**Background:** This study was performed during an era of partial vaccination with varicella vaccine in Israel to characterize ambulatory pediatric herpes zoster (HZ) cases in a population with partial varicella vaccination coverage.

**Methods:** Data were collected from computerized databases of a population of 114,000 children. Records of children aged 0–18 years, diagnosed with HZ during 2006 to 2008 were reviewed by pediatric infectious diseases experts. Telephone interviews were done with a sample of the parents to get further clinical details.

**Results:** Of 692 medical records reviewed, 450 cases were approved for analysis, and 77 interviews were conducted. Incidence of HZ was 130 of 100,000 person-life-years. Peak incidence was detected in children aged 9–11 years (222/100,000 person-life-years). Pain and fever accompanied 52% and 13% of episodes, respectively. Higher risk for HZ was found in children who had varicella during their first year of life (relative risk and 95% confidence interval: 13.5 [9.6–18.8]; $P < 0.001$), and in children who had varicella during the second year of life (relative risk $= 2 [1.5–2.6]; P < 0.001$). Vaccination was found to be protective against HZ (relative risk $= 0.42 [0.33–0.55]; P < 0.001$).

**Conclusions:** The epidemiology of HZ seems to be changing in a population with partial varicella vaccination rate. Our results may suggest that children who contracted chicken pox in their first year of life may benefit from varicella vaccination.

**Key Words:** children, herpes zoster, vaccination, varicella

**Patients and Methods**

This retrospective study was done with collaboration of Maccabi Health Services, which is the second largest health maintenance organization in Israel that uses a computerized database for recording all medical information of its patients. We retrieved the details of children who were 0–18 years of age, residing in Hasharon County in Central Israel, who were insured by Maccabi Health Services and were diagnosed with HZ by using International Classification of Diseases codes (053 group) from January 2006 until December 2008.

The records were evaluated by 2 pediatric infectious disease experts to confirm the diagnoses. We excluded cases where there was no satisfactory description of the rash, when the diagnosis was not conclusive or the clinical description was not compatible with HZ.

From the computerized files, we retrieved clinical information about HZ episodes and epidemiologic information regarding
Incidence

Maccabi Health Services provides medical care to about 114,000 children residing in Hasharon County. Based on these data, we calculated a mean incidence of 130 of 100,000 person-years. Peak incidence was noted in children 9–11 years of age—222 of 100,000 person-years (Fig., Supplemental Digital Content 1, http://links.lww.com/INF/B247).

Varicella Vaccination

Varicella vaccine had been recommended by the Israeli Society of Pediatrics since 2000 but was not funded by the Israeli Ministry of Health until 2008 when routine varicella vaccination was begun.

Fifty-five children with HZ were vaccinated against varicella, whereas 31,920 children residing in the county were vaccinated for varicella as compared with 395 cases of zoster among 82,080 children who presumably had natural varicella. Therefore, the protective effect of varicella vaccine for the emergence of HZ during childhood was found to be 0.36, (95% confidence interval: 0.27–0.48; *P* < 0.001).

Location

Detailed clinical information regarding the location of the rash was available in 442 files. The detailed distribution of the rash is shown in Table 1. We found that vaccinated children were more likely to have the rash on the head, neck, and lower extremities and less likely to have the rash in the lower trunk compared with non-vaccinated children.

Telephone Interviews

Telephone interviews were performed with 77 families chosen randomly. Forty parents (54.8%) noted that the zoster episode was accompanied by pain. The pain preceded the rash in 35%, and continued after the resolution of the rash in 7.5% of the 40 cases of HZ accompanied by pain. There were no cases of postherpetic neuralgia. Only 13 parents reported use of analgesics (paracetamol, ibuprofen or dipyrone) for pain relief. Ten parents (15.6%) had reported accompanying fever.

The median durations of the rash, pain and fever were 8, 7.6 and 4.3 days, respectively. Only 5.6% of responders noted exposure to patients with chicken pox before zoster appearance. The exposure was either at school or in households.

Acyclovir Treatment

One hundred ninety-eight (44%) children received systemic treatment with acyclovir, 130 (28.8%) were treated only topically and 52 children (13.6%) received both systemic and topical treatment.

Underlying Illnesses

Three patients had some degree of immunodeficiency. One child received methotrexate for juvenile rheumatoid arthritis, one had chronic renal failure and one patient had insulin-dependent diabetes mellitus.

**TABLE 1.** Location of Herpes Zoster Rash in Vaccinated and Unvaccinated Children

| Location of the Rash† | Total Group % (n = 442) | Vaccinated Children % (n = 52) | Nonvaccinated Children % (n = 390) | *P*
|----------------------|-------------------------|-------------------------------|-------------------------------|------
| Head and neck        | 9.3 (n = 41)            | 19.2 (n = 10)                 | 7.94 (n = 31)                 | 0.017
| Upper extremity      | 9.9 (n = 44)            | 15.4 (n = 8)                  | 9.2 (n = 36)                  | NS
| Upper trunk          | 46.3 (n = 205)          | 36.5 (n = 19)                 | 47.6 (n = 186)                | NS
| Lower trunk          | 21.7 (n = 96)           | 7.7 (n = 4)                   | 23.8 (n = 92)                 | 0.01
| Lower extremity      | 12.6 (n = 56)           | 21.1 (n = 11)                 | 11.5 (n = 45)                 | 0.009

†Some children had rash in more than one location, for example, involvement of both the neck, and the upper extremity.

‡For the difference between vaccinated and unvaccinated children.

NS indicates not significant.
Age of Contracting Varicella

Records regarding primary infection with varicella were available for 147 of the 450 children with HZ. The age of contracting varicella in this group was compared with that of the other children in the county to determine the RR for HZ according to the age of contracting varicella (Figs., Supplemental Digital Content 2 and 3, http://links.lww.com/INF/B248 and http://links.lww.com/INF/B249).

A significantly increased risk for HZ was found in children who contracted varicella during the first year (RR: 13.5 [9.6–18.8]; P < 0.001) and also in the second year of life (RR: 2 [1.5–2.6]; P < 0.001). In addition, there was a significant correlation between the age of contracting chicken pox and the time interval to zoster breakout (RR = 0.16; P < 0.05). Specifically, the time period between varicella infection to HZ was shorter in children who had chicken pox before 2 years of age compared with children who had chicken pox at an older age (5.07 ± 3.36 versus 6.08 ± 3.5 years, respectively; P = 0.039).

Varicella in Vaccinated Children

Nine of the 55 children with zoster who were vaccinated for varicella had a history of varicella (Table, Supplemental Digital Content 4, http://links.lww.com/INF/B250). Five of them contracted varicella after vaccination (breakthrough varicella), whereas 4 children had varicella during the first year of life, before vaccination. None of these patients had the zoster rash over the upper extremities, and only 1 child had the zoster rash over the lower extremities.

**DISCUSSION**

HZ, a well-characterized entity in adults, has not been extensively investigated in healthy pediatric populations, and a large amount of the data about its incidence and associated risk factors are derived from studies performed several decades ago. In addition, there are only a few reports with regard to pediatric HZ in the era of varicella vaccination.14–16

Our study was conducted in a population that was partially vaccinated for chicken pox, because this vaccine was recommended by the Israeli Society of Pediatrics but was not funded by the Israeli Ministry of Health. The average coverage in the pediatric population of Hasharon County with varicella vaccine during the study period (2006–2008) was 28%.

As reported previously, HZ in the immune-competent child is a mild and self-limited illness that generally does not result in postherpetic neuralgia. The incidence found in the present study was higher than reported historically: 130 versus 42 cases per 100,000 person-years. This rate may either reflect a real increase in childhood HZ rate, or may reflect a recording bias, as our study was based on analysis of computerized data where there was better access to medical records. The higher rate found in our study is probably not related to the introduction of varicella vaccine, because a similarly high rate was already found in a study done before varicella vaccination era in Iceland. A recent study from California also demonstrated rates that were close to our finding.

However, as opposed to previous series showing a steady rise in the rate of childhood zoster with increasing age, our data demonstrated a significant peak in the incidence of HZ in children 9–16 years of age, with the highest incidence in children 9–11 years of age. This finding, which was consistent throughout each of the 3 study years, could be due to the effect of partial varicella vaccination; children 9–16 years of age were more likely to be infected with wild-type virus, but subsequently had limited re-exposure to chicken pox because of the introduction of varicella vaccination. On the other hand, older children had presumably more re-exposure since varicella vaccine was introduced in Israel in the year 2000. Evidence supporting this assumption can be found in the recent population-based active surveillance of Civen et al among residents of Atelope Valley, CA. This survey demonstrated an age-specific effect of the implementation of varicella vaccination on the incidence of HZ in children. Although the incidence of HZ among children < 10 years of age declined by 55%, the incidence among children 10–19 years of age increased by 63%. Civen et al’s and our results are in accord with theoretical models that predicted the epidemiologic effect of varicella vaccination on the incidence of HZ.

This situation is apparently only temporary, because universal vaccination (that has already been used in Israel since 2008) is eventually supposed to result in a lower incidence of HZ. The RR for HZ in vaccinated children was 0.36 (0.27–0.48) compared with unvaccinated children. In addition, only 1 of the 9 patients who were vaccinated and also contracted varicella before or after vaccination had the zoster rash over the extremities, suggesting that zoster in at least part of these cases might have been caused by wild-type varicella virus rather than by vaccine virus. Our study, comparing the rates of HZ in vaccinated and unvaccinated children in a population with partial varicella vaccination rate, has suggested that there is a protective effect of varicella vaccination on the incidence of HZ. This effect has been demonstrated previously in clinical studies and also in surveillance studies.

These results are reassuring with regard to the long-term effect of routine varicella vaccination on the incidence of HZ.

The age for contracting varicella has been found in earlier studies to be a major factor for the early appearance of HZ, but this finding has not been demonstrated subsequently. We found that children who were younger than 1 year of age while contracting varicella had higher incidence of HZ (RR: 13.5 [9.6–18.8]). Moreover, our study is the first to suggest that even children who had chicken pox during their second year of life had a substantial rise in HZ incidence (RR: 2 [1.5–2.6]). In contrast to previous reports, there was a significant correlation between the age of contracting varicella and the time period from primary varicella infection to the appearance of HZ, and the time period between varicella infection and HZ was shorter in children who had chicken pox before 2 years of age. Current guidelines do not recommend administering varicella vaccine to children who are infected before 1 year of age. Our finding may suggest that the cellular immune response to varicella in this group of children is less robust and they may benefit from varicella vaccination.

**Limitations**

The main limitations of our study are the retrospective nature of data collection and the absence of virologic diagnosis. However, HZ has a distinct clinical presentation and data were meticulously reviewed by infectious diseases experts minimize misdiagnosis of HZ. In addition, there are no reference data regarding the incidence of pediatric HZ in Israel before the introduction of varicella vaccine.

We were able to retrieve the age of contracting varicella in only 147 patients. This could be either due to the fact that some children had varicella without reporting it to their pediatricians. Another explanation is that many children, especially older children, had their varicella infection before their pediatricians were enrolled in the computerized recording system; therefore, the office visit for varicella infection was not recorded in the computerized system.

**REFERENCES**


