The effect of sex difference on compositions of urinary calculi

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Abstract

To evaluate the effect of sex on the quantitative analysis of urinary calculi, fifty-two calculi were enrolled in this study. Calculi obtained from 52 patients (age 13—55 years)were divided according to the sex of patients. There were 14 urinary calculi isolated from females and 38 were isolated from males. The calculi were subjected to quantitative analysis and sought for calcium, uric acid, phosphorus, oxalate, magnesium, and ammonium ion contents. Significant ($p<0.05$) elevation of oxalate percentage was indicated in calculi of females when compared with that of males. Calcium oxalate calculi were demonstrated to be the most common produced in females while calcium phosphate calculi were predominated in males.

تأثير اختلاف الجنس على مكونات حصى المجاري البولية

الخلاصة

لغرض تقيم تاثير اختلاف الجنس على مكونات حصى المجاري البولية تم تقدير مكونات حصى المجاري البولية تقديراً كمياً.تضمنت الدراسة ٥٢ حصاة(الأعمار للمرضى ١٣ــــ٥٥ سنة) أخذت من٣٨ رجل و ١٤ امرأة مصابين بحصى المجاري البولية. تم تحليل الحصى بطريقة التحليل الكمي واستخدمت البيانات لحساب كلاً من الكالسيوم وحامض اليوريك والفوسفات والاوكزالات وايون الامونيوم . اظهرت نتائج تقدير نسبة الاوكزالات زيادة معنوية في حصى النساء عند مقارنتها بحصى الرجال وكانت حصى اوكزالات الكالسيوم هي الاكثر شيوعاً لدى النساء بينما كانت حصى فوسفات الكالسيوم هي الاكثر في الر جال.

Introduction

Urinary stones are hard masses of crystals formed in the kidney or urinary tract. They have afflicted human kind since antiquity. It would be interesting to know that first evidence of urinary stones dates back to 4800 b.c., when a bladder stones discovered in Egyptian mummy at El Amarh-Egypt (1, 2).

Urolithiasis is a common world problem (3). It is a complex process that involves multiple factors.The calculus is frequently composed of nucleus surrounded by the layers. Uroliths can be found in kidneys, ureters, bladder or urethra. They vary considerably in size from small "gravel like" stones to large "staghorn'" calculi. The calculi may stay in the position in which are formed, or migrate down the urinary tract producing symptomes along the way (4).

The knowledge of composition of urinary stones is important because uorlithiasis is a recurrent disease in many people and preventive measure must be based on such information. Uric acid and cystine stones are relatively insoluble in acidic urine and quite soluble in alkaline urine, phosphate stones are relatively insoluble in alkaline urine and acidification may be theoretically practical in some cases (5).

Most stones consist of calcium, combined with either oxalate, phosphate (or both) and these types of stones account the majority of calculi in the population (6). Ten percent of stones are formed of uric acid and often associated with gout (7-9).

One of the benefits of the quantitative estimation of urinary calculi contents which may improve the protocol regime of treatment. However, in this study we attempted to study the effect of sex on the quantitative contents of urinary calculi.

Materials and Methods

Patients and collection of specimens:

Fifty-two calculi obtained from patients afflicted with urolithiasis were enrolled in this study**.** They were 38 males and 14 females (age 13---55 years). All of them were attended the hospitals of Middle Euphrate province. The study was carried out at the department of Biochemistry, College of Medicine, University of Kufa during 2005-2006.

Chemical and Apparatus:

All laboratory chemicals and reagents were of analar grade. Potassium permanganate, Sulphuric acid, Sodium hydroxide and Sodium hypochlorite, were obtained from Merk Company(United State), Ethylenediamine tetra acetic acid was obtained from BDH Company(England), Nitric acid from Fluka Company(Switzerland). Sodium tungstate from Fisher Company(England), Polyvinyl alcohol and Titan yellow, Ammonium sulphate, and Phenol were obtained from BDH Company, Disodium hydrogen orthophosphate from Fluka Company, Unico UV-2100 spectrophotometer, United products and instruments U.S.A., Julabo Water bath, super-mixer, PH meter, HANA from Italy Company were used during our study.

Collection of specimens:

Stones were obtained by surgery, passed spontaneously or by other endourological procedures(cystoscopy,Dormia basket,..). The calculi were washed to remove any dried blood or other matter, dried in an incubator at 37 Cº, and weighed. The residue after drying was divided into aliquots for chemical analysis. The calculi were subjected to quantitative analysis to determine their compositions.

Preparation of aliquots:

Two aliquots of stone powder were weighed; the first contained 40 mg of such powder. It was mixed with 8 ml of concentrated nitric acid and used for determination of calcium, magnesium, phosphate by conventional methods. The second contained 100 mg of stone powder, it was mixed with 20 ml of ethylenediamine tetra acetic acid (5 %) adjusted at pH 7.8 with NaOH. It was used for estimation of uric acid (10).

Methods:

Calcium concentration was measured in stones of subjects according to the method of Hodgkinson (11). The concentration of calcium calculi was estimated from the equation, calcium (mg /dl) = (At-Ac / Ast-Ab) ×10. Uric acid concentration was measured according to the enzymatic colorimetric method. Uric acid concentration was calculated from the standard curve constructed in the range of 1-6 mg/dl. Phosphorus concentration was measured in stones according to the method of Henry(12). Phosphorus concentration was calculated from the standard curve constructed in the range of 0.5-5 mg/dl. Oxalate concentration was estimated according to the permanganate titration method (13). The concentration of oxalate found in the stones was calculated from the volume of the equivalent potassium permanganate solution. Magnesium concentration was determined according to the titan yellow method (14). Magnesium concentration was estimated from the standard curve constructed in the range of 0.5-2 mg/dl. Ammonium ion concentration was estimated according to the McCullough's modified method, which was based on the indophenol reaction of ammonium ion (15). The concentration of ammonia in a stone sample was calculated as follows: Stone ammonia (µg NH_3- N /100 ml) = (At- Ac / Ast-Ab) × st con.

Biostatatical analysis:

The results were expressed as mean ± SD and analyzed statistically. The difference between the results of sex of patients with urinary calculi was assessed by student's t test. Significant variation was considered when p value less than 0.05

Results and Discussion

To estimate the effect of sex on the compositions of urinary calculi, the enrolled calculi were divided according to the sex of patients. They were 38 males and 14 females.

A higher rate of urinary calculi disease is reported in males than in females, about three males are afflicted for every female.

One of the benefit of urinary calculi analysis in the patients afflicted with urolithaisis is use of such analysis in the explaining the difference in tendency for calculi formation between two sex. Citraturia excretion is higher in females than in males, thus lowering the incidence of urinary calculi formation (16, 17).In addition, the lower risk of urinary calculi formation in female may be due to the decreased urinary saturation with calculi forming salts (18). Curhan et al (19) and Asplin et al (20) demonstrated decreased incidence of urinary calculi formation in females as compared with males.

The student's t test revealed that significant ($p < 0.05$) elevation for oxalate in females when compared with those of males. Calcium, phosphate, magnesium, ammonium, and uric acid did not show any variation during a comparable analysis (table 1).

The reason of these observations may be attributed to the overweight of the patients. However, unfortunately the body mass index was not measured during the period of the project. It has been found a direct proportion between the BMI and urinary oxalate excretion in females. In these patients there is excessive endogenous production or enhanced intestinal absorption of oxalate (20-24). In addition BMI was found to be positively correlated with urinary calcium excretion in males. Some authors mentioned other causes for calcium oxalate predomenancy, Rall et al (25) found associated urinary high uric acid concentration with reduced inhibitory activity of glycosaminoglycans since the latter compounds concentration is more higher in women than in men and considered as naturally inhibitor for calcium oxalate calculi formation.

The determination of the structural formula of the urinary calculi indicated that females are more prone for development of calcium oxalate rich calculi (fig 1) while males are susceptible for the development of calcium phosphate rich calculi (fig 2).The linear regression analysis stated a significant ($r = 0.31$ $p < 0.01$) negative correlation for phosphate with oxalate in males, while in females a similar correlation was obtained with a doubled value ($r = 0.62$, $p < 0.05$) of the correlation factor (figs 3 , 4 and table 2).

Some reports mentioned incompatible data with those reported herein. It has been found a higher average of calcium oxalate in male calculi in comparison with those of female calculi (26).However, it is believed that testosterone increases endogenous production by liver while estrogens decrease urinary oxalate excretion (27). Citrate was found to play several important roles in protecting females against urolothiasis i.e.urine excretion of females for citrate is higher than that of males(28-30).

Changes of uric acid and magnesium ammonium phosphate (struvite) in males and females were found to be insignificant. These results are in agreement with those reported by others (31-35).

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Table 1 Sex differences of urinary calculi compositions.

Parameter	Subjects	Mean ± SD	Range	P value
Calcium	**Male**	**25.56 ± 11.56**	**1.30 – 42.25**	**N.S**
	Female	**28.21 ± 10.64**	**4.30 – 41.00**	
Oxalate	**Male**	**15.38 ± 11.89**	**1.10 – 41.10**	**<0.05**
	Female	**22.36 ± 14.41**	**2.20 – 45.10**	
Phosphate	**Male**	**13.60 ± 9.24**	**0.55 – 41.70**	**N.S**
	Female	**12.85 ± 9.55**	**4.40 – 41.15**	
Magnesium	**Male**	**9.59 ± 9.97**	**0.05 – 29.60**	**N.S**
	Female	**5.31 ± 4.87**	**0.65 – 13.30**	
Ammonium	**Male**	**1.60 ± 0.99**	**0.24 – 4.20**	**N.S**
	Female	**1.41 ± 1.07**	**0.33 – 4.20**	
Uric acid	**Male**	**29.92 ± 25.38**	**1.50 – 98.70**	**N.S**
	Female	**23.71 ± 18.58**	**0.19 – 61.67**	

Table 2 The Correlation of oxalic acid with phosphorus percentage in male and female calculi patients.

		Phosphorus		Oxalic acid	
		R	p	r	p
Males	phosphorus	**–**	**–**	**- 0.31**	**0.01**
	oxalic acid	**- 0.31**	**0.01**	**–**	**–**
Females	Phosphorus	**–**	**–**	**- 0.62**	**0.05**
	oxalic acid	**- 0.62**	**0.05**	**–**	**–**

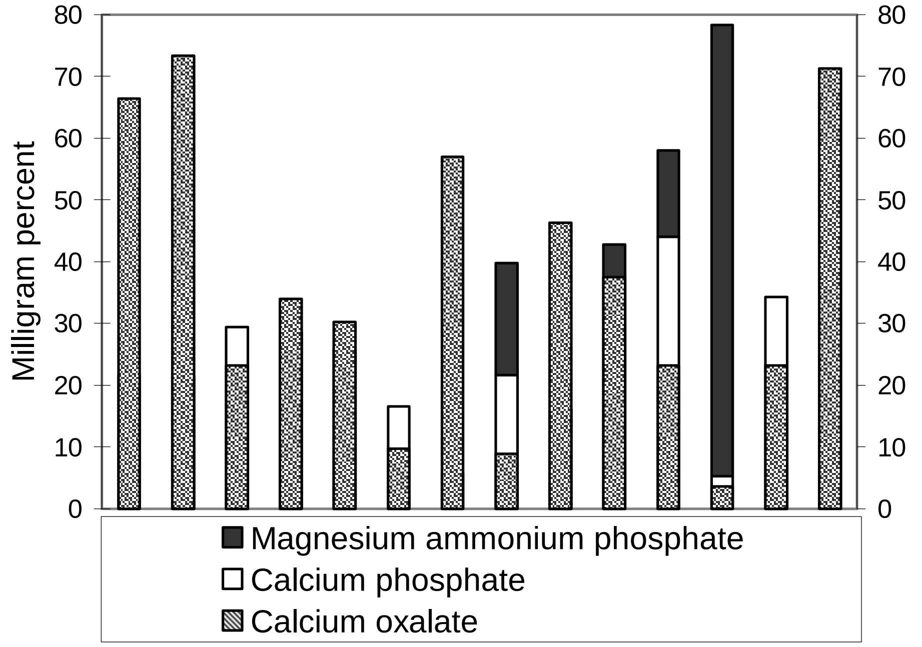

Fig 1 Compositions of calculi (kidney and bladder) from14 female patients, arranged in order of calcium phosphate content.

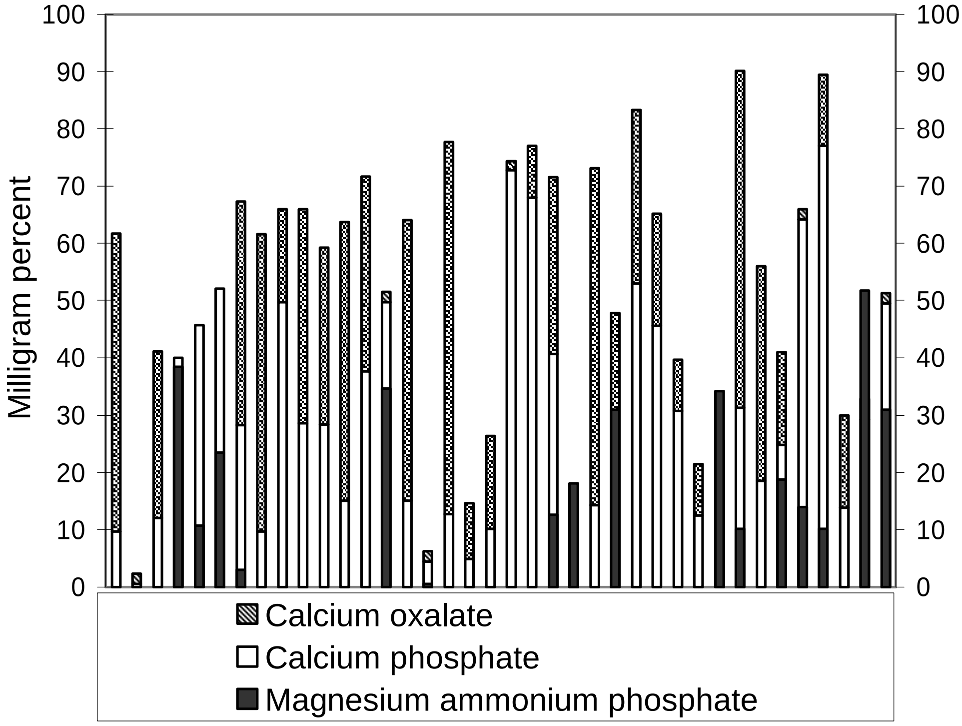

Fig 2 Compositions of calculi (kidney and bladder) from 38 male patients, arranged in order of calcium phosphate content.

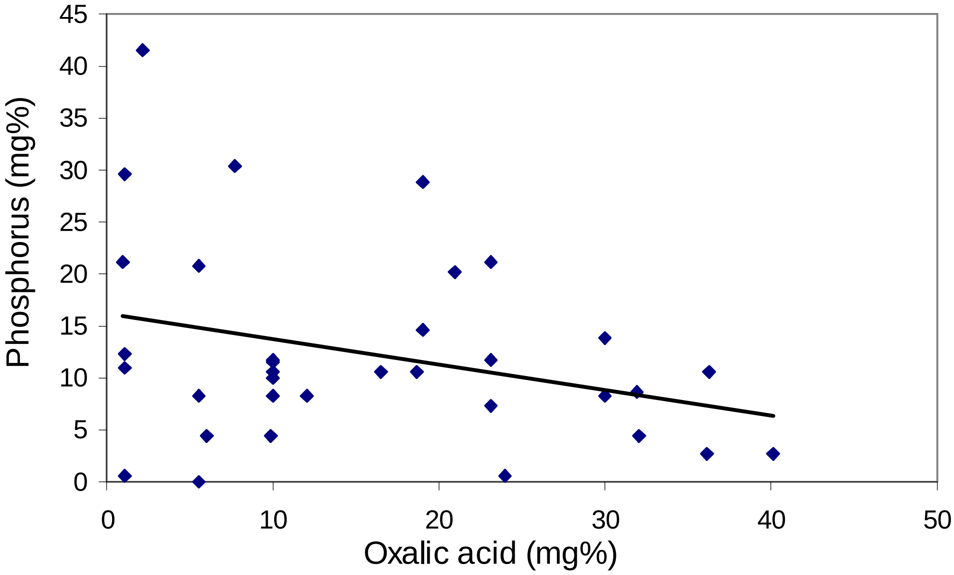

Fig 3 The correlation between oxalic acid and phosphorus contents in calculi of male patients.

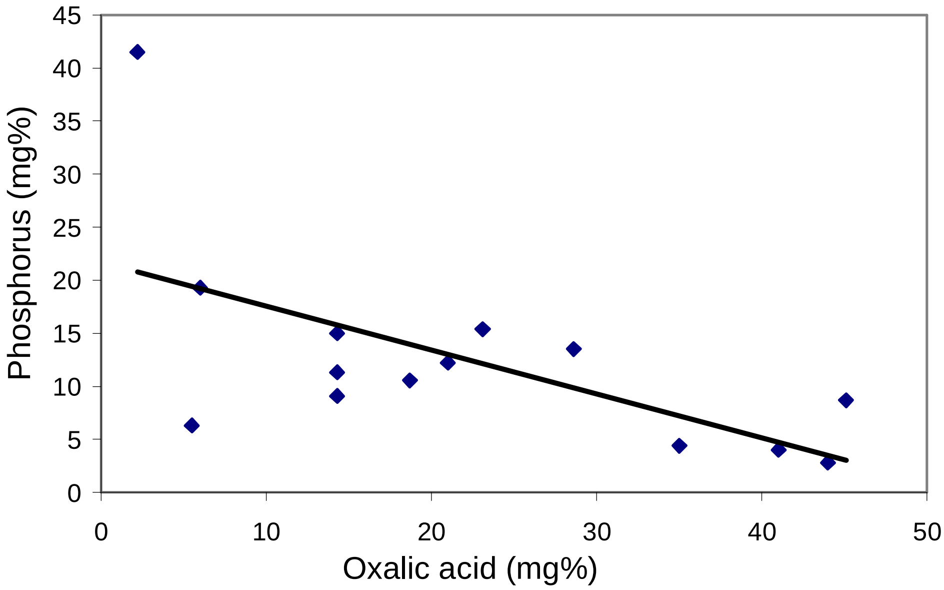

Fig4 The correlation between oxalic acid and phosphorus contents in calculi of female patients.