Innovative Journal of Medical and Healthcare Research (IJMHR)
Volume-1 Issue-2 March-2024

Study Of Serum Hs-C Reactive Protein And Serum Uric Acid In Type-II Diabetic Patients

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ABSTRACT

A complex metabolic condition, diabetes affects the body's glucose level in several ways. Hyperglycemia and impaired glucose tolerance are the hallmarks of type 2 diabetes, which may be caused by either a relative or total lack of insulin or a resistance to its effects. End organ malfunction and failure may occur as a consequence of chronic hyperglycemia in people with diabetes. This can happen to the retina, kidneys, nerves, heart, and blood vessels. Patients with diabetes have a substantially increased risk for cardiovascular disease (CVD), and there is strong clinical evidence linking diabetes to atherosclerotic cardiovascular disease. Among the many factors that contribute to the development and advancement of accelerated atherosclerosis in people who have type 2 diabetes mellitus, inflammation is a key player. Therefore, new biomarkers of inflammation, such as high-sensitivity C-reactive protein, may be used to predict the likelihood of cardiovascular disease. A variety of morbidity statuses, such as hypertension, metabolic syndrome, renal illness, and cardiovascular disease, are linked to hyperuricemia. The current research aims to assess the serum uric acid and high sensitivity C reactive protein levels in individuals with type 2 diabetes.

In order to measure the concentrations of high-sensitivity C-reactive protein in individuals with type 2 diabetes. In order to measure the serum uric acid levels in individuals with type 2 diabetes and If there is a relationship between hs-CRP and serum uric acid, we want to know about it. Seventy healthy individuals and seventy people with type 2 diabetes were among the 140 people who participated in the study. The immunoturbidimetry was used to evaluate the amounts of uric acid and high-sensitivity C-reactive protein (hs-CRP) in the serum. The statistical study was conducted using Spearman's Rank Correlation and an independent Students' t-test.

There was no significant link between hs-CRP and Uric acid, although there was a substantial rise in both serum uric acid levels and high-sensitivity C-reactive protein ($p < 0.001$) in type 2 diabetes participants compared to controls.

Researchers discovered that high-sensitivity C-reactive protein levels were significantly higher in those with type 2 diabetes compared to healthy controls. Glycated haemoglobin, high-sensitivity C-reactive protein, and fasting serum glucose are strongly correlated. Patients with type 2 diabetes had significantly higher blood uric acid levels than non-diabetic controls, according to our research. Additionally, hs-CRP and uric acid did not correlate significantly. Patients with type 2 diabetes mellitus are at increased risk for complications and disease-related morbidity due in large part to serum uric acid levels. In individuals with type 2 diabetes, elevated levels of hs-CRP and serum uric acid indicate the likelihood of future cardiovascular problems.

Key words: Type 2 Diabetes Mellitus, Glycated hemoglobin, High-sensitivity C-reactive protein, Uric acid.

I. INTRODUCTION

DIABETES MELLITUS

Hyperglycemia is a hallmark of the metabolic diseases collectively known as diabetes mellitus. Multiple forms of diabetes mellitus (DM) result from a complicated interplay between hereditary and environmental variables. Hypoglycemia occurs when the body does not produce enough insulin, uses glucose less efficiently, and produces more glucose than it needs.

Both the diabetic person and the healthcare system endure immense strain as a result of secondary pathophysiologic alterations brought on by metabolic dysregulation and affecting many organ systems.

Type 2 diabetes mellitus has a growing global incidence, elevating the illness to a level of critical concern. According to recent figures, over 336 million individuals globally were diagnosed with type 2 diabetes mellitus in 2011. By 2030, experts predict that there will be 552 million instances, a much greater prevalence. Also, as long as global obesity rates are high, the majority of academics believe that this prevalence will keep climbing sharply. For this reason, preventing type 2 diabetes mellitus requires first identifying the variables that put people at risk for developing the condition.

HIGH-SENSITIVITY C-REACTIVE PROTEIN (hs-CRP):

The five subunits that make up C-reactive protein are the same as those in the pentraxin protein family. The C-reactive protein is named so because it has an affinity for the C-polysaccharide found in pneumococcal capsules. When it comes to inflammatory indicators, hs-CRP stands out as a "golden marker of inflammation" due to its significance in diabetic patients.

Recent years have seen an uptick in interest in the inflammatory process and its underlying causes in the study of cardiovascular disease and diabetes. It is well acknowledged that inflammation is a key factor in the development and advancement of atherosclerosis in individuals diagnosed with diabetes.

The characteristic of inflammation is the elevation of C-reactive protein (CRP) and fibrinogen levels in the blood plasma, which are acute-phase proteins produced by the liver. Hepatocytes generate CRP, an acute phase response protein with a half-life of 19 hours, in reaction to many stimuli, the most common of which are interleukin-6 (IL-6), interleukin-1 (IL-1), or tumour necrosis factor (TNF). CRP levels are significantly elevated in inflammatory and viral disorders.

A more precise way to assess CRP levels is using high sensitivity C-reactive protein, or hs-CRP. More than a hundred times more sensitive than standard CRP testing, with a lower limit of detection of 0.01 mg/L. Patients with low, moderate, and high risk for future cardiovascular events are identified by levels <1, 1-3, and >3 mg/L, respectively.

Systemic inflammation is often accompanied with hs-CRP values more than 10 mg/L. Serum hs-CRP estimates in the early stages of type 2 diabetes patients may be enthusiastic since it is utilised as a biomarker of chronic inflammation throughout the disease and aids patients in making early decisions about their macrovascular risk prognosis.

URIC ACID

The intermediates are used in the conversion of adenosine and guanosine, two main purine nucleosides, to uric acid in humans. A serum level of 2.6–6.0 mg/dl is considered normal for women and 3.5–7.0 mg/dl for males. Some cases of hyperuricemia are due to enzyme deficiencies, but many more are a result of disorders that increase tissue turnover, such psoriasis or cancer.

It has been suggested that diabetic problems may be caused by an increase in urinary acid levels after tissue damage. Recent research has linked hyperuricemia to endothelial dysfunction, pathologic vascular diseases, decreased renal function, stroke, poor glycemic management, hypertension, cardiovascular risk, and myocardial infarction. An early sign of diabetic nephropathy caused by damage to the basement membrane, microalbuminuria, has been linked to higher blood uric acid levels.

High levels of uric acid in the blood and a high rate of renal clearance have been linked to poor glucose management and early impairment of renal function. Multiple studies have linked elevated uric acid levels to an increased risk of developing the condition.

As an independent predictor of stroke, cardiovascular risk with poor outcome, essential hypertension, myocardial infarction, and classical risk factors like C-reactive protein and insulin resistance, hyperuricemia is a powerful predictor of cardiovascular risk.

Renal vasoconstriction, endothelial dysfunction, inflammatory response, oxidative stress, and autoregulation abnormalities are all symptoms of renal failure, and serum uric acid may serve as a marker for these pathogens.

It has been linked to endothelial dysfunction, which hinders nitric oxide release, and uric acid (UA) overproduction by ischemic tissues. Uric acid and its precursors were thus thought to be damage signals in renal ischemia. In renal disorders, microalbuminuria and decreased glomerular filtration rate were also highly related with serum uric acid level 9.

The importance of glycemic management and uric acid levels may be better understood if more research into Type 2 Diabetes mellitus focuses on serum uric acid and hs-CRP.

II. AIMS AND OBJECTIVES

1. In order to measure the concentrations of high-sensitivity C-reactive protein in individuals with type 2 diabetes.
2. The goal is to measure the serum uric acid levels of people with type 2 diabetes.
3. If there is a relationship between hs-CRP and serum uric acid, we want to know about it.

III. REVIEW OF LITERATURE

EPIDEMIOLOGY:

An "ice berg" illness is diabetes. From an estimated 30 million cases in 1985 to 285 million in 2010, the prevalence of Diabetes Mellitus has grown considerably during the previous twenty years.

The International Diabetes Federation predicts that 438 million people will develop diabetes by 2030 if present trends continue.

Worldwide, the incidence of both type 1 and type 2 diabetes mellitus is on the rise, but type 2 is developing at a much faster rate. This is likely due to factors such as an ageing population, a decline in physical activity levels as a result of industrialization, and the prevalence of obesity.

Multiple studies have shown that diabetes is probably underreported as a cause of death, despite the fact that it is a leading cause of death overall. Diabetes, according to a recent assessment, ranks as the world's fourth worst killer. Adults in rural India have a disease prevalence of 2.4%, but those in urban areas have a prevalence of 4.1% to 11.6%. Studies have indicated that impaired glucose tolerance is rather common, with rates ranging from 3.6% to 9.1%. This suggests that the frequency of diabetes mellitus might continue to climb in the next decade.

HISTORY

Scholars of Hindu origin first described diabetes in their works about 1500 BC. The name diabetes, which meant "to go through" or "syphon" since the ailment caused a person to lose more fluid than they could absorb, was likely invented by Apollonius of Memphis about 250 BC. Because it produced delicious urine, the Latin term "mellitus" was later added.

In the second century AD, Arataeus of Cappadocia in Asia Minor provided the earliest account of diabetes. The name "diabetes," originally from the Greek for "syphon," was also coined by Aretaeus. This is because the fluid does not stay in the body but rather utilises it as a conduit to exit. The disease's relentless pee flow, insatiable thirst, "melting down of the flesh and limbs into urine," and limited survival were all emphasised in his vivid description of the illness.

Charaka and Sushrutha, two Hindu doctors who lived between 400 and 500 BC, were likely the first to notice that diabetic pee tastes sweet. A simple observation—that ants gathered around the urine—or a taste test confirmed the diagnosis.

Inactive, overweight, and gluttonous people who ate a lot of sugar and fat were the ones most likely to have the condition, according to Charaka and Sushrutha.

The first adult-use, frequent, automated, and non-invasive glucose monitor was the Cygnus GlucoWatch Biographer, which received FDA approval in 2001.

Officially, Type 2 Diabetes Mellitus was renamed Non-Insulin Dependent Diabetes Mellitus (NIDDM) in 2003, while Type 1 Diabetes Mellitus was legally abandoned in the same year.

Aruna D et al two indicators of systemic inflammation, C-reactive protein (CRP) and interleukin-6 (IL-6), were identified as risk factors for type 2 diabetes mellitus (T2DM) in a 2001 prospective study of seemingly healthy middle-aged women. After controlling for obesity, clinical risk factors, and fasting insulin levels, CRP remained a strong independent predictor. Similar correlations were seen for IL-6, however they were of lesser strength and showed just a hint of statistical significance after multivariate analysis. Both obese and nonobese people consistently showed these results, and they held up in sensitivity studies that only included persons with a baseline haemoglobin A1c of 0% or below.

In the same year 2010, Mahajan A et al "High Sensitivity C-reactive protein levels and type 2 Diabetes in urban north Indians" was the subject of a cross-sectional research. Researchers observed that compared to healthy controls, those with type 2 diabetes had much higher median hs-CRP levels.

A.K.M. Fazlul haque et al study in year 2010 carried out by selecting 70 individuals with diabetes who did not have any other health issues or comorbidities, as well as 35 healthy controls who did not have diabetes or any other disorders. Both groups were evaluated for hs-CRP level and HbA1c%; they were also non-smokers, non-alcoholics, and non-hypertensive. In the diabetes group, the mean hs-CRP was 1.13 mg/L, while in the healthy group, it was 0.39 mg/L. There is a statistically significant difference between the mean hs-CRP levels of normal healthy people (0.39 mg/L) and diabetes patients (1.13 mg/L). Among healthy, normal people, the mean hs-CRP level was less than 1 mg/L, which is considered the lowest level of risk for cardiovascular disease.

Andreas pfutzner et al study in the year 2010 shown a significant increase in the risk of cardiovascular complications in insulin-resistant individuals. Insulin resistance, type 2 diabetes, and an increased risk of cardiovascular illnesses have all been extensively associated with low-grade inflammation, according to research conducted in the last

few decades. A dependable biomarker for the subclinical inflammatory state is elevated levels of high sensitivity C-reactive protein. There is mounting evidence that measuring hsCRP may be helpful for assessing vascular risk and therapy effectiveness in both non-diabetic and insulin-resistant diabetic patients.

Tiange wange et al study in year 2011 shown that uric acid levels in the blood were a reliable indicator of the likelihood of developing type 2 diabetes in middle-aged and older Chinese people. Insulin resistance is a key component in the development of type 2 diabetes, however the findings showed that the association between serum uric acid and incidence did not rely on it.

IV. MATERIALS AND METHODS

a) Source of data:

From May 2021 to October 2022, researchers at Khaja Banda Nawaz Teaching and General Hospital in Kalaburagi studied hs-CRP and uric acid levels in patients with type 2 diabetes and healthy controls who were matched for age and sex.

The study's use of human participants was approved by the Ethical Council of the Faculty of Medicine at Khaja Banda Nawaz University in Kalaburagi.

Participants gave their written informed permission before the research began.

The individuals and controls in the research were recruited willingly. Cases and controls alike underwent comprehensive medical histories and pertinent clinical tests. According to the inclusion and exclusion criteria, about 70 individuals with type 2 diabetes and 70 healthy controls of the same age and gender were included.

b) Inclusion Criteria:

Cases: 70 Individuals in the 40-60 age range who have just been diagnosed with type 2 diabetes mellitus and are now symptom-free. We established that all patients with type 2 diabetes met the World Health Organisation criteria, which include fasting blood sugar levels of 126 mg/dl or more and haemoglobin A1c levels greater than 6.5%.

Controls: There were the same number of healthy controls of the same age and gender as there were cases.

c) Exclusion criteria

- Type 1 diabetic patients.
- Preschoolers and teenagers.
- Factors that are known to affect hs-CRP blood levels include a history of myocardial infarction and angina
- Factors that are known to affect ferritin and hs-CRP levels in the blood include a history of liver, renal, acute sickness, thyroid, anaemia, and hemochromatosis.
- Hypoglycemia During Pregnancy
- A family history of polycystic ovary syndrome, an ovarian cyst that affects insulin levels in the blood
- People whose blood hs-CRP levels are known to be affected by the statins and metformin they take for treatment
- Serum hs-CRP levels in women on hormone replacement treatment are known to be affected. This patient is receiving immuno suppressants and chemotherapy.

d) Method of sample collection:

The research participants' antecubital veins were numbed using a sterile disposable syringe to extract about 6 mL of fasting venous blood in accordance with aseptic procedures. In a normal vacutainer, 4 mL was taken, and in an EDTA-containing vacutainer, 2 mL was taken.

The serum was isolated by centrifugation from a plain vacutainer that contained 4 mL of blood.

The biochemical parameters were examined using the Immuno Turbidimetric technique and the Chemiluminiscence immuno assay.

e) Parameters measured:

In the present study following parameters were estimated.

I. Serum was used for the estimation of following parameters

1) Fasting serum glucose,
2) Post Prandial glucose
3) Uric acid
4) High Sensitivity C-reactive protein,

II. Whole blood was used for the estimation of Glycated hemoglobin

Cases and controls that are age and sex matched are included in this research following informed permission, according to the inclusion and exclusion criteria. Important details and patient data were recorded using a proforma.

Analytical kits from the Beckman Coulter AU480 chemical analyzer were used to measure the serum concentrations of glucose and uric acid.

Using immunoturbidimetric kits from Turbodyne, the amounts of hs-CRP and glycated haemoglobin in the serum were estimated.

V. SAMPLE SIZE

70 Patient and 70 Controls.

Prevalence p= 72% = 0.72q=100-p=28%
d= allowable error= 5-15% of p = 15% of 72=10.8
Formula :

Sample size (n)= $4pq/d^2$

= $4 \times 72 \times 28 / (10.8)^2$

= 69.1

Therefore sample size comes as 70.

VI. RESULTS

Distribution based on age and sex

Table No 1. Age and sex distribution of the study population.

Age and gender distribution among 2 groups						
Variable	Category	Cases		Control		P-Value
		Mean	SD	Mean	SD	
Age	Mean	49.41	6.89	49.70	5.95	0.68[a]
	Range	37 - 69		40 – 60		
		n	%	n	%	
Sex	Males	55	78.6 %	52	74.3 %	0.55[b]
	Females	15	21.4 %	18	25.7 %	

The average age in the Case group was 49.41 ± 6.89, with participants' ages ranging from 37 to 69, whereas in the Control group it was 49.70 ± 5.95, with participants' ages ranging from 40 to 60. Between the case and control groups, there was no statistically significant difference in mean age (p=0.68). Compared to the female counterparts, there were more men in the case group [78.6%] and the control group [74.3%]. The gender distribution did not vary significantly between the two groups (p=0.55).

Comparison of mean levels of Glycemic parameters between Cases & Control group

Table no.2 - Comparison of mean levels of Glycemic parameters between Cases &Control group

Comparison of mean levels of Glycemic parameters between Cases & Control group using Mann Whitney Test						
Parameter	Groups	N	Mean	SD	Mean Diff	P-Value
FBS	Case	70	173.27	35.23	88.10	<0.001*
	Control	70	85.17	11.01		
PPBS	Case	70	262.51	58.42	149.34	<0.001*
	Control	70	113.17	12.78		
HbA1c	Case	70	8.63	1.64	3.66	<0.001*
	Control	70	4.97	0.56		

* - Statistically Significant

The Case group had a substantially higher mean FBS level (173.27 ± 35.23) compared to the Control group (85.17 ± 11.01), with a significant difference (p<0.001). The Case group had a substantially higher mean PPBS level (262.51 ± 113.17) compared to the Control group (113.17 ± 12.78), with a significant difference (p<0.001).

The Case group had a considerably higher mean HbA1c level (8.63 ± 1.64), compared to the Control group (4.97 ± 0.56), with a significant difference (p<0.001).

Comparison of mean Serum Uric Acid Levels (in mg/dL) between Cases & Controlgroup using Independent

Student t Test

Table no.3- Comparison of mean Serum Uric Acid Levels (in mg/dL) between Cases& Control group using Independent Student t Test

Comparison of mean Serum Uric Acid Levels (in mg/dL) between Cases & Control group using Independent Student t Test						
Parameter	**Groups**	**N**	**Mean**	**SD**	**Mean Diff**	**P-Value**
Serum Uric Acid Levels	Case	70	5.38	1.46	0.57	0.01*
	Control	70	4.81	1.22		

* - Statistically Significant

The control group had considerably lower serum uric acid levels [4.81 ± 1.22] compared to the case group, which had significantly higher levels [5.38 ± 1.46]. The statistical significance of the difference between the two groups was established at p=0.01.

Comparison of mean hs-CRP Levels (in mg/L) between Cases & Control groupusing Mann Whitney Test

Table no. 4- Comparison of mean hs-CRP Levels (in mg/L) between Cases & Control group using Mann Whitney Test

Comparison of mean hs-CRP Levels (in mg/L) between Cases & Control group using Mann Whitney Test						
Parameter	**Groups**	**N**	**Mean**	**SD**	**Mean Diff**	**P-Value**
hs-CRP levels	Case	70	6.31	2.81	4.47	<0.001*
	Control	70	1.84	0.99		

* - Statistically Significant

At a p<0.001, the mean difference in hs-CRP levels between the two groups was statistically significant, with the Case group having considerably higher levels (6.31 ± 2.81) than the Control group (1.84 ± 0.99).

Correlation test to assess the relationship b/w Serum Uric Acid & hs-CRP Levelsamong study subjects

Table no.5- Correlation test to assess the relationship b/w Serum Uric Acid & hs-CRP Levels among study subjects

Spearman's Rank Correlation test to assess the relationship b/w Serum Uric Acid & hs-CRP Levels among study subjects

Variable	Cases		Control		Overall	
Serum Uric Acid & hs-CRP Levels	rho	p-value	rho	p-value	rho	p-value
	0.07	0.55	0.09	0.46	0.17	0.04*

* - Statistically Significant

Rho is the abbreviation for the correlation coefficients. Denoting negative association, the minus sign Interval for the correlation coefficient: 0.0 to no Correlation

0.01 - 0.20 - Very Weak Correlation

0.21 - 0.40 - Weak Correlation

0.41 - 0.60 - Moderate Correlation

0.61 - 0.80 - Strong Correlation

0.81 - 1.00 - Very Strong Correlation

In the case group, there is a slight positive connection between the levels of serum uric acid and hs-CRP [rho=0.07, p-value=0.55]. Also, in the control group, there is a very slight positive connection with hs-CRP levels [rho=0.09, p-value=0.46]. Statistical analysis failed to reveal a correlation between case and control group levels of hs-CRP and serum uric acid. An very weak positive correlation (rho=0.17) between serum uric acid and high-sensitivity C-reactive protein levels was seen in all samples, and the observed association between the two variables was statistically significant (p=0.04).

VII. CONCLUSION

- Worldwide, diabetes mellitus is a major public health concern.
- A major contributor to the development of diabetes and its consequences is inflammation. One way to gauge the likelihood of cardiovascular disease and kidney disease is to look at inflammatory biomarkers, such as high-sensitivity C-reactive protein.
- Compared to healthy controls, those with type 2 diabetes had significantly higher levels of high-sensitivity C-reactive protein in our research. Blood sugar levels, glycated haemoglobin, and high-sensitivity C-reactive protein are strongly correlated when measured during fasting.
- To better manage diabetes and its consequences, it is important to identify and monitor the inflammatory marker hs-CRP early on as a predictor of diabetic nephropathy.
- Patients with type 2 diabetes had significantly higher blood uric acid levels than non-diabetic controls, according to our research. Uric acid and hsCRP did not correlate significantly either.
- Additional research is needed to understand the function of uric acid in the development of diabetes and identify potential treatments that might help prevent the condition. Nevertheless, it is a significant risk factor.
- Complications in type 2 diabetes mellitus are much more likely to occur in patients with hyperuricemia. As serum uric

acid levels rise, the risk of problems rises as well. The diagnosis of problems and the monitoring of blood uric acid levels are therefore of greater importance in clinical practice.

- At reduced amounts of body fat, the effect of uric acid on the development of diabetes may be different; so, studies with bigger samples might shed light on this mystery.
- As a result, our research shows that hs-CRP and serum uric acid are both utilised to identify diabetes and its consequences.

VIII. SUMMARY

The purpose of this research was to examine the relationship between uric acid and hs-CRP levels in individuals with type 2 diabetes.

In this research, 70 people who had just been diagnosed with diabetes and 70 healthy controls, matched for age and sex, participated. The research does not include diseases or variables that impact hs-CRP or serum uric acid levels. In addition to a physical and clinical evaluation, blood parameters such as serum uric acid and hs-CRP were evaluated using the uricase and immunoturbidimetric methods, respectively.

In comparison to non-diabetic persons, our research found that diabetes patients had much higher hs-CRP readings. Patients with type 2 diabetes also had significantly higher blood uric acid levels. Additionally, hs-CRP and uric acid did not show any association.

Insulin resistance, type 2 diabetes, and an increased risk of cardiovascular illnesses have all been extensively associated with low-grade inflammation, according to research conducted in the last few decades. A dependable biomarker for the subclinical inflammatory state is elevated levels of high sensitivity C-reactive protein. There is strong evidence that measuring hs-CRP may be helpful for assessing cardiovascular risk and in patient therapy.

A number of studies have shown a strong correlation between diabetes and elevated levels of acute phase reactants in the blood, such as uric acid. Hyperuricemia has been linked in several studies to endothelial dysfunction, a pathogenic process that contributes to a host of local and systemic problems in long-term diabetes.

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