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Early diagnosis of acute kidney injury by measurement of Interleukin-6 (IL-6) and Hepcidin levels in patients following cardiac catheterization

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Abstract

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 serum urea, Interleukin-6 (IL-6) and Hepcidin levels in patients with acute renal injury (AKI) following cardiac catheterization. The study included 81 patients (64 males and 17 females) ranging in age from 40 to 75 years. Data from most patients is reported in the form of an age, gender and smoking background questionnaire. The results indicate a significant increase in serum urea, Interleukin-6 (IL-6) and Hepcidin levels in patients with severe renal insufficiency after cardiac catheterization in (79%) males versus (21%) females. According to the outcomes of this study, improved risk prediction could improve patient monitoring and treatment after surgery, as well as direct patient treatment and decision making. Also, the findings show that they enhance participation in AKI interventional trials.

Keywords: Serum Interleukin-6(IL-6), Hepcidin, AKI, Chronic kidney disease, Cardiac surgery

Introduction

Chronic kidney disease (CKD) is one of the most common diseases afflicting people worldwide. 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 sex of the patient[4]. Behavioral risk factors consist of the patient's daily activities, such as alcohol and unhealthful food[5]. It is worth noting that

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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 has been independently linked with micro albuminuria[7]. A cross-sectional analysis of 7,476 people without diabetes found that the amount of urinary albumin excretion is related to the amount of cigarette smoking, lethargy, and malnutrition[8]. The biomedical section covers people with diabetes, elevated blood pressure, 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 of 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 for not detecting 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 edema, 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 creatine in the blood and gradual renal failure. 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 characterized by a significant increase in serum creatine of > 0.3 mg/dL or > from baseline or a decrease in urinary volume of 0.5 ml/kg/hour[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 has grown 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 and diagnose these diseases and the complex aspects of AKI. Creatine and urea analyses are critical markers 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, and Hepcidin may be one of the biomarkers. 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 [17]. The second marker is an Interleukin-6 (IL-6) cytokine that is one of the key factors controlling the defense mechanisms of the body through multi-directional actions. IL-6 activity plays a significant role in its inclusion in the immune response, hematopoiesis, and inflammatory processes. This marker is thought to be one of the key proinflammatory human cytokines and is also active

in those processes, which may explain the rise in the serum level of this cytokine during chronic damage to the kidney and acute kidney[18].

According to the above survey, a lot of studies have employed different types of tests, such as blood tests that reveal the percentage of waste products in the blood, such as creatine and urea. But there are a few studies using the rate of Hepcidin and Interleukin-6 (IL-6) cytokines to diagnose AKI. As a result, the study's goal is to follow the condition of patients before and after heart surgery, rather than relying on traditional methods of monitoring "kidney function" and measuring the level of creatine in the blood.

Materials and Methods

This study was 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 is 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 IL-6 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 left for 15 min, after which the coagulated part was separated from the clear solution using a centrifuge (Win-com Company Ltd.China) at a speed (min / 10000 g) for a period of 15 min. The laboratory investigations for (serum IL-6 and Hepcidin) are immediately performed by the ELI-SA technique using a (Cloud clone corp. USA) ELISA kit.

Statistical analysis

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

Result

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 a result, as shown in table (2), the number and percentage of cigarette smokers patients were 33(40.7%) compared to non-smokers 31 (38.3%) and 17 (21%), respectively. Table (3) indicates a significant increase in mean serum Interleukin-6 (IL-6) levels from (22.08) to (71.21) (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.

Discussion

Before and after cardiac surgery, two biomarkers, Interleukin-6 (IL-6) and hepcidin, were examined and evaluated in relation to the issues associated with acute kidney injury. 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[19].As a result, improvement of renal function after acute renal injury in elderly individuals is at risk and "age" should be considered as a possible diagnostic rate after acute renal impairment. These findings are consistent with a study in a pediatric patient group that recorded a potential 3- to 5-year follow-up of 245 children with acute renal impairment treated at Texas Children's Hospital between January

1998 and June 2001[20]. As shown in Table 2, the results revealed the majority of male cases were in patients with severe renal insufficiency. This finding differs from other research that showed a greater risk of females developing renal dysfunction compared to males. The effects of gender distribution were inconsistent with our findings as males were more prominent in our sample, and this could be due to the presence of patients with rheumatoid arthritis as well as environmental and health factors in the study area.As shown in Table 1, the body mass index (BMI) is high in the infected people studied, as it is thought to be an important predictor of many disease cases. Forexamples, chronic obstructive pulmonary disease, chronic renal impairment and cancer have increased mortality in underweight patients [21]. The findings of increased body mass index (BMI) in patients with significant renal impairment were in line with previous research.

Woersching, J. (2019) Reported the association between BMI and the incidence of acute renal injury in 445 patients undergoing cardiac surgery. Also, the findings refer to how a higher BMI was separately associated with an increased risk of developing acute renal impairment, as well as that obesity was found as an independent risk factor for developing CKD. 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 micro albuminuria, this is consistent with the research involving 40619 people aged 28 to 75 years. It was noted that smoking was a significant influence on people without diabetes or hypertension and was independently associated with albumin structure[23] .According to a report performed by Pinto et. al. (8) on 7,476 non-diabetic participants, the rate of excretion of urinary albumin is related to the amount of cigarettes smoked. Table (3) shows significant differences in IL-6 levels before and after cardiac catheterization procedures. The inverse correlation of glomerular filtration rate (GFR) with circulating levels of pro-inflammatory markers, including IL-6, is additional evidence of a connection between IL-6 and kidney disease, as seen in Fig.1.

In patients with diffuse inflammatory marker levels such as IL-6, which were higher than those of healthy subjects.The GFR incidence was slightly lower; elevated serum interleukin (IL)-6, IL-8, IL-1β, and IL-10 levels were observed. Also, in patients with acute renal dysfunction of AKI, tumour necrosis factor alpha (TNF-alpha). The results indicate an increase 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.

Conclusion

1. The findings suggest that the concentration of Interleukin-6 (IL-6), hepcidin are increased in the serum of adults who have undergone heart surgery and this is a sign of acute nephritis. IL-6 and hepcidin are good biomarkers of chronic kidney damage in acute-stage survivors after surgery.
2. 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.
3. 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.
4. 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.
5. “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.

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