Reports of Biochemistry & Molecular Biology
Vol.10, No.2, Jul 2021

Original article

www.RBMB.net

Evaluation of Serum Cyclooxygenase, Hepcidin Levels in Acute Renal Injury (AKI) Patients Following Cardiac Catheterization

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Abstract

Background: Acute kidney damage is a severe condition common in patients who have undergone heart surgery (catheterization) and secondary injury is also referred to as being synonymous with surgery. The goal of this research is to determine the rate of cyclooxygenase and hepcidin levels in patients with acute renal injury (AKI) following cardiac catheterization.

Methods: The study is performed on (81) patients (64 males and 17 females) aged 40-75 years. Data from most patients are reported in the form of age, gender, and smoking background questionnaire.

Results: The results indicate a significant increase in serum levels of cyclooxygenase and hepcidin levels in patients with severe renal insufficiency after cardiac catheterization by (79%) males versus (21%) females.

Conclusions: In this study, improved risk prediction could enhance patient monitoring and treatment after surgery, direct patient treatment and decision making, and enhance participation in AKI interventional trials.

Keywords: AKI, Cardiac surgery, Chronic kidney disease, Cyclooxygenase, Hepcidin.

Introduction

Chronic kidney disease (CKD) is one of the most prevalent disorders of people in the world. The relative rise in the number of cases is due to old age and related conditions such as diabetes and high blood pressure (1). Recently, CKD cases have been reported to have risen by 10-15% worldwide (2). Statistics in the United States (US) show that more than 10% of the adult population has CKD. The number of cases of chronic kidney disease in Asian countries ranges from 13 to 17.5 % (3). One of the most important risk factors, such as cardiovascular disease, which is associated with other chronic diseases, is a common factor in patients with chronic renal inflammation. The risk drivers of CKD can be classified into three major categories: chronic, behavioral, and biomedical. The fixed group includes family history, age of the patient, prior cases of kidney failure, low birth weight, and gender of the patient (4).

Behavioral risk factors consist of the patient's daily activities, alcohol, and unhealthful food consumption (5). It is worth noting that smoking raises the accumulation of urinary albumin. In a sample of 40,619 people aged 28 to 75 years, concentrations of albumin increased below the level of micro-albuminuria (6). Even in non-diabetic and hypertensive people, smoking obesity has been independently linked with micro-albuminuria (7). A cross-sectional analysis in 7,476 people without diabetes found that the amount of urinary albumin excretion is related to the number of cigarettes smoking, the lethargy, and the malnutrition (8). The biomedical section covers people with diabetes, elevated blood pressure,

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Received: 9 Jan, 2021; Accepted: 8 Feb, 2021

[DOI: 10.52547/rbmb.10.2.197]

cardiovascular disease, chronic renal inflammation, overweight, and obesity (9). In addition to risk factors, the most important of which are renal artery disorder, diabetic renal dysfunction, glomerulonephritis and inherited renal disease are common triggers, chronic kidney disorder (10). Surgery is one of the major causes of acute kidney injury, the most important of which is cardiac surgery, and its risks, such as inflammation and elevated toxicity to the kidneys as they interact with each other and inflict acute kidney injury (11).

One of the most important reasons not to detect chronic kidney disease early is that it has no signs and is known as a silent disease, as it is detected after a patient loses about 90% of kidney function and symptoms begin to emerge.

Among the major signs associated with chronic kidney disease are elevated blood pressure, changes in urine (decreased or increased urinary frequency during the night), peripheral oedema, kidney discomfort, weakness, loss of appetite, difficulty sleeping, fever, lack of focus, itching and restlessness Respiration, nausea, and diabetes-like symptoms of loss of appetite.

Acute renal injury (AKI) is a complex condition that arises in a number of clinical conditions. Its signs include a mild rise in creatinine in the blood and gradual renal failure. Acute renal injury (AKI) is an expression of the full spectrum of renal disease, in addition to acute renal failure (ARF), the primary symptom of which is a drastic decline in renal function within 48 hours.

Renal dysfunction is followed by a substantial rise in serum creatinine either> 0.3 mg/dL or > 50% from baseline or a drop in urinary volume < 0.5 ml/kg/hour for > 6 hours (12). One of the most common issues is the failure to clinically identify patients with renal insufficiency because long-term effects are dangerous and occur immediately (13). The number of cases and deaths in intensive care units due to AKI grows from 5% to 30% relative to other diseases. Despite technical advances in clinical treatment, acute nephritis-related deaths remain high as the practitioner can only give preventive care such as hemodialysis due to elevated amounts of creatine in the blood (14). In general, several studies have found that CI-AKI and possibly AKI have declined in patients who have undergone heart surgery over the past 10 years, with the exception of those who had postoperative coronary angiography and tested positive for AKI that required dialysis (AKI-D) (15).

Many biomarkers are helpful in the detection of acute renal dysfunction at different stages of the condition, from the onset of symptoms to the progression of symptoms such as serum creatine and urea concentration (16). However, this method is deemed inadequate to detect diagnose the diseases, complex aspects of AKI.

Creatine and urea analyses are a critical marker for the detection of diseases as well as for clinical assessment. However, this criterion is resistant to extreme changes in renal activity and can differ depending on several factors, such as age, gender, and diet. In cases of intact kidneys, an increase in this criterion could be due to renal ischemia. This criterion is often assumed to be insufficient because, in most clinical cases, its meaning is unclear, which makes it impossible to diagnose.

New diagnostic strategies, for example, renal biomarkers and enzymes, can be useful for early diagnoses such as Interleukin 6 (IL-6) (17), hepcidin and Cyclooxygenase (18). Several laboratory studies have shown that hepcidin has distinct and overlapping roles; the effects of hepcidin can cause systemic iron deficiency, reduced availability of iron for erythropoiesis, and resistance to endogenous and exogenous erythropoietin. Along with impaired kidney production of erythropoietin, hepcidin-mediated iron restriction contributes to anemia of chronic kidney (19).

The second marker is Cyclooxygenase include TxA2 and PGI2, synthesized by COX-1 and COX-2 respectively, two forms of cyclooxygenase have at least 60% of homology.

This enzyme is responsible for physiological functions in the body, is mainly expressed and especially the kidneys as a

[DOI: 10.52547/rbmb.10.2.197]

structural isoform. The function of the enzyme is to work on the flow of blood into the blood vessels through the production of prostaglandins responsible for lowering the resistance of blood vessels and ensuring adequate blood supply (20).

According to the above survey, a lot of studies employed different types of tests such as blood tests reveal the percentage of waste products, such as creatinine and urea. But there are few studies using the rate of Cyclooxygenase, hepcidin to diagnose AKI. Therefore, the study aimed at following up the condition of patients before and after undergoing heart surgery, not relying on traditional methods of following up the "kidney function" and measuring the level of Creatine in the blood.

Materials and Methods

This study is conducted on (81) patients (64 males and 17 females) whose ages ranged between (40-75) years, mean (58.56) years, and attended the Medical city hospital and Ibn Al-Bitar hospital and underwent cardiac catheterizations during the period from January to July 2020. The patients included in the study developed acute kidney injury (AKI) after catheterization. Data from all the patients are recorded in a questionnaire form regarding age, gender, and smoking history. The body mass index of patients is calculated from their height and weight. Laboratory investigations including estimation of serum cyclooxygenase and hepcidin are performed at private laboratories in Baghdad / Iraq. Venous blood samples are collected by means of disposable syringes from each patient before and after cardiac catheterization. Blood samples were collected in clean, dry tubes and leave it for (15 min), after which the coagulated part is separated from the clear solution using a centrifuge (Wincom company Ltd. China) at a speed (min/10000 g) for a period of (15) min. The laboratory investigations for (serum cyclooxygenase and Hepcidin) are immediately performed by ELISA technique using (Cloud-clone corp. USA) ELISA kit.

Statistical analysis

Statistical analysis was performed using SPSS Statistical Package for Social Sciences (version 20). Data are presented as mean±SD or number and percentage as applicable. Comparison between before and after catheterization procedure was done using Paired Student's t-test. Unpaired Student's t-test and ANOVA test were used to study the effect of gender, other complications, and smoking. P-value of <0.05 was considered as statistically significant.

Results

The results in Table (1) showed that the mean age of the patients with AKI was 58.56 years, while the mean BMI was 34.87 years. Gender distribution findings among AKI patients revealed that the number and percentage of males were 64 (79%) and the number and percentage of females were 17 (21%). As well as the number and percentage of cigarette smoker patients were 33 (40.7%) compared to non-smokers 31 (38.3%) and 17 (21%) had stopped smoking as seen in the graph (2). Table (3) indicates a significant increase in mean serum cyclooxygenase levels from (14.85) to (21.25) (p= 0.005) following cardiac catheterization. There was also a significant rise in mean serum Hepcidin levels (114.21) and was (47.94) (p= 0.005) among AKI patients after cardiac catheterization.

Table 1. Mean age and BMI of the studied patients.

	Mean	SD	Min.	Max.
Age	58.56	8.13	40.00	75.00
BMI	34.87	5.84	20.00	43.00

[DOI: 10.52547/rbmb.10.2.197]

Table 2. No. and percentage of gender and smoking status in the studied patients.

		No.	(%)
Gender	Male	64	79.0%
	Female	17	21.0%
Smoking	Smoker	33	40.7%
	None-smoker	31	38.3%
	Quit smoking	17	21.0%

Table 3. Mean Cyclooxygenase, Hepcidin levels before and after cardiac catheterization.

	Mean	SEM	Min.	Max.
PTGS2 before (ng/ml)	14.85	0.48676	8.21	25.38
PTGS2 after (ng/ml) p= 0.005*	21.25	0.57986	6.72	27.90
HEPCL before (ng/ml)	114.21	2.59173	74.18	211.32
HEPCL after (ng/ml) p= 0.005*	47.94	1.65161	23.08	96.44

Discussion

Two biomarkers cyclooxygenase, hepcidin were examined evaluated with associated acute kidney injury before and after cardiac surgery. The results revealed that the number and percentage of male patients were higher than females and obese, with an average BMI of 34.87. The results of our analysis also revealed a slight increase in the number and percentage of smokers. As shown in Table 1, depending on the age of patients with severe renal impairment, the mean age of the patients was (58.56) years, indicating that damage is roughly related to ageing. Ageing is associated with a decrease in renal function and an associated decrease in the estimated glomerular filtration rate, which reduces normal kidney function and increases the predisposition to severe renal impairment after surgery, and this is in agreement with (21,22).

As shown in Table 2, the results revealed the majority of male cases in patients with severe renal insufficiency. As stated in Table 1, the body mass index (BMI) is high in the infected persons who were examined, as it is considered an important evidence to predict many disease cases. The results for increased body mass index (BMI) in patients with significant renal impairment was well consistent with the previous literature.

Billings & Frederic et al. reported that the association between BMI and the incidence of acute renal injury in 445 patients undergoing cardiac surgery. In an analysis of conditions that help increase the occurrence of acute renal failure, the proportion of smokers was higher than non-smokers, as seen in the table (2). As smoking raises the accumulation of urinary albumin, even in a group with albumin concentrations below the threshold of microalbuminuria, this is consistent with the research involving 40619 people aged 28 to 75 years. It was noted that smoking was a significant influence on persons without diabetes or hypertension and was independently associated with albumin structure (24). According to a report (8) on 7,476 non-diabetic participants, the rate of excretion of urinary albumin is related to the number of cigarettes smoked.

Table 3 showed significant differences in the levels of cyclooxygenase and hepcidin between before and after cardiac catheterization. In the current study, there was a significant increase in cyclooxygenase

[DOI: 10.52547/rbmb.10.2.197]

enzyme levels between before and after cardiac catheterization in AKI patients. Cyclic oxidative enzymes (prostaglandins) in the kidneys are an important factor in vascular cohesion and the regulation of salt and water.

Cyclooxygenase (prostaglandin synthase G2/H2) is active in the mechanism of transforming arachidonic to prostaglandin (PG) G2 and then to PGH2, which is then metabolized by tissue-specific isomerize to PGs and thromboxane.

These findings are consistent with previous literature that inflammation (25), especially with an elevated PGE2 rate, is the cause of kidney damage. While PGE2 contributes to maintaining renal equilibrium in normal physiological conditions, it may be responsible in pathological cases or release of a damaging process. In multiple clinical contexts, this disparity in the PGE2 protocol is due to its binding to four receptors, EP1, EP2, EP3 and EP4 (26). The results indicate an increased concentration of hepcidin in the urine of patients with acute kidney inflammation following cardiac surgery. The increased concentration results in the isolation of iron inside the cells, which leads to renal perfusion as well as causing severe anemia due to decreased renal clearance and inflammatory state.

The findings suggest that the concentration of cyclooxygenase, hepcidin are increased in the serum of adults who have undergone heart surgery, and this is a sign of acute nephritis. Cyclooxygenase and hepcidin are good biomarkers of chronic kidney damage in acute-stage survivors after surgery.

The current study showed that the age of the patient plays a significant role in the preparation of AKI, particularly after cardiac surgery, as the rate of infection increased in adults aged 58 to 75 years.

Dietary and behavioral habits, such as smoking, are considered a contributing factor in raising the prevalence of infection, particularly for people who have kidney and urinary system issues in addition to respiratory disorders.

The Body Mass Index (BMI) is an additional cause for developing AKI due to associated complications with obesity and related disorders such as high blood pressure, diabetes, and diabetic nephropathy.

The findings of this analysis suggest that genetics and psychological and social influences could be the driving force behind the gender related variation found in patients with chronic kidney disease, where the proportion of adult males affected was 79% higher than females 21% 79% more than women and 21% of 81 samples of the patients who underwent the examination.

Acknowledgements

The authors would like to warmly thank the Medical city hospital and Ibn Al-Bitar hospital in Baghdad/Iraq.
The authors declare no conflicts of interest.

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