

# Evaluation of Serum IL-6 and FABP Levels in Acute Kidney Injury (AKI) Patients Following Cardiac Catheterization

Hind F. Aref<sup>1</sup>, Nazar A. Naji<sup>2</sup>, Hadaf D. Ibrahim<sup>3</sup>

<sup>1</sup>Researcher, <sup>2</sup>Professor, Department of Chemistry, College of Science, University of Tikrit, Salah Al Deen -34001, Iraq, <sup>3</sup>Professor, Department of Clinical Biochemistry, College of Medicine, University of Baghdad, Baghdad 10013, Iraq

## 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 interleukin-6 (IL-6) and fatty acid-related protein (FABP) in patients with acute renal injury (AKI) following cardiac catheterization. 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. The results indicate a significant increase in serum levels of IL-6 and FABP in patients with severe renal insufficiency after cardiac catheterization by (79%) males versus (21%) females. 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:** Serum IL-6, FABP protein, AKI, Chronic kidney disease, Cardiac surgery

## 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<sup>1</sup>. Recently, CKD cases have been reported to have risen by 10-15% worldwide<sup>2</sup>. 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 %<sup>3</sup>. 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<sup>4</sup>.

Behavioral risk factors consist of the patient's daily activities, such as alcohol and unhealthy food<sup>5</sup>. 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 microalbuminuria<sup>6</sup>.

Even in non-diabetic and hypertensive people, smoking has been independently linked with microalbuminuria<sup>7</sup>. A cross-sectional analysis in 7,476 people without diabetes found that the amount of urinary albumin excretion is related to the amount of cigarettes smoking, the lethargy, and the malnutrition<sup>8</sup>. The biomedical section covers people with diabetes, elevated blood pressure, cardiovascular disease, chronic renal inflammation, overweight and obesity<sup>2</sup>. 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<sup>9</sup>. 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

---

### Corresponding author:

**Hind Fawzi Aref**

Email: hindarif02@gmail.com

Mobile: 009647802649598

each other and inflict acute kidney injury<sup>10</sup>.

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. 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<sup>11</sup>. 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<sup>12</sup>. 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<sup>13</sup>. 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)<sup>14</sup>.

New diagnostic strategies (for example, renal biomarkers and enzymes) can be useful for early diagnoses, and liver fatty acid binding protein may be one of the biomarkers (L-FABP). Multiple laboratory studies have shown that individual FABPs have both distinct

and overlapping roles, some of which are dependent on basic protein structure elements<sup>15</sup>. Previous research on various forms of FABPs have shown that these proteins are associated with tissue damage, including myocardial injury and damage to other tissues, such as the liver, kidneys, intestines and lungs<sup>16</sup>.

The second marker is 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 pro-inflammatory 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<sup>17</sup>.

According to the above survey, a lot of studies employed different types of test such as blood tests reveal the percentage of waste products, such as creatinine and urea. But there are few studies using the rate of interleukin-6 (IL-6) and fatty acid-related protein (FABP) 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 IL-6, FABP 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 (15min),

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 IL-6 and FABP) 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  $\pm$  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 average age of patients with the failure renal disease was 58.56 years, while the average body mass index was 34.87, as seen in Table (1). The findings of the gender distribution among patients with acute renal injury showed that 64 (79%) were the number and percentage of males and 17 (21%) were the number and percentage of females, while 33 was the number and percentage of patients who smoked cigarettes. 31 (38.3 %), and 17 (21 %) of them gave up smoking (40.7 %) relative to non-smokers, as seen in Table (2). Table 3 displays the serum and urinary concentrations of IL-6 as a measure of AKI in the adult group following cardiac catheterization. Compared to stable individuals, a slightly higher concentration (71.21) ( $P = 0.005$ ) was observed in the serum and urine. In comparison to the control group, the FABP level was also higher in the serum and urine of the research group, roughly after cardiac catheterization (1.54) ( $p = 0.005$ ).

**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

**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 IL-6 and FABP levels before and after cardiac catheterization**

	Mean	SEM	Min.	Max.
IL-6 before (pg/ml)	22.08	3.67063	0.10	192.44
IL-6 after (pg/ml) P=0.005*	71.21	6.91036	23.44	521.53
FABP8 before (ng/ml)	0.43	0.06915	0.10	3.63
FABP8 after (ng/ml) P=0.005*	1.54	0.16138	0.42	12.05

### Discussion

Two biomarkers (IL-6) and fatty acid bound protein (FABP) were examined and 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 <sup>18</sup>.

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 <sup>19</sup> recorded a potential 3 to 5-year follow-up of 245 children with acute renal impairment who were treated at Texas Children’s Hospital between January 1998 and June 2001.

As shown in Table (2), the results revealed the majority of male cases 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. 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.

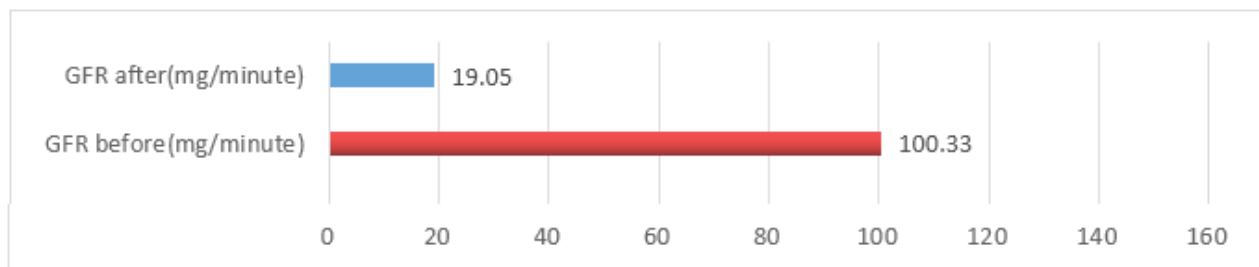
As stated in Table (1), the body mass index (BMI) is high in the infected persons who were examined, as it is considered an important evidence to predict many disease cases.

For example, chronic obstructive pulmonary disease, chronic renal impairment and cancer have increased mortality in underweight patients and these results are consistent with previous results by Guo et al. <sup>20</sup>. The results for increased body mass index (BMI) in patients with significant renal impairment were well consistent with the previous literature. Woerschling<sup>21</sup> reported the association between BMI and the incidence of acute renal injury in 445 patients undergoing cardiac surgery, and reported that a higher BMI was separately associated with an increased risk of developing acute renal impairment. 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 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 microalbuminuria<sup>22</sup>. According to a report performed by

Pinto et al.<sup>8</sup> on 7,476 non-diabetic participants, the rate of excretion of urinary albumin is related to the amount of cigarettes smoked.

Important variations in IL-6 and FABP levels before and after cardiac catheterization procedures were seen in the Table (3). 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.



**Figure 1: Differences between before and after catheterization values of the GFR**

In patients with diffuse inflammatory marker levels such as IL-6, which were higher than those of healthy subjects, the eGFR incidence was slightly lower; elevated serum interleukin (IL)-6, IL-8, IL-1 $\beta$ , and IL-10 levels were observed. And in patients with acute renal dysfunction of AKI, tumour necrosis factor alpha (TNF-alpha). FABP increased in a brief period of time from minutes to hours after renal damage, through the evidence collected from the study of patient serum, FABP is a significant biological marker for early detection of AKI. These results are in agreement with results of Ref.<sup>23</sup>.

### Conclusion

- 1- The findings suggest that the concentration of FABP and IL-6 is increased in the serum of adults who have undergone heart surgery and this is a sign of acute nephritis. L-FABP and IL-6 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 sex-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.

**Acknowledgement:** The authors would like to warmly thank the Medical city hospital and Ibn Al-Bitar hospital in Baghdad/Iraq

**Conflicts of Interest:** The authors declare no conflicts of interest.

**Ethical Clearance:** Taken from College of Science, University of Tikrit.

**Source of Funding:** Self.

### References

- Janssen WM, Hillege H, Pinto-Sietsma SJ, Bak AA, De Zeeuw D, de Jong PE. Low levels of urinary albumin excretion are associated with cardiovascular risk factors in the general population. *Clinical Chemistry and Laboratory Medicine (CCLM)*. 2000 Nov 12;38(11):1107-10.
- Levin A, Tonelli M, Bonventre J, Coresh J, Donner JA, Fogo AB, Fox CS, Gansevoort RT, Heerspink HJ, Jardine M, Kasiske B. Global kidney health 2017 and beyond: a roadmap for closing gaps in care, research, and policy. *The Lancet*. 2017 Oct 21;390(10105):1888-917.
- LI PK, Chow KM, Matsuo S, Yang CW, Jha V, Becker G, Chen N, Sharma SK, Chittinandana A, Chowdhury S, Harris DC. Asian chronic kidney disease best practice recommendations: positional statements for early detection of chronic kidney disease from Asian Forum for Chronic Kidney Disease Initiatives (AFCKDI). *Nephrology*. 2011 Sep;16(7):633-41.
- Tomson C, Bailey P. Management of chronic kidney disease. *Medicine*. 2011 Jul 1;39(7):407-13.
- Yacoub R, Habib H, Lahdo A, Al Ali R, Varjabedian L, Atalla G, Akl NK, Aldakheel S, Alahdab S, Albitar S. Association between smoking and chronic kidney disease: a case control study. *BMC public health*. 2010 Dec;10(1):1-6.
- Janssen WM, Hillege H, Pinto-Sietsma SJ, Bak AA, De Zeeuw D, de Jong PE. Low levels of urinary albumin excretion are associated with cardiovascular risk factors in the general population. *Clinical Chemistry and Laboratory Medicine (CCLM)*. 2000 Nov 12;38(11):1107-10.
- Hillege HL, Janssen WM, Bak AA, Diercks GF, Grobbee DE, Crijs HJ, Van Gilst WH, De Zeeuw D, De Jong PE, Prevend Study Group. Microalbuminuria is common, also in a nondiabetic, nonhypertensive population, and an independent indicator of cardiovascular risk factors and cardiovascular morbidity. *Journal of internal medicine*. 2001 Jun;249(6):519-26.
- Pinto-Sietsma SJ, Mulder J, Janssen WM, Hillege HL, de Zeeuw D, de Jong PE. Smoking is related to albuminuria and abnormal renal function in nondiabetic persons. *Annals of internal medicine*. 2000 Oct 17;133(8):585-91.
- Zhang J, Wang Z, Healy HG, Venuthurupalli SK, Tan KS, Fassett RG, Cameron A, Hoy WE. An overview of patients with chronic kidney disease, and their outcomes, in the Australian CKD. QLD registry (2011-2015). *Nephrol*. 2017;21.
- Mariscalco G, Lorusso R, Dominici C, Renzulli A, Sala A. Acute kidney injury: a relevant complication after cardiac surgery. *The Annals of thoracic surgery*. 2011 Oct 1;92(4):1539-47.
- Thakar CV. Perioperative acute kidney injury. *Advances in chronic kidney disease*. 2013 Jan 1;20(1):67-75.
- Moore E, Bellomo R, Nichol A. Biomarkers of acute kidney injury in anesthesia, intensive care and major surgery: from the bench to clinical research to clinical practice. *Minerva Anesthesiol*. 2010 Jun 1;76(6):425-0.
- Nazar CM. Significance of diet in chronic kidney disease. *Journal of Nephro pharmacology*. 2013;2(2):37.
- Heung M, Faubel S, Watnick S, Cruz DN, Koyner JL, Mour G, Liu KD, Cerda J, Okusa MD, Lukaszewski M, Vijayan A. Outpatient dialysis for patients with AKI: a policy approach to improving care. *Clinical Journal of the American Society of Nephrology*. 2015 Oct 7;10(10):1868-74.
- Devraj R, Wallace LS. Application of the content expert process to develop a clinically useful low-literacy Chronic Kidney Disease Self-Management Knowledge Tool (CKD-SMKT). *Research in Social and Administrative Pharmacy*. 2013 Sep 1;9(5):633-9.
- Ikizler TA, Cano NJ, Franch H, Fouque D, Himmelfarb J, Kalantar-Zadeh K, Kuhlmann MK, Stenvinkel P, TerWee P, Teta D, Wang AY. Prevention and treatment of protein energy wasting in chronic kidney disease patients: a consensus statement by the International Society of Renal Nutrition and Metabolism. *Kidney international*. 2013 Dec 1;84(6):1096-107.
- Fattori V, Borghi SM, Guazelli CF, Giroldo AC, Crespigio J, Bussmann AJ, Coelho-Silva L,

- Ludwig NG, Mazzuco TL, Casagrande R, Verri Jr WA. Vinpocetine reduces diclofenac-induced acute kidney injury through inhibition of oxidative stress, apoptosis, cytokine production, and NF- $\kappa$ B activation in mice. *Pharmacological research*. 2017 Jun 1;120:10-22.
18. Hoste EA, Clermont G, Kersten A, Venkataraman R, Angus DC, De Bacquer D, Kellum JA. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. *Critical care*. 2006 Jun 1;10(3):R73.
  19. McCracken C, Spector LG, Menk JS, Knight JH, Vinocur JM, Thomas AS, Oster ME, St Louis JD, Moller JH, Kochilas L. Mortality following pediatric congenital heart surgery: An analysis of the causes of death derived from the national death index. *Journal of the American Heart Association*. 2018 Nov 20;7(22):e010624.
  20. Guo Y, Zhang T, Wang Z, Yu F, Xu Q, Guo W, Wu C, He J. Body mass index and mortality in chronic obstructive pulmonary disease: A dose-response meta-analysis. *Medicine*. 2016 Jul;95(28).
  21. Woerschling J. Evaluating the Association between Mental Health Disorders, Substance Use Disorders and Healthcare Utilization in an Underserved Population Diagnosed with Head and Neck Cancer (Doctoral dissertation, New York University).
  22. Moeintaghavi A, Arab HR, Rezaee SA, Naderi H, Shiehzadeh F, Sadeghi S, Anvari N. The effects of smoking on expression of IL-12 and IL-1 $\beta$  in gingival tissues of patients with chronic periodontitis. *The open dentistry journal*. 2017;11:595.
  23. Beker BM, Corleto MG, Fieiras C, Musso CG. Novel acute kidney injury biomarkers: their characteristics, utility and concerns. *International Urology and Nephrology*. 2018 Apr 1;50(4):705-13.