

Causal-Effect of Uric Acid and Caries Experience in Ischemic Heart Diseases: A Case-Control Study

Amir Al-Mumin¹, Mazin Jaafar Mousa², Ahlam Kadhim Abbood³, Hussein O. M. Al-Dahmoshi⁴, Noor S. K. Al-Khafaji⁴

¹Interventional Cardiologist, Hammurabi Medical College, University of Babylon, Iraq.

²Histopathologist, College of Pharmacy, University of Babylon, Iraq.

³Medical Physiology, College of medicine, University of Babylon, Iraq.

⁴Biology Department, College of Science, University of Babylon, Iraq.

Corresponding author: Hussein O. M. Al-Dahmoshi

E-mail: husein_gst@yahoo.com

ABSTRACT

Background: both ischemic heart disease (IHD) and dental caries (DCr) are a chronic multifactorial disorder sharing several etiopathological risk factors. Uric acid (UA) has a proved pro inflammatory effect. This work is an attempt evaluate the causal effect of UA in carious experience in IHD patients.

Material and Methods: 118 IHD patients clinically assessed by cardiologist and 50 healthy subjects has been selected as a control group. One-way ANOVA was applied to correlate SUA level with groups of DMFT index. DCr was evaluated according to DMFT-index based on WHO-recommendations 1997. All participants were divided according to their carious status into three classes in which a DMFT index. All participants investigated for serum levels of uric acid, creatinine, urea nitrogen, according to available conventional techniques, and their serum UA/creatinine ratio had been calculated. Then again, studied subjects divided into normouricemic and hyperuricemic, using a cutoff level of 7.0mg/dl for males and 6.0mg/dl for females were assigned. Results are presented as mean±SD. The variation and correlation among variables were allocated significant for all the tests, once p-value ≤0.05. The data was processed and analyzed using SPSS version25 IBM-USA.

Results: The overall index of DCr in studied subjects was 11.7. Higher, not significant levels of SUA observed among patients (p=0.43). Significantly higher DMFT among IHD patients compared to control [14.6±10.8, vis 5.0±5.0, p=0.00 one-to-one]. Mean SUA/creatinine ratio was significantly higher in the patients' group (0.017). Gender revealed no impact regarding variation in the mean sera levels of UA and carious status among all studied subjects. Its observed that about half of the applicants had bad carious scores (DMFT>10). DMFT-scores increased bluntly as the ratio of mean SUA/creatinine increased among IHD patients but not in control group.

Conclusion: Patients with IHD had significantly higher caries experiences. Positive nonsignificant association of DCr with hyperuricemic subjects. Positive nonsignificant association of hyperuricemia and IHD. Significant higher SUA/creatinine ratio among the IHD as well as among those with carious experience.

Keywords: uric acid, heart diseases, hyperuricemia

Correspondence:

Hussein O. M. Al – Dahmoshi
Biology Department
College of Science
University of Babylon
Iraq

E-mail Address:

Hussein_gst@yahoo.com

Submitted: 25-04-2020

Revision: 27-05-2020

Accepted Date: 22-06-2020

DOI: 10.31838/jcdr.2020.11.02.21

INTRODUCTION

Worldwide, ischemic heart disease (IHD) signifies multifactorial pathology and the most common cause of morbidity that have a mortality rate of around 12% of total death causes (1-4). It is a well-recognized fact that several multisystemic disorders manifest in the oral cavity, and the best way is to treat the primary reason initially before the symptomatic therapy. One of the commonest systemic illnesses in dental practice in the general populace is IHD (5). Dental caries (DCr) is a long-lasting, most prevalent and complex multifactorial disease considered as one of the chief worries of WHO about oral health (6-8). In the face of inordinate global successes in oral health, difficulties remain in many societies, predominantly among deprived publics in the developing countries.

Uric acid is a heterocyclic-purine end-product, the normal upper limit is 6 mg/dl for females and 7.0 mg/dl for males (9, 10). As an inflammatory mediator, UA could enhance dysfunctioning endothelium and proliferating smooth-muscle cells, thereby promote atherogenesis (9). Then again, with continued mouth uncleaning, UA would contribute to dental calculus synthesis (11). Moreover, higher UA levels in healthy teeth may be ascribed to the formation of ammonia

which in favor mineralization/demineralization steadiness, sharing in plaque pH homeostasis, inhibiting a cariogenic microbiota that is the main obstacle to the progress of DCr (12).

This study aimed to evaluate the causal-effect of SUA and caries status in IHD in Babylon city (central Iraq).

MATERIAL AND METHODS

Source of Data

The study was carried out in Merjan medical city, during the period from the 1st of April to the 15th December 2019. We had examined 118 patients identified as IHD clinically assessed by a cardiologist and 50 healthy subjects (free from any cardiac disorders) been selected from the patients' attendants. A detailed history of smoking, hypertension and diabetes had been taken. Body mass index has also been calculated for all participants.

Settings and Design

This was a retrospective study, aimed to estimate and correlate the serum uric acid (SUA) levels with DCr in both study groups. All the participants were enlightened about

the aim of this observational study in local linguistic and their consent was obtained.

Assessment of Carious Status

DCr was evaluated according to DMFT-index: [the sum of D-decayed, M-missed, F-filled teeth] based on "(13, 14). The smooth/occlusal teeth-exterior have been cleaned with a soft brush, dried out, and examined with dental-mirror and explorer. The DMFT values will be interpreted according to DMF scoring scale.

Grouping of Study Participants

All participants were divided according to their carious status into three classes in which a DMFT value of (1-4) reflects low caries status, (5-9) is moderate and a value greater than 9 is high caries status (15, 16). Then again, for the division of studied subjects into normouricemic and hyperuricemic, a cutoff level of 7.0mg/dl for males and 6.0mg/dl for females were assigned (17).

Biochemical Assays

All participants investigated for serum levels of UA, creatinine, urea nitrogen, according to available conventional techniques, and their serum UA/creatinine ratio had been calculated.

Statistical Study

One-way ANOVA was applied to correlate SUA level with groups of DMFT index. Results are presented as mean±SD. The variation and correlation among variables were allocated significant for all the tests, once *p*-value ≤0.05. The Cronbach's Alpha reliability test for study parameters was >0.83. The data was processed and analyzed using SPSS version25 IBM-USA.

RESULT

Characteristics of Study Parameters

The overall index of DCr in studied subjects was 11.7±10.4, which have mean ages of IHD patients higher than control [59.5 vis 38.5 years respectively]. Out of 168 subjects in this study, males were predominant in both IHD and control groups (77% vis 86% correspondingly). Higher, not significant levels of SUA observed among patients (*p*-0.43). Significantly higher DMFT among IHD patients [14.6±10.8, vis 5.0±5.0, *p*-0.00 one-to-one]. Whereas mean levels of creatinine, blood urea, and BMI were comparable among study subjects. Mean SUA/creatinine ratio was significantly higher in the patients' group (0.017). Risk factors in term of incidence of DM, hypertension, and smoking were significantly higher among IHD patients (table-1).

Table 1: Characteristics of Studied Participants

	IHD	Control	P-value
Age	59.5±13.4	38.5±11.7	0.00
Sex			> 0.05
Male (No %)	91 (77.1%)	43 (86%)	
Serum uric acid	5.7±1.9	4.9±1.3	0.43
Index of Carious State	14.6±10.8	5.0±5.0	0.00
Serum creatinine	79.3±30.4	59.4±28.5	> 0.05
Blood urea	15.8±26.3	17.1±13.8	> 0.05
SUA/Creatinine Ratio	9.8±2.0	2.8±3.1	0.017
Diabetes mellitus (No %)	50 (42.4%)	4 (8%)	0.00
Hypertension (No %)	57 (48%)	3 (6%)	0.00
BMI (kg/m ²)	27.2±5.2	27.5±4.7	> 0.05
Smokers (No %)	48 (40%)	11 (22%)	0.00

Gender Variations

Gender revealed no impact regarding variation in the mean sera levels of UA and carious status among all studied subjects (*p*>0.05). Likewise, all other study variables not

affected by gender other smoking and number of filled teeth (results not appeared); both of them were significantly higher in males (table-2).

Table 2: DMFT Index and SUA categorized According to the Gender (Chi-square test)

	Sex	N	Mean	Std. Deviation	P-value
Index of Caries States	M	134	11.83	10.464	> 0.05
	F	34	11.47	10.337	
Serum Uric acid	M	134	5.503	1.6155	> 0.05
	F	34	5.429	2.4049	

Evaluation of Carious Status

It is observed that about half of the applicants had bad carious scores (DMFT>10), while the other half of them had

comparable carious status distributed equally among other DMFT scores (figure-1).

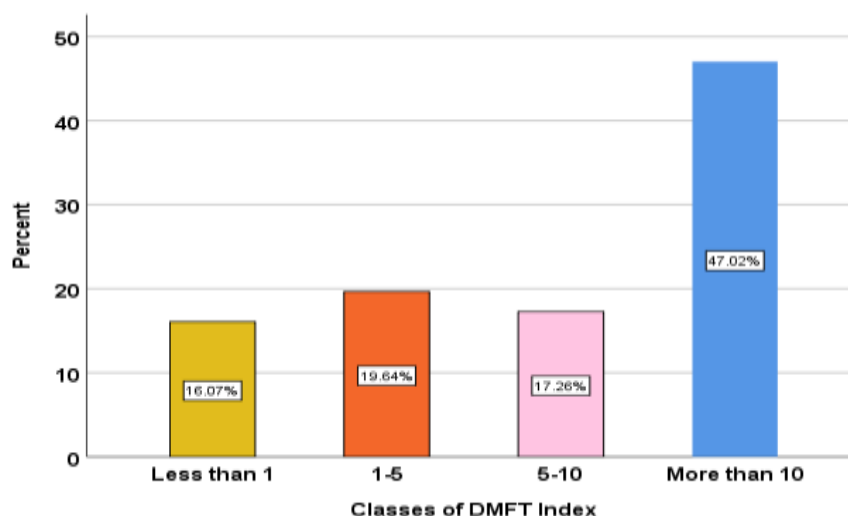


Figure 1: Percent Distribution of Caries Experience (Scores of DMFT) Among Study Subjects

Correlation of Uric Acid and Carious Experience

The data generated in this study display a trend for a SUA to have a positive correlation with waning carious state of both IHD and control subjects, although it does not reach a

statistical significance. DMFT-scores increased bluntly as the ratio of mean SUA/creatinine increased among IHD patients but not in control group (figure-2).

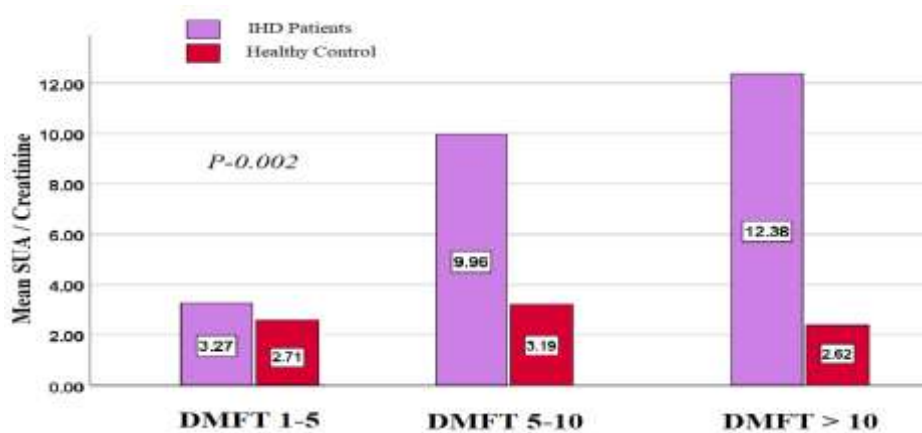


Figure 2: Distribution of Classes of Dental Caries According to Means of SUA / Creatinine Ratio in IHD patients vs Healthy Control

Conversely, carious experiences were not increased obviously among hyperuricemic compared to normouricemic individuals (table-3).

Table 3: Caries Experience Differences Between Hyperuricemic and Normouricemic

	SUA Categories	Number	Mean	Std. Deviation	P-value
Caries Index	Hyperuricemic	51	14.27	11.098	> 0.05
	Normouricemic	117	12.10	11.402	

DMFT-scoring, according to levels of SUA in both IHD patients and control show positive nonsignificant increases of caries experiences with incremental SUA levels (figure-3).

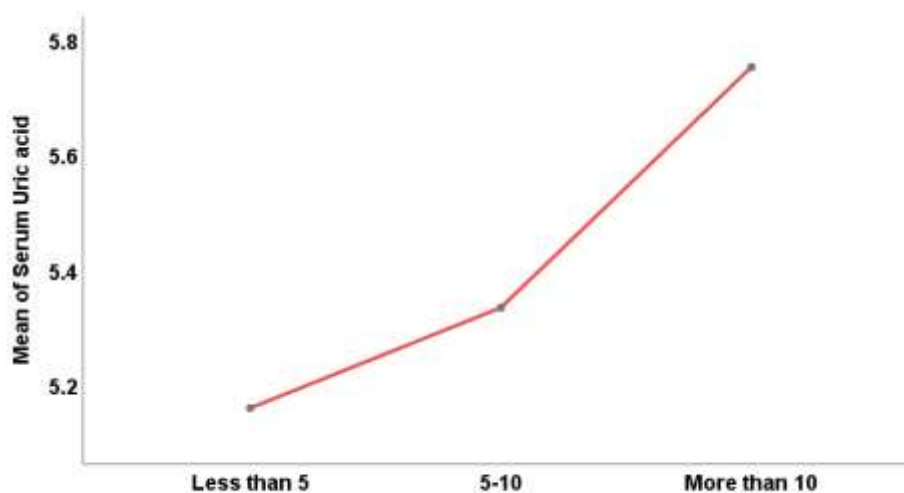


Figure-3: Distribution of Classes of Dental Caries According to Means of SUA / Creatinine Ratio in IHD patients vis Healthy Control

DISCUSSION

A lot of studies have concerted on the risk factors in CVD, of these risk factors is the oral health and the presence or absence of dental disease demonstrated to be associated with IHD (1, 15, 18). This case-control study demonstrated a link between high SUA and DCr in IHD patients. Patients with IHD experienced higher DCr scores compared to the control group. Our finding is close to outcomes published by Leng, et al who found a statistically significant association between oral infectious disease and IHD (18). Kyuwoong Kim and colleagues demonstrated that patients with progressive DCr significantly associated with IHD (19). One of the studies tried to inspect the relation between DCr and atherosclerosis reported a direct correlation between carious experience and atherosclerosis (20). A lot of studies documented this link between atherosclerotic changes and oral disease (1, 15, 21). Till now the actual pathogenesis of the link between DCr and IHD is indistinct. This could be explained as bacteria from DCr spread and cause inflammation in coronary endothelium, besides DCr may aggravate cardiac risk factors of metabolic nature (19). One of the important bacteria that is responsible for DCr is *Streptococcus Mutans*, which was found in the plaques of the vascular wall (22), indicating a proatherogenic role of DCr (20). The authors suggest considering "dental care" in parallel with other risk factors and the physician can consider the worsening of DCr as a bad sign for IHD.

The higher mean age among IHD with a predominance of male sex in this study, is rational as both of them considered one of the risk factor in IHD as inflammation and atherosclerotic events take time to reach to a state of ischemia, and male sex is risk-factor especially in those < 60 years, but still, the female gender is of worse prognosis (23). The age per se is the sharing factor for IHD and DCr, both progress with aging being more in male-gender (24).

Assessment of cardiac troponins is considered the "gold standard" biomarker for diagnosis of IHD (25-27). However, in concordance to other studies (26), our study showed high SUA in IHD patients, though some studies decreasing the risk association of SUA in IHD (28). There is a growing body of evidence suggests that SUA induce

proliferation of vascular smooth muscle fibers with the formation of materials that aid in inflammation, oxidation, and vasoconstriction (29). Uric acid was found in some atheromatous-plaque (30) enhancing the accumulation of platelets (31) in addition to its oxidative role on the endothelium (32).

There is a high incidence of risk factors in this work; like hypertension, diabetes, and smoking in IHD patients. This may reflect the association of hyperuricemia with cardiovascular risk factors besides male sex and age which is also observed by Rathmann et al (33).

There was no significant gender difference of SUA in this study contrary to Masayuki K. et al outcomes that reported lower SUA in females (34). Similarly, the gender had no significant difference in carious status, a finding that does not coincide with scholars that revealed a female predominance in developing DCr. This might be due to hormonal fluctuations during adolescence, menstrual period, and pregnancy that may affect saliva composition and oral health (35). These differences in results could reflect the limitation of the study regarding sample size and especially female sample size.

In this study, we used the SUA/creatinine ratio, and up to our information, no other studies used this ratio in IHD. Of note, the SUA/creatinine ratio was used in other clinical conditions like lung disease (36) renal disease (37) and metabolic syndrome with diabetes mellitus of type-II (38). Other study reported that in most patient suffering halitosis, SUA/Creatinine ratio was higher in patients than in the control group (39). This can empower our finding of a significantly higher level of this ratio in IHD patients henceforth, SUA/creatinine ratio can be considered as a marker in IHD patients as well as metabolic syndrome.

This study demonstrates a positive correlation between SUA with the carious state of participants. One of several factors that affect oral health is the mouth normal flora, which has a vital role in protection against infection although it is affected by the PH of the oral cavity. In hyperuricemic subjects, high salivary urate secretion reduces PH and aggravate the oral disease (40). One of the oral bacteria is

Prevotella Intermedia was documented with high abundance in hyperuricemic subjects (41).

More than one explanation is proposed to clarify the association between hyperuricemia. Changes of PH during hyperuricemic state predispose for poor oral hygiene (40). It has been described that in caries-resistant subjects a more alkaline biofilm is encountered (42). Bacteria can invade the circulation and stimulate immune response with cytokines formation and stimulate innate and adaptive immunity, can affect cardiovascular inflammatory response (43). Other bacterial types like *Streptococcus Anginosus* also found in DCr (44), particularly in the saliva of a hyperuricemic patient (43). Subsequently, the hyperuricemic patient must take care of oral hygiene to reduce the risk of IHD.

In this paper, and under the light of above-attained results, although carious experiences were statistically of no difference among hyperuricemic compared to normouricemic individuals. Yet, it is more in hyperuricemic patients and this argues to increase the sample size of hyperuricemic patients. The authors claim that the association of hyperuricemia and caries experiences in IHD is crucial, to an extent that those with IHD should be frequently examined by dentists for proper care. Again SUA/creatinine ratio was of remarkable value in the DMFT-scores as this score increased bluntly as the ratio increased among IHD patients. Further researches in this field could expose much about the exact causal-effect relationship of SUA and DCr, and help to guide IHD patients, dentists and cardiologists for better management of IHD.

CONCLUSION

Patients with IHD had significantly higher caries experiences. Positive nonsignificant association of DCr with hyperuricemic subjects. Positive nonsignificant association of hyperuricemia and IHD. Significant higher SUA/creatinine ratio among the IHD as well as among those with carious experience.

FINANCIAL SUPPORT AND SPONSORSHIP

Nil.

CONFLICTS OF INTEREST

The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or nonfinancial in this article.

REFERENCES

1. Hayder Abdul- Amir Maki Al-hindi SFA-S, Basim MH Zwain, Thekra Abid Al-Kashwan Jaber Relationship of Salivary & Plasma Troponin Levels of Patients with AMI in Merjan medical city of Babylon Province: Cross-Sectional Clinical Stud. Al-Kufa University Journal for Biology. 2016;8 (3):6.
2. Hayder Abdul-Amir Maki Al-hindi MJM, Thekra Abid Jaber Al-kashwan, Ahmed Sudan, Saja Ahmed Abdul-Razzaq. On Admission Levels of High Sensitive C-Reactive Protein as A Biomarker in Acute Myocardial Infarction: A Case-Control Study. Indian Journal of Public Health Research & Development. 2019;10(4):5.
3. Abed DA, Jasim R, Al-Hindy HA-A, Obaid AW. Cystatin-C in patients with acute coronary syndrome: Correlation with ventricular dysfunction, and affected coronary vessels. Journal of Contemporary Medical Sciences. 2020;6(1).
4. Asseel KS, Raghdan A-S, Raad J, Hayder Abdul-Amir Makki A-H. Biochemical Significance of Cystatin-C and High-Sensitive CRP in Patients with Acute Coronary Syndrome; any Clinical Correlation with Diagnosis and Ejection Fraction. SRP. 2020;11(3):301.
5. Swathi M RT, Reddy RS, Begum MR, Rajesh N, Reshmi T. Oral manifestations in diabetic patients under treatment for ischemic heart diseases: A comparative observational study. J Indian Acad Oral Med Radiol. 2018;30(4):7.
6. Shaki F A-NM, Maleki F, Yazdani Charati J, Nahvi A. Evaluation of Some Caries-Related Factors in the Saliva of 3-5 Year Old Children in Sari, Northern Iran. Int J Pediatr. 2020;8(8):9.
7. Mithra N. Hegde SK, Nidarsh D. Hegde & Shilpa S. Shetty. RELATION BETWEEN SALIVARY AND SERUM VITAMINC LEVELS AND DENTAL CARIES EXPERIENCE IN ADULTS - A BIOCHEMICAL STUDY. NUJHS 2013;3(4):4.
8. Shrestha S SR. Correlation Between Oral Health and Body Mass Index among Nepalese Teachers. KATHMANDU UNIVERSITY MEDICAL JOURNAL. 2016;55(3):4.
9. Hayder Abdul-Amir Maki Al-Hindi MJM, Thekra Abid Jaber Al-Kashwan, Ahmed Sudan, Saja Ahmed Abdul-Razzaq. Correlation of on Admission Levels of Serum Uric Acid with Acute Myocardial Infarction: Case-Control Study. Journal of Global Pharma Technology 2019;11(7):6.
10. Shani M, Vinker S, Dinour D, Leiba M, Twig G, Holtzman EJ, et al. High Normal Uric Acid Levels Are Associated with an Increased Risk of Diabetes in Lean, Normoglycemic Healthy Women. The Journal of Clinical Endocrinology & Metabolism. 2016;101(10):3772-8.
11. Shibasaki K, Ueda J, Ikarashi R, Kitagawa T, Yamaguchi A. Uric Acid in Saliva and Involvement in Dental Calculus Formation 2010.
12. Nireeksha MNHaSKN. Salivary Urea and Uric Acid Levels as Biomarkers in Dental Caries. Oral Health and Dentistry 2018;3(1):4.
13. Patel RN, Eaton KA, Pitts N, Schulte A, Pieper K, White S. Variation in methods used to determine national mean DMFT scores for 12-year-old children in European countries. Community dental health. 2016;33:286-91.
14. WHO. World Health Organization, oral health survey: basic methods. Third Edition ed: Geneva; 1987.
15. Hayder Abdul- Amir Maki Al-hindy ASAM, Basim MH Zwain. Decayed, Missed, Filled Teeth Scores in Iraqi Patients with Acute Myocardial Infarction. Al-Kufa University Journal for Biology. 2016;8(3):7.
16. Shirazi U-e-R, Naz F, Yousuf M. DMFT INDEX AMONG DENTAL UNDERGRADUATES OF LAHORE MEDICAL AND DENTAL COLLEGE IN

- DIFFERENT PROFESSIONAL YEARS OF DENTISTRY. *Pakistan Oral and Dental Journal*. 2013;33:156-9.
17. Papavasileiou MV PS, Moustakas G, Vrakas CS, Kalogeropoulos P, Karamanou A and Pittaras A. The Role of Uric Acid in Carbohydrate Metabolism among Hypertensive Individuals *Haematology International Journal*. 2018;2(1):10.
 18. Leng W-D, Zeng X-T, Kwong JSW, Hua X-P. Periodontal disease and risk of coronary heart disease: An updated meta-analysis of prospective cohort studies. *International Journal of Cardiology*. 2015;201:469-72.
 19. Kim K, Choi S, Chang J, Kim SM, Kim SJ, Kim RJ-Y, et al. Severity of dental caries and risk of coronary heart disease in middle-aged men and women: a population-based cohort study of Korean adults, 2002–2013. *Scientific Reports*. 2019;9(1):10491.
 20. Glodny B, Nasser P, Crismani A, Schoenherr E, Luger AK, Bertl K, et al. The occurrence of dental caries is associated with atherosclerosis. *Clinics (Sao Paulo)*. 2013;68(7):946-53.
 21. Dhadse P, Gattani D, Mishra R. The link between periodontal disease and cardiovascular disease: How far we have come in last two decades ? *J Indian Soc Periodontol*. 2010;14(3):148-54.
 22. Nakano K, Inaba H, Nomura R, Nemoto H, Takeda M, Yoshioka H, et al. Detection of cariogenic *Streptococcus mutans* in extirpated heart valve and atheromatous plaque specimens. *J Clin Microbiol*. 2006;44(9):3313-7.
 23. Tomaszewski M, Topyła W, Kijewski BG, Miotła P, Waciński P. Does gender influence the outcome of ischemic heart disease? *Prz Menopauzalny*. 2019;18(1):51-6.
 24. Josphipura KJ, Rimm EB, Douglass CW, Trichopoulos D, Ascherio A, Willett WC. Poor oral health and coronary heart disease. *J Dent Res*. 1996;75(9):1631-6.
 25. Ali Kareem Hameed GSH, Amir Sahib Al-Mumin. D-dimer and troponin T Biomarkers in Acute Coronary Syndrome in Hilla City. *International Journal of Chem Tech Research*. 2016;9(11):13.
 26. Hajir Karim Abdul-Hussein FSD, Ameera Jasim Al-Aaraji, Hayder Abdul-Amir Makki Al-Hindy, Mazin Jaafar Mousa. Biochemical causal-effect of circulatory uric acid, and HSCRP and their diagnostic correlation in admitted patients with ischemic heart diseases. *Journal of Cardiovascular Disease Research* 2020;11(4).
 27. Hayder Abdul-Amir Maki Al-hindy MJM, Nawrass J Alsalihi. Circulating Atrial Natriuretic Peptide (NT-proBNP) vis Cardiac-Troponin (cT-I) After Acute Coronary Syndrome: Relationship with Left Ventricular Ejection Fraction and Number of Affected Vessels by Coronary Angiography. *Biochemical and Cellular Archives*. 2020;20(2).
 28. Cheong E, Ryu S, Lee JY, Lee SH, Sung JW, Cho DS, et al. Association between serum uric acid and cardiovascular mortality and all-cause mortality: a cohort study. *J Hypertens*. 2017;35 Suppl 1:S3-s9.
 29. Kang DH, Park SK, Lee IK, Johnson RJ. Uric acid-induced C-reactive protein expression: implication on cell proliferation and nitric oxide production of human vascular cells. *J Am Soc Nephrol*. 2005;16(12):3553-62.
 30. Corry DB, Eslami P, Yamamoto K, Nyby MD, Makino H, Tuck ML. Uric acid stimulates vascular smooth muscle cell proliferation and oxidative stress via the vascular renin-angiotensin system. *J Hypertens*. 2008;26(2):269-75.
 31. Suarna C, Dean RT, May J, Stocker R. Human atherosclerotic plaque contains both oxidized lipids and relatively large amounts of alpha-tocopherol and ascorbate. *Arterioscler Thromb Vasc Biol*. 1995;15(10):1616-24.
 32. Ginsberg MH, Kozin F, O'Malley M, McCarty DJ. Release of platelet constituents by monosodium urate crystals. *J Clin Invest*. 1977;60(5):999-1007.
 33. Rathmann W, Funkhouser E, Dyer AR, Roseman JM. Relations of hyperuricemia with the various components of the insulin resistance syndrome in young black and white adults: the CARDIA study. *Coronary Artery Risk Development in Young Adults*. *Ann Epidemiol*. 1998;8(4):250-61.
 34. Kawabe M, Sato A, Hoshi T, Sakai S, Hiraya D, Watabe H, et al. Gender differences in the association between serum uric acid and prognosis in patients with acute coronary syndrome. *J Cardiol*. 2016;67(2):170-6.
 35. Lukacs JR, Largaespada LL. Explaining sex differences in dental caries prevalence: saliva, hormones, and "life-history" etiologies. *Am J Hum Biol*. 2006;18(4):540-55.
 36. Durmus Kocak N, Sasak G, Aka Akturk U, Akgun M, Boga S, Sengul A, et al. Serum Uric Acid Levels and Uric Acid/Creatinine Ratios in Stable Chronic Obstructive Pulmonary Disease (COPD) Patients: Are These Parameters Efficient Predictors of Patients at Risk for Exacerbation and/or Severity of Disease? *Med Sci Monit*. 2016;22:4169-76.
 37. Gu L, Huang L, Wu H, Lou Q, Bian R. Serum uric acid to creatinine ratio: A predictor of incident chronic kidney disease in type 2 diabetes mellitus patients with preserved kidney function. *Diab Vasc Dis Res*. 2017;14(3):221-5.
 38. Al-Daghri NM, Al-Attas OS, Wani K, Sabico S, Alokail MS. Serum Uric Acid to Creatinine Ratio and Risk of Metabolic Syndrome in Saudi Type 2 Diabetic Patients. *Scientific reports*. 2017;7(1):12104-.
 39. Khozeimeh F, Torabinia N, Shahnasari S, Shafaei H, Mousavi SA. Determination of salivary urea and uric acid of patients with halitosis. *Dent Res J (Isfahan)*. 2017;14(4):241-5.
 40. Zhao J, Huang Y. Salivary uric acid as a noninvasive biomarker for monitoring the efficacy of urate-lowering therapy in a patient with chronic gouty arthropathy. *Clin Chim Acta*. 2015;450:115-20.
 41. Kamma JJ, Nakou M, Manti FA. Microbiota of rapidly progressive periodontitis lesions in association with clinical parameters. *J Periodontol*. 1994;65(11):1073-8.

42. Loesche WJ. Role of Streptococcus mutans in human dental decay. Microbiological reviews. 1986;50(4):353-80.
43. Liu J, Cui L, Yan X, Zhao X, Cheng J, Zhou L, et al. Analysis of Oral Microbiota Revealed High Abundance of Prevotella Intermedia in Gout Patients. Cell Physiol Biochem. 2018;49(5):1804-12.
44. Rawlinson A, Duerden BI, Goodwin L. New findings on the microbial flora associated with adult periodontitis. J Dent. 1993;21(3):179-84.