

Article

The Role of the Activity of the Enzyme Glutathione-S-Transferase and Some Biochemical Variables In Patients with Acute Renal Failure

Layali Msaher Mshaal^{1*}, Wasan Nazhan Assi²

¹² Tikrit University, College of Education for Pure Sciences, Department of Chemistry

*Correspondence: lm230012pep@st.tu.edu.iq

Citation: Mshaal, L. M. The Role Of The Activity Of The Enzyme Glutathione-S-Transferase and Some Biochemical Variables In Patients With Acute Renal Failure. American Journal Of Bioscience And Clinical Integrity 2024, 1(12), 14-21.

Received: 10th Sept 2024

Revised: 11th Oct 2024

Accepted: 24th Nov 2024

Published: 21th Dec 2024



Copyright: © 2024 by the authors. Submitted for open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>)

Abstract: A study was conducted to determine the effect of glutathione-S-transferase (GST) enzyme in patients with acute renal failure, in addition to studying the changes in the levels of urea, creatinine, uric acid, the antioxidant nitric oxide, as well as the levels of albumin, thiol group, sodium, and potassium ions. The results of the study showed a slight increase in the level of GST enzyme as well as nitric oxide. In contrast, other variables showed a significant increase in their levels, such as urea, creatinine, and uric acid. As for the thiol group, albumin and sodium ions showed a decrease in their levels compared to the control group.

Keywords: Acute Renal Failure, Glutathione-S transferase, Uric Acid, Urea, Creatinine, Albumin, Sodium

Introduction

Acute Renal Failure represents a sudden and reversible decrease in kidney function that is sufficient to cause a significant disturbance in the internal environment of the body and cause the accumulation and collection of harmful nitrogenous compounds inside the body [1]. Usually, kidney function is fully restored after treatment of this type, which lasts for a few days or weeks [2]. Acute renal failure can be diagnosed based on clinical signs, and kidney function can be estimated using known tests such as blood urea and creatinine tests and urine analysis [3]. Acute renal failure (ARF) is a distinct clinical entity and a significant cause of death [4]. The results of treatment for the disease are better in patients of middle age due to the lack of diseases accompanying the condition, and deaths from renal failure decrease immediately after dialysis. In general, acute renal failure occurs at the moment when the kidneys stop entirely performing their function [5], and the role of the artificial alternative (dialysis) becomes necessary to protect the patient's life until recovery and return to normal function are achieved.

Glutathione-S transferase (GST) is classified as a transporter enzyme. GST is found in the liver and is produced by glutathione, which is composed of three amino acids: glycine, glutamic acid, and cysteine. It consists of two ends: carbon (C-term) and nitrogen (N-term). It is a powerful antioxidant and is used to remove toxins, heavy metals, and drugs from reactive oxygen species (ROS) from the body, as it inhibits the formation of free radicals and protects cells from damage. GST is a vital defense enzyme that helps protect the body from the harmful effects of radiation exposure and chemotherapy

for cancer and greatly helps in treating liver and blood diseases. GST is one of the enzymes whose genes are associated with eliminating oxidative stress, and it has a role in stimulating the coupling of hydrophobic compounds and electrolytes with reduced glutathione GSH and is excreted in urine and feces after coupling with GSH[6].

Uric Acid is one of the non-protein nitrogenous organic compounds in the blood. It is characterized by being difficult to dissolve in water, so most of it must be excreted in urine, as about (75%) is filtered through the kidneys [7]. Its formation depends on the extent of the protein content of the food, as well as the extent of the free purine bases in the food, as is the case in tea and coffee, as well as on the demolition processes that occur in the cells. It represents the final product of the decomposition of purines in mammals. After the formation of uric acid in the last step, it will undergo additional metabolism in humans and then be excreted through the kidney and intestinal tract, as it is filtered in the kidney and reabsorbed or excreted through the renal tubule, mostly through the process of urate transport [8]. Hyperuricaemia increases the chance of kidney disease progressing and developing.

Urea, also known as carbamide, is a water-soluble organic nitrogenous compound. It is produced during the urea cycle in the liver from ammonia, which is produced by deamination of amino acids. It is, therefore, the final product of protein breakdown. Ammonia that is converted into urea is very harmful, so the body converts it into urea [9]. The most essential function of the kidneys is to excrete nitrogenous products of protein breakdown, the vast majority of which is urea. Nitrogen represents the percentage of urea formed in the liver. The expected value of blood urea for both sexes is 15-40 mg/100 ml [10].

Creatinine is a cyclic anhydride that belongs to the class of non-protein nitrogenous compounds and is produced from the final metabolism of nitrogen in the body. It has the structural formula ($C_4H_7N_3O$), and its molecular weight is 113 Daltons. It is produced from the loss of a water molecule from the creatine compound that is built in the liver. After its formation, creatinine is transported to the kidneys through the blood, where it is filtered by the renal glomeruli and excreted through the urine without being reabsorbed by the tiny renal tubules. If the concentration of creatinine in the blood serum is high, this suggests the presence of moderate or severe kidney damage. This can be confirmed by a test called creatinine clearance, which is considered one of the most sensitive tests for measuring the glomerular filtration rate GFR[11].

Albumin The normal serum albumin concentration is 3.5-5.5 g/dL. Albumin differs from blood proteins in that it does not have a glycosyl group added to it. In hypoalbuminemia, albumin levels in the blood are low, i.e. less than 3.5 g/dL. On the contrary, high albumin levels in the body are uncommon and indicate the presence of severe problems, such as dehydration [12]. **Sodium** Healthy kidneys maintain a constant level of sodium in the body by adjusting the amount excreted in the urine. An imbalance in the amount of sodium taken in and lost affects the total amount of sodium in the body. The amount of sodium concentration in the blood can be [13].

Materials and Methods

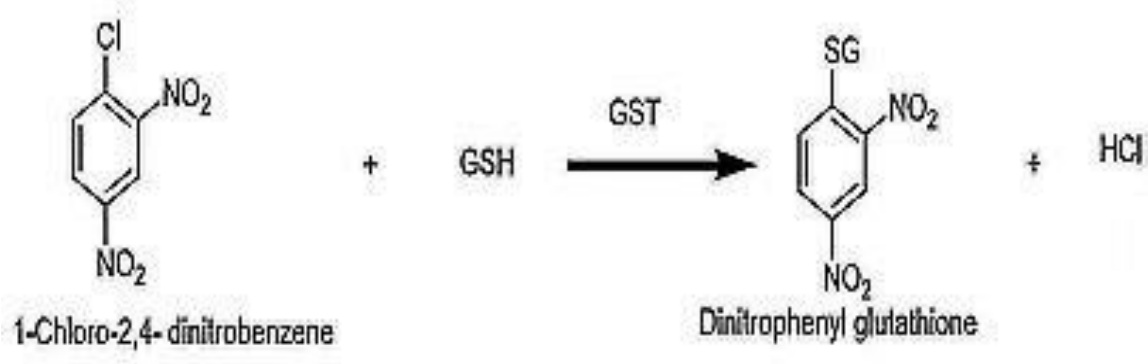
1. Collection Of Blood Samples

Blood was drawn from the vein using a (medical syringe) with a volume of (5) ml and placed in plastic tubes free of any additives Plain tubes, sterile made of polystyrene. It was left for (15) minutes, after which the blood serum was separated from the clotted part by centrifugation (Centrifuge) at a speed of (4000 rpm for (10) minutes, then the clear blood serum was drawn and stored in the freezer [14].

2. Estimation the activity of the enzyme Glutathione-S-transferase

A. The Principle

The method of measuring the activity of the GST enzyme depends on the coupling of GSH with 1-chloro-2,4-dinitrobenzene (CDNB-1) and the absorbance of the complex formed is measured at 340 nm [15]. The activity of GST can be defined as the amount of enzyme required to coupling 1-micromol of CDNB with GSH per minute as shown in the equation:



B. Reagents

- 1) Glutathione solution (29.93 mM)
- 2) 22.463 mM solution of 1-chloro-2,4-dinitrobenzene (CDNB)
- 3) Phosphate buffer solution PH 6.25

C. Methodes

Blank	Sample	Reagents
2.7 ml	2.7 ml	phosphate buffer pH 6.25
....	100 µl	Serum
100 µl		DW
100 µl	100 µl	CDNB solution 22.463 mM
100 µl	100 µl	After 3 minutes, add 29.93 mM GST solution.

Then all the tubes are mixed and the first absorbance is read at the first minute and the last absorbance at the tenth minute at a wavelength of 340 nm.

D. Calculations

$$\text{Activity of GST (U/L)} = \frac{\Delta A / 10 \times V_t \times 1000}{\epsilon \times V_s \times d}$$

ΔA represents the difference between the first and last absorbances

V_t represents the total volume = 3 ml

V_s represents the volume of the sample = 0.1 ml

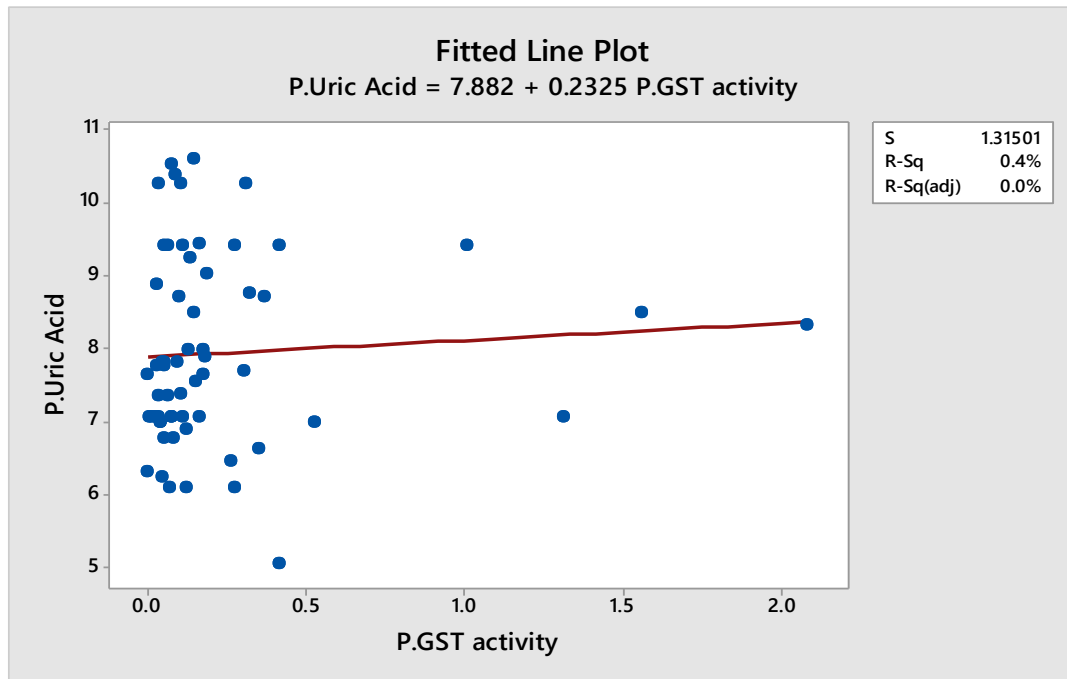
ϵ Represents the absorbance coefficient .9.6 mM⁻¹ /cm⁻¹

d represents the light path

Result and Discussions

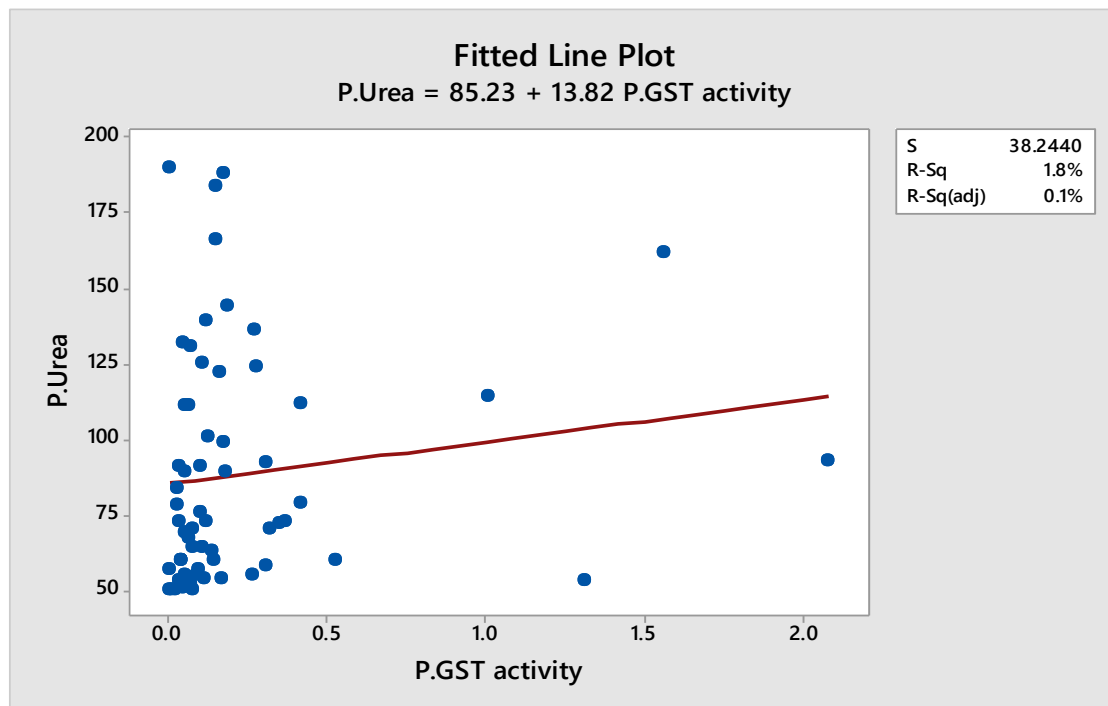
1. Correlation between GST and uric acid concentration level:

The relationship between them is direct and the value of the correlation coefficient for them is $r = 0.067$, meaning that with an increase in the level of the GST enzyme, the concentration of uric acid increases [16].



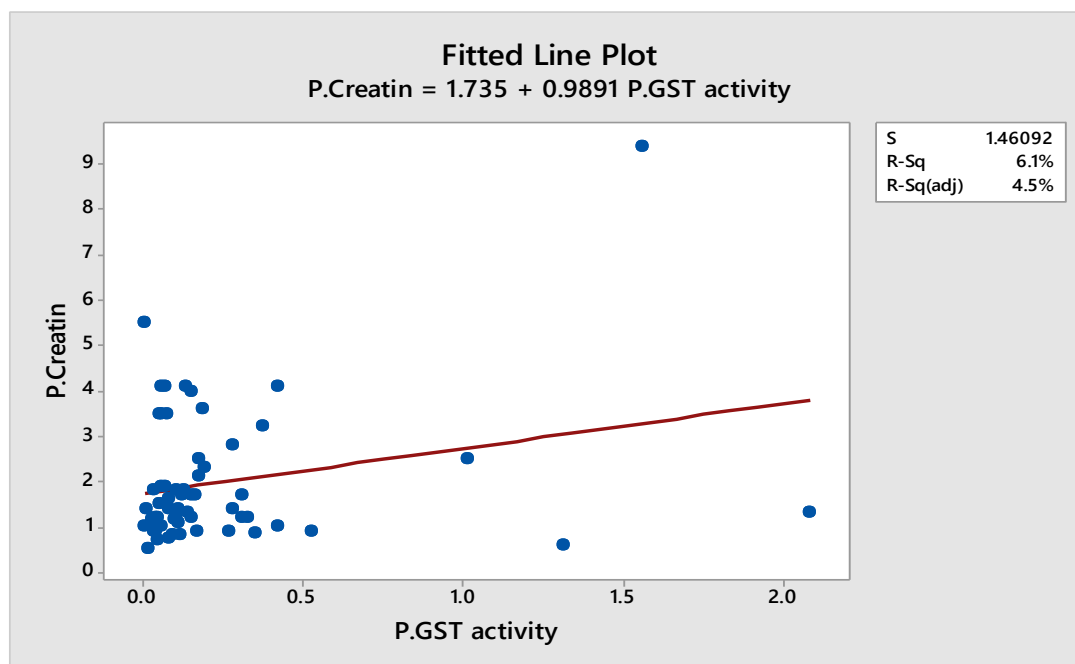
2. Correlation between GST and uric acid concentration level:

The relationship between them is direct and the value of the correlation coefficient for them is $r = 0.067$, meaning that with an increase in the level of the GST enzyme, the concentration of uric acid increases [17].



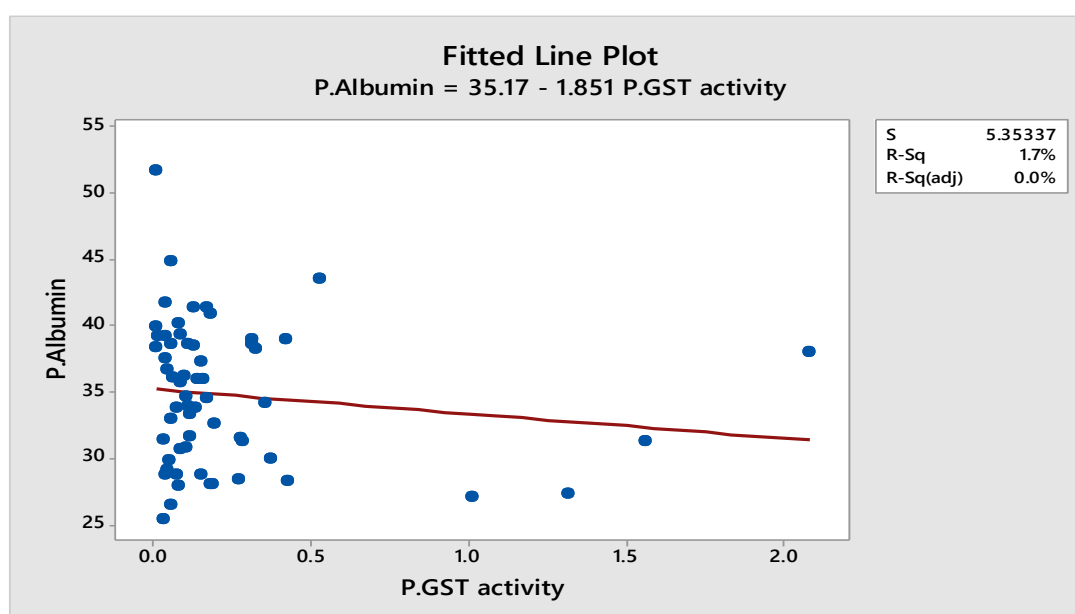
3. Correlation between GST and creatinine concentration level:

The relationship between them is direct and the value of the correlation coefficient for them is $r = 0.247$, meaning that with an increase in the level of the GST enzyme, the concentration of creatinine increases.



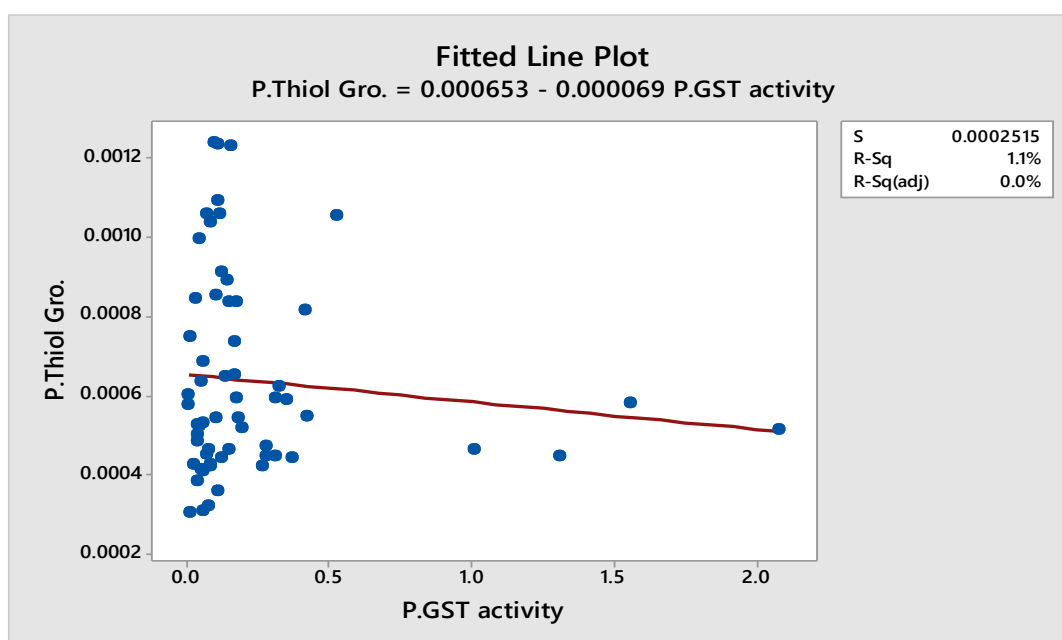
4. Correlation between GST and albumin concentration level:

The relationship between them is inverse and the value of the correlation coefficient for them is $r = -0.129$, meaning that when the level of the GST enzyme increases, the concentration of albumin decreases [18].



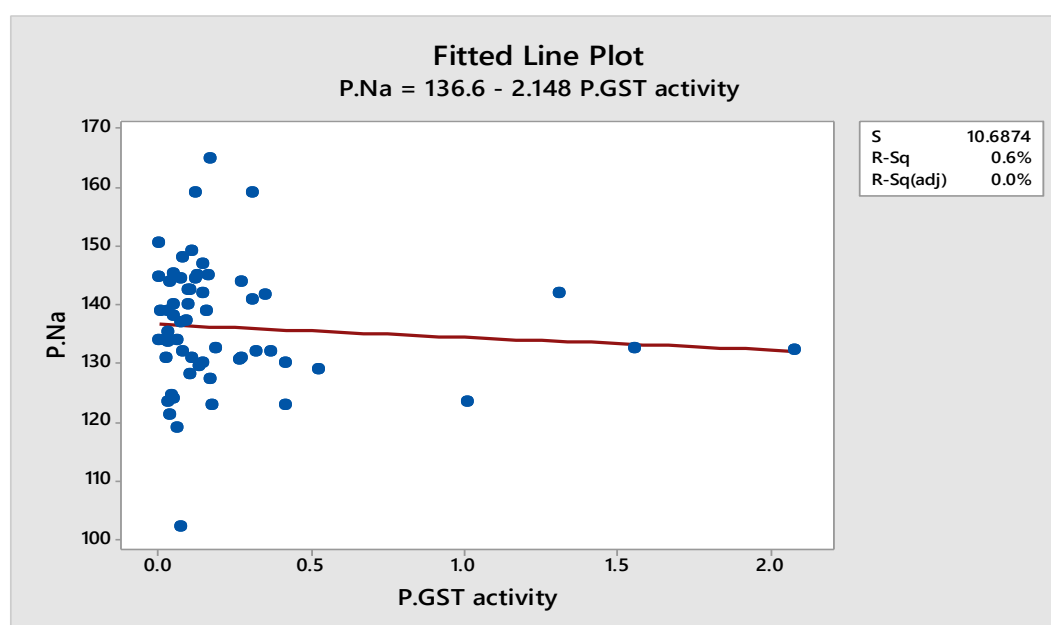
5. Correlation between GST and thiol group concentration:

The relationship between them is inverse and the value of the correlation coefficient for them is $r = -0.103$, meaning that when the level of the GST enzyme increases, the concentration of the thiol group decreases [19].



6. Correlation between GST and sodium ion concentration level:

The relationship between them is inverse and the value of the correlation coefficient for them is $r = -0.076$, meaning that when the level of the GST enzyme increases, the concentration of sodium ions decreases.



Conclusion

These results are consistent with previous studies that have shown an early decrease in glutathione S transferase (GST) activity during various types of acute kidney injury. This enzyme is one of the detoxification enzymes that stimulate tissue protection through the conjugation of GST to foreign substances and reactive oxygen molecules. The possible changes in GST enzyme expression during acute kidney injury have pathophysiological significance in detecting the severity of the injury [20].

REFERENCES

- Gorelik, Yuri, et al. "Acute renal failure following near-drowning." *Kidney international reports* 3.4 (2018): 833-840.
- Paller, Mark S. "Pathophysiologic mechanisms of acute renal failure." *Mechanisms of injury in renal disease and toxicity*. CRC Press, 2020. 3-13.
- Shirakabe, Akihiro, et al. "Worsening renal function definition is insufficient for evaluating acute renal failure in acute heart failure." *ESC heart failure* 5.3 (2018): 322-331.
- Vijayan, Anitha, et al. "Effect of frequent dialysis on renal recovery: results from the acute renal failure trial network study." *Kidney International Reports* 3.2 (2018): 456-463.
- Abdurakhmanovich, Khamidov Obid, et al. "Role of Kidney Ultrasound in the Choice of Tactics for Treatment of Acute Renal Failure." *Central Asian Journal of Medical and Natural Science* 2.4 (2021): 132-134.
- Noor, F. A. M., Elias, S. M., Bakar, S. A., Aris, A. Z., & Md, H. (2022). Blood Heavy Metals (Arsenic, Cadmium and Lead) Concentration and Genetic Polymorphism of Glutathione S-transferase Genes Among Adults in Coastal Area of Melaka, Malaysia. *Malaysian Journal of Medicine and Health Sciences* (eISSN 2636-9346) *Mal J Med Health Sci* 18(SUPP5): 45-52.
- النساء الحوامل صالح، نادية احمد دراسة العلاقة بين الفسفور وفعالية انزيم الفوسفاتيز القاعدي في مصل دم المصابات بمرض الفشل الكلوي في محافظة صلاح الدين مجلة تكريت للعلوم الصرفة. المجلد (١١)، العدد (٢)، صفحة ٦١-٥٦، ٢٠٠٦.
- Enomoto, A., Kimura, H., Chairoungdua, A., Shigeta, Y., Jutabha, P., Ho Cha, S., ... & Endou, H. (2002). Molecular identification of a renal urate-anion exchanger that regulates blood urate levels. *Nature*, 417(6887), 447-452.
- Verzì, A. E., Musumeci, M. L., Lacarrubba, F., & Micali, G. (2020). History of urea as a dermatological agent in clinical practice. *International Journal of Clinical Practice*, 74, e13621.
- Chen, C. C., Hsieh, J. C., Chao, C. H., Yang, W. S., Cheng, H. T., Chan, C. K., ... & Zan, H. W. (2020). Correlation between breath ammonia and blood urea nitrogen levels in chronic kidney disease and dialysis patients. *Journal of breath research*, 14(3), 036002
- Reynolds, K., & Valdes, R. (2016). *Pharmacogenomics and Precision Medicine, An Issue of the Clinics in Laboratory Medicine* (Vol. 36, No. 3). Elsevier Health Sciences.
- Belinskaia, D. A., Voronina, P. A., Batalova, A. A., & Goncharov, N. V. (2020). Serum albumin. *Encyclopedia*, 1(1), 65-75.
- Lim, Y. S., Larson, T. S., Benson, J. T., Kamath, P. S., Kremers, W. K., Therneau, T. M., & Kim, W. R. (2010). Serum sodium, renal function, and survival of patients with end-stage liver disease. *Journal of hepatology*, 52(4), 523-528.
- O. Atakisi, "The Role of Reduced Glutathione on the Activity of Adenosine Deaminase, Antioxidative System, and Aluminum and Zinc Levels in Experimental Aluminum Toxicity," *Biol Trace Elem Res*, vol. 201, no. 9, pp. 4429–4436, 2023, doi: 10.1007/s12011-022-03503-0.
- S. A. Sheweita, "The deleterious effects of cadmium on oxidative stress markers, drug-metabolizing, and antioxidant enzyme activities: Role of Silymarin and Garlic as Antioxidants," *Environmental Science and Pollution Research*, vol. 30, no. 52, pp. 112490–112502, 2023, doi: 10.1007/s11356-023-30197-1.

16. C. Li, "Role of Escin in breast cancer therapy: potential mechanism for inducing ferroptosis and synergistic antitumor activity with cisplatin," *Apoptosis*, vol. 28, no. 7, pp. 1154–1167, 2023, doi: 10.1007/s10495-023-01849-x.
17. Madhu, "Modulation in gene expression and enzyme activity suggested the roles of monodehydroascorbate reductase in development and stress response in bread wheat," *Plant Science*, vol. 338, 2024, doi: 10.1016/j.plantsci.2023.111902.
18. M. Işık, "Evaluation of the relationship among gene expressions and enzyme activities with antioxidant role and presenilin 1 expression in Alzheimer's disease," *J Cell Mol Med*, vol. 27, no. 21, pp. 3388–3394, 2023, doi: 10.1111/jcmm.17953.
19. C. S. Dzah, "Anti- and pro-oxidant properties of polyphenols and their role in modulating glutathione synthesis, activity and cellular redox potential: Potential synergies for disease management," *Advances in Redox Research*, vol. 11, 2024, doi: 10.1016/j.arres.2024.100099.
20. B. S. Ajisebiola, "Echis ocellatus venom-induced sperm functional deficits, pro-apoptotic and inflammatory activities in male reproductive organs in rats: antagonistic role of kaempferol," *BMC Pharmacol Toxicol*, vol. 25, no. 1, 2024, doi: 10.1186/s40360-024-00776-0.