



LEVELS OF SERUM AMYLASE, URIC ACID AND LIPID PROFILE IN TYPE-2-DIABETES MELLITUS: A PILOT STUDY IN ROHILKHAND REGION

Biochemistry

Dr. Ashish Jain Assistant Professor, Biochemistry Dept., FH Medical College, Agra, Uttar Pradesh

Dr. Veena Gupta* Professor, Biochemistry Dept., FH Medical College, Agra, Uttar Pradesh *Corresponding Author

Dr. KV Thimmaraju Professor, Biochemistry Dept., Rohilkhand Medical College, Bareilly, Uttar Pradesh

ABSTRACT

Type-2 Diabetes mellitus [T2DM] is a metabolic disorder characterized by chronic hyperglycemia with disturbance in carbohydrate, fat and protein metabolism. These metabolic abnormalities lead to long-term damage of various organs, causing their dysfunction and failure. Complications of T2DM are among the leading cause of mortality worldwide. The aim of the present study is to study and compare the lipid profile, serum amylase and UA in T2DM with controls. The present study was carried out in the department of Biochemistry of Rohilkhand Medical College, includes total 120 subjects: 60 known cases of T2DM and 60 age and sex matched healthy adult as control subjects. Based on the results of the present study and data available, it is clear that in Diabetes the serum level of lipid profile, UA and serum amylase were altered. This pilot study proves to be significant in respect of diabetes and diagnosis protocol.

KEYWORDS

T2DM, uric acid, amylase, lipid profile.

INTRODUCTION:

Type-2 Diabetes mellitus [T2DM] is a metabolic disorder characterized by chronic hyperglycemia with disturbance in carbohydrate, fat and protein metabolism. The two major pathophysiological defects are impaired insulin secretion and insulin action.[1] These metabolic abnormalities lead to long-term damage of various organs, causing their dysfunction and failure. Diabetes related microvascular complications are responsible for the majority of new cases of blindness, kidney failure and amputation (non traumatic). Further more macro vascular complications such as stroke and cardiovascular diseases (CVD) related death are 2-4 times more frequent in adult with diabetes then in the general population. These complications of T2DM are among the leading cause of mortality worldwide and cause a significant decrease in the life expectancy of diabetic patient.

The threat of a diabetes epidemic is gaining momentum and arousing global concern.[2] India now has 40.9 million people with diabetes and projected estimate for the 2025 is 69.9 million.[3] The World Health Organisation[WHO] estimates that approximately 180 million individuals are affected worldwide and this number is expected to be doubled by the 2030. Moreover the age of onset of T2DM is decreasing and it is increasingly observed in children.[4]

The new classification system given by American Diabetic Association (ADA) and World Health Organisation identify four types Diabetes mellitus (DM). Type-1, Type-2, other specific types and gestational diabetes. The occurrence of early onset T2DM between the age of 25-39 year was first described by O Rahilly [5] as a distinct clinical and genetic syndrome resulting from Inheritance of a diabetic genes or genes passed from parents. T2DM in the young and usually has higher prevalence in female and is often associated with relatively higher body mass index (BMI), dyslipidemia and hypertension. Insulin resistance (IR) is defined as a subnormal biological response to give an insulin concentration.[6] IR has been implicated as the central process in pathogenesis of T2DM. In patient with T2DM both plasma insulin and c-peptide concentrations are usually high reflecting underline IR. Raised serum VLDL, triglycerides and low levels of HDL cholesterol are the most frequently lipid abnormalities in patients with deranged glycemia, first degree relatives of T2DM and individuals with IR.[7-8]

Uric acid (UA) is the final oxidation product of purine metabolism. Excess UA accumulation can lead to various disease notably gouty Arthritis. Increased serum concentration of UA has been implicated in cardiovascular disease. High serum UA level may also be a sensitive

Marker for underlying vascular inflammation and re-modelling with the arterial vessel wall.[12] DM is caused by a derangement in the secretion of function of the endocrine function of the pancreas. In T2DM wherever the blood glucose was higher the serum amylase activity was found to be significantly lower. This reflected the derangement in the endocrine and exocrine axis of the pancreas, as a disease which affected by any portion of an organ would affect the adjoining area of that organs functionally.

Even though the prevalence of microvascular complications of diabetes like retinopathy and nephropathy are comparatively lower in the Indians the prevalence of premature coronary artery disease is much higher in Indian compared to the other ethnic groups. Hence the aims of the present study are to study and compare the lipid profile, serum amylase and UA in T2DM with controls. To find the correlation between biochemical parameters and diabetes.

MATERIAL AND METHODS:

The present study was carried out in the department of Biochemistry of Rohilkhand Medical College and Hospital Bareilly, Uttar Pradesh, India. After getting approval from institutional ethical committee written informed consent was taken from each enrolled patient prior to their inclusion into the study. This study includes total 120 subjects: 60 known cases of T2DM and 60 age and sex matched healthy adult as control subjects.

Exclusion criteria of patients were as follows:

- Fasting serum triglyceride is > 250 mg/dl.
- Inherited disorder of lipoprotein or family history of such disorder.
- Deranged liver function test.
- Patient on drugs affecting lipid metabolism like Beta blocker, diuretics, antihypertensive lipid lowering drugs and alcohol.
- Patient taking vitamin supplements for antioxidant for last 2 weeks.
- Clinical or biochemical evidence of hypothyroidism or Cushing's syndrome.
- Smoker and patient with congestive heart failure and hypercholesterolemia > 250 mg/dl.
- Patient with nephropathy as evidence by protein urea for raised blood urea and serum creatinine.

All subjects were called on post absorptive stage after 12 hours of fasting and 4 ml of venous blood was drawn for estimation of fasting blood sugar(FBS), Lipid profile (TC, TG, HDL, LDL, VLDL) UA, Amylase. After that 2 hours Post prandial blood sample (PPBS) was also drawn for the estimation of PPBS.

NORMAL RANGES

| S. No | PARAMETER | GOOD | FAIR | POOR |
|-------|----------------------------------------|--------------------------|---------|------------------------|
| 1. | Fasting Blood Sugar (mg/dl) | 65-100 | 100-120 | >120 |
| 2. | 2 hr Post Prandial Blood Sugar (mg/dl) | 100-135 | 135-170 | >170 |
| 3. | Total Cholesterol (mg/dl) | <200 | 200-240 | >240 |
| 4. | HDL Cholesterol (mg/dl) | >45 | 34-45 | <35 |
| 5. | LDL Cholesterol (mg/dl) | <130 | 130-160 | >160 |
| 6. | Serum Triglycerides (mg/dl) | <150 | 150-200 | >200 |
| 7. | Serum Uric Acid (mg/dl) | 2.4 (Female), 3.4 (Male) | - | >6 (Female), >7 (Male) |
| 8. | Serum Amylase (IU/L) | 0-137 | - | > 137 |

Anthropometric measurement included (Height, Weight and BMI) in all cases and controls.

Statistical analysis-

The data was analysed by using SPSS software. Values were given as mean \pm SD. The student T test is used to find the significant difference between cases and control.

OBSERVATIONS AND RESULTS:**Table: 1- Comparison Of Anthropometric Parameters In Case And Control Groups**

| Parameters | Case (N=60) | Range Case (N=60) | Control (N=60) | Range Control(N=60) | P Value |
|--------------------------|-----------------|-------------------|------------------|---------------------|---------|
| | Mean \pm SD | | Mean \pm SD | | |
| Height (cm) | 165 \pm 8.5 | 151-189 | 166.5 \pm 11.8 | 150-189 | 0.05 |
| Weight (kg) | 71.6 \pm 9.1 | 53-97 | 70.2 \pm 10.3 | 50-94 | 0.05 |
| BMI (kg/m ²) | 26.26 \pm 3.2 | 20-34 | 25.71 \pm 3.8 | 20-84 | 0.05 |

p Value is Significant if p < 0.005

TABLE: 2- COMPARISON OF GLYCEMIC PARAMETERS IN CASE AND CONTROL GROUPS

| Parameters | Case (N=60) | Range Case (N=60) | Control (N=60) | Range Control (N=60) | P Value |
|--------------|-------------------|-------------------|-----------------|----------------------|---------|
| | Mean \pm SD | | Mean \pm SD | | |
| FBS (mg/dl) | 174.05 \pm 27.8 | 140-260 | 88.2 \pm 8.6 | 66-102 | 0.0005 |
| PPBS (mg/dl) | 232.1 \pm 6.7 | 210-240 | 110.1 \pm 7.8 | 96-125 | 0.0005 |

p Value is Significant if p < 0.005

TABLE: 3- COMPARISON OF BIOCHEMICAL PARAMETERS IN CASE AND CONTROL GROUPS

| PARAMETERS | Case (N=60) | RANGE CASE (N=60) | Control (N=60) | RANGE CONTROL (N=60) | p VALUE |
|---------------------|------------------|-------------------|------------------|----------------------|---------|
| | Mean \pm SD | | Mean \pm SD | | |
| Cholesterol (mg/dl) | 168.2 \pm 42.3 | 116-305 | 167.2 \pm 25.5 | 110-220 | 0.05 |
| TG (mg/dl) | 151.8 \pm 32.2 | 79-204 | 134.7 \pm 41.3 | 75-275 | 0.0005 |
| HDL (mg/dl) | 41.05 \pm 5.9 | 30-55 | 45.6 \pm 4.1 | 38-54 | 0.0005 |
| LDL (mg/dl) | 105.3 \pm 36.7 | 62-236 | 89.3 \pm 25.5 | 32-133 | 0.05 |
| VLDL (mg/dl) | 30.3 \pm 6.4 | 15.8-40.8 | 28.6 \pm 8.5 | 15-55 | 0.05 |
| UA (mg/dl) | 4.8 \pm 1.4 | 3.4-12.8 | 3.76 \pm 1.1 | 1.9-7 | 0.0005 |
| Amylase (IU/L) | 54.2 \pm 11.4 | 24-88 | 55.3 \pm 12.01 | 24-88 | 0.05 |

p Value is Significant if p < 0.005

DISCUSSION:

In our study baseline clinical characteristics of cases and control includes demographic profile which has the study consisted of 60 cases patients and 60 control with a mean age of 46.28 \pm 8.8 and 34.68 \pm 12.03 years respectively.

There were 30 males 30 females in case group. There were 29 males and 31 females in control group therefore the data shows that there is female predominance in the study group. Our study is consistent with previous study conducted by Josna VP et al.[13] Anthropometric parameters include the mean height and weight were 165.5 \pm 8.5 cm and 71.6 \pm 9.1 kg in the patient group and 160.65 \pm 11.8 cm and 7.2 \pm 10.3 kg in control group. The mean BMI of cases was 26.6 \pm 3.2 and for control it was 25.7 \pm 3.8 kg/m² respectively. {Table1}

According to ATP-3/WHO recommendation criteria BMI was in abnormal range more than 25 kg / m² which was 40 (66.6%) in patients and 28 (46.6%) in controls. This signifies the presence of obesity in youth onset T2DM and their first degree relatives. On comparing with previous study done by Mishra et al[14] and Vikram et al[15] there is significant rise in percentage number of patient with higher BMI in our study. Therefore our studies suggest that youth onset T2DM are getting obese in North India. We have observed irregular eating habits and lack of physical exercise activity in both the groups which could be its probable cause.

The mean of FBS in cases group was 174.05 \pm 27.8 mg/dl and 88.2 \pm 8.6 mg/dl in control. Mean PPBS was 232.1 \pm 6.7 mg/dl in cases and 110 \pm 7.8 mg/dl in control.(Table-2) Study done by Vikram et al showed that presence of T2DM in first degree relatives was 82.3 percent in North India. Therefore, our study also shows that family history is very significant in young onset diabetics. Study suggests screening of all first degree relative at least for DM Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance(IGT).

Cholesterol in patient group with mean value was 168.2 \pm 42.3 mg/dl, HDL with mean value was 41.05 \pm 5.9 mg/dl and triglyceride was 151.8 \pm 32.2, raised in 12 patient in this group. In controls mean serum cholesterol was 167.2 \pm 25.5 mg/dl, mean HDL was 45.6 \pm 4.1 the mean triglyceride was 134.7 \pm 41.3 mg/dl. It was raised in 32 patients. Mean value for LDL was 89.3 \pm 25.5 mg/dl in control. HDL was lower in 34 patient in control group which was very significant.(Table-3) Thus majority of cases in our study had abnormal lipid profile. These results are coincides with previous studies. [15]

Usually the elevation is moderate 1.5-3 folds as compared with non diabetic subject matched for sex age and body mass index.[9-10]The concentration of HDLC is on an average reduced by 10 to 20%. The decrease HDLC occur primarily in the HDL to subfraction, the subtraction most closely associated with protection action against CAD[11] High triglyceride level have been shown to the strongly associated with the lower HDL level and with small HDL size in patient with insulin resistance.

There has been increase in prevalence of youth onset T2DM that is decreasing trend of age, may be due to heredity, strong family history, obesity, physical inactivity and poor eating habits leading to obesity, all probably contributing to premature development of T2DM and metabolic syndrome. The family history of diabetes, high BMI, adiposity, deranged lipid profile, absence of recent weight loss, no requirement for insulin in past and science of IR revealed striking different among T1DM and T2DM of young.

These can be used as simple marker of segregation in situation where marker of autoimmunity genetic marker and c-peptide assay are not available. Thus T2DM in young patient can be clinically diagnosed based on criteria given above. In our study, we reported robust predictions of DM in youth and their first degree relative including

family history of diabetes, high BMI, raised total triglycerides, T2DM and its fore runner, pre-diabetes provide fertile ground for incorporating family history information into an efficient screening strategy. In general history of DM in a first degree relative doubles an individual risk of developing the disease in future. In our study family history was seen in 60% of young Diabetics which is very significant because of metabolic phenotypes sharing between early onset DM and their first degree relatives. Therefore we suggest all first degree relative should be screened for metabolic and biochemical parameters, to prevent, overt risk.

Our findings suggest a strong renal involvement in the balance of plasma UA and may also reflect certain dietary pattern, such as high intake of protein, fat and certain local vegetables. Many predictor variables and their interactions were analysed along with the reason for the high plasma UA level in persons with IGT and for the low plasma UA level in Diabetic patients which coincides with previous study done by Jaakko tuomilehto et al[16] In our study the mean serum UA level was 4.8 ± 1.4 in case group and 3.76 ± 1.1 in control group. These findings are similar to study done by A.Costa et al[17] p value was highly significant. Recent studies have introduced serum UA as a potential risk factor for developing diabetes, hypertension, stroke and CVD. The value of elevated level of UA in serum as a risk factor for diabetes development is still under scrutiny. Recent data suggest that clearance of UA is being reduced with increase in insulin resistance and UA as a marker of prediabetes period. With aging, level of UA increased in serum of diabetic patients.[18] Low serum amylase levels may reflect impaired exocrine and endocrine relationship in the pancreas. Serum amylase was associated with the pathogenesis of impaired insulin action, metabolic syndrome and diabetes. Clinical variables except for age and estimated glomerular filtration rate, shifted favorably with increasing serum amylase levels. The mean serum amylase level in our study was 55.3 ± 12.01 in cases and 54.2 ± 11.4 in control group.(Table-3) This is similar in study done by Nakajima et al. Low serum amylase is also associated with insulin deficiency in patient with T1DM and less commonly with T2DM. In terms of risk factor, only kidney dysfunction contributes to elevation in serum amylase level because the kidney play the main role in elimination circulating amylase. Regarding the cause effect relationship, low serum amylase level were believed to be due to deficiency of insulin activity.

CONCLUSION :

Based on the results of the present study and data available from literature it is clear that in Diabetes the serum level of lipid profile, UA and serum amylase were altered, but it remains to be unknown whether these changes are a cause or consequences of the disease. It is not clear which is the primary event that trigger the neuropathy diabetic, nephropathy and retinopathy. Many studies as shown that hyperuricemia and increase level of triglyceride play a role in severity and outcome of diabetes. Low serum amylase level may reflect impaired exocrine and endocrine relationship in the pancreas. It may be due to deficiency of insulin activity, serum UA as a potential risk factor for developing diabetes, hypertension, stroke and CVD.

Future perspectives:

This study is just a drop in the ocean of diabetes researches and need to be done with large sample to find more statistically significant data and probabilities. New outcomes and possibilities are definite for this research.

REFERENCES:

- World Health Organization: Definition, Diagnosis and classification of Diabetes Mellitus and its Complications. Part-1: Diagnosis and classification of Diabetes Mellitus. Geneva, Department of non communicable Disease Surveillance, 1999.
- King H, Rewers M, Global estimates for prevalence of diabetes mellitus and impaired glucose tolerance in adult. WHO AdHoc Diabetic reporting Group, Diabetes care 1993; 16:157-177.
- International Diabetes Federation (IDF), Diabetes Atlas, 3rd ed., 2007.
- Ferrante AWJ, Obesity induced inflammation a metabolic dialogue in the language of inflammation. J in-term Med.2007;262:408-14.
- O Rahilly S, Spirey RR, Nugent Z, Clark A, Turner RC. Type-II diabetes of the early onset: a distinct clinical and genetic syndrome? BMJ 1987; 294: 923-28.
- Khan CR Insulin resistance, insulin sensitivity and insulin unresponsiveness: a necessary distinction metabolism 1978; 27: 1893-1902.
- Taskinen M, Quantitative and qualitative lipoprotein abnormalities in diabetes mellitus. Diabetes 1992; 41: 12-17.
- Taskinen MR, Hyperlipidemia in diabetes. Baillieres clinical Endocrinol Metab 1990; 4: 743-45.
- Brunzell JD, Hazzard WR, Motulsky AG et al, Evidence for diabetes mellitus and genetic forms of hypertriglyceridemia as independent titles. Metabolism 1975; 24: 1115-21.
- Axisen M, Smith U, Eriksson JW, Taskinen MR et al, Post prandial hypertriglyceridemia and insulin resistance in normoglycemic first degree relatives of patients with Type-2 diabetes. Ann Intern Med 1999; 131: 27-31
- Syvanne M, Ahola M, Subfractions in non insulin dependent diabetes mellitus and coronary artery disease. J lipid Res 1995; 36: 573-82
- Melvin Hayden, Uric acid-new look at CVD and metabolic syndrome. Nutrition and metabolism 2004, 1: 10
- Jyotsna VP et al, Clinical and biochemical profiles of young diabetes in North-Eastern India. J Assoc Phy Ind 2002; 50: 1130-34.
- Mishra A et al, Simple anthropometric measures identify fasting hyperinsulinemia and clustering of cardiovascular risk factors in Asian Indian adolescents. Metab Clinical Experimental 2006; 55: 1569-73.
- Vikram NK, Tandon N, Mishra A et al, Correlates of Type-2 Diabetes mellitus in children adolescents and young adults in north India: a multisite collaborative case control study. Diabet Med 2005; 23: 293-98.
- Jaakko Tuomilehto, Paul Z, Eva W, et al, Plasma uric acid level and its association with diabetes mellitus and some biologic parameters in a biracial population of Fiji. Am. J. Epidemiol 1988; 127(2): 321-336.
- Costa A, Iguá I, Bedini J et al, Uric acid concentration in subjects as risks of Type-2 diabetes mellitus: Relationship to components of the metabolic syndrome. 2002; 51(3): 372-75.
- Causevic A, Semiz S, Macic Drankovic A et al, Relevance of uric acid in progression of Type-2 diabetes mellitus. Bosn J Basic Med Sci. 2010;10(1): 54-9.