Epidemiology of Pediatric Herpes Zoster After Varicella Infection: A Population-Based Study

Su-Ying Wen, MD[a,b], Wen-Liang Liu, PhD[c,d]

abstract

BACKGROUND: There are limited population-based data regarding pediatric herpes zoster (HZ).

METHODS: Children aged <12 years with varicella infections between 2000 and 2006 were identified from a national population-based database and followed-up for a diagnosis of HZ until December 2008. Since a routine varicella vaccination program was started in 2004, vaccinated children without medically attended varicella were identified between 2004 and 2006, and followed-up for a diagnosis of HZ until December 2008.

RESULTS: Of 27 517 children with medically attended varicella, 428 developed HZ. The incidence of HZ was 262.1 per 100 000 person-years. Of 25 132 vaccinated children without medically attended varicella, 106 developed HZ. The incidence of HZ was 93.3 per 100 000 person-years. The mean duration from varicella to HZ was 4.12 years. Children diagnosed with varicella at aged <2 years had a higher incidence ($P < .001$) and shorter duration ($P = .04$) than those diagnosed aged ≧2 years. Children diagnosed with varicella aged ≥2 but <8 years had a significantly increased incidence of HZ after than before the vaccination program (relative risk = 1.85 at 3 years of follow-up, $P = .03$). Children with varicella infections had a significantly greater risk of HZ than vaccinated children without a history of varicella (relative risk = 2.31 at 4 years of follow-up, $P < .001$).

CONCLUSIONS: This study demonstrates the population-based epidemiologic characteristics of pediatric HZ among those who contracted varicella. In the early postvaricella vaccination period, an increased HZ incidence was observed among children with varicella infection aged ≥2 years.

FREE

[a]*Department of Dermatology, Taipei City Hospital, Renai Branch, Taipei, Taiwan;* [b]*Center for General Education, Mackay Junior College of Medicine, Nursing, and Management, Taipei, Taiwan;* [c]*Institute of Clinical Research and Training, Taipei City Hospital, Taipei, Taiwan and* [d]*Department of Nursing, National Taipei University of Nursing and Health Sciences, Taipei, Taiwan*

Dr Wen conceptualized and designed the study and drafted and revised the manuscript; Dr Liu carried out the initial analysis and reviewed the manuscript; and all authors approved the final manuscript as submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2013-4037

DOI: 10.1542/peds.2013-4037

Accepted for publication Dec 17, 2014

Address correspondence to Wen-Liang Liu, PhD, Institute of Clinical Research and Training, Taipei City Hospital, Taipei, Taiwan, No. 10, Sec. 4, Renai Rd, Da-An District, Taipei City 106, Taiwan. E-mail: suyinwen@ms15.hinet.net

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

WHAT'S KNOWN ON THIS SUBJECT: This is the first population-based study regarding the epidemiologic characteristics of pediatric zoster among only those who had contracted varicella.

WHAT THIS STUDY ADDS: The herpes zoster (HZ) incidence among only children with varicella infection is higher than previously reported. The HZ incidence increased for children contracting varicella aged <2 years. After a vaccination program, the HZ risk increased for those contracting varicella aged ≥2 years.

Herpes zoster (HZ) is caused by the reactivation of latent varicella-zoster virus (VZV), the virus that initially produces varicella. Although HZ is considered a disease of the elderly, it can affect individuals at any age, including children. The incidence of pediatric zoster has been reported to range from 42 to 238.5 per 100 000 person-years.[1–11] Previous studies have suggested that the incidence rate of HZ should include only individuals with VZV infection rather than an age-adjusted population including those without varicella infection. This is even more important when estimating pediatric HZ, because most adults but not children have previously had a VZV infection.[2,5] Very few studies have revealed the duration from contracting varicella to the occurrence of pediatric HZ, with a duration ranging from 5 to 8.8 years.[3,4,6,12] HZ in children and adolescents has been reported to be associated with immunosuppressive conditions such as malignancy,[6,12–14] especially leukemia,[12–14] and HIV infection.[15] It has also been reported in otherwise healthy children, and most frequently in those with varicella infection in the first year of life.[1,7,16–19]

Several studies have indicated that exposure to VZV provides a protective effect against reactivation of VZV by boosting specific immunity to the virus.[20,21] Varicella vaccination programs have led to a reduction in the number of cases of varicella, and the reduced exposure to VZV may influence the incidence rates of HZ. However, few population-based studies are available on the effects of varicella vaccination on the incidence of pediatric HZ.[7,9–11]

Studies regarding HZ among children are limited, and no previous population-based epidemiologic studies of pediatric HZ among only those infected with varicella have been published. In this nationwide population-based study with a retrospective cohort design, we investigated the incidence of pediatric HZ before and after the introduction of a vaccination program in children with medically attended varicella. The effects of hospitalization and systemic antiviral therapy for varicella on pediatric HZ were examined. Because HZ can be caused by the reactivation of the wild-type or vaccine strain of VZV, the incidence of HZ in children without a medical history of varicella who received the varicella vaccine was also assessed. The aim of this study was to establish population-based pediatric HZ data from only those who had varicella infection and assess the early effect of routine varicella vaccinations on the incidence of pediatric zoster.

METHODS

Data Source

The National Health Insurance Research Database (NHIRD) in Taiwan consists of detailed medical claims data from >25.68 million enrollees. In this population-based retrospective cohort study, data were obtained from a representative 1 million subjects randomly sampled from all enrollees of the National Health Insurance program, which was initiated in Taiwan in 1995. The National Health Insurance program covers ~99% of the population in Taiwan and has contracts with >95% of hospitals and clinics nationwide. All beneficiaries are eligible to receive medical services by paying only a small copayment or free of charge for people of low socioeconomic status. Hospitals and clinics in Taiwan are densely distributed, highly accessible, and very low cost. Thus, there is a very strong motivation for people in Taiwan to use these services. In the NHIRD, all diagnostic codes, in the form of *International Classification of Diseases, Ninth Revision, Clinical Modification* codes, are assigned by the board-certified clinicians who saw the patients. Varicella and HZ were mainly diagnosed by pediatricians, dermatologists, and family medicine physicians.

In 2004, a nationwide free varicella vaccination program was implemented in Taiwan, since when all 1-year-old children (born after 2003) are required to receive a varicella vaccination. There is no catch-up for this vaccination program. The coverage rate increased from 90% in 2004 to 97% in 2006.[22]

Study Population

Because HZ might be caused by wild type VZV, as well as the vaccine strain of VZV, this study included children with medically attended varicella and those without a medical history of varicella but who received the varicella vaccine.

Group A

Children diagnosed with varicella (*International Classification of Diseases, Ninth Revision, Clinical Modification* code: 052.XX) aged younger than 12 years between January 1, 2000, and December 31, 2006, were identified from inpatient, outpatient, and emergency department files. Subjects in this group were either unvaccinated or vaccinated.

Group B

Children aged 1 year between 2004 and 2006 (birth year: 2003–2005) who were vaccinated with the varicella vaccine but without any medical history of varicella infection were included in this group.

Follow-up Period

The children in group A were followed up from a diagnosis of varicella to a diagnosis of HZ or until December 31, 2008. The children in group B were followed up from 43 days after the vaccination to a diagnosis of HZ or until December 31, 2008.

Covariates

Demographic factors including age and gender were obtained for all of

TABLE 1 Demographic Characteristics of Children With Medically Attended Varicella (Group A) and Those Who Developed Pediatric HZ

Varicella, n = 27 517			HZ, n = 428	
Gender, n (%)			Gender, n (%)	
Boy	14 526 (52.8)		Boy	224 (52.3)
Girl	12 991 (47.2)		Girl	204 (47.7)
Age (mean ± SD)	5.24 ± 2.41		Age (mean ± SD)	8.40 ± 3.40
Age at diagnosis of varicella, n (%)		Duration from varicella to HZ	Age at diagnosis of HZ, n (%)	
<1	1060 (3.9)	3.75 ± 2.01	<2	12 (2.8)
1	1600 (5.8)	3.74 ± 1.90	2–7	188 (43.9)
2–7	21 244 (77.2)	4.31 ± 2.37	≥8	228 (53.3)
≥8	3613 (13.1)	3.40 ± 2.62		
Mean duration from varicella to HZ, y		4.12 ± 2.31		

the included children from the NHIRD. Children in group A who received systemic antiviral drugs for varicella infection were defined as users of antiviral therapy. In Taiwan, systemic antiviral drugs (acyclovir) are indicated for immunocompromised patients, neonatal varicella, varicella pneumonia, varicella meningitis, and hospitalized varicella patients with fever >38°C. The recommended dose for varicella is 20 mg/kg per dose orally 4 times daily for 5 days, or 10 mg/kg per dose intravenously 3 times daily for 7 days. Comorbid chronic medical conditions of the children who received antiviral therapy for varicella were reviewed.

Statistical Analysis

Descriptive statistics were used to summarize the characteristics of the study subjects. Continuous variables were reported as mean ± SD and categorical variables as percentages. The incidence rate of HZ in group A was calculated by dividing the number of incident HZ cases by the number of person-years of follow-up for the subjects in group A who had a medical history of varicella. The incidence rates of HZ in the children in group A were further compared by age at the diagnosis of varicella at 2, 5, and 8 years of follow-up. To access the influence of the implementation of the national varicella vaccination program (since 2004) on the incidence of HZ, the children in group A with complete follow-up before versus after 2004 were further analyzed. Only children having both primary infection and HZ either before or after 2004 were included. The maximum follow-up period for the prevaccination era (2000– 2003) was 3 years. The HZ incidences were compared by age group at the diagnosis of varicella (aged <1, 1 to <2, 2 to <8, and ≥8 years) at 2 and 3 years of follow-up. We also estimated the HZ incidence of group A according to the status of receiving antiviral therapy or being hospitalized for varicella. The incidence rate of HZ in the children who received antiviral therapy for varicella was further examined by dividing them into those with and those without comorbid chronic medical conditions. The incidence rate of HZ in group B was calculated by dividing the number of incident HZ cases by the number of person-years of follow-up for the vaccinated subjects in group B who did not have any medical history of varicella infection. To assess the risk of zoster after primary infection versus the vaccination, we compared the incidence of HZ between groups A and B at 2, 3, and 4 years of follow-up.

The duration from varicella to zoster for group A was defined as the period between the first date of diagnosis of varicella and the date of diagnosis of zoster.

In a Cox regression model, patients with varicella who did not develop HZ or were lost to follow-up in the study period were censored. All analyses were performed by using SAS software version 9.3 (SAS Institute, Inc, Cary, NC). The Mantel-Haenszel χ^2 procedure was used to estimate the relative risks (RRs) and 95% confidence intervals (CIs).

This study was approved by the Institutional Review Board of Taipei City Hospital (TCHIRB-1011005-E).

RESULTS

There were 27 517 children in group A, including 428 who developed HZ in the follow-up period. Of these 428 cases, 82.0% developed HZ at an age older than 5 years. The mean age at the diagnosis of varicella was 5.24 years, and 8.40 years for HZ. There were no significant differences between gender in the incidence of varicella or HZ. The mean duration from varicella to HZ was 4.12 years (Table 1). In group A, the peak duration between varicella and HZ differed by the age at the diagnosis of varicella. For those diagnosed with varicella aged <1 year, the peak duration of HZ occurred between 49 and 60 months, with 25.5% developing HZ during this time. The development of HZ peaked between 37 and 48 months for those aged ≥1 year but <2 years, and between 61 and 72 months for those aged ≥2 years. The mean duration for children diagnosed with varicella aged <1, ≥1 but <2, and ≥2 years were 3.75 ± 2.01, 3.74 ± 1.90, and 4.23 ± 2.40 years, respectively. The mean duration was significantly shorter for those diagnosed with varicella aged <2 compared with those diagnosed aged ≥2 but <7 years (P = .04).

There were 25 132 children in group B, including 106 who developed HZ during the follow-up period. Of these 106 HZ cases, 48 were boys and 58 girls, with no significant difference between gender in the incidence of HZ. The mean age of the HZ cases was

TABLE 2 Incidence Rate (1/100 000 Person Years) of HZ Among Children by Age at the Diagnosis of Varicella (Group A)

Age,[a] y	Year 2000–2008				At 2 y of Follow-up				At 5 y of Follow-up				At 8 y of Follow-up			
	Total Varicella	Total HZ	IR	95% CI	No. of Varicella	No. HZ	IR	95% CI	No. of Varicella	No. HZ	IR	95% CI	No. of Varicella	No. HZ	IR	95% CI
<1	1060	47	714.8	531.2–942.3	1060	14	518.4	295.1–849.2	774	36	855.5	608.2–1172	284	14	589.7	335.7–966.0
1	1600	51	494.3	371.9–644.8	1600	13	318.5	177.2–531.0	1277	43	614.2	450.1–819.7	428	12	332.3	180.1–565.0
2	2076	37	276.5	197.6–377.2	2076	9	168.5	82.2–309.2	1596	25	281.8	186.4–409.9	594	16	315.6	186.8–501.6
3	3189	52	259.4	195.8–337.6	3189	17	208.3	125.4–326.8	2288	29	229.1	156.3–324.7	880	23	308.7	200.4–455.9
4	5168	75	239.3	189.6–298.3	5168	22	167.7	107.7–249.7	3461	40	208.8	151.2–281.5	1270	28	258.6	175.2–368.8
5	5292	68	218.4	170.9–275.2	5292	23	170.9	110.0–252.4	3473	27	140.2	94.3–201.2	1105	20	212.2	133.3–322.0
6	3565	48	232.5	173.4–305.7	3565	12	131.0	71.0–222.8	2279	20	157.8	99.1–239.4	658	16	285.1	168.7–453.0
7	1954	23	215.4	139.9–318.1	1954	6	120.2	48.7–249.9	1107	11	179.1	94.2–311.2	269	5	216.8	79.4–480.6
8	1387	11	148.5	78.1–258.0	1387	3	84.3	21.5–229.5	728	7	173.3	75.8–342.8	189	4	248.0	78.8–480.6
9	978	5	96.51	35.36–213.9	978	4	160.7	51.1–387.6	517	2	69.5	11.7–229.8	138	0	0	N/A
10-	749	8	199.8	92.8–379.5	749	0	0	N/A	391	3	137.6	35.0–374.4	113	3	310.2	89.9–844.3
11	499	3	114.4	29.1–311.2	499	2	168.5	82.2–309.2	244	2	147.7	24.8–488.0	80	1	143.5	7.18–707.6
<2	2660	98	580.2	473.5–703.9	2660	27	398.2	261.8–571.3	2048	79	704.9	561.8–873.8	712	26	434.5	289.9–627.5
2–7	21 244	303	238.2	212.5–266.2	21 244	89	164.1	132.6–201.0	14 204	152	193.0	164.1–225.6	4776	108	265.4	218.8–319.2
≥8	3613	27	140.5	94.5–201.6	3613	9	97.4	47.5–178.7	1880	14	134.0	76.3–219.4	520	8	179.0	83.1–339.9

IR, incidence rate.

[a] Age at diagnosis of varicella.

2.51 years (range, 1.36–4.78 years), which was significantly younger than the children in group A ($P < .001$).

In group A, the incidence of pediatric HZ was 262.1 per 100 000 person-years for the whole observation period (2000–2008). The children diagnosed with varicella when they were younger than 1 year of age had a significantly greater risk for HZ ($P < .001$), with incidence rates of 518.4, 855.5, and 589.7 per 100 000 person-years at 2, 5, and 8 years of follow-up. The incidence rates of HZ for the children diagnosed with varicella aged ≥1 but <2 years were significantly higher at 2 and 5 years of follow-up than those aged ≥2 years ($P < .001$; Table 2).

In group A, 11 of 134 (8.21%) children who received systemic antiviral treatment of varicella developed HZ, compared with 417 (1.52%) of the 27 383 children who did not receive antiviral treatment. Among the 134 children who received antiviral therapy for varicella, 13 had immunocompromised diseases (7 lymphoma/leukemia, 5 other malignancies, and 1 polyarteritis nodosa). Among the children who received antiviral therapy for varicella, those with immunocompromised diseases had a higher risk of developing HZ than those without immunocompromised diseases.

The risk of developing HZ in the children diagnosed with varicella aged <1 year was insignificantly lower after than before the vaccination program. In contrast, the children diagnosed with varicella aged ≥2 had a higher incidence rate of HZ after 2004, and this difference was significantly higher for those aged ≥2 but <8 years (P = .02 and P = .03 at 2 and 3 years of follow-up, respectively; Table 3). The children in group A had a significantly higher risk of developing HZ than the children in group B at 2, 3, and 4 years of follow-up ($P < .001$). The incidence of HZ in the children in

TABLE 3 Incidence of Pediatric HZ in the Children With Medically Attended Varicella (Group A) Before and After the Implementation of a Varicella Vaccination Program (in 2004)

Age Group, y	Follow-up Period, y	Before 2004				After 2004				After Versus Before 2004		
		No. of Varicella	No. of HZ	IR	95% CI of IR	No. of Varicella	No. of HZ	IR	95% CI of IR	RR	95% CI of RR	*P*
<1	2	898	7	611.9	267.6–1210	289	2	271.4	45.5–896.6	0.44	0.06–1.99	.30
	3	284	6	597.6	242.2–1243	230	3	371.7	94.6–1012	0.62	0.13–2.50	.50
1	2	696	5	287.5	105.3–637.3	323	0	0	N/A	N/A	N/A	N/A
	3	428	6	395.8	160.4–803.2	256	1	108.7	5.4–536.1	0.27	0.01–1.86	.20
2–7	2	7372	22	116.5	79.4–173.5	7040	39	218.5	157.6–295.8	1.88	1.12–3.21	.02
	3	4776	19	111.2	68.9–170.4	5113	37	205.3	146.7–280.0	1.85	1.07–3.27	.03
≥8	2	811	1	48.0	24.0–236.7	1733	4	361.0	114.7–870.8	1.89	0.24–46.80	.78
	3	521	1	53.3	26.7–262.9	1176	6	132.9	53.9–276.4	2.71	0.40–62.74	.34

IR, incidence rate (in 100 000 person years).

group A was 2.31-fold higher than in group B at 4 years of follow-up (Table 4).

DISCUSSION

To the best of our knowledge, this is the first population-based study to report the epidemiologic characteristics of pediatric HZ among only those who contracted varicella. Weinmann et al[11] reported a population-based study of HZ in children, in which the incidence rate was calculated by the number of laboratory-confirmed HZ cases divided by the total person-years of observation in patients aged younger than 18 years, which differs from the current study cohort.

The reported incidence rates of pediatric HZ vary widely, and are drawn from different populations and based on different methodologies. Guess et al[1] reported an incidence rate of 42 per 100 000 person-years for those aged 0 to 19 years, compared with rates of 160 and 220 per 100 000 person-years among the same age group reported by Petursson et al[3] and Chidiac et al,[8] respectively. Insinga et al[5] reported an incidence of 110 per 100 000 person-years in children aged 0 to 14 years, and Weinmann et al[11] and Civen et al[9] reported rates of 230 per 100 000 and 238.5 per 100 000 person-years respectively, which are similar to the findings of the current study. The higher incidence in this study may be because pediatric HZ was measured in a cohort of children who were all infected with varicella rather than including individuals free of varicella infection in the denominator.

In the current study, the mean age at the diagnosis of zoster was 8.4 years, which is similar to the findings of Takayama et al[12] and Wootton et al,[6] but younger than that reported by Petursson et al[3] (11.8 years). The mean duration from varicella to HZ was 4.12 years in the current study, which is shorter than in previous studies (range, 5–8.8 years).[3,4,6,18] We also found that the mean duration (3.75 ± 1.94 years) among the children who contracted varicella aged <2 years was significantly shorter than those aged ≥2 years ($P = .04$). These findings are similar to those of Stein et al[10] but different from the reports by Petursson et al[3] and Takayama et al[12] in that there were no significant correlations between age at the diagnosis of varicella and the time interval to develop pediatric HZ.

This study adds robust additional data to existing literature that contracting varicella in the first year of life greatly increases the risk for pediatric HZ.[16–20] The children who contracted varicella aged <2 years had a significantly higher risk of developing childhood zoster than those contracting varicella aged ≥2 years ($P < .001$). This may be explained by a decreased level of immunity to VZV when varicella occurs at a much younger age.[17]

In this study, the children who received systemic antiviral therapy for varicella had a higher risk of developing HZ than those who did not receive antiviral therapy. Immunocompromised children are prone to contract pediatric HZ, and this may have led to the higher incidence of HZ in the cases receiving

TABLE 4 Incidence of Pediatric HZ in Children With Medical Attended Varicella (Group A) and Those Without a Medical History of Varicella but Who Received the Varicella Vaccine (Group B)

Follow-up Period, y	Group A				Group B				Group A Versus Group B		
	No. of Varicella	No. of HZ	IR	95% CI of IR	No. of Varicella	No. of HZ	IR	95% CI of IR	RR	95% CI of RR	*P*
2	27 517	91	165.7	134.2–202.5	25 132	51	96.1	72.3–125.3	1.73	(1.23–2.04)	.0016
3	24 907	126	169.1	141.4–200.6	17 844	51	95.4	71.8–124.5	1.77	(1.29–2.47)	<.001
4	21 689	158	183.7	155.9–213.0	8629	31	79.1	54.1–114.0	2.31	(1.59–3.44)	<.001

IR, incidence rate (in 100 000 person years).

systemic antiviral therapy for varicella. Regardless of immune status, systemic antiviral therapy for varicella in Taiwan is also indicated for hospitalized children with fever >38°C. The lack of clinical signs and symptoms further limits the interpretation of the influence of antiviral therapy for varicella on pediatric HZ.

In this study, the mean age at the diagnosis of HZ in varicella-vaccinated children without a medical history of varicella was 2.5 years, which is similar to a report of laboratory-confirmed HZ in vaccinated subjects with the vaccine strain of HZ (mean age, 2 years).[5] Lin and Hadler[23] proposed that young subjects may be a target group for the initial monitoring of the impact of decreased circulation of VZV on the occurrence of HZ. Modeling studies have hypothesized that a reduction in varicella cases will consequently lead to an initial increase in HZ, followed by an eventual decline.[24,25] During this early postvaccine period, we found an increased incidence of HZ in the children diagnosed with varicella aged ≥2 years, with a significant difference in those aged ≥2 but <8 years. Civen et al[9] observed a trend of an increasing incidence of zoster among children and adolescents who had had varicella, and suggested that widespread varicella vaccinations may increase the incidence of HZ.

A lower HZ incidence rate in children who have been vaccinated compared with those with natural infection has also been reported.[9,23,26] It has been proposed that the vaccine strain of the virus is attenuated, which may mean that it has less frequent access to sensory nerves to establish latency and is thus less able to reactivate compared with the wild-type virus.[27] Civen et al[9] reported that the risk of HZ among vaccinated children aged <10 years is 4 to 12 times lower than that among children of a similar age with a history of varicella. In addition, Weinmann et al[11] reported a 79% lower incidence of HZ in vaccinated children than in unvaccinated children. A RR for HZ in vaccinated children of 0.36 (0.27–0.48) compared with unvaccinated children has been reported in a partially vaccinated pediatric population.[10] The current study revealed a higher incidence of HZ in vaccinated children compared with other studies (ranging from 15 to 48 per 100 000 person-years),[9,11] but a lower rate more similar to a partially vaccinated pediatric population reported in central Israel (28% average coverage).[10] Such findings may be related to the early postvaricella vaccination period, as the trend of pediatric HZ declines with time after a varicella vaccination program has been introduced.[11] In the current study, the HZ in the vaccinated children without a medical history of varicella might be due to vaccine strain VZV or wild-type strain from indolent natural varicella infection before or after the vaccination.

This study has several limitations. Children with very mild symptoms may not seek medical attention. Thus, the results may underestimate the actual incidence of zoster. The validity of the estimates depends on the accuracy of physician diagnosis coding in the administrative claims database. Nevertheless, the appearance of varicella and HZ is sufficiently distinctive that a clinical diagnosis is generally regarded as reliable. The influence of varicella vaccination on HZ is limited by the short time period since the implementation of the vaccination program in Taiwan. Longer follow-up is needed to understand the impact of the varicella vaccination program on the epidemiology of pediatric HZ.

CONCLUSIONS

This study presents the population-based epidemiologic characteristics of pediatric HZ in a cohort of children who were all infected with varicella. The incidence rate in the current study is higher than in previous studies, and children younger than 2 years at the diagnosis of varicella had a significantly higher risk and shorter duration of developing HZ. In the early postvaricella vaccination period, the incidence of HZ among the children diagnosed with varicella aged ≥2 but <8 years significantly increased compared with before the implementation of the vaccination program. A higher incidence of HZ in vaccinated children without medically attended varicella was observed compared with previous reports of the incidence of HZ in vaccinated children in the late postvaccination period. The results of the current study may serve as baseline data for the early effects of varicella vaccinations on pediatric HZ. Long-term studies are required to monitor the impact of a varicella vaccination program on pediatric HZ.

REFERENCES

1. Guess HA, Broughton DD, Melton LJ III, Kurland LT. Epidemiology of herpes zoster in children and adolescents: a population-based study. *Pediatrics*. 1985;76(4):512–517
2. Donahue JG, Choo PW, Manson JE, Platt R. The incidence of herpes zoster. *Arch Intern Med*. 1995;155(15):1605–1609
3. Petursson G, Helgason S, Gudmundsson S, Sigurdsson JA. Herpes zoster in children and adolescents. *Pediatr Infect Dis J*. 1998;17(10):905–908
4. Kakourou T, Theodoridou M, Mostrou G, Syriopoulou V, Papadogeorgaki H, Constantopoulos A. Herpes zoster in children. *J Am Acad Dermatol*. 1998;39(2 pt 1):207–210
5. Insinga RP, Itzler RF, Pellissier JM, Saddier P, Nikas AA. The incidence of herpes zoster in a United States administrative database. *J Gen Intern Med*. 2005;20(8):748–753
6. Wootton SH, Law B, Tan B, Mozel M, Scheifele DW, Halperin S; IMPACT Investigators. The epidemiology of children hospitalized with herpes zoster in Canada: Immunization Monitoring Program, Active (IMPACT), 1991-2005. *Pediatr Infect Dis J*. 2008;27(2):112–118

7. Tseng HF, Smith N, Marcy SM, Sy LS, Jacobsen SJ. Incidence of herpes zoster among children vaccinated with varicella vaccine in a prepaid health care plan in the United States, 2002-2008. *Pediatr Infect Dis J*. 2009;28(12):1069–1072
8. Chidiac C, Bruxelle J, Daures JP, et al. Characteristics of patients with herpes zoster on presentation to practitioners in France. *Clin Infect Dis*. 2001;33(1):62–69
9. Civen R, Chaves SS, Jumaan A, et al. The incidence and clinical characteristics of herpes zoster among children and adolescents after implementation of varicella vaccination. *Pediatr Infect Dis J*. 2009;28(11):954–959
10. Stein M, Cohen R, Bromberg M, Tasher D, Shohat T, Somekh E. Herpes zoster in a partially vaccinated pediatric population in central Israel. *Pediatr Infect Dis J*. 2012;31(9):906–909
11. Weinmann S, Chun C, Schmid DS, et al. Incidence and clinical characteristics of herpes zoster among children in the varicella vaccine era, 2005-2009. *J Infect Dis*. 2013;208(11):1859–1868
12. Takayama N, Yamada H, Kaku H, Minamitani M. Herpes zoster in immunocompetent and immunocompromised Japanese children. *Pediatr Int*. 2000;42(3):275–279
13. Novelli VM, Brunell PA, Geiser CF, Narkewicz S, Frierson L. Herpes zoster in children with acute lymphocytic leukemia. *Am J Dis Child*. 1988;142(1):71–72
14. Sørensen GV, Rosthøj S, Würtz M, Danielsen TK, Schrøder H. The epidemiology of herpes zoster in 226 children with acute lymphoblastic leukemia. *Pediatr Blood Cancer*. 2011;57(6):993–997
15. Wood SM, Shah SS, Steenhoff AP, Rutstein RM. Primary varicella and herpes zoster among HIV-infected children from 1989 to 2006. *Pediatrics*. 2008;121(1). Available at: www.pediatrics.org/cgi/content/full/121/1/e150
16. Huang JL, Sun PC, Hung IJ. Herpes zoster in infancy after intrauterine exposure to varicella zoster virus: report of two cases. *J Formos Med Assoc*. 1994;93(1):75–77
17. Baba K, Yabuuchi H, Takahashi M, Ogra PL. Increased incidence of herpes zoster in normal children infected with varicella zoster virus during infancy: community-based follow-up study. *J Pediatr*. 1986;108(3):372–377
18. Terada K, Kawano S, Yoshihiro K, Miyashima H, Morita T. Characteristics of herpes zoster in otherwise normal children. *Pediatr Infect Dis J*. 1993;12(11):960–961
19. Feder HM Jr, Hoss DM. Herpes zoster in otherwise healthy children. *Pediatr Infect Dis J*. 2004;23(5):451–457, quiz 458–460
20. Brisson M, Gay NJ, Edmunds WJ, Andrews NJ. Exposure to varicella boosts immunity to herpes-zoster: implications for mass vaccination against chickenpox. *Vaccine*. 2002;20(19–20):2500–2507
21. Thomas SL, Hall AJ. What does epidemiology tell us about risk factors for herpes zoster? *Lancet Infect Dis*. 2004;4(1):26–33
22. Centers for Disease Control and Prevention. Statistics of Communicable Diseases and Surveillance Report. Available at: www.cdc.gov.tw/infectionreport.aspx?treeid=075874dc882a5bfd&nowtreeid=995e575b9810625b. Updated December 23, 2013. Accessed April 15, 2014
23. Lin F, Hadler JL. Epidemiology of primary varicella and herpes zoster hospitalizations: the pre-varicella vaccine era. *J Infect Dis*. 2000;181(6):1897–1905
24. Brisson M, Edmunds WJ, Gay NJ, Miller E. Varicella vaccine and shingles. *JAMA*. 2002;287(17):2211–2212, author reply 2211–2212
25. Edmunds WJ, Brisson M. The effect of vaccination on the epidemiology of varicella zoster virus. *J Infect*. 2002;44(4):211–219
26. Tanuseputro P, Zagorski B, Chan KJ, Kwong JC. Population-based incidence of herpes zoster after introduction of a publicly funded varicella vaccination program. *Vaccine*. 2011;29(47):8580–8584
27. Chen JJ, Zhu Z, Gershon AA, Gershon MD. Mannose 6-phosphate receptor dependence of varicella zoster virus infection in vitro and in the epidermis during varicella and zoster. *Cell*. 2004;119(7):915–926

Epidemiology of Pediatric Herpes Zoster After Varicella Infection: A Population-Based Study

Su-Ying Wen and Wen-Liang Liu

Pediatrics 2015;135;e565
DOI: 10.1542/peds.2013-4037 originally published online February 23, 2015;

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Epidemiology of Pediatric Herpes Zoster After Varicella Infection: A Population-Based Study

Su-Ying Wen and Wen-Liang Liu

Pediatrics 2015;135;e565
DOI: 10.1542/peds.2013-4037 originally published online February 23, 2015;