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Biochemical and Hematological Parameters in a Group of Chronic Kidney Disease Patients in Albania

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Abstract: Chronic kidney disease is a serious, life threatening health problem. It is also known as chronic kidney failure, as it is a process of irreversible loss of nephrons, which at the end stage leads to kidney failure. There are many different reasons that lead to kidney failure, such as: hypertension, diabetes, polycystic kidney disease, glomerulonephritis, parathyroid glands dysfunction, etc. The aim of this study was to evaluate the biochemical and hematological profile in a group of chronic kidney patients in Albania. A group of 247 chronic kidney disease patients is included in this study (170 adult males and 77 adult females). A group of biochemical parameters, such as urea, CRP, albuminemia, HbA1C, creatinine, ALT, AST, calcium, phosphate, CaxP product, sodium, potassium and hematological parameters, such as hemoglobin, red blood cells, white blood cells and PTH, were measured and compared to the findings from the control group. Results were analyzed statistically using SPSS 20 program for windows. From data analysis, we found a reduced count of red blood cells and hemoglobin, statistically significant change, compared to the control group ($p < 0.05$). High levels of PTH, serum urea, creatinine and hyperphosphatemia, accompanied by hypocalcemia, were found statistically significant compared to the control group ($p < 0.05$). From our observations, hypertension, diabetes and kidney stones were the main causes leading to chronic kidney disease. Evaluation of these parameters, results to be significant in the differentiation and management of the health state of these patients.

Keywords: Chronic kidney disease, Albanian population, Biochemical and hematological parameters, Urea, Hemoglobin

Introduction

Chronic kidney disease is a serious, life threatening health problem. It is also known as chronic kidney failure, as it is a process of irreversible loss of nephrons, which at the end stage leads to kidney failure. There are many different reasons that lead to kidney failure, such as: hypertension, diabetes, polycystic kidney disease, glomerulonephritis, parathyroid glands dysfunction, etc. Chronic kidney disease is a broad term used to describe a situation of renal function decrease that happens for more than three months. As we know one of the main functions of the kidneys is to maintain blood parameters homeostasis and remove waste from the blood. Kidneys play a key role also in keeping steady the electrolytes and maintaining the amount of water in our body. Another function of the kidneys is to produce hormones, such as erythropoietin and vitamin D which is not a hormone, but behaves like a hormone in the human body. Renal function is monitored and assessed by the glomerular filtration rate which is one of the most important and accurate markers. Chronic kidney disease

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(CKD) is defined as the presence of kidney damage or an estimated glomerular filtration rate (eGFR) less than 60 ml/min per 1.73 square meters, persisting for 3 months or more (De Broe et al., 2020).

This glomerular filtrate rate is observed to be slightly less in women compared to men and affected by age (in older ages the glomerular filtrate rate is less). An abnormally low glomerular filtration rate (GFR) often escapes medical notice in the earliest, most treatable stage, so that an increasing number of patients progress to end-stage renal failure. Its main causes are hypertension and diabetes mellitus (Thomas et al., 2009). In hypertension according to the literature, there are changes related to the arteries that supply the kidneys, their walls get thicker in order to withstand the high pressure. This leads to a narrow lumen, providing less blood and oxygen for the kidneys, damaging so the structural and functional parts of the kidneys (nephrons). The same final result comes due to diabetes and the fact that excess glucose in the blood, sticks to the proteins via a non enzymatic process of glycation. This process will affect mostly the efferent arteriole, causing so arteriosclerosis and creating an obstruction which will make it difficult for blood to leave the glomerulus. This will increase the pressure inside the glomerulus and will lead to hyperfiltration.

Chronic kidney disease (CKD) is considered a global public health problem and about 200,000 persons landed into terminal kidney failure every year and millions more suffer from lesser forms of kidney diseases (National Kidney Foundation 2006). In the United States, more than 1 in 7 adults—15% of the adult population, or 37 million people—are estimated to have chronic kidney disease (CKD), 9 in 10 adults with CKD do not know they have CKD and about 2 in 5 adults with severe CKD do not know they have CKD. One reason is the rapidly increasing worldwide incidence of diabetes and hypertension (Ansari et al., 2021). The prevalence of CKD is higher in developing countries than in the developed world. Diabetes mellitus is becoming increasingly prevalent in these countries. Therefore, it is expected that there will be a proportionate increase in vascular and renal disease (Ansari et al., 2021). Diabetic kidney disease is the commonest cause of end stage Kidney disease (ESKD) in the world (Wild S. et al. 2004). End-Stage Renal Disease (ESRD) is the final stage of CRF characterized by progressive, irreversible deterioration in renal function and body fails to maintain fluid and electrolyte balance resulting in uremia. ESRD is characterized by a decrease in GFR and evidence of less than 10% nephron function remaining (Poothullil et al., 1975).

Kidney diseases are associated with a change in various biochemical and hematological parameters. Biochemical and hematological profiles are commonly affected in CKD and this becomes more apparent as the disease progress which further complicates the condition of the patient, making the patient more vulnerable for cardiovascular complications (Habib et al., 2017). During hemodialysis elements such as Na⁺, K⁺, Ca⁺⁺, Mg⁺, Cl⁻, and H⁺ must be kept in a rather narrow physiological range, otherwise life-threatening events may occur (Daugirdas, 1985). ALT levels are also higher in CKD patients (Ochiai, 2020). Many abnormalities are observed in the hematological parameters, such as anemia, decrease in platelet count, tendency to abnormal bleeding and bruising, etc. (Brown et al., 1922; Marc et al., 2020; Castaldi, 1966; Gouva, 2006).

Method

A group of 247 chronic kidney disease patients, undergoing hemodialysis, is included in this study. The study was carried out during the period of time from 2017 to 2019. These patients were diagnosed with chronic kidney disease problems and followed the treatment in the University Hospital “Mother Teresa” in Tirana and in the Regional Hospital of Elbasan (Dialysis center) as well. In order to evaluate and understand how chronic kidney problems affect the biochemical and hematological parameters in this group of patients, all the biochemical and hematological data are observed and collected from the register of patients periodically.

A group of biochemical parameters, such as urea, CRP, albuminemia, HbA1C, creatinine, ALT, AST, calcium, phosphate, CaxP product, sodium, potassium and hematological parameters, such as hemoglobin, red blood cells, white blood cells and PTH, were measured and compared to the findings from the control group. Ten ml fasting venous blood sample was collected each time in prechilled tubes with anticoagulants. The results were analyzed statistically using SPSS 20 program for windows and are presented as mean ± standard deviation (± SD) and P-value considered significant ($p \leq 0.05$).

Exclusion criteria

- Pediatric age was excluded from this study as well as pregnant and lactating women.

- All individuals who didn't have regular laboratory data (who had some missing values), were excluded also.

Results and Discussion

In total, the biochemical and hematological parameters of 247 adult individuals with chronic kidney disease are observed and evaluated in this study. As we can see from the results of this study, male are more affected than female by chronic kidney disease, 170/247 (68.83%) and 77/247 (31.17%) respectively, with significant level between them $P < 0.0001$. The patients' age varies from 18 to 79 years old, with a mean age 56.64 (± 14.21) years old. As we can see from the table below (Table 1), most of the patients belong to the age-group of 50-59 years old with a number of cases of 79 patients (31.98 %), 52 males and 27 females, followed by the age-group of 60-69 years old with a number of cases 76 (30.77 %), 58 males and 18 females.

Table 1. Age and gender distribution in chronic kidney disease patients

Age (years)	Female	Male	Total no (%)
18-39	12	13	25 (10.12)
40-49	11	27	38 (15.39)
50-59	27	52	79 (31.98)
60-69	18	58	76 (30.77)
≥ 70	9	20	29 (11.74)
Total	77 (31.17%)	170 (68.83%)	247 (100%)

It is noticed that males are more affected by chronic kidney disease and maintained on dialysis when compared to females as shown in table 1. Similar data are presented in other studies of the same profile, showing a predominance of male compared to female as mentioned by Singh et al. 2018 and Islam et al. 2015 and by Ansari et al. 2021. From the data distribution we can see that the more problematic age is from 50 to 69 years old as shown in table 1 and figure 1. These findings are comparable to other studies done by Singh S et.al JMMIHS.2018;4(1):4-11²⁵, in Nepal, where the majority of the patients were in the age group of 41-60 years old. According to other studies in the nearby countries, e.g. by Cozzolino et.al. 2018, we can see comparable data in Italy also, where male with chronic kidney disease predominate to female in the patients enrolled in the study (59.7% males, aged 66.2 ± 14.6 years). According to Sombolos et al.2014, based on a similar study in Greece, patients on average were older (mean age 66.2 ± 14.6 years, median: 69.6 years), predominantly male (54.9%). From other population based studies in Turkey, according to Süleymanlar G. et al.2011, we can see that chronic renal diseases affect younger ages and mostly women (mean age 40.5 ± 16.3 years; 55.7% women).

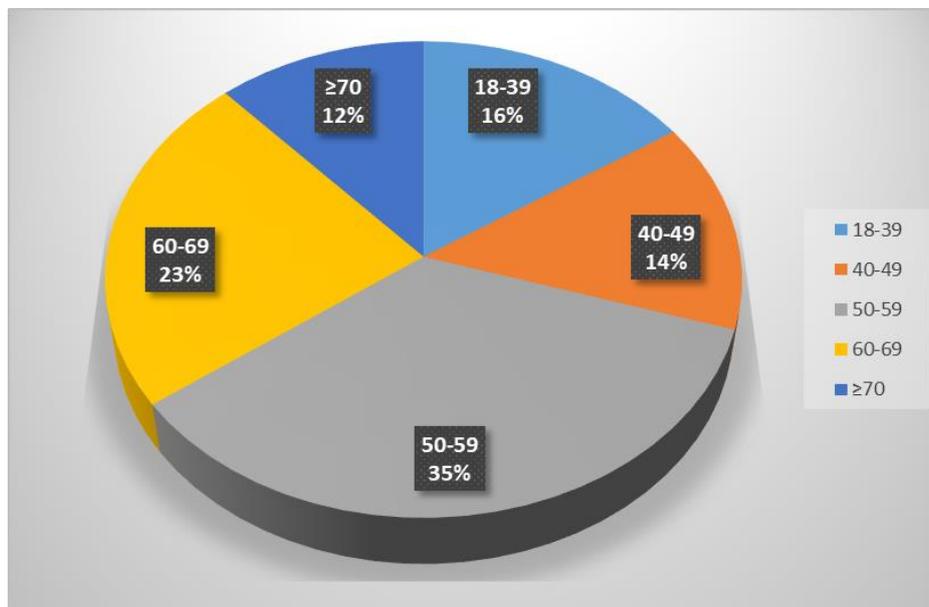


Figure 1. Age distribution in chronic kidney disease patients

From data analysis on the etiology of chronic kidney disease in this group, based on our observations, the most common etiology was the combination of hypertension and cardiovascular diseases (39.97 %), followed by the

combination hypertension and diabetes mellitus (15.36 %), hypertension (21 %), Diabetes (13.39 %), Glomerulonephritis (7.31 %), Pyelonephritis (5.24 %) and other issues such as Nephrolithiasis, Rheumatoid arthritis and others (3.73 %) as shown in figure 2.

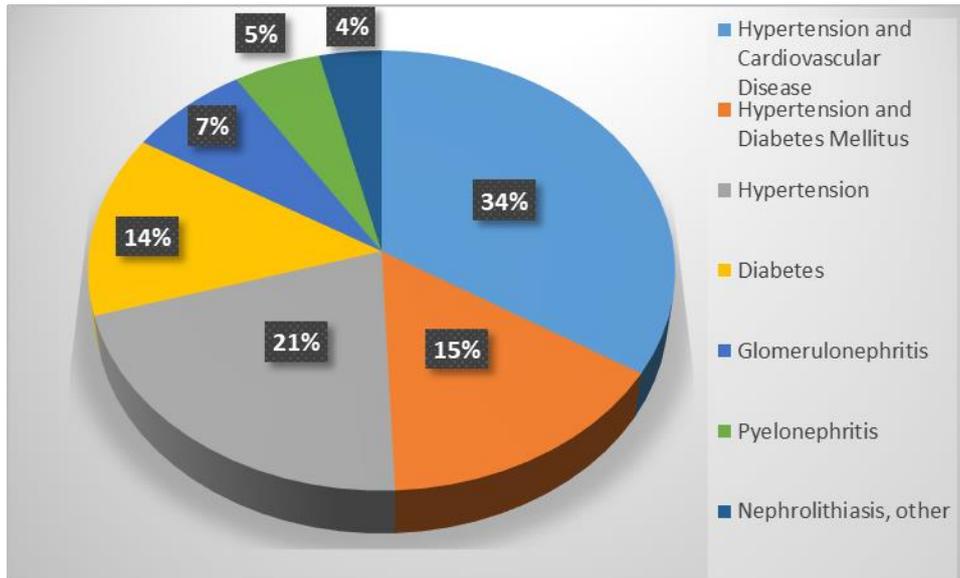


Figure 2. Etiology of chronic kidney disease

Both biochemical and hematological parameters as is shown in table 2, seems to have significant changes compared to the control group and the reference values. The mean values of PTH, phosphates, total calcium, CaxP product, potassium, sodium, albumin, urea and creatinine were 645.15 (± 475.37) mg/dl, 5.32(± 1.39) mg/dl, 8.4 (± 0.94) mg/dl, 46.11 (± 10.5) mg²/dl², 5.6 (± 0.74) mmol/l, 5.6 (± 0.74) mmol/l, 133.27 (± 6.12) mmol/l, 3.81 (± 0.47) g/dl, 100.57 (± 53.74) mg/dl and 11.2 (± 2.1) g/dl.

Very high levels of PTH are observed in this group, which was statistically very significant, when compared to control group ($p < 0.05$). PTH is essential and plays a central role in calcium homeostasis. In this group of patients, with a reduced nephron activity, vitamin D maturation (last stage of hydroxylation in the level of proximal tubule) is not possible due to kidney dysfunction. In these conditions, vitamin D which is crucial in the absorbance of calcium from the intestines, is not active and calcium is not absorbed enough, which is presented as hypocalcemia. In this case, parathyroid glands are stimulated to produce more PTH in order to maintain the level of circulating calcium, leading in most of the cases in secondary hyperparathyroidism. Several studies has discovered a strong affiliation among mortality and abnormal mineral metabolism; probably mediated by vascular calcification. The disturbances embrace calcium, phosphorous, vitamin D, and PTH homeostasis. So, mineral metabolism results are gaining significance in hemodialysis treatment (Singh S. et al. 2012). On the other hand, similar results to ours are mentioned in other studies from RusulArif 2018 and Freethi et al. 2016, where significant hypocalcemia is observed in CKD patients.

Serum phosphates, CaxP product, urea and creatinine were highly increased in those patients, while calcium levels are significantly decreased compared to control group and reference level ($p < 0.05$). The kidneys play a central role in maintaining the phosphorous homeostasis by proper excretion of phosphorus through the urine in response to its high levels to make certain that their serum concentrations are good enough for the performance of numerous functions. Decreased GFR will increase serum phosphorus levels as its excretion will be reduced (García et al. 2017).

Creatinine is generated from creatine with the aid of non-enzymatic dehydration, while urea is the main product of protein and amino acids catabolism (through the urea cycle in the liver). In the urea cycle, ammonia is transformed to urea, which is carried by means of blood to the kidneys for its elimination from the body. Elevated levels of urea within the blood may additionally indicate renal failure (National Kidney Foundation, 2006). Normal levels of albuminemia and aspartate aminotransferase (AST) are observed in this patients, as is shown in the table 2. On the other hand we can notice high levels of Serum alkaline phosphatase (ALP) when compared to the control group and reference level 190.93 (± 195.7) U/l, statistically significant. Based on other studies on chronic kidney disease patients high levels of ALP are observed and linked with the severity and stage of the disease in these patients. According to Kovesdy CP. Et.al, Serum alkaline phosphatase (ALP)

increases in patients with chronic kidney disease (CKD) and high-turnover bone disease. ALP may represent an adjunct marker of high bone turnover devoid of drawbacks of serum parathyroid hormone (PTH), and it may also be associated with cardiovascular calcification in CKD. Higher ALP has been recently associated with increased mortality and coronary calcification in dialysis patients.

Table 1. Biochemical and hematological parameters in chronic kidney disease patients

Parameters	CKD patients (Mean)	Control (Mean)	Reference rate
PTH (mg/dl)	645.15 (±475.37)	55.33(±11.29)	10 - 65
Phosphates (mg/dl)	5.32(±1.39)	4.06(±0.27)	2.6 – 4.5
Total Calcium in serum (mg/dl)	8.4 (±0.94)	8.89(±0.95)	8.6 - 10.2
CaxP (mg ² /dl ²)	46.11 (±10.5)	43.6(±11.35)	<55
K (mmol/l)	5.6 (±0.74)	4.03(±0.29)	3.5 – 5.3
Na (mmol/l)	133.27 (±6.12)	137.42(±4.25)	135 – 148
Albuminemia (g/dl)	3.81 (±0.47)	3.64(±0.9)	3.56 – 4.61
ALP (U/l)	190.93 (±195.7)	93(±19)	< 130
AST (U/l)	21.6 (±21.7)	17(±9.75)	< 37
Urea (mg/dl)	100.57 (±53.74)	25.17(±7.19)	15-50
Creatinine (mg/dl)	7.12 (±3.27)	0.79±0.32	0.5-1.2
Hemoglobin (g/dl)	11.2 (±2.1)	13.07(±1.92)	14 – 18 (In males) 12 – 16 (In females)
HbA1c (%)	6.78	5.3(±0.7)	4.8-5.9
Hematocrit (%)	25.94 (±5.11)	41.9(±3.14)	35.0-52.0
RBC (million/mm ³)	2.85(±0.96)	4.67(±0.24)	4.00-5.50
WBC (Thousands/mm ³)	7358.29(±1496.13)	8316.11(±1548.3)	4.23-10.00
Platelet count	205926.25(±71339.18)	311572.67(±75403.26)	150000.00-400000.00

The hematological parameters studied in this group of patients results to be reduced compared to control group and to the reference intervals for this parameters. The mean values for hemoglobin, HbA1c, hematocrit, red blood cell count, white blood cell count (total leucocyte count) and platelet count in this group of patients with chronic kidney disease, were 11.2 (±2.1) g/dl, 6.78 %, 25.94 (±5.11) %, 2.85 (±0.96) million/mm³, 7358.29 (±1496.13) thousands/mm³ and 205926.25 (±71339.18) respectively. These values are lower than the control group, which is statistically significant change (p<0.5). Similar result are mentioned in other studies in chronic kidney disease patients, as mentioned from Singh et. al., 2018, Habib et al. 2017, Suresh et al. 2012, Yassein et al. 2016 and Alghythan et al., 2013.

The reduction of these blood cells parameters, such as red blood cells, hemoglobin, hematocrit and platelets, comes as a result of lower levels of the hormone erythropoietin production, because of kidney failure. In chronic renal disease because of impaired erythropoietin secretion, increased destruction of red blood cells, leads to a fall in red blood cell count, which reduces the hemoglobin concentration and haematocrit. A decrease in haematocrit is apparent even among patients with mild to moderate renal insufficiency (Wintrobe, 2008; George C, et al. 2018).

From our observations and data analysis of the observed parameters in this group, we can say that the degree of changes, in both hematological and biochemical parameters, depends on the severity of renal failure. Except the fact that it is difficult to point an abnormally low glomerular filtration rate (GFR), which often escapes medical notice in the earliest stage and leads to end-stage renal failure (Thomas et al., 2009), socioeconomic difficulties affect self examination and the frequency one is going to the doctor for a routine check up, etc. (Zeng et al. 2018), leading so in severe forms of chronic kidney disease in the population. We found out that most of these patients are living in low income 42.1% (less than 200 euro and only 7.2% of the patients are living in the categorized high income living group (more than 400 euro per month). This can be also a significant factor affecting the situation of chronic kidney disease in this group.

Conclusion

As a conclusion of this study we can say that male are more affected than female by chronic kidney disease and that hypertension combined with cardiovascular diseases and diabetes are the main causes leading to chronic

kidney disease. Chronic kidney disease is associated with significant disorders in various biochemical and hematological parameters, which is mandatory to be evaluated regularly. Monitoring those abnormalities will help the stratification of patients and will reduce the morbidity and mortality in this group of patients.

Limitations of the study

There are some limitations in this study linked to the relatively small number of subjects, especially females and lack of information because of the high number of deaths in this group of patients, which makes it difficult to assess the situation over the years.

Scientific Ethics Declaration

The authors declare that the scientific ethical and legal responsibility of this article published in EPHELS journal belongs to the authors.

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