DISTRIBUTION OF THE SIZES OF KIDNEY STONES IN A COMMUNITY

Amorn PREMGAMONE,[1] Eim-on MAIRIANG,[2] Srinoi MASKASEM,[1] Vitoon PRASONGWATANA,[3] Wattana DITSATAPORNCHAROEN[1]

ABSTRACT

Background: Small stone is easy to manage but difficult to diagnose. We aimed to determine the size distribution of kidney stones (KS) in rural community using 256-grey-scale ultrasonography (US) with multiple anatomical approaches.

Method: The modified fist test (MFT) and urine strip test by the urine analyzer(UriluxS S) was performed. The presence of hyperechoic foci (HYF) were considered to be significant when fulfilled with the 3 criteria: i.e., denser, unusual place, and nearby calyectasis.

Results: A total of 1,423 subjects, aged between 18 and 72 years were enrolled and HYF were detected in 606 subjects (42.6%). HYF findings were significantly associated ($p < 0.05$, Pearson Chi-Square) with eight chronic health complaints: myofascial pain, back pain, dyspepsia, arthralgia, fatigue, frank paresthesia, dysuria and any of these aggravated by purine-rich foods. Another four significantly associated variables including: [1] a positive MFT, [2] blood relative with KS, [3] age >45, and [4] the presence of red blood cells. We calculated the expected number of KS in each size by the number of HYF and the figures from part 1. The expected percentage distribution of KS was 54.3, 23.9,13.1, 4.5, 1.7, 1.4 and 1.1 % percent in stone size 5.0, 5.1-7.5, 7.6-10.0, 10.1-12.5, 12.6-15.0, 15.1-20.0 and >20.0 mm, respectively.

Conclusions: We concluded that nine from ten of the KS detected in the community were small (≤10 mm), thus active management at the community level should be the prime concern.

Key words: dyspepsia, hyperechoic foci, myofascial pain, purine rich food, ultrasound

INTRODUCTION

Worldwide, regional differences in the incidence of urolithiasis have resulted in certain high incidence areas being called stone belts1.[1] In Thailand, epidemiological analysis has indicated that stone belts lay over the northern and northeastern regions where incidence is 3 to 5 times higher than in other parts of the country.[2] The patterns of urinary stone disease in Thailand, as in other parts of the world, have changed from a predominance of lower urinary tract or bladder stones to upper urinary tract or kidney stones (KS).[3-5] However, preliminary studies and anecdotal evidence suggests that the burden of stone disease at the community level is more extensive than evidenced in the hospital records. In one epidemiological survey for

[1] Department of Community Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand 40002
[2] Department of Radiology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand 40002
[3] Department of Biochemistry, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand 40002

the prevalence of bladder stones indicated that, for every patient hospitalized for stone removal three persons pass their stones spontaneously and eight have presumptive symptoms.[3] The sizes of stone are the major determinant for the choice of treatment. Stones < 5 mm in diameter have a high chance of passing spontaneously, in comparison with only 50% for those 5-7 mm. KS over 7 mm in diameter usually require urological intervention.[6] Most hospital admitted cases having open stone surgery (OSS) or extracorporeal shock wave lithotripsy (ESWL) represent for only those stones >10 mm. ESWL has become the treatment of choice for most calculi of the upper urinary tract and the need for OSS has declined considerably. However, stone recurrence is often encountered as a long-term problem requiring re-treatment. The rate of recurrence after ESWL varies according to the stone types but the higher is the infected stone. If stone fragments are retained, the re-growth rate is about 33% at 3.6 years.[7] Kosar *et al.*[8] reported that the rate of recurrence was 31.8% within a mean of 40 months in the OSS group, whereas this figure was 13.9% with a mean interval period of 46 months in the ESWL group. However, the mean diameter of KS in both groups reported by Kosar et al. were different (29±8 *vs.* 14±11 mm, respectively). A study in the Northeast Thailand reported a recurrence of 25 and 49 percent at 12 and 24 months respectively after OSS.[9] To gain more understanding of the size distribution of KS and their associated symptoms, we conducted a field survey in 20 rural villages. By simple random sampling, some of these subjects with or without HYF by ultrasonography (US) were sent to the university hospital for unenhanced helical computed tomography(UHCT) for comparisons, and the figures obtained were use to calculate the expected number of different sizes of KS.

MFT = Modified Fist Test
KS = Kidney Stone
HYF = Hyperechoic Foci
US = Ultrasonography
ESWL = Extracorporeal Shock Wave Lithotripsy
UHCT = Unenhanced Helied Computed Tomography
OSS = Open Stone Surgery
HYF = Hyperechoic Foci

METHODS

Sampling Method and Estimation of Sample Size

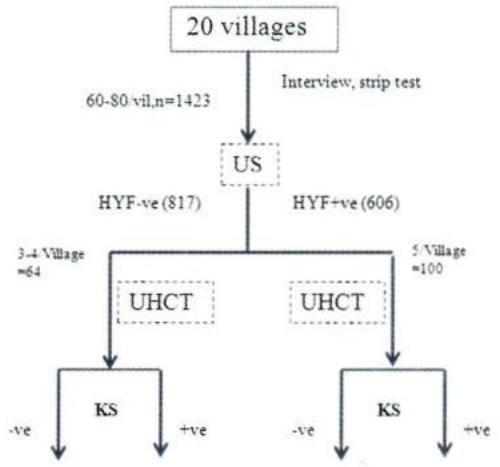
The sample size was calculated based on the purpose to demonstrate the percent distribution of the sizes of small KS, ≤ 5.0, 5.1-7.5 and > 7.5 mm, in the community. We assumed that the 5.1-7.5 mm group was 25% and the worst acceptable value was 20%, so we needed at least 263 KS to answer the question. We estimated that about 50% of HYF detected by US were confirmed as KS, so we had to study at least 526 subjects with HYF. The previous study revealed that the prevalence of HYF in voluntary villager seeking for free examination of urinary stones by ultrasonography was not less than 40%. So the sample size for ultrasonography screening was 1,315 persons (400/0.35). To answer the question about sensitivity and specificity of US as compared to the UHCT, we made the assumption that the sensitivity and specificity was 0.75 and 0.65, respectively. The sample size for detection of the sensitivity and specificity was 73 and 88 kidneys, if we allowed the 0.10 difference. So we needed at least 88 normal kidneys (or 44 negative subjects) and 88 positive kidneys to enrolled in the study. We decided to use 100 subjects with HYF and 64 normal subjects in step 2 of the study.

Data Collection Step1: Screening for HYF

Free US checks for kidney abnormality were offered through the village health volunteer network in 2 districts of Khon Kaen Province in the Northeast Thailand. There were 20 rural villages willing to participate in all the 2 step of the study. Participants in the study joined voluntarily and were interviewed for demographic information and the presence of 9 common multiple chronic health complaints (MCHC), including: [i] myofascial pain, [ii] back pain or lower abdominal pain, [iii] dyspepsia, [iv] arthralgia, [v] headache, [vi] fatigue, [vii] frank paresthesia, [viii] dysuria, and [ix] any of these variables aggravated by the consumption of purine-rich foods (PRF) or alcoholic beverages. Participants had their costo-vertebral angle area repeatedly percussed with equal

force by the examiner's fist to see which side had more dull pain (i.e., a positive fist test). Then each subject underwent a spot urinalysis for the presence of red blood cells (hematuria) and white blood cells (pyuria) using a strip (Combur[10] Test M, Roche, Basel, Switzerland) read by a portable urine analyzer (UriluxS, Roche, Basel, Switzerland). The presence of significant hyperechoic focus (HYF) was determined using 256-grey-scale US scanner with a multiple anatomical approach, which included the prone, decubitus and supine views obtained in the transverse, longitudinal and oblique planes. Characteristically, small stones diagnosed in the present study appeared as a significant HYF with or without acoustic shadowing. It was denser than the renal vascular tissue and its location was not coincide with the distribution of vascular tissue and had related calyectasis. The longest diameter of the biggest HYF was measured and recorded when there were multiple foci.

Fig 1 Details of patients enrolled in the study



KS=kidney stone; HYF=Hyperechoic foci; UHCT= unenhanced helical CT

Step 2: UHCT for KS (Unenhanced Helical Computed Tomography for Kidney Stone)

From the 20 villages willing to participate in step1, we performed the simple random sampling of 5-6 subjects who had the HYF size < 10.1 mm and 3-4 normal subjects for each village for step 2. These subjects were sent for UHCT in the university hospital within 48 hour after screening by US. The radiologist was blind for the US result. The Details of the results in step2 would be in another report. We extracted the rate of positive KS at different sizes of HYF to calculate the expected numbers of KS in the survey. The results are presented as the percents, means (SD). For comparison between groups, the Student-*t* tests and $\chi 2$-test were used. A probability of $p < 0.05$ was considered statistically significant. Logistic regression models were use to investigate the variables associated with HYF.

This study was funded by Khon Kaen University. The protocol was approved by the Ethics Committee of Khon Kaen University (HE 450309).

HYF = Hyperechoic Foci
MCHC = Multiple Chronic Health Complaints
PRF = Purine Rich Foods

RESULTS

Participants

A total of 1,423 subjects (65.8% females) were enrolled in step1. The subjects were between 18 and 72 years of age and were divided into three groups: under 30, 30-59 and ≥ 60 years old. Those between 30 and 59 constituted the largest group (79.2%) (Table1).

HYF findings

US imaging detected significant HYF in 606 subjects (42.2%). When a comparison was made among the groups for the prevalence of HYF, the 60 and over group was the highest (53.7%) while those under 30 was the lowest (18.7%) (Table1). For step 2, we random sampled 103 subjects who had HYF in their kidneys and 3 subjects were unavailable at the appointed time. The total subjects in step 2 was 164, 100 subjects were positive for HYF in at least one kidney (118 positive kidneys HYF and 82 normal kidneys) and 64 subjects without HYF (128 kidneys with negative HYF) were willing to join.

Table 1 Age and sex distribution of participants and ultrasonography findings

Character	Negative n (%)	Positive For HYF n (%)	Total (%)
Sex Male	280(60.3)	193(39.7)	486 [34.2]
Female	497(55.9)	413(44.1)	937 [65.8]
Total	817(57.4)	606(42.6)	1,423 [100]
Age < 30	109(81.3)	25(18.7)	134 [9.4]
30-59	633(56.2)	494(43.8)	1,127 [79.2]
≥ 60	75(42.3)	87(53.7)	162 [11.4]
Total	817(57.4)	606(42.6)	1,423 [100]

( ), % within row; [ ], % within column; HYF, hyperechoic foci

Distribution of HYF sizes and kidney stone sizes

At first we arranged the distribution of the HYF, and then calculated the expected number of KS. The HYF were classified into seven groups according to their sizes (range, ≤ 5.0 to > 20.0 mm in diameter). The average (SD) size of the detected HYF was 5.22 (4.7) mm in diameter: 66.0, 23.6, 6.3, 2.1, 0.8, 0.6 and 0.5 percent were 5, 5.1-7.5, 7.6-10.0, 10.1-12.5, 12.6-15.0, 15.1-20.0 and >20.0 mm. Two-third of the HYF were ≤ 5.0 mm and less than 5% were > 10.0 mm (column 5, Table 2). The step 2 data revealed the rates of detection of KS from the finding of the HYF depend on their sizes, which was 29.5, 48.0 and 100.0% for stone size 5, 5.1-7.5, and >7.5 mm, respectively (column3, Table 2). The percentage of positive KS despite negative HYF was 4.7%. From these figures, we calculated the expected number of stones for each size (column 4, Table 2). After the adjustment, the expected percentage stone size distribution was 40.8, 23.9, 13.1, 4.5, 1.7, 1.4 and 1.1 % in 5, 5.1-7.5, 7.6-10.0, 10.1-12.5, 12.6-15.0, 15.1-20.0 and > 20.0 mm, respectively. For the negative HYF, 39 stones (13.5%) were expected. Only 8.7% of the KS was bigger than 10 mm. From one kidney stone of the size bigger than 1.0 mm found there were more than ten KS or twenty KS existed in the community. The distributions of KS by size after the adjustment are presented in Figure 2.

Association between chronic symptoms and HYF

Our results showed that eight of the nine MCHC parameters, except headache, were significantly associated with the finding of HYF i.e., myofascial pain (odds ratio(OR) = 1.82, 95% confidence interval (CI): 1.44, 2.30), back pain or lower abdominal pain (OR=1.71, 95%CI: 1.36, 2.16), dyspepsia (OR=1.55, 95%CI: 1.25, 1.92), arthralgia (OR=1.43, 95%CI: 1.16, 1.77, dysuria (OR=2.33, 95%CI: 1.84, 2.97), fatigue (OR= 1.32, 95%CI: 1.05, 1.65), frank paresthesia (OR=1.75, 95%CI: 1.35, 2.26) and MCHC aggravated by PRF (OR= 2.34, 95%CI: 1.9, 2.92) (Table 3). Besides the MCHC parameters, there were four other variables which were significantly associated with HYF. These four variables were: the fist test, blood relative with KS, age over 45, and urine RBC. When logistic regression models were performed only two MCHC variables and three other variables were significantly associated with the finding of stones. These were [i] dysuria [(adjusted OR =1.69 (95%CI:1.26 ,2.26)], [ii] MCHC aggravated by PRF [adjusted OR=1.59 (95%CI:1.21,2.09)], [iii] positive fist test [adjusted OR= 2.32(95% CI: 1.76 ,3.04)], [iv] at least one

kidney-stone blood relative [adjusted OR=1.81 (95% CI:1.33,2.47)] and [v] age over 45 years [adjusted OR=1.55 (95%CI: 1.15,2.01)]. MCHC were significantly associated with HYF and pyuria. Subjects with HYF had more chronic symptoms than the ones without HYF (p<0.0001, Student-t tests). The respective mean (SD) of MCHC parameters in subject with and without HYF was 5.1(2.2) and 3.9(2.0). Subjects with pyuria also had significantly (p<0.0001, Student-*t* tests) more chronic symptoms than the one without urine WBC (Table 4). Subjects with HYF had a higher rate hematuria (46.5%) than those without (41.1%); however, the difference was not significant (Table 3).

Fig.1 Distribution of the sizes of kidney stones by US (adjusted by UHCT)

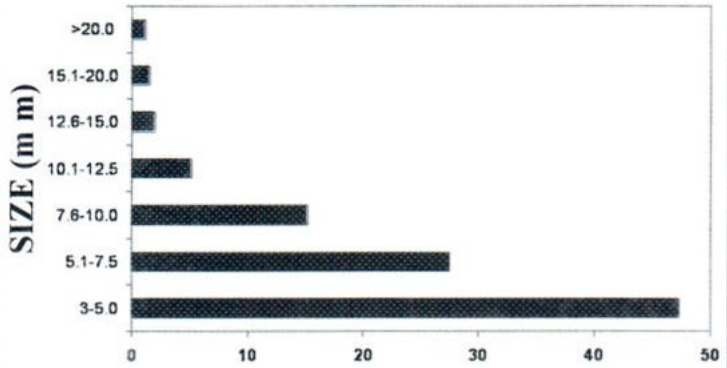


Table 2 Distributions of the sizes of hyperechoic foci (HYF), kidney stones

HYF size (mm)†	No. with HYF, n (%)	%KS (UHCT)‡	Expected No. of KS, n (%)	% Cum. of HYF	%Cum. of KS
Not found	817	4.7	39 (13.5)	0	13.5
? 5.0	400 (66.0)	29.5	118 (40.8)	66.0	54.3
5.1-7.5	143 (23.6)	48	69 (23.9)	89.6	78.2
7.6-10.0	38 (6.3)	100	38 (13.1)	95.9	91.3
10.1-12.5	13 (2.1)	100	13 (4.5)	98.0	95.8
12.6-15.0	5 (0.8)	100	5 (1.7)	98.8	97.5
15.1-20.0	4 (0.7)	100	4 (1.4)	99.5	98.9
> 20.0	3 (0.5)	100	3 (1.1)	100.0	100
Total	06 (100)		§289 (100)		

†, Mean SD = 5.22 4.7 mm;
‡, When unenhanced helical computed tomography (UHCT) is the reference ;
KS, kidney stones; %Cum, Cumulative percent;
§ Prevalence of KS = (100x289)/1423 = 20.3%

Table 3 Association between chronic health complaints, urinary findings, other variables and hyperechoic foci (HYF)

Variable	HYF (%)			OR(95%CI)	Adj OR† (95%CI)
	Neg	Pos	All		
Myofascial pain	61.9	74.8	67.5	1.82(1.44,2.30)	1.28(0.95,1.72)
Back pain	61.5	73.3	66.7	1.71(1.36,2.16)	
Dyspepsia	45.3	56.1	50.0	1.55(1.25,1.92)	
Arthralgia	41.4	50.4	45.3	1.43(1.16,1.77)	
Dysuria	20.1	37.0	27.6	2.33(1.84,2.97)	1.69(1.26,2.26)
Fatigue	28.4	34.3	31.0	1.32(1.05,1.65)	
Frank paresthesia	17.9	27.6	22.1	1.75(1.35,2.26)	
Aggravated by PRF‡	30.6	50.8	39.5	2.34(1.90,2.92)	1.59(1.21,2.09)
Headache	52.8	57.6	54.9	1.22(0.98,1.51)	
Positive MFT§	23.4	45.8	32.6	2.77(2.15,3.57)	2.32(1.76,3.04)
Blood-relative with KS	16.8	27.7	21.4	1.90(1.43,2.53)	1.81(1.33,2.47)
Age >45 years	46.5	60.9	52.9	1.77(1.42,2.21)	1.55(1.15,2.01)
Pyuria	40.3	48.0	43.7	1.37(1.11,1.70)	1.28(0.99,1.65)
Hematuria	41.1	46.5	43.7	1.24(0.99, 1.53)	

† By multiple logistic regression;
‡ Purine rich food; ? Modified fist test

Table 4 Hyperechoic foci (HYF), pyuria and multiple chronic health complaints (MCHC)

Variable		Subjects	No. of MCHC mean (SD)	p-value †
HYF	positive	606	5.1(2.2)	<0.001
	negative	817	3.9(2.0)	
Pyuria	positive	603	4.9(2.1)	<0.001
	negative	780	4.2(2.1)	

†, Student-t tests

DISCUSSION

Summary of Main Findings

The percentage of KS size 5, 5.1-7.5, 7.6-10.0, 10.1-12.5 and 12.6-15.0 mm were 54.3, 23.9, 13.1, 4.5 and 1.7%, respectively. For ten KS in the community, only one was bigger than 10.0 mm, so this showed that the diagnosed KS in the hospital based treatment was only the tip of iceberg when compared with the burden of the disease. More than half of the HYF size < 7.5 mm found in this study was not the KS. The HYF was associated with purine-rich food problems, pyuria, and multiple chronic complaints (dyspepsia, arthritis, myofascial pain, back pain, fatigue and positive Modified Fist Test). The

HYF which was not the KS may be the sludge and can be the nest of bacterial infection.

Where This Fits with Other Literature

The finding also suggesting that the number of nephrolithiasis admitted to the hospital represents a small fraction of the real burden in community. This is similar to a report on bladder stones in the region.[3] The HYF in this study was associated with pyuria and the MCHC. Vrtiska and coworker10 postulated that the HYF might be sludge or milk for uric acid or calcium. The HYF could be a nest for microorganisms and chronic infection, which may be the cause of symptoms in the MCHC. One study reported that all MCHC subsided when treated kidney stones presenting with antibiotic plus Orthosiphon grandiflorus.[11]

The distribution of KS size in this study can explain the variation in the figure of stone prevalence when different instruments were used. If we can use the gold standard UHCT in a survey to detect KS of all sizes, the prevalence rate will be higher than ordinary instruments. The increasing intensity in arthralgia, myofascial pain and dyspepsia after consuming purine-rich foods or alcoholic beverages suggested the subjects might be suffering from uric acid over-production. Hyperuricosuria as a consequence of uric overproduction can promote stones formation by heterogeneous nucleation of calcium oxalate by uric acid crystals or reduction of urine crystal growth inhibitors. Uric acid stones are known to form because of dehydration, excessive sweating, intestinal alkali loss and purine overload or overproduction.[11-13] A study found that 38.4% of urolithiasis in Kuwait had abnormal mineral metabolic screen of which hyperuricosuria accounted for 79.8% of those abnormalities.[14] Primary gout, where urinary pH is low, is associated with uric acid crystallization and stone formation15. In the present study, although the symptoms of gouty arthritis were aggravated by PRF, joint pain was less severe than in overt gouty arthritis and most of the patients were female. Further study about the composition of the kidney stones and purine metabolism in this group of subjects should be undertaken. There was a strong association between the finding of HYF and the pain on percussion at the CVA. Our Modified Fist Test (MFT) was performed as follows: the examiner lightly percussed with his fist 4-5 times on the costo-vertebral area of one side then switched to the other and repeats at least 4-5 times. The subjects who were positive for MFT felt only a small difference in dull pain between sides. The severity of pain was less intense than acute pyelonephritis. The authors want to name this technique the "modified fist test" (MFT). A positive MFT showed the strongest association with HYF (adjusted OR 2.32, 95%CI: 1.76, 3.04).

Strengths and Limitations

This study was the first attempt to reveal the important of small KS and the HYF. The 256 grey -scale US used in this study was widely used in clinics and community hospitals in Thailand, so the result can be generalized for the general practitioners who regularly use the machine. On different point of view, the high resolution US and the better surrounding in the scanning may be more accurate and may alter the percentage distribution of the KS. The authors agreed with this idea and it should be performed where the resources and technologies are available.

This study did not aim to report the stone prevalence, so we did not randomly select the subjects in the enrollment. The 42.6% of HYF (Table 1) and 20.3 % of KS (Table2) in this study does not represent the real prevalence because of the selection bias. The mean (SD) MCHC variables in the subjects with HYF and without HYF in this study was 5.1(2.2) and 3.9(2.0) (Table 4). The participants might choose to join the project because they already had some symptoms of MCHC, which were perhaps related to the presence of stones or HYF in the urinary tract. The true prevalence may therefore be lower if a rigorous sampling technique is implemented.

Implications

The majority of community kidney stones were small, more than half under 5 mm and 90%

under 10 mm, which is crucial for the control of kidney stone via health education in the community level. Subjects with multiple chronic symptoms (MCHC) might have sludge/small kidney stones, so clinicians encountering patient with MCHC should consider the appropriate investigations or treatments.

A history of chronic symptoms aggravated by PRF, the new finding in the present study, should not miss in the history taking process.

MCHC = Multiple Chronic Health Complaints

ACKNOWLEDGEMENTS

The authors thank the Faculty of Medicine, Khon Kaen University for its funding support, Prof. A J Hedley for his valuable comments and Mr. Bryan Roderick Hamman for assistance with the English -language presentation of the manuscript.

REFERENCES

1. Swift Joly J. The etiology of stone. J Urol 1934; 32:541.
2. Unakul S. Urinary stones in Thailand: A statistical survey. Siriraj Hosp Gaz 1958; 13: 199-214.
3. Halstead SB, Valyasevi A. Studies of bladder stone disease in Thailand: III Epidemiologic studies in Ubol province. Am J Clin Nutr 1967; 20:1329-39.
4. Sriboonlue P, Prasongwatana V, Chata K, Tungsanga K. Prevalence of upper urinary tract stone disease in a rural community of north-east Thailand. Br J Urol 1983; 55: 353-5.
5. Yanagawa M, Kawamura J, Onishi T, Soga N, Kameda K, Sriboonlue P, Prasongwatana V, Bowornpadungkitti S. Incidence of urolithiasis in northeast Thailand. Int J Urol 1997; 4: 537-540.
6. Coe FL, Evan A and Worcester E. Kidney stone disease J. Clin. Invest (2005). 115: 2598-2608.
7. Lahme S, Wilbert DM, Schneider M, Bichler KH. Fate of clinically insignificant residual fragment (CIRF) after ESWL. In: Rodgers AL, Hibbert BE, Hess B, Kahn SR, Preminger GM, editors. Urolithiasis 2000. Proceedings of the 9th International Symposium on Urolithiasis; 2000 Feb 13-17; Cape Town (South Africa). Rondebosch (South Africa): University of Cape Town Publishers; 2000. P.748-9.
8. Kosar A, Sarica K, Aydos K, Kupeli S, Turkolmez K, Gogus O. Comparative study of long-term stone recurrence after extracorporeal shock wave lithotripsy and open stone surgery for kidney stones. Int J Urol 1999 Mar; 6 (3): 125-9.
9. Bowornpadungkitti S, Sriboonlue P, Tungsanga K. Post operative kidney stone recurrence in Khon Kaen Regional Hospital. Thai J Urol 1992; 13: 21-6.
10. Vrtiska TJ, Hattery RR, King BF, Charboneau JW, et al. Role of Ultrasound in Medical Management of Patients with Renal Stone Disease.Urol Radiol14: 131-138(1992)
11. Premgamone A, Sriboonlue P, Ditsataporn-jaroen W, Maskasem S, Sinsupan N and Apinives C. A long-term study on the efficacy of a herbal plant, Orthosiphon grandiflorus, and sodium potassium citrate in treatment renal calculi. Southeast Asian J Trop Med Public Health 32: 654-60.
12. FL, Moron E, Kavalieh AG: The contribution of dietary purine over consumption to hyperuricosuria in calcium oxalate stone formers. J Chronic Dis 1976; 29: 793-800.
13. FL, Kavalich AG: Hypercalciuria and hyperuricosuria in patients with calcium nephrolithiasis. N Engl J Med 1974; 291: 1344-1350.
14. Reshaid K, Mughal H, Kapoor M, Epidemiological profile, mineral metabolic pattern and crystallographic analysis of urolithiasis in Kuwait.Eur J Epidemiol 1997;13(2):229-234
15. Gutman AB, Yu TF. Uric acid nephrolithiasis. Am J Med1995; 45: 756-779.