زانکۆی سەلاحەدین - هەولێر
Salahaddin University-Erbil

Some biochemical complication before hemodialysis in patients with chronic renal failure in Erbil city

Research Project

Submitted to the department of biology in partial fulfillment of the requirements for the degree of B.A in biology

By:

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Supervised by:

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May-2023

DECLARATION

I declare that the Bachelor project research entitled: **Some biochemical complication before hemodialysis in patients with chronic renal failure in Erbil city** is our own original work, and hereby certify that unless stated, all work contained within this project research is our own independent research and has not been submitted for the award of any other degree at any institution, except where due acknowledgment is made in the text.

Signature:

Student: Name: Hana ------- and Shayma ----------

Date: / /2023

SUPERVISOR CERTIFICATE

This project research has been written under our supervision and has been submitted for the award of the degree of Bachelor of Science in **Biology/Blood Physiology** with our approval as supervisor.

Signature Name: **Asst. Prof. Dr. Sarbaz I. Mohammed**

Date

I confirm that all requirements have been fulfilled.

Signature:

Name: **Mr. Mohammed Ali Saleem**

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Date:

ACKNOWLEDGEMENTS

First and foremost, thanks for **Allah** to whom be ascribed all perfection and majesty for all the boons and for giving us strength and health to achieve this project research.

I would love to express our sincere gratitude to our advisor **Asst. Prof. Dr. Sarbaz I. Mohammed**, for the continuous support of my B.A project research. study, for his patience, motivation, and immense knowledge. His guidance helped us during the researching and writing of this project research. I could not imagine having a better advisor and mentor for our B.A. study.

A special thanks to **Mr. Mohammed Ali Saleem**, the head of Biology Department for his continuous help during this study. To all staffs in the ---------- Hospital in Erbil city

And from the bottom of our heart a special feeling of gratitude to my beloved parents, brothers and sisters whose words of encouragement and all the support they have provided me over the years were the greatest gift anyone has ever given us.

Hana & Shayma

DEDICATION

To our lovely parents

And

To our sweet sisters

To our kindly brothers

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ABSTRACT

Background: Chronic kidney disease is a worldwide public health problem. It is associated with various biochemical abnormalities that lead to morbidity and mortality. This study aimed to evaluate the biochemical parameters in chronic kidney disease patients before the dialysis process. **Methods**: This is a prospective cross-sectional study conducted on 94 chronic kidney disease patients before dialysis at Kumari Hospital, Erbil-Iraq. Biochemical parameters such as urea, creatinine, Albumin, serum glucose, GOT, GPT, calcium, ALP, sodium, potassium and chloride were measured using standard techniques using Cobas 311 in chronic kidney disease cases and the findings were compared with age-sex-matched controls. Results were analyzed using GraphPad 8 program. **Results**: In biochemical parameters, serum glucose, creatinine, urea, ALP, Cl- and K+ were increased and GPT and TSB levels were reduced significantly as compared to controls ($p<0.001$). **Conclusion**: Biochemical parameters are impacted in patients with chronic kidney disease. Routine evaluation of these parameters is useful in the management of these patients.

Keywords: Chronic kidney disease, Biochemical, Creatinine, urea

Introduction

The term renal failure denotes the inability of the kidneys to perform excretory function leading to the retention of nitrogenous waste products from the blood. **Acute Renal Failure (ARF)** is the syndrome in which glomerular filtration declines abruptly (hours to days) and is usually reversible. According to the KDIGO criteria in 2012, AKI can be diagnosed with any one of the following: (1) creatinine increases of 0.3 mg/dL in 48 hours, (2) creatinine increases to 1.5 times baseline within the last 7 days, or (3) urine volume less than 0.5 mL/kg per hour for 6 hours. Recently the term acute kidney injury (AKI) has replaced ARF because AKI denotes the entire clinical spectrum from a mild increase in serum creatinine to overt renal failure (Chertow et al., 2005, Luo et al., 2014, Bindroo et al., 2022, Kampmann et al., 2023).

Chronic Renal Failure (CRF) or chronic kidney disease (CKD) is defined as a one of the diseases of human that have variety of causes. It can be defined as a heterogeneous disorders affecting kidney structure and function. Guidelines for definition and classification of this disease represented an important shift towards its recognition as a worldwide public health problem that should be managed in its early stages by general internists. This disease and management are classified according to stages of disease severity, which are assessed from glomerular filtration rate can be classified into five stages depending on the GFR, in which in each stage it decreased (Webster et al., 2017, Conte et al., 2023).

Chronic kidney disease (CKD) arises from many heterogeneous disease pathways that alter the function and structure of the kidney irreversibly, over months or years. this condition as decreased kidney function shown by glomerular filtration rate (GFR) of less than 60 mL/min per 1·73 m^2, or markers of kidney damage, or both, of at least 3 months duration, regardless of the underlying cause. GFR which equals the total amount of fluid filtered through all of the functioning nephrons per unit of time. (Chertow et al., 2005, Luo et al., 2014, Bindroo et al., 2022).

Incidence, prevalence, and progression of CKD also vary within countries by ethnicity and social determinants of health, possibly through epigenetic influence. Many people are asymptomatic or have non-specific symptoms such as lethargy, itch, or loss of appetite. Diagnosis is commonly made after chance findings from screening tests (urinary dipstick or blood tests), or when symptoms become severe. CKD is associated with increased risk of death, cardiovascular disease (CVD), and high health care costs. The majority of CKD patients have diabetes (DM), hypertension (HT) and/or CVD, driven by a reciprocal relationship among these four major chronic diseases which complicates relevant treatment. The number of patients affected by end-stage kidney disease (ESKD) has grown in the world, causing an economic impact on public health services. Until a few decades ago, people with CKD had a much lower life expectancy than the general population, and access to renal replacement treatment in many countries was conditioned by age and comorbid conditions (Webster et al., 2017, Conte et al., 2023).

Presence of proteinuria is associated with increased risk of progression of CKD and death. Kidney biopsy samples can show definitive evidence of CKD, through common changes such as glomerular sclerosis, tubular atrophy, and interstitial fibrosis. Complications include anemia due to reduced production of erythropoietin by the kidney; reduced red blood cell survival and iron deficiency; and mineral bone disease caused by disturbed vitamin D, calcium, and phosphate metabolism. People with CKD are five to ten times more likely to die prematurely than they are to progress to end stage kidney disease. This increased risk of death rises exponentially as kidney function worsens and is largely attributable to death from cardiovascular disease, although cancer incidence and mortality are also increased (Nakagawa and Nishio, 2022).

In general, a large number of risk factors including age, sex, family history of kidney disease, primary kidney disease, urinary tract infections, cardiovascular disease, diabetes mellitus, and nephrotoxins (non-steroidal anti-inflammatory drugs, antibiotics) are known as predisposing and initiating factors of CKD. Environmental pollution of water by heavy metals and of soil by organic compounds (including pesticides) have also been implicated in geographically localized epidemics of CKD (Ghelichi-Ghojogh et al., 2022).

CDK is classified by kidney disease: Improving Global Out-Comes (KDIGO) into 5 stages. Stages 1 and 2 require Presence of kidney damage e.g., proteinuria. Stages 3–5 are defined by glomerular filtration rate below 60ml/min/1.73m2 Over at least 3months. Stages 3 And 4 (GFR 59-15ml/min/1.73m2) represent loss of 50% Of normal kidney function and are seen as a cut-off for Clinically significant CKD. CKD stage 3 is further Divided into CKD stage 3a (59-45ml/min/1.73m2) and 3b (44-30ml/min/1.73m2). Stage 5 covers GFR under 15ml/Min/1.73m2 (Ghelichi-Ghojogh et al., 2022, Kampmann et al., 2023).

The definition of acute kidney injury indicates that a rise in creatinine has occurred within 48 hours, although in the outpatient setting, it may be hard to ascertain when the rise happened. A high serum creatinine level in a patient with a previously normal documented level suggests an acute process,

whereas a rise over weeks to months represents a subacute or chronic process (Rahman et al., 2012).

Serum creatinine is used as a marker to evaluate kidney function and estimate glomerular filtration rate because of its complete filtration by the kidney. However, there are disadvantages to using creatinine as an indicator of kidney function. Serum creatinine levels can be influenced by age, sex, muscle mass, diet, and chronic illness. Creatinine is formed from creatine. Muscle contains the most significant stores of creatine and creatine phosphate, which play a critical role in cellular energy metabolism (Staples et al., 2010, Mian and Schwartz, 2017, Wong Vega et al., 2020).

Urea, a marker of uraemic retention in chronic kidney disease (CKD) and of the adequacy of intradialytic solute removal, has traditionally been considered to be biologically inert. However, several recent experimental data suggest that urea is toxic at concentrations representative of CKD. First of all, at least several recent studies indicate that urea itself induces molecular changes related to insulin resistance, free radical production, apoptosis and disruption of the protective intestinal barrier. Second, urea is at the origin of the generation of cyanate, ammonia and carbamylated compounds, which as such all have been linked to biological changes. Especially carbamylation has been held responsible for post-translational protein modifications that are involved in atherogenesis and other functional changes(Vanholder et al., 2018).

In observational clinical studies, these carbamylated compounds were associated with cardiovascular and overall morbidity and mortality. Yet, also the views that the kinetics of urea is not representative of the kinetics of several other uraemic retention solutes and that urea cannot be held responsible for all complex metabolic and clinical changes responsible for the uraemic syndrome, remain valid. Future efforts to improve the outcome of patients with CKD might be directed at further improving the removal of solutes implied in the uraemic syndrome, including but not restricted to urea, also taking into account the impact of the intestine and (residual) renal function on solute concentration (Vanholder et al., 2018).

Material and Methods

A total of 94 (49 females and 45 males) diagnosed adult chronic kidney failure patients' prior dialysis process and thirty control without kidney diseases were conducted in the study in the department of ---------- from December 2022 to march 2023. The median age of the total participants was 57 (45.75-65) years. The patient was diagnosed with renal failure for both sexes based on the history, clinical examination and taking renal function test. The subject was fasting for 12-14 hr. at the time of blood withdrawal.

Collection of samples

Samples from 94 patients with Chronic Renal Failure were collected. 2– 3 ml of peripheral venous blood was drawn using standard procedure. 2.0 ml of blood was transferred into a plain vacutainer for the estimation of biochemical parameters. Biochemical tests including sodium, potassium, phosphorus, calcium, urea and creatinine were tested in an automated biochemistry analyzer (Cobas C311). Sample collection is done by trained laboratory technicians working in the hospital and leads to proper testing for further analysis

Statistical Analysis

Data were analyzed using Statistical Package for Social Science (GraphPad 8.1) for Windows. An Independent t-test was used for statistical analysis. A p-value less than 0.05 was considered statistically significant.

Results and Discussion

The result of ninety-four (49 females and 45 males) patients with kidney failure before the dialysis process and thirty control without kidney diseases contributed to the study were shown in Tables 1 & 2. The median age of the total participants was 57 (45.75-65) years. The biochemical data showed serum glucose, creatinine, urea, ALP, Cl- and K+ were significantly higher in kidney failure patients as compared to the control group in both sexes, whereas GPT and TSB levels were found significantly lower in kidney failure patients as compared to an individual without kidney failure in both sexes, while Hb, GOT, and calcium level decreased significantly only in male patients. In a similar study done by Singh et al., serum urea, creatinine and phosphorous were highly increased in CKD patients and calcium level was

decreased as compared to control statistically significant subjects ($p<0.05$)(Singh and Bhatta, 2018).

The results show a significant ($P< 0.001$) increase in urea and creatinine concentration in chronic renal failure patients when compared with those of the control group (Merza and Hasson, 2015, Afzal et al., 2022). There was a significant difference in the levels of serum urea and creatinine observed before and after hemodialysis concerning different age groups. Generally, urea accumulation in the blood serum of kidney failure patients arises from the degradation of food and tissues such as muscle. The increasing level of creatinine in serum may cause itching and damage to nerve endings. Hemodialysis portrayed an effective impact on serum creatinine levels which reduced to near normal value (ChaitanyaShree et al., 2019, Nisha et al., 2017).

In agreement with Mehta et al., who indicate that increase in serum creatinine of more than or equal to 0.3 mg/dl (≥ 26.4 μmol/l) from baseline in the first stage. To more than 200 % to 300 % (> 2- to 3-fold) from baseline in the second stage. In the last stage increase in serum creatinine to more than 300 % (> 3-fold) from baseline (or serum creatinine of more than or equal to 4.0 mg/dl [≥ 354 μmol/l] with an acute increase of at least 0.5 mg/dl [44 μmol/l])(Mehta et al., 2007, Afzal et al., 2022). In the previous study, blood urea and serum creatinine showed a significant increase in their levels in patients with CRF when compared to those of controls (Wali et al., 2020).

In patients with hyperglycemia, the renal maximum glucose re-absorptive capacity, and the threshold for glucose passage into the urine, are higher and contribute to the hyperglycemic state (Gronda et al., 2020). One of the causes of kidney failure is high blood glucose (sugar) levels. Over time, the high levels of sugar in the blood damage the millions of tiny filtering units within each kidney. In hyperglycemia, the kidneys may play an exacerbating role by reabsorbing excess glucose, ultimately contributing to chronic hyperglycemia, which in turn contributes to chronic glycemic burden and the risk of microvascular consequences. the glomeruli become damaged and are unable to filter blood efficiently and glomerular membranes leak protein (more than 50% of the protein is albumin) into the urine. In patients with diabetes, the kidneys may be particularly susceptible to the effects of

hyperglycemia, as many kidney cells are unable to sufficiently decrease glucose transport rates to prevent intracellular hyperglycemia in states of increased glucose concentration (Forbes et al., 2008, Pavkov et al., 2018).

The concentrations of serum aminotransferases in both patients on chronic dialysis and those with non-dialysis chronic kidney disease most commonly fall within the lower end of the range of normal values. Although the exact cause is unknown, possible underlying reasons may be related to pyridoxine deficiency (pyridoxal phosphate is a necessary coenzyme for ALT and AST) and/or the presence of an inhibitory substance in the uremic milieu (Fabrizi et al., 2001).

Table 1: Impact of some biochemical parameters in female kidney failure patients in Erbil-city

	Parameters	**Kidney failed**	**Control**	**P<0.05**
1	Glu (mmol/L)	122.0 (97.00 - 163.5)	96.00 ± 1.817	0.05
2	Creatinine (mg/dL)	8.941 ± 0.4867	0.7400 ± 0.04301	0.001
3	Urea (mg/dl)	161 (115.8-191)	34 (31.5-36.5)	0.001
4	GOT (U/L)	13.10 (9.600 - 18.25)	18.00 (13 – 23)	NS
5	GPT (U/L)	10.30 (7.65-17.15)	23 (21-29.5)	0.001
6	T.S.B (mg/dL)	0.3 (0.2-0.4)	0.59 (0.55-0.635)	0.001
7	ALB (g/L)	3.8 (3.5-4.2)	4.2 (3.7-4.35)	NS
8	ALP (IU/L)	297 (198-406)	100.5 (95.15-120.4)	0.001
9	K+ (mmol/L)	5.695 ± 0.1411	4.506 ± 0.095	0.01
10	Na+ (mmol/L)	136 (135-138)	136 (135.2-137.5)	NS
11	Ca+ (mmol/L)	1.052 ± 0.02635	1.152 ± 0.02131	NS
12	Cl^- (mmol/L)	108 (106-111.5)	99 (98-100.5)	0.001

Table 2: Impact of some biochemical parameters in male kidney failure patients in Erbil-city

	Parameters	**Kidney frailer**	**Control**	**P<0.05**
1	Glucose (mmol/L)	134.0 (109 - 185)	99.00 (97.00 - 101.0)	0.05
2	Creatinine (mg/dl)	9.9 (7.3-12.4)	0.6 (0.505- 0.920)	0.001
3	Urea (mg/dL)	161.3 ± 6.784	32.40 ± 2.502	0.001
4	GOT (U/L)	11.90 (9.850- 15.65)	34.00 (27.50-37.50)	0.001
5	GPT (U/L)	11.3 (7.8-17.95)	34 (25.5-36)	0.001
6	T.S.B (mg/dl)	0.3 (0.2-0.395)	0.63 (0.56-0.665)	0.05
7	ALB (g/L)	3.9 (3.45-4.4)	3.8 (3.395-4.05)	NS
8	ALP (IU/L)	211 (161.5-324)	159 (155-163)	0.05
9	K+ (mmol/L)	5.411± 0.1248	4.320 ± 0.1068	0.01
10	Na+ (mmol/L)	137 (135-138)	139 (134.5-187)	NS
11	Ca+ (mmol/L)	1.05 (0.895-1.09)	1.6 (1.26-1.85)	0.0001
12	Cl- (mmol/L)	109 (107-111)	100.2 (99.5-103.5)	0.001

Conclusion

A firm association were observed between serum creatinine, serum urea, glucose, liver function test, K+, Cl- and ALP levels among renal failure patients presenting information on renal function among varied age individuals. Both serum creatinine and serum urea are widely accepted biomarkers to assess renal functions.

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whole or in part to any company. Tufts Medical Center, Johns Hopkins University, and Metabolon, Inc. have a collaboration agreement to develop a product to estimate glomerular filtration rate from a panel of markers (June 25, 2016). Dr. Coresh is a member of the Global Hyperkalemia Council (sponsored by Relypsa, no personal compensation). National Institute of Diabetes and Digestive and Kidney Diseases (US).

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