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Estimation of Endothelin-1 and Vitamin D Levels in Patients with Some Renal disease

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ABSTRACT

Chronic renal disease is a worldwide public health problem with an increasing incidence, prevalence, poor outcomes, and high cost. A cross-sectional study was carried out in balad city from 10th of November 2018 to 15th of March 2019. The number of patients under study were 60 patients with renal disease (30 acute renal disease and 30 chronic renal disease under hemodialysis). Their ages were between (20-75) years. Patients with acute renal disease were admitted to Balad general hospital and patients with chronic renal disease who admitted to Salahaddin general hospital for hemodialysis. The study included 30 apparently healthy subject as control group. The results showed that the highest mean level of endothelin-1 was found in patients with chronic renal disease (13.15 ± 7.81) pg/ml followed by patients with acute renal disease (1.78 ± 1.49) pg/ml compared with the control group (0.41 ± 0.31) pg/ml. These result were significant higher ($P < 0.01$). The results showed that the lowest mean level of vitamin D was found in patients with chronic renal disease (14.45 ± 5.92) ng/ml followed by patients with acute renal disease (23.49 ± 13.14) ng/ml compared with the control group (24.02 ± 8.22) ng/ml. The results were significant higher than control ($P \leq 0.01$). The study showed that patients with acute renal disease were distributed equally to male and female (1:1) while 56.67% of patients with chronic renal disease were males. The conclude from this study that the endothelin elevated in chronic renal disease patients and vitamin D was reduced.

Introduction

Unlimited renal disease is a worldwide public health problem with an increasing incidence and prevalence, poor outcomes, and high cost. Outcomes of chronic renal disease include not only kidney failure but also complications of decreased kidney function and cardiovascular disease[1]. Current evidence suggests that some of these adverse outcomes can be prevented or delayed by early detection and treatment [2,3]. The major outcomes of chronic renal disease, regardless of cause, include progression to kidney failure, complications of decreased kidney function, and cardiovascular disease (CVD). strikingly the unlimited renal disease is underdiagnosed and undertreated, resulting the opinion for uniform application of simple tests for detection and evaluation [1].

Over the last decade, a pivotal role for the Endothelin-1 system has been documented in normal

renal function, as well as in renal disease. In the kidney, Endothelin-1 acts in an autocrine and paracrine manner in renal vessels and nephron segments, modulating renal hemodynamics and tubular water and sodium reabsorption, respectively [4]. Therefore, Endothelin-1 is a key factor contributing to the extracellular volume and blood pressure homeostasis. Alterations of the Endothelin-1 system have been documented in renal diseases in which cardiovascular illness including hypertension and endothelial dysfunction coexist [5]. Individuals obtain vitamin D either through consuming vitamin D-rich foods (oily fish, dairy products) or supplements, or through the skin's exposure to ultraviolet B radiation producing vitamin D [6]. Under physiological conditions, $1,25(\text{OH})_2\text{-VD}$ is mainly metabolized in the kidneys but in abnormal conditions, such as pregnancy, chronic kidney failure,

rheumatoid arthritis and granulomatous diseases, other cell types can also contribute to its circulating levels. Moreover, there is an increasing body of evidence about the pivotal role of extra-renal 1α -hydroxylation for autocrine and paracrine effect [7,8]. The study aimed at estimation of Endothelin-1 and vitamin D in sera of in patients with renal failure and normal healthy control.

Materials and Methods

A cross sectional study was carried out in balad city for the period between the 10th of November 2018 to 15th of March 2019. The number of patients under study were 60 patients with renal disease (30 acute renal disease and 30 chronic renal disease under hemodialysis). Their ages were between (20-75) years. Patients with acute renal disease were admitted to Balad general hospital and patients with chronic renal disease who admitted to Salahaddin general hospital for hemodialysis. The study included 30 apparently healthy subject as control group, whose age were between (15-70) years.

Methods Five ml of blood sample was taken by vein puncture from each subject enrolled in this study. Blood samples were centrifuged, the serum were separated and keep for estimation of human endothelin-1 by ELISA and vitamin D by immunofluorescence assay.

Statistical analysis

Computerized statistically analysis was performed using Minitab ver. 18 statistic program. Comparison was carried out using T-Test for determination of probability (P) value. The P value < 0.05 was considered statistically significant and P value greater than 0.05 considered non-significant statistically.

Results

The results showed that the highest mean level of Endothelin-1 was found in patients with chronic renal disease (13.15±7.81) pg/ml followed by patients with acute renal disease (1.78±1.49) pg/ml compared with the control group (0.41±0.31) pg/ml. These results were significant higher than control ($P < 0.01$), as shown in Table 1.

The results showed that the lowest mean level of vitamin D was found in patients with chronic renal disease (14.45±5.92) ng/ml followed by patients with acute renal disease (23.49±13.14) ng/ml compared with as show in the control group (24.02 ±8.22) ng/ml. The result were significant higher than control ($P < 0.001$), Table 1.

Table (1): Level of Endothelin-1 and Vitamin D in patients with renal disease and the control group.

Biochemical parameters	Healthy control Mean±SD NO=30	Patients with renal disease		P. value
		Acute mean±SD NO=30	Chronic mean±SD NO=30	
Endothelin-1 Level (pg/ml)	0.41±0.31	1.78±1.49*	13.15±7.81*	0.0048
Vitamin D Level (ng/ml)	24.02±8.22	23.49±13.14*	14.45±5.92*	0.0002

*Significant different between control at ($p \leq 0.001$)

The study showed that patients with acute renal disease were distributed equally to male and female (1:1) while 56.67% of patients with chronic renal disease were males, as show in Figure 1.

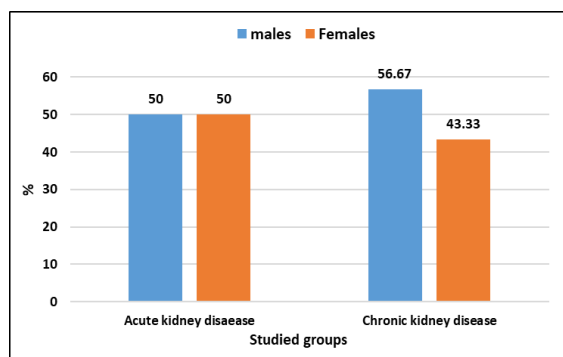


Fig. 1: Distribution of patients in the study according to sex

Discussion

The result of the current study was in consistence with Larivière, *et al* [9] study, who showed that, plasma Endothelin-1 concentrations are markedly increased in patients with end-stage renal disease undergoing dialysis as compared with healthy individuals. Rebholz, *et al* [10] also found that Endothelin-1 was more likely to be elevated in hemodialysis patients. Shah, [11] indicated that Endothelin-1 was activated in several diseases, including renal failure and arterial hypertension. Additionally, El-Shafey, *et al* [12] found that level of Endothelin-1 was significantly higher in dialysis patients compared to the controls ($P < 0.001$). Dhaun, *et al* [13] demonstrated that Endothelin-1 level was significantly correlated with the progression of Chronic renal disease and the highest level was found in end stage hemodialysis patients and the minimum level was among healthy control. These increases in ET-1 in chronic renal disease patients are likely due in part to reduced renal clearance from the circulation and/or to increases in synthesis [14]. There is also strong evidence that the activation of the endothelin system directly promotes renal fibrosis, as rats with transgenic overexpression of endothelin-1 develop severe glomerulosclerosis and interstitial fibrosis [15]. Cell culture studies have further shown that exposure to protein overload, as a general model of proteinuric

nephropathies, and exposure to shigatoxin, as a model for the haemolytic uraemic syndrome, both upregulate Endothelin-1 expression in cultured podocytes [16]. The release of Endothelin-1 then results in further deterioration of podocyte structure and function by an autocrine mechanism [15]. In agreement with our findings, in Firth, *et al* [17] study, plasma levels of endothelin-1 and/or renal expression of endothelin-1 have been reported to be elevated acute renal disease. Endothelin-1 may play a role in the development of acute renal failure, which most commonly arises due to renal vasoconstriction and subsequent ischemic necrosis of renal tubules [18].

Over the years, studies have improved the understanding of the biological and clinical consequences of the interaction between disordered vitamin D metabolism and chronic renal disease. Vitamin D deficiency are now becoming a global epidemic problem in patients with chronic renal disease [19]. Several observational studies have demonstrated an important link between vitamin D deficiency, impaired glomerular filtration rate (GFR), and increased mortality in patients with chronic renal disease [20,21]. Moreover, Lundwall, *et al* [22] found that activated vitamin D treatment reduces all-cause and cardiovascular mortality rates in patients with chronic renal disease and those undergoing hemodialysis. The critical role of the vitamin D endocrine system in disease prevention extends beyond the classic regulation of calcium and phosphorous homeostasis and skeletal integrity, to its potentially pleiotropic effects on extra-mineral metabolism, including kidney function [6].

High prevalence of vitamin D deficiency or insufficiency in patients with Chronic renal disease has been well documented in recent epidemiological studies [23,24]. In a previous study, a serum 1,25(OH)₂D decline was observed during early stages of chronic renal disease, comparing with healthy control [25]. Interestingly, a retrospective study showed that serum 25(OH)D is an independent inverse predictor of renal disease patients with earlier stages of Chronic renal disease [26]. These clinical

data suggest that the association between vitamin D and renal disease.

Patients with chronic renal disease, especially on hemodialysis, are likely to have less sunlight exposure [6]. Valle, *et al* [27] showed that 84% of the hemodialysis patients with vitamin D deficiency had inadequate sunlight exposure. Uremia may also decrease the response of plasma vitamin D to ultraviolet B irradiation [28]. Chronic hemodialysis patients exhibited a lower vitamin D response than normal individuals when exposed to a physiologically equivalent dose of ultraviolet B [29].

Nutritional factors may also contribute to suboptimal 25(OH)-vitamin D status in Chronic renal disease. Patients with Chronic renal disease frequently have low food intake due to numerous reasons such as reduced appetite, uremic-related gastrointestinal symptoms and dietary restrictions, i.e., low protein (especially in those on preservation is the board) and low phosphate diets [25,30].

Because differences in men's and women's physiology have widely been recognized, researchers are encouraged to evaluate clinical study data by sex [7,8]. Important sex-specific distinctions have been recognized in several of the most prevalent medical conditions, such as obesity, type 2 diabetes mellitus, cardiovascular disease, and depression [31]. Many of these conditions coexist with, or may have contributed to, chronic renal disease [32]. Chronic renal disease in itself raises numerous gender questions, for example, regarding sex-dependent prevalence and disease awareness [33]. Sex-specific differences in the characteristics, treatment, and outcomes for individuals on renal replacement therapy have, however, only once previously been the primary theme in an international study, and with focus on mortality patterns at the start of dialysis [7,8].

Conclusions

It was concluded from our result that endothelin elevated in chronic renal disease patients and vitamin D was reduced.

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تقدير مستويات الاندوثيلين-1 وفيتامين-د في المرضى الذين يعانون من بعض أمراض الكلى

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الملخص

مرض الكلى المزمن هو مشكلة صحية عامة في جميع أنحاء العالم مع زيادة معدل الإصابة، والانتشار، ونتائج سيئة، وارتفاع تكلفة. أجريت هذه الدراسة في مدينة بلد في الفترة من 10 نوفمبر 2018 إلى 15 مارس 2019. وكان عدد المرضى قيد الدراسة 60 مريضاً يعانون من مرض كلوي (30 مريضاً يعانون من مرض كلوي حاد و30 مريضاً يعانون من مرض كلوي مزمن يخضعون إلى غسيل الكلى). تتراوح أعمارهم بين (20-75) سنة. تم إدخال المرضى الذين يعانون من مرض كلوي حاد في مستشفى بلد العام والمرضى الذين يعانون من مرض كلوي مزمن الذين دخلوا مستشفى صلاح الدين العام لغسيل الكلى في وحدة الكلية الصناعية. وشملت الدراسة أيضاً 30 من الأشخاص الأصحاء كمجموعة سيطرة. أظهرت النتائج أن أعلى متوسط لمستوى الإندوثيلين-1 تم العثور عليه في المرضى الذين يعانون من مرض كلوي مزمن $(13.15 \pm 7.81) \text{pg/ml}$ يليه المرضى الذين يعانون من مرض كلوي حاد $(1.78 \pm 1.49) \text{pg/ml}$ مقارنة مع مجموعة السيطرة $(0.41 \pm 0.31) \text{pg/ml}$ وكانت هذه النتائج تشير إلى ارتفاع معنوي عند مستوى احتمالية ($P < 0.01$). كما وأظهرت هذه النتائج إلى أن أدنى مستوى لفيتامين (D) وجد في المرضى الذين يعانون من مرض كلوي مزمن $(14.45 \pm 5.92) \text{ng/ml}$ يليه المرضى الذين يعانون من مرض كلوي حاد $(23.49 \pm 13.14) \text{ng/ml}$ مقارنة مع مجموعة السيطرة $(24.02 \pm 8.22) \text{ng/ml}$ وكانت هذه النتائج تشير إلى ارتفاع معنوي أعلى بكثير من مجموعة السيطرة وعند مستوى احتمالية ($P \leq 0.01$). وأظهرت هذه الدراسة أن المرضى الذين يعانون من مرض كلوي حاد تم توزيعهم بالتساوي على الذكور والإناث (1:1) في حين أن 56,67% من المرضى الذين يعانون من مرض كلوي مزمن كانوا من الذكور. خلاصة هذه الدراسة تشير إلى ارتفاع مستويات الإندوثيلين-1 في مرضى الكلى المزمن وانخفاض فيتامين (D)