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THE RELATION OF SERUM URIC ACID WITH A RISK MARKERS **OF** CARDIOVASCULAR DISEASE **PATIENTS** | 17 |

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Abstract

Uric acid is the last **product of purine metabolism** . There has been **a** | 8 |

recent rise in the prevalence of cardiovascular disorders which have been associated to

elevated levels of serum uric acid | 12 |

(SUA). This study evaluated a group of people with cardiovascular disease to see whether there was any correlation

between serum uric acid and a range of | 29 |

biochemical markers. Thrombosis,

ischemic heart disease (IHD), and cardiovascular **disease** | 12 |

(CVD)

patients were all **included in the** research, which had **a total** enrollment **of** 150. **Patients**

| 18 |

with IHD and CVD who had higher

uric acid, glucose, cholesterol, triglycerides , urea, **and**

| 10 |

creatinine levels as well as lower HDL .Thromboembolism patients had elevated

levels of uric acid, glucose, cholesterol , triglyceride, urea, **and**

| 10 |

creatinine, and lower levels of HDL. logistic regression analysis showed a significant link

between elevated uric acid levels (hyperuricemia) **and** an **increased risk of**

| 20 |

ischemic heart disease (IHD).We concluded that hyperuricemia has a significant influence in the development of cardiovascular vascular illnesses

such as ischemic heart disease and

| 34 |

thromboembolism. Keywords: Uric acid, Cardiovascular disease, Ischemic heart disease, Thromboembolism, D-dimer, Troponin.

1. Introduction Uric acid (UA) is the last **product of purine metabolism. The**

| 14 |

body's UA production and excretion are in equilibrium under normal circumstances. Hyperuricemia results from a disturbance in this delicate equilibrium. A UA level of 7

mg/dL or higher **in males and** 6 **mg/dL or** higher **in females** is considered to **be**

| 13 |

hyperuricemia[1]. the UA level threshold increased risk much lower than clinical diagnostic criteria for overall

> **mortality (4.7 mg/dL) and cardiovascular mortality (5 mg/dL** | 5 |

), respectively [2]. Hyperuricemia has superseded hypertension, hyperglycemia, and hyperlipidemia as the "fourth greatest" risk factor for cardiovascular disease, according to a new research [1,3-5]. Metabolic syndrome may be caused by hyperuricemia, according to certain theories [6,7]. Myocardial infarction, coronary artery disease, heart failure, and thromboembolism may all be predicted by uric acid levels in healthy individuals, as well as troponin and D-Dimer [8,9].

> **In the present study, we aimed to**   illuminate   **the risk** | 21 |

ratio and the relation

> **of serum uric acid**   with   **risk**   marker   **of cardiovascular disease** | 33 |

like troponin and D-Dimer.

> **2. Materials and Methods 2.1. Subjects**   Our   **study conducted on** | 7 |

150 patients divided in to 3 groups which diagnosed by physicians, first group suffering from IHD Troponin-I positive >0.3 (ng/mL), the seconed group was within thrombosis D-Dimer positive >500 (mg/dL) and thired group was within CVD under control. The mean of age for all patients was 40-70 years old. Study samples were collected from patients attending to Respirotory care unit and cardiac care unit at Baghdad teaching hospital/ Medical city from January 2022 to July 2022.

> **All participants were informed about the study procedure through a written consent form before participation. The study complied with the Declaration of Helsinki, and the research protocol was approved by** | 2 |

Medical City Research Ethics Committee (Decision date: 01.06.2022, Decision no: 2022/21853). *Corresponding author. e-mail address: haydarjassim5@gmail.com. A

> **body mass index BMI (Kg/m2**   ) and   **blood pressure**   category (**mm Hg** | 16 |

) was defien according to American Heart Association (AHA) [10].

Blood samples were obtained from the subjects by venipuncture **and centrifuged** | 6

immediately, and serum samples were analyzed directly without storage. In the central laboratory of Baghdad Teaching Hospital, a serum concentration of total serum uric acid, cholestero, triglyceride high density lipoprotien (HDL), urea and creatinin was measured by enzymatic methods, whereas

plasma glucose was measured by the hexokinase method | 32

by an autoanalyzer. Troponin-I and D-Dimer levels were assayed by the chemiluminescent immunoassay technique by an autoanalyzer. 2.2

Statistical Analysis Chi-square (X2) **tests were used to** compare percentages in **the** | 19

present study's data. t. A test to compare two numerical variables was used. Measurement of the linear connection

between two variables was done **using Pearson correlation test** | 22

. A significance threshold of 0.05 was used in the test. Logistic regression analysis and its 95% confidence intervals was used to measured odd ratio. SPSS v.23 programs used to analyze current data 3.

Results and Discussion 3. **1** . Results **The** mean ages **of the studied groups** | 1

were within fifth to sixth decades, and this

difference was statistically non- **significant (P= 0** .2). Also, **the** results **of** | 3

this table documented that most cases of Ischemic patients and cardiovascular under control were among male groups with 42(84.0%), 32(64.0%) respectively, while most cases of Thrombolisim in patients with Covid-Positive were recorded among female groups 32(64.0%), and these differences were

statistically highly significant (P< 0.001) as shown in table 1 | 15

. Table 1. Demographical picture of studied groups (N=150) Parameters Test Ischemic group (N=50) Thrombolisim group (N=50) Cardiovascular under Control (N=50) Sig. Age (Years) M± SD 60.46±10.67 56.56±14.05 57.68±10.74 P-value=0.2 (N.S) (30-44) N (%) 2 (4.0%) 10 (20.0%) 5 (10.0%) Chi- (45-59) N (%) 25 (50.0%) 18 (36.0%) 24 (48.0%) sequare=7.6 (60-74) N (%) 17 (34.0%) 18 (36.0%) 17 (34.0%) P-value=0.2 (75-89) N (%) 6 (12.0%) 4 (8.0%) 4 (8.0%) (N.S) Male 42 (84.0%) 18 (36.0%) 32 (64.0%) Chi- Gender N (%) Female 8 (16.0%) 32(64.0%) 18 (36.0%) sequare=24.5 P-value <0.001 (H.S) Normal weight 3 (6.0%) 2(4.0%) 4 (8.0%) Chi- BMI (Kg/m2) Overweight 23 (46.0%) 16 (32.0%) 16 (32.0%) sequare=3.6 Obese 24 (48.0%) 32 (64.0%) 30 (60.0%) P-value= 0.4 (N.S) Blood Normal 10 (20.0%) 16 (32.0%) 11 (22.0%) Chi- sequare=3.7 pressure Hypotension 7 (14.0%) 9 (18.0%) 6 (12.0%) P-value= 0.4 Hypertension 33 (66.0%) 25 (50.0%) 33 (66.0%) (N.S) Table 2 demonstrated that there was increased in serum glucose levels in the three groups (<110 mg/dL) Ischemic group, Thromboembolism group and Cardiovascular under control with means and standard deviation (S.Ds) value (209.04±133.20, 140.20±73.22, 197.22±89.38) respectively, with this highly significant differences (P= 0.001).In regard to cholesterol (mg/dL) and triglyceride (mg/dL) levels, there was an increase in their levels among the three groups above the normal value of both indicated by the increase in their mean and (S.Ds) value Table 2. Means of biochemical parameters among the studied groups (N=150). Parameter Studied group Mean+SD *P value Glucose Ischemic group (N=50) 209.04±133.20 0.002 (H.S) Thrombolisim group (N=50) 140.20±73.22 Cardiovascular under Control (N=50) 197.22±89.38 Ischemic group (N=50) 199.74±49.56 Cholesterol Thrombolisim group (N=50) 162.24±55.21 0.009 Cardiovascular under Control (N=50) 184.82±74.73 (H.S) Ischemic group (N=50) 183.74±101.60 Triglycerdie Thrombolisim group (N=50) 176.40±97.67 0.04 Cardiovascular under Control (N=50) 243.78±206.04 (S) Ischemic group (N=50) 46.64±15.86, 43.84±10.93 HDL Thrombolisim group (N=50) 38.68±14.07 0.01 Cardiovascular under Control (N=50) 43.84±10.93 (S) Tn-I Ischemic group (N=50) 7.62±7.09, <0.001 (H.S) Thrombolisim group (N=50) 0.034±0.03 Cardiovascular under Control (N=50) 0.026±0.03 D-Dimer Ischemic group (N=50) 318.10±78.95 Thrombolisim group (N=50) 2089.76±1560.34 <0.001 (H.S) Cardiovascular under Control (N=50) 307.82±85.88 Uric acid Ischemic group (N=50) 6.42±2.06 0.1 Cardiovascular under Control (N=50) 5.66±2.11 Thrombolisim group (N=50) 5.71±1.98 (N.S) Ischemic group (N=50) 51.24±25.06 Urea Thrombolisim group (N=50) 49.56±20.91 0.3 Cardiovascular under Control (N=50) 43.80±18.95 (N.S) Creatinine Ischemic group (N=50) 1.17±0.9, 1.14±0.54, 1.13±0.59 0.2 Cardiovascular under Control (N=50) 1.13±0.59 Thrombolisim group (N=50) 1.14±0.54 (N.S) (199.74±49.56, 162.24±55.21, 184.82±74.73) , (183.74±101.60, 176.40±97.67, 243.78±206.04) respectively, and these differences ranged from highly significant to significant (

P= 0.009, P= 0.04) respectively. On the other hand   , the   **levels of** | 11 |

HDL were normal (40-60) mg/dL among the Ischemic and Cardiovascular under control groups with means and (S.Ds) values (46.64±15.86, 43.84±10.93) respectively versus lower levels of of HDL (> 40 mg/dL) with mean and (S.Ds) (38.68±14.07) among thromboembolism group, with a statistically

significant difference (P= 0.01). The results of the current study   also   **showed that the levels of** | 1 |

Tn-I were increased among the Ischemic groups (< 0.3 ng/mL) compared to normal levels up to 0.3 ng/mL among the thromboembolism and cardiovascular under control groups with mean and (S.Ds) values (7.62±7.09, 0.034±0.03, 0.026±0.03) respectively, with highly significant differences (P= 0.001). It was found that the levels of D- dimer were highly elevated (<400 mg/dL) among patients attacked with Thromboembolism and Covid-19 with means and (S.Ds) values of (2089.76±1560.34), while the levels among the Ischemic and cardiovascular under control group were within the normal range (up to 500 mg/dL), with a

highly significant difference (P= 0.01). The results of   1

this table also revealed that the levels of uric acid were within normal among the three groups (> 7.2 mg/dL) with different range of means and (S.Ds), with non-significant differences (P= 0.1). In regard to renal function tests including urea, there was an increase in urea levels among ischemic and Thromboembolism group with means and (SDs) values (51.24±25.06, 49.56±20.91) versus the cardiovascular under control group (43.80±18.95), with non-significant difference (P=0.3). While the levels of the creatinine were found to be normal among the three groups with different means and (SDs) values (1.17±0.9, 1.14±0.54, 1.13±0.59) respectively, with non-significant differences (P=0.2). Results in Table 3 showed that 21(42.0%) cases out of 50 cases of Ischemic group suffered from hyperuricemia versus 29(58.0%) had normal uric acid, and lower cases of hyperuricemia were found among cardiovascular under control group 11(22.0%) out of 50, while the rest cases 39(78.0%) under the same group were having normal uric acids, and only 15(30.0%) cases out of 50 of Thromboembolism group had hyperuricemia versus 35(70.0%) were having normal uric acid, with non−significant differences (Chi-square= 4.7, P= 0.09). Table 3. Comparison of serum uric acid according to cutoff point among studied groups (N=150). Categorial uric acid levels (mg/dL) N (%) Ischemic group (N=50) Thrombolisim group (

N=50) Study Groups (N   =150) Cardiovascular under   **Control (N=50**   23

) Total 2.5-7.2 Normal N (%) 29 (58.0%) 35 (70.0%) 39 (78.0%) 103 (68.7%) >7.2 Hyper N (%) 21 (42.0%) 15 (30.0%) 11 (22.0%) 47 (31.3%)

Total N (%) 50 (100.0%) 50 (100.0   %) 50 (**100.0**   %) 150 (100.0%)   **Chi**   -sequare 4.7   **P**   3

-value 0.09 (N.S) In logistic regression analysis, the assessment of ischemic risk was based on three models, in crude analysis we assessed the effect of hyperuricemia as predictor of ischemia in unadjusted analysis hyperuricemia considerable as a risk factor in model 1 and 2 with 1.165% and 1.16% respectively, in model 3 after removing most of the confounder there was significant association with 1.36.6% increased risk of ischemic with hyperuricemia which indicate that hyperuricemia is dependent predictor of ischemia, as illustrated in Table 4. In all models including crude analysis,

there was no significant association between hyperuricemia **and** increased **risk** | 30 |

of thrombotic events, as illustrated

in Table 4. Table 4. Logistic regression analysis | 31 |

and its 95% confidence intervals for both ischemic and thromboembolic groups according to uric acid levels. OR 95%CI p-value Ischemic group risk assessment Crude analysis 1.197 0.983 − 1.457 0.074 Model 1 1.165 0.951 − 1.428 0.141 Model 2 1.16 0.916 − 1.468 0.219 Model 3 1.366 1.013 − 1.841 0.041 Thromboembolic group risk assessment Crude analysis 1.013 0.835 − 1.229 0.898 Model 1 1.023 0.835 − 1.253 0.829 Model 2 0.908 0.712 − 1.159 0.440 Model 3 0.846 0.636 − 1.129 0.256

Model 1: age and gender Model 2: Model 1 + BMI , urea, and creatinine **Model 3: Model 2** | 9 |

+ HDL, TG, cholesterol, glucose, D-Dimer (were excluded in the second group) OR: odd ratio, CI: confidence interval 3.2. Discussion The average age of the patients evaluated of our study was found to be between the fifth and sixth decades. There were more instances of thromboembolism in patients with Covid-Positive in women than men, which further supports the notion that males are more likely to suffer from ischemic heart disease and have their cardiovascular systems under control. AHA reports that the incidence of cardiovascular disease (CVD)

among men and women in the United States | 27 |

is approximately 40% between the ages of 40 and 59, and approximately 75% between the ages of 60 and 79 [12]. Most cardiovascular disease (CVD) fatalities occur between the ages of 60 and 79, according to the AHA's 2019 Heart Disease and Stroke Statistical Update, which is conduct with our study [11,12]. In the three groups we analyzed, thromboembolism, ischemic heart disease, and cardiovascular disease under control, we found an increase in glucose, cholesterol, triglycerides, troponin, and urea, while HDL levels were normal in the aforementioned categories and dropped in the thromboembolism cases. In thromboembolism, D-dimer levels were shown to be elevated, but they were unaltered in CVD and ischemic heart disease. However, creatinine levels were found to be within the normal range in all three groups investigated. T2DM patients

have a greater risk of cardiovascular disease (CVD) **and** | 26 |

a still remarkable cardiovascular mortality, despite advancements in many risk factors targeting T2DM patients [13].

People with diabetes have a two to three **times greater risk of developing cardiovascular disease** 4 and mortality **than** those **without the**

condition. People with diabetes over the age of 40 have a shortened life expectancy of 6–7 years, and this decrease is compounded in individuals with chronic cardiovascular disease, which is identical to our study finding [14]. Dyslipidemia is now well recognized as a risk factor for heart disease (CVD). Lowering LDL-C levels with statins reduces one's chance of developing a life-threatening cardiovascular illness [15]. In epidemiological studies, elevated triglyceride levels have been related to a greater risk of cardiovascular disease (CV) [16]. According to scientific investigations, persons with high triglyceride levels are less likely to develop cardiovascular disease (CVD) [17]. Biochemical indicators such as glucose, cholesterol, triglyceride, D-Dimer and Troponin are important biomarkers for the identification of cardiovascular diseases, according to our study. fibrin breakdown product that has been cross-linked Solvent degradation generates D-dimer, which is a soluble by-product. D-dimer levels are associated with thrombosis-related illnesses [18]. D-dimer is often used to diagnose and monitor thrombosis, pulmonary embolism, and blood clots [19]. People with coronary artery disease

have been shown **to** have **an elevated risk of cardiovascular** 24

disease and an even worse prognosis if their D-dimer levels are high [20]. Using cardiac troponin is the gold standard for diagnosing acute coronary syndrome or acute myocardial infarction [21]. As more cardiac troponin testing is available and used, more people are showing elevated cardiac troponin levels that may be clinically relevant [22]. Greater troponin levels in the early and mid-stages after a heart attack are now shown in retrospective clinical trial populations to be related with

a higher risk of recurrent **cardiovascular events [23]. The** 25

findings showed a rise in uric acid in most instances of cardiovascular disease (CVD) under management, IHD and thromboembolism, as well as associated risk factors, as serum uric acid levels were significantly connected. After hypertension, high blood sugar, and high cholesterol, it is currently the "fourth highest" risk factor for cardiovascular disease. There are around 170 million Chinese and 32,5 million Americans who are affected by hyperuricemia, according to these estimates, which is conduct with our study [1,3]. According to our results from an analysis using logistic regression, excessive levels of uric acid (hyperuricemia) are linked to a higher risk of ischemic heart disease (IHD). Several long-term investigations

have shown an association between increased levels of **uric acid** in the blood **and** 28

various cardiovascular diseases, strokes included[24]. According to current studies, a high SUA level may worsen cardiovascular disease, such as heart attacks and strokes [25,26] According to a recent study [27,28], hyperuricemia has been linked to an increase in intracellular oxidative stress, inflammation, vascular constriction, and an endothelial dysfunction that leads to atherosclerosis and cardiovascular disease[9]. For future studies, we recommend increase the sample size of the study patients to obtain more precise results. Include other types of cardiovascular types and complication within the study a several health issues like excessive blood pressure and coronary artery disease as well as congenital and heart failure are addressed. Acknowledgment The author would like to dedicate this research to the soul of the martyr Bassam AL-KHALIDI. References [1] Hao, Y., Li, H., Cao, Y., Chen, Y., Lei, M., Zhang, T. and Qian, Z. 2019. Uricase and horseradish peroxidase hybrid CaHPO4 nanoflower integrated with transcutaneous patches for treatment of hyperuricemia. Journal of Biomedical Nanotechnology, 15(5): 951-965.342. [2] Virdis, A., Masi, S., Casiglia, E., Tikhonoff, V., Cicero, A. F. G. and Ungar, A. 2020. Identification of the Uric Acid Thresholds Predicting an Increased Total and Cardiovascular Mortality Over 20 Years. Hypertension, 75 (2): 302–308. [3] Singh, G., Lingala, B. and Mithal, A. 2019. Gout and hyperuricaemia in the USA: prevalence and trends. Rheumatol. (Oxford)., 58 (12): 2177–2180. [4] Kuwabara, M., Niwa, K., Hisatome, I., Nakagawa, T., Roncal-Jimenez, C. A. andres-Hernando, A. and Johnson, R. J. 2017. Asymptomatic hyperuricemia without comorbidities predicts cardiometabolic diseases: five-year Japanese cohort study. Hypertension., 69(6): 1036-1044. [5] Maruhashi, T., Hisatome, I., Kihara, Y. and Higashi, Y. 2018. Hyperuricemia and endothelial function: from molecular background to clinical perspectives. Atherosclerosis., 278: 226-231. [6] Fujimoto, T. and Parton, R. G. 2011. Not just fat: the structure and function of the lipid droplet. Cold Spring Harbor perspectives in biology., 3(3): a004838. [7] Rana, J. S., Liu, J. Y., Moffet, H. H., Boklage, S. H., Khan, I. and Karter, A. J. 2018. Risk of incident atherosclerotic cardiovascular DiseaseEvents by achieved Atherogenic lipid levels Among62, 428 statin- treated individuals with diabetes mellitus. The American Journal of Cardiology., 122(5): 762-767. [8] Go, A. S., Mozaffarian, D., Roger, V. L., Benjamin, E. J., Berry, J. D., Borden, W. B. and Turner, M. B. 2013. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. Circulation., 127(1): e6-e245. [9] Zhao, G., Huang, L., Song, M. and Song, Y. 2013. Baseline serum uric acid level as a predictor of cardiovascular disease related mortality and all-cause mortality: a meta-analysis of prospective studies. Atherosclerosis., 231(1): 61-68. [10] American Heart Association. 2014. Heart Attack and Strocke Symtomps. [11] Yazdanyar, A. and Newman, A. B. 2009. The burden of cardiovascular disease in the elderly: morbidity, mortality, and costs. Clinics in geriatric medicine., 25(4): 563-577. [12] Benjamin, E. J., Muntner, P., Alonso, A., Bittencourt, M. S., Callaway, C. W., Carson, A. P. and American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. 2019. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. Circulation., 139(10): e56-e528. [13] Rawshani, A., Rawshani, A., Franzén, S., Eliasson, B., Svensson, A. M., Miftaraj, M. and Gudbjörnsdottir, S. 2017. Mortality and cardiovascular disease in type 1 and type 2 diabetes. New England journal of medicine., 376(15): 1407-1418. [14] Menotti, A., Lanti, M., Kromhout, D., Kafatos, A., Nedeljkovic, S. and Nissinen, A. 2005. Short and long term association of a single serum cholesterol measurement in middLe-aged men in prediction of fatal coronary and other cardiovascular events: a cross-cultural comparison through Europe. European journal of epidemiology., 20(7): 597-604. [15] Rana, J. S., Liu, J. Y., Moffet, H. H., Boklage, S. H., Khan, I. and Karter, A. J. 2018. Risk of incident atherosclerotic cardiovascular DiseaseEvents by achieved Atherogenic lipid levels Among62, 428 statin- treated individuals with diabetes mellitus. The American Journal of Cardiology., 122(5): 762-767. [16] Boullart, A. C. I., De Graaf, J. and Stalenhoef, A. F. 2012. Serum triglycerides and risk of cardiovascular disease. Biochimica et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids., 1821(5): 867-875. [17] Miller, M., Stone, N. J., Ballantyne, C., Bittner, V., Criqui, M. H., Ginsberg, H. N. and

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