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Relationship Between Branched Chain Amino Acids, β- Catenin and Serotonin in Patients with Chronic Kidney Disease in Thi-Qar Province/ Iraq

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ABSTRACT

Background and Aims: Chronic kidney disease (CKD) is a major global health problem with increasing incidence and mortality rates. Its early stages are often asymptomatic, delaying diagnosis and treatment. This study aimed to evaluate the relationship between branched-chain amino acids (BCAAs), serotonin, and β-catenin in CKD patients in Thi-Qar province, Iraq.

Methods: A case-control study was conducted involving 88 patients with CKD and 40 healthy controls. Blood samples were collected, and serum levels of BCAAs, serotonin and β-catenin and were measured using enzyme-linked immunosorbent assay (ELISA) kits (Sunlong Biotech, China). Data were analyzed using SPSS version 11.5. The Mann-Whitney U test compared group means, and Spearman's rank correlation assessed associations between variables. Statistical significance was defined as P<0.05.

Results: BCAA concentrations were significantly lower in CKD patients compared with controls (35.53 ± 3.37 µg/ml vs 61.06 ± 5.39 µg/ml; P<0.001). β- catenin levels were also significantly reduced in CKD patients: (39.55 ± 9.62 pg/ml vs. 48.81 ± 13.74 pg/ml) (P <0.001), while serotonin levels were significantly elevated in patients with CKD: (21.69 ± 6.95 ng/ml vs. 18.88 ± 3.3 ng/ml) (P < 0.001). There is a negative correlation between serum branched-chain amino acids and β-catenin and serotonin with correlation coefficients (r = -0.0761) and (r = -0.0949) respectively.

Conclusion: The findings suggest that low levels of branched-chain amino acids (BCAAs) in patients with CKD may be associated with impaired β-catenin synthesis and elevated serotonin levels. These could be vital monitoring indicators in disease management. Early nutritional interventions, including amino acid supplementation, may benefit patients and warrant further investigation.

KEYWORD: β- Catenin, Serotonin ,Branched chain amino acids and patients.

1. INTRODUCTION

The kidneys are an important part of the body's biological balance of several substance they play an active role in reabsorbing, converting, and regulating their levels in the blood(Brenner and Rector's.;2019). The kidneys serve a crucial function in the metabolic processing of branched-chain amino acids (BCAAs), specifically comprising leucine, isoleucine, and valine [1]. These organs function not merely as excretory systems, but also contribute to the regulation of amino acid concentrations within the circulatory system [2]. Following the filtration process in the glomeruli, amino acids are reabsorbed in the proximal convoluted tubules of the nephrons, thereby mitigating their excretion through urine [3]. The kidneys exhibit a significantly elevated activity of the enzyme branched-chain amino acid transaminase (BCAT), which facilitates the removal of the amino group from BCAAs, leading to their conversion into the respective keto acids. This biochemical reaction predominantly transpires within the muscles, brain, and kidneys, contrasting with the hepatic. Metabolism observed with the majority of amino acids [4]. In the context of chronic kidney disease, the metabolic pathways governing BCAAs are markedly disrupted, resulting in imbalances in nitrogen homeostasis and potentially serving as a biomarker for the progression of renal dysfunction [5]. Branched Chain Amino Acids: Branched-Chain Amino Acids (BCAAs), specifically valine, leucine and isoleucine, represent a category of indispensable amino acids that are not capable of being synthesized through de novo pathways. The role of BCAAs is pivotal in both developmental processes and the aging continuum [6]. These amino acids are frequently present in dietary proteins, constituting approximately 15%–20% of total protein consumption, thereby exerting both direct and indirect metabolic influences (e.g., modulation of body weight, facilitation of muscle protein synthesis, maintenance of energy homeostasis, regulation of food intake, and stabilization of glucose homeostasis) [7 , 8]. BCAAs account for 35% of the essential amino acids present in muscle tissue, 40% of the protein requirements, and 50% of the essential amino acids available in dietary sources [9]. Circulating BCAAs are actively absorbed by skeletal muscle and utilized for energy production, muscular repair, or hypertrophy. Consequently, BCAAs are indispensable for the preservation of muscle mass and the promotion of anabolic processes, as they enhance protein synthesis and mitigate the rate of protein degradation [10].In the context of chronic kidney disease (CKD), the deterioration of renal function, augmented catabolism of muscle proteins, and metabolic aberrations result in diminished concentrations of branched-chain amino acids (BCAAs) in the bloodstream[11]. This reduction serves as an indicator of malnutrition and compromised amino acid metabolism, while also acting as a biomarker for the progression of the disease and the nutritional status of the affected individual[12]. This condition disrupts the equilibrium of proteins, as the kidneys' capacity to reabsorb amino acids within the proximal tubules is impaired, which may consequently result in their excretion in urine, particularly in instances where proteinuria is present[13].Furthermore, the excessive degradation of proteins and heightened muscle metabolism contribute to the utilization of BCAAs as an energy substrate, thereby lowering their levels in the blood [14]. The catabolic degradation of branched-chain amino acids (BCAAs) constitutes a multifaceted biochemical process that necessitates a series of enzymatic reactions[15], unlike the majority of amino acids, the preliminary phase of branched-chain amino acid (BCAA) catabolism occurs outside the liver due to the diminished hepatic activity of branched-chain-amino-acid aminotransferase (BCAT), which is the initial enzyme involved in the BCAA catabolic pathway. Consequently, following the ingestion of proteins, the concentration of BCAAs in systemic circulation escalates rapidly and becomes readily accessible to extra hepatic tissues. This particular occurrence confers a distinctive advantage to BCAA-based nutritional formulations in comparison to others, particularly those aimed at promoting muscle and cerebral function. [16]. The initial two stages of this catabolic pathway are uniform across all three BCAAs [17]. In contrast to other amino acids, which are primarily subjected to catabolism within the hepatic tissue [18], the preliminary step in the catabolism of BCAAs is uniquely not conducted in the liver, a phenomenon attributed to the diminished hepatic expression of branched-chain amino acid aminotransferase (BCAT), the inaugural enzyme activated within the BCAA catabolic pathway. The predominant locus for the majority of BCAA catabolic activities resides within skeletal muscle, attributable to the elevated activity of BCAT in these specific tissues [16], which is encoded by the BCAT2 gene. The absence of the BCAT2 gene inhibits the synthesis of BCAA metabolites within peripheral tissues. In the presence of BCAT2, BCAAs undergo conversion to branched-chain α-ketoacids through the process of amino group removal. Subsequently, the α-ketoacids are subjected to decarboxylation by branched-chain α-ketoacid dehydrogenase (BCKD)[19].Ultimately, the metabolites of BCAAs are further catabolized through a succession of enzymatic reactions, yielding their terminal products, acetyl-CoA and succinyl-CoA, which subsequently enter the tricarboxylic acid (TCA) cycle [20].

2. MATERIALS AND METHODS:

This clinical study included 88 patients referred to Nasiriyah Teaching Hospital in Thi Qar, Iraq. Participants were diagnosed with chronic kidney disease (CKD) after evaluation by specialist physicians. Patients with prostate cancer and other malignancies, as well as those with heart disease, hepatitis, and arthritis, were excluded from the study. All CKD patients with obesity, hypertension, and diabetes were included. These data were used to identify differences. Blood samples were collected from the patients, both male and female, aged 35–70 years, and from a control group of males and females aged 35–50 years. Serum serotonin and β-catenin concentrations were measured using enzyme-linked immunosorbent assay (ELISA), following the steps provided with the assay kit developed by Sunlong Biotechnology Co., Ltd. in Hangzhou, China. This method is based on competitive binding. The technique is based on sandwich ELISA. A hormone-specific antibody was deposited onto the ELISA microchip included with the kit. The appropriate wells of the ELISA microplate were filled with standard or reference samples and then mixed with the specific antibody. Each ELISA microplate was then completely coated with a horseradish peroxidase (HRP) antibody and incubated. Free fragments were removed by washing. TMB substrate solution was added to each well. Upon addition of the stop solution, wells containing only the hormone and HRP antibody changed color from blue to yellow. Optical density (OD) was measured using a spectrophotometer at 450 nm. Hormone concentration is directly related to OD. By comparing the OD of the samples to a standard curve, hormone levels could be determined. Serum branched-chain amino acids (BCAAs) were determined following the instructions supplied with the test kit, which was developed by Sunlong Biotechnology Co., Ltd. in Hangzhou, China. The quantities of branched-chain amino acids (BCAAs), namely valine, leucine, and isoleucine, were determined using enzyme-linked immunosorbent assay (ELISA) [21]. This system is based on competitive binding and employs a sandwich ELISA technique. The system consists of a microELISA slide coated with antibodies specific to the BCAAs. The appropriate cavities of the microELISA slide are filled with standard or sample samples, which are then mixed with the selected antibody. Next, a horseradish peroxidase (HRP)-specific antibody is added to each cavity of the microELISA slide, and the area is incubated. Free fragments are removed by washing. A TMB substrate solution is added to each cavity. Upon the addition of the stop solution, only the wells containing the BCAAs and the HRP-conjugated antibodies turn blue and yellow, respectively. A spectrophotometer set to 450 nm is used to determine the optical density. The concentration of branched-chain amino acids (BCAAs) is correlated with optical density. By comparing the optical density of the samples to a standard curve, the BCAA content can be determined. All values obtained are presented as mean ± standard deviation. The difference in means between the study and control groups was compared using the Mann-Whitney U test. Statistical significance was defined as a p-value less than 0.05. The relationship between hormones and BCAAs was investigated using Spearman's rank correlation analysis. SPSS for Windows, version 11.5, was used for statistical analysis.

3. RESULTS:

Our current study involved measuring the concentration of BCAAs, serotonin, and β-catenin in the blood serum of patients with CKD to monitor the decline in their kidney function. According to the study results, CKD patients had significantly lower levels of BCAAs in their blood serum ($P < 0.005$). The mean concentration was (35.53 ± 3.37 µg/ml) Compared to the concentration level in the serum of control group (61.06 ± 5.39 µg/ml), as shown in Table (1) and Figure(1).

Table (1): Mean concentration level (BCAA) and standard deviation in the blood serum of control and patients with CKD.

	Groups	Number	Mean	Std. Deviation	T-value	P-value
BCAA	Control	40	61.06 µg/ml	5.39	24.96	0.001
	Patients	88	35.53 µg/ml	3.37		

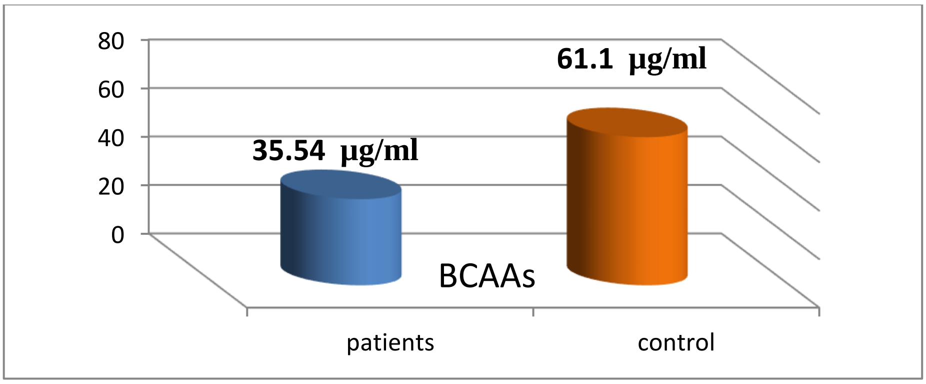

Fig. (1): mean concentration of BCAAs in the serum of patients with CKD compared to control . Where there is a significant and clear decrease in patients as a result of the pathological causes mentioned in the discussion.

The results showed that the serum serotonin level in the control group was (18.88± 3.3 ng/ml), compared to (21.69 ± 6.95 ng/ml) in the serum of patients with chronic kidney disease. Meanwhile, the concentration of β-catenin protein was (39.55 ± 9.62 pg/ml) in the serum of patients with chronic kidney disease, compared to (48.81 ± 13.74 pg/ml) in the control group, as shown in Table 2.

Table (2): Mean concentration of dopamine, epinephrine and norepinephrine hormones ± standard deviation in blood serum.

Parameters	**Groups**	**No.**	**Mean**	**Std. Deviation**	**P-value**
Serotonin	**Patient**	**88**	**21.69**	**6.95**	**0.001**
	Control	**40**	**18.88**	**3.3**	
β-catenin	**Patient**	**88**	**39.55**	**9.62**	**0.001**
	Control	**40**	**48.81**	**13.74**	

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The results for serotonin hormone and beta-catenin protein showed significant differences between the control group and chronic kidney disease patients in the blood serum at a probability level ($P < 0.005$), as shown in Figures (2,3).

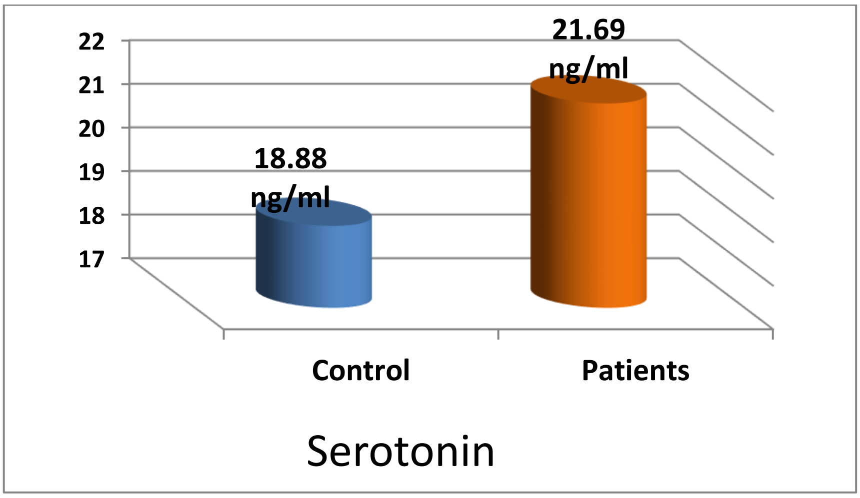

Fig. (2): serotonin mean concentration in CKD patients' serum as compared to the control group. Where there is a significant and clear increase in patients as a result of the pathological causes mentioned in the discussion

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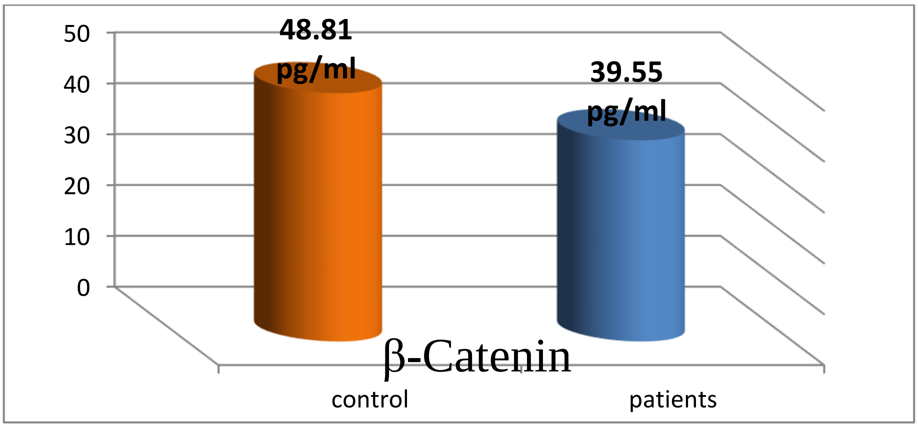

Fig. (3): Mean concentration of β-catenin in the serum of CKD patients compared to control group. Where there is a significant and clear decrease in patients as a result of the pathological causes mentioned in the discussion .

The linear correlation coefficient (r) of branched-chain amino acids in blood serum with β-catenin and serotonin in CKD patients is negative, as shown in Figures (4, 5).

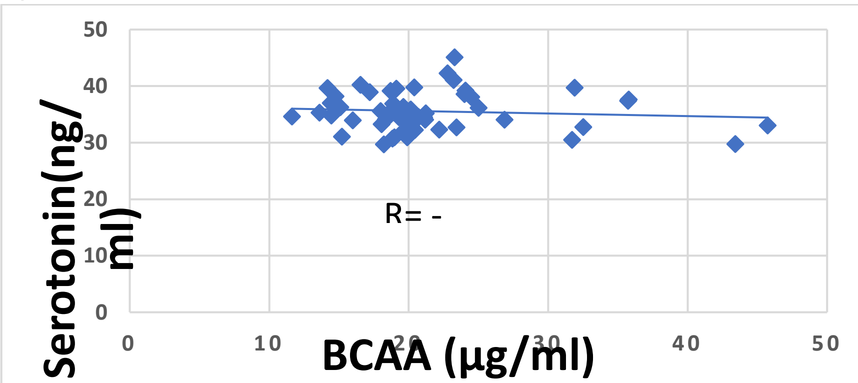

Fig. (4): The patients' blood serum's linear correlation between the BCAA and the serotonin hormone. Shows the negative correlation between serum BCAA and serotonin with a correlation coefficient of (r= -0.0949) .

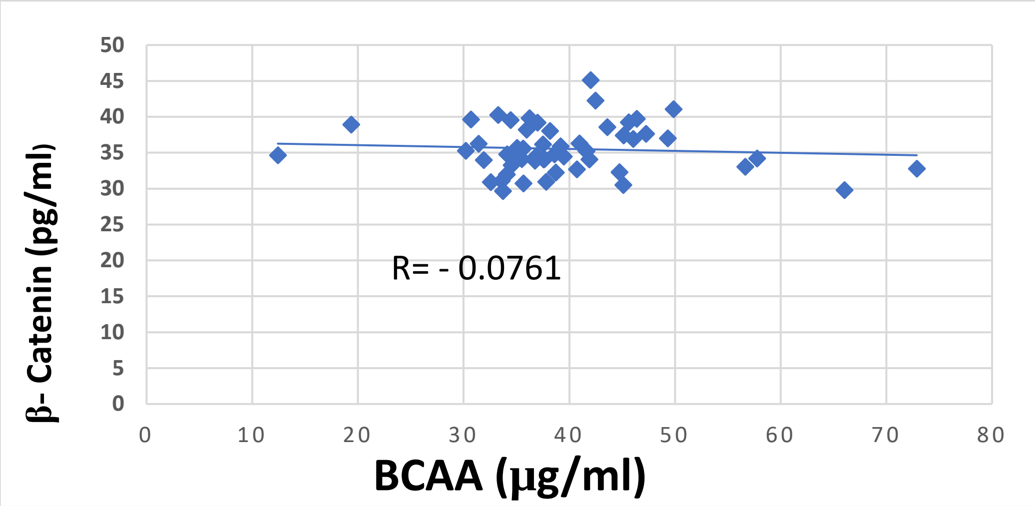

Fig. (5): The patients' blood serum's linear correlation between the BCAA and the Epinephrine hormone. Shows the negative correlation between serum BCAA and Epinphrine with a correlation coefficient of (r=-0.0761).

4. DISCUSSION:

In chronic kidney disease (CKD), a significant decrease in serum branched-chain amino acid (BCAA) concentrations has been observed in the patient group compared to the control group ($p<0.001$). Studies suggest a strong correlation between this decrease and its side effects, resulting from a combination of increased muscle breakdown, malnutrition, chronic inflammation, metabolic acidosis, and impaired amino acid absorption. These factors all contribute to a reduction in serum BCAA concentrations. In a study of patients diagnosed with CKD, Pickering et al. (2002) demonstrated that a decrease in total serum BCAAs is associated with a significant decrease in muscle ubiquitin (mRNA) content compared to the healthy control group. This indicates that impaired muscle protein metabolism leads to excessive protein breakdown in skeletal muscle, increasing the consumption of BCAAs as an energy source and consequently increasing the activity of branched-chain amino acid transaminases (BCATs) in muscle, which in turn increases the consumption of these amino acids [22]. Since chronic kidney disease (CKD) is a chronic inflammatory condition, cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) are released. These cytokines stimulate muscle protein breakdown and reduce branched-chain amino acids (BCAAs), thereby suppressing appetite and reducing protein intake [23]. Additionally, gut microbiota may play a significant role in regulating satiety. Total ghrelin levels are elevated in CKD patients, as ghrelin is primarily metabolized in the kidneys; however, this elevation is associated with an increase in the obistatin and decyl forms of ghrelin, which may have effects opposing those of the appetite-stimulating active form of ghrelin, acylghrelin, which reduces appetite [24]. On the other hand, with decreased kidney function, blood leptin levels, an antagonist of ghrelin, increase, further amplifying the loss of appetite [25]. The concentration of β-catenin in the serum of patients with chronic kidney disease (CKD) is lower than in the control group ($p<0.001$). In CKD, the Wnt/β-catenin signaling pathway is disrupted, and oxidative stress and signaling disturbances lead to increased activity of protein kinases such as GSK-3β. This results in increased phosphorylation of β-catenin, leading to decreased circulating levels and subsequent proteasome degradation [26]. CKD also impairs metabolic waste product clearance and the accumulation of free radicals (ROS). These ROS directly or indirectly oxidize β-catenin by affecting its binding proteins (such as Axin and APC), further increasing the rate of β-catenin degradation due to oxidative stress. Axin and APC are both essential proteins in the Wnt signaling pathway. Axin acts as a support protein in the Wnt pathway, assembling other proteins to form a complex called the "destruction complex." Another protein, colonic adenomatous protein (APC), plays a pivotal role in the destruction complex and helps regulate β-catenin levels in the cell. In the absence of Wnt signaling, the destruction complex degrades β-catenin by activating the transcription of specific genes. In summary, Axin and APC work together in the Wnt signaling pathway to regulate β-catenin levels, and any disruption to this process can have serious consequences for cell health [27]. Diseased kidneys reduce the clearance of uremia-related protein toxins produced by protein metabolism in the liver and muscles, disrupting protein synthesis pathways. The protein breakdown resulting from uremia also reduces the production of structural and regulatory proteins, including β-catenin. Consequently, its levels are reduced in the serum of patients with chronic kidney disease [28]. Chronic inflammation in the human body produces elevated levels of inflammatory cytokines (such as TNF-α and IL-6). These cytokines activate pathways such as NF-κB, which reduces β-catenin stability and increases the expression of its hydrolytic enzymes. Since CKD is a chronic inflammatory disease, this pathway is activated, leading to decreased β-catenin levels in the serum of patients with this disease, according to the findings

[29]. It is noted that patients with chronic kidney disease (CKD) have decreased renal excretion of serotonin and its metabolite, 5-HIAA, as the kidney is the organ that contributes to the disposal of serotonin and 5-HIAA. As eGFR decreases, excretion weakens, resulting in increased plasma serotonin. CKD patients exhibit an inverse relationship between eGFR and plasma serotonin concentration, suggesting a plausible reason for the elevated serum serotonin levels in patients with CKD [30]. Platelet storage or uptake of serotonin is impaired due to elevated uremia or dialysis in CKD. Most peripheral serotonin is stored within platelets. In CKD, platelet dysfunction impairs serotonin uptake (SERT) and increases its release, with elevated "free" forms in plasma. Dialysis sessions themselves may also trigger platelet activation that releases serotonin. This supports clinical evidence showing decreased platelet content and elevated plasma levels in patients with CKD [31,32]. Enterochromaffin (EC) cells synthesize 95% of the body's 5-HT and release it in response to mechanical or chemical stimulation. 5-HT in EC cells has physiological effects on intestinal motility, secretion, and visceral sensation. Abnormal regulation of 5-HT results in increased intestinal serotonin synthesis due to chronic inflammation, a result of microbiome dysfunction, as 90–95% of serotonin is synthesized in Enterochromaffin cells. In chronic inflammation and microbiome alterations, which are common in CKD, TPH1 expression/activity, EC cell number, or secretion are increased, leading to increased peripheral serotonin production [33]. Serotonin metabolism plays a pivotal role in both physiology and pathophysiology. The physiological and pathological mechanisms mediated by EC cells mentioned above are affected differently but remain closely interconnected. Furthermore, serotonin metabolism is directly or indirectly modulated by the gut microbiota, reinforcing the essential roles of EC cells in regulating this axis that links inflammation and increased serotonin secretion [34].

5. CONCLUSION:

The results showed a clear correlation between low beta-catenin concentration and low branched-chain amino acid (BCAA) concentrations in the blood of patients with chronic kidney disease (CKD). This correlation, along with elevated serotonin levels in these patients, suggests a relative risk factor for CKD in the general population. Therefore, it is recommended to initiate basic interventions, such as amino acid supplementation, as early as possible before dialysis to reduce morbidity and mortality rates in these patients. Further research is urgently needed to explore the potential mechanisms underlying this disease.

6. DECLARATIONS

6.1 Acknowledgments:

We are grateful to the doctors and nurses at Al-Nasiriya Teaching Hospital for their life-saving efforts, as well as the laboratory assistants for their technical assistance in obtaining blood samples from patients.

6.2 Ethical Considerations:

This study obtained ethical approval, with all patients providing written consent for the use of their data in clinical research. The study adhered to the principles outlined in the latest version of the Declaration of Helsinki. Ethical approval was obtained from the Thi-Qar Health Directorate, the Training and Human Development Center of University of Thi-Qar (Approval No. REC0774803, dated July 22, 2024).

6.3 Author Contributions:

Writing - preparation of the original draft, A.H.M., M.A.A. and H.M.A.; writing - review and editing, A.H.M.The authors read and approved the final manuscript.

6.4 Conflict of Interest:

The authors declare no conflict of interest.

6.5 Funding or Financial Support:

This research was not funded by any public, commercial, or not-for-profit funding agency.

6.6 Use of Artificial Intelligence Tools:

The researchers refrained from employing artificial intelligence instruments.

REFERENCES

1) **Zhe N; Jiang Y; & Wu J. (2023).** Amino acid metabolism in health and disease. *Signal Transduction and Targeted Therapy*, *8*(345): 1–32. https://doi.org/10.1038/s41392-023-01569-3.ces
2) **Pedro H; & Nilufar M.(2022).** Kidney metabolism and acid–base control: back to the basics. European J. Physiology, 474: 919-934.

3) **Martine G; Wulfmeyer V; Müller R; & Rinschen M. (2024).** Amino acid metabolism in kidney health and disease. *Nature Reviews Nephrology*, *20*: 771–788.
4) **Neinast M; Jang C; Hui S; Murashige D; Chu Q; Morscher R; Li X; Zhan L; White E; Anthony T; Rabinowitz J; & Arany Z. (2019).** Quantitative Analysis of the Whole-Body Metabolic Fate of Branched-Chain Amino Acids. *Cell Metabolism*, *29*: 417–429.
5) **Pinelopi K. (2025).** Fueling kidney recovery: boosting BCAA metabolism to overcome nephrotoxic AKI. *Am J Physiol Renal Physiol*, *328*: 596–598, doi:10.1152/ajprenal.00024.2025.
6) **Philipp R; & Zimmermann A. (2024).** Branched-chain amino acids: physico-chemical properties, industrial synthesis and role in signaling, metabolism and energy production. *Amino Acids*, *56*(51): 1–27. https://doi.org/10.1007/s00726-024-03417-2.
7) **Layman K; & Walker D. (2006).** Potential importance of leucine in treatment of obesity and the metabolic syndrome. *J.Nutr.*, *136*(1): 319–323.
8) **Lynch, C; & Adams S. (2014).** Branched-chain amino acids in metabolic signaling and insulin resistance. *Nature Reviews Endocrinology*, *10*(12):723–736. https://doi.org/10.1038/nrendo.2014.171.
9) **Okekunle A; Zhang M; Wang Z; Liu X; Liu Y; & Wei W. (2019).** Dietary branched-chain amino acids intake exhibited a different relationship with type 2 diabetes and obesity risk: a meta-analysis. *Acta Diabetologica*, *56*: 187–195. https://doi.org/10.1007/s00592-018-1243-7.
10) **Gagandeep M; Mora S; Madu G; & Adegoke O. (2021).** Branched-chain amino acids: catabolism in skeletal muscle and implications for muscle and whole-body metabolism. *Frontiers in Physiology*, *12*: 1-26.
11) **Mahbub M; Arima K; Ikeda K; Fukunaga S; Yonemoto A; & Nakashima E. (2021).** Association of plasma branched-chain and aromatic amino acids with reduction in kidney function evaluated in apparently healthy adults. *J. Clin. Med.*, *10*(22): 5234. https://doi.org/10.3390/jcm10225234
12) **Shafi S; Khan H; & Bajpai P. (2024).** Protein metabolism and its profiling for the diagnosis of metabolic disorders. Clinical applications of biomolecules in disease diagnosis. *Springer, Singapore*: 1-448. https://doi.org/10.1007/978-981-97-4723-8_3.
13) **Knol . M; Wulfmeyer V; Müller R; & Rinschen M. (2024).** Amino acid metabolism in kidney health and disease. *Nature Reviews Nephrology*, *20*: 771–788. https://doi.org/10.1038/s41581-024-00872-8.
14) **Aikaterini D; Vasilis T; & Eleni B; Dimova. (2022).** The critical role of the branched chain amino acids (BCAAs) catabolism-regulating enzymes, branched-chain aminotransferase (BCAT) and branched-chain α-keto acid dehydrogenase (BCKD), in human pathophysiology. *Int. J. Mol. Sci.*, *23*(7): 4022.
15) **Haizhou J; Feifan G; & Fei X. (2025).** Role of branched-chain amino acid catabolism in the regulation of adipocyte metabolism. *Endocrinology*, *166*(7):1-13.
16) **Holeček M.(2018).** Branched-chain amino acids in health and disease: metabolism, alterations in blood plasma, and as supplements. *Nutrition & Metabolism*, *15*(33): 1–12. https://doi.org/10.1186/s12986-018-0271-1.
17) **Cole J. (2015).** Metabolism of BCAAs. Branched chain amino acids in clinical nutrition. *Humana Press, New York, NY.*: 1-30. https://doi.org/10.1007/978-1-4939-1923-9_2.
18) **Hou Y; Hu S; Li X; He W; & Wu G. (2020).** Amino acid metabolism in the liver: nutritional and physiological significance. *Advances in experimental medicine and biology, Springer, Cham.*, *1st ed*: 1-220.
19) https://doi.org/10.1016/ j.kint.2020.07.013.
20) **María M; López-Maside L; Donapetry-García C; Fernández-Fernández C; & Sixto-Leal C. (2017).** Enzymes involved in branched-chain amino acid metabolism in humans. *Amino Acids*, *49*(6): 1005–1028.
21) **Zhen Z; Müller D; Valdivia P; & Storch J. (2018).** Branched-chain amino acids as critical switches in health and disease. *Hypertension*, *72*: 1012–1022.
22) **Namkung SM, Choi JS, Park JH, Yang MG, Lee MW, Kim SW.(2017).** Detection of dopamine and serotonin by competitive enzyme-linked immunosorbent assay. Korean J Clin Lab Sci.;49(3):220-6. [DOI:10.15324/kjcls.2017.49.3.220].
23) **Tsai C; Huang S; Kao C; & Hsu P. (2022).** Muscle wasting in chronic kidney disease: mechanism and clinical implications—a narrative review. *International J. Molecular Sciences*, 23(11): 1-25.
24) **Ming T; Ou S; Chen H; Hsu H; & Chen T. (2021).** Relationship between circulating galectin-3, systemic inflammation, and protein-energy wasting in chronic hemodialysis patients. *Nutrients*, *13*(8): 1-13.
25) **Wang Y; Gao L; Yang Z; Chen F; & Zhang Y. (2018).** Effects of probiotics on ghrelin and lungs in children with acute lung injury: a double-blind randomized, controlledtrial. *PediatricPulmonology*, *53*(2):197-203. https:/doi.org/10.1002/ppul.23922.

26) **Bastings, J; Van Beek S; Van Der Laan S; & Van Marken Lichtenbelt W. (2023).** Influence of the gut microbiota on satiety signaling. *Trends in Endocrinology & Metabolism*, *34*(4): 243–255.
27) **Lingbo Z; Adjei I; Zhang H; & Wu J. (2023).** The WNT/β-catenin system in chronic kidney disease-mineral bone disorder syndrome. *International Urology and Nephrology*, *55*(10): 2527–2538.
28) **Ryan L; Qiu C; Zeyaei E; Baxter N; Han D; Wang A; Lock H; Chirikian O; Pruitt B; & Wilson M. Z. (2022).** Nucleation of the destruction complex on the centrosome accelerates degradation of β-catenin and regulates Wnt signal transmission. *Proceedings of the National Academy of Sciences*, *119*(36): 1-13. https://doi.org/10.1073/pnas.2204688119.
29) **Kuo-Chin H; Yao W; Liu Y; Yang H; Liao M; Chong K; Peng C; & Lu K. (2023).** The potential influence of uremic toxins on the homeostasis of bones and muscles in chronic kidney disease. *Biomedicines*, *11*(7): 1-25. https://doi.org/10.3390/biomedicines11072076.
30) **Ayesha M; Tauqir H; Ali S; Laiq I; Ali A; & Shakeel M. (2023).** Inflammatory process and role of cytokines in inflammation: An overview. *Punjab University J. Zoology*, *36*(2): 235–250.
31) **Adaway J; Dobson R; Walsh J; Rees -Smith B; Keevil B; & Coronavirus K. (2015).** Serum and plasma 5-hydroxyindoleacetic acid as an alternative to 24-h urine 5-hydroxyindoleacetic acid measurement. *Annals of Clinical Biochemistry*, *53*(5): 554–560. https://doi.org/10.1177/0004563215613109.
32) **Noordwest Z; & Piet C. (2006).** Platelet activation and serotonin release during treatment with haemodialysis. *Nederlands Tijdschrift Voor Klinische Chemie En Laboratoriumgeneeskunde*, *31*(3): 236–238.
33) **Baaten C; Sternkopf M; Henning T; Marx N; Bauwens M; Kuijpers M; Schurgers L; & Dekker L. (2021).** Platelet function in CKD: A systematic review and meta-analysis. *J. the American Society of Nephrology*, *32*(7): 1583–1598.
34) **Andromeda L; Ochoa-Cortez F; Beyder A; Soghomonyan S; Zuleta-Alarcon A; Coppola V; & Christofi F. (2016).** Mechanosensory signaling in enterochromaffin cells and 5-HT release: Potential implications for gut inflammation. *Frontiers in Neuroscience*, *10*: 1-13.
35) **Lai W; Rajan S; & Goli U. (2022).** Enterochromaffin cells–gut microbiota crosstalk: Underpinning the symptoms, pathogenesis, and pharmacotherapy in disorders of gut-brain interaction. *J. Neurogastroenterology and Motility*, *28*(3): 357–375. https://doi.org/10.5056/jnm22008.