



Economic Analysis of Herpes Zoster in a Hospital Setting in Hong Kong

Wai-kit MING^{1,2}, Wing-yin YU¹, Owen Tak-yin TSANG³, Paul Kay-sheung CHAN⁴ and Joyce Hoi-sze YOU¹

¹School of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, NT, Hong Kong, ²Harvard Medical School, Harvard University, Boston, Massachusetts, USA, ³Department of Medicine & Geriatrics, The Princess Margaret Hospital, Hospital Authority, and ⁴Department of Microbiology, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong. E-mail: joyceyou@cuhk.edu.hk
Accepted Jan 16, 2019; E-published Jan 17, 2019

Both old age and female sex are well-recognized risk factors in herpes zoster (HZ), and the rate of HZ-related hospitalization is also associated with age (1, 2). Hospitalization costs in Taiwan in 2006 were estimated as USD 1,427 per case of HZ (3). More than 50% of the Hong Kong population are female and 40% are 50 years or older (4). With an ageing population, the disease burden of HZ in Hong Kong is expected to increase.

Zoster vaccine is reported to be effective and safe in preventing HZ in adults aged 50 years and above (5, 6), yet it is not included in the current public vaccination programme in Hong Kong. The direct medical cost of treatment of patients hospitalized with HZ is a crucial factor in examining the potential health economic benefits of zoster vaccine against HZ incidence and HZ-related hospitalization. The present study therefore analysed the direct medical costs of HZ in older adult patients in the hospital setting.

METHODS

A retrospective observational study was conducted in 2 tertiary hospitals of Hong Kong. Patients aged 50 years or older with discharge diagnosis of HZ during the period between 1 January 2011 and 31 December 2013 were included. Patient demographics and utilization of healthcare resources for HZ were retrieved from medical records. The resource items were hospital length of stay (LOS), diagnostic tests, drug treatment for HZ and HZ-related complications. The study protocol was approved by the Joint Chinese University of Hong Kong–New Territories East Cluster Clinical Research Ethics Committee and the Kowloon West Cluster Clinical Research Ethics Committee.

The cost analysis was conducted with 2018 costs from the perspective of the public healthcare provider in Hong Kong. The Hospital Authority is non-profit making and subsidized by the government, and the hospitalization charge billed to non-Hong Kong residents was therefore assumed to represent the cost of healthcare services. The daily charges to non-Hong Kong residents for the general medical ward (USD 654 per day) and intensive care unit (USD 3,128 per day) were found in the Fees and Charges list (7), and the unit cost of medication and laboratory tests were obtained from the study hospitals.

Data analysis was conducted with Microsoft Excel 2017 (Microsoft Corporation, Redmond, USA) and SPSS 16.0 (SPSS Inc., Chicago, USA) for Windows. Continuous variables were compared by analysis of variance (ANOVA), and Pearson's χ^2 test was used for comparison of binary variables. To determine predictors of high treatment cost (defined as $\geq 75^{\text{th}}$ percentile of total direct medical cost), univariate analysis was performed on demographic and clinical factors (with frequency $\geq 5\%$). The factors with potential association ($p \leq 0.1$) were further investigated

using backward stepwise logistic models. The odds ratios with 95% confident interval (OR 95% CI) of significant predictors on high cost were reported. A p -value < 0.05 was considered statistically significant.

RESULTS

A total of 105 cases was reviewed, and 15 (14%) were immunocompromised patients (Table I). The age of immunocompromised (64 ± 10 years) and immunocompetent (71 ± 11 years) patients were not significantly different. Of 15 immunocompromised patients, use of immunosuppressant/high-dose corticosteroid was the common underlying cause.

The incidence of HZ-related complication (≥ 1 complication) was high in both immunocompromised (67%) and immunocompetent (43%) patients. Comparing with immunocompetent cases, higher rates of disseminated HZ (7% vs. 0%; $p = 0.01$) and HZ-related nervous system complications (13% vs. 1%; $p = 0.009$) occurred in the immunocompromised group. The hospital LOS was also longer in immunocompromised patients (14.7 ± 14.3 days) than in the immunocompetent group (5.9 ± 7.9 days) ($p < 0.001$).

The mean total direct medical cost of hospitalized cases ($n = 105$) was USD 4,883 \pm 6,271 (USD 1=HKD 7.8). The

Table I. Patient demographics, zoster-related complications and direct cost for hospitalized cases of herpes zoster (HZ)

	All patients ($n = 105$)	Immuno- compromised ($n = 15$)	Immuno- competent ($n = 90$)	p -value ^a
Age, years, mean \pm SD	70.2 \pm 11.4	64.3 \pm 10.0	71.2 \pm 11.4	0.63
Male, n (%)	50 (47.6)	8 (53)	42 (47)	0.03
Comorbidity, n (%)				
Cardiovascular disease ^b	68 (64.8)	10 (67)	58 (64)	0.87
Diabetes mellitus	29 (27.6)	3 (20)	26 (29)	0.48
Respiratory disease ^c	7 (6.7)	1 (7)	6 (7)	1.00
Herpes zoster (HZ) complication, n (%)				
One or more complication(s)	49 (47)	10 (67)	39 (43)	0.09
Post-herpetic neuralgia	41 (39)	8 (53)	33 (37)	0.22
HZ ophthalmicus	7 (7)	0 (0)	7 (8)	0.26
Disseminated HZ	1 (1)	1 (7)	0 (0)	0.01
Nervous system	3 (3)	2 (13)	1 (1)	0.009
Ramsay Hunt syndrome	2 (2)	1 (7)	1 (1)	0.15
Meningitis encephalitis	1 (1)	1 (7)	0 (0)	0.01
Length of stay, days, mean \pm SD	7.1 \pm 9.5	14.7 \pm 14.3	5.9 \pm 7.9	< 0.001
Cost (USD) ^d , mean \pm SD				
Laboratory	38 \pm 66	46 \pm 66	37 \pm 66	0.63
Medication	55 \pm 85	69 \pm 121	41 \pm 71	< 0.001
Hospitalization	4,792 \pm 6,236	9,713 \pm 9,355	3,971 \pm 5,187	< 0.001
Total direct medical cost	4,883 \pm 6,271	9,891 \pm 9,383	4,049 \pm 5,212	< 0.001

^a p -value for comparison of immunocompromised group vs. immunocompetent group.

^bCardiovascular diseases included congestive heart failure, dyslipidaemia, hypertension, ischaemic heart disease and atrial fibrillation. ^cRespiratory diseases included pneumonia, acute bronchitis, acute exacerbation of underlying chronic respiratory conditions, pneumonitis, respiratory failure and pneumothorax. ^dUSD 1 = HKD 7.8.

mean daily cost was highest for hospital stay (USD 689 ± 29 per day), followed by medication (USD 8 ± 10 per day) and laboratory (USD 6 ± 12 per day). The total direct medical cost in immunocompromised patients (USD 9,891 ± 9,383) was higher than the immunocompetent patients (USD 4,049 ± 5,212) ($p < 0.001$).

Univariate analysis found immunocompromised status as a positive predictor and age ≥ 65 years to be a negative predictor of high-cost hospitalized cases. In the final logistic regression model, only immunocompromised status was retained to be significantly associated with high-cost inpatient HZ treatment (OR = 9.25; 95% CI 2.78–30.77; $p < 0.001$).

DISCUSSION

In the present cohort, 47% cases developed one or more HZ-associated complications. These findings were similar to the incidence of complications in Taiwan (47%) and Italy (50%), but higher than in the USA (38%) (1, 8, 9).

The mean total direct medical cost per hospitalized case of our entire cohort was USD 4,883, and was similar to the cost per admission for HZ in England (approximately USD 4,946 when adjusted by 5% annual inflation rate to year 2018) reported by a population-based analysis of disease burden. The cost per case in our immunocompetent group (USD 4,049) was also consistent with the cost per admission in the immunocompetent population in England (approximately USD 4,819 when adjusted to year 2018 with 5% annual inflation rate) (10).

The total direct medical cost per case of HZ in the immunocompromised group was significantly (2.4-fold) higher than in the immunocompetent group. In the multiple logistic regression model, immunocompromised status was the only predictor found to be associated with high treatment cost. Similarly, a case-control study in Korea examined the association between immunity level and burden of HZ, and reported that management costs for HZ increased significantly with deterioration of immunity (11). The cost of HZ in immunocompromised patients was 1.3–4 times higher than in immunocompetent patients in Korean patients (11, 12), similar to the findings of the current analysis.

Older age (65 years or above) was identified as a negative predictor for high HZ treatment cost in the univariate analysis, despite the fact that it was not retained in the final logistic model. Older age was significantly associated with lower odds for intensive care in patients with influenza in Hong Kong (13). These findings suggest that physicians in Hong Kong are less likely to use an aggressive treatment approach toward older patients.

Health economic studies found vaccination for HZ to be cost-effective in older adults in different countries (14, 15). The current study provided important health economics parameters to the public healthcare policy decision-makers for estimation of the cost and benefits of zoster vaccination in reducing HZ-related hospitalization in Hong Kong.

The current study was limited by the retrospective design and small sample size. The availability of data was highly subject to the level of completeness of documentation in medical records.

In conclusion, the total direct medical costs for HZ in immunocompromised and immunocompetent patients in the hospital setting of Hong Kong are substantial. Implementation of a cost-effective zoster vaccine programme is highly warranted.

ACKNOWLEDGEMENTS

This study was supported by Health and Medical Research Fund (project number 15140432), Food and Health Bureau, The Government of the Hong Kong SAR, China.

All authors have no conflicts of interest to declare.

REFERENCES

- Lin YH, Huang LM, Chang IS, Tsai FY, Lu CY, Shao PL, et al. Disease burden and epidemiology of herpes zoster in pre-vaccine Taiwan. *Vaccine* 2010; 28: 1217–1220.
- Friesen KJ, Chateau D, Falk J, Alessi-Severini S, Bugden S. Cost of shingles: population based burden of disease analysis of herpes zoster and postherpetic neuralgia. *BMC Infect Dis* 2017; 17: 69.
- Census and Statistics Department, The Government of the HKSAR. Population. Accessed on 10 October 2018: <https://www.censtatd.gov.hk/hkstat/sub/so20.jsp>.
- Jih JS, Chen YJ, Lin MW, Chen YC, Chen TJ, Huang YL, et al. Epidemiological features and costs of herpes zoster in Taiwan: a national study 2000 to 2006. *Acta Derm Venereol* 2009; 89: 612–616.
- Schmader KE, Levin MJ, Gnann JW, Jr., McNeil SA, Vesikari T, Betts RF, et al. Efficacy, safety, and tolerability of herpes zoster vaccine in persons aged 50–59 years. *Clin Infect Dis* 2012; 54: 922–928.
- Cunningham AL, Lal H, Kovac M, Chlibek R, Hwang SJ, Díez-Domingo J, et al. Efficacy of the herpes zoster subunit vaccine in adults 70 years of age or older. *N Engl J Med* 2016; 375: 1019–1032.
- Hospital Authority. Fees and charges. Accessed on 10 October 2018: http://www.ha.org.hk/visitor/ha_visitor_index.asp?Content_ID=10045&Lang=ENG&Dimension=100&Parent_ID=10044.
- Gabutti G, Serenelli C, Cavallaro A, Ragni P. Herpes zoster associated hospital admissions in Italy: review of the hospital discharge forms. *Int J Environ Res Public Health* 2009; 6: 2344–2353.
- Lin F, Hadler JL. Epidemiology of primary varicella and herpes zoster hospitalizations: the pre-varicella vaccine era. *J Infect Dis* 2000; 181: 1897–1905.
- Hobbelen PH, Stowe J, Amirthalingam G, Miller L, van Hoek AJ. The burden of hospitalisation for varicella and herpes zoster in England from 2004 to 2013. *J Infect* 2016; 73: 241–253.
- Choi WS, Kwon SS, Lee J, Choi SM, Lee JS, Eom JS, et al. Immunity and the burden of herpes zoster. *J Med Virol* 2014; 86: 525–530.
- Cheong C, Lee TJ. Prevalence and healthcare utilization of herpes zoster and postherpetic neuralgia in South Korea: disparity among patients with different immune statuses. *Epidemiol Health* 2014; 36: e2014012.
- Chan YK, Wong RYK, Ip M, Lee NL, You JH. Economic outcomes of influenza in hospitalized elderly with and without ICU admission. *Antiviral Therapy* 2017; 22: 173–177.
- Preaud E, Uhart M, Bohm K, Aidselburger P, Anger D, Bianic F, et al. Cost-effectiveness analysis of a vaccination program for the prevention of herpes zoster and post-herpetic neuralgia in adults aged 50 and over in Germany. *Hum Vaccin Immunother* 2015; 11: 884–896.
- Le P, Rothberg MB. Cost-effectiveness of herpes zoster vaccine for persons aged 50 years. *Ann Intern Med* 2015; 163: 489–497.