Short Communication

Assessment of Arginase II with Biochemical Changes in Patients with Chronic Kidney Disease

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Abstract

Background: Chronic kidney disease (CKD) is defined as the presence of kidney damage or an estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 mt^2, persisting for 3 months or more, irrespective of the cause. Arginase activity has two major homeostatic aims: first, to detoxify of ammonia through urea synthesis, and second, to produce ornithine, the precursor for prolines and polyamines. Determine arginase activity represents a key feature of kidney failure. **Objective:** Evaluate the role of arginase II in the development of CKD. **Materials and Methods:** This research conducted a case–control study involving a total of 90 participants, split into two healthy groups of 45 each is misleading as it suggests both groups are healthy, which contradicts the earlier mention of a chronic kidney group. Blood samples were collected to measure arginase II. Other variables, including age and BMI, were also assessed. Statistical analyses, including ROC-curve analysis, were conducted to evaluate the diagnostic accuracy of ARGII. **Results:** The study found a significant increase in ARGII protein concentration in the CKD group compared to the control group ($P < 0.05$), additionally, the ARGII ROC resulted in a 98.8% area under the curve. **Conclusion:** The results emphasize the importance of arginase play a crucial role in CKD

Keywords: Arginase II, chronic kidney disease, patient

Introduction

Chronic kidney disease (CKD) has emerged as a significant public health concern in Babylon City. It is recognized as a devastating condition that has reached epidemic proportions due to the rising prevalence of its associated risk factors.[1] It is a condition where kidney function gradually declines and renal replacement therapy (dialysis or transplantation) becomes necessary. Pathologic abnormalities indicated by renal biopsy or imaging studies, abnormalities in urinary sediment, or elevated urinary albumin excretion rates are all considered forms of kidney damage.[2,3] In Iraq, CKD is among the top five life-threatening diseases, as reported by the Iraqi Ministry of Health.[4] Throughout the course of the disease, patients with CKD experience structural and functional changes within the kidneys, leading to injuries in the glomeruli, tubules, and blood vessels. Retinal fibrosis develops as a result of chronic inflammation, oxidative stress, and hypoxia, all of which are features of the disease's progression phase.[5,6] Arginine amidinase (EC 3.5.3.1), canavanase, L-arginase, and arginine transamidinase are manganese-containing enzymes. It influences the last stage that produces urea. As Figure 1 shows,[7] it is prevalent in every aspect of life.[8]

There are two varieties of this sort of enzyme in most mammals. Arginase I is the form that works in the urea cycle and is found in the cytoplasm of the liver cells.[9]Arginase II the second isozyme, controls the amounts of arginine and ornithine in cells. Additionally, it has a location in the mitochondria of several bodily

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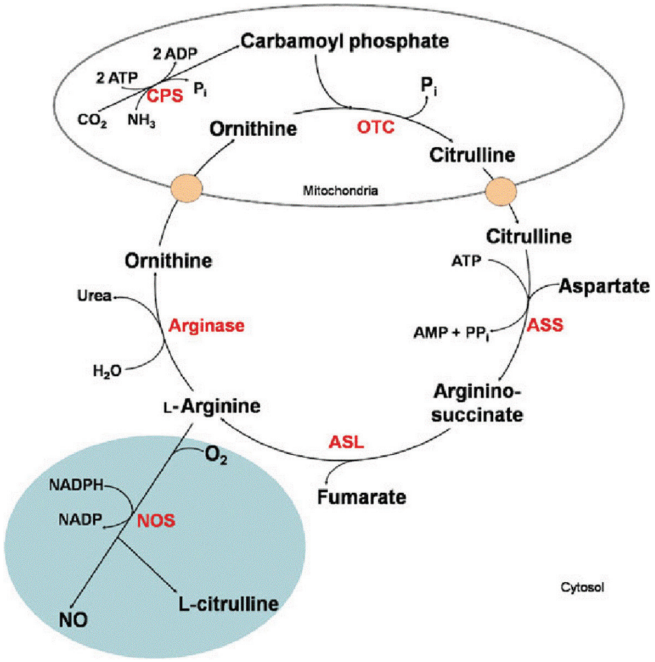


Figure 1: Urea cycle

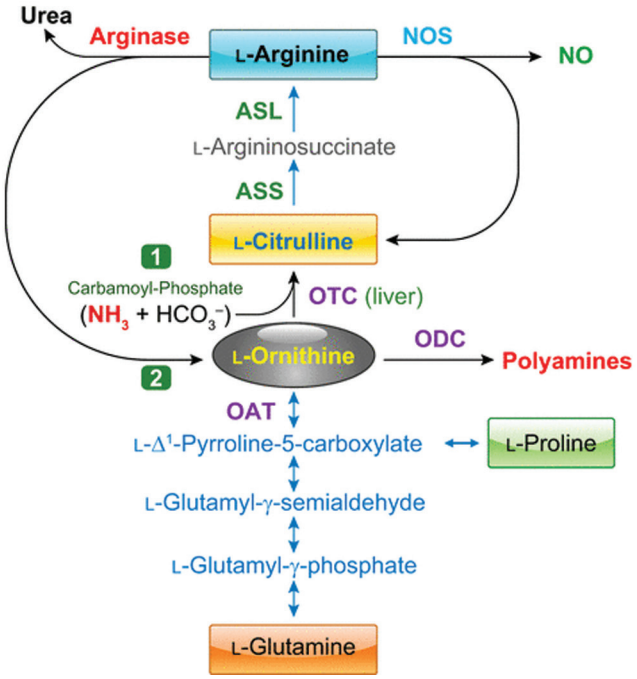


Figure 2: Shown the production of polyamines and proline from ornithine

tissues, including the kidneys and prostate, where it is highly prevalent. Additionally, the brain, nursing mammary glands, and macrophages may have them at lesser concentrations.[10] It is possible to identify a second isozyme even in the lack of additional urea cycle enzymes.[11]

There are two main homeostatic goals of arginase activity: first, it produces ornithine, a precursor of prolines and polyamines, and second, it removes ammonia through urea production.[8] ARG hydrolyzes L-arginine to produce L-ornithine and urea. As seen in Figure 2, ornithine aminotransferase (OAT) will convert L-ornithine to L-proline, and the ornithine decarboxylase (ODC) route will convert it to polyamines. Mammals use the ornithine generated from arginine for the production of proline, a polyamine, in the cytoplasm and glutamine in the mitochondria. They are necessary for inflammation, wound healing, tissue repair, and neural development in addition to their critical involvement in cell proliferation and growth.[12,13]

Materials and Methods

There were 90 participants in this case–control research study, of which 45 had chronic renal disease (females 20 with 25 males) and 45 appeared to be in good health (females 20 with 25 males). All of the samples had been collected during August and October of 2023. Samples were taken from the dialysis units at Babylon, Iraq's Marjan and Imam Al-Sadiq Teaching Hospitals.

They chose the patient groups based on selection criteria and exclusion criteria included smokers, the subjects under the age of 18, subjects with hyperglycemia, hypertension (HT), pregnancy, liver, cardiovascular, obesity, autoimmune disease, and then made the patient diagnoses.

A blood sample was collected from the vein of each participant, the patients sample was taken at prehemodialysis time. Blood push slowly in gel tube and let to clot at room temperature for 10-15 min, then centrifuged at 3000×*g* for 10 min. The serum was obtained and put in Eppendorf tubes and then used to determine serum arginase II.

The technique enzyme-linked immunosorbent assay (ELISA) using to determine the concentration of human serum ARGII in this study.

The Serum ARGII levels were measured using the enzyme-linked immunosorbent assay (ELISA) kits from Bioassay Technology Laboratory (Shanghai, China).

Ethics approval

Before collecting samples, all study participants were informed and allowed to verbally consent, and permission form by the document number [IRB: 5-25, August 8, 2023].

Statistical analysis

SPSS version 25 was used for statistical analysis. Both percentages and frequencies were used to represent categories of variables. The format for continuous variables was (means ± SD). The means of the two groups

were compared using the Student *t* test. The means of the two paired readings were compared using the paired *t* test. A significant *P* value was defined as <0.05. Utilizing a receiver operating characteristic (ROC) curve, the diagnostic accuracy of CKD was assessed.

Results

The study subject's demographic characteristics

The mean difference between the healthy and chronic kidney groups, as well as the correlation between the various patient parameters, were computed statistically using the *t* test in the current comparative analysis of the patient and healthy groups. About 90 persons in all were involved in the study, split into two healthy groups of 45 each. Table 1 shows the results of the 45 patient group, whose ages varied from 21 to 61 years old based on demographic information.

Age

The results were not statistically significant difference *P* value (0.548). The dispersion of age the rate malady is appeared in Table 1, the mean of patients (43.3 ± 11.22) compared with healthy control (42.08 ± 8.52), *P* value (0.548).

BMI

Showed that BMI was significantly higher in control ($P \leq 0.05$) the mean and SD was (26.91 ± 2.06) compared to patients of CKD the mean and SD was (24.84 ± 2.11), as illustrated in Table 1.

Sex

The sex distribution of the studied groups was 45 patients with CKD on hemodialysis, 25 (56%) male and 20 (44%) female, matching with controls and the results represented in Figure 3.

Figure 4 shows plasma arginase levels in CKD patients were significantly higher than in healthy controls, the mean and SD were (33.3 ± 5.7, 19.5 ± 3.7) for the patient and control respectively.

Table 2 presents the diagnostic accuracy of arginase (ARGII) overall, the table provides valuable insights into the variables being studied and their relevance to the patient population.

Table 1: The demographic characteristics of the study groups

Variable	Patients (mean ± SD)	Control (mean ± SD)	*P* value
Age (years)	43.3 ± 11.22	42.08 ± 8.52	0.548 NS
BMI (kg/m^2)	24.84 ± 2.11	26.91 ± 2.06	0.001*
Number	45	45	

NS: non-significant, * ($P \leq 0.05$)

Discussion

In this study, patients with CKD investigated to estimate the assessment of ARGII. The primary findings of this study were that the patients had high levels of ARGI. In mammals, raising levels of arginase activity have been correlated with malfunction and pathologies of the cardiovascular system, kidney, and also to dysfunction of the immune system.[14] There are two significant ways in which illnesses may be related to arginase's overactivity. First off, an excessive amount of arginase might deplete the L-arginine supply required for NO synthase to produce nitric oxide (NO). Second, an excessive amount of L-ornithine may cause anatomical issues with the vascular.[15]

The current study's findings concurred with those of a prior investigation conducted by Dalal *et al.*[16] Kidney disease (CKD) impairs the kidneys' capacity to filter and eliminate waste products, such as arginase. Consequently,

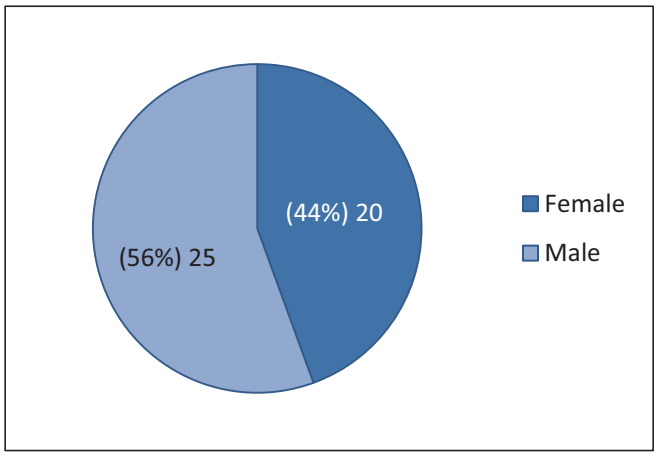


Figure 3: Sex distribution of patients and controls

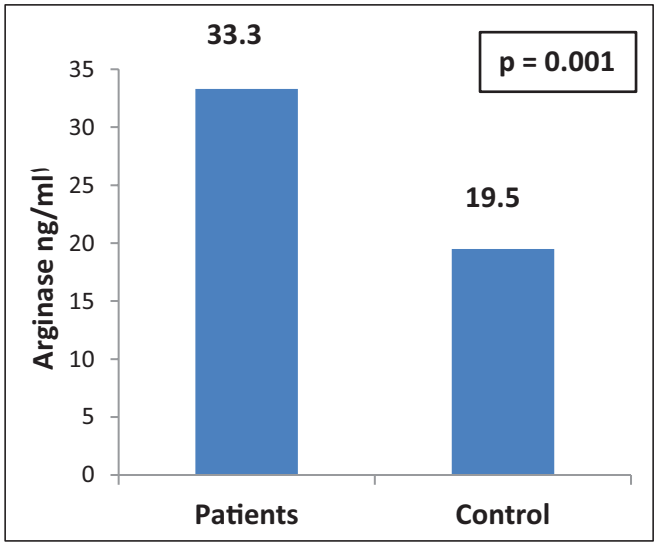
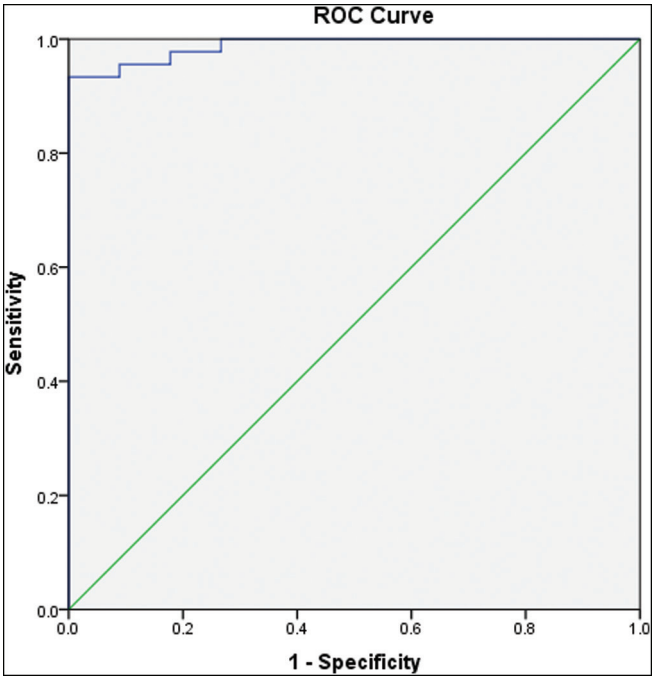


Figure 4: Represent arginase level in patients and control

Table 2: ROC-curve analyses of ARGII to predict patients with CKD

Variable	AUC	Sensitivity	Specificity	*P* value	Cutoff point
ARGII	0.988	95.0%	92.0%	0.00	24.751



there may be an accumulation of arginase in the blood, which would raise serum levels.

Further research conducted by Roumeliotis *et al.*[17] Endothelial dysfunction, or the compromised performance of the blood vessel lining cells, is a hallmark of CKD. Both changes in the arginine-NO pathway and the release of arginase from endothelial cells can result from endothelial dysfunction. Vascular health may be impacted by higher arginase activity as it may reduce the availability of arginine, a substrate for NO production.

Additional studies by Huang *et al.*[18] find that elevated arginase activity is linked to CKD. Dysregulation of several enzymes involved in arginine metabolism can cause changes in arginine metabolism, including elevated arginase activity, in CKD.

Age was not significantly different between groups in this study. This age matching aids in removing discrepancies in the parameters' results that might arise from a large age variance, that agree with previous study of Ranasinghe *et al.*[19] The most susceptible age group was between the ages of 21 and 61.

BMI was significantly higher in control compared to patients of CKD. Malnutrition is a serious danger for hemodialysis patients with CKD.[19]

In ROC analysis present results that indicate a good discriminative value, However, it cannot be considered a biomarker for diagnosing patients with CKD due to the limited number of study participants.

Conclusion

This study demonstrated Patients with CKD had greater levels of arginase II. Also ARGII could be guide the markers in diagnosis and follow-up.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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