Epidemiologic features of mumps in Taiwan from 2006 to 2011: a new challenge for public health policy

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Background: The adoption of a second dose of the measles-mumps-rubella (MMR) vaccine among Taiwanese school children began in 2001. However, during that time, mumps cases continued to occur. The purpose of the present study was to assess the epidemiology and vaccination policy for mumps in Taiwan.

Methods: We examined the data on mumps cases collected by the Taiwan Centers for Disease Control (Taiwan CDC) between 2006 and 2011.

Results: During the 6-year study period, a total of 6612 cases of mumps were reported to the Taiwan CDC. Of the patients with known vaccination status, 62% received one dose of the MMR vaccine or no vaccine. The incidence of mumps ranged from 4.18 to 5.28 per 100 000 population and peaked in 2007. Males had a higher incidence of mumps than females (5.9 vs. 3.7 per 100 000 population; P=0.024). Children between 5 and 6 years of age had the highest incidence of mumps, and those 20 years and older had the lowest incidence. Compared to those who received two doses of the MMR vaccine, patients who were not vaccinated or received a single dose of the vaccine had a higher risk of suffering from complications and/or hospitalization.

Conclusions: In Taiwan, more than 60% of mumps cases received either no dose or one dose of the MMR vaccine. Monitoring mumps through biological testing and instituting a second dose of the MMR vaccine for

World J Pediatr, Vol 11 No 2 · May 15, 2015 · www.wjpch.com

children is needed for the elimination of mumps in Taiwan.

World J Pediatr 2015;11(2):141-147

Key words: epidemiology; incidence; measles-mumps-rubella vaccine; mumps

Introduction

umps is an enveloped, single-stranded RNA virus belonging to the paramyxoviridae family that causes an acute infectious disease primarily in children and young adults.^[1] Transmission of mumps occurs by droplet contact, and humans are the only known host of mumps. Mumps is highly infectious and spreads rapidly in susceptible individuals living in close proximity. The infectious period begins 7 days before the onset of parotitis and continues for 9 days afterwards.^[2,3] The illness spectrum ranges from subclinical infection to severe meningoencephalitis, and severity increases with age.^[4] In the pre-vaccination era, the highest attack rate was among primary school children, and most adolescents showed evidence of previous infection.^[4,5] Complications of mumps include orchitis, oophoritis, aseptic meningitis, encephalitis, deafness and pancreatitis; at least one of these complications occurs in up to 42% of mumps patients.^[5-7]

Taiwan has a population of approximately 2.3 million people with a population density of 635/ km². The majority (95%) of the population lives in the western part of Taiwan, which is divided into northern, central, and southern regions. Only 5% of the population lives in eastern Taiwan, where medical care is sub-standard and socioeconomic status is classified as low. In Taiwan, measles, mumps, and rubella (MMR) vaccination for 15-month-old children began in 1992.^[8] There was a decrease in mumps cases immediately after the start of the vaccination program; the mean incidence fell from 10.4 (in 1992) to 1.3 (in 2006) per 100 000 population.^[8] However, mumps cases continued to be diagnosed, and individuals suffering from mumps were still hospitalized each year. In 2001, a second dose of

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doi: 10.1007/s12519-014-0525-6

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MMR was introduced for children at primary school entry (approximately 6-7 years old).^[9] During the same year, a supplementary dose of MMR vaccine was given to 8-11 years old children.^[8,9] Since then, all children routinely receive two doses of the MMR vaccine (the first dose at 12-15 months and the second dose at primary school entry). The current vaccination uptake rate for the first and second doses of the MMR vaccine in Taiwan are >95%.^[8] MMR vaccines, including Jeryl Lynn-based strain (level B) mumps vaccines, are used in Taiwan. Despite the current vaccination program, mumps cases still occur in Taiwan. While the disease epidemiology is changing, the persistent occurrence of mumps cases requires careful monitoring. The disease burden caused by mumps needs to be addressed, and effective public health measures should be adopted in Taiwan.

Original article

Methods

Data sources

Since 1999, the National Notifiable Disease Surveillance System (NNDSS) has reported mumps cases to the Centers for Disease Control, Taiwan (Taiwan CDC).^[8] Until 2005, only the number of mumps cases was reported to the Taiwan CDC. Since 2006, mumps has been a reportable disease by law in Taiwan. Physicians are required to report all cases of mumps by entering the data into local databases and electronically forwarding the data to the Taiwan CDC within one week of case ascertainment using Taiwan CDCdeveloped software.^[8-10] According to a survey in Taiwan,^[11] more than 84% of physicians indicated they would report notifiable diseases to the CDC if they diagnosed the disease.

We collected all mumps related data reported to NNDSS at the Taiwan CDC from January 2006 to December 2011. The reported information included the patient's age, gender, area of residence, geographic location of disease occurrence, vaccination status, and onset date for the swelling of parotid or other salivary glands. If the patient had been vaccinated, the vaccination date and the number of doses received were also reported. Additional clinical details were reported, including signs/symptoms and disease outcome (either complication or death). Serum samples were also collected from the patients for serological confirmation of the diagnosis. Serological testing was performed by the Taiwan CDC mumps virus laboratory. Serum specimens were tested for mumps IgM and/or IgG antibodies using a commercially available capture IgM EIA kit and a commercially available indirect IgG EIA kit (Denka Seiken Co., Ltd., Niigata, Japan) according to the manufacturer's instructions.^[12]

This study was approved by the Institutional Review Board of National Cheng Kung University Hospital.

Case definition

A probable case of mumps was defined as a patient who was ill with an acute onset of unilateral or bilateral tenderness and self-limited swelling of the parotid or other salivary glands that lasted for at least two days, without other apparent causes.^[13] A confirmed case was defined as a patient who had a positive laboratory test (presence of IgM antibodies and/or a four-fold increase in IgG antibodies) or who met the clinical case definition and was epidemiologically linked to a confirmed or probable case.^[7,13]

Statistical analysis

The annual incidence of mumps was calculated by dividing the number of physician reported mumps cases by the population of individuals of the same age, as reported between 2006 and 2011 in the Taiwan census data, and was expressed as the number of mumps cases per 100 000 population. Age-specific incidence rates were estimated for the following age groups: <1 year, 1-2 years old, 3-4 years old, 5-6 years old, 7-8 years old, 9-10 years old, 11-13 years old, 14-19 years old, and >20 years old, which were comparable to the age groups used by the Taiwan CDC for Taiwan health surveillance.^[8] All statistical analyses were performed using SAS V.9.2 (SAS Institute Inc., Cary, North Carolina, USA). We used the Chi-square test with Yates' correction for categorical data and Student's t test for continuous variables. The accepted level of significance for all analyses was P < 0.05.

Results

Surveillance

Fig. 1 shows the number of mumps cases reported by month to the Taiwan CDC between January 2006 and December 2011. During the six-year study period, seasonal peaks occurred every year during the summer, the highest of which occurred in 2007. The 2007 wave encompassed all four regions of Taiwan. The annual reported number of cases varied yearly (range: 948-1203 cases per year).

Morbidity

Between 2006 and 2011, a total of 6612 mumps cases were reported to the Taiwan CDC. The mean patient age was 16 years, and median patient age was 5.8 years (range: 1 month to 80 years old). There were 41 (0.6%) patients in the <1 year age group, 429 (6.5%) in the 1-2

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Fig. 2. The number of mumps cases by age group and by MMR vaccination dose (A), and the annual incidence of mumps by gender (B) and region (C) in Taiwan, China, 2006-2011.

years group, 898 (13.6%) in the 3-4 years group, 1072 (16.2%) in the 5-6 years group, 952 (14.4%) in the 7-8 years group, 631 (9.5%) in the 9-10 years group, 537 (8.1%) in the 11-13 years group, 328 (5.0%) in the 14-19 years group, and 1724 (26.1%) in the 20 years and older group. The number of male patients was 4077 (61.7%), and the number of female patients was 2535 (38.3%); the male-to-female ratio was 1.6:1. The numbers of patients residing in the different regions of Taiwan were as follows: 3676 (55.6%) in the northern region, 1342 (20.3%) in the central region, 1325 (20.0%) in the southern region, and 269 (4.1%) in the eastern region. The vaccination status was known for 6406 of the 6612 (96.9%) patients; 1716 (26.0%) were unvaccinated, 2319 (35.1%) received one dose of the vaccine, and 2371 (35.9%) received two doses of the vaccine. The vaccination status for 206 (3.1%) patients was unknown. Among the mumps cases, there were 718 (10.9%) hospitalizations and 2 (0.03%) deaths (Table 1). One of the deceased was 2 years old, and the other was 4 years old. Their deaths were a result of complications from encephalitis. Each had received one dose of the MMR vaccine.

The number of mumps cases by age group and by vaccination status is shown in Fig. 2A. Overall, children

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 Table 1. Demographic characteristics of patients with mumps in

 Taiwan, China, 2006-2011

Variables	Number of cases, <i>n</i> =6612	%	
Age group	· ·		
<1 y	41	0.6	
1-2 y	429	6.5	
3-4 y	898	13.6	
5-6 y	1072	16.2	
7-8 y	952	14.4	
9-10 y	631	9.5	
11-13 y	537	8.1	
14-19 y	328	5.0	
≥20 y	1724	26.1	
Gender			
Male	4077	61.7	
Female	2535	38.3	
Region of residence			
Northern	3676	55.6	
Central	1342	20.3	
Southern	1325	20.0	
Eastern	269	4.1	
Mumps vaccination status			
No vaccination	1716	26.0	
One dose	2319	35.1	
Two dose	2371	35.9	
Unknown	206	3.1	
Imported cases			
Yes	711	10.8	
No	5901	89.2	
Hospitalization			
Yes	718	10.9	
No	5894	89.1	
Death			
Yes	2	0.03	
No	6610	99.97	

aged 5-6 years had the highest number of cases and annual incidence rate ($38.0/100\ 000$), followed by those aged 3-4 years ($34.9/100\ 000$), 7-8 years ($30.6/100\ 000$), 9-10 years ($18.5/100\ 000$), 1-2 years ($17.8/100\ 000$), 11-13 years ($9.7/100\ 000$), <1 year ($3.7/100\ 000$) and 14-19 years ($2.8/100\ 000$). Adults aged 20 years and older had the lowest incidence rate ($1.6/100\ 000$).

There was no significant change in the annual incidence of mumps cases in males and females during the six-year study period (the Chi-square test for linear trend=0.170; P=0.680). Males had a higher average annual incidence rate than females between 2006 and 2011 (5.9 vs. 3.7 per 100 000; P=0.024). The annual incidence rates per 100 000 population for males and females were 5.0 and 3.4, respectively, in 2006, 6.7 and 5.3 in 2007, 6.3 and 5.0 in 2008, 5.6 and 4.6 in 2009, 6.0 and 4.9 in 2010, and 5.9 and 5.0 in 2011 (Fig. 2B).

Fig. 2C shows the incidence rates for the four regions of Taiwan. The eastern region had the highest incidence rate (7.8/100 000) between 2006 and 2011. The lowest incidence rate (3.5/100 000) was observed in the southern region.

Risk of complications and/or hospitalization by mumps vaccination status

From January 2006 through December 2011, there were 6406 mumps patients with a recorded MMR vaccination. The association between MMR vaccination status and complications and/or hospitalization is shown in Table 2. Unvaccinated patients were statistically more likely to have had complications and/or be hospitalized than patients who received a two-dose vaccination [risk ratio (RR): 1.97; 95% CI: 1.65-2.37; P<0.0001]. Patients who received a single dose of the vaccine had a 1.65-fold higher risk of complications and/or hospitalization than those who received a two-dose vaccination (RR: 1.65; 95% CI: 1.38-1.97, P< 0.0001).

Discussion

Through the use of the public database, this study provides an estimate of mumps morbidity in Taiwan between 2006 and 2011. The results detailed overall mumps incidence rates as well as age-specific rates and the vaccination status of patients. The epidemiological evidence supports the conclusion that mumps is a major public health concern in Taiwan. Of the reported mumps cases from 2006 to 2011, approximately 63% (4035 cases) received either no vaccination or a single dose of the MMR vaccine.

This study found that the mumps case counts between 2006 and 2011 in Taiwan were far below those of the pre-vaccination era, during which at least twice the number of cases were reported monthly (the average number of mumps cases reported in 1992 was 200).^[8] The incidence of mumps was the highest among school children between 5 and 6 years of age and among those who received a single dose of the mumps vaccine. Compared to other studies,^[13-15] some of the epidemiological features of mumps in Taiwan identified in this study were unusual. Why did children aged 5-6 years of age have the highest incidence of mumps in this study? One possible explanation is that children aged 3 to 6 years entered day-care center, which increased their risk with regard to intensive exposure (crowed, communal settings) and importation of the mumps virus from abroad (imported mumps cases constituted 10.8% of the total cases in this study).^[16] By the end of 2011, an estimated 460 000 permanent immigrants resided in Taiwan: 67% were from the mainland of China, 19% were from Vietnam, 6% were from Indonesia, 2% were from Thailand, and 6% were from other countries.^[17] These four areas are considered mumps-endemic.^[18]

Over the past several years, mumps has made a global resurgence.^[4,13,14] Whereas mumps was historically a disease of childhood, these global outbreaks have predominantly involved young adults, nearly all of whom had a history of mumps vaccination during childhood. Previous studies^[15,19] showed that individuals who contracted mumps had received a second dose of the MMR vaccine more than 10 years before, whereas their roommates who did not contract mumps had received a second dose within the previous 10 years. Another study^[20] showed lower levels of mumps-neutralizing antibodies in individuals who had been vaccinated with a second MMR dose 15 or more years ago than in those who had been vaccinated 1 to 5 years ago. However, no data in our study indicated that waning immunity played a significant role in the persistence of mumps in the

Table 2. Comparison of mumps cases with or without complications and/or hospitalization with MMR vaccination status

MMR vaccination status	No. cases (%) with complications and/or hospitalization	No. cases (%) without complications and/or hospitalization	Risk ratio (95% CI)
2 dose	178 (8)	2193 (92)	Reference
1 dose	287 (12)	2032 (88)	1.65 (1.38-1.97)*
0 dose	253 (15)	1455 (85)	1.97 (1.65-2.37)*

MMR: measles-mumps-rubella vaccine; CI: confidence intervals. *: P<0.0001.

population of Taiwan.

It also has been postulated that antigenic differences between the vaccine and outbreak strains of the mumps virus may allow for vaccine escape.^[21] Mumps viruses isolated from recent outbreaks cluster into genotype groupings distinct from those of the strains used in the vaccine.^[21] With few exceptions, genotype G strains of the mumps virus have been isolated from cases in the West,^[22] genotype J and F strains have been isolated from cases in the Asia-Pacific region,^[23] and genotype H strains have been isolated from cases in the Middle East.^[24] The mumps vaccines used in countries of these regions are predominantly genotype A Jervl Lynnbased vaccines, and to a lesser extent, the genotype B Urabe-AM9 vaccine, as well as the yet to be assigned genotype Leningrad-Zagreb vaccine.^[21] However, some studies^[13,14,21] have concluded that vaccine escape is not a significant factor in an outbreak. Our study showed that the mumps unequally affected the age groups. Vaccine escape was unlikely a strong explanation for children aged 5-6 years having the highest incidence rate of mumps in Taiwan.

The MMR vaccine has been used in the United States since 1978 and has eliminated more than 99% of all three diseases.^[25] In this study, we found that the majority (71%) of mumps cases occurred among previously vaccinated patients. Similar results have also been reported for some recent outbreaks in Western countries; for instance, in 2006 in the United States, 77% to 97% of mumps cases occurred in patients previously vaccinated with two doses,^[13] as did 69% of cases in outbreaks in Canada in 2005.^[6] This finding is unexpected because of the increased vaccination rate, but it does not necessarily mean that vaccination policies have failed. However, this change does suggest that the clinical efficacy of the mumps vaccine measured during clinical trials may not be replicated in a community setting. The effectiveness of the Jeryl Lynn strain against mumps is estimated to be 78% (range: 49%-92%) for 1 dose of MMR vaccine and 88% (range: 66%-95%) for 2 doses of MMR vaccine.^[26,27] A person's susceptibility to mumps is also influenced by the effectiveness of the vaccine received. Moreover, immunity conferred through vaccination may last for a shorter period than expected.^[28] The issue of immunity acquired through vaccination should be further studied in Taiwan, as a recent article on the sero-epidemiology of mumps in Europe describes methods for improving the mumps vaccination schedule.^[29]

The government's vaccine coverage goal is for more than 90% of those in Taiwan to have at least one dose of MMR.^[10] However, the estimated threshold for herd immunity against mumps ranges from 88% to 92%.^[30] Numerous outbreaks have occurred in populations with

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high one-dose coverage,^[31] and the effectiveness of a single dose of mumps vaccine of approximately 80% is considered to be inadequate to provide population protection.^[30,32] The effectiveness of two doses of vaccine has been less extensively studied, but ranges from 88% to 95%.^[30] Nevertheless, even 95% coverage with 95% vaccine effectiveness brings the population immunity (90%) effectiveness near the putative herd immunity threshold. Areas of high population densities and high contact rates, which facilitate transmission, may require an increased level of group-specific immunity.^[31,32]

In addition, we consider that children who would have received one dose, but were too old for the second recommended dose, may play a role in perpetuating mumps cases in the community. To prevent the spread of the mumps virus in this population, public health authorities should adopt a policy to identify such individuals and give them a second dose of mumpscontaining vaccine. In our study, the incidence of mumps in this cohort was consistently lower than the incidence in other cohorts from year to year.

In our study, male patients had a higher annual incidence rate than did female patients. In a mumps outbreak in the United States,^[13] female patients were disproportionately affected, accounting for 64% of cases. In a mumps outbreak in Guam,^[32] the ratio of male cases to female cases was 1:1. We are unable to explain this epidemiological finding but postulate that contributing factors may include different behavioral patterns or differential reporting patterns.

In our study, a high percentage (56%) of mumps cases occurred in the northern region. In Taiwan, the population in northern region has a high socioeconomic status, and approximately 40% or more of the Taiwanese population live in this area.^[33] The high proportion of mumps cases reflects this region's population density. In contrast, this study found that the eastern rural areas had the highest incidence of mumps. The underlying cause of this high incidence rate remains unknown. Lower numbers of cases, as a result of low population density (104 per km²), could be an explanation.

Notably, only two deaths were attributable to mumps over the six years of surveillance in Taiwan. No published international data on mumps mortality are available. In contrast to previous studies,^[7] our study had a higher proportion of hospitalized patients (3-4% *vs.* 10.9%). The higher hospitalization rate in Taiwan may be due to the health insurance system, through which people have greater access to hospital services.

Is low vaccine effectiveness a problem specific to mumps, or does it also apply to measles and rubella? Between 1999 and 2008, a total of 84 measles cases were reported in Taiwan, and the annual incidence varied from 0 to 1.5 per 1 000 000 people.^[10] Rubella is not a notifiable disease in Taiwan; therefore, we do not have information on the number of annual rubella cases. However, the seropostivity rate for rubella was 97.5%, which was higher than that in the USA, Finland, and Italy, and was high enough to meet the population immunity target (95%) for the elimination of rubella.^[34,35] Based on this information, vaccine effectiveness is only an isolated problem with respect to mumps.

Our study has several limitations. First, the data were obtained via a surveillance-based method. The completeness of reporting is important in determining the disease impact. Second, most cases were diagnosed by physicians according to their clinical presentation. Misdiagnosis and the underestimation of cases were likely to occur. Nonetheless, this information is a reasonable surrogate for population-level data.

In conclusion, the continuous occurrence of cases of mumps in Taiwan seems to be due to a combination of several factors: an insufficient vaccination rate for the second dose; settings of intense exposure, even after two vaccine doses; and the existence of cohorts of young adults who are not sufficiently vaccinated in the context of significant virus circulation reduction. Because of these results, the reliability of the estimation of mumps cases based on clinical diagnosis should be discussed. As a monitoring strategy, the inclusion of biological testing in the case definition of mumps seems necessary to establish whether the mumps virus remains in circulation in Taiwan.

Acknowledgements

We thank the Centers for Disease Control, Taiwan of China, for providing the National Surveillance and Laboratory Data on mumps infections.

Funding: This study was supported by a grant (NSC 101-2314-B-006-055) from the National Science Council, Taiwan of China. **Ethical approval:** Ethical approval for this study was obtained from the Institutional Review Board of National Cheng Kung University Hospital.

Competing interest: None.

Contributors: Chen CC and Lu CC contributed equally to this paper. All of the authors contributed to the manuscript conception, design, drafting, revision, and appraisal.

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Received December 21, 2013 Accepted after revision March 21, 2014