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STUDY OF THE RELATIONSHIP BETWEEN GHREL IN HORMONE AND NITRIC OXIDE IN PATIENTS WITH CHRONIC KIDNEY DISEASE IN THI-QAR GOVERNORATE – IRAQ

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Abstract

Objective: When abnormalities in kidney structure or function are evident for more than three months, it is referred to as chronic kidney disease (CKD), a complicated and progressive chronic disorder that can have devastating health effects. Either reduced glomerular filtration rate or indicators of renal injury could be evident. End-stage renal disease (ESRD) patients are increasingly choosing PD, HD, and kidney transplantation as treatments to extend their lives because of the development of renal replacement therapies, such as kidney transplantation, hemodialysis (HD), peritoneal dialysis (PD), and continuous renal replacement therapy (which is frequently used for acute renal failure). Loss of muscle mass may result from dialysis treatments that increase protein breakdown and decrease protein synthesis. These reactions continue after dialysis. The purpose of this research is to look into the connection between the ghrelin. Materials and Method: In order to determine the blood lipid profile and Ghrelin hormone levels, 90 individuals with Chronic Kidney Disease (CKD) on dialysis were divided into 45 males, 45 females, and 90 healthy subjects. The Ghrelin hormone concentration was compared with the other biochemical parameters, and the relationship between the hormones Ghrelin and Nitric Oxide was also found. Results: Ninety healthy subjects and ninety chronic kidney disease (CKD) patients with dialysis had their blood lipid profiles and Ghrelin hormone and nitric oxide levels measured. The results included a comparison of the hormone's concentration with other biochemical parameters and the identification of the hormone's relationship with nitric oxide. Results: When compared to the control group, dialysis patients' nitric oxide levels significantly decreased ($p \leq 0.05$). There were no discernible variations in the levels of serum nitric oxide between the sexes. ($p < 0.05$).Ghrelin levels in the blood serum of dialysis patients were significantly lower than those in the control group ($p \leq 0.05$). Additionally, it was demonstrated that the level of the hormone Ghrelin was significantly lower in females than in males ($p \leq 0.05$). Conclusion: When comparing dialysis patients to the control group, we detect a significant drop in the levels of Ghrelin Hormone and Nitric Oxide in patients with chronic kidney disease.It follows that low nitric oxide and ghrelin levels in chronic renal disease patients can cause kidney failure to progress to an advanced degree and eventually require dialysis.

Keywords: Chronic kidney disease, Ghrelin, Nitric Oxide.

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Introduction

In low-income nations, chronic kidney disease (CKD) is still mostly caused by poverty-related factors such high concentrations of disease-transmitting vectors, inadequate access to safe water, infectious diseases brought on by poor sanitation, and environmental pollutants [1]. Two of the main causes of chronic kidney disease (CKD) in many nations are interstitial nephritis and chronic glomerulonephritis [2].

If kidney function is reduced, the estimated glomerular filtration rate (eGFR) must be less than 60 ml/min/1.73 m2, or there must be signs of kidney damage, such as hematuria, albuminuria, or abnormalities shown on imaging, and they must be present for at least three months [3]. A more practical method in the office is to estimate GFR (estimated GFR, or eGFR) from the serum creatinine concentration, using either the Cockcroft-Gault or the Modification of Diet in Renal Disease (MDRD) Study estimating equations. Although creatinine clearances can be calculated from urine creatinine

concentration measured in a 24-hour urine collection and a concomitant serum creatinine concentration [4]. By area, there are significant differences in the occurrence of various aetiologies. Although the exact etiology of chronic kidney disease (CKD) is unknown, there are numerous reasons, including well-known and studied ones like diabetes, glomerulonephritis, and cystic kidney disorders. For example, although CKD and hypertension are closely associated, there is ongoing debate on whether hypertension causes or results from CKD [5].

A peptide hormone, ghrelin is primarily released by the small intestine and stomach. demonstrated that ghrelin causes body weight gain and fat utilization, which in turn causes obesity. This finding provides the first indication of ghrelin's function as an appetite-stimulating hormone, in addition to its effects on growth hormone release. In the hypothalamus, ghrelin stimulates the release of neuropeptide Y (NPY) and agoutirelated peptide (AgRP), two potent neuropeptides that stimulate appetite.Plasma ghrelin levels increase prior to meals and decrease thereafter. Gastritis and gastric motility are stimulated by ghrelin. Moreover, insulin secretion and glucose metabolism are impacted by it.It could have a significant impact on the etiology of inflammation, cardiovascular problems, and protein-energy wasting (PEW) in chronic kidney disease (CKD). Changes in these circulating ghrelin proteins have an effect on the CKD8 environment as a whole.Improved muscle metabolism and dietary alternatives may result from ghrelin's impact on hunger and muscle mitochondria [9]. Anorexia and cachexia symptoms, which are linked to a lower quality of life and a higher death rate, are frequently present in patients with chronic kidney disease (CKD). Anorexia, cachexia, renal osteodystrophy, and an increased risk of cardiovascular disease in individuals with chronic kidney disease (CKD) may all be attributed in part to chronic inflammation. Given its positive effects on appetite and meal enjoyment, ghrelin may be a useful treatment for CKD patients who suffer from anorexia. Ghrelin has been demonstrated to have anti-inflammatory qualities in addition to its ability to stimulate appetite [10].

Maintaining vascular homeostasis is facilitated by nitric oxide, a potent vasodilatory and anti-inflammatory signaling molecule with several functions. Endothelial dysfunction is characterized by a diminished capacity for nitric oxide generation and decreased nitric oxide sensitivity. Nitric oxide produced by endothelial cells is a vital regulator of this balance. This ultimately causes a prothrombotic, proinflammatory, and less compliant blood vessel wall by creating an imbalance in vascular homeostasis. In several pathophysiologic disorders, endothelial dysfunction plays a major role [11]. Endothelial nitric oxide synthase (eNOS) and neuronal NOS (nNOS) produce NO, which is involved in the control of the glomerular microcirculation, the recovery of renal function, and the prevention of platelet adhesion and aggregation. On the other hand, inducible NOS (iNOS) are the source of NO in pathological conditions such as inflammation. Furthermore, it has been demonstrated that glomerular damage and NO-induced oxidative stress significantly correlate [12].Activation of redox-sensitive proinflammatory transcription factors and signal transduction pathways may result in an inflammatory response and ultimately apoptosis, further exacerbating kidney injury [13].

Materials and Methods

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All samples for this prospective study were from patients who visited the dialysis unit at Al-Nassiryah Hospital and specialty clinics. comprised 90 blood samples from CKD patients on dialysis, 45 of whom were men, 45 of whom were women, and 90 healthy participants. Serum samples were separated and stored at -20°C until they were tested for nitric oxide and ghrelin hormone. Five milliliters of blood samples from CKD patients receiving dialysis and controls were taken, and they were allowed to clot at room temperature in empty disposable tubes before being centrifuged at 3000 revolutions per minute (rpm) for ten minutes.

ELISA Reader, USA used a kit provided by Elabscience, USA to assess serum levels of the hormones ghrelin and nitric oxide. Mean ± SD, or mean ± standard deviations, were used to express the results. To compare parameters among the various study groups, a one-way ANOVA test was employed. Statistical significance was defined as P-values ($P < 0.05$).

Results and Discussion

When dialysis patients' blood serum Ghrelin levels were compared to controls, there was a significant drop ($p \leq 0.05$) in the former group.These findings align with a prior study that found dialysis patients had decreased levels of ghrelin. The data also show that low ghrelin levels exacerbate the increased mortality risk linked to a state of (PEW), suggesting that

ghrelin is regulated by an individual's nutritional status. It is conceivable that these interactions could be amplified by the uremic phenotype, which is associated with a considerably higher prevalence of anorexia, protein-energy wasting (PEW), inflammation, and cardiovascular disease (CVD) [14,15]. Patients with end-stage renal disease (ESRD) receiving hemodialysis frequently struggle with malnutrition. Ghrelin may aid in the recovery of appetite and the fight against malnutrition because of its several concurrent functions, which include the release of growth hormone, fat accumulation, increased food intake, and activation of hypothalamic appetite centers.

Cachexia/PEW is strongly associated with inflammation, and systemic inflammation is frequent in CKD. The central nervous system is influenced by inflammatory mediators, which can change appetite and metabolism. In this regard, ghrelin might be a significant factor. Inflammation is reduced by ghrelin. Macrophages and leukocytes both express ghrelin receptors. The release of inflammatory cytokines is inhibited by ghrelin [17].

Additionally, it was demonstrated that the level of the hormone Ghrelin was significantly lower in females than in males ($p \leq 0.05$).These findings deviate from earlier research [18]. To elucidate gender disparities in ghrelin levels in hemodialysis (HD) patients, ghrelin levels were evaluated, and the link between ghrelin and pertinent clinical indicators was studied by gender. Given that plasma ghrelin levels are mostly determined by gastric atrophy. Serum pepsinogen levels can be used to identify atrophy of the gastric mucosa, particularly in the stomach body, where low renal clearance of pepsinogen causes elevated blood levels of the protein in individuals with kidney failure [19,20].

Table 1 :Serum Ghrelin hormone concentrations of (control) and (hemodialysis) groups.

Ghrelin Hormone				
Group of	**No.**	**Control Mean± SD**	**Ghrelin (µmol/L) Mean± SD**	**P-value**
Male	90	303.66±15.33	227.54±18.43	0.000
Female	90	280.36±16.00	210.34±13.73	0.000
P-value		0.001	0.010	

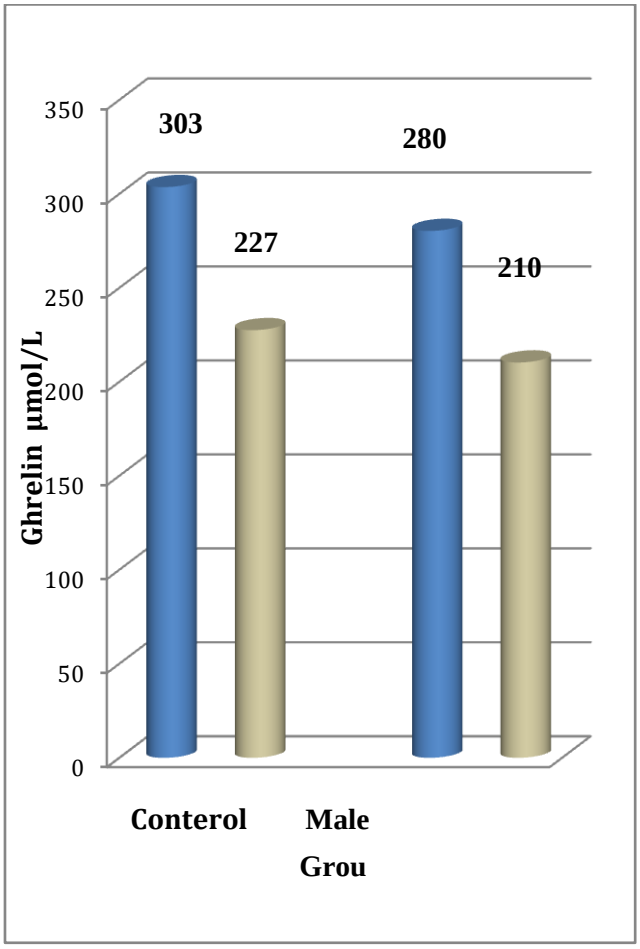

Figure 1 :Serum levels of ghrelin in control groups and both sexes in hemodialysis patients.

While Nitric oxide levels showed a significant decrease in patients with dialysis compared to control($p \leq 0.05$).It was found no significant differences in the concentration of serum nitric oxide between male and female. ($p \leq 0.05$).These results disagree with previous study[21].Reduced nitric oxide (NO) bioavailability is a hallmark of chronic kidney disease (CKD), with this disturbance being almost universal in patients who reach the most advanced phase of CKD, end-stage kidney disease (ESKD). Low NO bioavailability in CKD depends on several mechanisms affecting the expression and the activity of endothelial NO synthase (eNOS). Accumulation of endogenous inhibitors of eNOS, inflammation and oxidative stress and the anti-ageing vasculoprotective factor all impinge upon NO bioavailability and are the main risk factors to endothelial dysfunction in CKD[22].Vascular abnormalities are contribute to renal disease progression. Endothelial dysfunction and oxidative stress are evident in patients with renal disease, a major source of ROS in renal tubular epithelial cells and endothelial cells , induces mitochondrial abnormalities, contributing to endothelial dysfunction, vascular abnormalities, and renal disease progression[23].NO is generated from the conversion of L-arginine to L-citrulline by NOS that requires the cofactors tetrahydrobiopterin (BH4), flavin adenine dinucleotide, and flavin mononucleotide. Nitric Oxide deficiency in the kidney can be caused by: (1) L-arginine deficiency, (2) decreased abundance and activity of NOS, (3) inactivation of NO by increased oxidative stress, and (4) increased endogenous NOS inhibitor ADMA. Several lines of

evidence indicate that NO deficiency contributes to hypertension and kidney disease [24].

Table-2: Serum NO concentrations of (control) and (hemodialysis) groups.

NO				
Group of	**No.**	**Control Mean± SD**	**NO(µmol/L) Mean± SD**	**P-value**
Male	90	210.42±37.67	146.32±24.50	0.000
Female	90	182.37±20.12	143.32±28.57	0.000
P-value		0.021	0.768	

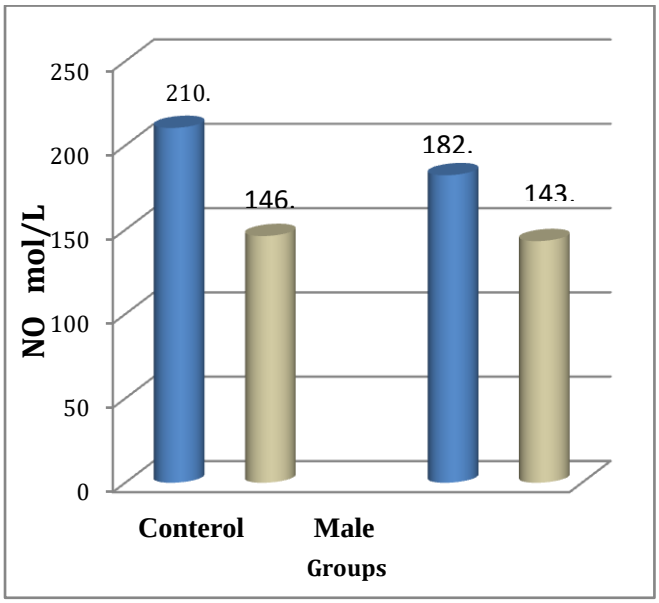

Figure 2: Serum levels of NO in control groups and both sexes in hemodialysis patients.

Conclusion

From the data presented in this study, we could obtain the following conclusions are In Chronic kidney disease patients with dialysis, we finding decrease in Nitric Oxide and Ghrelin hormone in Chronic kidney disease patients with dialysis as compared to control group.It was also shown that there was a significant decrease in the level of the Ghrelin hormone in female compared to male,Also, no significant differences were observed in nitric oxide levels between women and men.

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Conflict of Interest

No Conflict of Interest

Inform Consent

Each patients has Consent writing for study

Ethical Statement

Study Reflections ethical statement

Author Contribution

All authors participate in the work

Reference

1. Jha, V., Garcia-Garcia, G., Iseki, K., Li, Z., Naicker, S., Plattner, B., & Yang, C. W. (2013). Chronic kidney disease: global dimension and perspectives. The Lancet, 382(9888), 260-272.
2. Foundation, N. K. (2006). KDOQI clinical practice guidelines and clinical practice recommendations for anemia in chronic kidney disease.American journal of kidney diseases: the official journal of the National Kidney Foundation, 47(5 Suppl 3), S11-S145.
3. Webster, A. C., Nagler, E. V., Morton, R. L., & Masson, P. (2017). Chronic kidney disease. The lancet, 389(10075), 1238-1252.
4. Coresh, J., Astor, B. C., Greene, T., Eknoyan, G., &Levey, A. S. (2003). Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. American journal of kidney diseases, 41(1), 1-12.
5. Pearce, N., &Caplin, B. (2019). Let's take the heat out of the CKDu debate: more evidence is needed. Occupational and environmental medicine, 76(6), 357-359.
6. Tschöp, M., Smiley, D. L., &Heiman, M. L. (2000). Ghrelin induces adiposity in rodents. Nature, 407(6806), 908-913.
7. Cowley, M. A., Smith, R. G., Diano, S., Tschöp, M., Pronchuk, N., Grove, K. L., ...& Horvath, T. L. (2003). The distribution and mechanism of action of ghrelin in the CNS demonstrates a novel hypothalamic circuit regulating energy homeostasis. Neuron, 37(4), 649-661.
8. Gunta, S. S., &Mak, R. H. (2013). Ghrelin and leptin pathophysiology in chronic kidney disease. Pediatric Nephrology, 28, 611-616.
9. Derakhshandeh, S., &Ostad, A. N. (2022). The Impact of Ghrelin on Cachexia among Children with Chronic Kidney Disease. Journal of Nutrition, Fasting & Health, 10.
10. Cheung, W. W., &Mak, R. H. (2010). Ghrelin in chronic kidney disease. International Journal of Peptides, 2010.
11. Cyr, A. R., Huckaby, L. V., Shiva, S. S., &Zuckerbraun, B. S. (2020). Nitric oxide and endothelial dysfunction. Critical care clinics, 36(2), 307-321.
12. Snijder, P. M., Van Den Berg, E., Whiteman, M., Bakker, S. J. L., Leuvenink, H. G. D., & Van Goor, H. (2013). Emerging role of gasotransmitters in renal transplantation. American Journal of Transplantation, 13(12), 3067-3075.
13. Ozbek, E. (2012). Induction of oxidative stress in kidney. International journal of nephrology, 2012.
14. Carrero, J. J., Nakashima, A., Qureshi, A. R., Lindholm, B., Heimbürger, O., Bárány, P., &Stenvinkel, P. (2011). Protein-energy wasting modifies the association of ghrelin with inflammation, leptin, and mortality in hemodialysis patients. Kidney international, 79(7), 749-756.
15. Şahin, H. A. B. İ. B. E., Uyanik, F., Inanç, N., &Erdem, O. (2009). Serum zinc, plasma ghrelin, leptin levels, selected biochemical parameters and nutritional status in malnourished hemodialysis patients. Biological trace element research, 127, 191-199.

16. Amin, E., Eldesouky, A., Abdel-Aziz, H., &Rageb, O. (2019). Malnutrition Markers and Serum Ghrelin Levels in Hemodialysis Patients. GEGET, 14(2), 32-40.
17. Cheung, W. W., &Mak, R. H. (2010). Ghrelin in chronic kidney disease. International Journal of Peptides, 2010.
18. Sakao, Y., Ohashi, N., Sugimoto, M., Ichikawa, H., Sahara, S., Tsuji, T., ...& Yasuda, H. (2019). Gender differences in plasma ghrelin levels in hemodialysis patients. Therapeutic Apheresis and Dialysis, 23(1), 65-72.
19. Sakao, Y., Sugimoto, M., Ichikawa, H., Sahara, S., Tsuji, T., Ohashi, N., ...& Yasuda, H. (2016). Severity of gastric mucosal atrophy is the major determinant of plasma ghrelin level in hemodialysis patients. American Journal of Nephrology, 44(3), 224-233.
20. Sugimoto, M., Sahara, S., Ichikawa, H., Sakao, Y., Ohashi, N., Sugimoto, K., ...&Andoh, A. (2017). Natural course of Helicobacter pylori infection in Japanese hemodialysis patients. Digestion, 95(4), 302-309.
21. Carlström, M. (2021). Nitric oxide signalling in kidney regulation and cardiometabolic health. Nature reviews nephrology, 17(9), 575-590.
22. Roumeliotis, S., Mallamaci, F., &Zoccali, C. (2020). Endothelial dysfunction in chronic kidney disease, from biology to clinical outcomes: a 2020 update. Journal of Clinical Medicine, 9(8), 2359.
23. Kahveci, A. S., Barnatan, T. T., Kahveci, A., Adrian, A. E., Arroyo, J., Eirin, A., ... &Irazabal, M. V. (2020). Oxidative stress and mitochondrial abnormalities contribute to decreased endothelial nitric oxide synthase expression and renal disease progression in early experimental polycystic kidney disease. International journal of molecular sciences, 21(6), 1994.
24. Hsu, C. N., &Tain, Y. L. (2019). Regulation of nitric oxide production in the developmental programming of hypertension and kidney disease. International Journal of Molecular Sciences, 20(3), 681.