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Assessment the Role of Erythropoietin, Hepcidin and Albumin in Patients with Chronic Kidney Disease in Kirkuk-Iraq

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Abstract

The dys function of kidney dys functions is one of the most common diseases among people on a global scale. and the renal failure disease were classvided into five stages, which include decreafe glomerular filtration rate 60 ml min^{-1}, levels in serum. The aim of the current study was to estimate the concentrations of erythropoietin, hepcidin and albumin in people with chronic renal failure. The current study included 75 Patients of both gender, ages (40-70). They suffer from renal failure at different stages which has been classified into five stages and each stage include 15 sample as well as, 15 healthy people as a control group. the results showed a significant decrease ($P \leq 0.01$) in the concentration of erythropoietin in chronic kidney disease (CKD) patients compared with the control group, as the concentration of erythropoietin began to decrease gradually during the stages of renal failure due to the decline in renal function in CKD patients as a result of decreased filtration and secretion of this hormone. The results showed a significant increase ($P \leq 0.01$) in the concentration of hepcidin in CKD patients, except for the first stage, in which a significant difference was not observed when compared with the control group. Finally, the results also showed a significant ($P \leq 0.01$) decrease in albumin levels in patients with renal failure compared to the control group. Based on the results of the current study, both erythropoietin and hepcidin can be used as indicators of renal failure. Also, albumin is one of the most important criteria for detecting kidney function.

1. Introduction:

There is no wide awareness of the importance of chronic kidney disease among the general public, and various qualitative studies show that if members of the public are aware of kidney disease, their knowledge is generally limited to dialysis and transplantation [1], [2]. Kidney disease is often seen as an inevitable consequence of aging or as a long-term complication affecting a small number of people, rather than as a common and preventable chronic disease [3], [4]. Environmental pollutants, including metals and air pollutants can increase the risk of CKD and accelerate its progression [5]. Chronic renal failure results in a decrease in the level of the hormone Erythropoietin in the serum, and Erythropoietin is a hormone produced by the kidneys and its function is as a catalyst for the formation of red blood cells [6]. and the hormone has the ability to stimulate the production of RBCs in the bone marrow through the presence of special receptors for it on the surfaces of proerythroblast which are the progenitor cells of red blood cells. In the case of anemia and low hemoglobin in the blood, the kidneys will be sensitive to a lack of oxygen

and begin to secretion, which sequentially increases the production of red blood cells [7]. Hepcidin, a peptide hormone produced in the liver, was discovered in 2000 and appears to be a key regulator of iron homeostasis in humans Milkmaids Mammals [8]. As for humans, the gene responsible for the synthesis of hepcidin is HAMP (Hepcidin Antimicrobial Protein), And benefit from it [9]. hepcidin model assumes that the velocity of iron flow from the plasma depends mainly on the concentration of hepcidin in the plasma, when the level of iron is high , hepcidin synthesis increases, and iron released from intestinal cells and macrophages decreases in an opposite way [10]. So, the aim of the current study was to estimate the concentrations of erythropoietin, hepcidin and albumin in people with chronic renal failure.

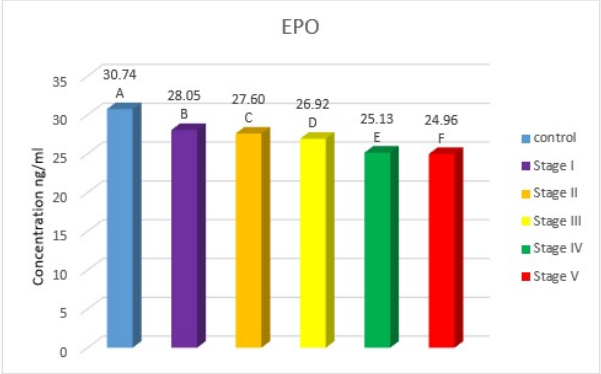

Figure 1. Concentrations of erythropoietin in serum of patients and healthy groups.

2. Materials and Methods:

2.1 Study Design:

This Case -design was conducted for the period from October 2022 to March 2023 in the specialized clinics in the city of Kirkuk, which included 75 patients with renal failure at different stages at ages 40-70 years, as well as 15 people who did not suffer from any disease symptoms as a control group.

2.2 Blood Samples:

5 ml of Blood from every patients with chronic renal failure , serum is separated by centrifugation at a speed of 3000 rpm to obtain blood serum.and stored at c (-20).

2.3 Biochemical Analysis:

The basic principle for estimating the concentration of erythropoietin and hepcidin by using the analysis kit from the company French Biolabo, enzyme linked immunosorbent assay (ELISA), using Demeditec Diagnostics EPO ELIZA GmbH • Lise-Meitner-Straße 2 • D-24145 Kiel (Germany).

2.4 Statistical Analysis:

Data recorded on a specially designed questionnaire, collected and entered in the computer then analyzed using appropriate data system which is called Statistical Package for Social Sciences (SPSS) version 24 and the results compared between patients with different variables, with a statistical significance level of ($p \leq 0.01$). The results presented as frequencies, percentages in tables and figures and analyzed using correlation and T tests.

3. Results and Discussions:

3.1 Erythropoietin:

The results of the current study are shown in Figure 1 There was a significant decrease in the concentrations of the hormone erythropoietin in the serum of CKD patients compared with the control group, and that the gradient in moral decline started from the first stage (28.05 ± 0.26 ng ml^{-1}) and the second stage (27.6 ± 0.37 ng ml^{-1}) and the third stage (26.92 ± 0.63 ng ml^{-1}) and the fourth stage (25.13 ± 0.75 ng ml^{-1}) up to the fifth stage (24.96 ± 0.58 ng ml^{-1}) compared to the control group (30.74 ± 0.99ng ml^{-1}).

The main reason for the decrease in erythropoietin concentration is attributed to the decline of renal function in patients with chronic renal failure. It was found from the results of our study that this hormone is inversely associated with the stages of advanced kidney failure, and its concentration decreases with the decline in kidney function in terms of filtration and secretion of this hormone. Among the cells whose performance declines are the cells that produce the hormone erythropoietin, which are located in the cortex layer of the kidney [11]. and that the decline in kidney function leads to severe anemia in patients with chronic renal failure as a result of a decrease in the production of erythropoietin, which in turn leads to a reduction in the production of blood cells called erythrocytes in the bone marrow and thus a decrease in the number of red blood cells. CKD patients are the majority of those who suffer from chronic diseases, especially diabetes and pressure, which leads to pressure on the kidney cells, especially the glomeruli and renal nephrons, in addition to the tubules that carry out the filtration process. The kidney, which negatively affects its efficiency, and thus reduces the secretion of the hormone erythropoietin from the kidney [12]. It is possible to measure the glomerular filtration rate by calculating creatinine clearance [13]. Studies have shown that the filtration rate from the glomeruli is associated with erythropoietin concentrations, and when the filtration level from the renal glomeruli drops to levels less than 60 ml min^{-1}, the erythropoietin secretion rates also decrease [14].

3.2 Hepcidin:

The results show in the Figure 2 that the concentrations of hepcidin increased significantly ($p \leq 0.01$) in all stages of renal failure compared with the control (except for the first stage), in which no significant difference was observed compared

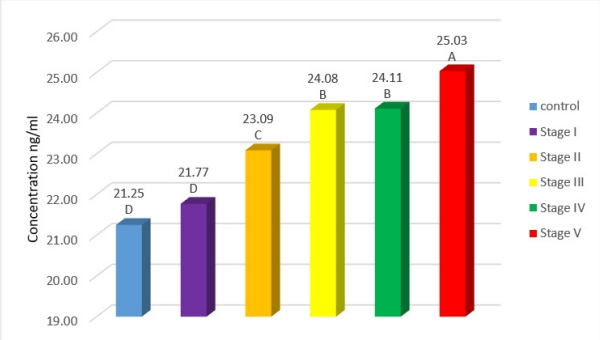

Figure 2. Serum hepcidin concentrations in patients and healthy groups.

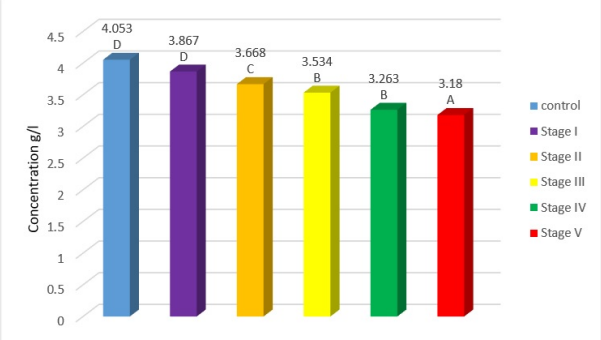

Figure 3. Albumin concentrations in the study groups.

with the control group, as it reached the rate of hepcidin in the first stage (21.77±0.76 ng ml^{-1}) and in the second stage (23.09±0.45 ng ml^{-1}) and in the third stage (24.08±0.22 ng ml^{-1}) and in the fourth stage (24.11±0.94 ng ml^{-1}) up to the fifth stage when it reached (25.03±0.6 ng ml^{-1}) compared to the control group, which amounted to (21.25 ± 0.69 ng ml^{-1}).

In the current study, the concentrations of the hepcidin hormone in patients with renal failure in all its stages (except for the first stage) were significantly higher than in healthy subjects. College [15]. Hepsidin concentrations were evaluated in patients undergoing periodic dialysis, and they found a significant increase in the rate of this hormone compared to healthy subjects [16]. The main reason for the high concentrations of hepcidin may be due to the fact that all groups included in the research are patients who suffer from chronic kidney diseases limited to acute to chronic renal failure, which requires frequent blood dialysis, which leads to a rise in the concentration of this hormone as a result of weakness It is secreted from the glomeruli and tubules of the kidneys, which in turn leads to its accumulation in the liver and bloodstream, which leads to damages represented in anemia and the lack of iron availability for the blood production process, which accompanies patients with kidney failure in particular [17][18], [19], [20] and [21]. The action of this hormone is involved in the regulation of iron concentrations in the blood plasma, and its rise leads to an imbalance in the amount of iron in the blood, as well as inhibiting the absorption of iron ions in the small intestine, especially in the duodenum, which leads to a decrease in iron concentrations in the medium term and thus a decrease in ferritin stores [22]. The concentration of this hormone stimulates its expression in several pathological conditions, including general infections, an increase in the concentration of iron in the body, and its inhibition may be associated with many cases, including hypoxia, and in cases of acute anemia resulting from iron deficiency [23].

3.3 Albumin Concentration:

The results of the current study show that there are significant differences ($p \leq 0.01$) in albumin concentrations between the groups of patients with kidney failure compared with the healthy group, as the mean albumin concentration in patients was in the following sequence: the first stage (3.867±0.09 g L^{-1}) in the second stage, (3.668±0.19 g L^{-1}), (3.534±0.14 g L^{-1}) in the third stage, (3.263 ± 0.11 g L^{-1}) in the fourth stage, (3.18±0.17 g L^{-1}) in the fifth stage, while it was (4.053±0.12g L^{-1}) in healthy subjects, as in Figure 3.

The results of the current study were in agreement with the results of another study conducted on patients with renal failure, and it proved a decrease in albumin concentration in CKD patients compared to the healthy group. The results of another study also showed that low concentrations of albumin in the serum were independently associated with a decline in kidney function in the elderly, whose ages ranged between 70 and 79 years, Also, the concentration of albumin in the blood was significantly associated with renal function and proteinuria [24]. The albumin in the blood is significantly associated with the deterioration of the renal glomeruli compared to the healthy group and the increased risk of progression to the last stages of chronic kidney disease, as well as the low concentration of albumin in the blood was associated with an increased probability of rapid deterioration in kidney function and an increased risk of chronic and acute kidney disease [23].

4. Conclusions:

Based on the results of the current study, both erythropoietin and hepcidin can be used as indicators of renal failure. Also, albumin is one of the most important criteria for detecting kidney function.

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Data Availability Statement: All of the data supporting the findings of the presented study are available from corresponding author on request.

Declarations:

Conflict of interest: The authors declare that they have no conflict of interest.

Ethical approval: The manuscript has not been published or submitted to another journal, nor is it under review.

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تقييم دور الارثروبيوتين، الهبسدين، الالبومين، لدى المصابين بالعجز الكلوي المزمن في كركوك لعراق.

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الخلاصة

يعد ضعف وظائف الكليتين من الامراض المنتشرة بين الناس وبكثرة وعلى صعيد عالمي. ويمكن ان تصنف هذه الامراض الى خمسة مراحل والتي تتضمن انخفاض في مستويات الترشيح الكلوي للدم وبمعدل يقل عن 60 مل هدفت الدراسة الحالية الى تقدير تراكيز هرمونات الأرثروبيوتين والهبسدين وتركيز بروتين الألبومين، تضمنت الدراسة (75) مريضا من كلا الجنسين وبأعمار من (70 – 40) مريضا يعانون من ضعف في وظائف الكلى بمختلف المراحل والتي تم تصنيفها الى خمسة مراحل وبواقع (15) عينة من كل مرحلة من مراحل عجز الكلى. اضافة الى (15) من اشخاص اصحاء لا يعانون من اية امراض كمجموعة سيطرة . واظهرت النتائج أنخفاضا معنويا (p \leq 0.01) في تركيز الأرثروبيوتين لدى المصابين بالعجز الكلوي المزمن مقارنة مع مجموعة السيطرة، أذ بدأ تركيز الأرثروبيوتين ينخفض تدريجيا خلال مراحل العجز الكلوي بسبب تراجع وظائف الكلى في المرضى الذين يعانون من العجز الكلوي المزمن نتيجة انخفاض الترشيح والافراز لهذا الهرمون . وأظهرت النتائج أرتفاعا معنويا (p \leq 0.01) في تركيز الهبسدين لدى المرضى المصابين بالعجز الكلوي المزمن ماعدا المرحلة الاولى التي لم يلاحظ فيها فرق معنوي عند المقارنة مع مجموعة السيطرة، أخيرًا، أظهرت النتائج أيضًا انخفاضًا معنويًا في مستويات الألبومين لدى مرضى الفشل الكلوي مقارنة بمجموعة التحكم. بناءً على نتائج الدراسة الحالية ، يمكن استخدام كل من إرثروبويتين وهيبسيدين كمؤشرات للفشل الكلوي. كما يعتبر الألبومين من أهم معايير الكشف عن وظائف الكلى.

الكلمات الدالة : الارثروبيوتين؛ الهبسدين؛ مرض الفشل الكلوي المزمن

التمويل: لايوجد.

بيان توفر البيانات: جميع البيانات الداعمة لنتائج الدراسة المقدمة يمكن طلبها من المؤلف المسؤول.

اقرارات:

تضارب المصالح: يقر المؤلفون أنه ليس لديهم تضارب في المصالح.

الموافقة الأخلاقية: لم يتم نشر المخطوطة أو تقديمها لمجلة أخرى، كما أنها ليست قيد المراجعة.