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PREVALENCE, INCIDENCE, AND ASSOCIATED RISK FACTORS OF UROLITHIASIS AMONG POPULATION OF SALAH-ALDEEN PROVINCE IN IRAQ

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ABSTRACT

Background: Nephrolithiasis is a urological disorder characterized by precipitation of ions and acid salts that combined together in concentrated urine. Diet, climate and occupation are giving rise to excessive sweating , obstruction of urinary tract, urinary tract infection(UTI), crystalluria, inherited disorders (cystinuria, xanthinuria), diseases of general metabolism (gout, hyperparathyroidism, abnormal intestinal absorption…etc) and idiopathic. **Methodology:** A total of 135 patients with urolithiasis were submitted to hospital based series study and 91 of them were males. Data were collected through direct interview using a questionnaire designed for the present study. Relative history was taken and physical examination was done for each patient entered the study who was either admitted to the ward of urology or visited the outpatient clinic of urology. **Results:** The frequency of urolithiasis with respect to family history, poverty, consumption of tape water, July, rural residence, July of the year, rural residence, 41-50 years age group, workers and males was 12.6,74.8, 45.2, 12.6, 54.8, 30.4, 11.1 and 67.4% respectively. Statistical analysis revealed most of the variation among risk factors was significant (P ≤0.5). **Conclusions:** The data presented here revealed a different patterns of urolithiasis with respect to risk factors

compared to the findings demonstrated elsewhere. These variation might be due to local habits and impacts of extreme weather and series of wars that population passed through.

KEYWORDS: urolithiasis, demography, risk factors, Iraq.

INTRODUCTION

Nephrolithiasis is a urological disorder characterized by precipitation of ions and acid salts that combined together in concentrated urine.[1] Most urinary calculi generally are composed primarily of a poorly soluble salt with a small amount of protein containing Ca++ as a main constituent.[2] The direct cause of calculi is mostly unknown and likely to be multifactorial, but urinary physiological abnormalities can be identified in more than 60% of the patients. Hypercalciuria is the most common of these abnormalities which increases the risk of stone formation by raising saturation of stone forming salt and reducing the endogenous stone inhibitors.[3] The prevalence of urolithiasis is approximately 2-3% of general population. The peak age of males is 30 years old, while in the women has bimodal age distribution with peaks at 35 and 55 years old. One kidney stone forms the probability that a second stone will form within 5-7 years in approximately 50%.[4] Stone disease is 2-3 times more common in men than in women and it occurs more often in adults than in elderly and more often in elderly than in children. Urolithiasis occurs more frequently in hot dry areas than in temperate regions.[12] A seasonal variation is also seen with urinary calcium oxalate (CaOx) saturation in men during summer and in women during early winter.[5] Diet, climate and occupation are giving rise to excessive sweating , obstruction of urinary tract, urinary tract infection(UTI), crystalluria, inherited disorders (cystinuria, xanthinuria), diseases of general metabolism (gout, hyperparathyroidism, abnormal intestinal absorption…etc) and idiopathic.[6] Obesity, medullary spongy kidney, associated tumors might cause urolithiasis.[7,8] A family history of kidney stone increases the risk by 3 times, insulin resistant state, history of hypertension, chronic metabolic acidosis and surgical menopause are all risk factors.[9] In postmenopausal women the occurrence of stone is associated with history of hypertension and low dietary intake of Mg++ and Ca++.[10] Incidence of stone is higher in patients with anatomical abnormalities of urinary tract and neurological disease that may result in urinary stasis.[11] Despite these recognized risks, it has been found that patients still have low awareness of kidney disease and its potential safety risks with communication lacking with doctors, which greatly increases the risk of disease.[12,13] It was found that identifying the risk factors associated with renal stones can serve as a valuable reference for

individuals, enabling them to implement preventive measures in their daily lives to reduce the incidence of this condition.

MATERIALS AND METHODS

Patients

This study was conducted in the Urology Department wards and outpatients clinics in Tikrit teaching hospital and in Salah-Aldeen hospital of Tikrit city. A total of 135 patients with urolithiasis were submitted to hospital based series study and 91 of them were males.

Data collection

Data were collected through direct interview using a questionnaire designed for the present study. Relative history was taken and physical examination was done for each patient entered the study who was either admitted to the ward of urology or visited the outpatient clinic of urology. The acceptance for participation in the present study was taken from all the participants whose native language is Arabic. They were not mentally retarded and they were completely healthy considering hearing and speaking. The control group composed of 20 subjects who were looked healthy and from other hand had comparable criteria to the patients and composed of 14 males and 6 females.[14,15]

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics such as means, standard deviations, and frequency distributions were computed to summarize the data.[16,17]

RESULTS

Gender

In this study, 135 patients were included, all of them were diagnosed to have urinary stones by means of clinical, radiological, ultrasound and laboratory investigations. It was shown that 91(67.4%) of them were males (Table 1, Figure 1). Chi-square test did not show a significant association between gender and urinary stone removal status ($\chi^2 = 0.00$, df = 1, p = 1.00).

Table 1: Distribution of urinary stones according to sex and removal of the stones.

Stone removal	Gender		Total No. (%)
	Male No. (%)	Female No. (%)	
Removed	36 (26.7)	18 (13.3)	54(40)
Non-removed	55(40.7)	26 (19.3)	81(60)
Total	91(67.4)	44(32.6)	135 (100%)

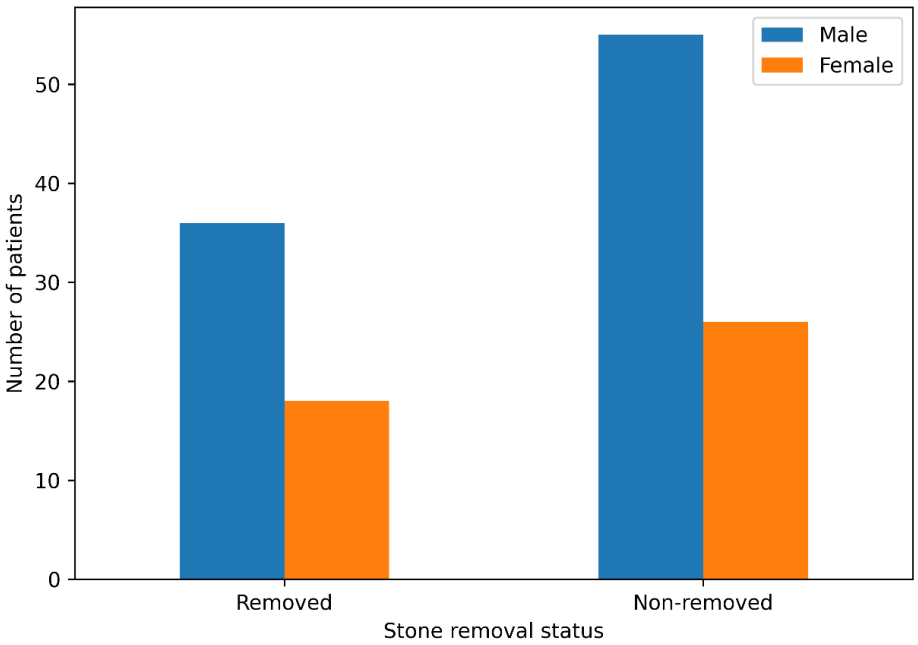

Figure 1. Distribution of urinary stone removal by gender.

Age

The present study showed that the patients included ranged between 2 and 68 years old and the highest frequency of patients was in the age groupof 41-50 years old which constituted 30.4% and the lowest frequency was of age group 11-20 years old (3.7%). The prevalence of urolithiasis in children was demonstrated within age group ≤10 years old was high (15.6%) and there were 3 children with congenital anomalies in the urinary tract. This situation can also be applied on the male patients when the highest percentage was in the age group 41-50 years old with frequency of 20.7% and the lowest percentage was among the age group 11-20 years old with frequency of 3.7%, and for female patients the highest frequency was demonstrated among 41-50 years age group with 9.6% but the lowest frequency was in the age group 11-20 years old (0%) as shown in Table 2. There wa a weak, non-significant linear relationship between age and urolithiasis ($p > 0.05$). The 41–50 year group revealed the highest frequency, but did not follow a linear pattern. The present study showed that the peak incidence of urolithiasis occurred in middle age rather than increasing steadily with age(Figure 2).

Table 2: Distribution of urinary stones according to age.

Age group	Male No. (%)	Female No. (%)	Total No. (%)
≤10	15 (11.1)	6 (4.4)	21 (15.6)
11-20	5 (3.7)	0	5 (3.7)
21-30	7 (5.2)	3 (2.2)	10 (7.4)
31-40	20(14.8)	8(5.9)	28(20.7)
41-50	28(20.&)	13(/9.6)	41(30.4)
51-60	9(6.7)	11(8.1)	20(14.8)
≥61	7(5.2)	3(6.8)	10(7.4)
Total	91(67.4)	44(32.6)	135(100)

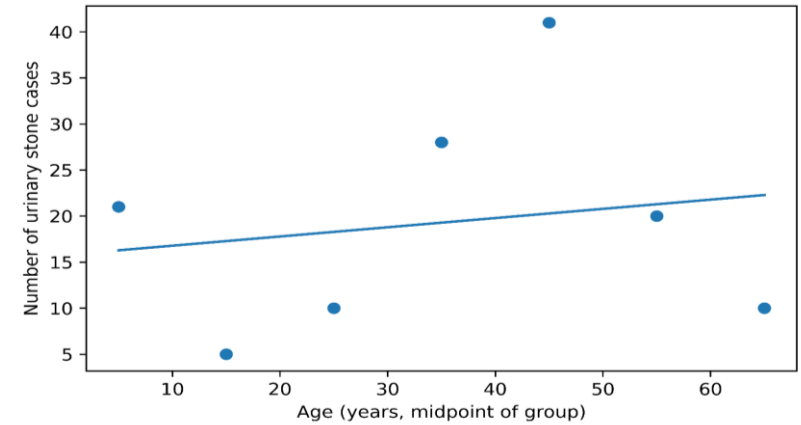

Figure 2. Age-wise distribution of urinary stones with linear regression.

Occupation

The distribution of patients according to their occupation was presented in Table 1.The highest incidence of urolithiasis of male patients was among drivers and the frequency was 15.6%. But the females revealed the highest frequency occurred among housewives with percentage 16.3. Farmer patients with kidney stones composed of 18.5% of the patients tested. Figure 3 of Forest plot demonstrated an odds ratio (OR) of urinary stone occurrence by occupation of male vs female with an overlaid linear regression trend. The dashed vertical line did not reveal gender difference i.e. OR = 1.

Table 3. Distribution of urinary stone patients according to occupation.

Occupation	Males No. (%)	Females No. (%)	Total No.(%)
Farmer	15 (11.1)	10 (7.4)	25 (18.5)
Driver	21 (15.6)	0	21 (15.6)
Policeman	5 (3.7)	0	5 (3.7)
Clerk	4 (3)	2 (1.5)	4 (3)
Teacher	4 (3)	2 (1.5)	6 (4.4)
Student	10 (7.4)	8 (5.9)	18 (13.3)
House wife	0	22 (16.3)	22 (16.3)
Engineer	2 (1.5)	0	2 (1.5)

Workers	15 (11.1)	0	15 (11.1)
Health employer	1 (0.7)	0	1 (0.7)
Others	14 (10.4)	2 (1.5)	16 (11.9)
Total	91 (67.4)	44 (32.6)	135 (100)

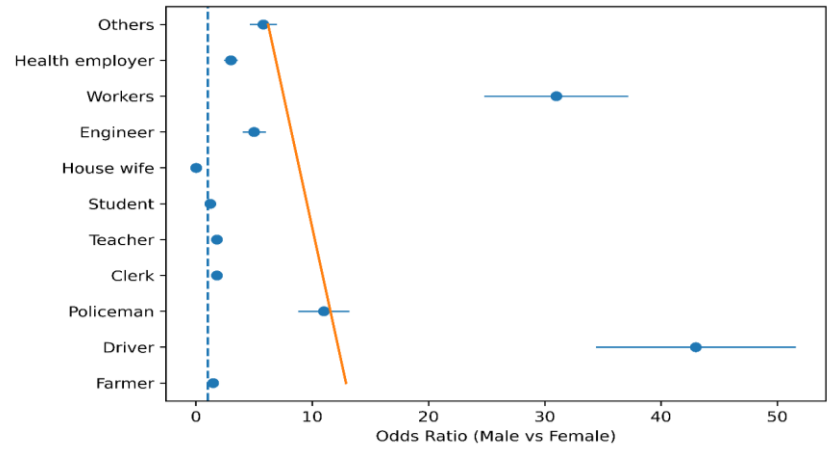

Figure 3. Forest plot of occupation-wise urinary stones with linear regression trend.

Residence

The present data revealed that 45.2% of the patients with urolithiasis were from urban area (Table 4). The Chi-square (χ^2) test of independence did not show statistically significant association between residence and gender incidence of patients with urolithiasis ($p > 0.05$). Both urban and rural populations showed a comparable gender distribution(Figure 4).

Table 4: Distribution of the urinary stones patients according to residence.

Residence	Males No. (%)	Females No. (%)	Total No.(%)
Urban	40 (29.6)	21 (15.6)	61 (45.2)
Rural	51 (37.8)	23 (17)	74 (54.8)
Total	91 (67.4)	44 (32.6)	135 (100)

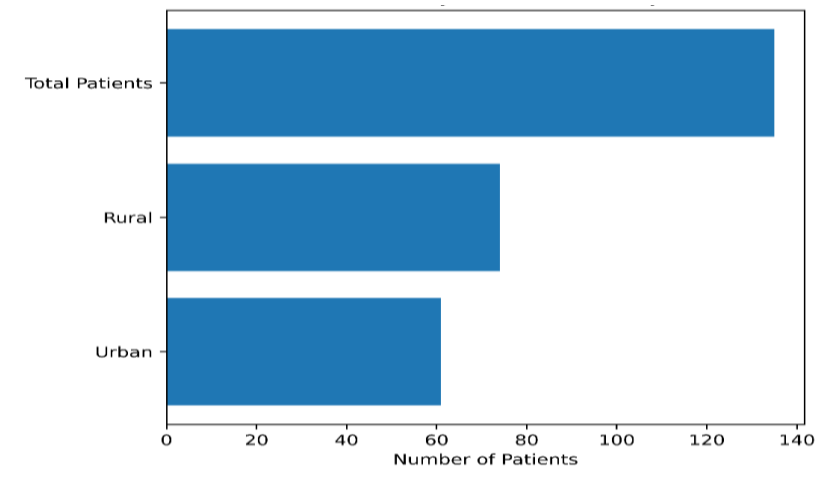

Figure 4. Funnel chart of urinary stone patients by residence.

Family history, economic status and drinking water

The family history of urolithiasis was found among 17 (12.6%) of patients (Table 5, Figure 5). Renal stones were markedly higher in patients without family history. Almost 25% were below the poverty line economic class whereas 74.82% of patients were above the poverty line economic class as shown in Table 5. The present data revealed that majority of urolithiasis patients (45.2%) of patients were consuming tape water whereas 26% of the patients tested utilized raw river water and 28.9% of the patients consumed raw well waters. Linear trend analysis showed a decreasing pattern of urolithiasis presence with positive family history and raw water consumption, but a positive trend was observed with higher economic status.

Table 5. Distribution of renal stones patients according to family history, economic status and drinking water.

Parameter	Variable	No. (%)
Family history	positive	17 (12.6)
	Negative	118 (87.4)
	Total	135 (100)
Economic status	Low	34 (25.2)
	High	101 (74.8)
	Total	135 (100)
Drinking water	Tape water	61 (45.2)
	Well water	39 (28.9)
	Raw water	35 (26.0)
	Total	135 (100)

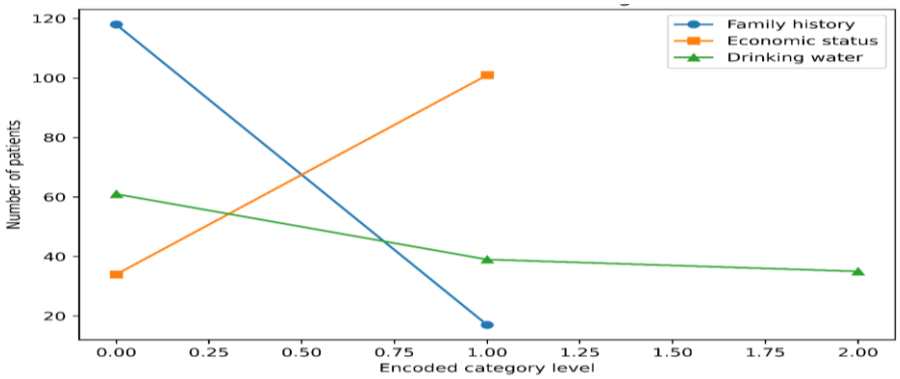

Figure 5. Renal stone distribution with linear regression trends.

Monthly distribution

The distribution of patients with urolithiasis according to months of study was shown in Table 6 and Figure 6. The data collected revealed that the higher frequency of male patients was recorded during hot months particularly July and August with 8.9 and 7.7% respectively.

Whereas the urolithiasis of females was demonstrated among August and September with 3.7% of both of them. Collectively, the highest frequency of 12.6 was recorded during July. Poisson regression showed a significant increase in urolithiasis cases across months (β = 0.057, p = 0.023), corresponding to a 5.9% monthly increase in incidence. Negative binomial regression accounting for overdispersion which showed a similar but non-significant trend (β = 0.054, p = 0.54), indicating variability of monthly recorded cases. Sex-stratified Poisson regression analysis revealed a significant monthly elevation in urolithiasis incidence among males (Incidence Rate Ratio, IRR ≈ 1.07). Females showed a lower and non-significant elevation (IRR ≈ 1.04). Forest plot demonstrated highlights of stronger seasonal and/or monthly effect in male patients, suggesting gender relevant differences in susceptibility to seasonal risk factors.

Table 6. Distribution of renal stones patients according to months.

Season	Males No.(%)	Females No,(%)	Total No.(%)
October	7(5.2)	3 (2.2)	10 (7.4)
November	6 (4.4)	5 (3.7)	11 (8.1)
December	6 (4.4)	2 (1.5)	8 (5.9)
January	5 (3.7)	2 (1.5)	7 (5.3)
February	7 (5.2)	3 (2.2)	10 (7.4)
March	5 (3.7)	3 (2.2)	8 (5.9)
April	7 (5.2)	3 (2.2)	10 (7.4)
May	7 (5.2)	4 (3.0)	11 (8.1)
June	10 (7.4)	4 (3.0)	14 (10.4)
July	12 (8.9)	5 (3.7)	17 (12.6)
August	10 (7.4)	5 (3.7)	15 (11.1)
September	9 (6,7)	5 (3.7)	14 (10.4)
Total	91 (67,4)	44 (32,6)	135 (100)

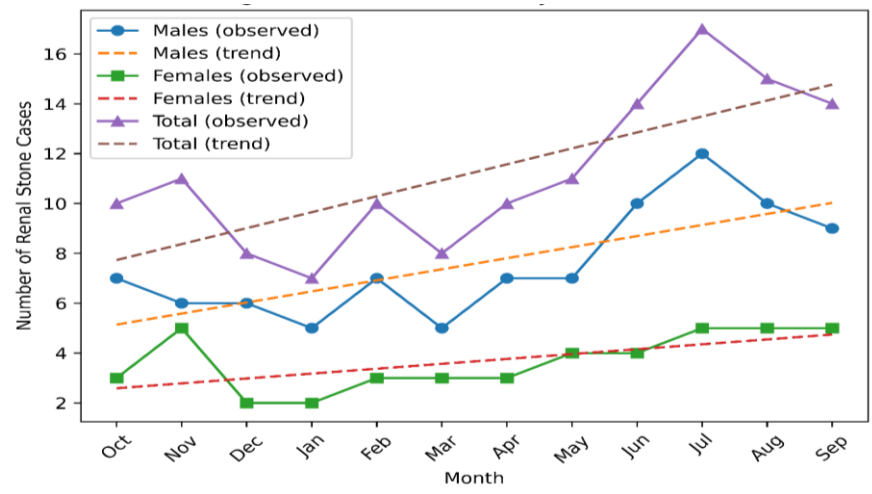

Figure 6. Linear regression trends of monthly renal stone incidence.

Hypertension

The prevalence of hypertension among patients and control was 25.9 and 10% respectively(Table 7, Figure 7). Sex-stratified analysis revealed an elevated hypertension among urolithiasis patients compared to controls of both males and females. It was noticed that female patients revealed a greater proportion of hypertension than males, whereas hypertension was infrequent among controls. Statistically there was no significant difference between the two groups (P> 0.05) using chi-square test.

Table 7. Distribution of renal stones patients according to blood pressure.

Parameter	Patients			Control			Total
	Male	Female	Total	Male	Female	Total	
Hypertension	21	14	35	1	1	2	37
Non-hypertension	70	30	100	13	5	18	118
Total	91	44	135	14	6	20	155

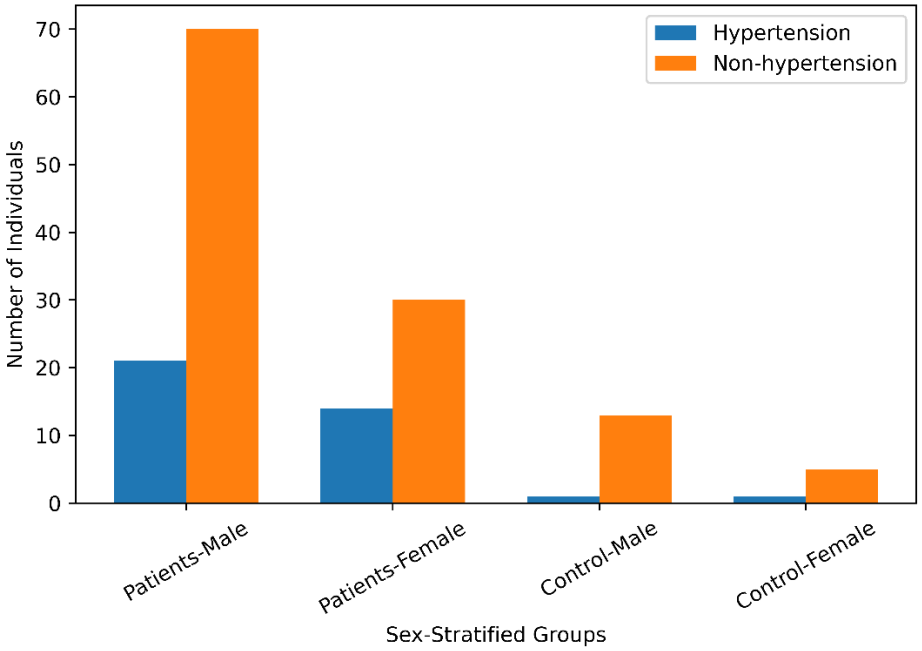

Figure 7. Sex-stratified distribution of hypertension in renal stone patients.

DISCUSSION

The present study showed that prevalence of renal stone was more in males than females with frequency of 57 %. The ratio between both sexes was almost 1.3:1. This results was almost similar to those of Al-Jebouri.[18] Obesity and weight gain with high BMI are considered as risk factors leading to the development of kidney stones among susceptible patients.[19] In the present study, the majority of the patients were obese with high BMI, indicating that obesity was a significant risk factor for kidney stone formation. However, Taylor et al. found out that

obesity may be an independent risk factor for renal stones.[20] Multivariate analysis revealed that obesity was statistically significantly associated with urinary stones.[20,21] Moreover, A BMI gradient trend was observed, with an increasing number of renal stone patients in higher BMI categories, particularly above 30 kg/m², indicating a possible positive relationship between obesity and renal stone occurrence. Flow chart of study design and analysis utilized by the present study demonstrated the following descriptive illustration of renal stone with reference to statistical analysis. Furthermore, other studies demonstrated a relation between body fatness and calculi formation.[22,23,24,25] A positive correlation between BMI and the development of kidney stones was reported in a study carried out by Taylor et al.[26] and Nowfar et al.[27]who concluded a direct association between kidney stone formation and obesity in both males and females. However, usually men have more kidney stones than women which is probably due to of the larger muscle mass as compared to women.[28] The daily break down of the tissue results in increased metabolic waste and a predisposition of stone formation. The other more significant cause is that male urinary tract being more complicated than the female urinary tract.[29,30,31] Moreover, it might be due to hormonal effect like in experimental animals, when testosterone promotes stone formation by suppressing osteopontin expression in the kidney and increasing urinary oxalate excretion. Estrogen seems to inhibit stone formation by increasing osteopontin expression in the kidney and decreasing urinary oxalate excretion. High urolithiasis inhibitory activity where some authors demonstrated increased urinary citrate concentrations in the urine of women. Moreover, the lower risk of stone formation in women may be due to the lower urinary saturation of stone forming salts.[32,33]

The present study shows the peak incidence was in the age group 36-50 years old with frequency of 40% of patients. The lowest percentage in the present study was found in the younger group 20-36 with a frequency of 22% of patients. Moreover, these result were similar to those found by Baker *et al*.[34] who reported that the peak age for the development of calcium oxalate stones ranged between 50 to 60 years of age. However, the incidence of stone formation with age may be correlated with diet and metabolism. The intestinal absorption of many nutrients that influence stone formation, such as calcium, may be reduced in the elderly. In men, the incidence of kidney stones declines markedly after 60 years of age and older stone former is excreted less urinary calcium than their younger counterparts.[35,36,37]

In this study, 78% of the patients were from urban areas. Statistically, there was a significant difference in urinary stone disease distribution according to the residence. These results were almost similar to those found elsewhere.[38] However, locally many people strive for their livelihood by working in construction sites under hot weather where the chances of dehydration are very high.[39] People are usually careless about their daily water intake. Foods containing oxalate and calcium are regular components of the diet in Iraq; thus, calcium oxalate stones are usually predominant in the country, whereas reports of cystine stones are few. Moreover, high protein intake leads to increased uric acid kidney stones because the acid load in the kidney will markedly elevated due to the amino acid purine a precursor of uric acid.[40]

The patients with hypertension had the tendency to develop urinary calculi more than the subjects with normal blood pressure as it was concluded by the present study. This is because hypertension leads to increase Ca^{+2} excretion in urine and there are two theories to explain this phenomena which are the renal calcium (Ca^{+2}) leak hypothesis which means an increase in

urinary excretion of calcium (Ca^{+2}) at each level of sodium (Na^{+2}) output in hypertensive patients. On high salt intake there would be a tendency to sodium (Na^{+2}) retention and as a compensatory. mechanism there will be an increase in arteriolar tone (raise the blood pressure) and increase in venous compliance (shift the blood to the center). This leads to expansion in central blood volume without real increment in total blood volume which could cause an increase in urinary calcium (Ca^{+2}) excretion leading to chain of compensatory mechanisms including secondary.

The examination of the patients in the present study revealed that the patients with positive family history having renal stones was 28% and 72 of renal stone patient have no family history with renal stone. This finding was almost similar to those found by other workers.[41,42] It has been found that genetic factor is very important factor in the etiology of urolithiasis.[43] It was implied that the occurrence of urolithiasis in the same family member may be promoted by living in the same environment along with having similar dietary habits, lifestyles and activities.[44] This emphasizes the contribution of extrinsic factors on stone formation. Nevertheless, genetic susceptibility of renal stone development has been suggested in many researches. Thus people with family history of kidney stones are at higher risk than

those without history.[45,46,47,48] Finally, More rigorous attempts with a larger and more representative population size are needed for verifying the results.

CONCLUSIONS

The data presented here revealed a different patterns of urolithiasis with respect to risk factors compared to the findings demonstrated elsewhere. These variation might be due to local habits and impacts of extreme weather and series of wars that population passed through.

Statement of Ethics

All the procedures involving human participation were conducted in strict accordance with ethical standards of Institutional Research Committee, Department of Scientific Research, Tikrit University as well as the 1964 Helsinki Declaration and its subsequent amendments or equivalent ethical norms.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of Interest Statement

The author declares that he has no conflicts of interest, financial or otherwise.

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