ISSN NO. 2320-5407

RESEARCH ARTICLE

RELATIONSHIP OF SERUM URIC ACID LEVELS AND ANGIOGRAPHIC SEVERITY OF CORONARY ARTERY DISEASE IN PATIENTS WITH ACUTE CORONARY SYNDROME USING SYNTAX SCORE.

Mustafa Hamed Rashed, Mohamed Yahia Abdel-Khalik, Abdullah Mohamed Alshehria, Ayman Mohamed Azoz, Shady Gamal, Alhanoof Dlaim Almalki.

Manuscript Info

Abstract

*Corresponding Author
....
Mustafa Hamed Rashed.

Background:- The relationship between elevated uric acid (UA) levels and the risk of major forms of atherosclerotic cardiovascular disease has been well demonstrated especially with chronic stable coronary artery disease, but still showing some debate in patients with acute coronary syndrome.

Aim:- This study was designed to detect the relationship between serum UA and the severity of coronary artery disease (CAD) in patients with acute coronary syndrome (ACS) as assessed by SYNTAX score.

Materials and Methods:- The study was carried on 80 patients who were admitted by ACS and underwent coronary angiography. All patients were assessed for the presence of cardiovascular risk factors .UA levels and other biochemical assessments were measured in all patients after 12 hour fasting before the procedure. The severity of CAD was assessed by the SYNTAX score. The relationship between the serum UA and the severity of CAD was statistically evaluated using IBM SPSS Statistics 21 for Windows.

Results:- This study was carried on 80 subjects, 70 of them were males (87.5%) and 10 subjects (12.5%) were females. The mean age in males was (53.6±11.2) years and it was (62.5±8.8) years in females. Among the studied population there were 57 (71.25%) current smokers, 8 (10%) ex-smokers and (18.75%) nonsmokers.

Forty-nine patients (81.25%) had hypertension on medical treatment while 35 patients (43.75 %) were diabetic (type 2 DM). the HbA1c was (8.16±2.41) in females and (7.43±1.97) in males.

Forty six patients (75.5%) had a history of abnormal lipid profile on medical treatment.

The level of uric acid was (5.45±2.45 mg/dl) in females and (5.33±1.61mg/dl) in males

Conclusion:- The level of serum uric acid showed no correlation with the calculated SYNTAX score among the studied population (p value = 0.198)

Introduction:-

Cardiovascular diseases are currently the leading cause of death in the world especially in industrialized countries and are expected to become so in emerging countries by 2020 (Murray et al.,1997). Coronary artery diseases (CAD) are the most prevalent manifestation and are associated with high mortality and morbidity (Go AS et al., 2013). CAD had many different presentations including chronic stable angina, unstable angina, myocardial infarction (MI), heart failure, and even sudden cardiac death. Patients presented with chest pain represent a very large proportion of all acute medical hospitalizations in Europe. It is very important to diagnose patients with ACS within the very large proportion with suspected cardiac pain which make it a diagnostic challenge, especially in individuals without clear symptoms or electrocardiographic changes which suggest the diagnosis (Berenson et al., 1998), (Freedman et al.,2001).

The mortality rate from ACS is still high especially acute myocardial infarction. All the Pathological, imaging, and biological observations have demonstrated that atherosclerotic plaque rupture or erosion, with superimposed thrombosis and distal embolization, resulting in myocardial infarction. And so, this may be a life-threatening state of atherothrombotic disease. The development of criteria for risk stratification have been proposed to allow the clinician to make timely decisions on pharmacological management as well as coronary revascularization strategies, tailored to the individual patient. Chest pain is still the leading symptom that initiates the diagnostic and therapeutic cascade, but the classification of patients is based on the electrocardiogram (ECG) (Steg et al., 2012).

Regarding ACS we have two categories of patients may be encountered:-
1. Patients with ST-elevation ACS (STE-ACS), these patients presented with acute chest pain and persistent (>20 min) ST-segment elevation. These ECG changes generally reflect an acute total coronary occlusion. Most of these patients will ultimately develop an ST-elevation MI (STEMI). The rapid diagnosis and proper management to achieve rapid, complete, and sustained reperfusion by primary angioplasty or fibrin lytic therapy is essential to decrease the mortality and hospitalization associated with such patients (Hamm et al., 2011),(Van et al., 2008).

2. The 2nd category is Patients with acute chest pain but without persistent ST-segment elevation. These patients have different ECG changes; they may have transient ST-segment deviation or T-wave inversion, flat T waves, pseudo-normalization of T waves, or no ECG changes at presentation. The initial strategy in these patients is to alleviate ischemic manifestations, to monitor the patient with serial ECGs, and to repeat measurements of markers of myocardial necrosis (Hamm et al., 2011),(Van et al., 2008).

3. In order to differentiate between the two types of non-ST-elevation ACS (NSTE-ACS), we measure chemical biomarkers called the cardiac enzymes, including the cardiac troponins. As a result, they will be further qualified as non-ST-elevation MI (NSTEMI) with increased biomarkers levels or unstable angina with normal levels. In a certain number of patients, coronary heart disease will subsequently be excluded as the cause of symptoms (Van et al., 2008).

Uric acid and Ischemic heart disease:-
Many investigators observed an association between serum uric acid and cardiovascular disease (CVD) since 19th century. CVD are the leading cause of death as mentioned Hence, huge epidemiologic data were collected and showed a relationship between serum uric acid with variety of CVDs. In these studies , there was an observation that hyperuricemia is associated with other cardiovascular risk factors for ischemic heart disease like male gender, old age, diabetes mellitus, hypertension, insulin resistance, hypertriglyceridemia and metabolic syndrome (Hamaguchi et al.,2011).

It has also been proved in different studies that there is strong association between hyperuricemia and adverse outcomes including recurrent ischemia and hospitalization in ischemic heart disease (IHD) especially in patients with heart failure (Gertler et al., 1951).

Biochemically, Uric acid is the end product of purine metabolism. Its immediate precursor, xanthine, is converted to uric acid by a serial of enzymatic reaction involving xanthine oxidoreductase (Kim SY et al., 2010).

Increased levels of serum uric acid has been observed to be associated with atherosclerotic changes at arteries including , endothelial dysfunction ,increased free oxygen radicals with high oxidative stress ,anti- proliferative

effects, and thrombus formation (Ter Arch, 2011) . Investigators suggest that hyperuricemia causing endothelial dysfunction which is the corner stone in initiation of the process of atherosclerosis. Patients with persistently elevated levels of uric acid in blood serum have significantly higher levels of endothelial dysfunction (ED) markers; albuminuria and plasma endothelin (Ong AT et al., 2006).

Routine laboratory measurement of serum uric acid levels is unlikely to enhance usefully the prediction of IHD in general populations. And that's why still uric acid has yet not been recognized as a CVD risk factor by major professional societies, and treatment of asymptomatic hyperuricemia to reduce CVD risk is not advised (Ong AT et al., 2006).

The SYNTAX score:-
The SYNTAX scoring system is a novel anatomical tool that helps in identifying the coronary vasculature. Importantly, the SYNTAX score grades the complexity of coronary artery disease and does not consider lesion treatment. Complex lesion anatomy creates a greater technical challenge and difficulty to the operator for making a decision and subsequently, a higher risk of adverse events when treated by percutaneous intervention. In contrast, CABG bypasses the lesion and is make lesion complexity less important to the surgeon. The goal of the SYNTAX score is to assist the clinician in selecting the optimal revascularization strategy (either PCI or CABG), resulting in the best possible outcome for the individual patient. Furthermore, the SYNTAX score is a useful tool to describe the extent of the coronary artery disease complexity for an individual patient allows for more comparison between patients and help the invasive cardiologist in taking a rapid step in revascularization. It can be calculated on line using smart phones or computers (Mach et al., 2009),(Serryy PW,2008),(Rakic MT et al., 1964).

Materials and Methods:-
It is a case series study, The study population was randomly selected from King Fahd Hospital of the University (KFUH) in AL Khobar , Saudi Arabia .Including all admissions with ACS who were subjected to coronary angiography to calculate the SYNTAX score .

All Patients underwent complete history evaluation, thorough clinical examination, Baseline resting electrocardiography was done upon admission.

Baseline blood tests: A venous blood sample was drawn from each patient for analysis of complete blood picture, renal and liver functions, HbA1C, total serum cholesterol (TC), triglycerides (TGs), high density lipoprotein (HDL), and low-density lipoprotein (LDL) cholesterol and serum uric acid.

Our exclusion criteria were: patients had a history of chronic kidney disease, patients on treatment of hyperurecemia and the category that did not do coronary angiography.

The severity of CAD was assessed by the SYNTAX score. This score grades the complexity of coronary artery disease and does not consider lesion treatment , so it can be used simply to assess the severity of the coronary lesion .It was calculated by using Version 2.11 of the SYNTAX Score calculator, easily used by smart phones or disk top computers, it contains the latest four-year SYNTAX trial results. The SYNTAX Score website now uses this version.

The relationship between the serum UA and the severity of CAD was statistically evaluated using IBM SPSS Statistics 21 for Windows.

Results:
This study was carried on 80 subjects, 70(87.5%) of them were males and 10 subjects (12.5%) were females, representing a random sample of acute coronary syndrome patients who were admitted to King Fahd Hospital of the University (KFUH), all patients were subjected to coronary angiography to calculate the SYNTAX score and the routine lab were extracted including serum uric acid level.

The mean age in males was (53.6±11.2) years and in Females was (62.5±8.8) years and this may reflect that the females had ACS at older age than the males (table 1).

Table 1: differences between males and females in the studied group.

	Female	Male
Age in years	62.5±8.8	53.6±11.2
Number and Percentage	(10)12.5%	(70)87.5%
Total cholesterol (mg/dl)	193.6±33.9	174.7±40.3
TG (mg/dl)	140.7±44.4	157.04±65.4
LDL (mg/dl)	122.2±40.2	110.3±43.6
HDL (mg/dl)	52.6±15.8	40.5±19.8
HbA1c (mg/dl)	8.16±2.41	7.43±1.97
S. Creatinine (mg/dl)	0.97±0.4	1.25±0.7
Uric acid (mg/dl)	5.45±2.45	5.33±1.61

Among the studied population there were 57 (71.25%) current smokers, 8 (10%) ex-smokers and 15 (18.75%) non smokers

Forty-nine patients (81.25%) had hypertension on medical treatment while 35 patients (43.75 %) were diabetic (type 2 DM). the HbA1c was (8.16±2.41) in females and (7.43±1.97) in males (table1).

Forty six patients (75.5%) had a history of abnormal lipid profile on medical treatment.

As regarding the lipid profile:
Females had a higher cholesterol, LDL and HDL levels (193.6±33.9mg/dl), (122.2±40.2 mg/dl) and (52.6±15.8 mg/dl) respectively compared to males (174.7±40.3mg/dl), (110.3±43.6 mg/dl) and (40.5±19.8 mg/dl) respectively. While males had higher triglycerides (157.04±65.4 mg/dl) than females (140.7±44.4mg/dl) as shone in (table 1) and (figure 1).

Serum uric acid levels (5.45±2.45 mg/dl) in females and (5.33±1.61mg/dl) in males

The level of serum uric acid showed no correlation with the calculated SYNTAX score among the studied population as shown in the Scatter graph (figure 2)

Also we use the liner regression test to compare the results and we find that the r square was low (0.02) this indicate that there is poor correlation between the studied parameters (p value = 0.198) (figure 3)

Discussion:-
A relationship between increased serum uric acid levels and CVD has been established since the 1900's. Hyperuricemia are a common finding in patients with hypertension, insulin resistance, and obesity which precipitate the development of IHD. Furthermore, uric acid as a CV risk factor has been addressed in numerous prospective and cohort studies (Rakic MT et al., 1964)

Also hyperucicemia have been observed in diabetics, hypertensive, obese and patients with abnormal lipid profile. A multiple risk factor clustering syndrome (Metabolic syndrome) has been considered to be responsible for high serum uric acid level in CAD questioning the role of serum uric acid level as independent risk factor (Puig JG et al., 2008).

Regarding the mean levels of serum UA, our present study showed levels consistent with the literature (Kaya EB et al., 2010). But in others, UA levels were higher than those measured in our study (Xiong Z et al., 2011), (Ehsan A et al., 2013).

The Gensini scoring system and the Syntax scoring system are the two most widely used scoring systems for assessing angiographic severity and complexity of IHD (Neeland IJ et al., 2012).Studies have proved their correlation and comparability, with none of them inferior to the other (Sinning C et al., 2013).

Duran M et al , studied the relationship of hyperuricemia and ACS using Gensini score instead of SYNTAX system in 246 non-diabetic and non-hypertensive patients of ACS and found a positive association of hyperuricemia with angiographic severity of ischemic heart disease (Duran M et al., 2012).

Also, Gur M et al, found an association between hyperuricemia and IHD using Gensini score. They observed positive correlation between serum uric acid levels and angiographic evidence of coronary lesions **but not** with severity of ischemic heart disease (Gur M et al., 2008).

Xiong Z et al, found that increased levels of serum UA to be prominently related to angiographic complexity (not severity) of coronary artery disease by Syntax score (Xiong Z et al., 2011).

In agreement of our study, Lu P et al, from China, reported that there was no relationship between serum uric acid levels and severity of IHD (Lu P et al., 2002).

In conclusion, this study has shown no association between the severity of CAD assessed by SYNTAX score and increased UA levels in the acute coronary syndrome patient's category. The limitations of the study were serum uric acid level was done once, study population was a limited number, and it included only patients with ACS.

References:-

1. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. Lancet 1997;349: 1498–1504.
2. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics–2013 update: A report from the American Heart Association ,Circulation, 127 (2013), pp. e6–e245
3. G.S. Berenson, S.R. Srinivasan, W. Bao. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart StudyN Engl J Med, 338 (1998), pp. 1650–1656
4. Freedman DS1, Khan LK, Dietz WH, Srinivasan SR, Berenson GS. , et al. Relationship of childhood obesity to coronary heart disease risk factors in adulthood: The Bogalusa Heart Study Pediatrics, 108 (2001), pp. 712–718
5. Steg PG, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, Borger MA, et al. Task force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J*. 2012;33(20):2569-2619.
6. Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: the task force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2011;32(23):2999-3054.
7. Van de Werf F, Bax J, Betriu A, Blomstrom-Lundqvist C, Crea F, Falk V, et al . Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J 2008;29:2909–2945.Rathmann W , 1998
8. Hamaguchi S, Furumoto T, Tsuchihashi-Makaya M, Goto K, Goto D, Yokota , et al . Hyperuricemia predicts adverse outcomes in patients with heart failure, 2011.
9. Gertler MM, Garn SM, Levine SA. Serum uric acid in relation to age and physique in health and in coronary heart disease, 1951 .
10. Kim SY, Guevara JP, Kim KM. Hyperuricemia and coronary heart disease: a systematic review and meta-analysis. Arthritis Care Res. 2010.
11. Ter Arkh. Clinical implication of endothelial dysfunction in patients with essential arterial hypertension and urate dysbolism with renal damage, 2011.
12. Ong AT, Serruys PW, Mohr FW, Morice MC, Kappetein AP, Holmes DR Jr, et al. The SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery (SYNTAX) study: design, rationale, and run-in phase. Am Heart J. 2006.
13. Mack MJ, Banning AP, Serruys PW, Morice MC, Taeymans Y, Van Nooten G, et al. Percutaneous coronary intervention versus coronary artery bypass grafting for severe coronary artery disease. N Engl J Med. 2009.
14. Serruys PW. The SYNTAX Score: a new angiographic tool to grade the complexity of coronary artery disease. Presented at the Transcatheter Cardiovascular Therapeutics annual meeting; 2008.

15. Rakic MT, Valkenburg HA, Davidson RT, Engels JP, Mikkelsen WM, Neel JV, et al. Observations on the natural history of hyperuricemia and gout. I. An eighteen year follow-up of nineteen gouty families. Am J Med. 1964;37:862-71.

16. Puig JG, Martínez MA. Hyperuricemia, gout and the metabolic syndrome. Curr Opin Rheumatol. 2008;20:187- 191.doi: 10.1097/BOR.0b013e3282f4b1ed.

17. Kaya EB, Yorgun H, Canpolat U, Hazırolan T, Sunman H, Ülgen A, et al. Serum uric acid levels predict the severity andmorphology of coronary atherosclerosis detected by multidetector computed tomography.Atherosclerosis, 2010; 213: 178-183.

18. Xiong Z, Zhu C, Qian X, Zhu J, Wu Z, Chen L. Predictors of clinical SYNTAX score in coronary artery disease: serum uric acid, smoking, and Framingham risk stratification. J Invasive Cardiol. 2011;23(12):501-504.

19. Ehsan Qureshi A, Hameed S, Noeman A. Relationship of serum uric Acid level and angiographic severity of coronary artery disease in male patients with acute coronary syndrome. Pak J Med Sci, 2013; 29: 1137-1141.

20. Neeland IJ, Patel RS, Eshtehardi P, Dhawan S, McDaniel MC, Rab ST. Coronary Angiographic Scoring SystemsAn Evaluation of Their Equivalence and Validity. Heart J. 2012;164(4):547-552.doi:10.1016/j.ahj.2012.07.007.

21. Sinning C, Lillpopp L, Appelbaum S, Ojeda F, Zeller T, Schnabel R, et al. Angiographic score assessment improves cardiovascular risk prediction: the clinical value of SYNTAX and Gensini application. Clin Res Cardiol. 2013;102(7):495- 503. doi:10.1007/s00392-013-0555-4.

22. Duran M, Kalay N, Akpek M, Orscelik O, Elcik D, Ocak A. High Levels of Serum Uric Acid predict severity of ischemic heart disease in Patients With Acute Coronary Syndrome. Angiology. 2012;63(6):448-452. doi: 10.1177/0003319711426868.

23. Gur M, Yilmaz R, Demirbag R, Aksoy N. Relation of serum uric acid levels with the presence and severity of angiographic coronary artery disease. Angiology. 2008;59(2):166-171. doi:10.1177/0003319706292010.

24. Lu P, Hu D, Lu J, Wang W, Chen B. The association between uric acid and coronary heart disease. ZhonghuaNeiKeZaZhi. 2002;41(8):526-529.