Iraqi journal of Bioscience and Biomedical
Published Online First: 30/ June /2025.
p-ISSN: 3007-5491 / e-ISSN:3007-5505

Assessment of serum uric acid, creatinine and cytokines concentrations in Iraqi patients with gouty arthritis

Ziad Sh .Ahmed [1*] and Risala R. Hussain [1]

[1] Molecular and Medical Biotechnology, College of Biotechnology, Al-Nahrain University, Baghdad, Iraq

*Corresponding author: ziadaltaee59@gmail.com

Received: 28/12/2024, Accepted: 03/02/2025, Published: 30/06/2025

Abstract

Gout is the mainly prevalent type of inflammatory arthritis that is characterized by deposition of monosodium uric acid crystals in and around peripheral joints. This study was aimed to examine the effect of some biochemical parameters (serum uric acid, serum creatinine) and some immunological parameters (TNF-α , IL1-β) in Iraqi patients with gouty arthritis .Samples of blood were drawn from 41 gout patients and 50 healthy individuals as the control group, spanned from December2023 to march 2024, at Rheumatology Department of clinical Counselor at AL-Yarmouk Hospital. Their ages ranged from 25 to 80 years old, Clinical assessments, including imaging and laboratory tests, led to the diagnosis of acute gouty arthritis in all patients. Serum uric acid and creatinine were measured, serum cytokines (IL-1β and TNF-α) were determined using enzyme-linked immunosorbent assay (ELISA). The results indicated that serum uric acid concentration was significantly higher in gout patients (6.05±1.85 mg/dl) as compared to controls (4.40±0.97 mg/dl). No significant change was observed in the concentration of serum creatinine. Both serum cytokines (IL-1β and TNF-α) were significantly higher in gout patients as compared to controls.

Keywords: gouty arthritis, serum uric acid, creatinine, TNF-α, beta IL1-β

Introduction

Gout is a public kind of inflammatory arthritis caused by excessive levels of serum uric acid (SUA), which can form needle-like crystals in joints. Patients with gout feel severe pain, redness, warmth, and edoema. Gout was observed with a mean frequency of 0.1-10% over the world[1]. Male arthritis patients over 40 years of age had the highest incidence of gouty arthritis[2] . Additionally, hypertension, obesity, and the use of certain medications are risk factors for incident gout[3]. in addition, the use of purine- rich foods, high fructose foods along with alcohol intake are positively associated with gout and/or hyperuricemia[4].Acute arthritis, persistent arthritis and tophi, gouty nephropathy, joint impairment, impaired kidney function, and metabolic syndrome-related disorders are clinical signs of gout[5].

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Hyperuricemia refers to an abnormally high concentration of uric acid in serum [5]Gout prevalence ranged from 1-4% worldwide, with incidence ranging from 0.1 to 0.3%. Gout is more common in men than in women by a ratio of 3:1 to 10:1. Gout incidence and prevalence increased with each decade of life, with prevalence increasing to 11-13% and 0.4% in those over the age of 80[6]. Uric acid the end product of purine metabolism, is a weak acid that circulates as the deprotonated urate anion under physiological conditions and interacts with sodium ions to produce MSU[7]. Epidemiological studies show that gout and hyperuricemia patients often have clinical and biochemical irregularities of metabolic syndrome, counting insulin resistance, obesity and hyperlipidemia[8]. Gout is mainly diagnosed by identification of the pathognomonic MSU crystals by joint fluid aspiration or in tophi aspirate[9]. In many mammals, urease converts uric acid to ammonia after uricase further breaks it down to allantoin[10].

However, because humans lack uricase, their serum uric acid levels are at the theoretical limit of solubility (6.8 mg/dl)[11]. Uric acid C5H4N4O3 is a weak organic acid formed as a product of purine metabolism largely by the liver[12].Uric acid levels in human blood typically vary from 1.5 to 6.0 mg/dL in women and 2.5 to 7.0 mg/dL in males. It is poorly soluble in both water and plasma, and when its concentration rises above 6.8 mg/dL, it reaches plasma saturation, which raises the possibility of urate crystal formation [13]. About 60% of the total plasma antioxidant capacity is made up of uric acid, which has two double bonds and is regarded as an excellent antioxidant[14]. Uric acid is primarily created by the liver as a byproduct of the metabolic route of purines nucleotides, a component of nucleic acids [15]Endogenous purines are acquired from de novo purine nucleotide synthesis, salvage synthesis of purine nucleotides, and nucleic acid degradation, whereas exogenous purines are mostly absorbed from the diet. Uric acid levels are influenced by the content of endogenous and exogenous purines[16] .Therefore, this study aimed to investigate the effect of serum uric acid, serum creatinine and serum concentrations of (TNF-α, IL1-β) in among of Iraqi patients with gouty arthritis.

Materials and Methods

A total of 91 subjects including 41 patients with gouty arthritis were enrolled at the Al-Yarmouk Hospital, Baghdad .The study also included 50 gout free controls The Ethics Committee of the college of biotechnology approved this study. Before the study began. Prior to blood collection, each patient provided written informed consent. Rheumatologists documented clinical information and laboratory results for each participant, including serum levels of GLU (glucose), SUA (serum uric acid), CREA (creatinine), age, height, weight and blood pressures. The body mass index was computed by multiplying the body weight in Kg by the height squared in meters. Hyperuricemia was characterized as a strangely elevated blood level of uric acid, commonly greater than 7 mg/dL in men and 6 mg/dL in women.

For each participating patient, 10 ml of venous blood was collected under sterile condition from the patient and controls, disposable syringe and transferred into EDTA tubes and gel tubes. About 3 ml of blood was put into gel tubes, then centrifuged at 4000 rpm for 5 min, half of the separated sera was used in uric acid and creatinine assays, the other half was placed into small aliquot and stored at – 20 C until used for the determination of TNF alpha and IL beta using enzyme-linked immunosorbent assay (ELISA).

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Results and Discussion

Patients' enrollment and characteristics

The general clinical data of the participants that include sex, age, BMI and hypertension as shown in Table (1)

Table (1): Anthropometric Indices of gout patients and controls.

Factor		Patients No. (%)	Control No. (%)	P-value
sex	Male	32 (78.05%)	36 (75.00%)	0.0074 **
	Female	9 (21.95%)	12 (25.00%)	
BMI (kg/m^2)	Normal (18.5-24.9)	7 (17.07%)	8 (16.67%)	0.0429 *
	Over weight (25-29.9)	11 (26.83%)	16 (33.33%)	
	Obese (≥30)	23 (56.10%)	24 (50.00%)	
Age group (year)	25-49	17 (41.46%)	19 (39.58%)	0.1631 NS
	50-75	24 (58.54%)	29 (60.42%)	
Hypertension	Yes	28 (68.29%)	25 (52.08%)	0.0496 *
	No	13 (31.71%)	23 (47.92%)	

* (P≤0.05), ** (P≤0.01).

Biochemical Parameters

Serum uric acid concentration

There is a significant increase in level of serum uric acid in gout patients (6.37±0.32mg/dl) as compared to control (4.75±0.19 mg/dl) (Figure 1).

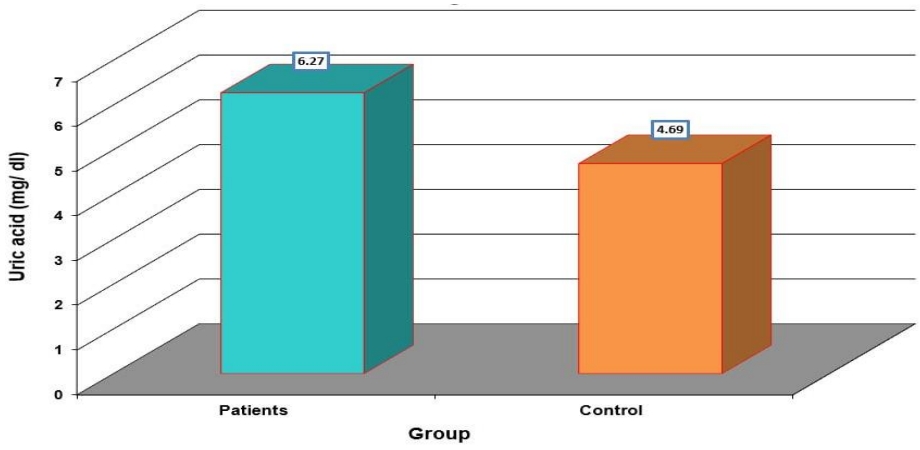

Figure (1): comparison between palatines and control groups in Unic Acid.

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Serum uric acid concentrations in gout patients and healthy controls are showed in Table (2) based on age, gender, BMI, and the presence or absence of hypertension.

Table (2): Serum uric acid concentrations according to gender, BMI, age and hypertension prevalence among gout patients and control.

Variables		Uric acid (mg/ dl)				
		N	Patients	N	Control	P-value
sex	Male	32	6.37 ±0.32	36	4.75 ±0.19	0.043 *
	Female	9	6.10 ±0.71	12	4.54 ±0.38	0.038 *
BMI (kg/m^2)	Normal (18.5-24.9)	7	5.21 ±0.68	8	4.21 ±0.28	0.048 *
	Over weight (25-29.9)	11	6.76 ±0.60	16	4.88 ±0.32	0.037 *
	Obese (≥30)	23	6.43 ±0.36	24	4.74 ±0.25	0.0091 **
Age (years)	25-49	17	6.05 ±0.43	19	4.86 ±0.31	0.045 *
	50-75	24	6.50 ±0.39	29	4.58 ±0.19	0.0089 **
Hypertension	Yes	28	6.59 ±0.39	25	5.05 ±0.27	0.047 *
	No	13	5.72 ±0.34	23	4.32 ±0.19	0.028 *

* (P≤0.05), ** (P≤0.01).

Values are means ±SD.

Similar letters represent no significant difference between the means of groups while different letterset and for significant differences between the means of the groups.

*** Significant differences.**

Serum uric acid levels in male and female gout patients were significantly higher than those in control groups in terms of sex. Serum uric acid concentrations in obese and overweight gout patients significantly increase in comparison to the comparable control groups, according to BMI categories. Serum uric acid values in all patient age groups are significantly (P<0.05) higher than in control groups**.**

Serum Creatinine Concentration

There is no significant difference in the Serum creatinine concentrations in gout patients (0.876±0.05 mg/dl) and controls (0.918±0.06 mg/dl) Figure (2).

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p-ISSN: 3007-5491 / e-ISSN:3007-5505

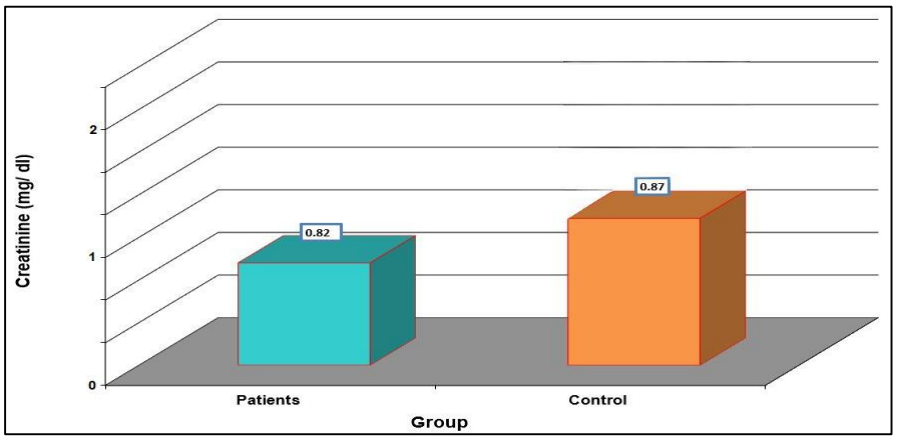

Figure (2): comparison between palatines and control groups in Creatinine.

The blood creatinine concentration in gout patients and controls is summarized in Table (3) based on age, gender, BMI, and the presence or absence of hypertension. Serum creatinine concentrations in gout patients, both male and female, do not differ significantly from controls in terms of gender. In all BMI categories (normal, overweight, and obese), it seems that all gout patients have somewhat higher serum creatinine concentrations than the control group, but the differences are not statistically significant. Serum creatinine concentrations in different age groups are studied, and the results show that older gout patients (50–75 years old) had much higher serum creatinine concentrations than younger gout patients (25–49 years old)Table (3) further shows that, in comparison to the matching control, gout patients with hypertension had a non-significantly higher serum creatinine concentration. Nonetheless, there is no discernible difference between the groups with and without hypertension.

Table (3): Serum creatinine concentrations distributed by sex, BMI, age and hypertension prevalence among gout patients and control.

Variables		Creatinine (mg/ dl)				
		N	Patients	N	Control	P-value
sex	Male	32	0.876 ±0.05	36	0.918 ±0.05	0.377 NS
	Female	9	0.695 ±0.05	12	0.724 ±0.06	0.402 NS
BMI (kg/m^2)	Normal (18.5-24.9)	7	0.695 ±0.05	8	0.796 ±0.11	0.394 NS
	Over weight (25-29.9)	11	0.832 ±0.09	16	0.955 ±0.09	0.429 NS
	Obese (≥30)	23	0.882 ±0.06	24	0.838 ±0.04	0.794 NS
Age (years)	25-49	17	0.717 ±0.06	19	0.801 ±0.06	0.347 NS
	50-75	24	0.922 ±0.06	29	0.920 ±0.05	0.903 NS
Hypertension	Yes	28	0.871 ±0.05	25	0.927 ±0.06	0.568 NS
	No	13	0.760 ±0.09	23	0.813 ±0.05	0.692 NS
NS: Non-Significant.						

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Values are means ±SD.

While distinct letters indicate significant variations between the group means, similar letters indicate no discernible difference between the group means.

Cytokines

Serum Interleukin 1 beta (IL-1β) concentration.

The serum concentrations of IL-1ß was significantly elevated in patients with GA (20.87±14.41 pg/ml) as compared with controls (12.63±8.57 pg/ml) Figure (3)

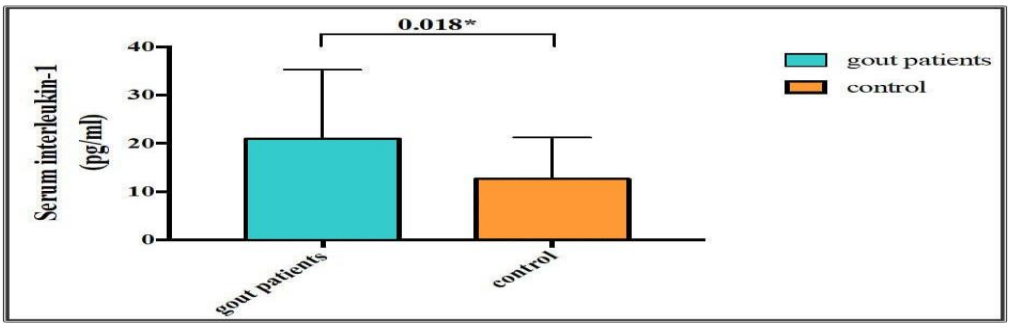

Figure (3): Serum IL-1βlevels in gout patients and control.

Serum tumor necrosis factor alpha (TNF-α)

The serum concentrations of TNF-α was significantly higher in patients with GA (12.35±10.15 pg/ml) as compared with controls (7.19±6.18 pg/ml) Figure (4).

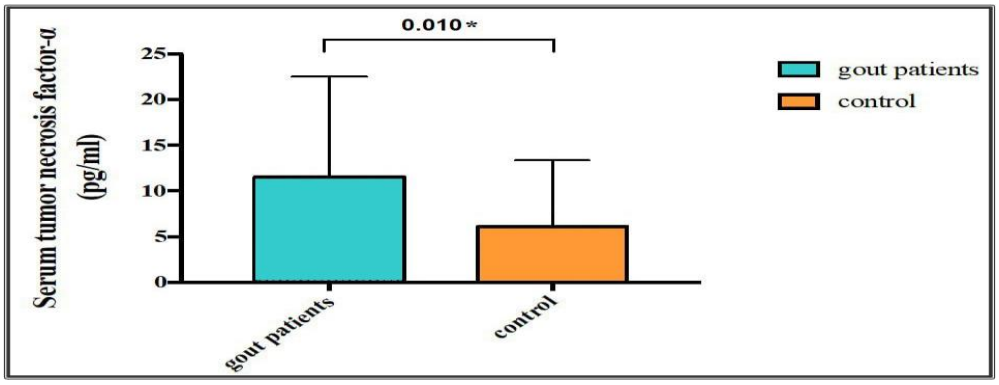

Figure (4): Serum TNF-α concentration in gout patients and control.

Discussion

Gout is frequently related with several risk factors, including excessive protein, alcohol, drugs, obesity, hypertension, and hyperuricemia[17].Meta-analyses and genome-wide association studies have revealed numerous genes related with gout risk[18,19]. Among these, the SLC22A12 and ABCG2 genes are

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recognized risk factors for gout in various demographics. As Vietnam's population grows increasingly overweight and obese, gout is becoming more common there[20,21].The data clearly shows that gout patients have significantly elevated serum uric acid levels compared to controls across diverse demographic factors. Elevated levels can lead to urate crystal formation in joints, which is characteristic of gout attacks. This finding aligns with existing literature that suggests hyperuricemia is a major risk factor for gout. This data is deal with many precedent research results and the relationship between gout and serum uric acid levels depending on demographics factors on the controls and patients samples and other risk factors e.g. purine-rich food and genetic change in the DNA, RNA and proteins[22,23] . Depending on the data that we got show that the serum uric acid levels in men is significantly higher than in women[24] .The liver produces uric acid, which is then eliminated by the kidneys and intestines as the final byproduct of purine metabolism[25] . Hyperuricemia, the primary etiological factor of gout, is brought on by either an excess or a lack of uric acid production because it can result in crystal formation and an inflammatory response[26,27].BMI has an impact on serum uric acid concentration as well. This was noted in the current investigation, where serum uric acid levels were significantly elevated in overweight and obese patients[28]shown a correlation between uric acid levels and BMI. Obesity in general and abdominal obesity in particular have been linked to elevated uric acid levels, possibly as a result of increased urate synthesis and decreased renal clearance. Additionally, it has been demonstrated that insulin resistance, which is closely linked to gout, is connected with overweight and obesity[29] . Serum uric acid concentration rose dramatically in older patients relative to the control group as they grew older. This could be called age-related renal function decline[30]. In addition, gout patients with or without hypertension had significantly higher serum uric acid concentrations in this study than in the control group. Hypertension itself, which is thought to be a part of the metabolic syndrome that is closely linked to gout, or glomerular arteriolar damage and glomerulosclerosis resulting from hypertension with subsequent renal damage and hyperuricemia could be the cause of this[31].

There was no discernible difference in the serum creatinine levels between the gout patients and the control group in this investigation. But stillrevealed a correlation between the concentration of uric acid and the blood creatinine level[32]. The breakdown product of creatine, of which 95% is found in muscle, is serum creatinine. The kidneys remove creatinine mostly from the blood by glomerular filtration, but they also do it by proximal tubular secretion, which is frequently used to gauge renal function[33]. Additionally, creatinine helps evaluate concomitant conditions in gout patients, particularly when measuring chronic renal illness[34]. In the current investigation, gout patients' serum levels of TNF-α and IL-1β were both considerably higher than those of the control group[35]. Indicated that there was no significant difference in the levels of IL-1β between the two groups, but that the levels of TNF-α in gout patients increased dramatically when compared to healthy controls. Still,[36].found that gout patients' IL-1β concentrations were noticeably greater than those of the controls. Furthermore, numerous investigations have demonstrated that gout patients' serum IL-1α and TNF-α concentrations did not significantly alter, and that IL-18 and IL-6 are the primary inflammatory mediators[37].

This is due to the fact that IL-1 regulates numerous inflammatory processes, making it a primary regulator of the innate immune response.[38,39].Innate immune cells, such as monocytes, macrophages, and dendritic cells, create the IL-1β precursor[40].Urate crystals are known to activate phagocytes and have a role in the inflammation signaling such as the maturation and secretion of IL-1β. Many other urate crystal-

induced inflammatory mediators are well characterized, including multiple prostaglandins, several leukotrienes and a host of cytokines, including IL-8 and many other chemokines, IL-6, and TNF-α.

Conclusions

1. Gout was associated with increased significantly serum uric acid in gout patients more than healthy controls, but not with creatinine concentrations.
2. Gout was associated with increased significantly cytokines (IL-1β and TNF-α) in gout patients comparatively to controls.
3. Gout disease and increase uric acid concentrations is not harm for kidneys and its function.
4. TNF-α and IL-1β are can be use as diagnostic parameters for gout disease.

Acknowledgments

The authors are grateful to their respective College of Biotechnology for their support.

Author's Declaration

- We hereby confirm that all the Figures and Tables in the manuscript are original and have been created by us.
- We have obtained ethical clearance for our study from the local ethical committee at [Al-Nahrain University/College of Biotechnology]. This approval underscores our commitment to ethical research practices and the well-being of our participants.
- Ethical Clearance: The project was approved by the local ethical committee at [Al-Nahrain University/College of Biotechnology], ensuring adherence to ethical standards and the protection of participants' rights and welfare.

Author's Contribution Statement

Ziad sh .Ahmed: Contributed to the conception and design of the study, conducted the experiments, data rearrangement and drafted the initial manuscript.

Risala R.hussain: contributed rearrangement the results, collection a part of literature review and conducted some characteristics of the products.

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