



Study of relationship between gout and infection with various kinds of renal stones in some biochemical variables

Muna H. Jankeer ^{1*}, Huda Y. Al-Attar ¹

¹ Sciences College, Biology Department, Mosul University, Mosul, IRAQ

*Corresponding author: munsbio12@uomosul.edu.iq

Abstract

The current study aimed to investigate the relationship between Biochemical variables which are considered an indicator to kidneys function with uric acid concentration in patients with gout and various kinds of renal stones. This study was included 76 patients (42 males & 34 females) infected in gout and various kinds of renal stones, whose ages ranged (15-75) years, attending to Al-Salam Teaching Hospital and the special laboratories in Mosul city, the patients whose cases were diagnosed by the specialist physicians. Moreover, 50 healthy of both sexes with the same ages of patients were used a control for comparison. The results showed a significant increase in concentration of each of uric acid, urea, and creatinine, associated with a significant decrease in conc. of each of the total protein, albumin, and calcium but showed non-significant decrease in conc. of globulin in compared with control. The results also showed existing of a strong (+) relationship between conc. of uric acid and conc. of each one of urea and creatinine in the male patients, but that relationship was found strong (+) between conc. of uric acid, and conc. of each one of total protein, and albumin was found with the female patients. While, rest of the studied Biochemical variables showed no relationship between them and uric acid. In this study, 90 stones were collected from those patients after surgical operations, or after dropping of the stone with the urine involuntarily, so the results showed that the high ratio of the infection with pure calcium oxalate stones at 23.3%, stone of pure uric acid at % 17.9, cystine stones at 15.6%, stones mixed with each of calcium oxalate and uric acid, stones mixed with pure calcium and calcium oxalate at the ratio of 10%, then the ratio of the stones composed of pure calcium reached 6.7%. We concluded that infection with gout and increasing conc. of uric acid led to infect in uric acid stones and other kinds of stones indicating to existing of metabolic dysfunction in the kidneys and urinary system.

Keywords: gout, renal stones, uric acid, biochemical variables

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INTRODUCTION

Gout (king's disease) is considered a chronic disease the most common one in what is called crystal arthritis, whereas it causes the males usually, thus they are more subject to be caused in it, and the females are subject to be caused in it after menopause. (Virsaladze *et al.*, 2007; Benjamin *et al.*, 2008; Klipple *et al.*, 2008). Gout is caused by increasing in conc. of uric acid in the blood serum of human being as a result of disorder purine metabolism, that is considered as the final product for the purine catabolism which share with nucleic acids component in liver, then excreted out of the body in the urine (Choi *et al.*, 2005; Nelson & Cox 2013; Saigal & Agrawal, 2015; Alosami *et al.*, 2019). Uric acid is considered of non-enzymatic antioxidants, and more than half of the antioxidants in the blood coming and producing from it (Heining & Jahnson, 2006). And it is considered as a basic indicator of gout, and its existing

in the serum helps in its diagnosis, whereas in the natural position uric acid is solved in the blood and excreted from the body through the urine excretion, but when its conc. increases more than normal rang, it leads to hyperuricemia in blood, gout is infected in (Siagal & Agrawal, 2015). One of the most important reasons for its increasing in the blood is known through decreasing the ability of the body to secret it through the urine and increasing the metabolism of the nucleic acids, causing its accumulation in the body tissues, also increasing which is taking place in the consumption of foods that are rich with the purines (like red meats and sea foods) which change to uric acid and increasing of its composition in the body for physiological or hereditary

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reasons (Klippel *et al.*, 2008). The high levels of uric acid in blood lead to deposition in tissues in form of crystals sodium urate salts, that cause arthritis especially on thumb, toe, or joints (Choi *et al.*, 2005; Virsaladze *et al.*, 2007).

Renal diseases (Nephritis) happens as a result of the renal filtration rate decrease of the uric acid because of the renal failure. Therefore, stones of the uric acid are the most spreading in the males associating usually the gout representing (5-10) % of the stones approximately (Marchini *et al.*, 2013; Cary & Curhan, 2017). Renal stones disease is considered one of the most common diseases that causes the urinary system in the males and females, whereas its spreading in the males more than the females. (Khurshid & Sharif., 2017). The stones are deposits formed in the kidney in form of micro particles resulting from crystallization of some urine components which in some natural cases are being solved in it. Many cofactors are working collectively or separately collaborate to prepare the circumstances for composing the nidus (Stoller, 2004). Renal stones differ in their sizes, and forms to be round, quinary, sinous, coarse, and the camel's horn. (Cavendish, 2008). Various kinds of stones are composed in the body of the human being, the most common of which in the world are the four kinds namely, calcium stones or often that related to the calcium oxalate or with phosphate as calcium phosphate, whereas those stones appear as a result of defect in the metabolism each of calcium and phosphate in the body and hypercalcemia and high and oxalate conc. in the urine (Moe, 2006), then uric acid stones, reasons of their composition were mentioned previously, cysteine stones and struvite stones. Thus, their spreading out increased continuously in the 20th century all. (Tamsaitye *et al.*, 2013)

Aim of this study:

Investigate the relationship between the Biochemical variables that are considered an indicator to kidney function with conc. of uric acid in the patients with gout and various kinds of renal stones, through introducing to the relationship between conc. of the uric acid and changes occurring in conc. of proteins and the nitrogenous compounds (urea, creatinine, and uric acid) in serum of those patients.

MATERIALS AND METHODS

Collection of Specimens

The current study included 76 patients suffering from gout and various kinds of renal stones form both sexes (42 males, and 34 females), whose ages ranged (15-75) years, attending to Al-Salam Teaching Hospital and the special laboratories in Mosul city, those patients after, tested by the diagnosticians, after their Infection was confirmed with renal stones depending on X-ray, Ultrasound ray, and general urine examination. Fifty healthy as control (25 males and 25 females) of the

Table 1. The methods used for estimating the number of biochemical variables in present study

Measured biochemical parameters	Method used	Reference
Uric acid conc.	Urease enzymatic method	Newman & Price, 1999
Urea conc.	Enzymatic method	Fawcett & Soctt, 1960
Creatinine conc.	Colorimetric method	Tietz, 1999
Total protein conc.	Biuret method	Gornall <i>et al.</i> , 1949
Albumin conc.	Bromocresol green method	Doumans <i>et al.</i> , 1971
Globulin conc.	According to the following law: Total protein – albumin	Richteich, 1969
Calcium conc.	Colorimetric method	Moorehead & Briggs, 1974

same age, after being sure of being not Infected in any case that effects on the results of the studied Biochemical variables.

Biochemical Tests of Blood Serum

The vein blood specimens were collected from the healthy and patients, and the blood was isolated to obtain the serum for estimation the conc. of some Biochemical variables by using methods of estimation referred to in **Table 1**, as a number of ready test were used from international companies such as French Biolabo company and BioMerierax company to estimate the conc. of those studied variables.

Collection of Renal Stones Specimens

Ninety stones were collected from those patients after surgical operations were made or when those stones were dropped involuntarily with urine, then each stone was put in a sterile bottle washed with the distilled and sterile water twice, then dried with 37°C for 12 hours and pounded by using the mortar to obtain its powder, then the quality of each stone was limited by using the stone analysis equipment from the French Biolabo company depending on the specific chemical method. (Winer *et al.*, 1943, Winer, 1959).

Statistical Analysis

Results were analyzed statistically by using program ready (SPSS) version 19 for window, whereas T. test was used for showing the difference between two groups at the probability level ($P \leq 0.001$ and $P \leq 0.05$), moreover for finding the linear correlation coefficient to find the relationship between the uric acid and the studied Biochemical variables of the patients. (Kik wood, 1988).

RESULT AND DISCUSSION

1. Relationship of Gout Infection with Sex and Age

The results in **Table 2** showed that the ratio of gout infection and various kinds of renal stones male cases was higher than that of the female cases, whereas it was with males 43%, but with females was 18% in gout. Thus, these results are agreed with the findings of (Conen *et al.*, 2004; Hak *et al.*, 2010; Kang *et al.*, 2017).

Table 2. The effect of sex on the ratio of infection gout in patients with various kinds of renal stones

Studied groups	Males		Females	
	No.	%	No.	%
Presence of Gout	18	43	6	18
Absence of Gout	24	57	28	82

Table 3. Ratio of infection gout in patients with various kinds of renal stones as age group and for both sexes

Sex	Males				Females			
	Presence of Gout		Absence of Gout		Presence of Gout		Absence of Gout	
Age group (year)	No.	%	No.	%	No.	%	No.	%
15 – 30	2	11.1	14	58	-	-	14	50.0
31 – 45	4	22.3	2	8	1	17	4	14.3
46 – 60	6	33.3	4	17	2	33	6	21.4
61 – 75	6	33.3	4	17	3	50	4	14.3
Total	18	100	24	100	6	100	28	100

Table 4. Concentration of some biochemical variables in serum of patients with gout disease and various kinds of renal stones compared with control of both sexes

Groups Variables (Conc.)	Control * (n= 50)			Patients (n= 76)		
	Mean \pm SE	% Conc.	% Change	Mean \pm SE+	% Conc.	% Change
Uric acid (mg/dl)	5.455 \pm 0.189	100	---	7.947 \pm 0.230 **	146	46+
Urea (mg/dl)	29.850 \pm 1.589	100	---	36.245 \pm 3.009 **	121	21+
Creatinine (mg/dl)	0.815 \pm 0.510	100	---	1.410 \pm 0.951 **	173	73+
Total protein (g/dl)	6.775 \pm 0.934	100	---	6.413 + 0.138**	95	5-
Albumin (g/dl)	4.025 \pm 0.106	100	---	3.855 \pm 0.127 *	95	4-
Globulin (g/dl)	2.750 \pm 0.114	100	---	2.557 + 0.761 NS	93	7-
Calcium (mg/dl)	9.210+ 0.128	100	---	8.234 \pm 0.156 *	89	11-

* Significant difference between control at (P \leq 0.05)
 ** Significant difference between control at (P \leq 0.01) NS: non-significant difference.

Hence, many studies indicated that the males infected ratio was higher than that of the females, the difference relates to the hormones such as estrogen, it is considered one of the factors which reduces the infection and leads to take of uric acid with the urine outside the body, and increasing of gout infection after menopause happens when estrogen hormone level

reduces (Alexandre et al.,2005; Mader, 2008; Hak et al., 2010).

2. Relationship of Gout Infection with Age

The results in **Table 3** showed that the high ratio of the gout infection in the males of age group ranged (46-60) and (61-75) years, that reached 33% whereas the ratio with the females of the same group age (46-60) and (61-75) years reached 33% and 50% respectively. It became clear from those results that the ratio of gout Infection with renal stones patients increases on the basis of age for both sexes, whereas the results of this study are agreed with previous studies concluded. (Roddy, et al, 2007; Weaver, 2008; Hussien, 2011) indicated to the increasing took place in the infection ratio with the females of the old age group after menopause.

3. Effect of Infection with Gout and Various Kinds of Renal Stones in Some Biochemical Variables

The results in **Table 4** showed a significant increase of conc. in each of: uric acid, urea and creatinine, associated by a significant decrease of conc. in each of: total protein, albumin, and calcium, but conc. of globulin showed non-significant decrease in the blood serum of patients infected with gout and various kinds of renal stones in comparison with conc. of those variables in serum of the healthy control.

Thus, the results in **Table 5** showed increase of conc. in each of uric acid, urea and creatinine in serum of the male and female patients infected in gout and various kinds of renal stones within approximate ratios, that means of increase ratio estimated at: 40%, 46% and 41% for males respectively, but also increase of ratio with females estimated at 47% ,46%, and 43% respectively in comparison with the healthy males and females. While, those results showed a significant decrease of conc. in each of total protein, albumin, globulin and calcium in serum of the male patients of the ratio 8%, 7%, 9%, and 7% respectively, and showed a non-significant decrease conc. of those studied variables in serum of the female patients infected in gout and various kinds of renal stones in comparison with the healthy males and females.

Table 5. Concentration of some biochemical variables in serum of patients with gout disease and various kinds of renal stones compared with control males and females

Groups Variables (Conc.)	Males						Females					
	Control (n= 25)			Patients (n= 42)			Control (n= 25)			Patients (n= 34)		
	Mean \pm S E	% Conc.	% Change	Mean \pm S E	% Conc.	% Change	Mean \pm S E	% Conc.	% Change	Mean \pm S E	% Conc.	% Change
Uric acid (mg/dl)	5.82 \pm 0.266	100	---	8.166 \pm 0.32 **	140	+40	5.090 \pm 0.225	100	---	7.505 \pm 0.280 **	147	+47
Urea (mg/dl)	25.60 \pm 1.299	100	---	37.29 \pm 4.935 *	146	+46	24.1 \pm 2.233	100	---	35.2 \pm 3.013 *	146	+46
Creatinine (mg/dl)	0.79 \pm 0.152	100	---	1.114 \pm 0.151 *	141	+41	0.84 \pm 0.476	100	---	1.20 \pm 0.102 *	143	+43
Total protein conc. (g/dl)	6.85 \pm 0.703	100	---	6.314 \pm 0.206 **	92	-8	6.70 \pm 0.175	100	---	6.535 \pm 0.177 NS	98	-2
Albumin (g/dl)	4.24 \pm 0.127	100	---	3.968 \pm 0.196 *	93	-7	3.81 \pm 0.144	100	---	3.752 \pm 0.151 NS	98	-2
Globulin (g/dl)	2.61 \pm 0.143	100	---	2.376 \pm 0.723 *	91	-9	2.89 \pm 0.175	100	---	2.782 \pm 0.127 NS	96	-4
Calcium (mg/dl)	8.98 \pm 0.151	100	---	8.39 \pm 0.22 *	93	-7	9.44 \pm 0.188	100	---	8.058+0.218 NS	85	-15

The results of this study are consistent with the conc. increase of each one of uric acid, urea, and creatinine with many studies (Luk & Simikin, 2005; Chen, 2009; Hussien, 2011; Sagiroglu et al., 2012; Humaish et al., 2016; Curhan, 2017; Jawad, 2017; Ajeel & Al-Mahdawi, 2018a; Al-Taii, 2020), those studies indicated to the reason of uric acid increasing that causes a deficiency of renal function, that can be inhibited of the vital utilization of nitric oxide in the endothelial cells, whereas the hyper increase in uric acid leads to a quick advancement in renal diseases, the renal stones are composed also as a result of uniting of calcium salts with the oxalate. (Khosla et al., 2005; Cirillo et al., 2006; De Oliveira & Burini, 2012). That is due to the large dysfunction the kidney as to the two processes namely secretion firstly and absorption secondly, leading to increasing in its conc.: a weakness in the renal function as a minimum limit. Moreover, the other reasons and the most common indicate that the gout is associated with some diseases including: renal stones, hypertension, cardiovascular diseases (Papachristou et al., 2002; Salih, 2012; Jawad 2017).

These studies indicated also to the reason of that increasing in the urea conc. belongs to a disorder in kidney function because it is the responsible for taking urea in the urine, therefore in infection of deficiency, disorder, or shortage function of the kidney that leading to a shortage in urea taking off that gathering and accumulating in the blood, then its conc. increasing (Zilva et al., 1989; Berl & Schrier, 2002). Beside, increasing of urea level in the blood serum represents the renal dysfunction and secreting disorders then the quick formation of urea, also this increasing depends on average of taking the proteins and their degradation, non-abundance of some persons by the nutrition system, and taking a large quantity of proteins lead all to increasing its level. (Schrier & Gottshalk, 1997) Those studies indicated to the reason of increasing in conc. of creatinine in serum leading to infection with renal disease that cause to fixed and continuous decreasing in the average of the glomerular filtration and creatinine release (Kirtane et al., 2005), creatinine conc. (which is non- protein nitrogen compounds) in serum a measure of glomerular filtration rate, and an indicator of the renal functions. (Perrone et al., 1992), and the most dependable than urea to reverse renal functions. Because creatinine can be filtrated in the glomerular fully and it can not be absorbed again then can not be subject to the tubal secretion. (Berl & Schrier, 2002; Schrier, 2008). Thus, increasing of creatinine leads to decreasing in the average of glomerular filtration and influx of the blood to the kidney, then increasing in absorption each of sodium and water again, that lead all to hypertension resulting from the contraction of the blood vessels in the kidney because of motivation of secretion of angiotecin and adrenal gland. (Schreir, 2008).

The results of this study showed a decrease in the conc. of the protein, albumin, and globulin in the serum of the patients, whereas those results are identical with what many researchers concluded (Al-Khafaji 2004; Khurshid & Sharif, 2017; Ajeel & Al-Mahdawi, 2018b). Cavendish (2008) indicated that accumulation of oxalate in the kidney leads to renal disorder and dysfunction causing an infection of decrease in the level of proteins in blood, or the reason may attributed to the increasing of taking off the proteins because of the damage caused by the stones to the tissues of the kidney, or because of using the amino acids (building units of proteins) in the process gluconeogenesis from building glucose from non-carbohydrate sources, leading to decrease in the level of proteins in serum, or the cells may resort to use the alternative sources of the energy existing in the body such as proteins and fats, causing increase in the process of compensation for the amino acids for energy production, resulting in composing a considerable amounts of urea as a casual product (Guyton & Hall, 2010).

Moreover, composition of stones in the kidneys weakens their functions which is considered an additional factor contributing to decrease albumin in serum through increasing its taking off average with the urine. Whereas (El-Nahas et al., 2007) indicated that losing of albumin considerably with the urine represents an indicator to a damage in the tissue of the kidneys resulting from continuous composition of the renal stones. Schianchi & Borghi (2002) indicated both that retention of the water in the bodies of those patients infected in renal stones because of renal dysfunction is considered a basic factor of albumin conc. decrease in the blood serum.

The results of this study showed a non-significant decrease in the conc. of the globulin in serum of the patients in comparison with the healthy, this decrease belongs to the chronic cases in renal stones composition affecting on the functions of the kidneys negatively and causing a lack in the number and efficiency of the general. Renal units in the kidneys, causing renal deficiency. Whereas, the blood proteins taking off average increases including globulins because of the disorder in the process of filtration (Al-Khafaji, 2004)

4. Relationship Between Uric Acid and Some of Biochemical Variables in Blood Serum of Patients Infected in Gout and Various Kinds of Renal Stones

To find the relationship between uric acid and some of Biochemical variables in the male and female patients, average linear correlation coefficient could be found. Thus, the results appeared on **Table 6** a positive and strong relationship between the conc. of urea and creatinine of the male patients, therefore the value of correlation coefficient was (+ 0.289) and (+0.279) respectively, but there was no relationship between uric

Table 6. The relationship between the concentration of uric acid and some of biochemical variables in serum of patients of males and females with gout disease and Various kind of Renal Stones

Variables (Conc.)	Sex	Males	Females
		Uric acid (mg/dl)	Uric acid (mg/dl)
Urea (mg/dl)		+ 0.289	- 0.179
Creatinine (g/dl)		+ 0.279	- 0.067
Total protein (g/dl)		+ 0.336	+ 0.077
Albumin (g/dl)		+ 0.214	+ 0.243
Globulin (g/dl)		+ 0.285	- 0.161
Calcium (mg/dl)		+ 0.147	- 0.089

acid and rest of Biochemical variables reason of which may belong to the relationship uric acid, urea, and creatinine with renal diseases.

Thus level testing each of creatinine and urea are used to evaluate functions of the kidneys. Because they are taken off from the kidneys basically, therefore they find out average of glomerular filtration (renal filtration) which is considered of clinical importance because it is an indicator of functions of the kidneys. Therefore, when their two levels mean decreasing of glomerular filtration average 50% (Jose & Salazar, 2014).

The results in **Table 6** also showed a strong (positive) relationship between conc. of uric acid and each of total protein then albumin in the female patients, whereas value of correlation coefficient was (+0.77) and (+0.243) respectively, but there is no relationship between uric acid and rest of the variables studied in the female patients. Those results show that the males have high conc. in each of urea and creatinine because they are stronger in the muscles and skeletal system than the females (Delanghe, 1989).

5. Numbers and Kinds of Various Stones Diagnosed in the Patients Infected with Gout

Ninety stones were collected in the present study from the patients infected in gout after being subject to the surgical operations or after dropping the stone involuntarily with the urine. The results in **Table 7** showed that high infection ratio was of the stones of pure calcium oxalate kind estimated 23.3% , followed by the stones composed of the pure uric acid the ratio of which was 17.9%, then cysteine stones 15.6 % , stones of mixture composed of calcium oxalate with uric acid 10%, the same ratio of mixture composed of pure calcium with calcium oxalate stones, then stones ratio composed of pure calcium 6.7% only, but the rest stones ratios was less than ratio and various kinds as shown on **Table 7**.

The results of this study are identical with what Al-Jawadi (2002) concluded to know the kinds of the stones in which the renal stones patients infected in Mosul city, whereas that study showed that 62.8% of stones

Table 7. Numbers and Kinds of Various stones diagnosed in the patients infected with gout after surgical operations or after dropping the stone involuntarily with the urine

Kind of stone	Number	%
Pure calcium	6	6.7
Pure calcium +calcium oxalate	9	10.0
Pure calcium + cysteine	3	3.3
Calcium oxalate + Uric acid	9	10.0
Calcium oxalate + Calcium phosphate	3	3.3
Calcium oxalate	21	23.3
Calcium phosphate	3	3.3
Calcium carbonate	3	3.3
Uric acid	16	17.9
Cystine	14	15.6
Magnesium ammonium phosphate	3	3.3
Total	90	100

belonging to calcium oxalate kind 26.8% of uric acid, 9.5 % phosphate kind, and 0.5% of cysteine kind. The results of this study are consistent with the findings of Hadad (2009) in study conducted on Biochemical analyses of urinary traces stones (urolithiasis) in Nineveh governorate, whereas stones ratio of pure calcium oxalate was 41.1%, pure uric acid stones was 35.3%, and calcium phosphate was 33.3 % . Stones are composed of complex physiological processes (metabolic disorder) include relatively basic factors the most important of which are responsible by: hyper saturation, crystallinity catalysts and inhibitors (Al-Jawadi,2002). The common stones in the world are of four kinds: calcium stones, uric acid, cysteine and struvite.

Infection ratio in these kinds differ according to the geographical location, nutrition systems followed by the nations, climate, and the level of health care. There are many possible factors, lead to infection such as the relative variety especially in the semi-crystal characteristics, anti-organic crystallinity in the urine, in addition to the nutrition factors which limit the pattern of changing in the infection ratio. Also, the average of its repetition increases in case of existing a metabolic disorder or structural malfunctions in the urinary system (Nass et al., 2001, Hadad, 2009). Then, the reason for increasing infecting ratio in pure uric acid stones may belong to the high conc. of uric acid in the serum of the patients infected in gout under study as it is shown in each of **Table 4**.

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