# Clinical Characteristics and Cost of Chickenpox Hospitalization in Thai Children

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**Background:** Although primary Varicella-Zoster-Virus (VZV) infection generally causes uncomplicated illness confined to skin and mucous membrane among healthy children, it infrequently causes life-threatening infection especially among immuno-suppressed hosts or young infants. Limited information is available regarding the clinical features, outcomes, and the financial burden incurred by severe primary varicella infection in Thai children who required hospitalization.

**Objective:** To determine clinical characteristics particularly the disease severity, prevalence of complication, case fatality rate, and use of healthcare resources in terms of length of stay as well as direct medical cost of varicella-associated hospitalization in children.

Material and Method: A retrospective descriptive study was conducted among children aged one month to 18 years who were hospitalized with chickenpox between 2007 and 2011 at the Queen Sirikit National Institute of Child Health, Bangkok, Thailand. Information on clinical manifestations, complications, and outcomes were obtained by medical record abstraction, and data on hospital charges were obtained from the hospital financial database.

Results: A total of 101 cases of chickenpox were identified, with a median (interquartile range IQR) age of 4 (0.8, 7.25) years. Underlying predisposing conditions for severe varicella infection were identified in 35 cases (34.7%). Seventy four of 101 (73.3%) patients developed complications, with skin and soft tissue infections being the most common (50.5%), followed by pneumonia (12.7%) and neurological complications (6.4%). There were no fatal cases. Median (IQR) duration of hospitalization and hospital charges were 6 (3, 9) days and US\$ 330.2 (\$139.3, \$1,013.5), respectively. Children with predisposing conditions for severe varicella were significantly older, incurring 6-fold higher hospital charges and 2-fold longer hospitalization compared to their counterparts.

**Conclusion:** The high rate of complicated varicella and financial burden reported in this study suggested that the severity of varicella complications in children might have been previously underestimated. This study provides relevant information regarding the burden of hospitalized varicella infection among both otherwise healthy children as well as children with predisposing immuno-suppression.

Keywords: Hospitalization, Chickenpox, Pediatrics, Thailand, Varicella-zoster virus (VZV) infection

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"Chickenpox" (or primary varicella zoster virus (VZV) infection) is a common childhood illness that is known to be highly contagious and has the ability to affect virtually the entire population. Although VZV generally causes uncomplicated illness confined to the skin and mucus membrane among healthy children, it occasionally causes life-threatening illnesses, especially among immuno-suppressed children or

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Phone: 08-5515-8299 E-mail: waruneep@gmail.com young infants.

Data from various active surveillances suggested that approximately 0.6-6% of all varicella cases require hospitalization<sup>(1-3)</sup>, and 1.5%<sup>(1)</sup> of cases develop certain complications. In addition, severe illness and fatalities due to varicella infection have been documented among healthy children<sup>(2-4)</sup>. Skin and soft tissue superinfection, respiratory, hematological, and neurological complications are among the most commonly reported complications in hospitalized cases<sup>(5-10)</sup>. Neurological involvement was considered one of the most serious but common complications, including cerebellar ataxia, febrile convulsion, meningoencephalitis, seizures, syncope, and cerebral vasculitis/

infarction. Up to 12% of those with neurological complications sustained long-term sequelae, such as ataxia, epilepsy, hemiparesis, cerebral nerve palsy, and dysesthesia<sup>(10)</sup>.

A population-based study of varicella complications in the US during the pre-varicella vaccine era showed that acute cerebellar ataxia was the leading neurologic complication of primary VZV infection, occurring in approximately one in 4,000 varicella cases among children younger than 15 years of age. In contrast, varicella pneumonia was the most common complication among adults, resulting in hospitalization for one of every 400 varicella cases<sup>(11)</sup>.

Unusually severe varicella meningitis was reported in an unimmunized immunocompetent adult from the United States (US), despite the use of varicella vaccines in the national immunization program<sup>(12)</sup>. Hemorrhagic pneumonitis was reported to be significantly higher among hospitalized adults than children (32.7% vs. 4.4%)<sup>(13)</sup>.

Of note, a recent report from Saudi Arabia indicated that the majority of cases with complications occurred among those who did not have major underlying disease<sup>(2)</sup>. From the same report, fatality cases had no predisposing co-morbidities; one adult died from pneumonia and one child died from group A streptococcal septicemia<sup>(1)</sup>. In addition, pneumonia and hospitalization were significantly more common among adults than children. Another recent report from Australia in the post-vaccination era showed that 2.6% of hospitalized pediatric cases who were immunocompetent and unimmunized had severe multiple complications requiring intensive care<sup>(14)</sup>. Varicella-associated pneumonia among hospitalized cases was also reported among 7-28%<sup>(1,9,15,16)</sup>.

Cost effectiveness analysis for the adoption of varicella vaccination in the Thai National Immunization Program was not available. This is probably due, at least in part, to lack of relevant information on disease severity and impact on healthcare resources. As a result, varicella vaccine has not been included in the Thai basic immunization scheme. Therefore, the objective of this study was to provide pertinent information regarding disease severity, prevalence of complications, case fatality rates, and use of healthcare resources in terms of duration and hospital charges of varicella-associated hospitalization of children.

# **Material and Method**

The authors conducted a retrospective

descriptive study among hospitalized children younger than 18 years who were diagnosed with primary varicella infection during the 5-year period from January 1, 2007 to December, 31 2011 at Oueen Sirikit National Institute of Child Health (QSNICH), a tertiary medical center in Bangkok, Thailand. To obtain medical records of those cases, we identified hospitalized children with the discharge diagnosis of varicella infection or chickenpox, using the ICD-10 code B01.0-B01.9. After reviewing patients' records, the authors included only cases admitted to the hospital for primary varicella infection or chickenpox. Those who were diagnosed with herpes zoster and/or those who developed clinical signs and symptoms of varicella during their hospitalization due to other unrelated diagnoses were excluded. Information on demographics, clinical presentations, co morbidities, complications, treatment, duration of hospitalization, and outcomes were obtained from medical record abstraction. Information on hospital charges was obtained from the finance department at OSNICH.

## Statistical analyses

The data were descriptively analyzed. Clinical features, complications, and hospital costs were compared between cases with or without predisposing conditions for severe varicella complications. Data were collected and analyzed, using SPSS 16.0 for Windows software (SPSS Inc., Chicago, IL). Descriptive analyses were used to obtain summary estimates for each variable. Univariate analyses compared differences between the two groups. Normally distributed continuous variables were analyzed using Student's ttest, whereas skewed continuous data (age, duration of admission, hospital costs) were analyzed using non-parametric methods. For comparison between categorical variables, Chi-square or Fisher exact test were used when appropriate. This study received approval from the QSNICH Ethics Committee (#54-049.2).

#### Results

A total of 117 cases were identified, using the ICD-10 code from the hospital discharge database during the 5-year study period. After careful review of inpatient records, primary varicella infection was correctly coded in 110 cases (91.8%), among whom 101 cases (91.8%) were hospitalized for chickenpox. A total of 79,605 hospitalizations were enumerated during the same period, indicating an estimated 0.13% of overall hospitalization due to chickenpox. The highest numbers

of cases were identified during January to April (late winter to summer). Diagnosis of chickenpox was based on clinical signs and symptoms in all cases. Tzank smears were taken from 34 cases (33.6%), among whom 22 (64.7%) were positive.

# Demographic characteristics

Among 101 cases hospitalized for primary varicella infection, males were slightly predominant, with a gender ratio of 1.15:1. Median (interquartile range/ IQR) age of cases was 4 (0.8, 7.25) years. Children younger than 5 years were the highest proportion

(55.4%) of cases; 26 cases (25.7%) were infants (<1 year), 23 (22.8%) were toddlers (1-3 years), 24 (23.8%) were preschoolers (4-6 years), and 15 (14.9%) were 10 years or older. Among infants, 12 cases (46.2%) were younger than 6 months.

# Clinical characteristics

Characteristics of hospitalized varicella cases with any pre-existing co-morbidities are shown in Table 1. Associated co-morbidities were identified in 43 cases (42.6%), with hematologic malignancies being the most common (22.8%), followed by central nervous system

Table 1. Characteristics of hospitalized varicella cases with co-morbidities

Prior varicella immunization       7 (12.1)       8 (18.6)       0.440       15 (14.9)         At least one dose       2 (3.4)       3 (7.0)       5 (5.0)         No data available       49 (84.5)       32 (74.4)       81 (80.2)         Acyclovir treatment       15 (25.9)       37 (86.0)       <0.001       52 (51.5)         Complications       42 (82.8)       26 (60.5)       0.012       74 (73.3)         CNS complications       2 (3.4)       5 (11.6)       0.132       7 (6.9)         Encephalitis       0 (0.0)       3 (7.0)       0.074       3 (3.0)         Cerebellar ataxia       1 (1.7)       0 (0.0)       0.387       1 (1.0)         Seizure       0 (0.0)       2 (4.7)       0.179       2 (2.0)         Febrile convulsion       1 (1.7)       2 (4.7)       0.573       3 (3.0)         Respiratory complications       3 (5.2)       11 (25.6)       0.003       14 (13.9)         Pneumonia       3 (5.2)       11 (25.6)       0.003       14 (13.9)         Respiratory failure       0 (0.0)       2 (4.7)       0.179       2 (2.0)         Pulmonary hemorrhage       0 (0.0)       1 (2.3)       0.426       1 (1.0)         Skin and soft tissue       3		Otherwise healthy children (n = 58)	Children with any co-morbidity (n = 43)	<i>p</i> -value	Total (n = 101)
Median age in years, (IQR)       2.5 (6)       6 (7)       <0.001	Male, n (%)	31 (53.4)	23 (53.5)	0.997	54 (53.5)
Median duration of hospital (days) (IQR)       4 (2,6)       8 (3,12)       <0.001		2.5 (6)	6 (7)	< 0.001	4(7)
Hospital charges in US\$, median (IQR)		4(2, 6)		< 0.001	
Prior varicella immunization       7 (12.1)       8 (18.6)       0.440       15 (14.9)         At least one dose       2 (3.4)       3 (7.0)       5 (5.0)         No data available       49 (84.5)       32 (74.4)       81 (80.2)         Acyclovir treatment       15 (25.9)       37 (86.0)       <0.001	Hospital charges in US\$, median (IQR)	187.1		< 0.001	330.2
None       7 (12.1)       8 (18.6)       0.440       15 (14.9)         At least one dose       2 (3.4)       3 (7.0)       5 (5.0)         No data available       49 (84.5)       32 (74.4)       81 (80.2)         Acyclovir treatment       15 (25.9)       37 (86.0)       <0.001		(105.8, 389.2)	(349, 1,493.2)		(139.3-1,013.5)
At least one dose       2 (3.4)       3 (7.0)       5 (5.0)         No data available       49 (84.5)       32 (74.4)       81 (80.2)         Acyclovir treatment       15 (25.9)       37 (86.0)       <0.001	Prior varicella immunization				
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Acyclovir treatment       15 (25.9)       37 (86.0)       <0.001	At least one dose	2 (3.4)	3 (7.0)		5 (5.0)
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Hepatitis 2 (3.4) 7 (16.3) 0.035 9 (8.9)	Other	22 (37.9)	8 (18.6)	0.036	30 (29.7)
	Diarrhea	8 (13.8)	1 (2.3)	0.045	9 (8.9)
$A(60) \qquad 2(47) \qquad 0(27) \qquad (60)$	Hepatitis	2 (3.4)	7 (16.3)	0.035	9 (8.9)
Supsis $4(0.9)$ $2(4.7)$ $0.057$ $6(5.9)$	Sepsis	4 (6.9)	2 (4.7)	0.637	6 (5.9)
Thrombocytopenia 0 (0.0) 3 (7.0) 0.074 3 (3.0)	Thrombocytopenia		3 (7.0)	0.074	3 (3.0)
Disseminated varicella $0 (0.0)$ $4 (9.3)$ $0.030$ $4 (4.0)$	Disseminated varicella	0 (0.0)	4 (9.3)	0.030	4 (4.0)
IAHS $0 (0.0)$ $2 (4.7)$ $0.179$ $2 (2.0)$	IAHS	0 (0.0)	2 (4.7)	0.179	2 (2.0)
UGI bleeding $0 (0.0)$ $2 (4.7)$ $0.179$ $2 (2.0)$	UGI bleeding	0 (0.0)	2 (4.7)	0.179	2 (2.0)

IAHS = infectious-associated hemophagocytic syndrome; UGI = upper gastrointestinal; \* exchange rate 1 US\$=30 THB

Table 2. Characteristics of hospitalized varicella cases with predisposing conditions for severe varicella infection

	Children without predisposing co-morbidity (n = 66)	Children with predisposing co-morbidity (mainly immunosuppression) (n = 35)	<i>p</i> -value	Total (n = 101)
Male, n (%)	35 (53.0)	19 (54.3)	0.904	54 (53.5)
Median age in years, (IQR)	2.7 (0.7-6.4)	6.8 (3.9-10.5)	0.001	4.3 (0.8-7.9)
Median duration of hospitalization	4.0 (2, 6)	9.0 (7, 14)	< 0.001	6.0 (3, 9)
(days) (IQR)	(=, -)	· · · ( · , · · · )		(-, -)
Hospital charges in US\$, median (IQR)	187.1	1,229.9	< 0.001	330.2
11, 11, 11, 12, 11, 11, 11, 11, 11, 11,	(105.8, 371.5)	(633.5, 1,493.2)		(139.3-1,013.5)
Prior varicella immunization	(, ,	(, , )		( , ,
None	9 (13.6)	6 (17.1)	0.398	15 (14.9)
At least one dose	2 (3.0)	3 (8.6)		5 (5.0)
No data available	55 (83.3)	26 (74.3)		81 (80.2)
Acyclovir treatment	17 (25.8)	35 (100.0)	< 0.001	52 (51.5)
Complications	54 (81.8)	20 (57.1)	0.008	74 (73.3)
CNS complications	4 (6.1)	3 (8.6)	0.691	7 (6.9)
Encephalitis	0 (0.0)	3 (8.6)	0.039	3 (3.0)
Cerebellar ataxia	1 (1.5)	0 (0.0)	0.464	1 (1.0)
Seizure	0 (0.0)	2 (5.7)	0.118	2(2.0)
Febrile convulsion	3 (4.5)	0 (0.0)	0.550	3 (3.0)
Respiratory	6 (9.1)	8 (22.9)	0.072	14 (13.9)
complications				
Any pneumonia	6 (9.1)	8 (22.9)	0.072	14 (13.9)
Respiratory failure	1 (1.5)	1 (2.9)	0.645	2 (2.0)
Pulmonary hemorrhage	0 (0.0)	1 (2.9)	0.347	1 (1.0)
Skin and soft tissue	37 (56.1)	14 (40.0)	0.124	51 (50.5)
Secondary bacterial infections	24 (36.4)	7 (20.0)	0.090	31 (30.7)
Cellulitis	13 (19.7)	6 (17.1)	0.755	19 (18.8)
Purpura fulminan	0 (0.0)	1 (2.9)	0.347	1 (1.0)
Other	20 (30.3)	10 (28.6)	0.856	30 (29.7)
Diarrhea	8 (12.1)	1 (2.9)	0.157	9 (8.9)
Hepatitis	1 (1.5)	8 (22.9)	0.001	9 (8.9)
Sepsis	3 (4.5)	3 (8.6)	0.415	6 (5.9)
Thrombocytopenia	0 (0.0)	3 (8.6)	0.039	3 (3.0)
Disseminated varicella	0 (0.0)	4 (11.4)	0.013	4 (4.0)
IAHS	0 (0.0)	2 (5.7)	0.118	2 (2.0)
UGI bleeding	0 (0.0)	2 (5.7)	0.118	2 (2.0)

IAHS = infectious-associated hemophagocytic syndrome; UGI = upper gastrointestinal; \* exchange rate 1 US\$ = 30 THB

diseases (mainly a history of febrile convulsions/epilepsy) (5.0%), chronic renal disease (4.0%), chronic lung disease (3%), and anemia (including iron deficiency anemia and thalassemia) (3.0%). Rates of varicella immunization were low, 7.0% among those with and 3.4% without any co-morbidity.

Characteristics of hospitalized varicella cases with underlying predisposing conditions for severe

varicella infection (i.e. immuno-suppressive conditions from various causes and severe malnutrition) are shown in Table 2. Underlying predisposing conditions for severe varicella infection were identified in 35 cases (34.7%), with chemotherapy being the most common (23.8%), followed by steroid treatment (5%), being a neonate (3%), human immunodeficiency virus infection (2%), and severe malnutrition (1%). Rates of varicella

immunization were rather low, 8.6% among those with and 3% without any predisposing co-morbidity.

#### Duration of hospitalization

Median duration of hospitalization was 6 (IQR: 3, 9) days. Overall duration of hospitalization was significantly longer for those with co-morbidities, with a median (IQR) of 4 (2, 6), 8 (3, 12), and 9 (7, 14) days for otherwise healthy children, children with any co-morbidities, and children with predisposing conditions for severe varicella infection, respectively. However, duration of hospitalization did not significantly differ between those with or without complications, with a median (IQR) of 6 (3, 9) vs. 7 (3, 8) days, respectively (Table 3).

# Complications of varicella

Seventy-four of 101 (73.3%) patients developed certain complications during the course of illness. The most common were skin and soft tissue infections, comprising 50.5% (n = 51) of all varicellaassociated hospitalization cases. The second most common complication was pneumonia, which was observed in 14 cases (13.9%), followed by neurological complications (n = 7; 6.9%), including febrile convulsions, seizure, aseptic meningitis, encephalitis, and cerebellar ataxia (Table 1). Thirty cases (29.8%) developed other complications, including diarrhea, hepatitis, clinical sepsis, thrombocytopenia, upper gastrointestinal hemorrhage, disseminated varicella, and infectious-associated hemophagocytic syndrome. One case with severe complications required intensive care admission. There were no fatal cases.

The differences between those with and without complications are shown in Table 3, which indicate that those with predisposing conditions for

severe varicella were significantly older, incurring 6fold higher hospital costs and two-fold longer hospitalization duration compared to their counterparts.

#### **Discussion**

The aim of the present study was to quantify the severity and burden of varicella-associated hospitalization in Thai children, which has not been previously described. However, as the study was retrospective in nature and based on a single tertiary setting, the authors are not able to obtain a complete picture of the overall severity and public health burden. In general, the predominantly benign features of this illness have a tendency to overshadow the potentially serious and complicated outcomes resulting in hospitalization and/or fatality. Previously, healthy children were reported to suffer from serious complications such as pneumonia, septic arthritis, osteomyelitis, sepsis, encephalitis, and death<sup>(17,18)</sup>. In terms of health care resource utilization, the 0.13% rate among all recorded hospitalizations within the study period is comparable to a report from Italy (0.16%) in 2005<sup>(19)</sup>, where varicella vaccine was not a part of routine vaccination.

The present study showed that the numbers of cases were high in late winter and summer, which differs from previous reports indicating that the peak incidence of varicella infection generally occurred during winter or the cooler season in Asia<sup>(16,20,21)</sup>. However, this may be misleading, as the proportion of varicella hospitalization among overall varicella infection may not be constant throughout the year. In addition, the authors were unable to define proper denominators to establish population incidence. Existing literature has suggested a relationship between low ambient temperature and humidity and increased

**Table 3.** Comparison between cases with and without complications

	Uncomplicated varicella $(n = 27)$	Complicated varicella $(n = 74)$	<i>p</i> -value
Male, n (%)	12 (44.4)	42 (56.8)	0.272
Median age in years, (IQR)	5.2 (3.2, 10.5)	3.9 (0.8, 7.0)	0.108
Median duration of hospitalization (days) (IQR)	7 (3, 8)	6 (3, 9)	0.672
Hospital charges in US\$, median (IQR)	394.0 (152.0, 833.7)	324.7 (137.7, 1,129.2)	0.951
Prior varicella immunization $(n = 5)$	4 (14.8)	1 (1.4)	0.006
Acyclovir treatment $(n = 52)$	18 (66.7)	34 (45.9)	0.065
Presence of any co-morbidity	17 (63.0)	26 (35.2)	0.012
Presence of predisposing co-morbidity	15 (55.6)	20 (27.0)	0.008

IAHS = infectious-associated hemophagocytic syndrome; UGI = upper gastrointestinal; \* exchange rate 1 US\$ = 30 THB

VZV transmission potential, especially in tropical regions<sup>(22)</sup>. In addition, early literature from Thailand showed that age-adjusted VZV seroprevalence was significantly higher in cooler regions(23). Further, a seroprevalence survey indicated that seroconversion tends to occur more frequently in higher population density areas<sup>(23)</sup> and in older children in tropical regions rather than in temperate climate areas<sup>(20)</sup>. A VZV serosurvey among healthy children and young adults in Thailand found that the overall seroprevalence rate was 52.8%, and increased from 15.5% in the 9 months to 4 years age group to 75.9% in the 20-29 year-old group. Another serosurvey among Thai undergraduate students indicated that up to one-fourth of this population remains susceptible to VZV due to lack of pre existing VZV antibodies<sup>(24)</sup>. As a result, a significant proportion of Thais are susceptible to later onset of disease occurrence, which is associated with more severe illness and risk of complications.

An epidemiological survey of varicella hospitalization in the United States (US) 1995-2005 indicated that the estimated ratios between varicella cases/varicella hospitalizations/varicella-related deaths were 26,290:170:1<sup>(1)</sup>. In this American study, the hospitalization rate among overall varicella cases was estimated at 0.6% for all symptomatic cases, and case fatality rates of overall varicella and hospitalized varicella cases were 0.004% and 0.6%, respectively. On the other hand, a more recent report from Saudi Arabia demonstrated a high varicellaassociated hospitalization rate of 2% among all varicella cases<sup>(1)</sup>. The higher rate of hospitalization in the latter study was likely to be attributable to the high proportion of the adult population, as late onset of primary varicella infection is more frequent in tropical countries compared to temperate climate countries. Data from the Thailand National Health Security Office indicated that there was a total of 7,267 hospitalized chickenpox cases in children vounger than 18 years during the same period as our study (2007-2011). Data showed that they incurred a total of 23,674 hospitalization days and a total hospital cost of US\$ 1,424,359 (42,730,798 Thai Baht/THB) or US\$ 284,871 per annum (exchange rate 1 US\$ = 30 THB). The average hospitalization cost per pediatric case was US\$203 (6,090 THB) (National Health Security Office, Thailand, personal communication, 2012).

The findings are comparable to previous reports indicating that young children, especially those younger than 5, constitute the majority of hospitalized cases<sup>(6,7,16,19,21)</sup>. This group of children is more likely to

be affected by both primary varicella infection and secondary skin and soft tissue infection as reflected in our sample whereas the majority of children with associated immune suppressive condition were 5 years or older. The highest rate of complication (89.3%) was identified among infants which is comparable to a recent survey on the economic impact of varicella-related hospitalizations in Turkey which indicated that up to one-third of hospitalized cases were those younger than one year<sup>(6)</sup>. Sixty-five percent of these hospitalized infants developed complications<sup>(25)</sup>. The rates of complications were inversely related to maternal antibody levels during the first year of life<sup>(25,26)</sup>.

The authors did not detect any fatalities in our sample of 101 hospitalized cases. In general, the overall case fatality rates of hospitalized varicella ranged from 0 to  $2.73\%^{(1,9,10,13,14,27-30)}$ , compared to 0.0025% overall fatalities in the US<sup>(32)</sup>.

Duration of hospitalization in our sample was comparable to other reports, with median and mean duration in hospital varying between 5-6 days<sup>(7,9)</sup> and 3.7-6.8 days<sup>(16,21,29,32)</sup>, respectively. Median hospital charges in the present study were at the lower end of those reported for chickenpox with complications, median and/or mean cost of hospitalization, ranging from US\$ 338 to 12,819<sup>(6,13,31,33)</sup>. Hospital duration and costs were significantly higher among those with underlying conditions compared to those without. In the US, the overall chickenpox—associated direct and indirect medical costs were estimated at \$400 million/year<sup>(34)</sup>.

Similar to existing literature, the majority of chickenpox-associated hospitalizations in children were among those without any co-morbidity<sup>(6,13,35)</sup>, which highlights the importance of vaccinating against primary varicella infection among susceptible young infants and children to prevent financial burden and varicella-associated morbidities and mortality.

In the present study, the complication rate was 73.3%, which is in the upper range of other reports, ranging from 39.1% to 87.2%<sup>(7-10,14,16,21,25,32,35,36)</sup>. Similar to existing literature, bacterial superinfection of skin lesions, respiratory and neurological complications were the most commonly reported<sup>(5-10)</sup>. The prevalence of neurological involvement in the present study was at the lower end of other reports, ranging from 7-25.4%<sup>(5-8,29,37)</sup>. However, the rate of cerebellar ataxia, an immunemediated, delayed onset complication was rather low in our sample as we included only those who developed complications during the active varicella infection. Although the overall rates of neurological

complications were comparable between children with and without predisposing conditions for severe varicella infection, the more serious neurological complications (e.g. encephalitis, seizures) were detected only among those with predisposing conditions. Another report from Turkey suggested a difference in terms of types of complications between those with and without underlying co morbidities<sup>(6)</sup>. This particular report showed that hematological complications were more commonly observed in children with underlying conditions, whereas secondary bacterial infections and neurological complications were more common among their healthy counterparts. Although our study showed that thrombocytopenia was significantly more frequent among children with predisposing conditions for severe varicella infection, the authors did not detect significant differences in terms of either neurological or respiratory complications between the two groups.

Similar to a previous report, the overall complication rate was high, and significantly higher among otherwise healthy children. However, the distribution of complications were rather different i.e. the rates of encephalitis, hepatitis, thrombocytopenia and disseminated varicella were significantly more frequent among children with immununo-suppression than otherwise healthy children. On the other hand, skin and soft tissue infections were more common in otherwise healthy children albeit not reaching statistical significance. This might be due to the fact that those with uncomplicated varicella among otherwise healthy children were unlikely to be hospitalized, due to the risk of airborne transmission during their hospitalization and their lower risk of disease severity. In addition, immunocompromised children, known to be at high risk for serious complications, were more likely to be hospitalized and treated with antiviral agents as soon as chickenpox was diagnosed, regardless of whether there were complications. In our sample, acyclovir was prescribed during the first 24 hours of admission for all cases with predisposing conditions for severe varicella infection. Furthermore, although the rate of varicella immunization was low in our sample, children with prior varicella immunization were less likely to experience complications during their hospitalization (Table 3) compared to their counterparts.

In addition, as seen in Table 3, more than half of complicated varicella cases were among otherwise healthy children, whereas only 35.2% was among those with any associated co-morbidity and 27% with predisposing co morbidities. This might explain the lack of significant differences in terms of hospitalization

duration and hospital charges between complicated and uncomplicated varicella. Nevertheless, certain serious and/or life-threatening complications, such as encephalitis, hepatitis, thrombocytopenia, and disseminated varicella, occurred significantly more frequently among children with predisposing conditions. The types of complications identified in this study were similar to those reported from both developed and developing countries(4,30,36,39). However, little information is available among less developed countries regarding disease burden and economic impact of the disease and its complications. According to our findings, it is likely that the disease burden, economically and socially, would be comparable or even higher in Thailand, as the rate of complications and hospitalization are substantially higher.

In the present study, only hospitalized primary varicella infection and resulting hospital charges were taken into consideration in the analysis. VZV infection can result in significant morbidities and mortality associated with both primary infection and herpes zoster reactivation. Further, it can incur additional direct costs and productivity loss from inadvertent exposure of vulnerable individuals, including healthcare personnel, in both community and hospital settings<sup>(31)</sup>. Therefore, the cost data obtained from the present study substantially underestimated the true economic impact of overall varicella infection. Previous reports from North America indicated that in the absence of hospitalization, the cost of primary varicella infection was estimated to be US\$313-452 per family(39-41). Data from Canada suggested a substantial economic burden from primary varicella infection. For example, among uncomplicated cases, the average total days missed from daycare and school attendance were 5.6-7.6 and 4.2-5.6 days, respectively(41,42). Among uncomplicated primary varicella infection cases, direct medical costs accounted for only 10% of total costs among children 1-9 years old, as the largest cost driver for patient care was caregivers' productivity loss(41). Nevertheless, the existing economic evaluation of the impact of varicella infection fails to take into consideration productivity loss from inadvertent exposure of susceptible individuals. Therefore, it is likely that the existing estimated economic impact herein is derived from conservative estimates(31).

The present study was undertaken to provide information regarding hospital charges and complications of primary varicella-associated hospitalizations, which have not been previously reported for Thailand. However, our data were collected

from a single tertiary center in the Bangkok metropolitan area, without additional data from other settings or regions, so it is difficult to know the general application of this finding to other parts of Thailand.

#### Conclusion

The high rate of varicella complications and financial burden reported in this study suggest that the severity of varicella complications in children might have been previously underestimated. Overall, varicella accounts for a significant proportion of hospitalizations and financial burden in our setting, and represents an important continuing public health burden.

# What is already known on this topic?

Chickenpox can infrequently cause lifethreatening infection especially among immunosuppressed hosts or young infants. The rates of complications and financial burden among hospitalized cases have not yet well recognized in Thailand as compared to in the industrialized countries.

# What this study adds?

Rates of varicella immunization were rather low in Thai children i.e. 8.6% and 3% among those with and without predisposing co-morbidity, respectively. Approximately three-fourth of hospitalized chickenpox cases had varicella-associated complications with skin and soft tissue infection being the most common followed by pneumonia and neurological complications. Median duration of hospitalization and hospital charge were 6 days and USD 330.2, respectively.

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# Potential conflict of interest

None.

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# ลักษณะทางคลินิกและคารักษาพยาบาลในเด็กไทยที่นอนโรงพยาบาลด้วยโรคสุกใส

# วารุณี พรรณพานิช วานเดอพิทท,์ สิริลักษณ์ จันทร์วีระชัย, สุชาดา ศรีศรัง

ภูมิหลัง: การติดเชื้อ Varicella Zoster Virus ชนิคปฐมภูมิมักทำให้เกิดการเจ็บป่วยที่ไม่รุ่นแรงโดยอาการมักจำกัดอยู่บริเวณผิวหนังหรือเยื่อบุ อยางไรก็ตาม อาจทำให้เกิดภาวะแทรกซ้อนที่รุ่นแรงได้ในเด็กที่มีภูมิคุ้มกันผิดปรกติ, ทารกหรือเด็กเล็ก ปัจจุบันข้อมูลในด้านอาการทางคลินิก ผลการรักษาและภาระ คารักษาในโรงพยาบาลในเด็กไทย ที่เข้ารับการรักษาแบบผู้ป่วยในยังมีจำกัด

วัตถุประสงค์: เพื่อศึกษาลักษณะทางคลินิกของผู้ป่วยเด็กที่นอนโรงพยาบาลค้วยโรคสุกใส เพื่อประเมินความรุนแรงของโรค, ความชุกของภาวะแทรกซ้อน ภาระในการรักษาพยาบาลในด้านของระยะเวลาการนอนโรงพยาบาล และค่าใช้จายที่เรียกเก็บจากโรงพยาบาล (Hospital charges)

วัสดุและวิธีการ: เป็นการศึกษาย้อนหลังเชิงพรรณนา โดยการเก็บข้อมูลของผู้ป่วยเด็กอายุตั้งแต่ 1 เดือนถึง 18 ปี ที่เข้ารับการรักษาแบบผู้ป่วยใน ที่สถาบันสุขภาพเด็กแห่งชาติมหาราชินี กรุงเทพมหานคร ระหวางปี พ.ศ. 2550-2554 โดยรวบรวมข้อมูลทางด้านอาการแสดงทางคลินิก, ภาวะแทรกซอน, ผลการรักษาจากเวชระเบียนและค่าใช้จายที่เรียกเก็บจากโรงพยาบาล จากฐานข้อมูลของโรงพยาบาล

ผลการศึกษา: มีผู้ป่วยที่จำนวนทั้งสิ้น 101 ราย ในเวลา 5 ปี โดยมีค่ามัธยฐาน (พิสัยระหวางควอร์ไทล) ของอายุที่ 4 (0.8, 7.25) ปี พบการเจ็บปวยร่วม ที่เป็นปัจจัยเสี่ยงต่อการเกิดภาวะแทรกซ้อนพองโรคสุกใสในผู้ป่วย 35 ราย (ร้อยละ 34.7) อัตราการเกิดภาวะแทรกซ้อนเท่ากับร้อยละ 73.3 (n = 74) ภาวะแทรกซ้อนที่พบบอย 3 อันดับแรกได้แก่ การติดเชื้อของผิวหนังและเนื้อเยื่ออ่อน ตามด้วยปอดอักเสบและความผิดปกติของระบบประสาท โดยพบเป็นร้อยละ 50.5, 12.7 และ 6.4 ตามลำดับ ไม่พบการเสียชีวิต ค่ามัธยฐานของระยะเวลาที่เข้าร่วมรับการรักษาในโรงพยาบาลและค่าใช้จ่าย ที่เรียกเก็บเท่ากับ 6 (3, 9) วัน และ 330.2 (139.3, 1,013.5) เหรียญคอลล่าห์สหรัฐ (หรือ 9,906 (4,179, 30,405 บาท)) ตามลำดับโดยพบวาเด็ก ที่มีภาวะเสี่ยงต่อการเจ็บป่วยที่รุ่นแรงมีอายุมากกวาเด็กที่ไม่มีภาวะเสี่ยงอย่างมีนัยสำคัญ เด็กกลุ่มเสี่ยงที่นอนโรงพยาบาลด้วยโรคสุกใสเมื่อเทียบกับเด็ก ที่ไม่มีปัจจัยเสี่ยงมีค่าใช้จ่ายประมาณสูงกวา 6 เท่าตัว และนอนโรงพยาบาลนานกวาประมาณ 2 เท่า

สรุป: เด็กที่เข้านอนโรงพยาบาลค้วยใรคสุกใส่ได้พบวามีความชุกของการเกิดภาวะแทรกซ้อนและค่าใช้จายที่ค่อนข้างสูง การศึกษานี้จึงเป็นข้อมูลเบื้องค้น ที่แสดงใหเ้ห็นวาโรคสุกใสอาจก่อใหเ้กิดการเจ็บป่วยที่รุ่นแรง และเกิดโรคแทรกซ้อนได้ในเด็กทั้งที่มีโรคประจำตัวและเด็กที่มีสุขภาพแข็งแรงดีมาก่อน