

Association between serum uric acid and blood glucose in diabetic individuals: NHANES 2017- Mar.2020

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Abstract. Studies have shown conceivable relationship among serum uric corrosive (SUA), blood glucose (BG) and diabetes mellitus (DM), yet there are not many which examine the association among SUA and BG. The goal of this study is to help or reject the past presumption of the examinations and further close the conceivable association of SUA, BG and DM. Concentrate on information is from Public Wellbeing and Nourishment Assessment Study (NHANES) 2017-2020 review data set. Correlations of various conceivable related qualities of a sum of 1221 members are incorporated by making sense of trademark table, univariate and multivariate straight relapse examination among SUA and BG. Information closes a potential negative relationship among's SUA and BG in the wake of representing all conceivable frustrating elements. In the univariate and multivariate models, it is shown that uric corrosive, Aspartate aminotransferase (AST), egg whites has negative relationship with expanding level of blood glucose, all out cholesterol, fatty substances, Alanine aminotransferase (ALT) has positive connection with expanding level of blood glucose. The affiliation stays huge in the awareness examination (P stays under 0.05). All in all, Serum uric corrosive may be adversely related with blood glucose in diabetic people.

Keywords: serum uric corrosive , NHANES, blood glucose, diabetes mellitus.

1. Introduction

Uric corrosive is a heterocyclic compound of carbon, nitrogen, oxygen and hydrogen, which is created when the body isolates food assortments that contain normal combinations called purines. Serum uric corrosive (SUA) level has been researched previously and is demonstrated to be connected with various guess of contamination in fundamentally ill patients. It is additionally connected with hazard of antagonistic results in patients with Coronavirus [1, 2]. Coronavirus, as a continuous pandemic that exists from one side of the planet to the other, has brought about an awkwardness of patients' digestion and made critical rise in blood glucose level. This can additionally bring about insulin opposition and hyperglycemia, which might be causal connected with diabetes mellitus [3].

Blood glucose (BG), or what is called glucose level, is the proportion of glucose packed in the blood. Glucose is the main energy hotspot for all organic entities, and is the fundamental sugar that is tracked down in human blood. Level of BG is found to be related with several diseases, including Diabetes Mellitus (DM) and Hypertension (HTN) [4]. As past examination concentrates on explored, the counting affection of type 2 diabetes mellitus has grown up to 462 million people, comparing to 6.28% of the

total populace, or a commonness pace of 6059 cases for each 100,000 individuals. With this conveyance, north of 1 million passings can be credited to diabetes alone, which makes it the 10th driving reason for mortality [5]. Also, as introduced before, COVID-19 happens to be a potential factor which can cause diabetes mellitus, the number of infections and death will possibly increase in the future, and the burden of controlling diabetes mellitus is becoming more and more important and severe.

As research shows the possible connection between SUA and diabetes mellitus [6], it is reasonable to think of the connection between SUA and BG, and then investigate the overall controlling effect of these two elements in the metabolism imbalance. However, there are relatively small research results that investigate this relationship alone. The existing study has a result which explains there might be a significant inverse correlation between SUA and BG [7], but the sample is based on a relatively small sample size. However, there also exists a controversial conclusion which explains there might be a positive correlation between SUA and BG [8]. The paper aims to additionally examine the conceivable genuine connection among SUA and BG by researching ongoing NHANES information tests, and further expect the relationship among these two components and diabetes mellitus.

2. Methods

2.1. Data source

Current review relies upon information from the Public Wellbeing and Nourishment Assessment Overview [9], which joins public study poll results and actual assessments. Itemized information source depiction including segment, dietary, clinical medicines, research facility tests, and so forth. Different datasets are divided into different age groups for convenience of use, and all data are publicly available and de-identified by the National Center for Statistics before publication. Participants are required to sign the informed consent before participating in different surveys and studies, hence the database can be publicly used by different associations to bring benefits to their research or experiment.

The sample population includes data from 2017 to March 2020, the lack of complete data in the year of 2020 is due to the pandemic of COVID-19. A sum of 15,560 members are remembered for the segment data set from the get go, then members more youthful than 20 years of age ($n = 6,328$), members with missing SUA and BG information ($n = 1,352$), members with no diabetes record ($n = 6,659$) are prohibited from the example populace. The final 1,221 participants are the sample that this study used as the data source.

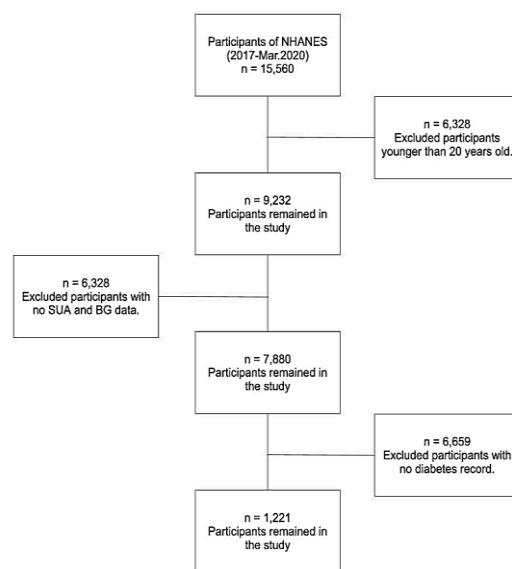


Figure 1. Flow chart of selecting sample population.

2.2. Variables

In the estimation of uric corrosive, a two point, end point response estimation occurring at 546 nm is utilized. In the estimation of blood glucose, a specific endpoint response estimation is used, which utilizes an enzymatic method that changes over glucose over totally to glucose-6-phosphate (G-6-P) by hexokinase inside seeing ATP, Glucose-6-phosphate dehydrogenase then changes the G-6-P over totally to gluconate-6-P inside seeing NADP⁺. As the NADP⁺ is diminished to NADPH during this response, the resulting development in absorbance at 340 nm (helper recurrence = 700 nm) is estimated[10]. Since the data are continuous and the result of correlation is desired for the two groups of data, dividing by interquartile range of the two elements is further used in the baseline characteristics table.

2.3. Covariates

In the estimation of uric corrosive, a two point, end point response estimation occurring at 546 nm is utilized. In the estimation of blood glucose, a specific endpoint response estimation is used, which utilizes an enzymatic method that changes over glucose over totally to glucose-6-phosphate (G-6-P) by hexokinase inside seeing ATP, Glucose-6-phosphate dehydrogenase then changes the G-6-P over totally to gluconate-6-P inside seeing NADP⁺. As the NADP⁺ is diminished to NADPH during this response, the resulting development in absorbance at 340 nm (helper recurrence = 700 nm) is estimated[10].

2.4. Statistical analysis

All information results were created utilizing R (adaptation 4.2.2)[11]. The ordinariness of the information relies upon past examination processes, which uses Kolmogorov-Smirnov commonness test to test the normality of the steady factors [15]. Conventionally coursed factors are shown as (mean \pm SD), non-commonly circled factors are shown as (middle \pm IQR). Among downright factors in various SUA and BG range gatherings, the chi-square test is utilized to dissect the rates of various gatherings. Among different SUA and BG intergroup correlations, the Bonferroni test is utilized to investigate the examination inside these numerous correlations[12-14]. As the dispersion of blood glucose level is slanted right (made sense of in the outcome), it is log-changed to fit the relapse examination. Then, for the relationship between's serum uric corrosive and glucose (and the other covariates that is recorded previously), univariate and multivariate direct relapse model is utilized to decide the relapse coefficient, standard blunders and P-esteem (with blood glucose level as the reliant variable). Finally, a responsiveness examination is performed by barring exceptions who have blood glucose levels >269.9 mg/dL or <1.5 mg/dL (characterized by upper and lower walls determined by interquartile range) [16]. A two-sided $P < 0.05$ is viewed as genuinely critical.

2.5. Results

Total of $n = 1,221$ participants who fall into five different ethnicity groups are included in the study, detailed of $n = 164$ Mexican Americans, $n = 125$ Other Hispanic, $n = 400$ Non-Hispanic White, $n = 335$ Non-Hispanic Black, and $n = 197$ Other Race. The mean SUA level is 336.9 ± 95.2 $\mu\text{mol/L}$ (micro mol per liter) and mean BG level is 146.2 ± 66.1 mg/dL (Milligrams Per Deciliter). The table is characterized into 4 SUA level groups by SUA quartiles: Q1 ($\text{SUA} \leq 267.7$ $\mu\text{mol/L}$), Q2 (267.7 $\mu\text{mol/L} < \text{SUA} \leq 327.1$ $\mu\text{mol/L}$), Q3 (327.1 $\mu\text{mol/L} < \text{SUA} \leq 398.5$ $\mu\text{mol/L}$), Q4 ($\text{SUA} > 398.5$ $\mu\text{mol/L}$). Detailed characteristics of different covariates are summarized in Table 1. The Bonferroni test is used for group comparisons which have $P < 0.05$, and it can be found that with the rising quartile of SUA, the extent of obese individuals has largely increased, while the level of Blood Glucose level ($P < 0.001$) is decreasing continuously.

Table 1. Clinical history record of sample population characterized by quartiles of SUA. NHANES 2017-Mar.2020 (n=1,221).

Characteristics	Uric Acid Quartiles				p
	Q1	Q2	Q3	Q4	
Number of subjects	323	311	297	290	
Age (year)	59.21 (12.61)	62.24 (12.49)	64.36 (12.11)	64.37 (11.57)	<0.001
Uric Acid (umol/L)	237.90 (47.6)	303.30 (29.7)	362.80 (35.7)	446.10 (71.4)	<0.001
Glucose (mg/dL)	136.00 (96.5)	126.00 (65.0)	121.00 (61.0)	123.00 (56.0)	<0.001
Total Cholesterol (mg/dL)	165.00 (56.5)	165.00 (50.0)	167.00 (61.0)	166.00 (50.0)	0.941
Triglycerides (mg/dL)	127.00 (93.0)	136.00 (98.0)	141.00 (114.0)	148.50 (104.5)	<0.001
Alanine Aminotransferase (U/L)	17.00 (13.0)	18.00 (12.0)	19.00 (14.0)	18.00 (13.0)	0.270
Aspartate Aminotransferase (U/L)	18.00 (8.0)	18.00 (8.0)	20.00 (9.0)	19.00 (10.0)	<0.001
Albumin (g/dL)	4.00 (0.45)	4.00 (0.4)	4.00 (0.4)	3.90 (0.5)	0.013
Total Protein (g/dL)	7.00 (0.6)	7.10 (0.6)	7.20 (0.7)	7.20 (0.5)	0.032
Race (%)					0.024
Mexican American	51 (15.8)	47 (15.1)	44 (14.8)	22 (7.6)	
Other Hispanic	44 (13.6)	30 (9.6)	28 (9.4)	23 (7.9)	
White	104 (32.2)	95 (30.5)	99 (33.3)	102 (35.2)	
Black	79 (24.5)	82 (26.4)	77 (25.9)	97 (33.4)	
Other Race	45 (13.9)	57 (18.3)	49 (16.5)	46 (15.9)	
Gender = Female (%)	189 (58.5)	150 (48.2)	101 (34.0)	112 (38.6)	<0.001
BMICAT (%)					<0.001
Normal (<25 kg/m ²)	53 (16.8)	34 (11.2)	36 (12.5)	22 (7.8)	
Overweight (≥25 and <30 kg/m ²)	147 (46.5)	186 (61.4)	171 (59.2)	194 (68.8)	
Obesity (≥30 kg/m ²)	116 (36.7)	83 (27.4)	82 (28.4)	66 (23.4)	

The characteristics that are summarized with the increasing quartile range of BG is shown in Table 2. The table is characterized into 4 groups by BG quartiles: Q1(BG ≤ 102 mg/dL), Q2 (102 mg/dL < BG

≤ 126 mg/dL), Q3($126 \text{ umol/dL} < \text{BG} \leq 169 \text{ umol/dL}$), Q4($\text{BG} > 169 \text{ umol/dL}$). The Bonferroni test is used for group comparisons which has $P < 0.05$, and it can be found that with the increasing quartile of BG, the level of SUA level ($P < 0.001$) is decreasing, while the level of ALT and Triglycerides is increasing continuously.

The result of univariate and multivariate linear regression analysis of every autonomous variable and log-transformed blood glucose level is displayed in Table 3. For univariate regression analysis results, there are multiple significant variables with $P < 0.05$, including Gender (negatively correlated $B = -0.050$), Race (negatively correlated $B = -0.032$), SUA (negatively correlated $B = -0.001$), Total Cholesterol (positively correlated $B = 0.001$), Triglycerides (positively correlated $B = 0.001$), ALT (positively correlated $B = 0.002$), Albumin (negatively correlated $B = -0.064$), associated with $\log(\text{BG})$. For multivariate regression analysis results, the significant variables (with $P < 0.05$) include: Gender (negatively correlated $B = -0.078$), Race (negatively correlated $B = -0.018$), SUA (negatively correlated $B = -0.001$), Total Cholesterol (positively correlated $B < 0.001$), Triglycerides (positively correlated $B < 0.001$), ALT (positively correlated $B = 0.008$), AST (negatively correlated $B = -0.008$), Albumin (negatively correlated $B = -0.153$). In both univariate and multivariate models, SUA is shown to be negatively correlated with $\log(\text{BG})$. The sensitivity analysis which exclude the outliers that are outside of the fences of the interquartile range are shown in Table 4. The correlations described in the regression analysis with significant level $P < 0.05$ are still significant in the sensitivity table ($P < 0.05$) excluding Total Cholesterol ($P = 0.3144$) and Race ($P = 0.077$).

Table 2. Clinical history record of sample population characterized by quartiles of serum blood glucose. NHANES 2017-Mar.2020 (n=1,221).

Characteristics	Blood Glucose Quartiles				p
	Q1	Q2	Q3	Q4	
Number of subjects	309	311	297	304	
Age (year)	61.92 (13.21)	63.98 (11.88)	64.15 (11.57)	59.81 (12.36)	<0.001
Uric Acid (umol/L)	333.10 (124.9)	333.10 (124.9)	333.10 (130.9)	309.30 (136.8)	<0.001
Glucose (mg/dL)	90.00 (13.0)	113.00 (12.0)	146.00 (19.0)	220.00 (78.75)	<0.001
Total Cholesterol (mg/dL)	164.00 (51.0)	160.00 (50.0)	162.50 (50.0)	178.50 (65.5)	<0.001
Triglycerides (mg/dL)	123.00 (100.0)	126.00 (73.5)	140.00 (89.0)	167.00 (125.5)	<0.001
Alanine Aminotransferase (U/L)	16.00 (12.0)	17.00 (11.0)	19.00 (13.0)	19.50 (13.25)	<0.001
Aspartate Aminotransferase (U/L)	19.00 (9.25)	18.00 (7.5)	19.00 (10.0)	18.00 (11.0)	0.059
Albumin (g/dL)	4.00 (0.5)	4.00 (0.5)	4.00 (0.4)	3.90 (0.4)	0.013
Total Protein (g/dL)	7.20 (0.6)	7.10 (0.6)	7.10 (0.7)	7.10 (0.6)	0.374
Race (%)					0.027

Table 2. (continued).

Mexican American	30 (9.7)	42 (13.5)	50 (16.8)	42 (13.8)	
Other Hispanic	26 (8.4)	31 (10.0)	26 (8.8)	42 (13.8)	
White	94 (30.4)	105 (33.8)	95 (32.0)	106 (34.9)	
Black	107 (34.6)	80 (25.7)	73 (24.6)	75 (24.7)	
Other Race	52 (16.8)	53 (17.0)	53 (17.8)	39 (12.8)	
Gender = Female (%)	150 (48.5)	159 (51.1)	119 (40.1)	124 (40.8)	0.010
BMICAT (%)					0.166
Normal (<25 kg/m ²)	46 (15.1)	33 (10.9)	42 (14.5)	24 (8.2)	
Overweight (≥25 and <30 kg/m ²)	172 (56.4)	186 (61.2)	163 (56.2)	177 (60.8)	
Obesity (≥30 kg/m ²)	87 (28.5)	85 (28.0)	85 (29.3)	90 (30.9)	

Table 3. Univariate and multivariate linear regression analysis predicting log-transformed serum blood glucose. NHANES 2017-Mar.2020 (n=1,221).

Univariable Linear Regression Analysis					Multivariable Linear Regression Analysis			
Variables	R squared	B	SE	P-value	Adj. R squared	B	SE	P-value
Age (years)	0.009	-0.003	<0.001	0.001	0.111	<0.001	0.001	0.936
Gender	0.004	-0.050	0.023	0.027		-0.078	0.024	<0.001
Race	0.010	-0.032	0.009	<0.001		-0.018	0.009	0.040
BMI (kg/m ²)	<0.001	<0.001	0.001	0.536		<0.001	0.002	0.851
Uric Acid (umol/L)	0.016	-0.001	<0.001	<0.001		-0.001	<0.001	<0.001
Total Cholesterol (mg/dL)	0.017	0.001	<0.001	<0.001		<0.001	<0.001	0.027
Triglycerides (mg/dL)	0.046	0.001	<0.001	<0.001		<0.001	<0.001	<0.001
ALT (U/L)	0.010	0.002	<0.001	<0.001		0.008	0.001	<0.001
AST (U/L)	<0.001	<0.001	<0.001	0.913		-0.008	0.001	<0.001
Albumin (g/dL)	0.003	-0.064	0.031	0.040		-0.153	0.035	<0.001
Total Protein (g/dL)	<0.001	-0.010	0.023	0.664		0.030	0.025	0.230

Table 4. Univariate and multivariate linear regression analysis predicting log-transformed serum blood glucose (sensitivity analysis performed: outlier or extreme value excluded). NHANES 2017-Mar.2020 (n=1,143).

Univariable Linear Regression Analysis					Multivariable Linear Regression Analysis			
Variables	R squared	B	SE	P-value	Adj. R squared	B	SE	P-value
Age (years)	0.001	-0.001	<0.001	0.193	0.052	0.001	0.001	0.463
Gender	0.004	-0.040	0.019	0.040		-0.051	0.021	0.014
Race	0.007	-0.022	0.008	0.005		-0.014	0.008	0.077
BMI (kg/m2))	0.001	0.001	0.001	0.239		0.001	0.001	0.310
Uric Acid (umol/L)	0.005	>-0.001	<0.001	0.013		-0.0003	<0.001	0.0009
Total Cholesterol (mg/dL)	0.005	<0.001	<0.001	0.017		<0.001	<0.001	0.3144
Triglycerides (mg/dL)	0.024	<0.001	<0.001	<0.001		<0.001	<0.001	<0.001
ALT (U/L)	0.009	0.002	<0.001	0.001		0.005	0.001	<0.001
AST (U/L)	<0.001	<0.001	<0.001	0.649		-0.005	0.001	<0.001
Albumin (g/dL)	<0.001	-0.020	0.027	0.469		-0.067	0.032	0.035
Total Protein (g/dL)	<0.001	-0.019	0.020	0.340		0.002	0.022	0.916

3. Discussion

The general outcomes from univariate and multivariate straight relapse shows that the serum uric corrosive level and blood glucose level in diabetic patients may be adversely related. The past concentrate by Tangigul Haque, Sadaqur Rahman, Shiful Islam, Noyan Hossain Molla and Nurshad Ali which controlled the covariates and the kind of people to research the conceivable relationship between's serum uric corrosive level and glucose level has a similar in general end which shows that they may be adversely connected [7]. In any case, what's different is that it shows a positive connection in the solid populace. The possible reason for this present circumstance is that SUA could be a piece of the huge determinant which changed the blood glucose level, there could in any case be different elements which may likewise cause the problem of the BG digestion. As indicated by what J.A.M. Andrade, H.C. Kang, S. Greffin, M.L. Garcia Rosa, and J.R. Lugon has written in their investigation of the connection among SUA and glucose jumble digestion, the presence of glycosuria is by all accounts went with the more elevated level of SUA and different side effects in diabetic patients, which may likewise prompt dysglycemia [17].

As serum uric acid might only be involved in the early stage of the disorder of blood glucose, which leads to the prediabetic stage or even advanced stages of diabetes, the assurance of prediabetes and diabetes mellitus should consider larger percent of the whole metabolism imbalance, but not considering only the serum uric acid level and what it leads to the blood glucose level. Hence, SUA may not be the

proper only predictor for the BG metabolism imbalance. This assumption is further supported by this study since the same experiment result is concluded by using datasets from different countries with different living environments.

Also what can be derived is that the relationship of different groups of elements are significantly related (Albumin for instance, significant negative correlation with BG), with positive or negative correlation. For future studies, if more evidence is concluded about the association of these imbalancing elements that happen in a diabetic patients, it may be easier to predict what must be controlled in order to cure from the diabetes mellitus or even prevent it from happening. Previous studies have made assumptions about controlling lifestyle and dietary to control this element [18], the clear relationship between these elements which caused the imbalance of metabolism will help to determine the better lifestyle and dietary.

What is limited in this study including the data sample size. Since COVID-19 crisis happened during the year of 2020, the data only extended to the month of March 2020. This largely decreases the sample amount and completeness during these three years. If a larger dataset of diabetic individuals is used, it is possible to derive a much clearer relationship. Also what is not included in the study is the excluding of anti-diabetic medications. As the medication may improve the situation of imbalancing metabolism, it might affect the association between serum uric acid level and blood glucose level [19-21]. Non-diabetic people's serum uric corrosive and blood glucose affiliation can be likewise involved to contrast and the diabetic people, which prompts a more grounded connection between these two components.

4. Conclusion

Serum uric acid level is decreasing toward a lower stage as the blood glucose level is increasing gradually, with the increasing amount of other elements including Alanine aminotransferase and Triglycerides. This study further agrees with the assumption that these two elements are negatively correlated and should not be considered alone as the factor of predicting diabetes mellitus. Additionally it concurs that serum uric corrosive can be engaged with the phase of digestion unevenness which further prompts diabetes mellitus. Bigger information size and non-diabetic people investment are expected to analyze the more grounded connection between serum uric corrosive and blood glucose.

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