

Selected Summaries

Epidemiological investigation and containment of a measles outbreak in New York: Critical appraisal and public health implications for India

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SUMMARY

Background

Measles is one of the most important preventable public health problems across the world. This is attested by the high burden of the disease and mortality despite the availability of efficacious vaccines delivered through well-developed vaccination programmes. As late as August 2018, WHO confirmed measles in 181 of 194 member states during the first 8 months of the year alone.¹ Unfortunately, the 11 countries comprising the WHO South-East Asia Region had the largest burden, with over 63 000 suspected cases and more than 42 000 confirmed cases. Among these, India alone had an estimated 38 500 confirmed cases,¹ reflecting the highest burden. It is interesting that although measles was declared eliminated from the USA in 2000, cases have been reported every year since then. This ranged from 37 in 2004 to 667 in 2014.² In the USA, the occurrence of three or more epidemiologically linked cases is termed an outbreak.

Analysis of some of the latest outbreaks in the USA reported that the 2008 outbreak was related to the rapid spread of infection in communities having unvaccinated individuals. The 2011 spike was related to the importation of cases from France, where there was a large outbreak. The year 2014 witnessed an unprecedented 23 outbreaks that were explained by spread among unvaccinated individuals as well as importation from the Philippines.² Similarly in 2013, there were 11 outbreaks including one in New York city. Of late, a group of investigators meticulously reported the public health consequences of this outbreak in the article being reviewed and critically appraised.

The article

The article gives a detailed epidemiological investigation of a measles outbreak, containment measures and the financial cost of these activities. An unimmunized adolescent returned to New York city on 13 March 2013; within 10 days, suspected measles cases began to be reported to the healthcare system—both by astute clinicians and laboratories notifying positive results. Detailed contact tracing was done. Based on presumed or confirmed immunity against measles, contacts were quarantined at home during their infectious period. All exposed contacts were offered measles, mumps and rubella vaccine if they were identified within 3 days of exposure or immunoglobulin within 6 days of exposure. Additionally, vaccination was anticipated to 6 months (from the usual age of 12 months) for infants residing in the affected communities.

The outbreak lasted about 12 weeks and affected 58 individuals—all belonging to a close-knit community residing in two areas of New

York. In addition, over 3300 exposed individuals were identified. Laboratory confirmation was available for 48 of 58 cases, whereas the other 10 cases were based on epidemiological linkage to laboratory-confirmed cases. None of the affected individuals were immunized, although 78% were eligible for vaccination. The remaining were infants who had not reached the age of routine measles vaccination. Over 70% of the affected cases belonged to eight extended families, and over 50% of cases probably acquired the infection from a family member. Less than 50% of cases were suspected as measles when they presented to the healthcare system and over a third of the cases did not present to the system at all.

Three-quarters of the exposed contacts had direct or indirect evidence of immunity against measles, while about one-fourth were deemed susceptible. A total of 191 individuals received timely administration of vaccine/immunoglobulin, thereby breaking the transmission chain.

Extensive physician and public education was conducted by facilitating heightened clinical suspicion, quarantine measures, rapid laboratory diagnosis and sensitization of the general public.

The total financial cost of investigating, managing and containing the outbreak over a period of 12 weeks was about US\$ 400 000. Of this, 84% was related to workforce costs on account of >10 000 work-hours spent by 87 personnel across diverse disciplines. The expenses in the non-workforce domain comprised only 16% of the total, with almost half of this being spent on advertising.

COMMENT

Critical appraisal

This article reports a meticulous epidemiological investigation starting from a single case of measles. Although the precise details of the source case are sketchy (in terms of age, symptoms, features bringing him to the attention of the public health system, basis for suspecting measles, etc.), all subsequent cases were investigated to identify the possible sources of exposure, infectious period and possibility of further spread. Robust criteria were used to define confirmed cases, suspected cases and contacts. Laboratory investigations to confirm measles included anti-measles IgM antibodies by ELISA and also real-time-polymerase chain reaction for detecting measles virus RNA. Further, measles virus genotyping was undertaken, which confirmed that 17 cases had the same type as was circulating in the UK (where the source case had travelled). These methodological refinements confirm the internal validity and raise confidence in the data.

Vaccination records of cases and contacts were also reviewed, besides the detection of anti-measles IgG antibodies to confirm protection. This is much superior to the presumption of immunity based on self-reported vaccination (which is the usual practice).

Cost calculations included expenses related to equipment, consumables, logistics, staff salaries, vaccine/immunoglobulin, courier/postage services and public health advertising. Staff salaries were related to work-hours spent in four domains, namely epidemiological investigation, outreach to the community, laboratory activities and administrative functions. Costs of items were calculated by adding the actual expenses, while staff costs were calculated by retrospectively counting the self-reported work-hours spent on managing the outbreak. On balance, the methods used for calculating costs in this study and the total cost reported appear to be similar to other such outbreaks in the USA.

For example, the total cost of managing a single case in Iowa state in 2004 was about US\$ 142 000,³ and containment of an outbreak with 34 cases in Indiana state in 2005 was about US\$ 168 000.² Similarly, California had an outbreak with 12 cases that cost about US\$ 125 000,⁴ and roughly US\$ 330 000 was spent on two outbreaks involving 13 cases in Utah state.² In contrast, the management of 16 outbreaks across the USA in 2011 had a cost estimate ranging from US\$ 2.7 to 5.3 million.⁵

Implications for public health in India

This epidemiological investigation has several lessons for public health in India (with reference to measles as well as other infectious diseases). In the New York outbreak, all the cases occurred in people who were unvaccinated. It is well known that high population immunity permits measles to be contained and hopefully eliminated. Thus, in developed countries, outbreaks are generally restricted to unvaccinated individuals and communities.

In India, the bulk of measles reported during the 12 months from July 2017 to June 2018⁶ occurred among children between 1 and 9 years of age, followed by older children (11–14 years) and infants <1 year. Few cases were reported among adults, although this would indicate lower health-seeking behaviour as well as poorer sensitization among physicians caring for adults (as compared to paediatricians). The majority of cases had no (or unclear) measles vaccination; however, cases occurred among those who had received one and even two doses of vaccine.⁶

This leads one to wonder about the population-level immunity in India. Older persons are presumed to be protected through natural infection acquired years/decades before, while infants, children and adolescents are expected to be protected through vaccination and/or development of subclinical or frank measles. Unfortunately, population immunity across various age groups has not been studied in detail. This lacuna is being addressed by a team of investigators based at the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, in collaboration with the University of Michigan, USA. A representative sample of individuals from birth to 60 years of age residing in Chandigarh underwent evaluation of vaccination status (by record and recall) and testing for anti-measles IgG antibodies. The preliminary analysis suggests pockets of susceptibility across all age groups even among those who were vaccinated or recalled having measles.

In contrast, the vaccination status of infants is readily available through the National Family Health Survey (NFHS) series. The 2015–16 NFHS-4 report suggests that 83.2% of infants between 1 and 2 years received measles vaccine.⁷ This represents a significant increase from 58.8% in the survey conducted 10 years ago.⁸ This heartening trend was observed for other vaccines also. It is encouraging that there were small differences between rural and urban children and boys and girls in the latest survey. However, there were stark differences based on maternal education status, religion, caste and economic status. The average figure also masks the wide variation between states such as Nagaland with 50% measles vaccination and Goa with over 96% coverage. In such a scenario, the average vaccination coverage for a whole country, or state or even a district, is meaningless unless the range is presented and the pockets with poorest immunization are identified. Only then can measles be contained. In other words, the public health focus (and consequent strategies) must shift from merely enhancing coverage, to identifying and managing the pockets of susceptibility.

One serious limitation of the NFHS estimates of measles

vaccination coverage is that it describes only vaccination status among 12- to 23-month-old infants without giving the actual age of vaccination. The New York outbreak (the article being reviewed) showed that infants who were eligible, but delayed vaccination, also suffered from measles. This highlights the necessity of estimating vaccination timeliness rather than coverage alone. A recent report highlighted the considerable gap between vaccination coverage and timely immunization with routine vaccines administered in India.⁹

Another issue, highlighted in the present study, is that over 20% of cases occurred among infants before the age of vaccination. In India, clinical experience and isolated reports suggest that measles occurs among infants younger than 9 months of age. This is not surprising considering that small hospital-based studies at Chandigarh as well as a large population-based study have all shown that infants lose protective maternal antibodies as early as 3–6 months of age.^{10–14} This raises the question whether anticipated vaccination could protect this vulnerable segment of the population. However, earlier vaccination in infants could be compromised by the unpredictable presence of maternally derived antibodies that will interfere with the infants' immune response, which in turn will necessitate additional closely spaced doses. The optimal age for anticipated measles vaccination in India is being currently addressed through a randomized controlled trial that compares seroprotection through vaccination at 6 months, 7.5 months and the conventional 9 months.¹⁵

What are the implications of the cost calculations in this study for a country such as India? Although the overall cost of containing the outbreak in New York cannot be directly compared to the expected cost in India, some aspects deserve attention. The cost of extensive laboratory investigations was only the equivalent of US\$ 0.65 million (₹6.5 lakhs), which indicates the existence of a well-designed laboratory set-up with ready availability of equipment, consumables and disposables. The cost for laboratory testing is likely to be much higher in India. On the other hand, the cost of each dose of vaccine was about US\$ 1400 (presumably this includes disposables required to administer the vaccine as well), which is much lower in India. One interesting point is that the total expense for using government vehicles over 12 weeks was merely US\$ 32. This is expected to be several fold higher in India.

Conclusion

This report highlights a multipronged approach involving assiduous epidemiological investigation, community mobilization, public health advertising, rapid administration of vaccine/immunoglobulin and overall tight administration to effectively contain the spread of measles among susceptible individuals in a developed healthcare system. The real-world financial cost is overshadowed by the huge scale of public health benefit.

Conflicts of interest. None declared

REFERENCES

- 1 World Health Organization. *Global measles and rubella*. Geneva:WHO; 2018. Available at www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/active/Global_MR_Update_August_2018.pdf?ua=1 (accessed on 5 Sep 2018).
- 2 Centers for Disease Control. Measles data and statistics. Available at www.cdc.gov/measles/downloads/measlesdataandstatsslideset.pdf (accessed on 5 Sep 2018).
- 3 Dayan GH, Ortega-Sánchez IR, LeBaron CW, Quinlisk MP, Iowa Measles Response Team. The cost of containing one case of measles: The economic impact on the public health infrastructure—Iowa, 2004. *Pediatrics* 2005;**116**:e1–4.
- 4 Sugerman DE, Barskey AE, Delea MG, Ortega-Sanchez IR, Bi D, Ralston KJ, *et al.* Measles outbreak in a highly vaccinated population, San Diego, 2008: Role of the intentionally undervaccinated. *Pediatrics* 2010;**125**:747–55.

- 5 Ortega-Sanchez IR, Vijayaraghavan M, Barskey AE, Wallace GS. The economic burden of sixteen measles outbreaks on United States public health departments in 2011. *Vaccine* 2014;**32**:1311–17.
- 6 World Health Organization. *Country slides (measles)*. Available at www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/Country_slides_measles.pdf?ua=1 (accessed on 3 Sep 2018).
- 7 International Institute for Population Sciences and ICF. *National Family Health Survey (NFHS-4), 2015–16: India*. Mumbai:International Institute for Population Sciences; 2017. Available at www.rchiips.org/NFHS/NFHS-4Reports/India.pdf (accessed on 1 Sep 2018).
- 8 International Institute for Population Sciences and Macro International. *National Family Health Survey (NFHS-3), 2005–06: India. Vol. 1*. Mumbai:International Institute for Population Sciences; 2007. Available at http://rchiips.org/NFHS/NFHS-3%20Data/VOL-1/India_volume_1_corrected_17oct08.pdf (accessed on 1 Sep 2018).
- 9 Shrivastwa N, Gillespie BW, Lepkowski JM, Boulton ML. Vaccination timeliness in children under India's universal immunization program. *Pediatr Infect Dis J* 2016; **35**:955–60.
- 10 Mathew JL, Ratho RK, Ahmed N, Dutta S. Evaluation of protection from measles in a cohort of infants through serial estimation of measles antibodies from birth to 9 months. *Int J Infect Dis* 2014;**21S**:115.
- 11 Mathew JL, Ahmed N, Ratho RK, Dutta S. Decline in transplacental measles antibodies and its potential public health impact: A prospective cohort study. Cape Town, South Africa: Oral Presentation at 8th World Congress of the World Society for Pediatric Infectious Diseases; 19–22 November 2013.
- 12 Mathew JL, Banerjee SN, Ahmed N, Ratho RK, Dutta S. Susceptibility of infants to measles prior to vaccination, and changing trends over time: Two cohort studies from Chandigarh, India. Madrid: Presentation at the 35th Annual Meeting of European Society of Pediatric Infectious Diseases (ESPID 2017); 23–27 May 2017.
- 13 Mathew JL, Wagner A, Suri V, Carlson BF, Ratho RK, Dutta S, *et al*. Community-based, prospective cohort study evaluating susceptibility to measles during the first year of life among infants in India. *Int J Infect Dis* 2018;**73**:394.
- 14 Boulton M, Mathew JL, Carlson BF, Suri V, Ratho RK, Dutta S, *et al*. Maternal measles antibodies and infant susceptibility in Chandigarh, India. *Int J Infect Dis* 2018;**73**:229.
- 15 ClinicalTrials.gov. Randomized controlled trial of measles vaccination schedule. Available at www.clinicaltrials.gov/ct2/show/NCT03170765 (accessed on 4 Sept 2018).

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