Effectiveness of previous mumps vaccination during the 2014–2015 outbreak in Lebanon

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Abstract

Background: In Lebanon, MMR was introduced at 12 months and 4-5 years in 1996. In 2014, the 2nd MMR dose was shifted to 18 months. Despite a national MMR coverage estimated at 79%, a six-fold increase in mumps national incidence was observed in December 2014.

Aims: The objective of this study is to determine mumps vaccine effectiveness (VE) among Lebanese population to guide immunization policies.

Methods: Clinical and confirmed mumps cases reported to the Epidemiological Surveillance Programme between week 46 of 2014 and week 11 of 2015 were included. Age matched controls were randomly selected from the same areas. Information was collected by structured telephone interview. Mumps vaccination status was based on documented valid dates for MMR vaccination. Vaccine effectiveness of 1 and 2 doses and odds ratios for acquiring mumps were estimated using conditional logistic regression.

Results: We selected 91 cases and 91 controls. Only 36% of cases had vaccination cards, compared with 71% of controls ($P < 0.001$); 94% of cases were not vaccinated compared with 51% of controls ($P < 0.001$). Vaccine effectiveness was estimated at 60% [95% confidence interval (CI) = –27–88) for 1 dose and 88% (95% CI = 60–96) for 2 doses.

Conclusions: Conclusions: This outbreak can be explained by suboptimal MMR2 coverage. Efforts should focus on achieving high MMR coverage and raising population's awareness about preserving vaccination documentation.

Keywords: mumps, vaccination, vaccine effectiveness, Lebanon

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Introduction

Mumps is a viral contagious infection transmitted from person to person by direct contact, droplets or contaminated fomites. The incubation period is about 15–24 (median 19) days (*1*). A person infected with mumps is generally contagious 1–2 days before the onset of clinical symptoms until 7–8 days afterwards. The disease is characterized by a painful swelling of the parotid gland, which occurs in 60–70% of infections. About a third of mumps infections arise without recognized symptoms. Clinically manifest infections might start with a short prodromal phase of low-grade fever, anorexia, malaise and headache. Aseptic meningitis (up to 10% of infections) and encephalitis (1%) are common complications of mumps together with orchitis in adult men; other complications include deafness and pancreatitis (*2*).

Mumps vaccines consist of live attenuated virus and are available as a monovalent vaccine, or most often in combination with measles and rubella vaccines (MMR). In the late 1960s, the original randomized clinical trials yielded efficacy estimates of more than 95% for the monovalent vaccine containing the Jeryl Lynn strain (*3*). Vaccine effectiveness is assessed, after a vaccine has been introduced into general use, commonly in the occasional outbreak situations. Thus, mumps vaccine effectiveness of prior vaccination with 1 dose of vaccine ranged from 64% to 80% and for 2 doses from 88% to 95% in outbreak studies (*4–8*). Of note over the last few years, large outbreaks have indeed affected highly vaccinated populations in England (*7*), Germany (*9*), Belgium (*10*), Netherlands (*11*), and the United States of America (*5,8,12–14*).

In Lebanon, vaccination against mumps was initiated in 1996 by administering a first dose of MMR vaccine at age 12 months and a second dose at age 4–5 years. In 2014, the timing of the second dose was shifted to age 18 months (*15*). In parallel, the monovalent vaccine is administered in the public health sector at age 9 months. Therefore, vaccination coverage for mumps is assessed by the second dose of the measles-containing vaccine (MCV2, which can be MMR1 or MMR2, depending on the provider). Before 2007, national mumps vaccination coverage, defined at that time as first dose of MMR (MMR1), was below 50% according to official national administrative estimates (*16*). This coverage increased to 71% in 2008, ranged between 86% and 89% between 2009 and 2012, and started decreasing in 2013 to reach 69% in 2014 (*16*). On the other hand, MMR1 coverage was estimated by WHO–UNICEF at 85% in 2008 (*17*). To date, no studies on the effectiveness of a mumps-containing vaccine have been conducted in Lebanon.

The identification of a suspected mumps case requires immediate notification to the Epidemiological Surveillance Programme at the Lebanese Ministry of Public Health (ESUMOH) and information on reported mumps cases is entered in the national database. Classification

relies on clinical and laboratory findings. A suspected case of mumps is defined by the acute onset of unilateral or bilateral tenderness and self-limited swelling of the parotid or other salivary gland, lasting 2 or more days without other apparent cause. A confirmed case is defined by positive results for at least 1 of the following tests: virus isolation, positive serological testing for mumps-specific IgM antibodies or at least a 4-fold rise in serum mumps IgG titre in the absence of mumps immunization in the preceding 6 weeks. Since laboratory confirmation for mumps is not routinely performed in Lebanon, most of the reported cases are suspected cases (*18*).

Over the past decade, national mumps incidence decreased from 5 per 100 000 in 2007 to less than 1 per 100 000 in 2010 and up to 2013. In 2014, Lebanon was hit by a national outbreak affecting both the Lebanese population and Syrian refugees with similar incidence. Among the Lebanese population, the mumps incidence was 12.74 per 100 000 in 2014, increasing to 23.3 per 100 000 in 2015. The highest region-specific incidence rates (greater than 57 per 100 000) were recorded in the provinces of Bekaa and North Lebanon. Similar incidence patterns were observed among Syrian refugees (*19*). This study focuses on the mumps outbreak among the Lebanese population only.

According to ESUMOH, among the Lebanese population, children 5–9 years old were the most affected (52 per 100 000), followed by the age groups 10–19 years (46 per 100 000) and 0–4 years (27 per 100 000). Approximately 83% of the cases reported in this outbreak were aged 1–19 years, and were eligible to receive ≥ 1 MMR dose. Around 36% of these cases were vaccinated (and 30% had an unknown vaccination status). However, this information is recorded by health care providers without verification of the vaccination card.

Therefore, given that the mumps outbreak occurred, it is important to understand the risk factors for mumps and to estimate the effectiveness of the mumps vaccine among Lebanese population in order to inform immunization policies and appropriate interventions.

Methods

Ethical considerations

A case–control study was conducted among reported Lebanese mumps cases and community controls matched by age and locality. As there is no institutional review board or ethics committee within the Lebanese Ministry of Public Health, the study protocol was reviewed by several scientific researchers of different affiliations external to ESUMOH in order to endorse the study methodology and conformity with ethical considerations.

Selection of cases and controls

A case was defined as a suspected or a laboratory-confirmed mumps case, registered in the ESUMOH central database, with date of onset between week 46 of 2014 and week 11 of 2015. Only Lebanese children with mumps aged between 1.5 and 19 years at time of onset, and contactable by phone, were included. Suitable controls were identified through an iterative selection process starting with systematic random sampling from the latest version of the national phone book (version 2005). Matching was conducted for locality of residence and age (±1 year for cases < 5 years old). If not applicable, the first sibling within a 4 year age range was selected for cases older than 10 years (by choosing the closer in age). Controls were eligible if they were Lebanese, never diagnosed with mumps, and not in contact with a mumps case during the 25 days preceding the telephone interview.

Data collection

A structured questionnaire was administered orally through phone call interviews with the subject's parents conducted by local ESUMOH staff. After obtaining oral consent, information was collected regarding their sociodemographic characteristics (highest education level of study participant and mother, number of persons living in the household, number of household rooms, etc.), vaccination status and illness history. For mumps vaccination status, respondents (who were mainly parents, given the young age range of study subjects) were asked to report whether the subject was vaccinated against mumps. Subsequently, they were asked to provide their vaccination card and the reported vaccination history was verified against it. To further assess the vaccination status of subjects reported as not having any vaccination card, parents were asked about the place of vaccination (if any, whether in the public or private sector) and the reason for not being vaccinated.

Sample size calculation

The sample size to estimate mumps vaccine effectiveness was calculated using *OpenEpi*. Assuming a 75% exposure prevalence among controls (based on WHO-estimated MMR1 coverage), 80% power and 95% confidence interval, 94 cases and 94 controls were needed to detection a minimal odds ratio of 0.4.

Data analysis

Epidata, version 3, was used for data entry and *Stata*, version 13, for data cleaning and analysis. "Crowding index" was generated as the number of persons living in the same household divided by the number of household rooms. Comparisons between cases and controls were conducted

using the independent samples *t*-test for means and McNemar's test for frequencies. The odds ratios and 95% confidence intervals were calculated using conditional logistic regression.

The variable "ever been vaccinated" was generated as follows: study subjects for whom a vaccination card was provided were classified as having a "documented vaccination status". Only those who had vaccination date specified on the card were considered "vaccinated against mumps". Study subjects were considered "not vaccinated against mumps" if they reported not being vaccinated at all, not having a vaccination card, or having a vaccination card lacking vaccination dates. This categorization aimed to rely only on documented vaccination status in an attempt to prevent any recall or reporting bias from the participants. Subsequently, mumps vaccine effectiveness (VE) was calculated for 1 and 2 doses using the following formula among those study subjects fulfilling the "vaccinated against mumps" criteria:

VE (%) = (1 – odds ratio) × 100

Results

We identified 133 eligible cases with date of onset between week 46 of 2014 and week 11 of 2015; of these, 41 were not reachable and 1 refused to participate in the study. In total, 91 cases and 91 controls aged 4–20 years were enrolled (Table 1). Around 4% of the cases reported orchitis. There were no significant differences between cases and controls with respect to age [11 years, standard deviation (SD) 4.11, $P = 0.42$] and sex (53% males, $P = 0.76$). On average, around 95% were students ($P = 0.305$), and for 47% their highest education level was primary school ($P = 0.345$). Cases (55%) were significantly more likely than controls (12%) to have mothers with a primary education level or below ($P < 0.001$) (Table 1). In addition, the household crowding index was significantly higher among cases (1.8, SD 0.7) than among controls (1.2, SD 0.6) ($P < 0.001$).

Just over half of the cases (53%) reported being vaccinated against mumps, compared with 97% among controls ($P < 0.001$) (Table 2). However, the documentation of the vaccination status was available for only 36% of cases ($n = 33$) and 71% of controls ($n = 63$) ($P < 0.001$). Of interest, the availability of the vaccination card was not dependent on age.

The classification of mumps vaccination status was limited to subjects with vaccination cards. "Zero mumps dose" was found for 16 cases and 12 controls, "1 dose" for 8 cases and 12 controls, "2 doses" for 4 cases and 32 controls, "more than 2 doses" for 5 cases and 7 controls ($P < 0.001$) (Table 2). The mean age at second mumps vaccination was significantly higher for cases (6.2, SD 3.7 years) than controls (4.2, SD 1.4 years) ($P = 0.03$).

Considering only subjects with documented vaccination dates, mumps vaccine effectiveness was calculated at 60% (95% CI: –27–88) for 1 mumps dose and 88% (95% CI: 63–95) for 2 doses (Table 3). The crude odds ratio for cases ever being vaccinated against mumps compared with controls was 0.11 (95% CI: 0.03–0.38) ($P < 0.001$), resulting in a crude overall vaccine effectiveness of 82% (95% CI: 57–93) (Table 3). Calculated by the number of doses, the crude vaccine effectiveness was 60% (95% CI: –27–88) for 1 dose and 88% (95% CI: 62–97).

Discussion

The 11-fold increase in the national mumps incidence in Lebanon in 2014 was preceded by low MCV2 coverage estimates over the previous years. The consequent accumulation of susceptible individuals may explain this 2014–2015 mumps outbreak, as evidenced by the significant difference in the proportion of cases (65%) and controls (26%) non-properly vaccinated, i.e. with less than 2 doses. The study was not designed to look at vaccine effectiveness by age group and in the absence of data on administrative vaccination coverage by age or birth cohort, it is difficult to argue further. It should also be considered that MCV2 coverage does not equate to MMR2 in Lebanon since monovalent mumps vaccine was also administered. Since only 76% of the controls in this study were vaccinated with 2 doses, herd immunity was less than optimum to block the spread of the outbreak in high-risk settings for exposure such as schools or overcrowded areas. Of note, Anderson and May (*20*) and models developed later (*21*) suggested an 88–92% herd immunity threshold to prevent mumps community transmission and outbreaks.

Indeed, living with a large number of housemates increased the risk of mumps infection; high population density provides increased opportunities for close contact and higher dose exposure to mumps virus. As mentioned before, most of the recent large mumps outbreaks in highly vaccinated population have occurred in communal living situations, such as dormitories or boarding schools (*12,22*).

Low level of education among mothers was also associated with an increased risk of mumps. It may be related to lack of awareness of the vaccine as our most effective technology to prevent infectious diseases or of where and how to get them for free. Similar findings have also been documented in studies on sociodemographic characteristics of MMR vaccination uptake in France (*23*) and Belgium (*24*).

Another factor contributing to the moderate effectiveness of the 2-dose mumps vaccine (88% in this study) could be related to the combination of vaccine strains used in Lebanon since the Jeryl Lynn strain seems to offer greater protection than the Urabe strain (80.7% versus 54.4%) (*25*). Unfortunately, the vaccine strain administered was almost never documented on the vaccination card and vaccine strains used in the public and private sector may differ. All in all, the Jeryl Lynn strain most widely used as the mumps component in MMR vaccine is derived from genotype A

and is less effective against the serogroup G wild strains (*26*) currently circulating in the Middle East (*27*).

Lastly, potential bias due to non-random distribution of outbreak sizes and resulting in the underestimation of vaccine effectiveness has been discussed as a common drawback in outbreak studies. Precisely, outbreak investigations will tend to underestimate vaccination efficacy to an extent which is related directly to the size of the epidemic, the vaccination coverage in the community, and the extent of clustering of vaccination failures in the population, and is inversely related to the size of, and contact intensity within, the investigated community (*28*). The main limitation of the study is that classification of mumps cases relies on clinical description rather than laboratory confirmation. Other viral infections (Epstein–Barr virus, parainfluenza virus 1 and 3, influenza a virus, coxsackievirus, adenovirus, parvovirus B19) can also cause parotitis (*29*) but not on an epidemic scale; such etiologies are rather considered when the incidence rate of mumps is low. Thus, if here was any misclassification of cases, it should have been very small. As for the assessment of the vaccination status, only study participants with a vaccination card available were considered as vaccinated. Since cases seem slightly more prone to not having their vaccination card, this may have led to an overestimation of the vaccine effectiveness.

A curious finding is the 1-year delayed second dose of mumps vaccination among cases; however, in view of the low number of cases involved, it cannot be interpreted. In Lebanon, the second dose of MMR was shifted from 5–6 years old to 18 months in 2014. An increased in the proportion of unvaccinated individuals and those vaccinated with only 1 dose a year after the change in the booster schedule has been described elsewhere (*30*). All in all, with most countries nowadays using a routine 2-dose schedule, but very large variation in age at the second dose (*2*), the ideal schedule for mumps vaccination in different settings is an unresolved issue, which deserves major attention.

Conclusion and recommendations

Our findings suggest that the 2014–2015 mumps outbreak in Lebanon can be explained by suboptimal uptake of the MMR vaccine. This outbreak is a wake-up call to the growing numbers of children and young people not adequately protected in Lebanon. Future outbreaks can be prevented by improving vaccination rates, by raising awareness about the importance of vaccination and, specifically in this case, enhancing routine MMR (1 and 2) vaccination among children. In addition, there is a substantial need to raise awareness about the importance of keeping the vaccination card even if one has completed all essential vaccinations. Establishing electronic immunization records is a possible opportunity for a better assessment of the vaccination status and gaps in the general population. Finally, strengthening laboratory capacities in the country is critical in order to confirm future outbreaks.

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Table 1. Demographic characteristics of mumps cases and controls aged 1.5–19 years, Lebanon, 2015

Characteristic	**Cases (*n* = 91)**		**Controls (*n* = 91)**		***P*-value**
Age (years) (SD)	11.4 (4.06)		10.9 (4.17)		0.419
Crowding index (SD)	1.8 (0.07)		1.2 (0.05)		< 0.001
	No.	**%**	**No.**	**%**	
Sex					
Male	54	59	52	57	0.764
Female	37	41	39	43	
Occupation status					
Non student	6	7	3	3	0.305
Student/employee	85	93	88	97	
Highest education level					
Kindergarten	11	12	8	9	0.345
Primary	46	51	40	45	
Intermediate	25	27	27	31	
Secondary	7	8	12	14	
University	2	2	1	1	
Mother's highest education level					
Primary or less	47	55	10	12	< 0.001
Intermediate and above	39	45	73	88	

SD = standard deviation.

Table 2. Distribution of mumps vaccination status among mumps cases and controls aged 1.5–19 years, Lebanon, 2015

Mumps vaccination	Cases (*n* = 91)		Controls (*n* = 91)		*P*-value
	No.	%	No.	%	
Reported as vaccinated					
Yes	48	53	88	97	< 0.001
No/unknown	43	38	3	3	
Vaccination card available					
Yes (documented)	33	36	63	71	< 0.001
No/unknown (not documented)	58	64	26	29	
No. of doses					
0	16	48.5	12	19	–
1	8	24.2	12	19	0.242
2	4	12.1	32	51	< 0.001
> 2	5	15.2	7	11	0.369
Mean (SD) age at 1st dose (years)	1.8 (1.4) (*n* = 11)		1.3 (0.9) (*n* = 41)		0.1782
Mean (SD) age at 2nd dose (years)	6.2 (3.7) (*n* = 5)		4.2 (1.38) (*n* = 31)		0.0307

Table 3. Mumps vaccine effectiveness in Lebanon, 2015

Vaccination status	Cases (*n* = 91)	Controls (*n* = 91)	Matched OR	VE (%)	95% CI
	Overall effectiveness				
	No. (%)	**No. (%)**			
Ever vaccinated	13 (14)	40 (44)	1		
Not vaccinated	78 (86)	51 (56)	0.18	82	57 to 93
	Effectiveness according to number of doses				
	No.	**No.**			
Not vaccinated[a]	76	46	–	–	–
1 dose	8	12	0.4	60	–27 to 88
2 doses	4	30	0.12	88	62 to 97

OR = odds ratio; VE = vaccine effectiveness; CI = confidence interval

[a]Defined here as: reported as not vaccinated, or without vaccination card, or having a vaccination card with no vaccination dates.