Original Article

Assessment of β-Catenin Levels and Related Biomarkers in Patients with Chronic Kidney Disease

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ABSTRACT

Objective: To contrast the alterations in serum concentrations of insulin-like growth factor-1 (IGF-1), β-catenin, calcium, vitamin D, parathyroid hormone (PTH), and phosphorus in renal failure patients with those in normal controls, and to contrast between-group differences to further define the biochemical derangements in renal failure.
Study Design: Comparative study
Place and Duration of Study: This study was conducted at the Iraqi hospitals and kidney disease centers from 7th August 2022 to 1st April 2023.
Methods: The study included 400 samples, control 100 and patients 300. Three groups were formed; each group was made up of 100 patients. These groups varied in age. Patients with cancer, and pregnant women were not included.
Results: Insulin-like growth factor-1, β-catenin, calcium and vitamin D, levels and increase in parameters parathyroid hormone and phosphorus varied significantly amongst the groups, according to the data. The first group, followed by the second and third groups, showed the lowest levels, while all three groups showed lower levels than the control group.
Conclusion: The reduction in the levels of IGF-1, β-catenin, calcium and vitamin D and increase in parameters parathyroid hormone and phosphorus.
Key Words: Chronic kidney disease, Insulin-like growth factor-1, β-catenin, vitamin D
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INTRODUCTION

Kidney failure, a life-threatening condition characterized by the loss of kidney function, is an enormous cost to healthcare systems globally. The kidneys, vital organs that filter waste, balance electrolytes, and regulate blood pressure, can be permanently damaged by chronic kidney disease (CKD) or acute kidney injury (AKI). CKD, a chronic decline in renal function, affects over 850 million people worldwide, with diabetes mellitus and hypertension accounting for nearly two-thirds of the burden. AKI, which is an acute renal failure, affects 13.3 million patients yearly, with sepsis, dehydration, or nephrotoxic medications frequently initiating it. Both conditions enhance morbidity and mortality, particularly in the aging population and in low-resources.[1,2]

The pathophysiology of renal failure is complex, with interaction between genetic, environmental, and lifestyle determinants. For instance, diabetic nephropathy, a leading cause of CKD, is due to chronic hyperglycemia-induced renal vasculature damage. Similarly, hypertension accelerates glomerulosclerosis, diminishing filtration potential. Emerging risk factors include obesity, smoking, and genetic predispositions, e.g, APOL1 gene variants in African ancestry populations. Socioeconomic disparities also exacerbate outcomes; marginalized communities have delayed diagnoses due to limited access to healthcare.[3]

If left untreated, kidney failure progresses to end-stage renal disease (ESRD) and necessitates dialysis or transplantation. Furthermore, CKD enhances cardiovascular risk, and cardiovascular mortality is 10–20-fold more probable in dialysis patients.[4]

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METHODS

The study was conducted in some Iraqi hospitals and kidney disease centers, during the period from 7th August 2022 to 1st April 2023. The study included 400 sample, control 100 and patients 300. Three groups were formed; each group was made up of 100 patients: There were (400) sample, control and patients with euthyroid goiter aged 25-70 years were considered as a sample of this study. They were categorized into four groups as group A (patients, CKD) includes100 patients aged 55 to 70 years, group B (patients, CKD) includes 100 patients aged 40 to 55 years, group C (patients, CKD) includes 100 patients aged 25 to 40 years and group D (control) consisted of 100 healthy subjects aged 25-70 years. Blood of patients was analyzed through medical tests, i.e, (IGF-1, β-catenin, calcium, vitamin D, PTH and phosphorus using the ELISA device. The data was entered and analyzed through SPSS-25.

RESULTS

The outcomes were reflected in Table 2, indicated the decline in insulin-like growth factor, β-catenin, and calcium, vitamin D and increase in parameters PTH, and phosphorus characteristics of the microorganisms of interest. Specifically, the outcome indicated a discernible decline in the three groups of patients as compared to the control group Kidney failure. In addition, the outcomes of the three groups varied from one another, and the variation is clearly depicted in Tables 1-2 and Figures 1-6.

Table No.1: Descriptive statistics of studied groups

Group	Mean±SD
A	61.96±6.00
B	48.13±6.42
C	36.23±6.3
D	47.06±5.6

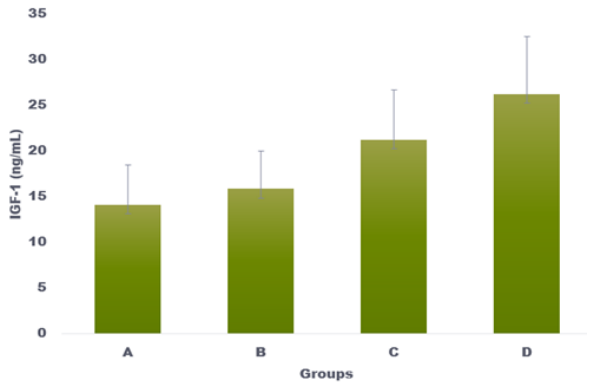

Figure No. 1: IGF-1 serum level of the patient groups and control group

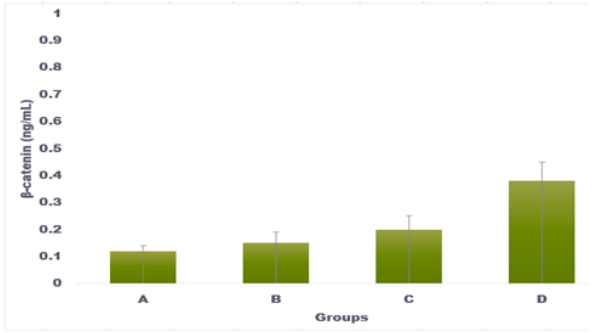

Figure No. 2: β-catenin serum level of the patient groups and control group

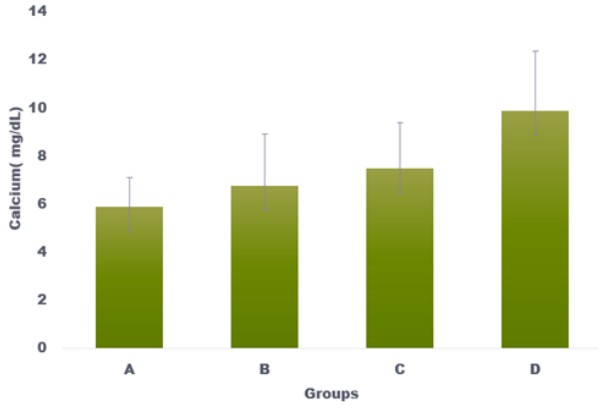

Figure No. 3: Calcium serum level of the three patient groups and control group

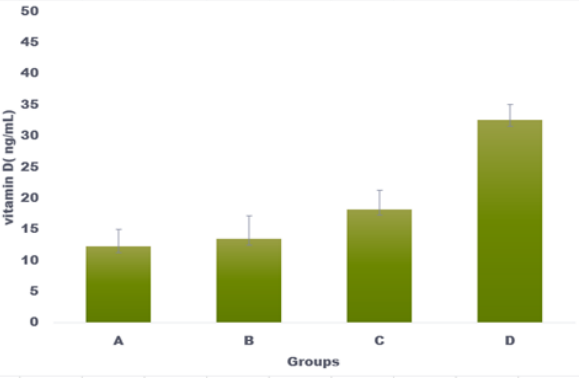

Figure No. 4: Vitamin D serum level of the three patient groups and control group

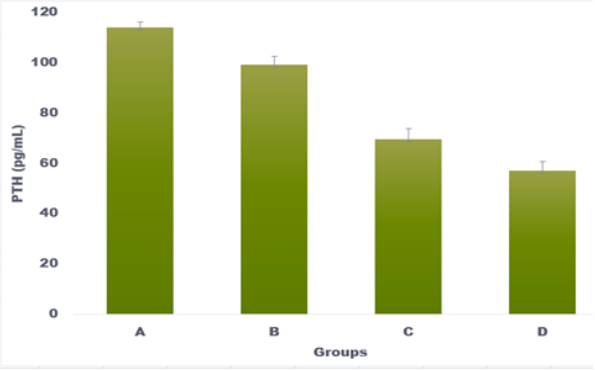

Figure No. 5 Vitamin D serum level of the three patient groups and control group

Table No.2: IGF-1, β-catenin, calcium, vitamin D, PTH and Phosphorus tests for studied groups

Group	IGF-1 (ng/mL)	β-catenin (ng/mL)	Calcium (mg/dL)	vitamin D (ng/mL)	PTH (pg/mL)	Phosphorus (mmol/L)
Group A	14.10±4.32^{b}	0.16±0.03^{b}	5.87±1.24^{c}	12.24±2.69^{c}	113.73±2.36^{c}	11.2±0.97^{d}
Group B	15.82±4.17^{b}	0.19±0.05^{b}	6.75±2.17^{b}	13.45±3.74^{c}	98.91±3.45^{bc}	9.88±1.03^{c}
Group C	21.21±5.42^{b}	0.22±0.06^{b}	7.49±1.90^{b}	18.22±2.99^{b}	69.35± 4.40^{b}	7.6±1.06^{b}
Group D	26.21±6.28^{a}	0.35±0.08^{a}	9.88±2.48^{a}	32.51±2.54^{a}	56.83±3.88^{a}	4.14±1.07^{a}
L.S.D	8.9	0.11	0.75	2.11	7.79	0.61

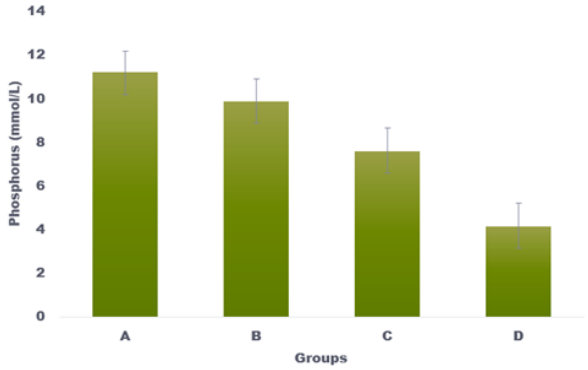

Figure No. 6: Phosphorus serum level of the three patient groups and control group

DISCUSSION

The IGF axis contains IGF-I, IGF-II, their receptor, and a family of IGF binding proteins (IGFBPs). It is essential for cell proliferation, tissue repair, and metabolism. In kidney disease (CKD) and renal failure, the following most important changes have been observed in this system. Renal failure patients have reduced circulating IGF-I in the body. This is because circulating IGF-I levels are reduced primarily as a result of an increase in the binding concentration of IGFBPs with IGF-I to limit bioavailability. These high levels of IGFBPs not only sequester IGF-I but also induce a condition of resistance of growth hormone and hence undermine any normal anabolic actions mediated through IGF-I.[5,6]

Muscle wasting, diminished physical capacity, and unfavorable nutritional status have been described due to decreased activity of IGF-I in CKD. These all contribute to the overall morbidity caused by chronic kidney failure in patients and have much more direct consequences on their health state. IGF-I is involved in renal development as well as repair, and in addition to systemic action, it has organ-specific action. In progressive renal failure, the deficiency of proper IGF-I action may impair the kidney's capacity to regenerate and recover from injury, further extending progression in renal dysfunction.[7,8]

Kidney failure is also associated with profound disruption of the IGF axis, specifically decreased levels and activity of IGF-I, which may be responsible for both systemic manifestations such as muscle wasting and additional renal function impairment. These observations make targeting the IGF system a potential therapeutic intervention in CKD, but further studies are required to elucidate the precise mechanisms and develop safe and effective interventions.[9,10]

The Wnt/β-catenin pathway is a key regulator of embryonic development and adult tissue homeostasis. In renal failure, particularly in chronic kidney disease (CKD), dysregulation of this pathway has been implicated in the formation of renal fibrosis, podocyte injury, and the deterioration of kidney function. Wnt/β-catenin signaling in the normal adult kidney is relatively quiescent; however, in response to injury such as ischemia-reperfusion injury or toxin-induced injury, the pathway reactivates. Transient activation of β-catenin is apparently beneficial in acute injury by initiating repair mechanisms, but chronic or uncontrolled activation is deleterious. Chronic activation causes transcription of profibrotic genes (such as fibronectin, matrix metalloproteinase-7, and plasminogen activator inhibitor-1) and induces epithelial-to-mesenchymal transition (EMT), which collectively results in interstitial fibrosis.[11,12]

The relationship between β-catenin and kidney failure is a twofold one: while transient activation may be involved in repair, chronic β-catenin activity promotes fibrotic alterations leading to progressive kidney failure. Thus, therapeutic strategies targeting the selective modulation of β-catenin signalling may be capable of reducing fibrosis and improving renal function in CKD patients.[13,14]

Chronic kidney disease is also closely related to mineral and bone metabolism abnormalities and thus a disorder referred to as CKD-mineral and bone disorder (CKD–MBD). One of the central aspects of CKD–MBD is secondary hyperparathyroidism (SHPT), where the parathyroid glands release PTH at a raised level chronically in response to an abnormal calcium, phosphate, and vitamin D metabolism. In CKD, decreased renal clearance of phosphate, decreased conversion of vitamin D to its biologically active form, and consequent hypocalcemia cause a compensatory rise in secretion of PTH. With time, this chronic stimulation leads to hyperplasia of the parathyroid glands and autonomous secretion of PTH, thereby aggravating metabolic derangements.[15,16]

Hyper PTH in CKD not only induces high-turnover bone disease (osteitisfibrosa) but also extra skeletal complications. Therefore, for instance, elevated PTH chronically can induce adipose tissue browning and enhanced energy expenditure resulting in wasting - a process which has been linked to poor clinical outcomes in patients on dialysis. Furthermore, PTH-induced bone resorption releases calcium and phosphate from the skeleton, resulting in vascular calcification and increasing the risk of cardiovascular events and mortality.[17,18]

The drug-induced effect has been shown to reduce PTH alongside serum calcium and phosphate concentrations and could potentially improve cardiovascular outcomes. At the same time, parathyroidectomy is a definitive treatment for advanced SHPT, and observational studies have linked its application with improved survival in dialysis patients. Overall, the CKD-PTH interaction is multifaceted, as CKD-stimulated abnormalities in mineral metabolism cause SHPT, whose contribution is to skeletal and cardiovascular morbidity. Treatment of elevated PTH by medical or surgical intervention is crucial in regulating the adverse outcomes secondary to CKD–MBD.[19,20]

CONCLUSION

The decline in insulin-like growth factor, β-catenin, and calcium, vitamin D and increase in parameters PTH, and phosphorus with increasing age. The oldest cohort exhibited the most pronounced reductions, followed by the middle-aged group, and finally the youngest group, which showed a slight decrease, but parathyroid hormone and inorganic phosphorus showed the exact opposite suggesting that these parameters could serve as biomarkers for diagnosing CDK.

Author's Contribution:

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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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