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Research Article

Evaluate the Influence of Renalase Enzyme on Catecholamine Levels Before and After Dialysis in Patients with Renal Failure in Kirkuk City

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Abstract

Objective: This study was done to evaluate dialysis's impact on serum renalase and catecholamines (epinephrine, dopamine, and norepinephrine) in Kirkuk City patients with end-stage renal disease.

Method: The study was conducted at the Al-Amal Kidney Dialysis Unit in Kirkuk from December 1, 2023, to March 1, 2024. A total of 180 individuals were allocated into three distinct groups for the study. Initial participants in renal dialysis. The second group underwent a 4-hour dialysis treatment, whereas the third group consisted of healthy individuals without chronic renal disease. Before and after dialysis, Renalase and Catecholamine levels were assessed in all study participants.

Results: study results reveled to, after 4 hours from dialysis, patients with end stage renal disease exhibit improvement in the level of renalase enzyme comparing with renalase level before dialysis, while the level of catecholamines showed lowering in end stage renal disease patients after 4 hours from dialysis comparing with its levels before dialysis.

Conclusion: Dialysis elevated renalase levels, resulting in a reduction of circulating catecholamines such as epinephrine, norepinephrine, and dopamine. Patients suffering from advanced kidney failure and heart disease necessitate dialysis due to the ability of renalase to lower the levels of circulating catecholamines, thereby mitigating cardiovascular damage.

Keywords: End Stage Renal Disease; Dialysis; Renalase Enzyme; Catecholamines; Kirkuk City

Abbreviations

CKD: Chronic Kidney Disease

Introduction

end-stage renal disease, occurs when the kidneys function at less than 15% of their usual capacity, resulting in the inability to remove waste from the blood [1]. Acute renal failure manifests rapidly and may be managed. However, chronic kidney failure progresses gradually and often cannot be reversed [2]. Possible symptoms include edema, lethargy, emesis, and confusion [1]. Acute and chronic failure may lead to uremia, hyperkalemia, and volume overload [3]. Additional complications associated with chronic failure included cardiovascular disease, hypertension, and anemia [4,5].

Hemolytic uremic syndrome, hypotension, rhabdomyolysis, drugs side effects, and urinary tract blockage are all potential causes of acute renal failure. Diabetes, high blood pressure, nephrotic syndrome, and polycystic kidney disease are some of the medical diseases that may lead to chronic kidney failure [2].

The identification of the underlying cause dictates the appropriate therapy for an acute failure. A kidney transplant, hemodialysis, or peritoneal dialysis are all options for treating chronic failure [7].

Renalase is an enzyme that is dependent on flavin adenine dinucleotide and acts as an amine oxidase. It is secreted into the bloodstream by the kidney., The structural analysis of renalase reveals that it functions as an oxidase that relies on FAD as a cofactor [9].

Renalase is an enzyme that degrades catecholamines like adrenaline and noradrenaline in the circulation. It was discovered and named in 2005 by a group at Yale School of Medicine led by Dr. Gary Desir [10]. Propose that the kidney secretes this protein to regulate blood pressure [11].

The controversial enzyme renalase may break down catecholamines, which have a role in the body's "fight or flight" response. When administered renalase, myocardial contractility, vascular resistance, blood pressure, and heart rate are momentarily reduced in rats [10], Under typical conditions, renalase in the circulation remains dormant. Upon entering the bloodstream, catecholamines trigger a rapid and significant increase in renalase activity, sustained for at least one hour. The early activation may be ascribed to circulating renalase, which is released 15 minutes later [12].

Renalase levels exhibit a significant decrease in individuals suffering from severe chronic kidney disease. [11,13,14]., Multiple Prior research has demonstrated that chronic kidney illness can affect the amounts of renalase in the bloodstream [15,17]., However, these studies lack an investigation into the association between end-stage renal disease and renalase levels and catecholamines levels in Iraqi patients, particularly in Kirkuk City. Our study aims to investigate the influence of dialysis on the serum concentrations of renalase and catecholamines in patients with renal failure in Kirkuk City.

Patients, Materials and Methods

Study population and study design

This study was conducted at the Al-Amal Kidney Dialysis Unit in Kirkuk City, with 180 participants. The research occurred from December 1, 2023, until March 1, 2024. The study had three distinct groups. The initial cohort comprised 70 adult patients who underwent renal dialysis. A senior resident nephrologist identified the patients as individuals with chronic kidney disease (CKD) who were undergoing hemodialysis.

The second group comprised the identical patients who had received dialysis within a time frame of 4 hours. Meanwhile, the third group comprised 40 healthy adults with no prior history of chronic kidney disease (CKD), who were designated as the control group. The study assessed the levels of serum Renalase, Dopamine, Catecholamine, and liver and renal function tests before and after dialysis in both the patients and the control group.

Clinical and biochemical measurements

The diagnosis of chronic kidney disease (CKD) was established based on clinical manifestations, biochemical markers, and imaging examinations. Every participant had a thorough medical health assessment.

measurement of biochemical parameters

Approximately 5 ml of blood was collected from patients with CKD before and after dialysis and a healthy individual in the control group. The blood samples were collected in test tubes without any anticoagulant. The samples were allowed to reach the ambient temperature for 10-15 minutes to expedite the coagulation process. The tube was centrifugated for 15 minutes at 3000 revolutions per minute (RPM). Various biochemical parameters were examined by transferring clear serum into Eppendorf tubes and storing them at a temperature of -20°C [17].

B T Lab in China distributed reagent kits for the quantification of blood Renalase, Dopamine, epinephrine, and norepinephrine. Concentrations were determined by following the directions provided by the manufacturer. The serum concentration of renalase was determined using a commercially available immunochemistry test called ELISA. This test utilized a monoclonal antibody targeting renalase and was obtained from B T Lab. in China [18].

Ethical approval

This study received approval from the Ethical Approval Committee of the University of Kirkuk College. We obtained the patient's consent before gathering their medical history.

Statistical analysis

Data analysis Utilizes IBM SPSS Statistics for Windows version 20. The data was analyzed by calculating qualitative variables' means and standard deviations. A T-test was performed to determine the significance of differences between groups of continuous variables, and a P-value was determined. The statistical testing utilized a significance level of 0.05 [19].

Results

The study revealed a significant disparity in renalase levels between persons with renal failure before and after dialysis compared to healthy subjects. The findings demonstrated an increase in the concentration of renalase enzyme in patients with renal failure after 4 hours of dialysis, compared to its concentration before dialysis. Table (1) figure (1), On the contrary, patients with renal failure had higher levels of catecholamines such as norepinephrine, epinephrine, and dopamine, in comparison to healthy persons. However, these levels dropped after four hours of undergoing dialysis, table (2-4), figure (2-4).

Factor	No	Mean ± SD
Control	40	61.78 ± 8.27 C
Before	70	25.72 ± 4.15 A
After	70	45.61 ± 6.97 B

Table 1: Renalase levels in patients with renal failure before and after undergoing dialysis.

SD: stander deviation, Distinct capital letters denote statistically significant differences (P< 0.05) between the means.

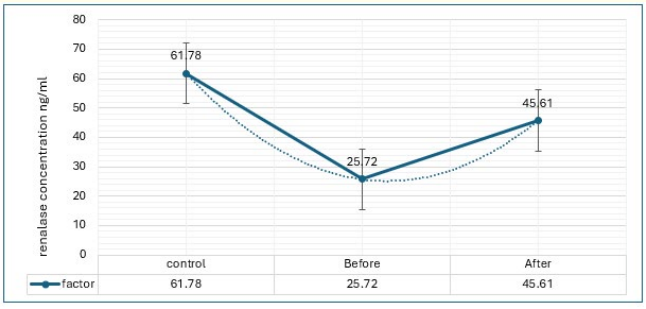

Figure 1: Renalase levels in patients with renal failure before and after undergoing dialysis.

Factor	No	Mean ± SD
Control	40	119.83 ± 14.49 C
Before	70	202.67 ± 26.18 A
After	70	161.50 ± 17.65 B

Table 2: Epinephrine levels in individuals with renal failure before and after dialysis.

SD: stander deviation, Distinct capital letters denote statistically significant differences (P < 0.05) between the means.

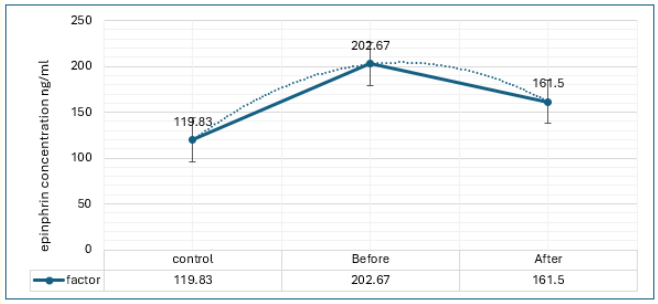

Figure 2: Epinephrine levels in individuals with renal failure before and after dialysis.

Factor	No	Mean ± SD
Control	40	1264.2 ± 55.7 C
Before	70	3636.8 ± 59.4 A
After	70	2289.3 ± 69.8 B

Table 3: Comparison between the level of norepinephrine in renal failure patients, before and after dialysis

SD: stander deviation, Distinct capital letters denote statistically significant differences (P< 0.05) between the means.

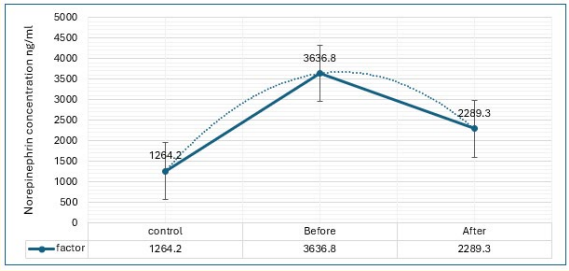

Figure 3: Comparison between the level of norepinephrine in renal failure patients, before and after dialysis.

Factor	No	Mean ± SD
Control	40	22.148 ± 4.638 C
Before	70	79.510 ± 9.700 A
After	70	44.620 ± 8.400 B

Table 4: comparison between the level of dopamine in renal failure patients before and after dialysis.

SD: Stander deviation, Distinct capital letters denote statistically significant differences (P < 0.05) between the means.

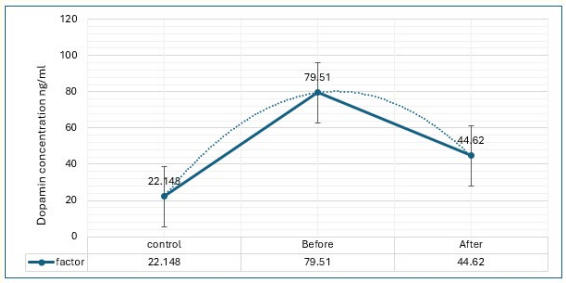

Figure 4: comparison between the level of dopamine in renal failure patients before and after dialysis.

Discussion

This study aimed to evaluate the impact of dialysis on the concentration of renalase enzyme in the blood and examine the correlation between renalase fluctuation and catecholamine levels. The study's findings indicated a rise in serum renalase levels in patients with chronic kidney disease (CKD) following dialysis compared to their pre-dialysis levels.

Our research findings corroborate another study that showed a significant decrease in Renalase levels in individuals with severe chronic kidney illness (end-stage renal disease) [15,20].

The kidney is considered the primary source of the renalase enzyme, unlike other sources of renalase, such as the heart and skeletal muscle, human liver cells, and the testes of mice. The blood level of renalase will indicate any decrease in kidney function [13,21], The renalase enzyme is released by the proximal convoluted tubules of the kidney, mainly in response to epinephrine. Any variables that influence the concentration of epinephrine can likewise alter the renalase concentration. Typically, individuals with end-stage renal illness encounter hypertension as a result of a response in the autonomic nervous system. This reflex causes a decline in epinephrine levels, leading to a decrease in the secretion of renalase by the kidney tubules [22-26].

This approach clarifies the results of our experiment on the levels of the renalase enzyme in patients suffering from end stage renal disease, in contrast. Our inquiry findings also showed a rise in the levels of catecholamines, notably adrenaline, norepinephrine, and dopamine. This finding is consistent with Renalase oxidizes catecholamines, with epinephrine oxidizing more than dopamine and norepinephrine [21].

Our study revealed that patients undergoing dialysis experienced an increase in renalase levels, resulting in a reduction in catecholamine levels. The observed outcome can be ascribed to renal failure caused by ischemia or toxic damage, leading to the buildup of waste substances like urea. The buildup of substances causes the demise of the cells that line the renal tubules, disturbing their normal functioning and resulting in substantial harm to the tissue. Consequently, the disruption of the internal cellular balance causes a decline in the functioning of the renal tubular epithelial cells [27-29], Dialysis helps restore the balance of the renal tubules by reducing the negative impact of metabolic waste products on the function of the renal tubular epithelium, leading to an improvement in the secretion of renalase by the kidney's nephrons [30,31], This process helps elucidate the results of our investigation, which demonstrate an enhancement in the concentration of renalase in the sera of patients after dialysis compared to its level prior to dialysis. Elucidate the decline in catecholamine levels in patients' sera following dialysis.

The study was limited by the small size of the study population, as it was conducted in a single town and for a limited duration.

Conclusion

The study revealed that dialysis treatment raised the concentration of renalase, resulting in a subsequent reduction in the levels of adrenaline, norepinephrine, and dopamine in the bloodstream. This enhancement is especially significant for patients who have both end stage renal disease and cardiovascular illness, as renalase plays a vital role in mitigating harm to the cardiovascular system by decreasing the amounts of circulating catecholamines.

Author Contributions

- Design and development
- Data collection and organization
- Statistical analysis and comprehension
- Composition of the article
- Reviewing the essay critically for key conceptual points
- Proficiency in statistical analysis
- Ultimate endorsement and guarantee of the article

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Conflicts of Interest

No conflicts of interest were found.

Bibliography

1. ADEYOMOYE OI., *et al*. "The biological roles of urea: A review of preclinical studies". *Indian Journal of Nephrology* 32 (2022): 539-545.
2. BLAKELEY S. "Renal failure and replacement therapies, Springer Science and Business Media.
3. CLATWORTHY M. "Nephrology: clinical cases uncovered, John Wiley and Sons (2010).
4. CORSELLO A., *et al*. "Walter E. Dandy: his contributions to pituitary surgery in the context of the overall Johns Hopkins Hospital Experience". *Pituitary* 20 (2017): 683-691.
5. DANZIGER J and HOENIG MPJAJOKD. "The role of the kidney in disorders of volume: core curriculum". American Journal of Kidney Disease 68 (2016): 808-816.
6. DESIR GV., *et al*. "Renalase lowers ambulatory blood pressure by metabolizing circulating adrenaline". *Journal of the American Heart Association* 1 (2012): e002634.
7. DESIR GVJKI. "Regulation of blood pressure and cardiovascular function by renalase". *Hypertension Research* 76 (2009): 366-370.
8. DIABETES MJN. "National Institute of Diabetes and Digestive and Kidney Diseases" (2017).
9. HAUSBERG M., *et al*. "Sympathetic nerve activity in end-stage renal disease". *Circulation* 106 (2002): 1974-1979.
10. JOLES JA and KOOMANS HAJH. "Causes and consequences of increased sympathetic activity in renal disease". *Hypertension* 43 (2004): 699-706.
11. JUMAA AH., *et al*. "Esomeprazole and Amygdalin combination cytotoxic effect on human cervical cancer cell line (Hela cancer cell line)". *Iraqi Journal of Cancer and Medical Genetics* 10 (2018): 2236-2241.
12. KERR JF., *et al*. "Apoptosis: a basic biological phenomenon with wide ranging implications in tissue kinetics". *British Journal of Cancer* 26 (1972): 239-257.
13. LANGER P and CHARNEY A. "Renal Case Report (2019).
14. LI G., *et al*. "Catecholamines regulate the activity, secretion, and synthesis of renalase". *Circulation* 117 (2008): 1277-1282.
15. LIAO MT., *et al*. "Insulin resistance in patients with chronic kidney disease". *BMC Nephrology* (2012).
16. MAHDI S., *et al*. "Effect of different concentrations of Bovine Serum Albumin on some of the frozen sperm characteristics of the rams". *Plant Archives* 19 (2019): 1486-1488.
17. MILANI M., *et al*. "FAD-binding site and NADP reactivity in human renalase: a new enzyme involved in blood pressure regulation". *Journal of Molecular Biology* 411 (2011): 463-473.
18. OGUZ EG., *et al*. "Increased serum renalase in hemodialysis patients: is it related to left ventricular hypertrophy?" *Renal Failure* 38 (2016): 1180-1186.
19. SALMAN IMJCHR. "Cardiovascular autonomic dysfunction in chronic kidney disease: a comprehensive review". *Current Hypertension Reports* 17 (2015): 1-20.
20. SCHNELLMANN RGJC. "DOULL'S TOXICOLOGY THE BASIC SCIENCE OF POISONS, N. Y. T. M.-H. 2001". Toxic Responses of the Kidney (2001).
21. SEBASTIAN M. "Renal toxicity. Handbook of Toxicology of Chemical Warfare Agents. Elsevier (2009).

22. SERWIN NM., *et al*. "Serum-to-urine renalase ratio and renalase fractional excretion in healthy adults and chronic kidney disease patients". *BMC Nephrology* 21 (2020): 1-7.

23. SEVERINA I., *et al*. "The history of renalase from amine oxidase to alpha-NAD (P) H-oxidase/anomerase". *Biochemistry (Moscow) Supplement Series B: Biomedical Chemistry* 61 (2015): 667-679.

24. SKRZYPCZYK P., *et al*. "Renalase in children with chronic kidney disease". *Biomarkers* 24 (2019): 638-644.

25. WANG F., *et al*. "Epinephrine evokes renalase secretion via a-adrenoceptor/NF-κB pathways in renal proximal tubular epithelial cells". *Kidney and Blood Pressure Research* 39 (2014): 252-259.

26. WANG F., *et al*. "Serum renalase is related to catecholamine levels and renal function". *Clinical and Experimental Nephrology* 19 (2015): 92-98.

27. WANG J., *et al*. "Identification, expression and tissue distribution of a renalase homologue from mouse". *Molecular Biology Reports* 35 (2008): 613-620.

28. WEXLER DJ., *et al*. "Research gaps in gestational diabetes mellitus: executive summary of a national institute of diabetes and digestive and kidney diseases workshop". *Obstetrics and Gynecology* 132 (2018): 496-505.

29. WISNIEWSKA M., *et al*. "Renalase in haemodialysis patients with chronic kidney disease". *Journal of Clinical Medicine* 10 (2021): 680.

30. XU J., *et al*. "Renalase is a novel, soluble monoamine oxidase that regulates cardiac function and blood pressure". *Journal of Clinical Investigation* 115 (2005): 1275-1280.

31. YASIN YS., *et al*. "Effect of Laetrile Vinblastine Combination on the Proliferation of the Hela Cancer Cell Line". *Asian Pacific Journal of Cancer Prevention* 24 (2023): 4329.