IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
**Research Article**
February 2017 Vol.:8, Issue:3


# Hypoadiponectinemia and Hyperuricemia as Risk Factors of Acute Coronary Syndrome in Kerbala Province

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

***Batool Luay Aziz, **Dr. Shaymaa Zahraw Nada, *** Prof. Dr. Ahmed Hussein Al- Mayali**

**, **, *** Department of Biochemistry (Clinical), College of Medicine, University of Karbala, Holy Karbala city, Iraq.*

**Submission:** 2 February 2017
**Accepted:** 7 February 2017
**Published:** 25 February 2017



**Keywords:** Acute coronary syndrome (ACS), Hypoadiponectinemia, hyperuricemia, uric acid, Adiponectin.

**ABSTRACT**

**Aim:** This study aimed to investigate and evaluate the Hypoadiponectinemia and hyperuricemia in acute coronary syndrome (ACS) patients in holy Kerbala city, Iraq.**Methods:** Case-control study conducted on 58 patients admitted with a diagnosis of ACS and 30 healthy subjects as control group. Measurement of Adiponectin and uric acid, triglyceride, total cholesterol and high-density lipoprotein cholesterol (HDL-C) levels in addition to BMI were measured for all subjects.**Results:** Adiponectin serum concentrations were significantly lower in persons with ACS compared with healthy control subjects. Uric acid serum concentrations were significantly higher in subjects with ACS compared with healthy control subjects; hyperuricemic patients significantly higher developed heart failure. **Conclusions:** Hypoadiponectinemia was negatively correlated with hyperuricemia in Patients with ACS. Level of serum adiponectin was significantly lower in patients ACS and level of serum uric acid was significantly higher in patients ACS.

## INTRODUCTION

Acute coronary syndrome (ACS) describes the range of myocardial ischemic states that contain unstable angina, non-ST elevated myocardial infarction (NSTEMI), or ST-elevated myocardial infarction (STEMI). The diagnosis and classification of ACS based on a thorough offer of clinical features, including electrocardiogram (ECG) findings and biochemical markers of myocardial necrosis [1]. Unstable angina is defined by the presence of ischemic symptoms without elevations in biomarkers and passing if any, ECG changes [2]. The term myocardial infarction (MI) used when there is evidence of myocardial necrosis in the setting of acute myocardial ischemia [3]. ACS occur because of the destabilization of atherosclerotic plaques, which may undergo tear or erosion [4]. Adiponectin is an adipocyte-specific protein amply present in the plasma. Since its discovery, numerous experimental and clinical studies have demonstrated that adiponectin has anti-atherogenic, anti-diabetic and anti-inflammatory properties. Hypoadiponectinemia plays a key role in the pathogenesis of metabolic syndrome [5]. Uric acid is the final breakdown product of purine decay in humans [6]. Elevated serum uric acid has proved to be risk factor for ischemic heart disease and other cardiovascular diseases in several epidemiologic studies [7, 8]. It is also linked with increased death from cardiac causes [9]. Experimental studies have shown a uric acid link to endothelial dysfunction [10, 11], impaired oxidative metabolism, platelet adhesiveness and platelet aggregation [12].

## MATERIALS AND METHODS

**Study Group:** Consecutive patients were enrolled from inpatients who underwent coronary angiography at Al-Hussein Teaching Hospital, Al-Hussein Medical City from May till August 2016. The control subjects were selected from male and female who visited hospital. Healthy controls were characterized by no history of ACS and another heart disease. Traditional risk factors of ACS like smoking, hypertension, dyslipidemia and family history of premature CAD were excluded.

**Subjects and experimental protocol:** In all participants, clinical history and complete physical examination including measurements of blood pressure and body mass index (BMI) were collected. Obesity was defined as BMI > 30kg/m$^2$. Diagnosis of hypertension was based on blood pressure measurement (>135/85mmHg) or antihypertensive medications and it was assessed using information by self-reported history. Diabetes mellitus was defined as fasting plasma glucose ≥126mg/dl or those with history of diabetes and use of anti-diabetic

medications. Diagnosis of dyslipidemia was based on serum High-density lipoprotein cholesterol (HDL-C) level <40mg/dl for males, HDL-C level <50mg/dl for females and triglycerides level >150mg/dl were considered abnormal. Continuous variables like age, height, weight, BMI and laboratory findings were calculated as mean and standard deviation. T-test and ANOVA were used to see significant relationship of study variables between ACS patient group and healthy control group. All data were entered and analyzed through SPSS. A p-value of 0.05 was considered statistically significant.

## RESULTS

The clinical characteristics of ACS patients and control subjects are shown in Table (1). Serum adiponectin levels in the ACS patients were significantly lower than those in healthy control subjects (P<0.0001), and Serum uric acid levels in the ACS patients were significantly higher than those in healthy control subjects (P<0.0001). In Table (2) no significant differences in the serum triglyceride, VLDL-C and LDL-C levels in comparison between ACS patient group and healthy control group (p>0.05), but there were significant differences in total cholesterol in ACS patients group in comparison with healthy control group (p<0.05). While Serum HDL-C recorded highly significant decreases in patients in comparison with healthy controls (p<0.001). Serum Hypoadiponectinemia was negatively correlated with hyperuricemia in Patients with ACS, as shown in figure (1).

**Table (1): Comparison between acute coronary syndrome patients group and healthy control group in the measured Adiponectin and uric acid.**

| **Parameters** | **Patients with ACS** | **Controls** | **t-test** |
|---|---|---|---|
| | **Mean ± SD** | **Mean± SD** | **p-value** |
| **Number** | **58** | **30** | |
| Adiponectin(ng/ml) | 21.888±6.531 | 36.09±3.88 | 0.000* |
| Uric acid (mg/dl) | 6.3446±1.04 | 4.748±0.848 | 0.000* |

*=Highly significant, SD=standard deviation, ACS= acute coronary syndrome, p-value derived from Student t-test, Significant: p<0.05, highly significant: p<0.001, No significant: p>0.05.

**Table (2): Comparison between acute coronary syndrome patients group and healthy control group in the measured parameters.**

| parameters | Patients with ACS | Controls | t-test p-value |
|---|---|---|---|
| | Mean ± SD | Mean± SD | |
| Number | **58** | **30** | |
| Age (years) | 58.21 ±8.57 | 56.96±9.01 | 0.526 |
| BMI (kg/m$^2$) | 27.14±2.82 | 27.01±2.92 | 0.84 |
| TG (mg/dl) | 199.49±99.42 | 165.18±56.6668 | 0.084 |
| TC (mg/dl) | 198.55±62.034 | 173.951±33.3128 | 0.046* |
| LDL (mg/dl) | 123.32±65.259 | 99.319±32.904 | 0.063 |
| HDL (mg/dl) | 35.33±6.166 | 41.59±6.163 | 0.000** |
| VLDL (mg/dl) | 39.899±19.88 | 33.036±11.333 | 0.084 |

*= Significant **= Highly significant, TG= triglycerides, TC= total cholesterol, HDL-C= high density lipoprotein- cholesterol, SD= standard deviation, LDL-C= low density lipoprotein-cholesterol, VLDL-C= very low-density lipoprotein cholesterol, BMI= body mass index, ACS= acute coronary syndrome, p-value derived from Student t-test, Significant: $p<0.05$, Highly significant: $p<0.001$, No significant: $p>0.05$

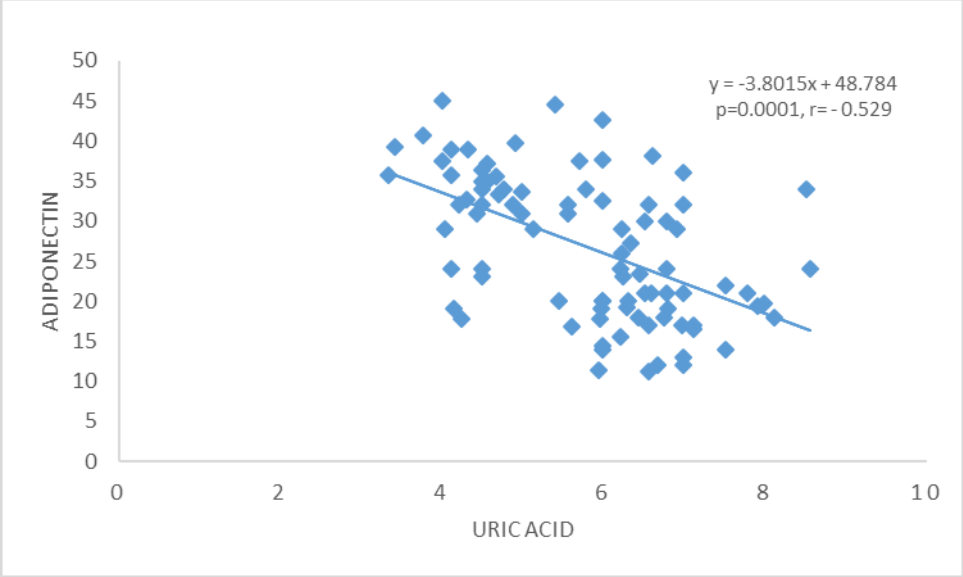


**Figure (1): Correlation between adiponectin and uric acid in acute coronary syndrome and healthy control group.**

In table (3) and table (4) the clinical and laboratory characteristics of the groups of acute coronary syndrome (ACS) patients and healthy control group in the measured parameters. Results obtained showed that serum uric acid was significantly higher in diabetic and non-diabetic ACS patients group in comparison with healthy control group ($p<0.001$), In addition, the results showed that there was a significantly lower in levels of adiponectin in diabetic and non-diabetic ACS patient group in comparison with healthy control group ($p<0.001$), and no significant differences in the serum triglyceride, TC, VLDL-C and LDL-C levels in comparison between diabetic and non-diabetic ACS patient group and healthy control group ($p>0.05$). While Serum HDL-C recorded highly significant decreases in patients in comparison with healthy controls ($p<0.001$). On the other hand, the age and BMI showed no significant difference between patients and healthy control group ($p>0.05$).

**Table (3): Comparison between diabetic and non-diabetic acute coronary syndrome patients groups and healthy control group in the measured parameters using ANOVA test.**

| **Parameters** | **Patient with ACS** | | **Control (30)** | **p-value** |
|---|---|---|---|---|
| | DM (26)<br>Mean± SD | Non-DM(32)<br>Mean± SD | Mean± SD | |
| Number | 26 | 32 | 30 | |
| Adiponectin (ng/ml) | 18.7±4.9 | 24.4±6.66 | 36.09±3.88 | 0.000* |
| Uric acid (mg/dl) | 6.5896±1.06 | 6.1±0.995 | 4.748±0.848 | 0.000* |

*= Highly significant, SD= standard deviation, ACS= acute coronary syndrome, p-value derived from ANOVA test, Significant: $p<0.05$, Highly significant: $p<0.001$, No significant: $p>0.05$.

**Table (4): Comparison between diabetic and non-diabetic acute coronary syndrome patients group and healthy control group in the measured parameters using ANOVA test.**

| Parameters | Patient with ACS | | Control (30) | p-value |
|---|---|---|---|---|
| | DM (26)<br>Mean± SD | Non-DM (32)<br>Mean± SD | Mean± SD | |
| Number | 26 | 32 | 30 | |
| Age | 59.53±8.72 | 57.12±8.43 | 56.93±9.018 | 0.480 |
| BMI | 27.8±2.95 | 26.6±2.6 | 27.01±2.94 | 0.275 |
| TC | 194.45±76.15 | 201.4±48.3 | 173.9±33.313 | 0.125 |
| TG | 211.34±102.12 | 189.93±97.4 | 165.1±56.666 | 0.149 |
| LDL-C | 121.32±83.8 | 124.9±47.3 | 99.319±32.90 | 0.175 |
| HDL-C | 31.48±6.98 | 38.5±2.726 | 41.5±6.163 | 0.000* |
| VLDL-C | 42.2±20.5 | 37.9±19.47 | 33.036±11.33 | 0.149 |

*= Highly significant, TG= triglycerides, TC= total cholesterol, HDL-C= high-density lipoprotein- cholesterol, SD= standard deviation, LDL-C= low-density lipoprotein-cholesterol, VLDL-C= very low-density lipoprotein cholesterol, BMI= body mass index, p-value derived from ANOVA test, Significant: $p<0.05$, Highly significant: $p<0.001$, No significant: $p>0.05$.

## DISCUSSION

In this study of participants with acute coronary syndrome (ACS), serum adiponectin levels were decreased and this suggests that adiponectin may respond to the acute phase of coronary artery disease (CAD). The exact mechanism of the decreased serum adiponectin levels shortly following the onset of ACS is not known, one possible explanation is that rupture of the coronary plaque may lead to decrease in plasma adiponectin levels, animals and human studies show that adiponectin was found in injured vessels rather than in intact vascular walls [13]. Therefore, it is possible that adiponectin targets ruptured plaques resulting in its consumption in the circulating plasma [13]. The findings of this study are in agreement with the previous study [13, 14]. High serum uric acid has been indicated as a risk factor for CAD [15, 16]. Many of authors such as Baruah *et al.*, Cheng *et al.* and Nadkar & Jain found statistically significant higher uric acid level in patients with acute MI than healthy controls [17, 18]. This study found that higher number of patients with hyperuricemia developed heart

failure than controls with normal serum uric acid level. The study also suggested that hyperuricemia is associated with the development of heart failure [19]. Kaya *et al* observed significantly higher hospital mortality and heart failure in patients with high uric acid levels, the mean ± SD of hospital stay of hyperuricemia group was significantly longer than healthy control [20, 21]. The measurement of serum uric acid level, an easily available and inexpensive biochemical tool, might turn out as a valuable risk marker for prediction of in-hospital outcomes in patients with ACS.

## CONCLUSION

Serum Hypoadiponectinemia was negatively correlated with hyperuricemia in Patients with ACS. It was found that a presence of significant association between Hypoadiponectinemia and hyperuricemia as risk factors of ACS in Kerbala province. Level of serum adiponectin was significantly lower in patients ACS and level of serum uric acid was significantly higher in ACS patients. Hypoadiponectinemia was significantly associated with the presence of ACS. High serum uric acid, increased total cholesterol, low HDL-C were significantly associated with the presence of ACS in patients admitted to C.C.U.

## REFERENCES

1. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. Circulation 2012; 126: 2020 –2035.
2. Smith JN., Negrelli JM., Manek MB, Hawes EM and Viera AJ. Diagnosis and Management of Acute Coronary Syndrome: An Evidence-Based Update. JABFM March–April 2015 Vol. 28 No. 2. J Am Board Fam Med 2015; 28: 283–293.
3. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of STelevation myocardial infarction: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013; 61:e78 – e140.
4. Maurizio Anselmia, Ulisse Garbin, Pierfrancesco Agostoni, Massimiliano Fusaroa, Anna Fratta Pasini, Cristina Nava, Dritan Keta, Marco Turri, Piero Zardini, Corrado Vassanelli, Vincenzo Lo Cascio, Luciano Cominacini. Plasma levels of oxidized low-density lipoproteins are higher in patients with unstable angina and correlated with angiographic coronary complex plaques. Atherosclerosis 2006; 185: 114–120.
5. Maedaa K and Matsuzawa Y. Discovery of Adiponectin and its Future Prospect. Journal of Diabetes and Obesity. J Diabetes Obes 2014; 1(1): 1-6.
6. Wortmann RL. Disorders of purine and pyrimidine metabolism. In: Kasper DL, Braunwald E, Fauci AS (eds). Harrison's Principles of Internal Medicine. 16th edn. New York: McGraw-Hill, 2005: 2308–2313.
7. Fang J, Alderman MH. Serum uric acid and cardiovascular mortality the NHANES I epidemiologic follow-up study, 1971-1992. National Health and Nutrition Examination Survey. J Am Med Assoc 2000; 283: 2404–2410.
8. Bos MJ, Koudstaal PJ, Hofman A, Witteman JC, Breteler MM. Uric acid is a risk factor for myocardial infarction and stroke: the Rotterdam Study. Stroke 2006; 37: 1503–1507.
9. Wong KY, MacWalter RS, Fraser HW, Crombie I, Ogston SA, Struthers AD. Urate predicts subsequent cardiac death in stroke survivors. Eur Heart J 2002; 23: 788–793.
10. Butler R, Morris AD, Belch JJ, Hill A, Struthers AD. Allopurinol normalizes endothelial dysfunction in type 2 diabetics with mild hypertension. Hypertension 2000; 35: 746–751.

11. Doehner W, Schoene N, Rauchhaus M, Leyva-leon F, Pavitt D, Reaveley D et al. Effects of xanthine oxidase inhibition with allopurinol on endothelial function and peripheral blood flow in hyperuricemic patients with chronic heart failure: results from 2 placebo-controlled studies. Circulation 2002; 105: 2619–2624.
12. Abu Sadique Abdullah, Noortaj Begum, Md. Aminul Haque Khan, Mofazzal Hossain, Shah Mohd.Eftar Jahan Kabir, Mohammad Sarwar Alam, Abdul Wadud Chowdhury, H. I. Lutfur Rahman Khan. Admission Serum Uric Acid Levels and In-Hospital Outcomes in Patients with Acute Coronary Syndrome. Journal of Enam. J Enam Med Col 2015; 5(1): 15–22.
13. Okamoto Y, Arita Y, Nishida M, et al. An adipocyte-derived plasma protein, adiponectin, adheres to injured vascular walls. Horm Metab Res 2000; 32: 47–50.
14. Ouchi N, Kihara S, Arita Y, et al. Adipocyte-derived plasma protein, adiponectin, suppresses lipid accumulation and class A scavenger receptor expression in human monocyte-derived macrophages. Circulation 2001; 103:1057–1063.
15. Allison TG. Coronary heart disease epidemiology. In: Murphy JG, Lloyd MA (eds). Mayo clinic cardiology. 3rd edn. Rochester (MN): Mayo Clinic Scientific Press, 2007: 687–693.
16. Brodov Y, Chouraqui P, Goldenberg I, Boyko V, Mandelzweig L, Behar S. Serum uric acid for risk stratification of patients with coronary artery disease. Cardiology 2009; 114: 300–305.
17. Baruah M, Nath CK, Chaudhury B, Devi R, Ivvala AS. A study of serum uric acid and C-reactive protein in acute myocardial infarction. International Journal of Basic Medical Sciences and Pharmacy (IJBMSP) 2012; 2: 21–24.
18. Nadkar MY, Jain VI. Serum uric acid in acute myocardial infarction. J Assoc Physicians India 2008; 56: 759–762.
19. Kojima S, Sakamoto T, Ishihara M, Kimura K, Miyazaki S, Yamagishi M et al. Prognostic usefulness of serum uric acid after acute myocardial infarction (the Japanese Acute Coronary Syndrome Study). Am J Cardiol 2005; 96: 489–495.
20. Kaya MG, Uyarel H, Akpek M, Kalay N, Erqlene M, Ayhan E et al. Prognostic value of uric acid in patients with STelevated myocardial infarction undergoing primary coronary intervention. Am J Cardiol 2012; 109(4): 486–491.
21. Abu Sadique Abdullah, Noortaj Begum, Md. Aminul Haque Khan, Mofazzal Hossain, Shah Mohd.Eftar Jahan Kabir, Mohammad Sarwar Alam, Abdul Wadud Chowdhury, H. I. Lutfur Rahman Khan. Admission Serum Uric Acid Levels and In-Hospital Outcomes in Patients with Acute Coronary Syndrome. J Enam Med Col 2015; 5(1): 15–22.