

Factors Influencing the Size and Duration of School Varicella Outbreaks in Shanghai, China, in the Era of Voluntary Single-Dose Vaccination

Qiangsong Wu,^{1,a} Linwei Zhang,^{2,a} Jingyi Liu,¹ Yuanfang Chen,¹ Qi Zhou,¹ Zeliang Xuan,¹ and Yi Hu³

¹Xuhui District Center for Disease Control and Prevention, Shanghai, China, ²School of Public Health, University of South China, Hunan Province, China, and ³Department of Epidemiology, China and Key Laboratory of Public Health Safety (Fudan University), School of Public Health, Fudan University, Ministry of Education, Shanghai, China

Varicella outbreaks continue to occur in schools. We assessed potential factors associated with the size and duration of 560 school-based outbreaks in Shanghai, China. Outbreaks occurring in primary and middle schools involved more cases and had longer durations, and conducting postexposure prophylaxis campaigns was an effective strategy for outbreak control.

Keywords. varicella; outbreak; postexposure prophylaxis; varicella vaccine.

In China, the varicella vaccine (VarV) was introduced in 1998 as a voluntary single-dose regimen for children aged ≥ 12 months. Although single-dose VarV coverage reached up to 90% of schoolchildren aged 3–14 years, outbreaks remained frequent in Shanghai from 2008 to 2014 [1]. The proportion of vaccinated cases, also known as breakthrough varicella (BV) cases, rose from 21% in 2008 to 86.1% in 2014 [1]. Although the symptoms of BV are mild, infectious BV cases can contribute to spread of outbreaks [1, 2]. Since 2013, single-dose VarV has been provided free of charge by the Shanghai government to schoolchildren with no history of VarV or who previously received single-dose VarV for >5 years as a postexposure prophylaxis (PEP) strategy for school-based outbreak control [3]. A workflow for PEP campaign implementation is shown in the [Supplementary Data](#). A voluntary 2-dose VarV regimen has been recommended in Shanghai since November 2017 and was included in Shanghai's immunization program starting in August 2018. The routine 2-dose regimen includes a first dose at

age 12 months, followed by a second dose at age 4 years. Older children can still receive the voluntary 2-dose VarV regimen.

Research on factors affecting the size and duration of school-based outbreaks is scarce in China and other low–middle income countries that have implemented a single-dose VarV regimen on a voluntary basis. In this study, we assessed potential factors influencing the size and duration of 560 school-based outbreaks occurring in Shanghai, China, from 2006 to 2017. Our aim in conducting this study was to inform rational strategies for controlling school-based outbreaks in China and in other countries where a 2-dose VarV regimen is not included in the national immunization program.

METHODS

School-based varicella outbreaks were defined as ≥ 2 epidemiologically linked clinical cases of varicella reported in a school within 21 days [4]. Shanghai's school system consists of kindergartens (age 4–6), primary schools (age 7–11), and middle schools (age 12–18). Xuhui District is located at the heart of Shanghai and was home to 1.2 million residents, 211 school settings, and 107 098 schoolchildren in 2017 ([Supplementary Data](#)).

The Xuhui District Center for Disease Control and Prevention in Shanghai conducted field epidemiological investigations of varicella outbreaks. Outbreak information was collected during the investigations, including type of school, number of cases, PEP campaigns, and the VarV immunization status of cases.

A database was established using Microsoft Excel, and statistical analyses were performed using SPSS 18.0. Differences between groups were assessed using χ^2 tests or Student *t* tests. Multivariate logistic regression or multivariable Cox proportional hazard models were used to identify potential factors associated with outbreak size (2–4 vs ≥ 5 cases) and duration, respectively. Type of school (kindergarten, primary, or middle school), number of students (<800 vs ≥ 800 individuals), time period (2006–2011 vs 2012–2017), proportion of BV cases ($<60\%$ vs $\geq 60\%$), number of outbreaks in the school (<4 vs ≥ 4 episodes), VarV immunization status of the index case (vaccinated vs unvaccinated), and PEP campaigns conducted during the outbreak (yes vs no) were included as variables in these 2 analyses. A 95% confidence interval (CI) that excluded 1 was considered statistically significant.

RESULTS

A total of 560 varicella outbreaks involving 4077 cases were reported in Shanghai schools from 2006 to 2017, including 87 outbreaks in kindergartens (15.5%), 264 outbreaks in primary schools (47.2%), and 209 outbreaks in

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aCo-first authors, equal contribution

Correspondence: Yi Hu, MD, PhD, MPH, School of Public Health, Fudan University, No. 130 Dongan Road, Xuhui District, Shanghai 200032, China (yhu@fudan.edu.cn).

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Table 1. School-Based Outbreak Characteristics

Outbreak Characteristics	2006–2011 (n = 195)		2012–2017 (n = 365)		P Value
	No.	%	No.	%	
Type of school					<.01
Kindergarten	12	6.2	75	20.5	
Primary school	105	53.8	159	43.6	
Middle school	78	40.0	131	35.9	
No. of students					.91
<800	95	48.7	176	48.2	
≥800	100	51.3	189	51.8	
VarV status of the index case					<.01
Unvaccinated	144	73.8	125	34.2	
Vaccinated	51	26.2	240	65.8	
Proportion of BV cases					<.01
<60%	158	81.0	128	35.1	
≥60%	37	19.0	237	64.9	
No. of outbreaks in the school					.19
1–3	58	29.7	90	24.7	
≥4	137	70.3	275	75.3	
PEP campaign					<.01
Yes	0	0.0	133	36.4	
No	195	100.0	232	63.6	
Size, mean ± SD	8.6 ± 12.6		6.6 ± 7.4		.03
Duration, mean ± SD	67.7 ± 21.2		63.0 ± 17.9		.01

Abbreviations: BV, breakthrough varicella; PEP, postexposure prophylaxis; VarV, varicella vaccine.

middle schools (37.3%). The average outbreak size involved 4.5, 8.2, and 7.3 cases, and the average outbreak duration was 56.1, 65.1, and 67.6 days in kindergartens, primary schools, and middle schools, respectively. The odds of ≥5 cases occurring in outbreaks in primary and middle schools were 1.6 times (odds ratio [OR], 1.60; 95% CI, 1.09–2.35) and 1.7 times (OR, 1.70; 95% CI, 1.11–2.58) higher than in kindergartens (Table 2). In addition, primary schools (hazard ratio [HR], 0.66; 95% CI, 0.50–0.87), middle schools (HR, 0.60; 95% CI, 0.44–0.81), and schools with >800 students (HR, 0.80; 95% CI, 0.66–0.96) had significantly longer outbreak durations (Table 2).

The total number of outbreaks and the number of outbreaks involving ≥60% of BV cases increased from 195 and 37, respectively, in 2006–2011 to 365 and 237, respectively, in 2012–2017. The average outbreak size decreased from 8.6 to 6.6 cases, and the average outbreak duration decreased from 67.7 and 63.0 days from the 2006–2011 period to the 2012–2017 period (Table 1).

In outbreaks involving ≥60% of BV cases, the odds of ≥5 cases occurring were 1.7 times higher than in outbreaks involving <60% of BV cases (OR, 1.73; 95% CI, 1.16–2.59). PEP campaigns were conducted in one-third of the outbreaks (36.4%) occurring from 2012 to 2017. Conducting PEP campaigns during outbreaks was associated with smaller outbreak size (OR, 0.69; 95% CI, 0.50–0.96).

DISCUSSION

In this study, we found that school-based varicella outbreaks occurring in primary and middle schools in Shanghai involved more cases and had longer durations compared with outbreaks occurring in kindergartens. At least 3 reasons may have contributed to this finding. First, children in Shanghai's kindergartens had higher single-dose VarV coverage than students in primary and middle schools in 2011 (87% vs 77%) [5]. Second, as the single-dose VarV regimen in Shanghai involves immunization at 12 months of age, most vaccinated students in primary and middle schools had received the VarV ≥5 years ago, which is a risk factor for breakthrough infection [6, 7]. Third, compared with primary and middle schools, kindergartens are smaller and have fewer students, which make it less likely that children would be exposed to varicella cases. Therefore, the government should focus their efforts on primary and middle schools to reduce the number of varicella cases during outbreaks.

We found that the number of outbreaks occurring from 2012 to 2017 was nearly twice that occurring during the preceding 5-year period (2006–2011). This finding may relate to changes in China's 1-child policy since 2007, which have contributed to a significant increase in the number of schoolchildren and kindergartens in the Xuhui District (Supplementary Data). In addition, according to China's education development report (2017), nearly half of schoolchildren participated in extracurricular training, which may increase the risk of transmission

Table 2. Potential Factors Associated With the Size and Duration of 560 School-Based Outbreaks in Shanghai, China

Variables ^a	Size of Outbreak ^b		Duration of Outbreak ^c	
	OR	95% CI	HR	95% CI
Type of school				
Kindergarten	1.00		1.00	
Primary school	1.60	1.09–2.35	0.66	0.50–0.87
Middle school	1.70	1.11–2.58	0.60	0.44–0.81
No. of students				
<800	-		1.00	
≥800	-		0.80	0.66–0.96
Proportion of BV cases				
<60%	1.00		-	
≥60%	1.73	1.16–2.59	-	-
Time period				
2006–2011	1.00		1.00	
2012–2017	0.44	0.30–0.65	1.30	1.06–1.59
PEP campaign				
No	1.00		-	
Yes	0.69	0.50–0.96	-	-

Abbreviations: BV, breakthrough varicella; CI, confidence interval; HR, hazard ratio; OR, odd ratio; PEP, postexposure prophylaxis.

^aIn addition to the statistically significant factors in the table, the number of outbreaks in the school (<4 vs ≥4 episodes) and the VarV immunization status of the index case (vaccinated vs unvaccinated) were simultaneously included in these 2 analyses.

^bAnalyzed using multivariate logistic regression.

^cAnalyzed using multivariable Cox proportional hazard models.

between schools [8]. Although the number of outbreaks from 2012 to 2017 increased, the average outbreak size was smaller and the average duration was shorter. This finding may be explained by the implementation of PEP campaigns in schools, beginning in 2013, as an effective outbreak control measure. The vaccine effectiveness of PEP among unvaccinated students and students who had received single-dose VarV was 42% and 77%, respectively [3]. The incidence rate of varicella decreased from 159.4 per 100 000 individuals in 2006–2011 to 111.5 per 100 000 individuals after conducting a PEP campaign in 2012 in Guangzhou, China [9]. To control the size of school outbreaks and reduce varicella incidence, it was recommended to implement PEP campaigns after identifying outbreaks.

We found no evidence that outbreaks with BV index cases lasted longer than other outbreaks, which was inconsistent with the findings of Zhu et al. [1]. However, we found that the sizes of outbreaks involving ≥60% of BV cases tended to be larger. This presumably relates to the mild or atypical symptoms of some BV cases, which are difficult to detect and isolate quickly, leading to increased risk that susceptible students will be exposed to contagious BV cases. However, in 1 middle school outbreak, the incidence of BV cases was lower than that of unvaccinated cases before a PEP campaign was conducted (4.0% vs 11.9%) [10]. Therefore, improving single-dose VarV coverage among students, along with early detection and isolation of BV cases, can effectively reduce the size of school outbreaks. In addition, the routine 2-dose VarV regimen is also an effective strategy to reduce the incidence of BV cases and the size of outbreaks [4, 11].

Our analysis included 560 outbreaks that were broadly representative of schools in cities across China, and data were available over a long period. However, there were also several limitations to our study. One limitation is that we only included outbreaks that occurred in Shanghai, which may not be generalizable to other areas with different vaccination policies or to those with different epidemiologic and demographic characteristics. Factors such as school buses, accommodations, and group activities may also contribute to the spread of outbreaks. We were not able to include these in our analysis.

In conclusion, our results indicate that there is a greater risk of larger varicella outbreaks occurring in primary and middle schools in Shanghai. In addition, the proportion of BV cases in school-based outbreaks showed an increasing trend over time [1, 12], which is another risk factor for large-scale outbreaks. Although the routine 2-dose VarV regimen can reduce the incidence of BV cases [11], as well as the number, size, and duration of varicella outbreaks [4], this regimen has not yet been widely adopted in other settings across the globe [13]. Therefore, conducting PEP campaigns during outbreaks is a cost-saving strategy [14] to reduce varicella incidence and control the size of school outbreaks in countries where routine 2-dose VarV has not been implemented.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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