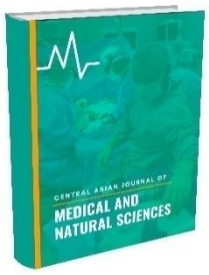
CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES



Volume: 05 Issue: 01 | Jan-Feb 2024 ISSN: 2660-4159

http://cajmns.centralasianstudies.org

STUDY SOME IMPORTANT BIOMARKERS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

1. Jalank Hameed Mahmoud

Received 20th Nov 2023,
Accepted 28th Dec 2023,
Online 19th Jan 2024

[1] Northern Technical University/Kirkuk Technical Institute/ Kirkuk, Iraq

Abstract: The current investigation was aimed to study some important biomarkers in patients with chronic kidney disease. Between June and October of 2023, 80 patients were recorded for CKD cases at Al-Jumhuri Hospital and Azadi Teaching Hospital. In Kirkuk, Iraq, at private laboratories, experimental work was conducted. The present study's participants had been divided up as follows: 40 healthy volunteers as control group. 80 patients with CKD as a second group. The results showed that creatinine level in patients (6.37±1.56 mg/dl) was indicated a substantial (P≤0.05) rise when compared to the normal individuals (0.95±0.17 mg/dl). Urea level in patients (154.02±25.84 mg/dl) indicated a substantial (P≤0.05) rise when compared to the normal individuals (29.17±5.32 mg/dl). The Copeptin level in patients (6.13±0.49 pmol/L) was indicated a substantial (P≤0.05) rise when compared to the normal individuals (3.04±0.58 pmol/L). B2MG level in patients (3.47±0.35 ng/ml) was indicated a substantial (P≤0.05) rise when compared to the normal individuals (2.28±0.21 ng/ml). The MDA level in patients (3.94±0.31 nmol/ml) was indicated a substantial (P≤0.05) rise when compared to the normal individuals (1.47±0.7 nmol/ml). GSH level in patients (0.2573±0.052 nmol/ml) was indicated a substantial (P≤0.05) reduce when compared to the normal individuals (0.4831±0.052 nmol/ml). Based on the current results, Copeptin, B2MG, Malondialdehyde and glutathione, in addition to urea and creatine, can be considered important criteria for diagnosing chronic renal failure.

Key words: CKD, Copeptin, B2MG, Malondialdehyde, glutathione.

Introduction

An estimated 850 million people worldwide suffer from CKD, which is acknowledged as a major public health issue [1-3]. In CKD, renal function declines gradually and irreversibly [4]. Therefore, it is now more crucial than ever to identify people at an early stage who are likely to develop end-stage renal disease (ESRD).

This classification is made possible by established metrics like proteinuria and estimated glomerular filtration rate (eGFR) [5–6]. Proteinuria is not a reliable biomarker of the course of CKD or the effectiveness of treatments, albeit [7]. As a result, new, verified biomarkers are needed to monitor the course of CKD and the risk of cardiovascular disease (CVD). Data on putative biomarkers in CKD will be obtained from proteomic investigations [8], but these need to be interpreted in the context of clinical practice [9]. Renal function is often assessed using the glomerular filtration rate, which calculates the volume of plasma filtered from all of the kidney's glomeruli in a given period of time. However, daily physiologic changes in the levels of albumin and protein in the urine—test items in a urinalysis—mean that there are many false positives and that accurately diagnosing chronic kidney disease (CKD) is difficult. Moreover, when the blood creatinine level exceeds the reference hematopoietic value, renal function has already decreased to around 40%, and it can be difficult to pinpoint the exact beginning of the reduction in renal function [10–11]. Many attempts have been made to compare the different expression amounts of proteins in plasma or urine between patients as well as healthy individuals in order to develop biomarkers for the diagnosis of CKD [121–13]. Conversely, oxidative stress, which encompasses numerous metabolic processes, is the term used to describe the oxidation of lipids, proteins, carbohydrates, and DNA in vivo. As a result, numerous substances are referred to as "biomarkers of oxidative stress." Oxidative stress indicators are more prevalent in CKD patients, according to cross-sectional investigations [14–15]. Determining GFR using formulas based on creatinine or creatinine and cystatin C is the main technique for assessing renal function. Due to the established constraints associated with these indicators, a number of substitutes have been examined, including β2-microglobulin (B2M), copeptin, angiotensin, and oxidative stress.

Materials & Methods

Subjects

Between June and October of 2023, 80 patients were recorded for CKD cases at Al-Jumhuri Hospital and Azadi Teaching Hospital. In Kirkuk, Iraq, at private laboratories, experimental work was conducted. The present study's participants had been divided up as follows:

- 40 healthy volunteers as control group.
- 80 patients with CKD as a second group.

Estimation of creatinine and urea levels

Using an assay kit that was sold commercially, the creatinine concentration was determined (BIOLABO – France).

Copeptin & B2MG

B2MG ELISA kit and Copeptin ELISA kit (Cusabio Biotech co., China). Following an overnight fast, blood samples were drawn, centrifuged, and frozen until analysis. The ELISA method was used to measure the amounts of copeptin and B2MG.

Plasma Peroxidation levels (MDA) and Glutathione

Using a spectrophotometer, MDA, also known as lipid peroxidation marker, was quantified in accordance with the reaction with thiobarbituric acid (TBA) [16]. Glutathione was tested using the Biovision-USA kits' standard protocol.

Statistical analysis

Minitab, a statistical tool, was utilized to evaluate the MDA and catalase data. ANOVA was used to examine the variation in the means of the experimental group.

Results & Discussion

Socio-demographic characteristics

Results of distribution of sample study according to gender in patients:

The gender of patients, were non-statistically significant at ($P \leq 0.05$) between male and female. The percentage of male patients at

(53.75%). Whereas, the percentage of female patients at (46.25%) (Table 1).

Table 1: Sample study distribution based on gender

Gender	No	Percentage (%)
Male	43	53.75
Female	37	46.25
Total	80	100%
P-value	---	0.097 NS
NS: Non-Significant.		

In this study, there was a noticeable male predominance (53.75%), with an approximate male to female ratio of 1.16:1. Males had a higher risk of chronic kidney disease (CKD) than females, according to a population-based case-control study conducted in Kirkuk City. This finding is consistent with previous research by Tain et al. (17) and Katsoufis et al. (18), which also found a 1.15:1 ratio. Although the current study contradicts the Turkish study by Bulum et al. (2013) (19), which indicated a female predominance with an M/F ratio of 0:84, this was because only relatives of CKD patients were included in the study.

Results of distribution of sample study according to age:

All patients with acne were distributed according to age as shown in Table (4-2). The age group (51-65 years) recorded the highest percentage (38.75%), followed by the group of (≥ 70 years), was (28.75%). While the lowest percentage showed in age group (≤ 20 years), representing (3.75%) (Table 2).

Table 2: Sample study distribution based on age

Age (year)	No	Percentage (%)
≤ 20	3	3.75
21-35	6	7.5
36-50	17	21.25
51-65	31	38.75
≥ 70	23	28.75
Total	80	100%
P-value	---	0.174 NS
NS: Non-Significant.		

This study clarifies that patients' ages rose with chronic renal failure condition. Reddy et al.'s [20] results showing that CRF patients' average age was 50 years [21] are in agreement with this result. In their case-control analysis, they also verify that the illness condition increased with age (45–54) years. The explanations might be what Rule et al. [22] speculated, citing higher rates of renal ischemia and fibrosis in older patients as reasons why their kidneys are more susceptible to the nephrotoxic effects of proteinuria. They based their hypothesis on research findings from Epstein [23], who described a decline in renal mass that occurs between the ages of 35 to 85 years, with the steepest decline occurring after 50.

Kidney functions

The creatinine level in patients (6.37±1.56 mg/dl) indicated a substantial (P≤0.05) rise when compared to the normal individuals (0.95±0.17 mg/dl). Urea level in patients (154.02±25.84 mg/dl) indicated a substantial (P≤0.05) rise when compared to the normal individuals (29.17± 5.32 mg/dl) as shown in the table (3).

Table (3): creatinine and urea levels in studied groups

Parameter	Control (40)	Patients (80)	P-Value
Creatinine mg/dl	0.95±0.17	6.37±1.56*	0.0001
Urea mg/dl	29.17±5.32	154.02±25.84*	0.0002

This study's urea results concurred with those of Al-Jumaili [24]. Both diabetic nephropathy and chronic renal failure can lower urine urea excretion, which is one of the causes of elevated urea levels. Low urea excretion from renal disorders leads to urea buildup and elevated blood concentrations. The absence of commitment is the second cause of elevated urea levels. Individuals who consume a lot of protein have higher blood urea concentrations [25, 26]. It was also found that blood urea concentrations are almost equal to blood creatinine concentrations, suggesting that renal filtration function problems may be present. A number of other serious diseases can result from elevated serum urea and creatinine levels, which have been noted by other researchers like Noor et al. [27] in individuals with CKD. Elevations in serum chemical levels signify kidney disease. Creatinine and urea are trustworthy markers of healthy renal function. renal injury caused creatinine levels to rise considerably, Moses and Johnkennedy [28] found, and this was followed by a decrease in glomerular filtration rate because of renal inflammation.

Copeptin & B2MG

The Copeptin level in patients (6.13±0.49 pmol/L) indicated a substantial (P≤0.05) rise when compared to the normal individuals (3.04±0.58 pmol/L). B2MG level in patients (3.47±0.35 ng/ml) indicated a substantial (P≤0.05) rise when compared to the normal individuals (2.28±0.21 ng/ml) as shown in the table (4).

Table (4): Copeptin & B2MG levels in studied groups

Parameter	Control (40)	Patients (80)	P-Value
Copeptin pmol/L	3.04±0.58	6.13±0.49*	0.0001
B2MG ng/ml	2.28±0.21	3.47±0.35*	0.0002

High plasma copeptin and B2MG levels were linked to CKD in the current study. In patients with type 1 or type 2 diabetes, A higher risk of major kidney effects, such as a doubling of plasma creatinine levels and/or a higher rate of end-stage renal disease (ESRD), has also been associated with plasma copeptin [29]. There has been a suggestion that individuals with CKD who have high copeptin levels may simply be reflecting a loss in GFR [30]. Copeptins may be cleared by the kidneys because they are tiny molecules. On the other hand, findings from a recent study indicate that renal clearance is not the main cause of circulating copeptin degradation [31]. Furthermore, B2M is a major predictor of death in these patients, even when controlling for other concomitant conditions such diabetes, starvation, persistent inflammation, and length of HD [32]. According to Liabeuf et al. [33], in patients with varying stages of chronic kidney disease, the plasma B2M level is predictive of both overall and cardiovascular mortality as well as cardiovascular events. Additionally, even after adjusting for CRP and GFR, In people with extensive asymptomatic carotid atherosclerosis, Amighi et al. [34] found a significant relationship between blood B2M level and cardiovascular events, with the severity of the comorbidity being similar to that of CKD patients. According to Shinkai et al. [35], plasma B2M level has a higher predictive value for mortality in the elderly population than other well-established prognostic markers including GFR, cystatin C, and CRP.

Malondialdehyde (MDA) & glutathione (GSH)

The MDA level in patients (3.94±0.31 nmol/ml) indicated a substantial (P≤0.05) rise when compared to the normal individuals (1.47±0.7 nmol/ml). GSH level in patients (0.2573±0.052 nmol/ml) indicated a substantial (P≤0.05) reduce when compared to the normal individuals (0.4831±0.052 nmol/ml) as shown in the table (5).

Table (5): MDA & GSH levels in studied groups

Parameter	Control (40)	Patients (80)	P-Value
MDA nmol/ml	1.47±0.73	3.94±0.31*	0.00001
GSH nmol/ml	0.4831±0.052	0.2573±0.052*	0.0001

According to the current study, individuals with chronic renal failure have mean serum levels of malondialdehyde (MDA) that are noticeably higher than those of healthy controls. The outcome was in line with earlier research by Vecchi et al. [36], Rusu et al. [37], and Sridhar [38]. Increased pro-oxidant levels and antioxidant depletion cause oxidative stress, which damages tissue by upsetting the balance between oxidative and anti-oxidative processes. [39] Suresh et al. 5 Lipid hydroperoxides can be produced when polyunsaturated fatty acids combine with reactive oxygen species (ROS) [37]. Lipid peroxidation is measured biochemically using malondialdehyde (MDA) as a marker. This study showed that the plasma or serum of CKD patients had low levels of GSH and high production of oxidative damage markers (MDA), which is consistent with [41–42].

Conclusions

Based on the current results, it is concluded that males are more likely to develop chronic renal failure, and that advancing age increases the chances of developing chronic renal failure. On the other hand, Copeptin, B2MG, Malondialdehyde and glutathione, in addition to urea and creatine, can be considered important criteria for diagnosing chronic renal failure.

References

1. Polenakovic MH, Dohcev S, Rambabova-Bushljetik I, et al. The Importance of the World Kidney Day World Kidney Day - 11 March 2021 - Living Well with Kidney Disease. Pril (Makedon Akad Nauk Umet Odd Med Nauki)2021; 42:19–40.
2. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, Hobbs FD. Global prevalence of chronic kidney disease—a systematic review and meta-analysis. PLoS ONE. 2016;11(7): e0158765.
3. Shabaka A, Cases-Corona C, Fernandez-Juarez G. Therapeutic insights in chronic kidney disease progression. Front Med (Lausanne). 2021;8: 645187.
4. Cao Q, Chen XM, Huang C, Pollock CA. MicroRNA as novel biomarkers and therapeutic targets in diabetic kidney disease: an update. FASEB Bioadv. 2019;1(6):375–88.
5. Hallan S.I., Ritz E., Lydersen S. Combining GFR and albuminuria to classify CKD improves prediction of ESRD. J Am Soc Nephrol, 20 (2009), pp. 1069-1077.
6. Hemmelgarn B.R., Zhang J., Manns B.J. Nephrology visits and health care resource use before and after reporting estimated glomerular filtration rate JAMA, 303 (2010), pp. 1151-1158.
7. Levey A.S., Cattran D., Friedman A. Proteinuria as a surrogate outcome in CKD: report of a scientific workshop sponsored by the National Kidney Foundation and the US Food and Drug Administration Am J Kidney Dis, 54 (2009), pp. 205-226.
8. Ben Ameur R., Molina L., Bolvin C. Proteomic approaches for discovering

biomarkers of diabetic nephropathy Nephrol Dial Transplant, 25 (2010), pp. 2866-2875.

9. Knepper M.A. Common sense approaches to urinary biomarker study design J Am Soc Nephrol, 20 (2009), pp. 1175-1178.
10. Zhang WR, Parikh CR. Biomarkers of acute and chronic kidney disease. Annu Rev Physiol. 2019;81:309–33.
11. Bidin MZ, Shah AM, Stanslas J, Seong CLT. Blood and urine biomarkers in chronic kidney disease: an update. Clin Chim Acta. 2019;495:239–50.
12. Taherkhani A, Farrokhi Yekta R, Mohseni M, Saidijam M, Arefi Oskouie A. Chronic kidney disease: a review of proteomic and metabolomic approaches to membranous glomerulonephritis, focal segmental glomerulosclerosis, and IgA nephropathy biomarkers. Proteome Sci. 2019;17:7.
13. Yamamoto A, Morioki H, Nakae T, Miyake Y, Harada T, Noda S, Mitsuoka S, Matsumoto K, Tomimatsu M, Kanemoto S, et al. Transcription factor old astrocyte specifically induced substance is a novel regulator of kidney fibrosis. FASEB J. 2021;35(2): e21158.
14. Dounousi E., Papavasiliou E., Makedou A. Oxidative stress is progressively enhanced with advancing stages of CKD Am J Kidney Dis, 48 (2006), pp. 752-760
15. Calabrese V., Mancuso C., Sapienza M. Oxidative stress and cellular stress response in diabetic nephropathy Cell Stress Chaperones, 12 (2007), pp. 299-306.
16. Mahmood, N. A. (2010). Glutathion-S-transferase Enzyme and Malondialdehyde (MDA) in Colorectal Cancer and in Healthy Control. J. Can. Med. Gen. 3(1): 21-26.
17. Tain YL, Luh H, Lin CY, et al. Incidence and risks of congenital anomalies of kidney and urinary tract in newborns: A population-based case-control study in Taiwan. Medicine (Baltimore). 2016; 95(5): e2659.
18. Katsoufis CP, DeFreitas MJ, Infante JC, et al. Risk Assessment of severe congenital anomalies of the kidney and urinary tract (CAKUT): A birth cohort. Front Pediatr. 2019; 7: 182.
19. Bulum B, Ozçakar ZB, Ustüner E, et al. High frequency of kidney and urinary tract anomalies in asymptomatic first-degree relatives of patients with CAKUT. Pediatr Nephrol. 2013; 28(11): 2143-7.
20. Reddy G. C., Ramakrishna D., Pragna R. (2013). iron indices in patients with functional anemia in chronic kidney disease. The Journal of the International Federation of Clinical Chemistry and Laboratory Medicine .vol.24, no.3-4
21. Elisabeth Ejerblad, C. Michael Fored, Per Lindblad, Jon Fryzek, Paul W. Dickman, Carl-Gustaf Elinder, Joseph K. Mclaughlin, and Olof Nyre´N. (2004). association between smoking and chronic renal failure in a nationwide populationbased case-control study. J Am Soc Nephrol 15: 2178–2185
22. Rule AD, Amer H, Cornell LD et al.(2010). The association between age and nephrosclerosis on renal biopsy among healthy adults. Ann Intern Med; 152: 561–567.
23. Epstein M.(1996). Aging and the Kidney. J Am Soc Nephrol;7:1106-1122.
24. Aljumaili, Wissam Sabhan Khalaf, "Partial purification of the hormone of the two copeptics and its relationship with some biochemical variables in patients with chronic renal failure in Kirkuk." Ph.D. Thesis, College of Education for Pure Sciences, Tikrit University. 2019.
25. Jumaa,I. A. (2013). Study of Some Biochemical Parameters in Blood Serum of Patients with Chronic Renal Failure. Journal of Basrah Researches (Sciences); 39: 4.

26. Bamanikar SA, Bamanikar AA, Arora A, Study of Serum urea and Creatinine in Diabetic and nondiabetic patients in in a tertiary teaching hospital . The Journal of Medical Research 2016; 2(1): 12-15.
27. Noor, U.A.; Raja, T.M.; Javaid, M.A.; Mudassar, Z. and Asad, M.R. (2014). Evaluating Urea and Creatinine Levels in Chronic Renal Failure Pre and Post Dialysis: A Prospective Study. Journal of cardiovascular disease, 2(2)
28. Moses, O. and Johnkennedy, N. (2013). The Alteration of Serum Glucose Urea and Creatinine Level of Malaria Patients in Obowo Local Government Area of Imo State Nigeria. International Journal of Advanced Medicine, (1): 1-6
29. Velho G, et al. Plasma copeptin, kidney outcomes, ischemic heart disease, and all-cause mortality in people with long-standing type 1 Diabetes. Diabetes Care. 2016;39(12):2288–2295.
30. Corradi V, et al. Copeptin levels and kidney function in ADPKD: case-control study. Clin Nephrol. 2016;86(9):147–153.
31. Ettema EM, et al. The effect of renal function and hemodialysis treatment on plasma vasopressin and copeptin levels. Kidney Int Rep. 2017;2(3):410–419.
32. Okuno S, Ishimura E, Kohno K, Fujino-Katoh Y, Maeno Y, Yamakawa T, et al. Serum beta2-microglobulin level is a significant predictor of mortality in maintenance haemodialysis patients. *Nephrol Dial Transplant.* 2009;24(2):571–7.
33. Liabeuf S, Lenglet A, Desjardins L, Neirynck N, Glorieux G, Lemke HD, et al. Plasma beta-2 microglobulin is associated with cardiovascular disease in uremic patients. Kidney Int. 2012;82(12):1297–303.
34. Amighi J, Hoke M, Mlekusch W, Schlager O, Exner M, Haumer M, et al. Beta 2 microglobulin and the risk for cardiovascular events in patients with asymptomatic carotid atherosclerosis. Stroke. 2011;42(7):1826–33.
35. Shinkai S, Chaves PH, Fujiwara Y, Watanabe S, Shibata H, Yoshida H, et al. Beta2-microglobulin for risk stratification of total mortality in the elderly population: comparison with cystatin C and C-reactive protein. Arch Intern Med. 2008;168(2):200–6.
36. Vecchi AFD, Bamonti F, Novembrino C, Ippolito S, Guerra L, et al. Free and total plasma malondialdehyde in chronic renal insufficiency and in dialysis patients. Nephrol Dialysis Transplant. 2009;24(8):2524–2529.
37. Rusu CC, Racasan S. Malondialdehyde can predict survival in hemodialysis patients. Med Pharm Rep. 2016;89(2):250–256.
38. Sridhar SN, Rao PVS, Sivakumar V. Study of oxidant and antioxidant status in patients with chronic kidney disease. J Clin Sci Res. 2018;7(3):124–154.
39. Suresh DR, Silvia CRWD, Agarwal R. Biochemical Markers of Oxidative Stress in Predialytic Chronic Renal Failure Patients. Hong Kong J Nephrol. 2008;10(2):69–73
40. Satyanarayana U, Chakrapani U. Biochemistry. In: Free radicals and antioxidants ;. p. 629–634
41. Duni A., Liakopoulos V., Roumeliotis S., Peschos D., Dounousi E. Oxidative Stress in the Pathogenesis and Evolution of Chronic Kidney Disease: Untangling Ariadne's Thread. Int. J. Mol. Sci. 2019;20:3711.
42. Podkowinska A., Formanowicz D. Chronic Kidney Disease as Oxidative Stress- and Inflammatory-Mediated Cardiovascular Disease. Antioxidants. 2020;9:752.