 (18)
Northwest Frontier Province	18	9 (50)	0	0
Punjab	8	4 (50)	0	0
Sindh	23	18 (78)	5	0

No samples came from Balochistan. These results from Islamabad include the outbreak investigation in Islamabad and Rawalpindi, but also include other tested cases not reported in Table I.

DISCUSSION

A mixed outbreak of measles and rubella in Islamabad and Rawalpindi was described. This investigation highlights the potential pitfall of relying only on a clinical measles case definition in areas with endemic rubella. The WHO case definition for measles does not exclude clinical rubella cases. Previous studies of measles in Pakistan have often relied on the clinical measles case definition.¹¹⁻¹⁴ In Egypt, where measles and rubella remain endemic and measles immunization coverage is relatively high, laboratory-based surveillance has identified frequent mixed outbreaks and similar seasonality of both diseases with peak disease incidence from March to May.¹⁵ Similarly, in-depth investigations of rash and fever outbreaks in Bangladesh have identified mixed outbreaks of measles and rubella, suggesting that mixed outbreaks may be relatively common in the region (WHO, unpublished data). A recent study in Karachi of the WHO Integrated Management of Childhood Illness case definition for measles found that it predicted measles only 75% of the time, and that many suspected measles cases had Dengue fever.¹⁶

There are some limitations to this investigation that warrant mention; not all households were contacted, a small number of samples were tested, and these results cannot be generalized to other regions.

In light of these findings and given the importance of reducing measles mortality, there is a great need to establish laboratory-based surveillance for measles in Pakistan, with emphasis on laboratory confirmation of disease. Because of the high disease burden of both diseases, laboratory testing for suspected measles and rubella cases should be used to investigate and confirm disease outbreaks.^{5,17} Furthermore, as the incidence of measles declines, e.g., after a country has completed offering all children a second opportunity for measles vaccination through Supplementary Immunization Activities (SIAs); laboratory confirmation will be critical, since the positive predictive value of the clinical case definition for measles will fall as disease prevalence declines. There is often a desire to obtain specimens on all cases in an outbreak, despite the fact that this may not be necessary in every case.^{10,18,19} The Pakistan MOH is planning to implement case-based surveillance for measles with serologic testing of each suspected measles case after conducting a nationwide measles vaccination campaign in 2007 and 2008. Although this investigation was conducted in June 2006, the lessons learned from this investigation are relevant for Pakistan now and for other countries who have recently completed nationwide measles vaccination campaigns. AFP surveillance infrastructure provides a good base to develop case-based surveillance for measles cases.²⁰

CONCLUSION

Laboratory confirmation of suspected measles cases is essential during measles elimination activities in Pakistan and other countries with endemic rubella. Implementation of case-based surveillance will provide a good opportunity to define the epidemiology of measles and rubella in Pakistan.

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