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EVALUATION OF KIM-1 LEVEL AND SOME BIOCHEMICAL VARIABLES IN PATIENTS WITH URINARY TRACT STONES

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Abstract: Urinary tract stones are a common disease, and the reason for this is the increasing number of people infected with it. It has a long medical history and the mechanism of stone formation has been studied at length, as it was one of the diseases that puzzled researchers and scientists. Renal stones are known as a solid mass that arises from crystals that somewhat resemble small mineral rocks that are formed or present in the kidneys or urinary tract. Kidney stones vary in their fine sizes between sand grains to the extent that they fill the cavity of the renal pelvis.

Keywords: Urinary tract stones, KIM-1, Uric acid, Urea, Creatinine, Calcium.

Introduction:

The formation of urinary tract stones, especially kidney stones, is a complex and multifactorial process resulting from a series of many physical and chemical steps[1]. It can form without any symptoms, or it can be associated with pain resulting from hematuria, obstruction of the renal tubules, or urinary tract infections. In some cases, it may lead to chronic kidney disease (CKD) in people with genetic disorders such as hyperoxaluria [2].KIM-1 is a membrane glycoprotein that has been evaluated in clinical trials as a biomarker for early acute kidney injury (AKI). Elevated KIM-1 levels have been shown to predict adverse clinical outcomes (need for dialysis or death) in patients with acute renal failure[3], Uric acid is the final product of the metabolism of a group of nitrogenous bases known as purines, which are part of the chemical composition of nucleic acids[4]. Urea belongs to the class of non-protein nitrogenous compounds. Urea is formed mainly inside the human body in the kidneys and in the liver cells from ammonia resulting from the process of removing ammonia from amino acids through the urea cycle [5]. When kidney disease occurs, the concentration of urea in the blood increases in addition to a decrease in blood flow to the kidneys. When kidney disorders occur, nitrogenous waste accumulates, which causes an abnormal increase in the level of urea in the blood. Urea is not completely filtered and part of it is reabsorbed through the renal tubules, so it is not completely reliable and is not suitable for measuring the glomerular filtration rate (GFR). For these reasons, measuring creatinine is the best and most accurate way to know kidney function [6]. Creatinine is a non-protein nitrogenous compound and is produced from the final metabolism of nitrogen in the body after losing a water molecule from the creatine compound [7]. Creatinine is transported to the kidneys through the blood after its formation, and is filtered by the renal glomeruli and excreted through the urine without being reabsorbed by the renal tubules [8]. Creatinine is one of the least variable non-protein nitrogenous compounds in the blood, as the concentration of plasma creatinine is almost constant in normal people and

under normal conditions or even if there is a slight defect in the function of the kidneys. Creatinine levels do not rise in kidney diseases in general unless there is significant damage to the kidney that prevents it from filtering and excreting waste [9]. Therefore, serum creatinine is a sensitive indicator of changes in kidney function and is of clinical importance, especially in kidney diseases of various types, as the level of creatinine in the blood increases when chronic or acute kidney diseases occur and urinary tract obstruction occurs [10]. Calcium ion (Ca^{2+}) is a positive ion present in the body in large quantities and is necessary in many life processes and is one of the basic elements that make up urinary tract stones [11].

Materials and Methods:

Sample Collection and Preparation

The current study included the collection of 180 samples divided into 100 samples for patients with kidney stones and 80 samples for healthy (control group), and ranging in age between (20-65 years) for both groups , Samples were collected from Tikrit Teaching Hospital in Salah al-Din Governorate from November 2022 to July 2023 After conducting medical and clinical examinations and presenting the patients to specialist doctors .

Estimation levels of kim-1 and some biochemical parameters:

kim-1 estimated using the ELISA Sandwich technique, where the kit provided by Bioassay Technology Lab. /china . while the kit from Biolabo Crop / France was used to estimate Uric acid,Urea,Creatinine ,Calcium .Using the colorimetric method, the absorbance is then measured.

Statistical analysis:

The results of the current research study were analyzed using the variance analysis program (IBM SPSS Statistics for Windows, Version 23.0. , NY: IBM Corp.), and the t-test and chi-square test were used to analyze the variance between two groups at the probability level ($P < 0.05$), and the correlation coefficient was found using (Pearsons Correlation Coefficient) to find the relationship between osteoprotein, Kim-1 and other biochemical variables in this research, and the graphs and tables were drawn using (Excel 2016) program.

Results and discussion:

The results of the current study included statistical values for each of the measurements of (uric acid, urea, creatinine) in blood serum, as well as the measurement of a number of vital variables in urine (Kim-1, calcium), which are considered important signs of kidney and urinary tract functions for both patients with urinary tract stones and healthy people (control group), whose ages ranged between (20-65) years and for both sexes at the probability level ($P < 0.05$). The results of the patient group were compared with the control group, and the standard deviation was found for each of the variables under study, as shown in Table (1).

Table (1): Average standard deviation of each Kim-1 and some biochemical variables in patients compared to control group

Parameter	Urinary tract stones Stone Patients	Control	P- Value
	Mean±S.D N=100	Mean±S.D N=80	
KIM-1 ng/ml	7.63 ± 1.58	1.25 ± 0.82	< 0.01
Uric acid mg/dl	8.67 ± 4.58	5.41 ± 3.25	< 0.05
Urea mg/dl	54.58 ± 14.86	26.12 ± 9.44	< 0.01
Creatinine mg/dl	1.42 ± 0.65	0.88 ± 0.31	< 0.05
Calcium mg/day	591.45 ± 167.52	288.23 ± 56.48	< 0.05

The concentration of the biomarker Kim-1 was estimated in the urine of patients with urinary tract stones compared to healthy people. The results of the current study showed that the level of Kim-1 was (7.63 ± 1.58 ng/ml) in the urine of patients with urinary tract stones, while it was (1.25 ± 0.82 ng/ml) in the urine of the control group. The results showed a significant increase at the probability level ($P < 0.01$) in the urine of patients with urinary tract stones compared to the control group, as shown in Figure (1).

The reason for the increase is due to damage or injury to the urinary tract, as stones vary in size and shape and may appear in one kidney or both kidneys. Stones can be very painful and can lead to kidney infections. Stones also cause wounds or blockage in the urinary tract, which leads to injury to the kidney tissue. The increase in Kim-1 in the urine can be a result of injury resulting from stones, and as a result, its level rises above the normal limit [12].

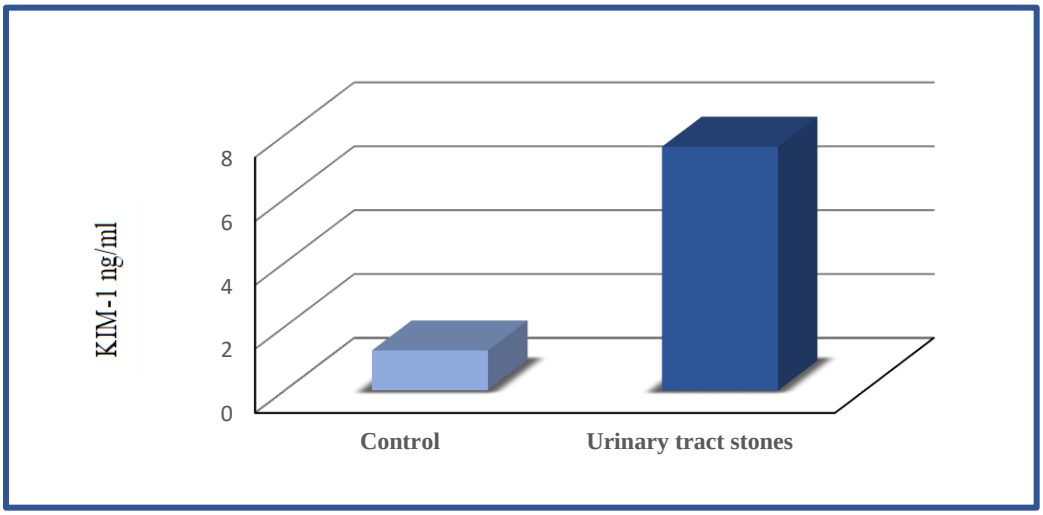


Figure (1): Kim-1 level in patients' urine compared to the control group

The concentration of the biomarker uric acid was estimated in the blood of patients with urinary tract stones compared to healthy people. The results of the current study showed that the level of uric acid was (8.67 ± 4.58 mg/dl) in the blood of patients with urinary tract stones, while it was (5.41 ± 3.25 mg/dl) in the blood of the control group. The results showed a significant increase at the probability level ($P< 0.05$) in the blood of patients with urinary tract stones compared to the control group, as shown in Figure (2).

The cause of high uric acid is attributed to the presence of a defect in the diet, or due to an unbalanced diet between plants and animals containing purines, as the diet plays a major role in increasing uric acid levels, and excessive daily consumption and a lot of foods containing high levels of purines such as red meat and lack of drinking fluids, especially water and fasting, and thus leads to an increase in the level of uric acid production above the normal limit in the blood and the inability of the kidneys to filter the excess [13]. Obesity and an unhealthy lifestyle may lead to increased levels of uric acid as a result of metabolic disorders. The cause may be attributed to digestive disorders and increased protein breakdown. People with insulin resistance or metabolic syndrome often have high levels of uric acid, or the increase occurs as a result of genetic factors, increased accumulation of nitrogenous waste in the blood, blood diseases, dysfunction of the kidney's secretion and filtration processes, gout, high blood pressure, kidney failure, or high levels of citrate in urine or thyroid disease [14].

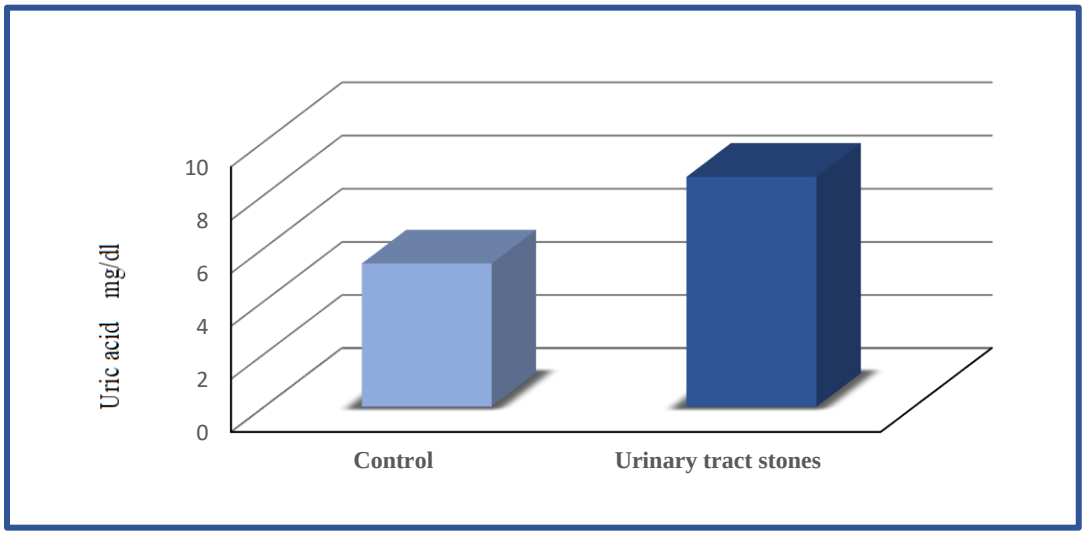


Figure (2): Uric acid level in patients' blood compared to the control group

The concentration of the biomarker urea was estimated in the blood of patients with urinary tract stones compared to healthy people. The results of the current study showed that the level of urea reached (54.58 ± 14.86 mg/dl) in the blood of patients with urinary tract stones, while it reached (26.12 ± 9.44 mg/dl) in the blood of the control group. The results showed a significant increase at the probability level ($P< 0.01$) in the blood of patients with urinary tract stones compared to the control group, as shown in Figure (3).

The reason for the increase is that urea is the basic nitrogenous substance resulting from metabolic wastes that are formed and excreted through urine. The excretion of harmful nitrogenous products in the process of protein metabolism is one of the most prominent and important functions performed by the kidney [15]. In the event of any damage or malfunction in the kidney function, this leads to a decrease in urea excreted through urine, which results in its accumulation in the blood and an increase in its concentration[16]. The other reason for the increase in urea levels is the failure of some patients to adhere to a healthy diet and their consumption of large amounts of protein, all of which leads to an increase in the urea level above the normal rate. The increase in urea concentration in the body depends on the severity of the damage and its progression in the kidney, as well as on the rate of protein intake and the rate of its breakdown. In other words, the increase in urea expresses a malfunction in the filtration function of the kidney [17].

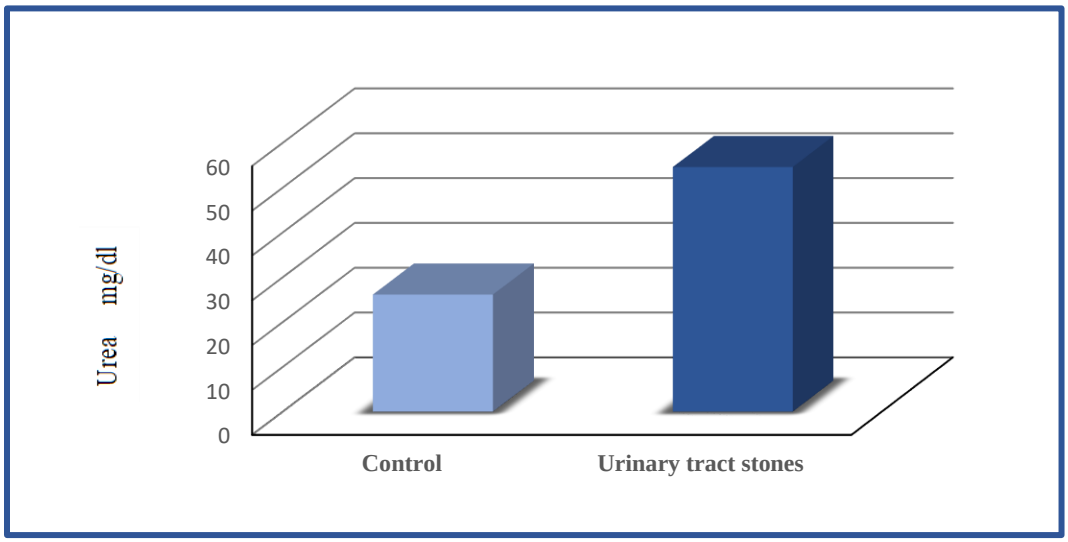


Figure (3): Urea level in patients' blood compared to the control group

The concentration of the biomarker creatinine was estimated in the blood of patients with urinary tract stones compared to healthy controls. The results of the current study showed that the level of creatinine was (1.42 ± 0.65 mg/dl) in the blood of patients with urinary tract stones, while it was (0.88 ± 0.31 mg/dl) in the blood of the control group. The results showed a significant increase at the probability level (P< 0.05) in the blood of patients with urinary tract stones compared to the control group, as shown in Figure (4).

The reason for the increase is attributed to the fact that creatinine is a nitrogenous metabolic waste that is formed in metabolic processes and is a result of the breakdown of creatine, which is a substance used in energy production in the muscles. Creatinine is filtered in healthy kidneys from the blood and is excreted with urine in normal conditions. However, when the kidneys are affected or in the event of a malfunction and deterioration in their function that prevents them from filtering, the kidneys gradually lose their functions and are unable to filter and excrete metabolic waste, which leads to an increase in the level of creatinine and its accumulation in the blood. This accumulation in the blood indicates that there is a problem in the kidneys' ability to get rid of waste effectively and that the kidneys are not doing their job effectively in filtering, and that the increase is a clear indicator of weak kidney function [18].

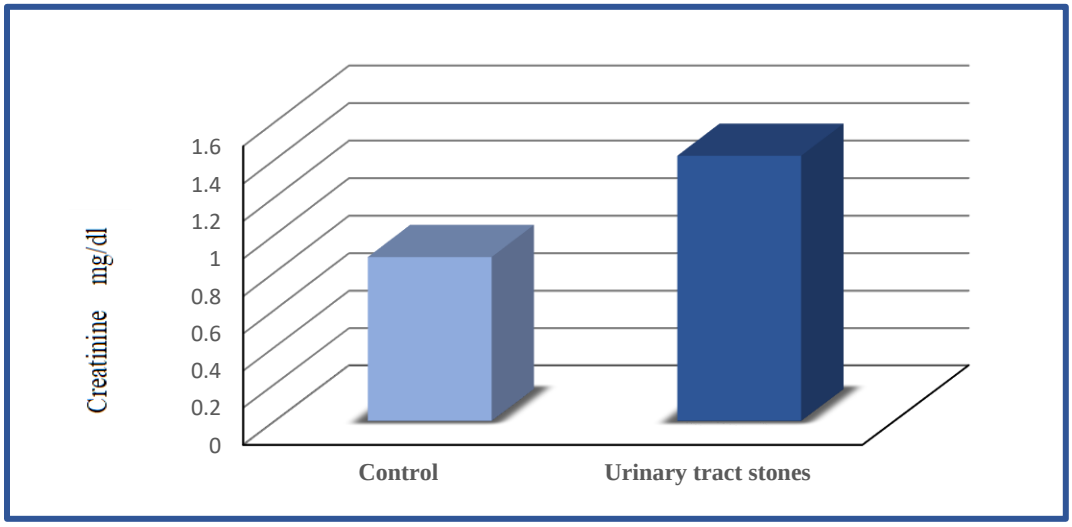


Figure (4): Creatinine level in patients'blood compared to the control group

The concentration of the calcium biomarker was estimated in the urine of patients with urinary tract stones compared to healthy people. The results of the current study showed that the calcium level reached (591.45 ± 167.52 mg/day) in the urine of patients with urinary tract stones, while it reached (288.23 ± 56.48 mg/day) in the urine of the control group. The results showed a significant increase at the probability level (P<0.05) in the urine of patients with urinary tract stones compared to the control group, as shown in Figure (5).

Calcium is an essential mineral for the body and plays a vital role in many vital functions such as building bones and regulating the heartbeat. When the concentration of calcium is excessively high in the blood and urine[19], it can directly contribute to the formation of urinary tract stones. The high concentration of calcium is due to several reasons, including consuming large amounts of dairy products, as dairy products are rich in calcium, which leads to increased levels of calcium in the blood and then in the urine. The reason may also be attributed to consuming excessive amounts of foods, red meat, and saturated fats, or to a lack of consumption of fruits and drinking water; because some water may contain a high percentage of minerals, calcium, and other dissolved elements that may affect the acidity, and thus these substances precipitate with oxalates and phosphates in the nephrons to form stones [20].

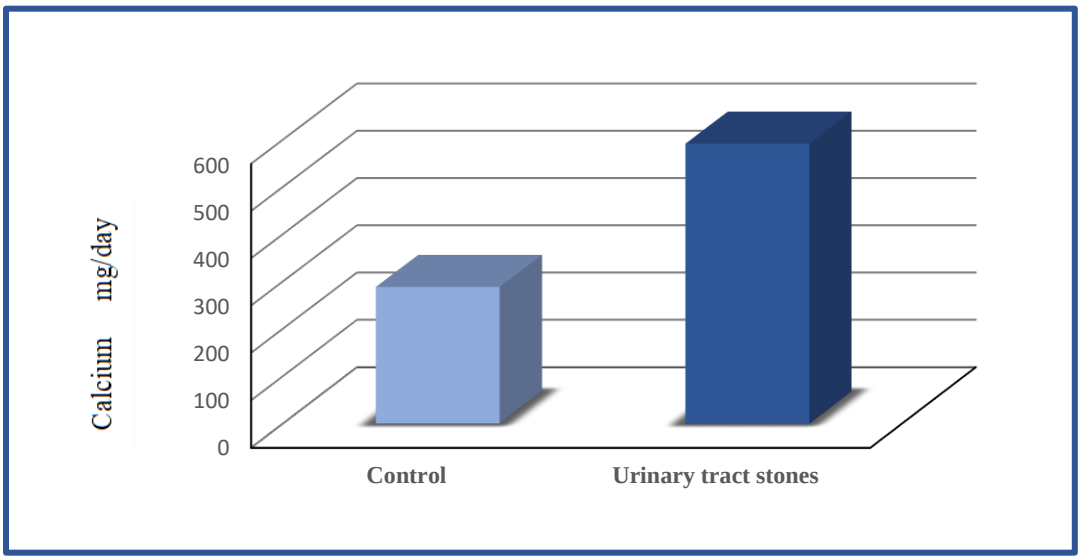


Figure (5): calcium level in patients' urine compared to the control group

Correlations:

Correlation between KIM-1 and Uric acid

The correlation between the biochemical variable, the kidney injury molecule Kim-1, and uric acid was studied, and through the effect of these variables on each other, it was found that there was a positive direct correlation (+ve) between them with values (r = 0.45, P = 0.001) as shown in Figure (6).

The direct relationship between the levels of Kim-1 and uric acid means that increasing the levels of Kim-1 leads to an increase in the level of uric acid, i.e. they directly affect each other in the formation of stones, because uric acid is secreted in healthy people effectively by the kidneys, and excessive secretion of uric acid is a risk factor for the formation of stones [21]. as crystals can accumulate and precipitate in the kidneys and act as a nucleus for the formation of kidney stones and thus cause kidney injury, and since Kim-1 is an accurate indicator for knowing kidney injury, it increases when uric acid increases, so any damage to the kidney works to increase the concentration of uric acid and thus increase the level of Kim-1 [22].

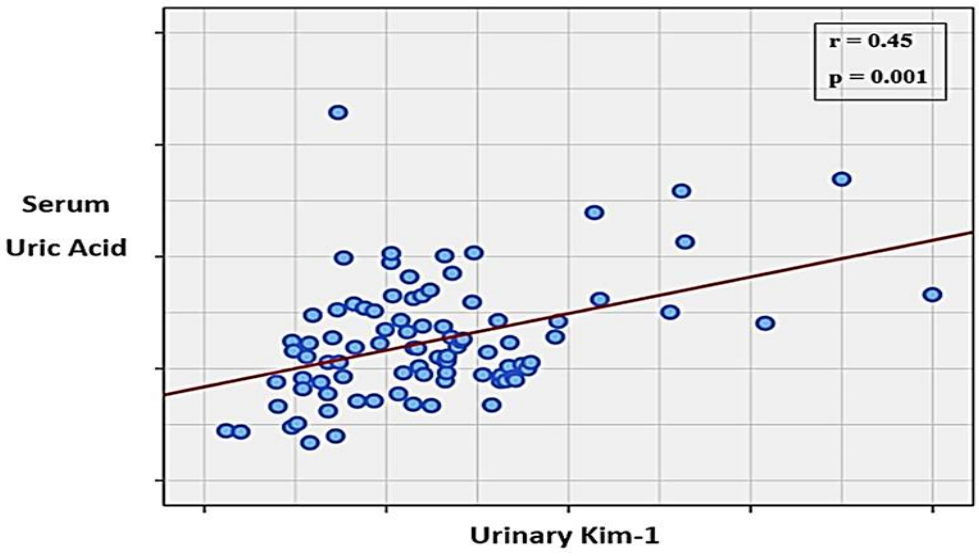


Figure (7): The relationship between Kim-1 and uric acid in patients

Correlation between KIM-1 and Creatinine

The correlation between the biochemical variable, the kidney injury molecule Kim-1, and creatinine was studied, and through the effect of these variables on each other, it was found that there was a positive direct correlation (+ve) between them with values (r = 0.38, P = 0.01) as shown in Figure (7).

The direct relationship between the levels of Kim-1 and creatinine means that an increase in the levels of Kim-1 leads to an increase in the level of creatinine, i.e. they directly affect each other in the formation of stones. This relationship can be explained by the fact that creatinine is a nitrogenous metabolic waste that is formed by metabolic processes [23].and it is filtered in the healthy kidneys from the blood and excreted with urine in healthy people. However, when the kidneys are affected by stones, it leads to a malfunction and deterioration in their filtration function, causing the accumulation of creatinine in the blood, and the increase is a clear indicator of weak kidney function, and since Kim-1 is a sensitive indicator of kidney injury, and as a result of this malfunction, the level of Kim-1 rises above the normal limit, and this is what the current study confirmed [24].

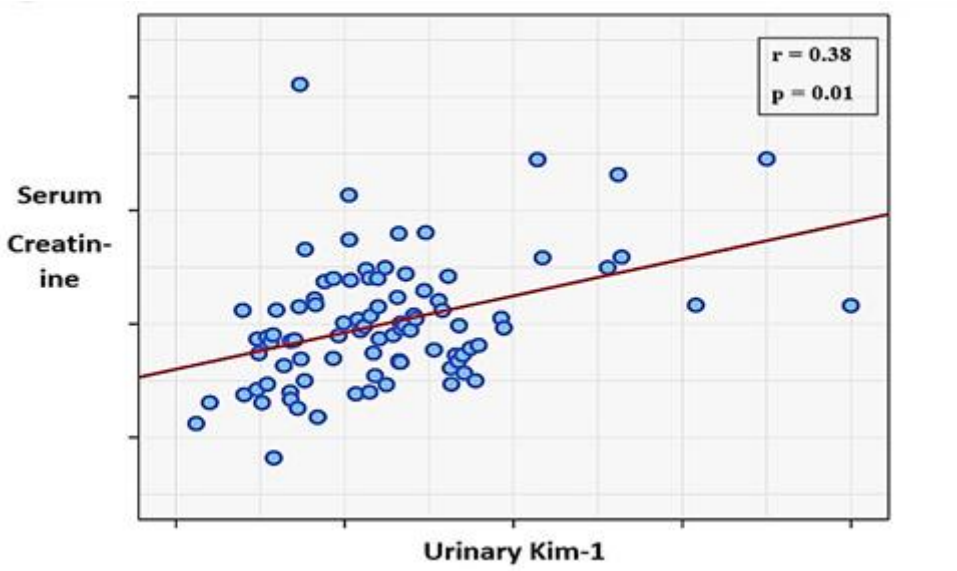


Figure (7): The correlation between KIM-1 and creatinine in patients

Conclusion:

We conclude from this study that people with urinary tract stones have a significant increase in the level of each of (Uric acid, Urea, Creatinine) in the blood, as well as a significant increase in the level of each of (KIM-1, Calcium) in the urine compared to the control group.

The correlation relationship was studied, and it was found that there is a positive direct correlation between (KIM-1 and uric acid), (KIM-1 and creatinine).

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