Hyperuricemia and smoking correlation in Egyptian young adults with coronary artery disease: Observational Study

Learning Objective:

HUA is significantly associated with the occurrence of CAD in non-smokers of young adults ≤ 35 years old. Unexpectedly, HUA and smoking have a contrast; the existence of these two risk factors in a patient is not remarkably associated with CAD occurrence compared to the statistical results of non-smokers.

Abstract

Background: Young adults, especially those under 35, are often overlooked; however, previous studies have shown that coronary artery disease (CAD) incidence increases rapidly. Previous studies proved many risk factors for CAD, such as hyperlipidemia, hypertension, diabetes, and smoking. The present study ultimately aimed to figure out the correlation between Hyperuricemia (HUA) and smoking in CAD Patients under the age of 35

Methods: This observational study included 100 young adults (18–35 years of age) suspected of CAD. We used the Gensini Score system to ascertain coronary angiography outcome and CAD; based on the number of affected vessels, localization of the segment, and the stenosis grade. The Gensini score being > 0 indicated the presence of CAD.

Results: In young adults under 35, there was a significant correlation between HUA and CAD. The interaction between HUA and smoking had a contrast for CAD that statistically shown the existence of CAD increased in patients who have hyperuricemia and non-smokers compared to smokers.

Conclusions: By monitoring various parameters in young adults ≤ 35 years old, This study strengthens the correlation between:1) hyperuricemia and the occurrence of CAD, 2) Smoking and the CAD. Furthermore, there is a clear association between HUA and the occurrence of CAD in non-smokers.

Keywords: Hyperuricemia, Smoking, Coronary Artery Disease

Introduction:

Coronary artery disease is the most frequent reason for mortality in cardiovascular diseases. Young adults, especially those under 35, are often overlooked; however, previous studies have shown that CAD incidence increases rapidly. Smoking and cigarette smoke are among the dominant risk factors for early or accelerated peripheral, coronary and cerebral atherosclerotic vascular disease. Kamceva et al.,[1] in a study to determine whether cigarette smoking, as a risk factor for CAD, affects antioxidant status. As a consequence, it raised oxidative stress and reduced antioxidant protection.

Hyperuricemia is linked with cardiovascular diseases (CVD), such as coronary artery disease (CAD), stroke, and hypertension[2], but the role of serum uric acid (SUA) as an independent risk factor for CVD remains unclear. Many previous studies have shown that hyperuricemia is commonly recorded in patients with CVD or at a high risk of CVD, such as hypertension, CAD, stroke, heart failure, metabolic syndrome, and peripheral vascular disease[3].

This study aimed to determine; a. the association between hyperuricemia and coronary artery disease. b. Studing the the association between HUA and CAD in smokers and non-smokers and Clarify the conflict effect between the risk factors of CAD.

Methods:

Study Design and Participants

This observational study was carried out at the cardiology department, Tanta University Hospital, after approval from Ethical Committee and obtaining written informed consent from each patient. The study involved 100 patients from October 2019 till March 2020. Eligibility criteria included all young adults (18–35 years of age) suspected to have CAD who underwent coronary angiography. The exclusion criteria were as follows: 1. Renal impairment (an estimated glomerular filtration rate [eGFR] < 60 mL/min/1.73 m2). 2. Active infections, autoimmune diseases, or neoplastic disease.3. Hepatic and hemolytic disorders. 4. Patient refusal.

Procedures / Study Protocol

A total of 100 patients went through a complete clinical record and accurate history taking. Thorough history taking with stress on age, sex, and history of risk factors for CAD, including hypertension, diabetes mellitus, smoking habits, dyslipidemia, and family history of ischemic heart diseases. Blood pressure under 140/90 mmHg patients described as hypertension or having Medication for anti-hypertension [4]. Taking insulin or oral hypoglycemic agents was a reason to consider the patient with diabetes. For patients with lack awareness about their diabetes history; we used the WHO criteria for 2006 diabetic diagnostic as follows: a. under 126 mg/dl for fasting blood glucose, and under 200 mg /dl for oral glucose tolerance or oral glucose tolerance test 2-hour plasma glucose ≥ 200 mg/dL. Smokers patients were defined as a patient smoking since six months or more. Suppose serum uric acid level was more than 7.0 mg/dl in men and 6.0 for women, defined as hyperuricemia[5]. Coronary artery disease is common in patients with positive family history.

A Standard twelve-lead electrocardiogram was done for all patients and analyzed for heart rate, rhythm, conduction abnormalities, ST-segment changes, and voltage criteria. By following the ECHO recommendations of American society, We have calculated the Left ventricular ejection fraction; besides, mitral pulsed-wave Doppler measurements with the transducer in the apical four-chamber view. Three consecutive beats were measured and averaged for each parameter [6]. Venous blood samples were obtained by the venipuncture of the large antecubital veins of the patients. Clinical examinations included blood sugar, serum creatinine, fasting blood sugar, blood urea, liver enzymes, lipid profile, cardiac enzymes, and serum uric acid.

All young patients with documented coronary angiography were selected. The coronary angiography was performed under local anesthesia via the femoral artery using the retrograde percutaneous transfemoral technique (Judkins's technique) by two experienced cardiologists blinded to the patients' clinical characteristics and laboratory results. We evaluated epicardial coronary arteries, including the left main, left anterior descending, left circumflex, right coronary artery, and the vessels' main branches. Ascertainment of outcome coronary

angiography and CAD was performed using (Gensini Score system) based on the number of affected vessels, localization of the segment, and the grade of the stenosis. These scores are multiplied by the coefficient defined for each coronary artery and segment, and the results are then added. The presence of CAD has been defined as the Gensini score being > 0 [7].

Statistical Analysis

In this study, SPSS version 20.0 was used for the statistical analysis and presentation. the mean and standard deviation present the continuous variables and data using t-test for comparing in normally distributed data; the median used for non normally distributed data

Results:

Study Population:

Between October 2019 and March 2020 in Tanta university hospital, 100 patients were divided into two groups suspected of CAD and non-CAD patients. All patients underwent an angiography scoring system that divided them into two groups; if the Gensini score was zero, the patients were non-coronary artery disease. This group included 40 male and ten females patients with a mean age (30 ± 3.5). If the Gensini score was higher than zero, the patients were defined as coronary artery disease patients. This group included 34 males and 16 females (mean age 31 ± 3)

Each group was subdivided according to sex into males and females with a mean age of 31.06 years. there was a nonsignificant statistical difference between the two groups regarding age (p=0.885) & sex (p=0.171). Regarding risk factors, smoking was the most frequent between the two groups Table (1). According to univariate analysis has shown a significant correlation between Hyperuricemia and CAD existence. This analysis results support the previous studies on CAD risk factors. All the data has been illustrated and recorded in Table 2.

HUA and Smoking Correlation in CAD patients

We have adjusted many factors present in table 2. We Found an unexpected difference between HUA and CAD correlation in smokers and non-smokers. In table 3, The Data presented a statistically significant association between HUA and CAD in non-smokers (p=0.045) compared with smokers (p=0.110).

Discussion:

In this study, regarding risk factors, 48% of the patients were smokers, 23% diabetic patients, 14% patients have a positive family history of CAD, and 46% hypertensive patients among the studied patients. The most affected artery was LAD (56%), followed by RCA (40%). There is a significant correlation between HUA and CAD in young adults ≤ 35 years old. In addition, HUA and smoking have statistical significance for CAD in young adults ≤ 35 years old. HUA is significantly associated with the occurrence of CAD in non-smokers of young adults ≤ 35 years

old. Unexpectedly, HUA and smoking have a contrast; the existence of these two risk factors in a patient is not remarkably associated with CAD occurrence compared to the statistical results of non-smokers.

A similar conclusion was reached by Lv et al. [8] that there is a contrast between smoking and HUA Patients for the existence of CAD; statistically, the non-smokers' patients with HUA were highly associated with CAD Compared to smokers in patients under35. In addition, Serum uric acid level was higher in patients with CAD [9]. In contrast to our study, Cheong et al. [10] concluded that Serum Uric Acid showed no significant association with all-cause and cardiovascular mortality. A large sample size in Cheong et al. [10] may be the cause as 356 960 patients were included vs. 100 patients in our study.

According to our results, there is an unexpected contrast between HUA and the cigarette effect on patients suspected of CAD. Different studies reached a similar conclusion that makes it a vital point for future researchers to focus on.

Study limitation

The present study has a significant limitation as follows; This observational study has a limited number of patients (100 patients), So it will be a must to apply it to a broader number of patients. The results were applied only to Egyptian patients and opening the sight for other researchers to apply it in different populations and races. Future research on smoking and hyperuricemia might explain the explanations of this contrast between them. Further studies on a large geographical scale and larger sample size The effect of anti-HUA drugs on the progression of CAD should be investigated further in large randomized trials, which may potentially provide new therapeutic approaches for the prevention and treatment of CAD.

Conclusion

By monitoring various parameters in young adults ≤ 35 years old, This study strengthens the correlation between:1) hyperuricemia and the occurrence of CAD, 2) Smoking and the CAD. Furthermore, there is a clear association between HUA and the occurrence of CAD in non-smokers.

References:

1. Kamceva, G., et al., *Cigarette Smoking and Oxidative Stress in Patients with Coronary Artery Disease.* Open Access Maced J Med Sci, 2016. **4**(4): p. 636-640.
2. Kim, S.Y., et al., *Hyperuricemia and coronary heart disease: a systematic review and meta-analysis.* Arthritis Care Res (Hoboken), 2010. **62**(2): p. 170-80.
3. Baker, J.F., et al., *Serum uric acid and cardiovascular disease: recent developments, and where do they leave us?* Am J Med, 2005. **118**(8): p. 816-26.
4. Ambrosio, G., et al., *Management of stable angina: A commentary on the European Society of Cardiology guidelines.* Eur J Prev Cardiol, 2016. **23**(13): p. 1401-12.
5. Toms, R., et al., *Geographic and area-level socioeconomic variation in cardiometabolic risk factor distribution: a systematic review of the literature.* Int J Health Geogr, 2019. **18**(1): p. 1.
6. Bhatnagar, P., et al., *The epidemiology of cardiovascular disease in the UK 2014.* Heart, 2015. **101**(15): p. 1182-9.
7. Wilmot, K.A., et al., *Coronary Heart Disease Mortality Declines in the United States From 1979 Through 2011: Evidence for Stagnation in Young Adults, Especially Women.* Circulation, 2015. **132**(11): p. 997-1002.
8. Lv, S., et al., *Hyperuricemia and smoking in young adults suspected of coronary artery disease ≤ 35 years of age: a hospital-based observational study.* BMC Cardiovasc Disord, 2018. **18**(1): p. 178.
9. Levine, G.N., et al., *2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention, 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease, 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction, 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes, and 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery.* Circulation, 2016. **134**(10): p. e123-55.
10. Cheong, E., et al., *Association between serum uric acid and cardiovascular mortality and all-cause mortality: a cohort study.* J Hypertens, 2017. **35 Suppl 1**: p. S3-s9.

Table 1: Demographic and clinical characteristics of the study population:

	(Group I) Non-CAD (n= 50)	(Group II) CAD (n= 50)	P
Sex (Male %)	40 (80%)	34 (68%)	0.171
Age	30.96 ± 3.50	31.06 ± 3.38	0.885
Diabetes Mellitus	7 (14%)	16 (32%)	0.032[*]
Hyperlipidemia	9 (18%)	18 (36%)	0.043[*]
Smoking	18 (36%)	30 (60%)	[*]0.016
Family history of CAD	3 (6%)	11 (22%)	0.021[*]
ECG (Abnormal %)	8 (16%)	38 (76%)	<0.001[*]
Echo (Abnormal %)	8 (16%)	39 (78%)	<0.001[*]
Fasting Blood Glucose	98.12 ± 16.30	107.16 ± 23.07	0.026[*]
RBS	95.0 (81.0 – 100.0)	94.50 (84.0 – 110.0)	0.358
Total cholesterol	171.0 (160.0 – 230.0)	176.50 (160.0 – 236.0)	0.997
TG	107.0 (90.0 – 128.0)	100.0 (83.0 – 160.0)	0.624
LDL	85.0(75.0 – 114.0)	114.0(85.0 – 132.0)	0.002[*]
HDL	50.0 (41.0 – 51.0)	48.50 (42.0 – 50.0)	0.687
Serum creatinine	0.77 ± 0.19	0.85 ± 0.21	0.035[*]
Uric Acid	3.90 (3.40 – 4.50)	4.55 (3.60 – 6.50)	0.001[*]

Echo: Echocardiography, ECG: Electrocardiogram, TG: Triglycerides, RBS: Random blood sugar,

Table 2: Univariate analysis of coronary artery disease (CAD) risk factors

	MEAN ± SD	NO. (%)	P	OR (95%C. I)
AGE	31.01 ± 3.42		0.883	1.009(0.899 – 1.132)
SEX				
MALE		74(74.0%)	1.0	1.882(0.756 – 4.690)
FEMALE		26(26.0%)	0.174	
SMOKING				
YES		48(48.0%)	0.017[*]	2.667(1.188 – 5.985)
NO		52(52.0%)	1.0	
HYPERURICEMIA				

			P	OR (95% C.I)
YES		18(18.0%)	0.014*	4.472(1.355 – 14.755)
NO		82(82.0%)	1.0	
HYPERTENSION				
YES		46(46.0%)	0.046*	2.263(1.013 – 5.052)
NO		54(54.0%)	1.0	
DIABETES MELLITUS				
YES		23(23.0%)	0.037*	2.891(1.068 – 7.823)
NO		77(77.0%)	1.0	
FAMILY HISTORY OF CAD				
YES		14(14.0%)	0.030*	4.419(1.151 – 16.966)
NO		86(86.0%)	1.0	
SERUM CREATININE	0.81 ± 0.20		0.039*	8.738(1.112 – 68.645)
TOTAL CHOLESTEROL				
≥200		32.0(32.0)	0.392	1.446(0.621 – 3.368)
<200		68(68.0%)	1.0	
TRIGLYCERIDES "TG"				
≥150		26(26.0%)	0.363	1.519(0.617 – 3.745)
<150		74(74.0%)	1.0	
LDL				
≥130		23(23.0%)	0.037*	2.891(1.068 – 7.823)
<130		77(77.0%)	1.0	
HDL				
<40		15(15.0%)	0.404	0.621(0.203 – 1.899)
≥40		85(85.0%)	1.0	

OR: Odd`s ratio, C.I: Confidence interval, LL: Lower limit, UL: Upper Limit

Table 3: Association between hyperuricemia and coronary artery disease (CAD) in smokers and non-smokers

	NO. OF PATIENTS	OR (95%C. I)			
		P	Crude	P	Model I[a]
NON-SMOKERS					
NORMOURICEMIA	41		Reference		Reference
HYPERURICEMIA	11	0.014*	6.444*(1.46 – 28.53)	0.045*	5.017*(1.83 – 30.31)
CURRENT SMOKERS					
NORMOURICEMIA	41		Reference		Reference
HYPERURICEMIA	7	0.199	4.250 (0.47 – 38.60)	0.110	9.409(0.60 – 147.29)

OR: Odd`s ratio, C.I: Confidence interval, LL: Lower limit, UL: Upper Limit