

The Biochemical Changes in Patients with Chronic Renal failure in District Hospital Shopian Jammu and Kashmir India

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ABSTRACT.

This study was carried out at District Hospital Shopian to evaluate various parameters in chronic renal failure (CRF) patients, including serum urea, creatinine, lipid profile (cholesterol, triglycerides [TG], high- density lipoprotein [HDL], and low-density lipoprotein [LDL]), and thyroid hormones (free triiodothyronine [FT3], free thyroxine [FT4], and thyroid- stimulating hormone [TSH]). A total of 41 patients participated in the study, consisting of 26 males and 16 females, with ages ranging from 17 to 88 years. The control group comprised 30 individuals without any signs or symptoms of renal disease, lipid disorders, or thyroid hormonedisorders, including 15 males and 10 females, with ages ranging from 22 to 66 years

The study findings revealed that serum urea and creatinine concentrations were significantly higher in CRF patients compared to the control group ($P<0.001$). Serum triglyceride concentrations in CRF patients were found to be within the normal range or not significantly increased when compared to the control group ($P>0.05$). There were no significant differences observed in serum cholesterol, HDL, and LDL concentrations between CRF patients and the control group. Similarly, no significant differences were found in serum FT3, FT4, and TSH concentrations between CRF patients and the control group. Furthermore, there were no significant associations identified between changes in lipid profile concentrations and changes in thyroid hormone concentrations.

INTRODUCTION

Renal failure refers to the condition where the kidneys are damaged, leading to a loss of their normal functions. This damage can be caused by various factors such as infections, autoimmune diseases, cancer, endocrine disorders like diabetes, and exposure to harmful substances. Renal failure is characterized by a decline in the kidney's ability to regulate bodily processes and urinary function. In the United States, it is the tenth leading cause of mortality and poses a significant burden in industrialized countries [1], [2]. Dyslipidemia and abnormalities in lipid metabolism are commonly observed in renal disease and are known

to contribute to glomerulosclerosis [3]. Post- transplant dyslipidemias have been shown to increase the risk of chronic rejection, altered graft function, and death [4], as well as an increased risk of ischemic heart disease. Several studies have investigated the impact of lipid disorders on renal function [5], with poor lipoprotein profiles identified as risk factors for progressive renal deterioration. Abnormal lipid profiles tend to develop soon after renal function starts to decline [6].

Thyroid hormones (TH) play a vital role in the growth, development, and maintenance of water and electrolyte balance in the kidneys. The kidneys are involved in the metabolism and elimination of TH. Both hypothyroidism and hyperthyroidism can cause significant changes in water and electrolyte metabolism and cardiovascular function, which have clinical implications. Changes in renal water and electrolyte management occur due to these effects. Furthermore, alterations in TH production, secretion, metabolism, and elimination occur concurrently with the decline in renal function. Patients with severe kidney disease often exhibit distinct features of thyroid dysfunction [8]. Additionally, medications used in the management of kidney and thyroid disorders can affect both thyroid and renal function. TH significantly influences the physiology, growth, and development of the kidneys [9], [10]. Hypothyroidism decreases the kidney-to-body weight ratio, while hyperthyroidism increases it [11]. Congenital renal abnormalities are more prevalent in children with congenital hypothyroidism, indicating the important role of TH in early embryogenesis [12]. Thyroid function also affects the balance of water and electrolytes in various bodily compartments [13]. The kidney serves as a crucial target organ for TH actions and contributes to the control of TH metabolism and elimination [14]. A decline in TH activity leads to an impaired ability to excrete excess water orally, which is attributed to a decrease in the glomerular filtration rate (GFR) rather than an inhibition of vasopressin synthesis or reduced reabsorption capacity of the renal tubule's dilutor segment [16]. Thyroid dysfunction results in significant alterations in renal function, including changes in renal blood flow, GFR, tubular electrolyte transport

activity, and electrolyte homeostasis [17]. Chronic renal failure is often associated with elevated cholesterol levels, dyslipoproteinemia, and triglycerides, as well as a decrease in polyunsaturated lipids. These abnormalities have been identified as independent risk factors for artery disease [18]. In patients undergoing dialysis, these lipid abnormalities tend to worsen [19].

Furthermore, there is a common occurrence of increased plasma homocysteine concentration in individuals with end-stage renal failure, which is considered an independent risk factor for atherosclerosis-related complications [22].

A recent study has issued a warning that relying heavily on a diet consisting of junk food or processed food may result in long-term harm to the kidneys and increase the risk of developing diabetes. Type 2 diabetes occurs when the body either doesn't produce enough insulin or doesn't respond adequately to it, leading to an accumulation of sugar (glucose) in the blood. This can have severe and lasting consequences for organs, particularly the kidneys, and contribute to the development of diabetic kidney disease.

"The western diet, which includes a substantial amount of processed junk food and high-fat content, has a well-established association with the rising prevalence of obesity and Type 2 diabetes," stated Havovi Chichger, the lead author of the study from Anglia Ruskin University in Britain. "Our study reveals that both Type 1 and Type 2 diabetes induce alterations in glucose transport in the kidneys, but a diet rich in junk food or high in fat produces changes that closely resemble those observed in Type 2 diabetes," Chichger added, as reported in the journal *Experimental Physiology*.

Although occasional indulgence in junk food is acceptable, it's important to be cautious about daily consumption. Regularly consuming junk food puts you at risk of developing type 2 diabetes and heart disease. It can also lead to digestive problems, fatigue, weakness, depression, and fluctuations in blood sugar levels. It's essential to strike a balance and prioritize a healthy and balanced diet to maintain overall well-being and kidney health.

MATERIAL AND METHODS

The objective of this study is to examine the alterations in multiple red blood cell (RBC) parameters, including hemoglobin concentration, hematocrit, RBC count, and RBC indices, among patients diagnosed with chronic kidney disease (CKD).

Additionally, we aim to compare these changes in RBC parameters across different stages of chronic renal failure.

ii MATERIAL AND METHODS.

The control group consisted of 30 non-hospitalized individuals without a history of systemic disease, matched for age and sex. The study group comprised 50 adult individuals diagnosed with chronic renal failure, based on their medical history, physical examination, and renal function test results. All participants had fasted for 12-14 hours prior to blood collection. The study included individuals aged 18 to 60, and high-quality chemicals and kits were used for analysis.

Blood samples were collected and the concentrations of various substances, including creatinine, urea, total cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH), were measured following established procedures. The study was conducted at the clinical laboratory of Kasturba Medical College and Hospital over a period of 2½ years, from November 2011 to June 2014. A total of 300 diagnosed

cases of CKD were included in this hospital-based retrospective and prospective study (ambispective study), selected according to the criteria of the National Kidney Foundation - Kidney Disease Outcomes Quality Initiative, irrespective of the primary cause of CKD. The glomerular filtration rate (GFR) was estimated using the MDRD study equation, and adjustments were made for women.

All CKD patients admitted to Kasturba Hospital were assessed for RBC count, hemoglobin (Hb), hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), serum iron profile (serum total iron, total iron-binding capacity, and serum ferritin levels), and peripheral smear analysis for anemia type and features of hemolysis, blood

urea, and serum creatinine. Clinical details were collected from the medical record department, and hematological and biochemical data were obtained from the hospital information system and research population data for complete blood count (CBC) analysis.

Patients and samples collection

A total of 145 samples were collected from Dist. Hospital Kulgam. Among these samples, 45 were from patients and 20 were from healthy individuals. Each set consisted of 26 males and 19 females, and the age range of the participants was between 17 and 88 years.

Serum Cholesterol

The cholesterol levels in the samples were measured using the CHOD-POD Enzymatic colorimetric method (Biolabo/France). The contents of vial R2 Enzymes (Cholesterol esterase (CHE) 300 U/L, Cholesterol oxidase (CHOD) 300U/L, Peroxidase (POD) 1250 U/L & 4 - Aminophenazone (4- AP) 0.4 mmol/L) were dissolved in the bottle of R 1 Buffer (PIPES 90 mmol/L and Phenol 26 mmol/L). After gently mixing and capping the solution, it was incubated for 5 minutes at 37°C at room temperature, and the absorption was read at 500 nm.

High serum cholesterol is a well-known cardiovascular risk factor in the general population. However, in patients with end-stage renal disease (ESRD), high cholesterol concentrations are associated with better survival, which is a phenomenon known as reverse epidemiology. This reverse association can be attributed, in part, to confounding factors such as malnutrition and chronic inflammation. The use of statins to lower serum cholesterol in this population remains a topic of debate. In ESRD, oxidative stress leads to modifications in LDL cholesterol, and these altered LDL particles play a crucial role in the development of atherosclerosis. The use of the antioxidant vitamin E to benefit this population has not been conclusively proven. This review aims to provide a comprehensive perspective on the available literature regarding dyslipidemia and oxidative stress in ESRD.

Serum Triglyceride The serum triglyceride levels were measured using the colorimetric method (Biolabo/France). The contents of vial R2 Enzymes (Lipase, Peroxydase, Glycerol 3 phosphate oxydase, Glycerol Kinase, 4 - Amino antipyrine, and Adenosine triphosphate) were added to vial R1 Buffer (PIPES 100 mmol/L, Magnesium chloride

9.8 mmol/L, and Chloro-4-phenol 3.5 mmol/L). The mixture was thoroughly mixed and left to stand for 5 minutes at 37°C at room temperature. The absorbencies were then recorded at 500 nm (480-520 nm) against the reagent blank.

Serum triglyceride levels ≥ 200 mg/dL were found to be independently associated with all-cause mortality in patients with Stage 3 and Stage 4 chronic kidney disease (CKD) who were younger than 65 years old. However, this association was not observed among patients aged 65 years and older. Further studies are

needed to validate these findings and explore the underlying mechanisms that may explain these associations.

A. Creatinine Assay

This test is used to measure the levels of creatinine in the blood and/or urine. Creatinine is a waste product produced by the muscles during regular daily activities. Normally, the kidneys filter creatinine from the blood and excrete it in the urine. However, if there is a kidney problem, creatinine may accumulate in the blood and be excreted in lower amounts in the urine. Abnormal levels of creatinine in the blood and/or urine can indicate kidney disease. You may need to undergo this test if you are experiencing symptoms of kidney disease, such as fatigue, puffiness around the eyes, swelling in the feet and/or ankles, decreased appetite, frequent and painful urination, or foamy or bloody urine. The conversion of creatine to creatinine occurs nonenzymatically, resulting in dehydration. The body produces creatinine at a consistent rate, and it is eliminated from the body by the glomerular filtration in the kidneys. Kidney disease can slow down the filtration rate of creatinine, leading to higher

concentrations of creatinine in the blood. Factors such as changes in muscle size, pregnancy, or the use of angiotensin receptor antagonists or inhibitors can also affect creatinine levels. In this test, the concentration of creatinine is measured using a linked enzyme process that produces a colorimetric measurement or fluorometric measurement (ex = 535 nm/em = 587 nm; 570 nm), which is directly proportional to the amount of creatinine present.

RESULTS

Enzymatic methods were employed to calculate the values of urea, creatinine, triglycerides (TG), total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and cholesterol from very low-density lipoprotein (VLDL-C). The levels of FT3, FT4, and TSH were determined using an ELISA approach.

Table I presents the biochemical indicators (urea, creatinine, cholesterol, TG, HDL, LDL, FT3, FT4, and TSH) in both male and female patients with chronic renal failure, as well as the control group.

Doctors evaluate renal function by analyzing plasma concentrations of waste products such as urea and creatinine. These tests are sufficient to detect the presence of renal disease in a patient. They help assess the kidneys' ability to filter blood and provide information about kidney function, including elevated levels of nitrogen and creatinine in the blood.

The glomerular filtration rate (GFR), determined by serum creatinine levels, is used to assess ongoing renal function and guide treatment decisions regarding the degree of renal disease.

Patients with chronic renal failure exhibited a non-significant ($P>0.05$) decrease in serum cholesterol, HDL cholesterol, and LDL cholesterol levels compared to the control group. Correlation analysis revealed no significant ($P>0.05$) association between thyroid hormone concentrations and lipid profile concentrations. Among the variables examined, triglyceride levels did not significantly differ between CRF patients and the control group ($p>0.05$). HDL levels showed no significant difference or were lower in CRF patients compared to the control group ($p>0.05$).

No significant changes ($p>0.05$) were observed in LDL and total cholesterol levels between CRF patients and the control group. Both hemodialysis and non-hemodialysis CRF patients had an increased risk of developing dyslipidemias characterized by elevated levels of hypertriglyceridemia and reduced HDL values of LDL and total cholesterol.

In patients with chronic kidney disease (CKD), serum TSH concentrations are generally normal or elevated, although the response of TSH to its hypothalamo-pituitary (TRH) is typically suboptimal. Uremia may be associated with intrathyroidal and pituitary abnormalities, as well as alterations in TSH glycosylation and circadian cycles. CKD patients commonly exhibit normal or low levels of free and total T3 and T4, with a frequent occurrence of decreased T3 levels (low T3 syndrome) attributed to reduced peripheral T3 synthesis from T4. The use of heparin during hemodialysis (HD) can occasionally lead to elevated free T4 levels by interfering with T4 binding proteins, while free and total T4 concentrations may be normal or significantly reduced. Studies have shown a correlation between T3 levels and mortality in uremic patients, but the association between TSH and survival in individuals with varying degrees of renal insufficiency requires further investigation.

Further research in this field will enhance our understanding of the biological significance

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