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Abstract

Background: The exact burden of varicella is not well quantified in Jordan.

Aims: This study aimed to estimate the varicella burden in paediatric patients in Jordan who sought care in a hospital-based setting.

Methods: This was a multicentre, retrospective review of medical records of patients aged 0–14 years with a primary varicella diagnosis in Jordan between 2013 and 2018. The data assessed were: use of health care resources for varicella (outpatient and inpatient visits, tests and procedures, and medication use), and clinical complications of the infection. Estimated costs were based on health care resources used (direct costs) and lost revenue to the child's caregiver (indirect costs) for outpatients and inpatients.

Results: In total, 140 children with varicella were included: 78 outpatients, mean age (standard deviation) 4.4 (3.2) years, and 62 inpatients, mean age 4.0 (3.8) years. No outpatients had varicella-related complications, while 32 (52%) inpatients had ≥ 1 complication. The use of health care resources was higher for inpatients than outpatients, including prescription medication use – 94% of inpatients versus 6% of outpatients. Total costs of varicella were estimated at US$ 66.1 (95% CI: 64.1-68.1) per outpatient and US$ 914.7 (95% CI: 455.6-1373.9) per inpatient.

Conclusions: Varicella is associated with considerable use of health care resources in Jordan and may be responsible for annual costs of US$ 11.5 million. These results support universal varicella vaccination in Jordan.

Keywords: chicken pox, child, outpatients, inpatients, costs, Jordan

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Introduction

Varicella is a highly contagious acute infectious disease caused by the varicella zoster virus that typically occurs in childhood. The annual incidence ranges from 2 to 16 cases per 1000 persons worldwide (1–3). The infection is characterized by mild symptoms, such as a pruritic vesicular rash, fever and malaise. Complications associated with varicella are known to occur and may include bacterial superinfections (skin, lungs or bones), cerebellar ataxia, encephalitis and aseptic meningitis (4).

In Jordan, no data exist on the incidence of varicella (5), however it has been estimated at 22 cases per 1000 persons (6). Treatment, rather than prevention, is the current approach to varicella infection in Jordan, where guidelines suggest that patients be provided with antipyretic and analgesic treatments and that they use disinfectant soap (7). Medical opinion in Jordan also discourages the use of antibiotics; however, an antiviral (acyclovir) is recommended in cases where immunodeficiency or severe eye and/or neurological complications are present (7).

As regards prevention, varicella vaccines have existed since the 1970s and mostly contain the live attenuated Oka strain (Mav strain licensed in South Korea only). The Oka vaccine is available for administration as a 1-dose or 2-dose schedule; both schedules using Oka-strain vaccines are highly effective at preventing varicella. The vaccine is well tolerated, with minimal side-effects (8–11). About 40 countries around the world have already included the varicella vaccine in their national immunization programmes (12). Many studies have demonstrated subsequent reductions in morbidity and mortality associated with varicella, as well as reductions in related use of health care resources (12).

The varicella vaccine is not currently included in Jordan's immunization programme, despite estimates that varicella infection likely represents a considerable health and economic burden that could be reduced through universal varicella vaccination (14-16). Jordanian health officials have spoken publicly about their planned tactic to combat communicable diseases in 2016–2020, including a strategy to introduce new vaccines to the national immunization programme (13).

Limited data exist on the epidemiology of varicella in Jordan, particularly data on the health burden and costs associated with varicella. The aim of this study was to provide evidence of the varicella burden in Jordan by assessing the complications of varicella and the use of health care resources and associated costs of the infection in paediatric patients in Jordan whose parents sought care for them in a hospital-based setting. These data can be used to quantify the overall economic burden of varicella in Jordan and evaluate the cost–effectiveness of varicella

interventions, including the potential inclusion of varicella vaccination in the national immunization programme.

Methods

Study design

This study was a retrospective, observational review of medical records conducted from October 2017 to September 2018 in three public hospitals in Jordan (King Abdullah University Hospital in Al-Ramtha, Princess Rahma Pediatric Hospital in Irbid and Al-Basheer Hospital in Amman). We conducted the study in accordance with the Guidelines for Good Pharmacoepidemiology Practice. This study is part of an ongoing multicountry project that includes the following countries: Argentina (14), Mexico (15), Poland (16), Peru (17) and Hungary (18).

Case selection

WH, ABI, AA, BM, MA and AH screened patient medical records for varicella infection in the past 5 years (between 2013 and 2018), starting with the most recent year. We reviewed each medical record from the date of first primary varicella infection until resolution of the disease, or the last date of contact with the patient. Given the descriptive nature of the study, we selected a convenience sample of 150 patients, with an approximate 1:1 ratio of outpatients and inpatients to allow generalizability of the results to both population groups.

Study population

We included children aged 0–14 years, treated as inpatients and outpatients for a primary diagnosis of varicella. The outpatient group included patients who visited either the outpatient clinic or department of a hospital or the emergency department, and were not hospitalized for varicella. Inpatients were children who were either immediately or eventually, admitted to a hospital for their primary varicella infection. We excluded patients who had received the varicella vaccination before, or who presented with either a second case of varicella or herpes zoster infection.

Outcome measures

The varicella-related clinical complications that we evaluated included, but were not limited to: skin and soft tissue infection, meningitis, encephalitis, pneumonia, sepsis, cerebellitis, keratitis, febrile seizure, dehydration, neutropenia, thrombocytopenia, cellulitis and gastroenteritis.

We also assessed the use of health care resources for varicella treatment and related

complications, which included: total number of outpatient visits (visits to the emergency room or hospital outpatient clinic); hospitalization and intensive care unit stay; use of non-prescription (over-the-counter) and prescription medications; tests and/or procedures performed; and allied health professional (e.g. dermatologist, ophthalmologist) consultations. Based on the health care resources used and lost revenue to the child's caregiver, we calculated direct and indirect costs per varicella case for both outpatients and inpatients. We then used these data to estimate the total annual cost related to varicella.

Statistical analysis

We included all eligible cases identified in the statistical analysis and did stratified analyses for outpatients and inpatients. We calculated the mean and standard deviation (SD) or 95% confidence interval (CI) for continuous variables, and frequencies for categorical variables.

We coded complications using the Medical Dictionary for Regulatory Activities (MedDRA) (19). To assess the varicella-related use of health care resources, we calculated the number and proportion of patients who used each health care resource, and the frequency or duration of use of the resource by the patient.

We determined the direct costs of varicella by multiplying the amount of resources (e.g. number of visits, days of hospitalization, days in the intensive care unit, number and duration of prescriptions) used per patient by the respective unit cost (20–23 and based on local expert opinion) of each resource in 2018 Jordanian dinars (JD), adjusting for inflation when necessary (24). We calculated the indirect costs as the lost revenue of the child's caregiver's using the national average monthly income (25) and the number of work days missed by the caregiver. We estimated the number of work days that the caregiver would have missed as the total number of days the patient was in hospital, including in the intensive care unit. For those treated as outpatients, we estimated 2.5 work days missed by the caregiver, as estimated in previous studies (26,27). All costs are 2018 costs in JD.

By extrapolation, we calculated annual costs of varicella for children younger than 15 years based on the mean costs per varicella case identified in our study, the number of annual varicella cases in Jordan, the proportion of these cases attributed to patients younger than 15 years, and the proportion of these younger patients who were hospitalized. We based all extrapolated costs on 2018 costs in JD, which we also converted to United States dollars (US$). The conversion rate at time of the analysis was JD 1 = US$ 1.41 (28).

We used SAS® software version 9.4 for statistical analyses and SPSS, version 24 for the cost analysis.

Ethical considerations

In accordance with local regulations, we notified the local ethics committees for all participating sites. The following ethics committees approved the study: Institutional Review Board, Jordan University of Science and Technology, King Abdulla University Hospital, and the Institutional Committee for the Study of Scientific Research at the Prince Hamzah Hospital. The study did not require patient consent as we collected data retrospectively from medical records identified only by an encrypted patient number.

Results

Table 1 shows the characteristics of the patients and their varicella presentation according to their inpatient or outpatient status. We included 78 outpatients and 62 inpatients aged 0–14 years in the study, with a mean (SD) age of 4.4 (3.4) and 4.0 (3.8) years, respectively. Most of the patients were boys: 53% of the outpatients and 61% of the inpatients. The greatest proportion of outpatients and inpatients (40% and 42%, respectively) presented with 50–249 skin lesions during the rash. A greater proportion of inpatients (14%) had > 500 lesions during the rash than outpatients (5%). Just over half of the inpatients (52%; 32/62) had one or more complication, among whom 9% (9/62) had two or more complications; no outpatients had complications. None of the patients was considered immunocompromised.

The most common complications in inpatients were: skin and soft tissue infection (24.1% of complications), pneumonia (20.7%), encephalitis (13.8%), sepsis (13.8%) and cerebellitis (10.3%); 17.2% were other types of complication, including neutropenia, thrombocytopenia, keratitis, cellulitis and gastroenteritis.

The use of health care resources associated with varicella is summarized by patient status in Table 2. For outpatients, 81% visited an emergency room while only 19% went to the hospital outpatient clinic. The mean number of visits per patient to both the emergency room and outpatient clinic was 1.0. For inpatients, 31% and 8% visited the emergency department or hospital outpatient clinic, respectively, before being admitted to hospital, both with a mean number of visits of 1.0 per patient. The mean (95% CI) length of stay in hospital was 5.6 (95% CI: 4.3–6.9) days. In addition, 2% of inpatients were admitted to the intensive care unit, with an average duration of stay of 2 days. The use of over-the-counter medication was high in both outpatients (96% of outpatients) and inpatients (60%); the mean number of medicines used per patient was 2.3 (95% CI: 2.2–2.5) for outpatients and 2.1 (95% CI: 1.8–2.4) for inpatients. The use of prescription medication was higher in inpatients than outpatients (94% of inpatients

versus 6% of outpatients); the mean number of prescription medications per patient was 2.2 for inpatients and 1.0 for outpatients. About two thirds of inpatients (68%) underwent tests and procedures and 18% had consultations with allied health professionals. The mean number of tests per inpatient was 5.0 (95% CI: 4.2–5.9) and the mean number of consultations with allied health professionals was 1.4 (95% CI: 1.0–1.7).

Antibiotics were prescribed for 69% of inpatients (Table 3); no outpatients were prescribed antibiotics. The mean number of antibiotics prescribed per inpatient was 1.7 (95% CI: 1.4–1.9), with a mean duration of 8.5 (95% CI: 7.1–9.9) days. The most commonly prescribed antibiotics were ceftriaxone (40%), piperacillin–tazobactam (13%), ampicillin (10%) and vancomycin (10%). The mean duration of use was 5.3 (95% CI: 4.2–6.4) days for ceftriaxone, 6.6 (95% CI: 6.0–7.2) for piperacillin–tazobactam, 3.0 (95% CI: 2.3–3.7) for ampicillin and 6.8 (95% CI: 5.2–8.5) days for vancomycin.

Table 4 presents the key unit costs that were used to calculate the varicella-associated costs of each resource used per patient. These cost per patients are shown in Table 5 for inpatients and outpatients. The mean overall total direct cost per outpatient was 9.7 (95% CI: 8.2–11.1) JD. The mean cost of emergency department visits was 6.0 (95% CI: 5.3–6.7) JD, which accounted for most of the overall total direct cost for outpatients. Visits to a hospital outpatient clinic (mean cost 1.6 (95% CI: 0.9–2.4) JD) and over-the-counter treatment (mean cost 1.8 (95% CI: 0.4–3.2) JD) also contributed to the total direct outpatient cost. For inpatients, the mean overall total direct cost was 565.5 (95% CI: 242.8–888.3) JD. Hospital stay (mean cost 270.1 (95% CI: 207.8–332.4) JD) and prescription medications (mean cost 240.2 (95% CI: 0.0–559.5) JD) accounted for most of the total direct cost for inpatients. Tests and procedures also made up a considerable portion of the total direct inpatient costs (mean cost 46.3 (95% CI: 28.1–64.5) JD). The mean indirect cost per outpatient was 37.2 JD and while this cost per inpatient was 83.0 (63.8–102.1). Thus the overall costs per patient for outpatients and inpatients were 46.8 (95% CI: 45.4–48.3) JD (US$ 66.1 (95% CI: 64.1-68.1)) and 648.5 (95% CI: 323.0–974.1) JD (US 914.7 (95% CI: 455.6–1373.9)), respectively.

The estimated annual direct and indirect costs associated with varicella among the paediatric population (