Original Article

DOI: 10.7860/JCDR/2018/36673.11706

Direct Medical Costs of Kidney Stone: A Retrospective Study

Public Health Section

TRUNG QUANG VO[1], TRAM THUY NGOC NGUYEN[2], THAO QUY THI LE[3], LUYEN DINH PHAM[4], QUANG VINH TRAN[5]

ABSTRACT

Introduction: Nephrolithiasis imposes a weighty economic burden on individuals and their families, the healthcare system, and society. In Vietnam, expenses related to nephrolithiasis are poorly investigated.

Aim: To assess the direct medical cost of treating nephrolithiasis and provide data on the economic burden of kidney stone disease in actual clinical practice in Vietnam.

Materials and Methods: A retrospective costs approach from a hospital perspective was employed. Data was collected from Binh-Dan Hospital – a public hospital in Ho Chi Minh City, Vietnam, to estimate direct medical costs. The Bootstraping method of 2,000 times of resampling was used due to a skewed data.

Results: A total of 57,332 nephrolithiasis patients from Binh-Dan Hospital were enrolled in the study. Throughout the study period, the per-episode direct medical cost of nephrolithiasis in the Inpatient Department (IPD) and outpatient department (OPD) was US$ 532.1 (95% CI, 524.8-539.9) and US$ 50.1 (95% CI, 49.7-50.4), respectively. The two most significant components of direct medical cost were medical procedures (24.7%) and pharmaceuticals (20.2%).

Conclusion: The findings indicate that nephrolithiasis places a considerable economic burden on public healthcare services in Vietnam. Analysis demonstrating the magnitude of the economic impact of nephrolithiasis management in Vietnam's healthcare system may help facilitate health and social policy interventions to improve the prevention and treatment of nephrolithiasis.

Keywords: Direct cost, Hospital, Kidney stone, Nephrolithiasis, Public, Vietnam

INTRODUCTION

Within the last few decades, kidney stone, or nephrolithiasis, has been deemed an important public health concern that impacts a wide range of people worldwide. In particular, more than eight percent of the United State (US) population is currently affected [1].

Various researches has showed that kidney stone disease is becoming more common globally [2,3]. As a whole, Western countries witnessed a higher incidence of nephrolithiasis among the adult population than did those in the Eastern region, despite the fact that the incidence rate was dramatically different among various parts of each country [4]. Nephrolithiasis exacts a significant burden of illness worldwide. The potential risk of stone formation varies in different regions of the world e.g., one to five percent in Asia, five to nine percent in Europe, 13 percent in North America and 20 percent in Saudi Arabia [5]. Romero et al. (2010), reported that the prevalence and incidence of kidney stone formation in Western countries ranged from two to 19 percent, with an increasing frequency among men [6]. Meanwhile, in Asia, China's prevalence of kidney stones in 2017 was estimated to be approximately four percent (4.8% in males and 3.0% in females) [7].

The National Health and Nutrition Examination Survey (NHANES) has shown that the prevalence of kidney stone in 1994 in US was 6.3 percent of males and 4.1 percent of females, and doubled in both genders by 2012 [1]. Data from the 2007-2010 of NHANES showed the rate of the US adult population affected by nephrolithiasis was approximately one out of eleven. On top of that, the longer the years after first occurrence were, the higher the recurrence rate of kidney stone disease would be, which is reported to be approximately ten percent during the first years after occurrence, 50 percent of five to ten years, and 75 percent of 20 years [8].

Reported as a public health problem since the 2000s, with high prevalence and mortality rates, nephrolithiasis places a huge economic burden on the healthcare system. By taking direct and indirect costs together, the total of both is estimated to exceed five billion US dollars (US$) [9,10]. In a study analysing the annual economic burden of nephrolithiasis, indirect costs were estimated to account for US$ 775 million (corresponding with 3.1 million lost workdays per year) among the privately insured [10]. Nonetheless, the true burden of nephrolithiasis predominantly comes from direct costs. In the US, Percutaneous Nephrolithotomy (PCNL) procedures account for a price of US$ 3,624, which is also the highest surgical treatment for this disease [10]. The average expenditures for open stone surgery, Extracorporeal Shock Wave Lithotripsy (ESWL) and Ureteroscopic Lithotripsy (URS) are US$ 2,916, US$ 2,295 and US$ 1,425, respectively [10]. Nephrolithiasis not only affects patients' quality of life but also puts them under financial pressure from high costs of treatment as well as work loss. This is regarded as a pivotal issue, especially in Vietnam and some other countries, since high burdens may consequently deter patients from receiving necessary care.

In Vietnam, the 2017 price data for surgeries and procedures in Hung-Vuong General Hospital, one of the largest hospitals in Ho Chi Minh City, showed that an ESWL procedure costs about US$ 102 whereas the expenditure for laserlithotripsy nearly triples to a cost of US$ 288. Meanwhile, the cost for a PCNL procedure ranges from US$ 350 to US$ 520 [11] {US$ 1 approximately equals 22,450 Vietnam Dong (VND) in 2017} [12]. On top of that, these costs do not consider other direct costs. Even though nephrolithiasis imposes a heavy economic burden on individuals and their families, the healthcare system, and society, nephrolithiasis cost research across the care continuum is lacking in Vietnam.

Thus, this retrospective study was conducted, which particularly concentrated on direct healthcare costs incurred by a population-based sample of people with kidney stones. It was carried out to

analyse hospital-level data from a Vietnamese population of around 57,000 patients at a downtown hospital between 2014 and 2017. To gather evidence on the undocumented economic burden of kidney stone in Vietnam, cost-of-illness study with standardized method was launched to provide researchers and policy-makers with a better understanding of the economic burden for nephrolithiasis disease.

MATERIALS AND METHODS

Study Design: The present study was conducted through a retrospective analysis of previously collected, non-identifiable information, from 2014 to 2017. Obtaining individual consent was not feasible, so patient records were anonymized and de-identified before analysis.

Data Source: Data on patient characteristics and costs over the period (2014-2017) was obtained from Binh-Dan Hospital's electronic database. The computerised information within the database comprises hospital identification (ID), demographic information, socioeconomic status (including age, gender, and health insurance status) and cost component information (including drugs, diagnostic procedures, laboratories, hospitalization, surgery).

Study Population: The data was derived from hospital electronic records of patients with a histopathological diagnosis of kidney stones as well as those hospitalized to receive disease treatment at the Department of Urology, Binh-Dan Hospital between January 2014 and December 2017. The patients were diagnosed with nephrolithiasis according to the World Health Organization's (WHO) International Classification of Diseases Code, Tenth edition (ICD-10). The ICD-10 code for nephrolithiasis is N20.0 (within N20 group), whereas the ICD codes for urolithiasis are much wider, from N20 to N23 [13].

Patients were required to be residents of Vietnam, including foreigners staying in Vietnam, for the duration of the study to ensure that all services could be accurately tracked. Individuals, who did not follow the hospital's treatment, changed the treatment hospital in the middle of the treatment process, or whose medical records were neither saved adequately nor fully available in the hospital database were excluded from this study.

Based on the whole sampling method for the prevalence rate, a total of 57,332 patients were included into the analysing stage. Some patients received re-treatment during four years; however, there were no death as well as lost to follow up cases. Therefore, the summary of the number of patients over the four years was higher than 57,332 due to the duplicated cases.

Cost Components: Direct medical costs comprised of `costs related to physician consultation, bed-days, laboratory tests, image techniques (e.g., X-ray, CT scan), pharmaceuticals (e.g., antibiotics, analgesics, anti-inflammatory, stone-eroding agents, vitamin supplements), medical procedures (e.g., shock wave lithotripsy, percutaneous nephrolithotomy, ureteroscopy), and medical supplies (e.g., bandage, syringe, needle). Patients who were not hospitalised represented zero costs for hospitalization. The breakdown of medical services costs collected during this study was reported in 2017 US$, using the then-current exchange rate of Vietnam (US$ 1 equals 22,450 VND) [12]. Each mentioned cost was calculated by multiplying the price per service by the number of services used. The cost for comorbidities treatment was not included in this study.

Statistical Analysis and Data Presentation: Descriptive statistics were employed to illustrate the characteristics of both insured and uninsured patients in the study population. The characteristics included sociodemographic characteristics, Outpatient (OPD) and Inpatient (IPD) expenses, direct medical costs, Length Of Stay (LOS) and health insurance reimbursement.

As with econometric data, cost distributions were heavily skewed. To solve this problem, the Bootstrap method for resampling with

Characteristics	2014 (N=16,963)		2015 (N=13,761)		2016 (N=16,946)		2017 (N=16,744)		2014-2017 (N=57,332)	
	IPD (n=1,408)	OPD (n=15,555)	IPD (n=1,593)	OPD (n=12,168)	IPD (n=1,702)	OPD (n=15,244)	IPD (n=1,793)	OPD (n=14,951)	IPD (n=5,921)	OPD (n=51,411)
Age (in years)										
Mean±SD	50.6±12.3	46.0±13.5	51.7±12.4	46.3±13.2	52.2±12.2	46.9±13.4	52.5±11.8	47.6±13.3	51.9±12.2	46.4±13.4
Median (Q1-Q3)	51.0 (42.0-59.0)	45.0 (36.0-55.0)	52.0 (43.0-60.0)	46.0 (36.0-56.0)	52.0 (44.0-61.0)	46.0 (37.0-56.0)	53.0 (45.0-61.0)	47.0 (38.0-57.0)	52.0 (44.0-60.0)	46.0 (36.0-56.0)
Range (Min-Max)	80.0 (14.0-94.0)	94.0 (2.0-96.0)	88.0 (6.0-94.0)	93.0 (7.0-100.0)	92.0 (4.0-96.0)	91.0 (3.0-94.0)	85.0 (5.0-90.0)	92.0 (2.0-94.0)	92.0 (4.0-96.0)	98.0 (2.0-100.0)
<30	54 (3.8)	1,711 (11.0)	58 (3.6)	1,168 (9.6)	54 (3.2)	1,433 (9.4)	47 (2.6)	1,246 (8.3)	194 (3.3)	5,216 (10.1)
30-39	228 (16.2)	3,635 (23.4)	217 (13.6)	2,857 (23.5)	204 (12.0)	3,323 (21.8)	193 (10.8)	3,171 (21.2)	773 (13.1)	11,840 (23.0)
40-49	361 (25.6)	4,088 (26.3)	386 (24.2)	3,321 (27.3)	432 (25.4)	4,145 (27.2)	457 (25.5)	3,971 (26.6)	1,482 (25.0)	13,712 (26.7)
50-59	434 (30.8)	3,561 (22.9)	506 (31.8)	2,795 (23.0)	538 (31.6)	3,601 (23.6)	583 (32.5)	3,645 (24.4)	1,873 (31.6)	11,799 (23.0)
≥60	331 (23.6)	2,560 (16.4)	426 (26.8)	2,027 (16.6)	474 (27.8)	2,742 (18.0)	513 (28.6)	2,918 (19.5)	1,599 (27.0)	8,844 (17.2)
Gender										
Male	578 (41.1)	7,240 (46.5)	665 (41.7)	5,649 (46.4)	734 (43.1)	7,351 (48.2)	784 (43.7)	7,412 (49.6)	2,489 (42.0)	24,345 (47.4)
Female	830 (58.9)	8,315 (53.5)	928 (58.3)	6,519 (53.6)	968 (56.9)	7,893 (51.8)	1009 (56.3)	7,539 (50.4)	3,432 (58.0)	27,066 (52.6)
Length of stay										
Mean±SD	9.3±4.5	-	9.2±4.6	-	8.4±5.3	-	8.0±4.5	-	8.7±4.8	-
Median (Q1-Q3)	8.0 (7.0-11.0)	-	8.0 (7.0-11.0)	-	7.0 (6.0-9.0)	-	7.0 (6.0-9.0)	-	8.0 (6.0-10.0)	-
Range (Min-Max)	46.0 (1.0-47.0)	-	49.0 (1.0-50.0)	-	53.0 (1.0-54.0)	-	34.0 (1.0-35.0)	-	53.0 (1.0-54.0)	-
Health Insurance Reimbursement Rate										
0% (Out of pocket)	450 (32.0)	10,311 (66.3)	507 (31.8)	10,380 (85.3)	394 (23.1)	12,415 (81.4)	262 (14.6)	11,539 (77.2)	1,509 (25.5)	39,821 (77.5)
80%	791 (56.2)	4,333 (27.9)	830 (52.1)	1,474 (12.1)	954 (56.1)	2,238 (14.7)	1,159 (64.6)	2,641 (17.7)	3,347 (56.5)	9,320 (18.1)
95%	78 (5.5)	456 (2.9)	103 (6.5)	140 (1.2)	109 (6.4)	235 (1.5)	111 (6.2)	264 (1.8)	368 (6.2)	962 (1.9)
100%	89 (6.3)	455 (2.9)	153 (9.6)	174 (1.4)	245 (14.4)	356 (2.3)	261 (14.6)	507 (3.4)	697 (11.8)	1,308 (2.5)

[Table/Fig-1]: Baseline sociodemographic characteristics of study population with nephrolithiasis in Binh-Dan Hospital throughout the 2014-2017 period {N=57,332, n (%)}
Abbreviations: IPD: Inpatient Department; OPD: Outpatient Department; SD: Standard Deviation; Q1: The 25% quartile; Q3: The 75% quartile

replacement was used. This process was repeated 2,000 times using the percentile method to compute mean values and 95 percent confidence level. Normality of continuous variables relating to costs was tested by the nonparametric one-sample Kolmogorov–Smirnov test. All these continuous variables were non-normally distributed. Thus, the Kruskal–Wallis H test was applied to determine the differences among ≥3 continuous variables. A p-value of less than 0.05 was considered statistically significant. All calculations were executed using Microsoft Excel 2013 for Window® and SPSS® 20.0 (SPSS Inc. Chicago, IL, USA).

Sensitivity Analysis: A one-way sensitivity analysis was carried out to determine the variance of total direct medical costs. Particularly, we adjusted each of the components of cost attributable to nephrolithiasis (except consultation and medical supplies) by ±5%, ±10%, ±20%, ±30%, ±50%, respectively. This would allow researchers and reviewers to assess the impact of these changes in a certain parameter will have on the model's results.

Ethics statement: This study has been reviewed and approved by the ethics committees of Binh-Dan Hospital (No. 114/BVBD-QĐ, date Jan 24, 2018).

RESULTS

Patient Characteristics: All sociodemographic characteristics are shown in [Table/Fig-1]. A total of 57,332 patients with nephrolithiasis participated in this study over the period of four years. The average age standard deviation for IPD and OPD service were 51.9±12.2 and 46.4±13.4, respectively. Considering the IPD service, patients in the 50 to 59 age group (n=1,873) represented the highest percentage, with approximately one-third of the total number (31.6%) of patients. In OPD, the 40 to 49 age group (n=13,712) accounted for the highest proportion (26.7%). IPD patients were older than OPD participants, and study participants were more likely female, which made up a figure of 58.0 percent (n=3,432) and 52.6 percent (n=27,006) for IPD and OPD, respectively, over the study period. Mean LOS in the study period was 8.7±4.8; however, it ranged from six to ten days. Most of the patients receiving IPD treatment had the health insurance reimbursement at 80 percent (n=3,347), representing more than a half of the total IPD patients. Meanwhile, most nephrolithiasis participants in the OPD group (n=39,821; 77.5%) had no insurance.

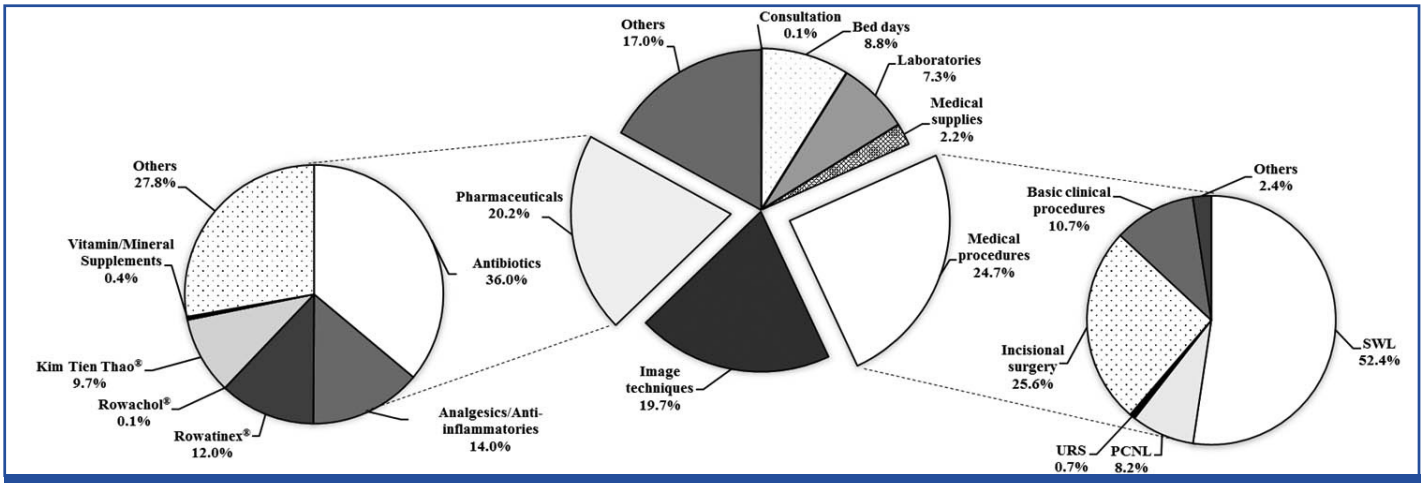
Direct Medical Costs: Per visit absolute costs incurred by those with nephrolithiasis [Table/Fig-2] illustrates the distribution of mean direct medical costs for four years in IPD and OPD by conducting Bootstrap method. The mean total direct medical cost per IPD visit, saw a gradual increase over time, in particular from US$ 415.3 (95% CI, 402.8-429.6) in 2014 to US$ 690.9 (95% CI, 673.9-708.1) in 2017. Likewise, there was a similar trend toward latter group; the mean total medical cost rose from US$ 38.4 (95% CI, 37.8-38.9) to US$ 60.2 (95% CI, 59.4-60.9), corresponding with 2014 and 2017. Both the mean cost per episode of IPD and OPD increased statistically significantly over time (p<0.001 for both), and so did the expenses on components of direct medical cost within the IPD group (p<0.001). The mean cost per visit for each service for the OPD group saw a statistically difference among four years (p<0.001); nevertheless, no statistically difference was identified in mean spending on medical supplies from 2014 to 2017 (p=0.457).

The relative distribution of total attributable costs by components is demonstrated in [Table/Fig-3]. The most significant components of direct medical cost were medical procedures (24.7%) and pharmaceuticals (20.2%). In terms of pharmaceuticals, antibiotics were the group for which cost represented the greatest proportion (36.0%) while that of vitamin/mineral supplements accounted for 0.4 percent, which was the lowest. Meanwhile, among types of medical procedures, more than 50 percent (52.4%) of costs were SWL cost, followed by 25.6 percent for incisional surgery. URS was the type of medical procedure which made up the lowest proportion of costs (0.7%).

The major areas of direct medical costs (consultation, bed-days, image techniques, laboratories, medical procedures, pharmaceuticals, medical supplies as well as others which contain the remaining factors) are summarized in [Table/Fig-4]. This is the description of the total cost and components of cost contributed to nephrolithiasis for the entire study population. Over the period of four years, the total cost of treatment saw progressive growth, with the figures of US$ 1,555,012.7; US$ 1,663,574; US$ 2,395,825.1; US$ 3,054,205 corresponding with 2014, 2015, 2016, 2017. Regarding the entire

Cost components	2014	2015	2016	2017	p-value*
IPD					
Physician consultation	0.9 (0.9-0.9)	1.0 (1-1.1)	1.1 (1.0-1.2)	2.1 (2.0-2.2)	<0.001
Bed days	70.7 (67.7-73.8)	93.6 (90.0-97.1)	98.7 (95.5-102.1)	157.5 (152.1-163.1)	<0.001
Laboratory tests	15 (13.4-16.7)	19.7 (18.2-21.4)	23.0 (21.4-24.5)	32.6 (31.1-34.1)	<0.001
Medical supplies	24 (18.9-33.2)	16.2 (14.7-17.8)	28.7 (26.6-30.9)	39.8 (36.9-43.3)	<0.001
Image techniques	25.3 (22.5-28.1)	36.0 (33.1-39.2)	30.2 (26.7-33.8)	24.0 (21.8-26.3)	<0.001
Medical procedures	117 (115.1-118.9)	123.2 (121.4-125.0)	144.6 (142.6-146.6)	173.6 (171.5-175.7)	<0.001
Pharmaceuticals	70 (64.7-76.2)	80.2 (74.6-86.4)	89.9 (83.6-97.3)	100.4 (92.3-109.8)	<0.001
Others	129.6 (124.5-135.2)	140.5 (135.0-146.2)	137.8 (132.5-143.3)	191.4 (184.2-198.9)	<0.001
Total	415.3 (402.8-429.6)	467.6 (455.5-480.1)	515.0 (502.6-527.9)	690.9 (673.9-708.1)	<0.001
OPD					
Physician consultation	0.7 (0.7-0.7)	4.5 (4.3-4.7)	4.4 (4.3-4.4)	4.3 (4.2-4.4)	<0.001
Bed days	1.8 (1.5-2.1)	1.6 (1.6-1.6)	2.7 (2.6-2.7)	4.4 (4.4-4.5)	<0.001
Laboratory tests	15.3 (15.1-15.6)	16.4 (16.0-16.7)	16.8 (16.5-17.1))	15.9 (15.6-16.2)	<0.001
Medical supplies	0.4 (0.2-0.9)	0.2 (0.1-0.3)	5.4 (3.8-6.9)	4.5 (2.0-9.0)	0.457
Image techniques	15.9 (15.6-16.3)	19.8 (19.3-20.2)	23.2 (22.7-23.7)	22.7 (22.2-23.1)	<0.001
Medical procedures	56.1 (54.9-57.3)	67.2 (66.1-68.3)	69.3 (68.4-70.3)	76.8 (75.9-77.8)	<0.001
Pharmaceuticals	21.1 (20.5-21.6)	18.8 (18.5-19.0)	19.9 (19.7-20.2)	21.3 (21.1-21.6)	<0.001
Others	23.6 (6.9-44.4)	42.8 (42.0-43.6)	66.6 (65.4-67.8)	69.6 (68.6-70.6)	<0.001
Total	38.4 (37.8-38.9)	45.9 (45.3-46.5)	53.1 (52.5-53.7)	60.2 (59.4-60.9)	<0.001

[Table/Fig-2]: Per visit absolute costs incurred by those with nephrolithiasis at Binh-Dan Hospital throughout the 2014-2017 period {2017 US$, Arithmetic mean (95% CI)}
Note: Arithmetic means are calculated by Bootstrapping method; *p-values are determined by Kruskal-Wallis H test
Abbreviations: CI: Confidence Interval; IPD: Inpatient Department; OPD: Outpatient Department



[Table/Fig-3]: Distribution of total economic burden of nephrolithiasis disease at Binh-Dan Hospital throughout the 2014-2017 period.

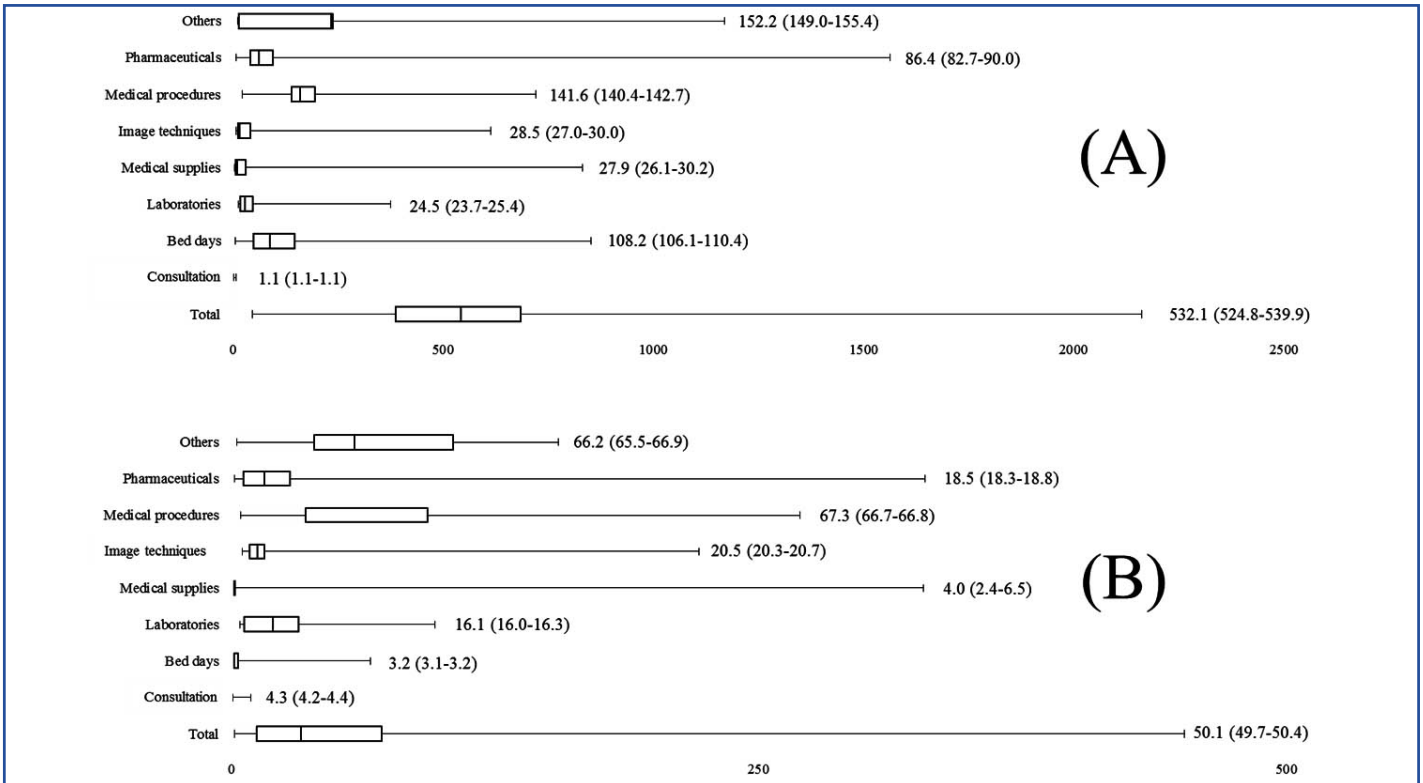
Economic Burden	2014 (N=16,963)		2015 (N=13,761)		2016 (N=16,946)		2017 (N=16,744)		2014-2017 (N=57,332)	
	n	Total cost (%)	n	Total cost (%)	n	Total cost (%)	n	Total cost (%)	n	Total cost (%)
Physician consultation	406	367.4 (0.1)	299	475.6 (0.1)	424	1,317.8 (0.1)	419	1,572.5 (0.1)	1,548	3,733.3 (0.1)
Bead days	1,445	101,523 (6.5)	3,295	157,417 (9.5)	4,980	187,414 (7.8)	5,222	318,154.6 (10.4)	14,942	764,509 (8.8)
Laboratory tests	7,873	120,466 (7.7)	6,730	113,630 (6.8)	10,240	180,531 (7.5)	11,692	216,314 (7.1)	36,535	630,942 (7.3)
Medical supplies	1,433	33,939 (2.2)	1,674	26,448.5 (1.6)	1,869	51,956 (2.2)	2,079	76,829.9 (2.5)	7,055	189,174 (2.2)
Image techniques	20,864	336,652 (21.6)	15,319	315,119 (18.9)	22,119	519,089 (21.7)	23,773	540,374.4 (17.7)	82,075	1,711,234 (19.7)
Medical procedures	5,662	402,282 (25.9)	5,497	458,267 (27.6)	6,572	574,105 (24.0)	6,934	708,827.1 (23.2)	24,665	2,143,481 (24.7)
SWL	406	233,573 (15.0)	299	253,273 (15.2)	424	292,012 (12.2)	419	343,541.1 (11.2)	1,548	1,122,399 (13.0)
PCNL	3,113	20,013 (1.3)	2,839	26,862.1 (1.6)	3,279	48,186 (2.0)	3,370	80,972.5 (2.7)	12,601	176,034 (2.0)
URS	32	2,822.2 (0.2)	50	5,959.1 (0.4)	55	4,127.7 (0.2)	37	3,008.8 (0.1)	174	15,917.8 (0.2)
Incisional surgery	948	92,061 (5.9)	1,058	121,160 (7.3)	1,072	152,287 (6.4)	1,085	183,459.6 (6.0)	4,163	548,969 (6.3)
Basic clinical procedures	2,590	48,358 (3.1)	2,698	36,403.5 (2.2)	3,319	60,955 (2.5)	3,002	83,011 (2.7)	11,609	228,727 (2.6)
Others procedures	71	5,454.2 (0.4)	146	14,609.4 (0.9)	146	16,538 (0.7)	115	14,834.1 (0.5)	478	51,435.3 (0.6)
Pharmaceuticals	15,037	386,018 (24.8)	13,228	349,512 (20.9)	17,041	465,751 (19.4)	18,719	551,906.2 (18.0)	64,025	1,753,187 (20.2)
Antibiotics	7,273	124,651 (8.0)	7,631	145,956 (8.7)	8,516	154,944 (6.5)	9,721	206,917.8 (6.7)	33,141	632,469 (7.2)
Beta-lactam	5,963	91,651 (5.9)	6,463	99,743.4 (6.0)	7,627	112,156 (4.7)	6,078	141,908.6 (4.6)	26,131	445,459 (5.1)
Aminoglycoside	306	3,265 (0.2)	458	3,697.3 (0.2)	267	2,725.4 (0.1)	568	8,229.7 (0.3)	1,599	17,917.4 (0.2)
Quinolone	1,341	12,995 (0.8)	1,131	9,043.5 (0.5)	755	4,910 (0.2)	1,096	8,488.8 (0.3)	4,323	35,437 (0.4)
Others antibiotics[a]	368	16,740.5 (1.1)	643	33,471.8 (2.0)	588	35,152.4 (1.5)	2,970	48,290.7 (1.5)	4,569	131,965 (1.5)
Analgesics, Anti-inflammatories	8,862	46,965 (3.0)	9,097	51,016.4 (3.1)	11,009	67,341 (2.8)	419	80,410.9 (2.6)	29,387	245,733 (2.8)
Rowatinex®	4,029	49,362 (3.2)	3,841	38,378.7 (2.3)	4,990	53,841 (2.2)	5,458	68,959.6 (2.2)	18,318	210,540 (2.4)
Rowachol®	-	-	-	-	-	-	52	457 (0.1)	52	457 (0.1)
Kim Tien Thao®	3,811	75,562 (4.9)	2,657	24,882.4 (1.5)	3,405	31,832 (1.3)	4,248	37,558.8 (1.2)	14,121	169,835 (2.0)
Vitamin Supplement	853	1,476.8 (0.1)	915	2,465.6 (0.1)	786	1,787.3 (0.1)	847	1,430.2 (0.1)	3,401	7,159.9 (0.1)
Others pharmaceuticals	9,063	88,002 (5.6)	9,262	86,812.7 (5.2)	11,577	156,007 (6.5)	11,552	156,171.9 (5.1)	41,454	486,993 (5.6)
Others services	1,349	173,765 (11.2)	2156	242,705 (14.6)	4,413	415,662 (17.3)	5,970	640,225.9 (21.0)	13,888	1,472,358 (17.0)
TOTAL	26,391	1,555,012.7 (100.0)	21,006	1,663,574 (100.0)	29,341	2,395,825.1 (100.0)	30,567	3,054,205 (100.0)	107,305	8,668,617(100.0)

[Table/Fig-4]: Economic burden costs to nephrolithiasis at Binh-Dan Hospital throughout the 2014-2017 period (2017 US$).
Note: n is total number of episode corresponding with each service, not the number of patients used each service; [a]Macrolide, Sulfonamide, Tetracycline, Peptide, and others
Abbreviations: SWL: Shock Wave Lithotripsy; PCNL: Percutaneous Nephrolithotomy; URS: Ureteroscopy

period, total expenditure for the study population (N=57,332) was nearly US$ 8.7 million. It can be seen that there was a noticeable difference among patient-associated costs. In particular, looking at the 2014 to 2017 period, the costs for consultation, bed-days, laboratory tests and medical supplies were US$ 3,733.3, US$ 764,509, US$ 630,942, US$ 189,174, respectively, which could be listed into the low-cost group. Conversely, patients incurred the highest expenses on the remaining services, with US$ 1,711,234 for image techniques, US$ 2,143,481 for medical procedures, US$ 1,753,187 for pharmaceuticals, and US$ 1,472,358 for others.

Throughout the entire study period, the mean direct medical cost of nephrolithiasis in the IPD per episode was US$ 532.1 (95% CI, 524.8-539.9), which was ten times that of OPD patients (US$ 50.1; 95% CI, 49.7-50.4). As shown in [Table/Fig-5], regarding per visit expenses, the 'others' group represented the highest cost, at US$ 152.2 (95% CI, 149.0-155.4). Meanwhile, OPD patients incurred the most costs on medical procedures per visit, with an expense of US$ 67.3 (95% CI, 66.7-66.8).

In the study period, the highest mean total direct medical cost per

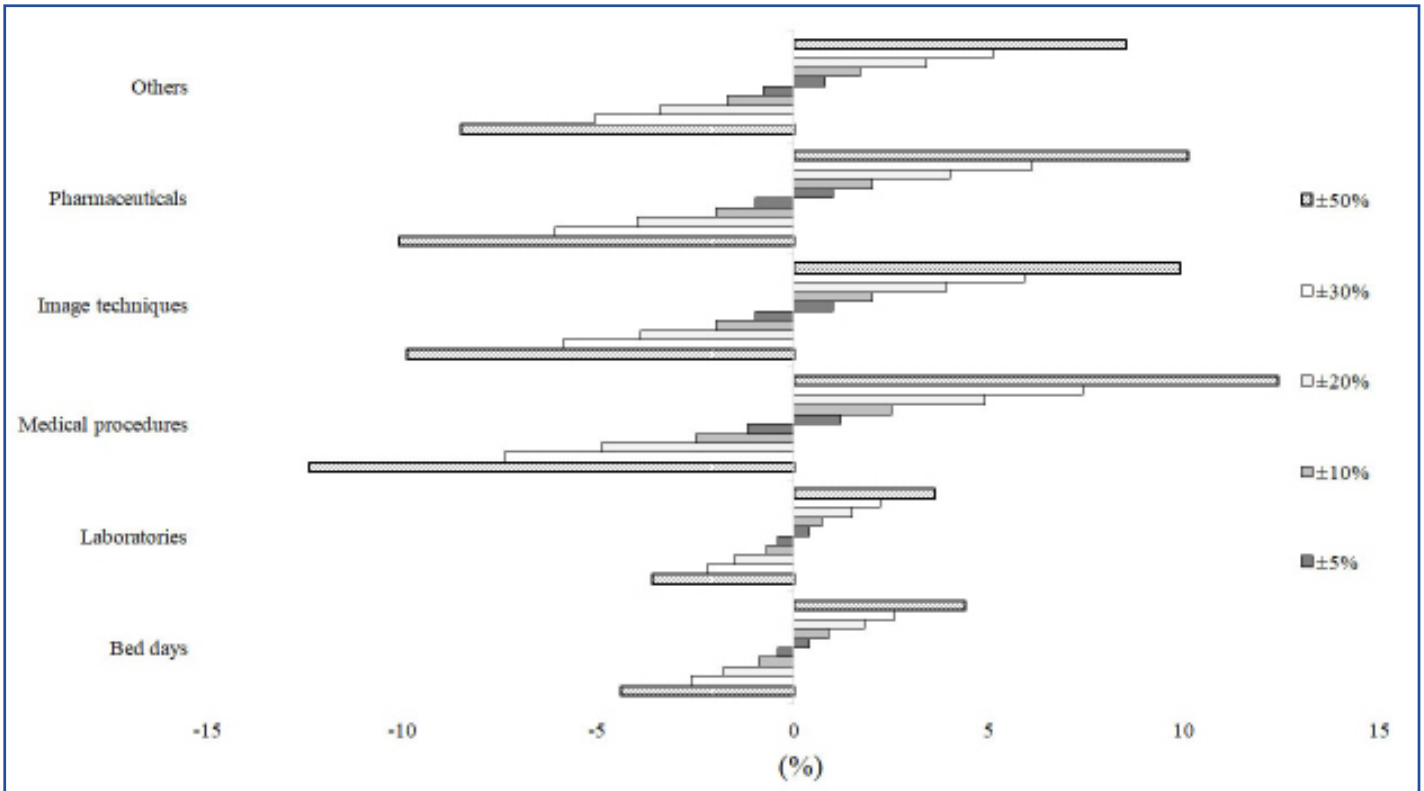


[Table/Fig-5]: Attributable and total cost per visit of patients with nephrolithiasis at Binh-Dan Hospital throughout the 2014-2017 period
(A): Cost per inpatient episode (IPD) {2017 US$, Arithmetic mean (95% CI)}
(B): Cost per outpatient episode (OPD) {2017 US$, Arithmetic mean (95% CI)}

	2014		2015		2016		2017		2014-2017	
	Arithmetic mean (95% CI)	p-value*	Arithmetic mean (95% CI)	p-value*	Arithmetic mean (95% CI)	p-value*	Arithmetic mean (95% CI)	p-value*	Arithmetic mean (95% CI)	p-value*
Age (in years)										
<30	42.1 (38.0-46.6)	<0.001	51.1 (46.9-55.5)	<0.001	55.3 (50.9-60.1)	<0.001	66.6 (61.0-72.5)	<0.001	53.4 (51.2-55.7)	<0.001
30-39	54.1 (51.0-57.7)		64.7 (61.4-68.2)		68.2 (65.4-71.0)		82.0 (77.7-86.6)		67.1 (65.4-69.0)	
40-49	59.0 (56.7-61.5)		75.5 (72.4-78.7)		79.3 (76.5-82.0)		101.0 (97.2-105.0)		79.8 (78.2-81.4)	
50-59	64.0 (61.3-66.8)		90.6 (86.3-94.9)		79.3 (76.6-82.2)		108.4 (104.3-112.6)		89.6 (87.7-91.4)	
≥60	65.2 (61.7-68.8)		96.3 (91.3-101.5)		95.3 (90.8-100.1)		111.2 (106.1-116.9)		93.8 (91.5-96.2)	
Gender										
Male	62.7 (60.7-64.7)	<0.001	83.8 (81.3-86.4)	<0.001	86.8 (84.6-89.1)	<0.001	108.9 (105.8-112.2)	<0.001	86.2 (84.9-87.5)	<0.001
Female	54.2 (52.5-56.1)		73.5 (70.9-76.3)		75.7 (73.3-78.0)		90.1 (87.3-93.0)		74.5 (73.2-75.7)	
Hospital services										
IPD	415.3 (402.8-429.6)	<0.001	467.6 (455.5-480.1)	<0.001	515.0 (502.6-527.9)	<0.001	690.9 (673.9-708.1)	<0.001	532.1 (524.8-539.9)	<0.001
OPD	38.4 (37.8-38.9)		45.9 (45.3-46.5)		53.1 (52.5-53.7)		60.2 (59.4-60.9)		50.1 (49.7-50.4)	
Health Insurance										
0%	50.3 (48.7-51.9)	0.01	55.8 (54.4-57.3)	<0.001	55.2 (54.0-56.4)	<0.001	59.2 (57.8-60.6)	<0.001	55.4 (54.6-56.1)	<0.001
80%	69.9 (67.3-72.6)		145.6 (139.2-151.7)		137.2 (132.7-141.9)		168.1 (162.5-173.8)		125.7 (123.3-128.0)	
95%	67.9 (60.8-75.8)		171.8 (149.1-195.6)		142.5 (129.9-155.7)		166.2 (150.1-185.6)		130.5 (122.8-138.3)	
100%	74.2 (65.2-85.0)		172.2 (155.2-189.6)		163.1 (149.9-177.2)		179.0 (165.0-193.5)		151.0 (143.8-158.3)	

[Table/Fig-6]: Differentials in expenditures per visit of nephrolithiasis patients by familial characteristics at Binh-Dan Hospital {2017US$, Arithmetic mean (95% CI)}.
Note: Arithmetic means are calculated by bootstrapping method; *p-values are determined by Kruskal-Wallis H test among sub-groups within one group
Abbreviations: CI: Confidence Interval; IPD: Inpatient Department; OPD: Outpatient Department

episode (US$ 93.8; 95% CI, 91.5-96.2) was incurred in the senior age group (≥60-year-old), and the lowest costs (US$ 53.4; 95% CI, 51.2-55.7) were incurred in the youngest age group (< 30-year-old) [Table/Fig-6]. However, the 40 to 49 and 50 to 59 age groups accounted for the highest proportion of patients [Table/Fig-1]. Males paid a higher total mean direct cost per visit than females did, with



[Table/Fig-7]: Tornado diagram for one-way sensitivity analysis of attributable and total costs of nephrolithiasis patients at Binh-Dan Hospital throughout the 2014-2017 period.

an average expense of US$ 86.2 (95% CI, 84.9-87.5) and US$ 74.5 (95% CI, 73.2-75.7), respectively. Mean cost per visit among levels of health insurance increased substantially with the level of health insurance, from US$ 55.4 (95% CI, 54.6-56.1) to US$ 151.0 (95% CI, 143.8-158.3), corresponding with 0% and 100% of insurance. All mean total direct medical costs of each sociodemographic group were statistically different (p<0.001).

Sensitivity Analysis: As shown in [Table/Fig-7], cost of medical procedures as well as pharmaceuticals, underwent the greatest variation. Varying the cost of medical procedures by 5%, 10%, 20%, 30%, 50% would yield, respectively, 1.2%, 2.5%, 4.9%, 7.4%, 12.4% changes in total direct medical cost. Likewise, the total direct medical cost of nephrolithiasis would rise by, respectively, 1.0%, 2.0%, 4.0%, 6.1%, 10.1% if the same analysis was carried out on pharmaceuticals cost. The results of sensitivity analysis on this research's cost estimates would contribute to support for health insurance in terms of adjusting costs at an appropriate percentage to reduce the economic burden for patients in the treatment of nephrolithiasis.

DISCUSSION

To the best of our knowledge, this is the first cost-of-illness study for nephrolithiasis in Vietnam. Our results showed direct medical costs related to the management and treatment of nephrolithiasis in Binh-Dan Hospital over the 2014 to 2017 period. In this study, more females than males suffered from nephrolithiasis, although several studies indicate that males usually outnumber females [10,14,15]. This difference might be a consequence of lifestyle-associated risk factors, such as dietaries and comorbidities. The mean ages within study population for IPD and OPD were 51.9±12.2 and 46.4±13.4, respectively; the number of patients in the 40 to 60 age group represented the highest proportion, which is similar to other studies (41.30±16.06) [16,17].

Within the last ten years, a modest number of researches have looked at the direct medical cost of nephrolithiasis, so it was difficult for this present study to give a systematic comparison with the results of similar studies. According to the results of the current study, the total inpatient cost per visit was US$ 532.1 (95% CI, 524.8-539.9), while cost per outpatient visit was significantly lower (US$ 50.1; 95% CI, 49.7-50.4). As expected, the mean total cost per visit increased along with age, particularly from US$ 53.4 (95% CI, 51.2-55.7) in the <30 age group to US$ 93.8 (95% CI, 91.5-96.2) in the ≥60 age group. This might be because of a physical decline in the elderly, and thus they need more care and treatment.

In all four years (2014-2017), males incurred a higher expense per visit than did females, even though more females than males suffered from nephrolithiasis in this study. Regarding the entire study population, all differences in terms of costs among sociodemographic sub-groups were statistically significant (p<0.001). US$ 8,668,617 was the amount of expense patients in this study (N=57,332) incurred between 2014 and 2017. Regarding the components of cost attributable to nephrolithiasis, medical procedures occupied the highest percentage of direct medical costs (24.7%), followed by pharmaceuticals (20.2%) and image techniques costs (19.7%).

This population-based study was based on a large sample size and used the bootstrapping technique, which solved the problem related to the skewness in the cost data. The objectives of public policies predominantly result from attempts to raise general health within the population, not from economic reasons. Assessing the economic impact on the whole community, however, would contribute to decision-making within the public health field. This study, which emphasized direct medical costs, can partly carry on such a pivotal mission. For instance, first, pointing out the non-health consequences of nephrolithiasis will enhance awareness of other interventions, for example, investing in the prevention of nephrolithiasis. Second, combined with studies of the health burden, this study may help prioritize the allocation of resources for prevention or research activities. Finally, this research, with the analysis of direct medical costs of nephrolithiasis within patients from Binh-Dan Hospital, a public hospital that specialized in urology, represents a useful step in the evaluation of the true cost of nephrolithiasis.

This present study also has some limitations. First, it included patients from a single hospital only; therefore, the results cannot be extrapolated to the whole population. Second, due to the lack of data regarding comorbidities, the relationship between comorbidities and nephrolithiasis direct costs were not be analysed.

CONCLUSION

Assessments in term of costs provide critical data for economic evaluations. The results of this study, which analysed direct medical costs for nephrolithiasis at a hospital in Vietnam, could be used as a reference for evaluation of the economic burden of nephrolithiasis in Vietnam's healthcare system. Our study group believes it would play an essential role as a cornerstone which can contribute to help policymakers in managing kidney stone as well as adjusting costs of the disease to reduce the long-term economic burden within the community.

ACKNOWLEDGEMENTS

We wish to thank the hospital authorities for giving us the permission to use data from their archived results for this study. We sincerely say thanks to the healthcare staffs of the Binh-Dan Hospital, Ho Chi Minh City for their co-operation and interest in this study.

DISCLAIMER

The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of any of their affiliated Research Institutions.

Contributors

Contributed essential policy database: TQV, TTQT. Conceived and designed the project: TQV, TTNN. Conceived and designed the analysis: TQV, TTNN, TTQT, LDP, QVT. Conducted the research and performed statistical analysis: TQV, TTNN. Analysed and interpreted the data: TQV, TTNN, QVT. Drafted original manuscript: TQV, TTNN. Edited and revised the paper: TQV, TTNN, TTQT, LDP, QVT.

FUNDING

None.

DISCLOSURE

The authors report no conflicts of interest in this work.

ABBREVIATIONS

CKD: Chronic Kidney Disease, CPI: Customer Price Index, CT: Computed tomography, ED: Emergency Department, ERSD: End-stage renal disease, ESWL: Extracorporeal shock wave lithotripsy, GDP: Gross Domestic Product, ID: Identification, INR: Indian Rupee, IPD: Inpatient, LOS: Length of stay, NHANES: National Health and Nutrition Examination Survey, OECD: Organization for Economic Cooperation and Development, OPD: Outpatient, PCNL: Percutaneous nephrolithotomy, SWL: Shock wave lithotripsy, URS: Ureteroscopy, US: United States, US$: United State Dollar, VND: Vietnam Dong, WHO: World Health Organization.

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PARTICULARS OF CONTRIBUTORS:
1. Lecturer, Department of Pharmacy Administration, Faculty of Pharmacy, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City 700000, Vietnam.
2. Undergraduate Student, Department of Pharmacy Administration, Faculty of Pharmacy, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City 700000, Vietnam.
3. Head of Department, Department of Pharmacy, Binh-Dan Hospital, Ho Chi Minh City 700000, Vietnam.
4. Lecturer, Department of Pharmacy Administration, Faculty of Pharmacy, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City 700000, Vietnam.
5. Undergraduate Student, Department of Pharmacy Administration, Faculty of Pharmacy, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City 700000, Vietnam.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Trung Quang Vo.,
Department of Pharmacy Administration, Faculty of Pharmacy, University of Medicine and Pharmacy at Ho Chi Minh City,
Ho Chi Minh City 700000, Vietnam.
E-mail: voquangtrungdk@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Apr 06, 2018**
Date of Peer Review: **May 04, 2018**
Date of Acceptance: **May 18, 2018**
Date of Publishing: **Jun 15, 2018**