

# WILLINGNESS TO PAY, QUALITY OF LIFE, AND KNOWLEDGE ON HERPES ZOSTER AMONG THAI PATIENTS PRIOR ZOSTER VACCINE ERA

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**Abstract.** Herpes zoster is a devastating condition affecting patients' wellbeing. Policy on zoster vaccine in developing countries needs more data on the disease burden. This study was designed to assess willingness to pay, quality of life, and the patients' knowledge on herpes zoster disease. All of the patients were asked to complete questionnaires about the willingness to pay for zoster treatment using the Dermatology Life Quality Index (DLQI) questionnaires in Thai version and basic knowledge about herpes zoster. The demographic and clinical data were all recorded. Eighty-two from one hundred and eighteen patients in this study were female (69.5%), and the mean (SD) age was 57.6 (14.9) years. The median of their willingness to pay for zoster treatment was THB500 (range of THB50-10,000) or only 4.2% of median income per month. The mean of total DLQI score (SD) was 10.7 (6.2), which indicated moderate to severe impact on quality of life. From multiple linear regression analysis, three factors were related to inferior patients' quality of life including facial involvement (regression coefficients,  $b=4.789$ ,  $p=0.001$ ), presence of zoster complications ( $b=5.018$ ,  $p=0.001$ ) and advanced pain score ( $b=0.883$ ,  $p<0.001$ ). Moreover, more than half of them still had mistaken knowledge about the disease.

**Keywords:** Herpes zoster, knowledge, quality of life, shingles, willingness to pay, Thailand

## INTRODUCTION

Herpes zoster (HZ), also known as shingles, is a disease manifested by one or more dermatomes-distributed vesicular lesions and is regularly accompanied by acute pain. The reactivation of varicella-

zoster virus (VZV) latent in dorsal-root ganglia since primary infection had played a role in HZ pathogenesis (Weller, 1983). This reactivation may be related to a decline in cell-mediated immunity, frequently from hosts with advanced age, or immunosuppressive condition. As a result, the incidence and severity of herpes zoster increase remarkably with age (Chaves *et al*, 2007; Weinberg, 2007). Overall, 10-20% of US population develop HZ at least once in their lifetimes (Katz *et al*, 2004).

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Besides, HZ was well established as a serious and devastating condition, either from the disease itself or its complications. It can affect multiple aspects of patients' wellbeing, including enjoyment of life, mood, sleep, leisure, and social activities (Schmader *et al*, 2007; Drolet *et al*, 2010). The most debilitating event for both patients and physicians is post-herpetic neuralgia (PHN), a persistent HZ-associated neuropathic pain syndrome, which can last long as years after the rash resolves. Apart from PHN, if the viral reactivation attacks the first division of the trigeminal nerve, the patient can develop herpes zoster ophthalmicus (HZO), which may lead to long-term vision damage (Weinberg, 2007). Or less frequently, when HZ targets at the sensory and/or motor division of the facial nerve with or without auditory and vestibular symptoms, it can cause Ramsay Hunt Syndrome (RHS). However, the rate of full recovery from RHS was observed in more than half of the cases (Rasmussen *et al*, 2014).

Because of its complications, the zoster vaccine was indicated to US residents in 2006 by the Advisory Committee on Immunization Practices (ACIP) to prevent HZ in elderly adults more than 60 years of age, because it had been demonstrated a decrease in the incidence and severity of HZ in this population (Oxman *et al*, 2005). Similarly, in Thailand, HZ vaccine was yet included in Recommend Adult and Elderly Immunization Schedule by The Royal College of Physicians of Thailand as optional vaccine since 2012 (Recommend Adult and Elderly Immunization Committee RCPT, 2012). Nevertheless, data on HZ-related impact on patients' wellbeing and HZ knowledge among Thai patients remain limited.

The aim of this study was to assess the willingness to pay for the zoster treatment

and the quality of life (QoL), as well as factors associated QoL in Thai HZ patients. Additionally, the authors would like to evaluate the patients' knowledge about HZ disease.

## MATERIALS AND METHODS

### Study site and population

The study design was cross sectional descriptive study. The zoster patients who were literate, with the age more than 18 years old from Dermatologic Clinic, Out-patient Department, Siriraj Hospital were enrolled during their first visit, between December 2013 and December 2014. All of them were asked to complete the questions about willingness to pay for zoster treatment. In addition, they were also asked to complete the Dermatology Life Quality Index (DLQI) questionnaire (Thai version) and about basic knowledge of herpes zoster. The patients' demographic data, underlying diseases, onset of the rash, pain score, which was rated on the VAS (Visual analog scale) of 0 ('No Pain') to 10 ('Pain as Bad as You Can Imagine'), previous history of chicken pox and herpes zoster, physical examination, investigation results, and prescribed treatment were all recorded in the case record forms.

### Instrument

The DLQI questionnaire was first described and pretested in 1994 by Finlay and Khan. It was comprised of 10 questions in 6 domains, which referred to the previous 7 days. The six domains consisted of symptoms and feelings, daily activities, leisure, working and studying, personal relationships, and treatment difficulties. Each question was short and easily understood. Each question had three possible scores: 'Very Much'=3, 'A Lot'=2, 'A Little'=1, and 'Not At All' or 'Not Relevant'=0.

The DLQI score was calculated by adding the score of each question, resulting in a minimum of 0 and a maximum of 30. The higher the score, the more quality of life is affected. The meaning of total DLQI scores can be categorized as follows: 0-1 = No Effect, 2-5 = Small Effect, 6-10 = Moderate Effect, 11-20 = Very Large Effect, and 21-31 = Extremely Large Effect on patient's life (Finlay and Khan, 1994). Finally, permission for use of the DLQI questionnaire was obtained and was reported to have high validity and good reliability for the Thai version (Kulthanan *et al*, 2004). Therefore, this instrument was applied to evaluate the quality of life of Thai herpes zoster patients in this study.

#### Statistical analysis

Descriptive statistics were used to describe the demographic and clinical data of the patients. Pearson chi-square test was used to test the association between two categorical variables. Unpaired *t*-test was employed to test the difference in mean between two groups. Multiple linear regression was performed to analyze the association between several patients' characteristics and DLQI scores. All statistical analyses were operated using PASW® (version 18; IBM, Armonk, NY). A *p*-value < 0.05 was considered to be statistically significant.

#### Ethical considerations

The Siriraj Hospital Institutional Review Board (SIRB) approved this study [Ref N° COA 708/2013, 682/2556(EC2); 2013 Dec 02].

## RESULTS

#### Demographic and clinical data

Eighty-two from one hundred and eighteen patients in this study were female (69.5%), and the mean (SD) age was

57.6 (14.9) years, with a range of 15-91 years old. Most of them were married (67.8%) and had highest level of education in the university or higher (43.2%). Only 16.9% of them were unemployed. Most of the cases (33.9%) were retired or homemakers, following by officers (28.8%). The median income per month of Thai populations was THB 12,000 (range of THB 0-80,000) (Table 1).

Regarding clinical characteristics, the most common dermatome involved in the population was thoracic (46.2%), following by head or face region (16%), cervical (15.1%), lumbar (15.1%) and sacral (7.6%) areas, respectively. Most of the respondents had occurrence of neuropathic pain before the rash (53.4%), and 7.6% of them did not experience the pain.

The median duration before the patients decide to visit the hospital was 4 days (range of 1-21 days). The mean (SD) of pain score during that first visit was 6.0 (2.9). Thirty-six of the cases (30.5%) were classified as immunocompromised hosts, including from diabetes mellitus (13.6%), malignancy (11%), chronic kidney disease (2.5%), HIV infection (2.5%), and steroid use (8.5%). Twenty-five of them (21.2%) had coexisting complications from herpes zoster disease, which were disseminated infection (8.4%), eye/ear involvement (8.4%), and secondary bacterial infection (5%). Most of the patients (69.5%) had once in their lifetime a history of chicken pox; though, only 15.2% of them had ever experienced herpes zoster disease.

Tzanck's smear was performed with 84 cases (71.2%), with positive result in almost all of the cases (81 cases). But direct immunofluorescence staining for VZV antigens was done in only 2 cases, with positive results in both cases. The common treatment applied in this study included

Table 1  
Demographic and clinical data of the patients (N=118).

Characteristics	n (%)
Gender	
Male	36 (30.5)
Female	82 (69.5)
Age, years – mean (SD)	57.6 (14.9)
< 45	17 (14.4)
45-65	68 (57.6)
> 65	33 (28.0)
Highest level of education	
No education	10 (8.5)
Primary/grade school	27 (22.9)
High school or equivalent	30 (25.4)
University or higher	51 (43.2)
Current income per month, THB – median (min-max)	12,000 (0-80,000)
No income	24 (20.3)
1-10,000	31 (26.3)
10,001-20,000	36 (30.5)
> 20,000	27 (22.9)
Dermatome involved <sup>a</sup>	
Head or face	19 (16.0)
C (cervical)	18 (15.1)
T (thoracic)	55 (46.2)
L (lumbar)	18 (15.1)
S (sacral)	9 (7.6)
Underlying diseases	
Diabetes mellitus	16 (13.6)
Chronic kidney disease	3 (2.5)
HIV infection	3 (2.5)
Malignancy	13 (11.0)
Steroid use (topical/systemic)	10 (8.5)
Complication associated Herpes zoster infection <sup>b</sup>	
No complication	93 (78.2)
Secondary bacterial infection	6 (5.0)
Eye/ear involvement	10 (8.4)
Disseminated herpes zoster infection	10 (8.4)

<sup>a</sup>One case had both C and T dermatomes involvement.

<sup>b</sup>One case had both secondary bacterial infection and disseminated herpes zoster.

systemic acyclovir (98.3%); analgesic drug, especially acetaminophen (60.2%); anxiolytic drugs (78%); vitamin B complex (50.8%); and topical antibiotics (76.3%).

#### Willingness to pay

The median of their willingness to pay for zoster treatment was THB 500 (range of THB 50-10,000) or 4.2% of their

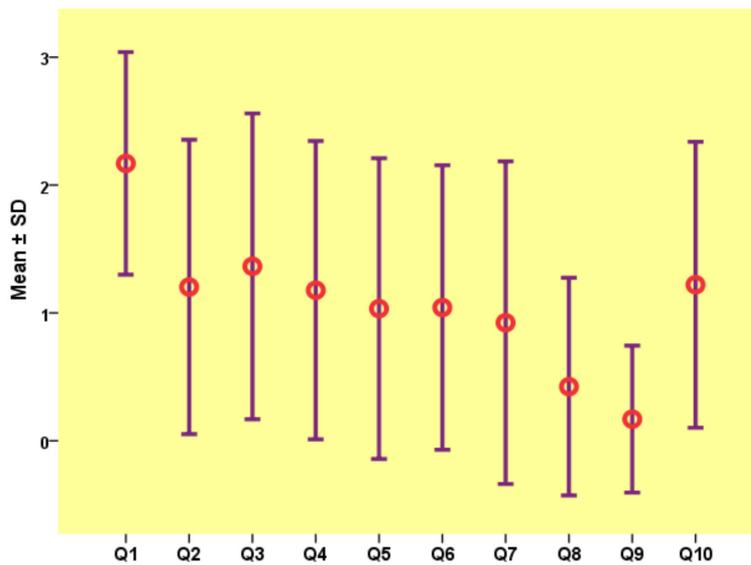


Fig 1–The mean and SD of DLQI score in each question.

median income per month (THB 12,000). The willingness to pay of patients in this study was not significantly associated with any demographic or clinical factors, income per month or DLQI scores.

#### DLQI score

The mean (SD) of total DLQI scores among patients in this study was 10.7 (6.2) (Fig 1).

The factors found to be significantly associated with higher score of DLQI or worse QoL in current study were young age (correlation coefficients,  $r=-0.216$ ,  $p=0.019$ ), patient's single or divorce status ( $p=0.047$ ), facial involvement ( $p=0.001$ ), presence of zoster complications ( $p=0.023$ ), and higher pain score ( $r=0.373$ ,  $p<0.001$ ) (Table 2).

However, according to multiple linear regression analysis, we observed only three robust factors related to inferior quality of patients' lives, including presence of facial lesions (regression coefficients,  $b=4.789$ ,  $p=0.001$ ), existence of complica-

tions ( $b=5.018$ ,  $p=0.001$ ), and advanced pain score ( $b=0.883$ ,  $p<0.001$ ).

#### Patients' knowledge about zoster

More than half of the patients still had mistaken knowledge about the pathogenesis, transmission route, manifestation, treatment, and prognosis of herpes zoster disease (Table 3). The mean (SD) of total scores from 10 questions in HZ patients was 3.9 (2.8). The total score was not found to be significantly associated with sex, age, and highest level of education or income per month.

#### DISCUSSION

Median income per month in population of this study was THB12,000, which was approximately four times the total healthcare costs for HZ in Thailand, according to one study (Aunhachoke *et al*, 2011). Median willingness to pay of this study was 4.2% of median income per month, compared to 11.7-35.9% of those of the US population (Lieu *et al*, 2008). This may raise concern about policy in zoster treatment and prevention in developing countries. The cost-effectiveness analysis of herpes zoster treatment and vaccine in developing countries; therefore, needs further study before being established in the future.

The mean DLQI score in this study was 10.7, which indicated the moderate to severe impact on patients' QoL. Comparing to previous studies in Thai patients, we observed higher mean DLQI scores in some diseases such as urticaria, psoriasis,

Table 2  
Patients' characteristics correlated with DLQI score.

Characteristics	n	Univariable analysis		Multivariable analysis <sup>a</sup>	
		DLQI score: mean (SD)	p-value	b <sup>b</sup>	p-value
Age (years)		r = -0.216	0.019	-0.064	0.066
Marital status					
Single/Divorce	38	12.3 (5.8)	0.047	1.661	0.120
Married	80	9.9 (6.2)		-	
Dermatome involved					
Face	19	14.3 (4.5)	0.001	4.789	0.001
Non-face	99	10.0 (6.2)		-	
Complication associated Herpes zoster infection					
No	103	10.2 (5.9)	0.023	-	
Yes	15	14.1 (7.1)		5.018	0.001
Pain score		r = 0.373	<0.001	0.883	<0.001

<sup>a</sup>Multiple linear regression.

<sup>b</sup>b, Unstandardized regression coefficients.

Table 3  
Patients' knowledge about zoster disease.

Questions (in Thai)	Correct answers n (%)
1. Is zoster caused from reactivation of latent zoster virus ?	63 (53.4)
2. Is zoster spread via the route of vesicle or bleb contact ?	43 (36.4)
3. Does zoster occur following chicken pox ?	38 (32.2)
4. Is zoster the disease that presented with generalized vesicles ?	42 (35.6)
5. Do everyone with HIV infection have to develop zoster ?	46 (39.0)
6. If zoster distributes to both sides of the body, will the patient die ?	25 (21.1)
7. Should we treated shingles with herbs or traditional medication ?	47 (39.8)
8. Can shingle be self-cured in normal healthy hosts ?	39 (33.1)
9. Can the patients have persistent pain after recovering form zoster ?	52 (44.1)
10. Do you really know the shingles or zoster ?	62 (52.5)
Total scores (each for 1 score, from 10 questions) – mean (SD)	3.9 (2.8)

riasis, and eczema (Kulthanan *et al*, 2004; Chularojanamontri *et al*, 2011). A previous study in Thailand also demonstrated significant burden of HZ to patients' well-being using Euro-QoL Five-Dimension Questionnaire (EQ-5D) (Aunhachoke *et al*, 2011). To the best of our knowledge, this

is the first study evaluate HZ patients' QoL using validated DLQI questionnaires.

From this study, the factors found to strongly associate with inferior QoL from multivariate analysis were facial involvement, presence of complications and greater pain score. Patients with

facial lesions may have more easily visible stigma. Presence of HZ associated complication, such as HZO, RHS, or disseminated infection may experience more suffering and need admission or advanced treatment from other specialists. And finally, as mentioned in previous studies, the greater the pain score was, the poorer QoL they experienced (Aunhachoke *et al*, 2011; Song *et al*, 2014).

About half of patients in this study mentioned that they had never known about HZ, which was considerably less than the results of a global survey (Paek and Johnson, 2010). Approximately 40% of Thai patients still had faith in traditional medicine for HZ treatment, more than the findings of a previous study, 31% (Paek and Johnson, 2010). Furthermore, these authors observed that patients with lower education and who came from Latin America or Asia were more likely to use alternative medicine than those in Europe.

However, from this study, 95% of the patients were prescribed the accurate dosage of acyclovir or valacyclovir, which was first-line antiviral therapy for HZ treatment, together with other appropriate supportive supplement therapy (Dworkin *et al*, 2007). In some cases, antiviral drug was not advised at the first appointment due to their late visit since the rash onset of more than a week, as the recommendation of beginning antiviral therapy was within 72 hours (Dworkin *et al*, 2007).

From our demographic data, most of cases were middle-aged female, which corresponded with the results from previous studies in Western countries, which demonstrated that advanced age of more than 50 years was one of the risk factors developing HZ (Lukas *et al*, 2012). Moreover, from studies in Thailand and USA, female predominance was observed as

well (Weinberg, 2007; Aunhachoke *et al*, 2011). These may be the result of the age-related decline in VZV-specific cell-mediated immunity (Chaves *et al*, 2007). And, females may have more concern about health problem, thus they have more tendency to visit the specialists at the hospital.

According to clinical data in this study, the median duration of symptoms was 4 days, which was the same trend compared to previous studies (Aunhachoke *et al*, 2011; Song *et al*, 2014). This may be explained by the new lesions of HZ often develop within 3-7 days, which may prompt patients to visit the hospital (Weinberg, 2007).

The most common dermatome involved of most cases in current study was thoracic dermatome, which was similar to the result of many previous studies (Arvin, 1996; Weinberg, 2007; Tsai *et al*, 2015).

HZ associated complication was noted in 21.8% of the cases in current study; the most common problems were eye/ear involvement and disseminated HZ infection. However, according to previous studies, PHN was indicated to be the most common complication with the incidence approximately 10-15% of the cases, and this may reach 28% in elderly populations (Helgason *et al*, 2000). From the literature, cut points used to differentiate PHN was varied from 1-to-6 months after HZ onset (Dworkin *et al*, 1994). Therefore, further prospective study may be recommended to evaluate cases with PHN.

Tzanck's smear was done in only 71.2% of the cases, which was matched to the study that the diagnosis of HZ can be made based on clinical syndrome (Weinberg, 2007). Direct immunofluorescence assay was performed in 2 atypical cases

of current study due to uncertain in the diagnosis from clinical pictures together with Tzanck's smear result. Regarding the dermatology practice in Thailand, direct immunofluorescence stain and real-time polymerase chain reaction are not the routine investigation. We reserve these for only unusual cases with problems in diagnosis and treatment.

Some limitations of this study are worth noting. Because it was a cross sectional study, the assessment of PHN and clinical response follow-up were impossible, so PHN was not included as one of the complications experienced by the patients in this study. In addition, misdiagnosis of the disease cannot be completely ruled out, given that some patients were not confirmed by laboratory investigation, which maybe due to their classic clinical presentations or extremely late rash duration at the first visit. Furthermore, because Siriraj Hospital was known as a super-tertiary care center, the prevalent cases may be more severe and complicated in either the diagnosis or management than those in the general population.

Only 4.2% of monthly income was considered acceptable for zoster treatment. The policy regarding zoster treatment and prevention needs further study. From DLQI score of herpes zoster patients in this study, it indicates the moderate to severe impact of the disease on QoL, especially in those who have lesions on the face, disease complications, and a greater pain score. The knowledge about herpes zoster among these patients is still lacking. Further education and evaluation is recommended.

#### ACKNOWLEDGEMENTS

The authors are grateful to Assist Prof Dr Chulaluk Komoltri from Division

of Clinical Epidemiology, Department of Health Research and Development, Faculty of Medicine, Siriraj Hospital, Mahidol University for her helpful statistical advice.

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