Correlation with renin-angiotensin-aldosterone and glomerular filtration rate in chronic renal failure patients

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Abstract

**Background:** One of the more significant hormonal systems, the renin-angiotensin-aldosterone system, controls the kidney function, adrenal gland through its effect on the balance of sodium and potassium, blood pressure, fluid volume, and also manages the functions of cardiovascular.

**Objective:** To clarify the interrelationship between renal dysfunction and renin-angiotensin-aldosterone system.

**Patients and Methods:** One hundred samples were collected from December 1, 2022, to February 18, 2023, from Al Shams Medical Laboratories (56 male, and 44) female, age range (of 45-60 years), all of them were volunteers suffering from chronic renal failure in the third stage the average glomerular filtration rate was 35.70 ± 0.37 125 mL/min/1.73m\(^2\). and under conservative treatment. Kidney function test, active renin, angiotensin II, and aldosterone were assessed in the serum of all subjects. The p - value of differences less than 0.05 is measured significant, and uses the statistical package for the social sciences (23) software to calculate the correlation coefficient between various parameters.

**Results:** The result shows relationship between the changes in GFR with creatinine, urea and active renin, the mean GFR showed significant negative correlated with mean creatinine (R = -0.76, p < 0.01). As well as the mean GFR with mean urea (R = -0.64, p < 0.01). The mean GFR also showed significant negative correlated with mean active renin in (R = -0.41, p < 0.01). Also, the mean serum active renin level was significantly positive correlated with mean aldosterone (R =0.33, p < 0.05).

**Conclusion:** Renin enzyme is inversely related to renal dysfunction, so when the glomerular filtration rate decrease, the higher the renin increased, and as a result, the increase in blood pressure in chronic renal failure patients.

**Keywords:** Renin, angiotensin II and renal dysfunction
Introduction

Chronic renal disease is a life-threatening condition often associated with kidney dysfunction, progression to kidney fibrosis, and hypertension, eventual chronic renal failure [1,2]. One of the more significant hormonal systems, the renin-angiotensin-aldosterone system (RAAS), controls the renal function, adrenal gland through its effect on the balance of sodium and potassium, blood pressure, fluid volume, and also manages the functions of cardiovascular [3]. The classical RAAS was found out further a century ago. In 1934 Goldblatt et al. found a link between renal function and renin and blood pressure. Angiotensinogen, which is formed in the liver and cleaved by renin released from kidney juxtaglomerular cells, is typically represented by the RAAS as an endocrine system [4]. Through this pathway, angiotensin I is formed, which, in turn, is more cleaved by angiotensin converting enzyme activity of the lungs into the active form of ANG II, then ANG II bind to with cortex of adrenal gland in specific receptors causing in release of aldosterone. In this way, the main function of the RAAS is keeping of blood pressure through ANG II encouraged vasoconstriction and aldosterone interceded sodium retention in the collecting duct [5]. The RAAS is a recognized manager of blood pressure and determinant of target-organ destruction. It regulates electrolyte balance and fluid via coordinated effects on the renal, heart and blood vessels. ANGII is the primary effector of the RAAS and uses its vasoconstrictor effect mainly on the postglomerular arterioles, thereby raising the hydraulic pressure of glomerular and the ultrafiltration of plasma proteins, effects that might contribute to development of chronic kidney failure, this explanation is showing that the role of RAAS in the progress of chronic kidney disease (CKD) [6]. Since when a defect occurs in the kidney function, renin is affected, and as a result, blood pressure is affected, objective of this study to clarify the interrelationship between renal dysfunction and renin-angiotensin-aldosterone system.

Patients and Methods

One hundred samples were collected from December 1, 2022, to February 18, 2023, from Al Shams Medical Laboratories (56 male, and 44) female, age range (of 45-60 years), all of them were volunteers suffering from chronic renal failure in the third stage the average glomerular filtration rate was $35.70 \pm 0.37 \, \text{125 mL/min/1.73m}^2$. and under conservative treatment.

A venous blood sample of 2.5 ml was taken from each patient involved in the study, and added into a gel tube used to estimate creatinine, urea, active renin, angiotensin II, and aldosterone, after centrifuging the blood samples at 2500g for 15 minutes, the serum was extracted.

A commercial ELISA Micro wells kit is used to measure the levels of active renin, angiotensin II, and aldosterone, after centrifuging the blood samples at 2500g for 15 minutes, the serum was extracted.

The automated quantitative COBAS INTEGRA 400 plus device (from Roche, Germany) was used to assay creatinine, and urea, in the serum of all sample, while GFR is estimated by using the equation eGFR-EPI. A commercial ELISA Micro wells kit is used to measure the levels of active renin, angiotensin II, and aldosterone in the serum of all patients.

Statistical Analysis

The $p$ - value of differences less than 0.05 is measured significant, and uses the
statistical package for the social sciences (23) software to calculate the correlation coefficient between various parameters.

**Results**

The result shows relationship between the changes in GFR with creatinine, urea and active renin, the mean GFR is significantly negative correlated with mean creatinine (R = -0.76, p < 0.01 Figure (1). As well as the mean GFR was significantly negative correlated with mean urea (R = -0.64, p < 0.01), Figure (2). The mean GFR also showed significant negative correlated with mean active renin in (R = -0.41, p < 0.01), Figure (3), Table (1).

**Table (1): Result of correlation coefficients between GFR with creatinine, urea, and active renin**

<table>
<thead>
<tr>
<th>Correlation coefficients</th>
<th>Creatinine</th>
<th>Urea</th>
<th>Active renin</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR</td>
<td>-0.76 **</td>
<td>-0.64 **</td>
<td>-0.41 **</td>
</tr>
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</table>

P-Value <0.05 significant

**Figure (1): Relation between GFR and creatinine in chronic renal failure**
Table (2) showed correlation among the changes in active renin concentration, ANGII, and aldosterone. While the mean active renin concentration showed non-correlated with mean ANGII, \( R = 0.19, p > 0.05 \), but the mean serum active renin Concentration was significantly positive correlated with mean aldosterone \( R = 0.34, p < 0.05 \), Figure (4).
Discussion

The RAAS is the best-known regulator of blood pressure (BP) and determinant of target-organ damage from hypertension. It also controls fluid and electrolyte balance through coordinated effects on the heart, blood vessels, and kidneys [7]. In this study, GFR showed significantly negative correlated with creatinine, increased levels of creatinine indicator a lower glomerular filtration rate, which reduces the kidneys' capacity to eliminate waste [8]. And also, GFR showed significantly negative correlated with urea, this is carried by a decrease in GFR in CRF patients. Plasma levels of creatinine and urea rise as the GFR decreases because these substances are removed by glomerular filtration and tubular secretion [9,10]. The previous study yielded an interesting finding that has not been analyzed in depth previously: an independent association between plasma aldosterone concentrations and renal filtration in hypertensive patients with "normal" renal function, such that the lower the renal filtration values, the higher the plasma aldosterone concentration [8].

The role of renin-angiotensin-aldosterone system in the progression of chronic kidney disease The renin-angiotensin-aldosterone system is a well-known regulator of blood pressure and determinant of target-organ damage. It controls fluid and electrolyte balance through coordinated effects on the heart, blood vessels, and kidneys. [11]. GFR showed significantly negative correlated with active renin. This maybe because reduced blood flow. That increased RAAS activity is also a main factor for numerous pathologic disorders because ANGII rises aldosterone.

<table>
<thead>
<tr>
<th>Correlation coefficients</th>
<th>Angiotensin II</th>
<th>Aldosterone</th>
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<tbody>
<tr>
<td>Active renin</td>
<td>0.18 NS</td>
<td>0.34 *</td>
</tr>
<tr>
<td>P-Value &lt;0.05 significant</td>
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</table>
level that led to increase blood pressure and contributes to the progress of end-organ injury via direct effects on heart, vascular, and kidney tissues [12]., so ANGII also decreases the glomerular filtration coefficient while rising resistances of afferent and efferent arteriolar, which contributes to the declines in GFR [13]. Juxtaglomerular epithelioid cells of afferent arterioles, which are the primary location of renin synthesis in the kidneys, result in reduced extracellular fluid and blood volume, lower arterial pressure, and increased sympathetic activity [14,15]. Active renin level was significantly positive correlated with mean aldosterone. That renin receptors are expressed in visceral and subcutaneous human adipose tissue [16]. Human adipocytes also have been found to produce aldosterone B [17].

Conclusions
Renin enzyme is inversely related to renal dysfunction, so when the glomerular filtration rate decrease, the higher the renin increased, and as a result, the increase in blood pressure in chronic renal failure patients.

Recommendations
The current study recommends that the levels of aldosterone be monitored periodically in patients with renal failure

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Ethical clearance: Ethical approval was obtained from the College of Medicine / University of Diyala ethical committee for this study.

Conflict of interest: Nil

References


الارتباط مع الرينين - أنجيوتنسين - الألدوسيرن و معدل الترشيح الكببي في مرضى الفشل الكلوي المزمن

فاطمة كاظم ابراهيم المهداوي1، مازن رزوق محمد2، مصطفى غني طاهر3، وسن عبد الوهاب الساعدي4، عمر القاضي 5، إيرينا بوتوروكو6، مروان شيمك7

الملخص

خلفية الدراسة: أحد أكثر الأنظمة الهرمونية أهمية، وهو نظام الرينين - أنجيوتنسين - الألدوسيرن، الذي يتحكم في وظائف الكلى والغدة الكظرية من خلال تأثيره على توازن الصوديوم والبوتاسيوم وضغط الدم وحجم السوائل، كما يتأثر على وظائف القلب والأوعية الدموية.

أهداف الدراسة: توضيح العلاقة المتبادلة بين وظائف الكلى ونظام الرينين - أنجيوتنسين - الألدوسيرن.

المرضى والطريقة: تم جمع مائة عينة من المتطوعين الذين يعانون من مرض الفشل الكلوي المزمن في المرحلة الثالثة من المرض للفترة من 1 ديسمبر 2022 حتى 18 فبراير 2023 من مختبرات الشمس الطبية (56 ذكور و44 أنثى)، تراجعت أعمارهم (45-60 سنة)، كان متوسط معدل الترشيح الكببي 35.37 ± 125 1.73 مل/ دقيقة/1.73 م. تحت العلاج المحافظ. تم تقييم اختبار وظائف الكلى والرينين النشط والأنجيوتنسين 2 والألدوسيرن في مصل جميع المرضى. تقدم قيمة الفروق الأقل من 0.05 معنوية، وتستخدم الحزمة الإحصائية لبرمجيات العلوم الاجتماعية (23) لحساب معامل p-value.

النتائج: أظهرت النتيجة علاقة بين التغييرات في معدل الترشيح الكببي مع الكرياتينين واليوريا والرينين النشط، حيث أظهر متوسط معدل الترشيح الكببي ارتباطاً سلبياً مع متوسط الكرياتينين (R = -0.76 %، p<0.01) وكذلك مع متوسط الألدوسيرن في اليماريا (R = -0.64 %، p<0.01). كما كان متوسط مستوى الرينين النشط في الدم مرتبطاً إيجابياً مع متوسط الألدوسيرن (R = -0.41 %، p<0.05).

الاستنتاجات: يرتبط إنزيم الرينين عكسيًا بالضعف بوظائف الكلى، لذلك عندما يخفض معدل الترشيح الكببي، يزداد ارتفاع الرينين، وتنتج عنه ارتفاع ضغط الدم لدى مرضى الفشل الكلوي المزمن.

الكلمات المفتاحية: الرينين، الأنجيوتنسين، الآفات والالدوستيرين - الألدوسيرن

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