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Incidence of herpes zoster amongst adults varies by severity of immunosuppression

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Summary *Objectives:* We examined the incidence of herpes zoster in immunocompromised adults (≥18 years) with different severities of immunosuppression and assessed the prevalence of complications and of various kinds of healthcare resource utilisation.
Methods: German claims data from more than ten million adults were used to calculate annual incidence rates of herpes zoster for the years 2006—2012 and to analyse the prevalence of complications, physician visits, hospitalisations, and antiviral and analgesic treatments using a cohort design. The analyses were stratified by age, sex, and severity of immunosuppression, defined by immunocompromising conditions and drug therapies.
Results: The incidence rate per 1000 person-years of herpes zoster was almost twice as high in immunocompromised patients (11.5 (95% confidence interval (CI): 11.4—11.6)) compared to immunocompetent subjects (5.9 (95% CI: 5.8—5.9)). The incidence rate was higher in highly immunocompromised patients (13.4 (95% CI: 13.2—13.6)) than in patients with a low severity of immunosuppression (10.0 (95% CI: 9.8—10.1)). These differences were observed for both sexes and in all age groups. Complications, outpatient physician visits, hospitalisations, and analgesic treatments occurred more frequently in immunocompromised patients as well.
Conclusions: Our results show that immunocompromised individuals are affected by the disease in particular and that the burden of herpes zoster is highest in severely immunocompromised patients.

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Introduction

Infection with the varicella zoster virus (VZV) usually occurs during infancy, causing chickenpox.[1] Decades later, the latent virus can be reactivated and result in herpes zoster (HZ) which is usually characterised by a painful skin rash.[2] Since the reactivation of the VZV is typically associated with a decline in cell-mediated immunity, older and immunocompromised (IC) individuals are at higher risk of developing HZ and its complications like postherpetic neuralgia (PHN) and VZV vasculopathy.[2–9] Accordingly, a recently published systematic review reported an HZ incidence rate (IR) between 6 and 8 per 1000 person-years (py) in 60-year-olds and between 8 and 12 per 1000 py at age 80.[10] Studies also observed much higher IRs in IC individuals.[11–13] Weitzman et al.,[11] for example, observed an HZ IR of 12.8 per 1000 py in IC subjects as compared to 3.5 per 1000 py in the total population. In a large study based on German health insurance data, Hillebrand et al.[12] found an HZ IR about 75% higher in IC patients than in immunocompetent ones.

While the epidemiology of HZ is generally well understood, data on the burden in different IC populations is more limited. So far, studies assessed the HZ incidence for single IC conditions[5,14,15] or distinguished between the general population or immunocompetent individuals and IC patients[12,16,17] but there was no further differentiation between different severities of immunosuppression. Such data is essential, however, since populations with different severities of immunosuppression may require different prevention strategies. This is for example the case with regard to vaccination where the currently available attenuated vaccine cannot be used in severely IC patients.

Therefore, the aim of this study was to estimate the incidence of HZ in a representative sample of German adults with different severities of immunosuppression. Besides, we assessed the prevalence of HZ complications and different aspects of healthcare resource utilisation in these populations.

Methods

Data source

The German Pharmacoepidemiological Research Database (GePaRD), which consists of claims data from four statutory health insurances (SHIs), was used for this study. At the time of the study's inception, GePaRD contained information on demographics, outpatient prescriptions, hospitalisations, and diagnoses for the years 2004–2012.[18] In the database, diagnoses are coded according to the International Classification of Diseases, 10th Version, German Modification (ICD-10-GM). Outpatient data include diagnoses (on a quarterly basis) with information on the diagnostic confidence (assured, suspected) and drug prescriptions. Prescription data contain the exact dates of prescription and pharmacy dispensation, information on the prescribing physician's speciality, as well as the Anatomical Therapeutic Chemical (ATC) code and the defined daily dose (DDD) of the drugs. Hospitalisation data comprise admission and discharge dates as well as admission and discharge diagnoses (including primary, secondary, and ancillary diagnoses).

Study design

We used a cohort design to examine the annual incidences of HZ and its manifestations for the years 2006–2012. Only individuals with an age of at least 18 years in the respective study year and continuous insurance coverage during the two years preceding cohort entry (baseline period) were included in the annual cohorts. In addition, subjects were not allowed to have a diagnosis of HZ in the 12 months preceding cohort entry to ensure that only incident cases were considered. Subjects entered the annual cohorts on January 1st, or, if an HZ diagnosis was coded in the year before the respective study year, on the day exactly one year after the last HZ diagnosis. Subjects exited the annual cohorts either on the date their insurance coverage ended, or on the date of an HZ diagnosis, or at the end of the respective study year.

To estimate the prevalences of HZ-related complications, concomitant diseases, and different kinds of healthcare resource utilisation among HZ patients, another cohort was built which included all subjects from the annual cohorts with at least one HZ diagnosis identified between 2006 and 2012. Cohort entry was on the date of the first HZ diagnosis. Subjects left this cohort either when their insurance coverage ended or at the end of the study period (December 31st, 2012).

Outcomes

Herpes zoster

HZ was defined as inpatient diagnosis (primary, secondary, or ancillary) or outpatient diagnosis (coded as "assured") of an ICD-10-GM code starting with B02. Using the fourth digit, the ICD-10-GM allows to differentiate between the HZ manifestations zoster encephalitis (B02.0), zoster meningitis (B02.1), zoster with other nervous system involvement (B02.2), zoster ocular disease (B02.3), disseminated zoster (B02.7), zoster with other complications (B02.8), and zoster without complications (B02.9). Diagnoses on the day of the first HZ diagnosis were used to define the HZ manifestations.

HZ-related complications

PHN was defined as inpatient diagnosis (primary, secondary, or ancillary) or outpatient diagnosis (coded as "assured") of the ICD-10-GM code G53.0 recorded in the quarter of the HZ diagnosis or in one of the two following quarters. The diagnosis PHN was also assumed if an HZ patient received pain medication (listed in Supplementary Table 1) during the quarter of the HZ diagnosis or during the following quarter. The ICD-10-GM codes listed in Supplementary Table 2 were used to identify cases of VZV vasculopathy. Only hospital main discharge diagnoses in the quarter of the HZ diagnosis and in the following two quarters were considered.

Concomitant diseases

Nerve palsies, lateral hemiparesis, pneumonia, hepatitis, and encephalitis, myelitis, encephalomyelitis were identified by inpatient diagnoses (primary, secondary, or ancillary) and outpatient diagnoses (coded as "assured") of the