Relationship between Uric acid, creatinine, Urea and Triglyceride production in Gout

Abstract

Background: Gout is a disorder that manifests as a spectrum of clinical and pathologic features built on a foundation of an excess body burden of uric acid, Hyperuricemia and gout are two of the most common metabolic diseases, there has been an increase in the prevalence and has attracted attention as an adult lifestyle-associated disease.

Objective: The present study was carried to determine the prevalence of goat and uric acid, creatinine , urea , and triglyceride production in patients with hyperuricemia .

Materials and methods: Cross sectional studay was done to examine associative between (November 2017 to February 2018). Totally 66 patient attended from (Hawler Private Hospital, Rezgari Governmental Hospital, Ankawa Private Laboratory) in Erbil and may have hyperuricemia can be developed to gout disease from both males (32) and females (34) .the age 18 up to 70 wew included in this study. Biochemical tests were performed for all patients (uric acid test, urea test, creatinine test, triglyceride test). These samples were analyzed by using blood serum, not depended on urine analyses.

Results: In male statistical analysis showed that significant correlation between high uric acid and age , the age group (41-60) years was significantly higher compared to other age groups ($P < 0.05$), and in female statistical analysis showed that significant correlation between high uric acid and age, the age group (61-80) years was significantly higher compared to other age groups ($P < 0.05$). In male statistical analysis showed that significant correlation between high creatinine and age , the age group (41-60) years was significantly higher compared to other age groups ($P < 0.05$), in female statistical analysis showed that significant correlation between high creatinine and age, the two age groups (41-60) & (61-80) years were significantly higher compared to other age group ($P < 0.05$). In male statistical analysis showed that significant correlation between high urea and age, the age group (41-60) years was significantly higher compared to other age groups ($P < 0.05$), in female statistical analysis showed that non-significant correlation between high urea and age groups ($P > 0.05$). In male statistical analysis showed that significant correlation between high TG and age , the age group (41-60) years was significantly higher compared to

other age groups ($P < 0.05$), in female statistical analysis showed that non-significant correlation between high TG and age groups ($P > 0.05$).

Conclusion: gout is a very common form of arthritis that may be increasing in prevalence as a result of changes in diet, lifestyle and environmental factors. Although not life-threatening, it has a significant impact on quality of life. The results provide support for possible linkage of influencing creatinine and triglyceride and uric acid and triglyceride with goat.

Keyward; Hyperuricemia and gout,creatinine,gender

Introduction

Uric acid is a heterocyclic compound of carbon, nitrogen, oxygen, and hydrogen with the formula C5H4N4O3). It forms ions and salts known as urates and acid urates, such as ammonium acid urate. Uric acid is a product of the metabolic breakdown of purine nucleotides, and it is a normal component of urine. High blood concentrations of uric acid can lead to gout and are associated with other medical conditions including diabetes and the formation of ammonium acid urate kidney stones [1]. Ammonia is extremely toxic, so most of it is very rapidly converted into urea in the liver. Human urinary wastes typically contain primarily urea with small amounts of ammonium and very little uric acid [2]. In most mammals, the enzyme uricase (urate oxidase) oxidizes uric acid to allantoin. Allantoin is highly soluble in water,therefore it does not accumulate in crystals and it is excreted unchanged through urine. Consequently, this makes urate oxidase very effective in lowering uric acid levels [5]. Unfortunately,urate oxidase is not a functional human enzyme, probably due tomutations occurring during the Myocene, and uric acid water-solubility is limited. As a result, humans but not other mammals can develop hyperuricemia and uric acid crystals can accumulate in human tissues and in the urinary tract, causing chronic hyperuricemia-related disease [6]. The serum uric acid level in the body is a function of balance between the breakdown of purine and the rate of urate excretion. The normal serum uric acid as measured by automated enzymatic (uricase) method is less than 7.0 mg/dl for adult male and any value more than 7.0 mg/dl is considered to represent hyperuricemia ,the normal rang in male(3.4-7.0 mg/dL) ,and in female (2.4-6.0 mg/dL) . The values however differ for women and children who have lower normal serum uric acid. This is so because the estrogenic compound in premenopausal women enhances renal urate clearance by inhibition of renal urate reabsorption via organic ion transporter [5.] Hyperuricemia occurs when there's too much uric acid in your blood. High uric acid levels can lead to several diseases, including a

painful type of arthritis called gout. Elevated uric acid levels are also associated with health conditions such as heart disease, diabetes, and kidney disease . Low uric acid (hypouricemia) can have numerous causes,low dietary zinc intakes cause lower uric acid levels. This effect can be even more pronounced in women taking oral contraceptive medication, a drug indicated for prevention of hyperphosphataemia in people with chronic renal failure, can significantly reduce serum uric acid [6]. Uric acid is formed when purines break down in your body. Purines are chemicals found in certain foods. Normally, your body rids itself of uric acid when you urinate. Hyperuricemia occurs when your body either makes too much uric acid or is unable to excrete enough of it. It usually happens because your kidneys aren't eliminating it quickly enough, Excess uric acid levels in your blood can lead to the formation of crystals. Although these can form anywhere in the body, they tend to form in and around your joints and in your kidneys. Your body's defensive white blood cells may attack the crystals, causing inflammation and pain [7]. Sometimes called gouty arthritis, occurs in about 20 percent of people with hyperuricemia, a rapid drop in uric acid levels can also trigger gout. Gout can affect any joint in your body, but flares often first appear in your large toe. Feet, ankles, knees, and elbows are also common sites of gout [6].Gout causes extreme pain in the affected joint, along with inflammation, and red and shiny skin. Often times this is accompanied by a mild fever. When this condition continues. over the course of one's life, it could create what is known as tophus (hard nodules formed by uric acid that has stuck to the area around the joint [8]. The symptoms of gout are often sudden, usually during the night without warning. The most common symptoms are: Acute pain in the affected joint: This disease usually affects the large toe, but it can occur in the foot, Ankle, knee, wrist, or hand. In many cases the pain is more severe during the first hours of its onset. Permanent feeling of discomfort: This feeling comes after the disappearance of the effects of the bout of inflammation, and continue for days or weeks. Subsequent seizures are more severe, and their effect lasts longer. Redness and inflammation of the joint injury: The morphology of the MSUM formed from uric acid was studied under various Na^+ ion concentrations, under conditions mimicking the body (pH 7.4, 37^{o}C). As the pH returns to normal, this converts to MSUM, causing an inflammatory response and generating a self-sustaining cycle, as shown in the diagram below [9.] The presence of hyaluronate, Na^+, K^+ and Ca^{2+} is found to affect the development of gout and a new MSUM "fishtail" morphology was observed in hyaluronate-, Na^+– and Ca^{2+}– containing solutions. A highly water soluble hyaluronate-Ca-urate complex was identified and authors suggest that disruption of this complex would lead to MSUM deposition, causing gout. Thus, people could have hyperuricemia but not develop gout, if their physiological

conditions maintain the complex [10]. Among women, unhealthy weight obesity. Among women, unhealthy weight gain, hypertension, and diuretic use are independent risk factors for increasing the incidence of gout and low-fat dairy consumption is associated with a lower incidence of gout [11]. Hyperuricemia can be caused by the overproduction of uric acid, but is more often the result of insufficient kidney uric acid excretion non-modifiable risk factors for gout include; male gender, increasing age, and menopause, Approximately 15% of uric acid clearance occurs via the gastrointestinal tract, and therefore small bowel disease can contribute to increased serum uric acid, A variety of medications can increase serum uric acid, including loop and thiazide diuretics. High intake of meat, shellfish, alcohol, and fructose also can cause hyperuricemia [12]. since urine pH is the major determinant of uric acid crystallization , Urinary pH and ammonium excretion are directly correlated with the number of metabolic syndrome features, with a greater urinary acidity and lower ammonium excretion correlated to more features.Serum creatinine (a blood measurement) is an important indicator of renal health because it is an easily measured byproduct of muscle metabolism that is excreted unchanged by the kidneys. Creatinine itself is produced via a biological system involving creatine, phosphocreatine (also known as creatine phosphate), and adenosine triphosphate (ATP, the body's immediate energy supply) [13].

Method

Sampling

Cross sectional study was done to examine associative between (November2017- February 2018). Totally 66 patient attended from (Hawler Private Hospital, Rizgari Governmental Hospital, Ankawa Private Laboratory) in Erbil and may have hyperuricemia can be developed to gout disease from both males (32) and females (34) the age 18 up to 70 years included in this study. Biochemical tests were performed for all patients (uric acid test, urea test, creatinine test, triglyceride test). These samples were analyzed by using blood serum, not depended on urine analyses.

Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers. Only the specimens listed below were tested and found acceptable.

-Serum or Plasma: Li-heparin and K2-EDTAplasma.

-EDTA plasma values are approximately 7%lower than serum values.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufactures were tested. Sample collection systems from various manufactures may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacture.

Stability in serum/plasma [14]:

7 days at 4-8 C

3 days at 20-25 C

6 months at -20 C

Test principle

" Brunner and Suddarth's Handbook of Laboratory and Diagnostic Tests"

Determination of Uric Acid in Serum, with Use of Uricase and a Tribromophenol-Aminoantipyrine Chromogen

A manual method is described for determining the hydrogen peroxide produced from uric acid with uricase (pH 9.2) after deproteinization of 1.00 ml of serum. In the method, 2,4,6-tribromophenol is coupled with 4-aminoantipyrine (pH 7.0) by peroxidase oxidative coupling. The sensitivity of the method is such that 25 C of uric acid from a fourth of the deproteinized serum (100 mg/liter) in a final volume of 5 ml of n-butyl acetate color extract gives a stable absorbance of 0.7 at 492 nm with a 1-cm cell. The method is reproducible, and many substances that may be encountered in serum do not interfere. Absorbances are linear for uric acid concentrations as high as 200 mg/liter. Uric acid is most specifically determined by use uricase.

Uricase cleaves uric acid to form allantoin and hydrogen peroxide.

$$\text{Uric acid} + 2H_2O + O_2 \xrightarrow{\text{Uricase}} \text{allantoin} + CO_2 + H_2O_2$$

In the presence of peroxidase, 4-aminophenazone is oxidized by hydrogen peroxide to a quinine-diimine dye.

$$2H_2O_2 + H^+ + \text{TOOS}^a + \text{4-aminophenazone} \xrightarrow{\text{peroxidasse}} \text{quinine-diimine dye} + 4\ H_2O$$

The color intensity of the quinine-diimine formed directly proportional to the uric acid concentration and is determined by measuring the increase in absorbance[14].

The decrease in absorbance is measured at 293 nm. To adapt the method to visible colorimeters, peroxidase methods have been developed for determining the generated hydrogen peroxide. Here, we extend this approach by a novel use of the well-known and sensitive 4- aminoantipyrine method for phenols. The normally used alkaline oxidative coupling agent, potassium ferricyanide, has been

replaced with the hydrogen peroxide-peroxidase couple (Equation 2) at pH 7. The major advantages of this method are that it uses non- carcinogenic reagents, the developed colo The major advantages of this method are that it uses non- carcinogenic reagents, the developed color is stable, and interference by reducing substances in serum is negligible[15.]

Nursing considerations

Before the rest

-Confirm the patient's identity using two patient identifiers according to facility policy.

-Explain to the patient that the uric acid test is used to detect gout and kidney dysfunction.

-Advise him that the test requires a blood sample or urine specimen. Explain who will perform the test, and how and when the serum or urine will be collected.

-Notify the laboratory and practitioner of medications the patient is taking that may affect test results; they may need to be restricted.

During the test

-Serum uric acid

Perform a venipuncture. Collect the sample in 3 or 4 ml clot activator tube[16].

Action required

Special wash programming: The use of special wash steps is mandatory when certain test combination is run together on Roche/Hitachi Cobas C systems. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. Cobas C 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the Cobas C link, manual input is not required. Where required, special wash carry-over evasion programming must be implemented prior to reporting results with the test[16].

Expected values

Serum plasma

Males:	3.4-7.0 mg/dl	(202.3-416.5 µmol/L)
Females:	2.4-6.0 mg/dl	(142.8-339.2 µmol/L)

Uric acid procedure

Bring the reagent to room temperature.

Pipette into labeled test tubes

Table (.1): Materials of uric acid test

Blank	standard	sample	
Distilled water	25µl	___	___
Uric acid standard(s)	___	25µl	___
Sample	___	___	25µl
Reagent (A)	1.0 ml	1.0 ml	1.0 ml

Mix thoroughly and incubate the tubes for 10 minutes at room temperature (16-25 C) or for 5 minutes at 37 C.

Measure the absorbance (A) of the standard and the sample at 520 nm against the blank.

The color is stable for at least 30 minutes.

Calculation

Roche Hitachi cobas C systems automatically calculate the analytic concentration of each Sample.

Conversion factors: mg/dl × 59.5 = µmol/L

Mg/dl × 10 = mg/L

Creatinine test procedure

Perform a vein puncture, collect the sample into gel tube.

Put the sample into the centrifuge to separate the serum.

Bring the reagent to room temperature.

Into a test tube, mix 500 micron of R1* + 500 micron of R2 + 100 micron of serum.

Incubate the tube for 5 minutes at 37 C.

Measure the absorbance (A) of the mixture at 520 nm with the spectrophotometer.

R: Reagent is a substance or compound added to a system to cause a chemical reaction. *

Urea test procedure

Perform a vein puncture, collect the sample into gel tube.

Put the sample into the centrifuge to separate the serum.

Bring the reagent to room temperature.

Into a test tube, mix 800 micron of R1 + 200 micron R2 + 10 micron of serum.

Incubate the test tube for 5 minutes at 37 C.

Measure the absorbance (A) of the mixture at 520 nm with the spectrophotometer.

Triglyceride test procedure

Perform a vein puncture, collect the sample into gel tube.

Put the sample into the centrifuge to separate the serum.

Bring the reagent to room temperature.

Into a test tube, mix 1000 micron of R1 + 10 micron serum.

Incubate the test tube for 5 minutes at 37 C.

Measure the absorbance (A) of the mixture at 520 nm with the spectrophotometer.

Statistical analyses

Data were presented as mean values ±SEM. Statistical evaluations were performed by use of parametrical test (t-test). $P < 0.05$ was considered significant, and n represents the total number of participants in each group. Statistical analysis was performed by use of Sigma Plot 10.0 software.

Results

Relationship between uric acid and age in male

Out of 66 patients samples 25 (38%) samples among 32 samples were positive (>7.0 mg /dL) means they have hyperuricemia compared to the normal rang (3.4-7.0 mg/dL), 7 (11%) samples among 32 samples were negative that's mean they have normal uric acid levels , in table (2) statistical analysis showed that significant correlation between high uric acid and age , the age group (41-60) years was significantly higher compared to other age groups ($P < 0.05$) .

Table (2) Relationship between uric acid and age in male

		Normal			Abnormal		
Age group		N	%	P	N	%	P
19-40		3	5%		6	9%	
41-60		4	6%		13	20%	
61-80		0	0%		6	9%	
Total		7	11%	0.21	25	38%	0.01
Total	32						
Mean	Age	35			53		
	Result	5.23 mg /dL			8.4 mg /dL		

Relationship between uric acid and age in female

Out of 66 patients samples 20 (30%) samples among 34 samples were positive (> 6.0 mg dL) means they have hyperuricemia compared to the normal rang (2.4-6.0 mg/dL) , 14 (21%) samples among 34 samples were negative that's mean they have normal uric acid levels , in table (3) statistical analysis showed that significant correlation between high uric acid and age , the age group (61-80) years was significantly higher compared to other age groups ($P < 0.05$) while figure (1) showed relation between gender(male and female) and uric acid, the high level of uric acid was in male (38%) more than in female (30%)

Table (3): Relationship between uric acid and age in female

		Normal			Abnormal		
Age group		N	%	P	N	%	P
19-40		8	12%		5	7.5%	
41-60		3	4.5%		6	9.1%	
61-80		3	4.5%		9	14%	
Total		14	21%	0.5	20	30%	0.006
Total	34						
Mean	Age	38			59		
	Result	5.4 mg /dL			8.4 mg /dL		

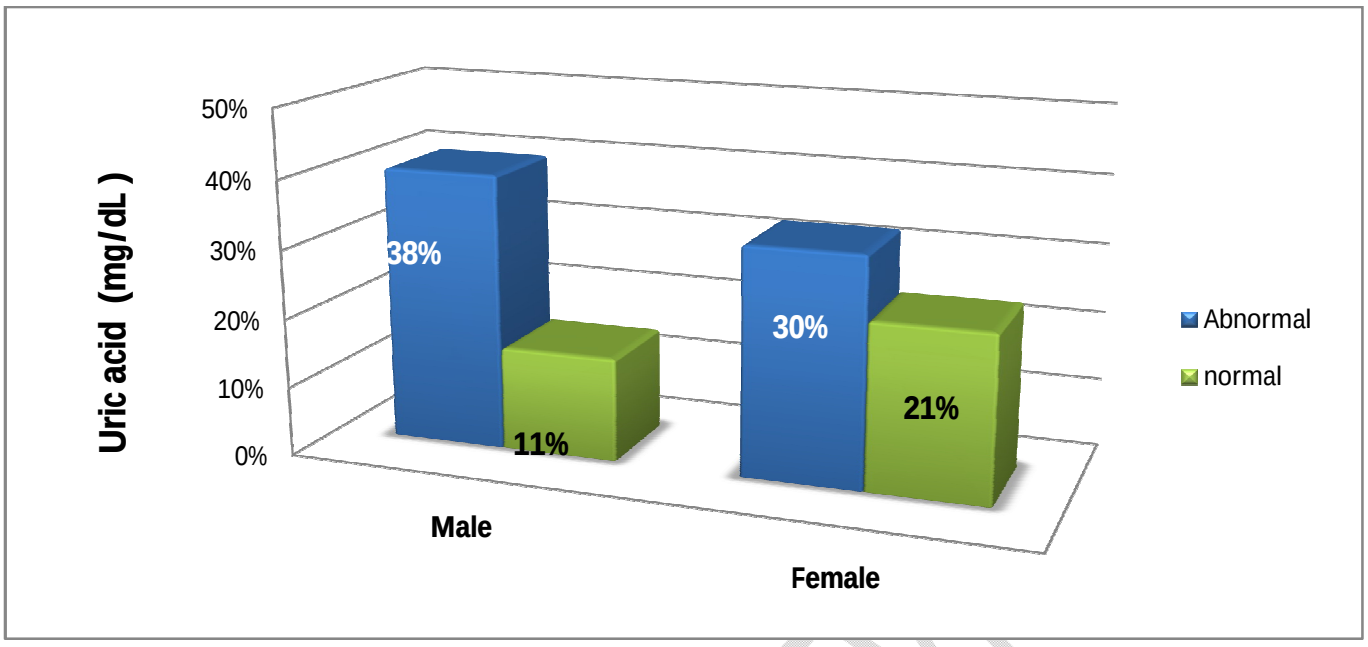

Figure (1) : Relation between uric acid and gender (Male , Female)

This figure showed relation between gender and uric acid, the high level of uric acid was in male (38%) more than in female (30%)

Relationship between creatinine and age in male

Out of 66 patients samples 22 (33.3%) samples among 32 samples were positive (>1.2 mg /dL) means they have high creatinine level compared to the normal rang (0.5-1.2 mg/dL) , 10 (15%) samples among 32 samples were negative that's mean they have normal creatinine levels , in table (4) statistical analysis showed that significant correlation between high creatinine and age , the age group (41-60) years was significantly higher compared to other age groups ($P < 0.05$) .

Table (4) Relationship between creatinine and age in male

	Normal			Abnormal		
Age group	N	%	P	N	%	P
19-40	6	9.1%		3	5%	
41-60	4	6.1%		13	20%	
61-80	0	0%		6	9.1%	
Total	10	15%	0.8	22	33.3%	0.09

Total	32		
Mean	Age	36	55
	Result	1.6 mg /dL	4.1 mg /dL

Relationship between creatinine and age in female

Out of 66 patients samples 20 (30%) samples among 34 samples were positive (> 1.1 mg /dL) means they have high creatinine level compared to the normal rang (0.4-1.1 mg/dL) , 14 (21.2%) samples among 34 samples were negative that's mean they have normal uric acid levels as in table (5) ,statistical analysis showed that significant correlation between high creatinine and age , the two age groups (41-60) & (61-80) years were significantly higher compared to other age group ($P < 0.05$) while figure (2) showed relation between gender(male and female) and creatinine, the high level of creatinine was in male (33%) more than in female (30%).

Table (5) Relationship between creatinine and age in female

		Normal			Abnormal		
Age group		N	%	P	N	%	P
19-40		7	11%		6	9.1%	
41-60		2	3%		7	11%	
61-80		5	8%		7	11%	
Total		14	21.2%	0.5	20	30%	0.01
Total	34						
Mean	Age	42			50		
	Result	1.4 mg /dL			4.8 mg /dL		

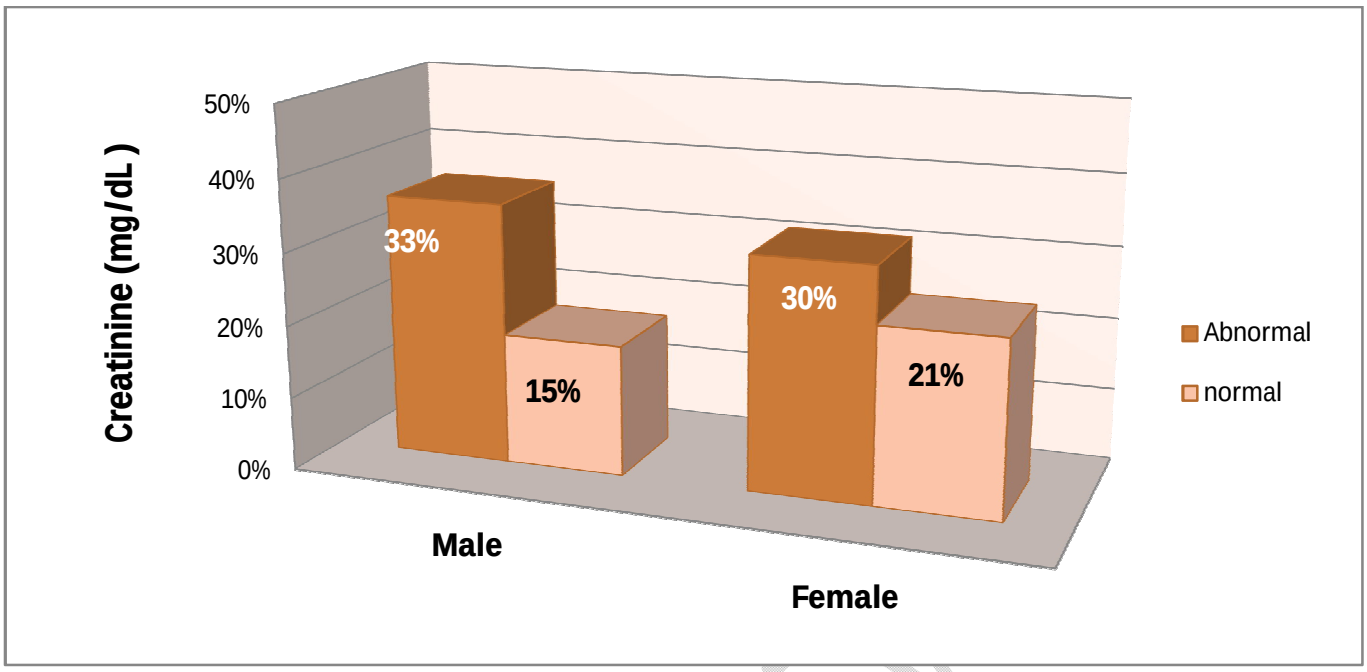

Figure (2): Relation between creatinine and gender (Male, Female)

This figure showed relation between gender and creatinine, the high level of creatinine was in male (33%) more than in female (30%).

Relationship between urea and age in male

Out of 66 patients samples 28 (42.4%) samples among 32 samples were positive (>20 mg /dL) means they have high urea level compared to the normal rang (7-20 mg/dL), 4 (6.1%) samples among 32 samples were negative that's mean they have normal urea levels , in table (6) statistical analysis showed that significant correlation between high urea and age , the age group (41-60) years was significantly higher compared to other age groups ($P < 0.05$) .

Table (6) Relationship between urea and age in male

		Normal			Abnormal		
Age group		N	%	P	N	%	P
19-40		4	6.1%		5	8%	
41-60		0	0%		17	26%	
61-80		0	0%		6	9.1%	
Total		4	6.1%	0.9	28	42.4%	0.02
Total	32						
Mean	Age	19			52		

Result 14 mg /dL 63 mg /dL Relationship between urea and age in female

Out of 66 patients samples 28 (42.4%) samples among 34 samples were positive (> 18 mg /dL) means they have high urea level compared to the normal rang (5-18 mg/dL) , 6 (9%) samples among 34 samples were negative that's mean they have normal urea level , in table (7) statistical analysis showed that non-significant correlation between high urea and age groups (P > 0.05) while figure (3) showed relation between gender(male and female) and urea, the high level of urea was the same in male and female (42%).

Table (7) Relationship between urea and age in female

	Normal			Abnormal		
Age group	N	%	P	N	%	P
19-40	4	6%		9	14%	
41-60	0	0%		9	14%	
61-80	2	3%		10	15%	
Total	6	9%	0.8	28	42.4%	0.6
Total	34					
Mean Age	34			50 mg /dL		
Result	10			41.1 mg /dL		

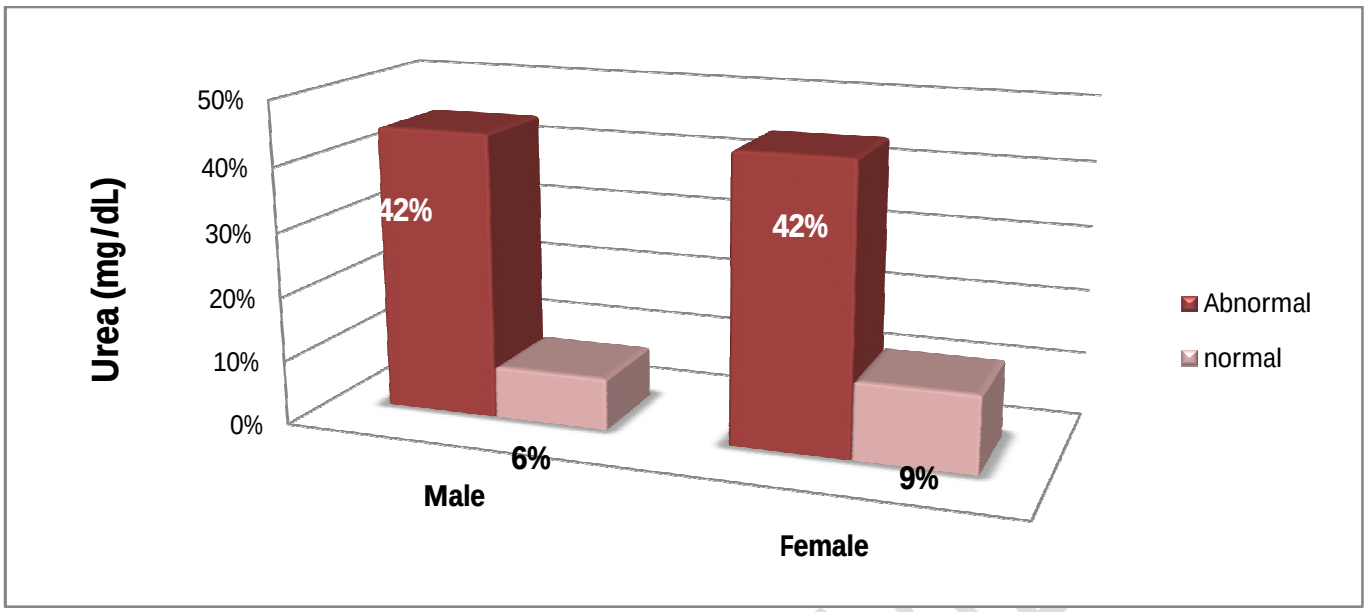

Figure (3): Relation between urea and gender (Male, Female)

This figure showed relation between gender and urea, the high level of urea was the same in male and female (42%).

Relationship between triglyceride and age in male

Out of 66 patients samples 20 (30%) samples among 32 samples were positive (>150 mg /dL) means they have high triglyceride level compared to the normal rang (<150 mg/dL), 12 (18.1%) samples among 32 samples were negative that's mean they have normal TG levels , in table (8) statistical analysis showed that significant correlation between high TG and age , the age group (41-60) years was significantly higher compared to other age groups ($P < 0.05$)

Table (8) Relationship between triglyceride and age in male

	Normal			Abnormal		
Age group	N	%	P	N	%	P
19-40	6	9.1%		3	5%	
41-60	6	9.1%		10	15%	
61-80	0	0%		6	9.1%	
Total	12	18.1%	0.3	20	30%	0.03
Total	32					
Mean Age	36			55		

Result	99 mg /dL	186 mg /dL

Relationship between triglyceride and age in female

Out of 66 patients samples 19 (29%) samples among 34 samples were positive (> 150 mg /dL) means they have high TG level compared to the normal rang (<150mg/dL), 15 (23%) samples among 34 samples were negative that's mean they have normal TG level, in table (9) statistical analysis showed that non-significant correlation between high TG and age groups (P > 0.05) while figure (4) showed relation between gender(male and female) and triglyceride, the high level of TG was in male (30%) more than in female (29%).

Table (9) Relationship between triglyceride and age in female

		Normal			Abnormal		
Age group		N	%	P	N	%	P
19-40		9	14%		4	6.1%	
41-60		1	1.5%		8	12.1%	
61-80		5	8%		7	11%	
Total		15	23%	0.8	19	29%	0.3
Total	34						
Mean	Age	40			53 mg /dL		
	Result	83			273 mg /dL		

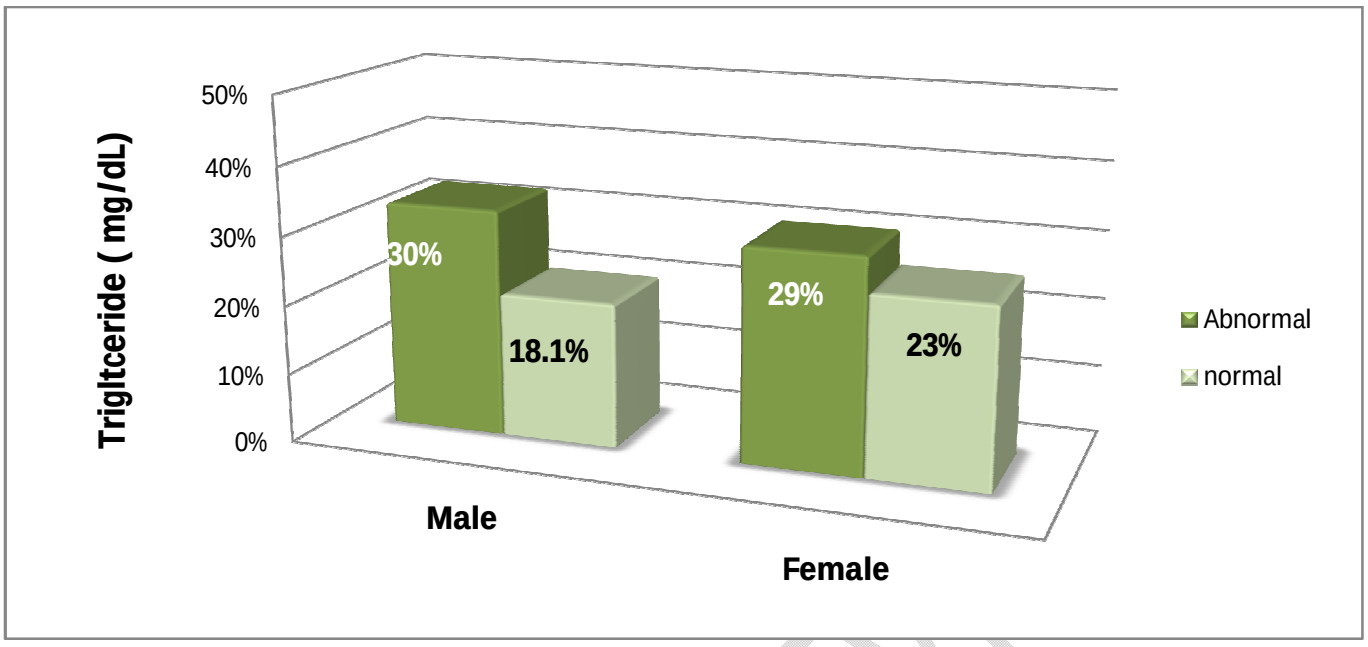

Figure (4): Relation between triglyceride and gender (Male, Female)

This figure showed relation between gender and triglyceride, the high level of TG was in male (30%) more than in female (29%).

Discussion

Relationship between uric acid with age and gender

Hyperuricemia is the cause of urate deposition diseases (such as gouty arthritis and renal damage) and is defined as serum urate levels of more than 7.0 mg/dL. The disease affects people of both genders and all ages. In the case that acute arthritis develops in the lower leg(s) of a male patient who has previously been diagnosed with hyperuricemia, there is a high possibility of gout, but differential diagnosis is necessary. Although hyperuricemia is well known, it must be noted that during the period in which gouty arthritis is developing, serum urate levels are maintained lower than usual in many cases[17]. Out of 66 samples we had 32(49%) males and 35(51%) females, in males total number 17(26%) of them were negative and 15(23%) of them were positive. In comparison with females 14(21%) were negative and 20(30%) were positive. In male statistical analysis showed that significant correlation between high uric acid and age , the age group (41-60) years was significantly higher compared to other age groups ($P < 0.05$), and in female statistical analysis showed that significant correlation between high uric acid and age, the age group (61-80) years was significantly higher compared to other age groups ($P < 0.05$) as compere with normal and our results concordant with other previous studies done by (Nicholls *et al*) [18]who reported that gout in women and young person's estrogen protects women from gout because of its association with enhanced renal excretion of uric acid ' estrogen in hormone

replacement therapy has a similar effect[19]. Also Harrold, *et al* [17] funded that gout occurs in only 0.2 per 1000 cases of women younger than 45 years. Women with gout tend to be older and have more comorbidity, such as obesity and kidney disease. Approximately 25% of patients with gout have a family history. However, in patients with early-onset gout (age <25 years), 80% have a family member with gout[20]. In Study compassion with prevalence of hyperuricemia and relation of serum uric acid with cardiovascular risk factors in a developing country research, the results of p-value for both males and females 0.040 and 0.004 which are significant. This explains the importance of monitoring serum uric acid levels, especially in patients with metabolic risk factors. As a matter of fact, patients who after a first acute episode do not monitor or treat serum uric acid levels, usually experience a second acute episode within two years[21]. Gout is the most common form of inflammatory arthritis in the United States, affecting 4% of the population, and its prevalence has been increasing. Its prevalence has also increased in other countries, which has been attributed to a westernized lifestyle, more comorbidities, and improved life expectancy.[61]Not all patients with hyperuricemia develop gout. In the United States, 21% of the population have hyperuricemia, and 4% have gout [22]. The epidemiology of gout is difficult to quantify precisely due to variations in methodology between studies, including differences in case definition and in the means of estimating incidence and prevalence[23]. Progression from asymptomatic hyperuricemia to urate deposition may take years.The Normative Aging Study is a longitudinal study that confirms the association between hyperuricemia and the development of rate deposition. A cohort of 2046 healthy volunteers has been monitored for 14.9 years. Urate deposition incidence was 0.1% in people with serum uric acid levels < 7.0 mg/dL, rising to 0.5% in people with uric acid levels from 7.0 to 8.9 mg/dL, and to 4.9% with uric acid levels higher than 9.0 mg/Dl[24], Cumulative incidence of urate deposition reached 22% after five years. It is particularly interesting to point out that incidence rates were three times higher for hypertensive patients than for normotensive patients ($p < 0.01$). The strongest predictors of gout were age body mass index, hypertension, cholesterol's level and alcohol intake[24]. Since the serum uric acid (SUA) level is balanced between hepatic production and excretion mainly through the kidney,a decrease in the excretion rate of urate results in hyperuricemia Although renal handling of urate is not yet fully understood [25].

Relationship between creatinine with age and gender

Gout is a disorder in which uric acid builds up in body and forms crystals in joints and/or kidneys and Gout has no a direct relation with high creatinine. However, gout can impair kidney

function, resulting in reduced renal function. High creatinine is a sign of Kidney Disease. The crystals in kidneys can cause inflammation in kidneys directly. Uncontrolled inflammation can cause scarring of kidney tissues. Once the kidneys are impaired, they will fail to remove creatinine from body adequately, thus resulting in high creatinine[26]. Out of 66 samples we had 32 (49%) males and 35(51%) females, in males total number 10 (15%) of them were negative. In the other side 22(33.3) of them were positive. In comparison with females 14(21.2%) were negative and 19(29 %) were positive. In male statistical analysis showed that significant correlation between high creatinine and age, the age group (41-60) years was significantly higher compared to other age groups ($P < 0.05$), in female statistical analysis showed that significant correlation between high creatinine and age , the two age groups (41-60) & (61-80) years were significantly higher compared to other age group ($P < 0.05$). as compere with normal and our results agreement with study done by Seegmiller *et al* [27] who reported that mean levels of body weight, plasma uric acid, and plasma creatinine in patients with gout were significantly higher than those of normal controls. The mean 24 hour urinary creatinine and urate excretions of patients with gout were also significantly higher than those of control subjects. There was no significant difference in the mean values of creatinine clearance between patients with gout and controls. The mean urate clearance in patients with gout was significantly lower than that of normal male controls . patients with gout had increased 24 hour urinary creatinine and uric acid excretion. Although in his study did not measure either endogenous creatinine or uric acid synthesis directly, it is possible that the hyperuricaemia seen in some patients with primary gout is due to accelerated endogenous creatinine synthesis.

Relationship between urea with age and gender

Out of 66 samples we had 32(49%) males 35(51%) females, in males total number 4(6.1%) of them were negative. In the other side (28 42.4%) of them were positive. In comparison with females total number 7(11%) were negative and 28(42.4%) were positive. In male statistical analysis showed that significant correlation between high urea and age, the age group (41-60) years was significantly higher compared to other age groups ($P < 0.05$), in female statistical analysis showed that non significant correlation between high urea and age groups ($P > 0.05$). as compere with normal and our results agreement with study done by Sarwar *et al* [28] who concluded that male are at more risk developing gout compared to women and this supported our results and also in there results comparing between Gout and urea in women and they found out differences in risk factors in young and older women results,. approximately most of women

with gout and highly urea in there study were over 50 years of age, confirming that this disease that mainly affects postmenopausal women, but a significant number of women under the age of 50 are now presenting with gout. In there conclusion, women who develop gout are more likely to be over the age of 50, have one or more comorbidity and are more likely to use diuretics.

Relationship between triglyceride with age and gender

High levels of triglycerides and uric acid have each been reported to be independently associated with an elevated risk for coronary heart disease. However, it is less well established whether high levels or triglycerides or uric acid, represent independent cardiovascular risk factors[28]. Out of 66 samples we had 32 (49%) males 35 (51%) females, in males total number 12 (18.1%) of them were negative in the other side 19 (28.7 %) of them were positive. In comparison with females total number 15 (23%) were negative and 19 (29 %) were positive. In male statistical analysis showed that significant correlation between high TG and age , the age group (41-60) years was significantly higher compared to other age groups ($P < 0.05$), in female statistical analysis showed that non-significant correlation between high TG and age groups ($P > 0.05$). as compere with normal and our results agreement with study done by Elaine *et al* [29] who concluded the significantly higher serum triglyceride concentration was the only abnormality among the lipid classes observed in gouty men patients compared with healthy men, the mean serum triglyceride level in the patients with gout (142 mg. per 100 ml.) was significantly higher ($p < 0.01$) than the mean triglyceride level of the healthy men. The results provide support for possible linkage of genetic factors influencing uric acid and triglyceride metabolism. Thus, although there is no direct relationship between hypertriglyceridemia and high uric acid levels, they are linked by a common denominator: a diet enriched in fructose. Fructose not only increases endogenous production of uric acid but also induces de novo lipid synthesis, thereby resulting in enhanced hepatic output of triglyceride-rich lipoproteins. High uric acid levels raise the likelihood of a person having elevated triglyceride levels, visceral obesity (increased waist circumference), insulin resistance, hypertension, and low high-density lipoprotein cholesterol levels, all of which represent features of the metabolic syndrome[29].

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