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Biochemistry

RELATIONSHIP OF SERUM MAGNESIUM, CALCIUM, LACTATE DEHYDROGENASE AND ADENOSINE DEAMINASE LEVELS TO THE GLYCEMIC STATUS IN TYPE 2 DIABETES MELLITUS PATIENTS.

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ABSTRACT Type 2 diabetes mellitus occurs when the body has developed insulin resistance and cannot use insulin properly. Micronutrients andd minerals are known to play a pivotal role in regulating various metabolic processes of living system. Its deficiencies or excess have been implicated in the aetiopathogenesis of several human diseases including diabetes. Magnesium plays important role in the insulin secretion, insulin receptor interaction, post receptor events involving tyrosine kinase mediated phosphorylation and normal carbohydrate utilization (by Mg dependent enzymes). A compromise in these functions leads to insulin resistance and poor glycemic status in magnesium depletion. Calcium plays an important role in glycemic control by affecting the biosynthesis and release of insulin from the beta cells of the pancreas. LDH is a glycolytic enzyme predominantly found normally in heart, liver and muscle tissues. Increased serum lactate dehydrogenase activity was seen in diabetics due to the influence of insulin on heart, liver and muscle with poor metabolic control. Adenosine deaminase is considered as a good marker of cell mediated immunity. Insulin enhances lymphocyte function, differentiation and proliferation, and also maintains the activated state of the T lymphocyte by enhancing the energy requirements and protein synthesis necessary for proper lymphocyte functioning. So, there will be a decrease in adenosine levels in insulin sensitive cells with higher ADA activity in type 2 diabetes mellitus. The purpose of this study is to predict the strong glycemic marker for assessing the glycemic status of recently diagnosed type 2 diabetes mellitus patients among the four parameters chosen for study. Comparison serum total cholesterol, FBS, BMI with HbA1c among the diabetic cases were statistically significant($p=0.08$, $p=0.028$, $p=0.00013$). Serum magnesium, calcium, lactate dehydrogenase, adenosine deaminase with HbA1c among diabetic cases show no correlation and was not significant ($p=0.91$, $p=0.25$, $p=0.34$, $p=0.51$). The study revealed no significant correlation between serum magnesium, calcium, lactate dehydrogenase and adenosine deaminase with HbA1c among type 2 diabetic mellitus patients

KEYWORDS : Magnesium, Calcium, Lactate Dehydrogenase, Adenosine deaminase, type 2 diabetes mellitu

INTRODUCTION

Diabetes is a group of metabolic diseases with high blood sugar levels over a prolonged period. Type 2 diabetes mellitus occurs due to insulin resistance and inadequate insulin secretion by the pancreatic β-cells. Insulin resistance leads to decreased glucose transport into muscle cells, elevated hepatic glucose production, and increased breakdown of fat which causes disturbance in carbohydrate, lipid and protein metabolism.[1]

In India, currently there are 62 million people with diabetes. By 2030, this number is estimated to rise to 80 million.[2]

Diabetes increases the risk to various macrovascular and microvascular complications due to chronic hyperglycemia. So, complications seen with diabetes, increase as a function of duration of glycemic status. Therefore attempt to reduce the blood sugar levels delays or prevents these complications.[3]

Several micronutrients enhance insulin action and they offer promise in countering the unpredictable consequences of hyperglycemia. Its deficiencies or excess have been implicated in the vascular complications of diabetes.

Magnesium is the second most abundant divalent component in the intra cellular compartment. Hypomagnesaemia often occurs in type 2 diabetes mellitus patients especially with poorly controlled glycemic status. Mg is involved in insulin secretion, binding and activity. Magnesium is the second messenger for post receptor events of insulin[4]. Hypomagnesaemia may worsen the existing diabetes by lessening the insulin secretion from the pancreatic β-cells due to Mg deficiency the tyrosine kinase and other protein kinase mediated autophosphorylation in the post receptor insulin signalling cascade are affected as they are dependent on Mg^{2+}.[5,6]

Calcium is an important element that plays a pivotal role in not only in skeletal mineralization but also in various biological activities. Hypocalcaemia is associated with uncontrolled hyperglycemia in patients with type 2 diabetes. Insulin secretion and insulin receptor phosphorylation is a calcium dependent process. So, any impairment of insulin secretion and insulin receptor phosphorylation leads to adverse effects on beta cell secretary function and impaired insulin signal transduction and decreased GLUT-4 activity respectively.[7]

Lactate Dehydrogenase(LDH) is a key enzyme for anaerobic glycolysis. Due to poor metabolic control in diabetic patient serum LDH activity will be increased. Normally low levels of LDH are maintained by Beta cells of islets of Langerhans, but in case of type 2 diabetes mellitus patients the activity of LDH is increased and the availability of glucose is normal. So it interferes with normal glycaemic index. Hence it causes defects in insulin secretion.[8]

Adenosine deaminase enzyme plays an important role in the development and maintenance of the immune system. Its main function is to eliminate a molecule called deoxyadenosine by deamination, which is the breakdown product of DNA.[9] Normally the activity of lymphocytes is increased by insulin and by increasing the energy needs. The active state of t-lymphocytes is also maintained by insulin. Adenosine is the factor that inhibits lipolysis by acting on A1 receptors of adipose tissues thereby reducing the free fatty acid levels and increases insulin sensitivity. In type 2 diabetes patients, the level of ADA is found high. Hence due to the increased activity of ADA in tissues which is more sensitive to insulin, glucose uptake by cells is reduced which results in hyperglycemia.[10]

Various studies have individually evaluated the association between micronutrients and metabolic enzymes with glycemic status in type 2 diabetes mellitus of different populations. Our study is first of its kind to examine the influence of glycemic control by the serum levels of magnesium, calcium, lactate dehydrogenase and adenosine deaminase in recently diagnosed type 2 diabetes mellitus patients in the same population.

Our present study is designed to predict the strong glycemic marker for assessing the glycemic status of recently diagnosed type 2 diabetes mellitus patients among the four parameters chosen for study.

AIMS & OBJECTIVES:

- The aim and objective of current study is,
- To assay the serum levels of Magnesium in type 2 diabetes mellitus patients

- To assay the serum levels of Calcium in type 2 diabetes mellitus patients.
- To assay the serum levels of lactate dehydrogenase in type 2 diabetes mellitus patients.
- To assay the serum levels of Adenosine deaminase in type 2 diabetes mellitus patients.
- To evaluate and compare the BMI, Lipid profile and HbA1c in type 2 diabetes mellitus patients and controls.
- To examine the relation between serum levels of Magnesium, Calcium, lactate dehydrogenase, Adenosine deaminase to Lipid profile, BMI and HbA1c in type 2 diabetes mellitus patients.

METHODOLOGY

This is a Case-Control study conducted in the month of May – June 2019 at the Department of Internal medicine, Tertiary care Hospital. The study included 60 recently diagnosed 30 – 55 years old type 2 diabetes mellitus patients of one year duration without complications. Known Type 2 Diabetes mellitus patients more than 1 year duration and with complications, Pregnant women, Type 1 diabetes mellitus, Serious infections, Smokers , known alcoholics, Patients with chronic hypertension, thyroid disease, cardiovascular disease, renal failure, chronic liver failure, lung disease, hemolysis, Under treatment of immunosuppressive drugs and drugs that affect magnesium levels were excluded from the study.

SAMPLE: 5ml of overnight fasting venous blood sample collected in red and grey vacutainer tube.

Fasting blood sugar concentration was determined by GOD/POD method (Enzymatic end point method). Blood urea concentration was determined by UV-GLDH method. Serum creatinine concentration was determined by Modified Jaffe's Reaction. Total Cholesterol (TC) concentration was determined by CHOD-PAP (Enzymatic End point Analysis). Triglyceride (TGL) concentration was determined by GPO-PAP (Enzymatic End point analysis). High density lipoprotein (HDL) concentration was determined by Phosphotungstate method. Low density lipoprotein (LDL) and very low density lipoprotein (VLDL) concentration was calculated using Friedewald formula, VLDL= TGL/5, LDL = TC-(HDL+VLDL). Hb1Ac levels were determined by Immunoturbidimetric Assay. Magnesium levels were determined by Xylidyl Blue Method. Calcium levels were determined by Arsenazo Method. Lactate dehydrogenase levels were determined by DGKC Method. Adenosine deaminase levels were determined by Enzymatic Method. All the parameters were estimated by enzymatic method using commercial kits in EM 360 autoanalyser. Body mass index (BMI) was calculated as weight in kilograms divided by height in meter square(kg/m^2). Waist-hip ratio was calculated as waist measurement divided by hip measurement (W ÷ H).

RESULTS

A total number of 120 samples were analyzed to study the levels of Fasting plasma glucose, lipid profile, BMI, serum magnesium, calcium, lactate dehydrogenase and adenosine deaminase in 60 age matched healthy controls and 60 diabetic patients as cases.

Statistical Analysis

- Statistical analysis performed using SPSS package v21.0
- The results were expressed as mean ± standard deviation (SD).
- Pearson correlation was applied to correlate between the parameters.
- Independent sample student's 't' test was used to compare mean values.
- P<0.05 was considered statistically significant.

The overall mean age of controls and case are 48 and 49(range 30 to 55 yrs). The mean value and standard deviation of BMI in controls (n=60) and diabetic cases (n=60) were 20.94±1.34 and27.14±4.2kg/m2 respectively. BMI among the groups were increased and statistically significant (p<0.0001).

The overall mean age of controls and case are 48 and 49(range 30 to 55 years). The mean value and standard deviation of W/H ratio in controls (n=60) and diabetic cases (n=60) were 0.90±0.23 and 1.90±0.03 kg/m2 respectively. BMI among the groups were increased and statistically significant (p<0.0001).

The mean value and standard deviation of fasting blood glucose in controls (n=60) and diabetic cases controls (n=60) were 99.7±19.8 and 209.1±80.2mg/dl respectively. FBG among the cases and controls were increased and statistically significant (p<0.0001).

The mean value and standard deviation of lipid profile parameters like Total cholesterol, Triglycerides , HDL, VLDL, LDL in controls (n=60) and diabetic cases(n=60) divided were increased and statistically significant (p<0.05).

The mean value and standard deviation of serum magnesium in controls (n=60) and diabetic cases were 1.98±1.03 and 1.98±1.03 mg/dl respectively and were not statistically significant (p=0.51).

The mean value and standard deviation of serum calcium in controls (n=60) and diabetic cases were 10.36±1.03and 9.58±1.02 g/dl respectively and were statistically significant (p=0.0001).

The mean value and standard deviation of serum lactate dehydrogenase in controls (n=60) and diabetic cases were 381.2±72.6 and 494.7±102.7 U/L respectively and were statistically significant (p<0.0001).

The mean value and standard deviation of serum adenosine deaminase in controls (n=60) and diabetic cases were 25.5±4.6and 14.67±6.44U/L respectively and were statistically significant (p<0.0001).

TABLE-1: Parameters (Mean±SD) among controls and diabetic cases.

S.no	Parameter	CONTROL	DIABETES MELLITUS
1	Glucose	99.7±19.8	209.1±80.2
2	TC	172.6±40.6	212.5±22.5
3	TGL	125.2±23	187.2±66.7
4	HDL	49.5±10.3	34.7±3.2
5	LDL	112.9±35.6	163.7±16.8
6	VLDL	25.2±7.6	37.4±13.3
7	BMI	20.94±1.34	27.14±4.2
8	W/H ratio	0.90±0.23	1.90±0.03
9	MG	1.98±1.03	1.98±1.03
10	ADA	25.5±4.6	14.67±6.44
11	LDH	381.2±72.6	494.7±102.7
12	CA	10.36±1.03	9.58±1.02
13	HbA1c	5.6±0.83	8.36±0.90

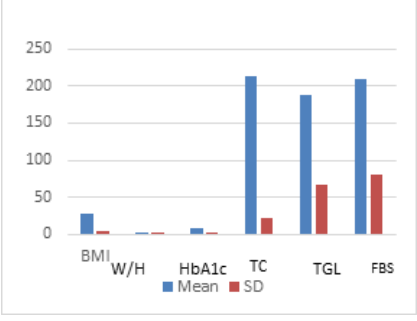

Figure 1: Comparison of BMI,W/H ratio, FBS, TC, TGL,HbA1c among diabetes cases.

This bar diagram shows the comparison between the BMI, W/H ratio, FBS , lipid profile, HbA1c among diabetic cases.

Comparison serum total cholesterol, FBS, BMI with HbA1c among the diabetic cases were statistically significant(p=0.08, p=0.028, p=0.00013)

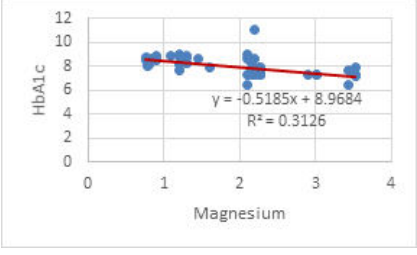

Figure 2: Correlation between serum magnesium and HbA1c among diabetic cases

Serum magnesium and HbA1c among diabetic cases show no correlation and was not significant (p=0.91)

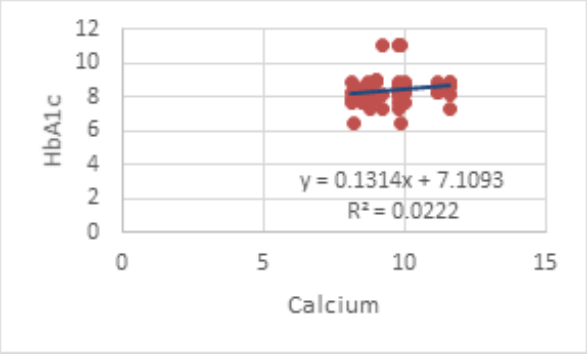

Figure 3: Correlation between serum calcium and HbA1c among diabetic case

Serum calcium and HbA1c among diabetic cases show no correlation and was not significant (p=0.25)

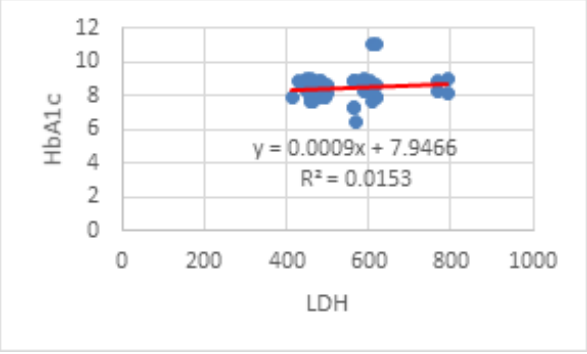

Figure 4: Correlation between serum lactate dehydrogenase and HbA1c among diabetic cases

Serum lactate dehydrogenase and HbA1c among diabetic cases show no correlation and was not significant (p=0.34)

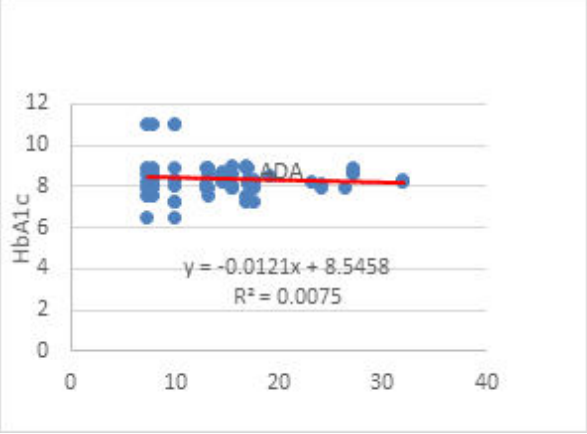

Figure 5: Correlation between serum adenosine deaminase and HbA1c among diabetic cases

Serum adenosine deaminase and HbA1c among diabetic cases show no correlation and was not significant (p=0.51).

DISCUSSION

In India, currently there are 62 million people with diabetes. By 2030, this number is estimated to rise to 80 million. Micro vascular and macro vascular complications seen with diabetes, increase as a function of duration of glycemic status. Micronutrients and minerals are known to play a pivotal role in regulating various metabolic processes of living system. Its deficiencies or excess have been implicated in the aetiopathogenesis of several human diseases including diabetes mellitus.

Arpaci et al, Arslanoglu et al, mather HM et al, Abdul wahid et al and many more studies showed poor glycemic regulation affects serum Magnesium levels.

Vineet kumar khemka et al, Mon Mohan Boro et al, T. Hoshino et al, J.G. Lee et al and many more studies showed higher serum adenosine deaminase levels in type 2 diabetes mellitus patients.

Rooney MR et al, sunghwan suh et al, and many more study showed elevated serum calcium was found to be associated with a greater risk of type 2 diabetes cases.

Vizir OO et al, Edward k. Ainscow et al studied the association of elevated lactate dehydrogenase in type 2 diabetes mellitus.

In our study, we found no significant correlation between serum magnesium, calcium, lactate dehydrogenase and adenosine deaminase with HbA1c among type 2 diabetic mellitus patients. We found significant correlation between fasting blood glucose, lipid profile, BMI and HbA1c among diabetic cases.

We found significant correlation between fasting blood glucose, lipid profile, BMI , HbA1c, serum calcium, serum lactate dehydrogenase and serum adenosine deaminase among diabetic casesand control groups.

Large multi centric trial with higher sample size may be needed to assess the correlation between serum magnesium, calcium, lactate dehydrogenase , adenosine deaminase and HbA1c among diabetic patients. We need to study the complications and duration of diabetes with these parameters.

CONCLUSION

Type 2 diabetes mellitus is an endocrinological disease associated with hyperglycemia characterized by both insulin resistance and defective insulin secretion.

Complications seen with diabetes, increase as a function of duration of glycemic status. Therefore attempt to reduce the blood sugar levels delays or prevents these complications. Micronutrients and minerals are known to play a important role in regulating various metabolic processes.

Magnesium is important for insulin secretion, insulin receptor interaction, post receptor events involving tyrosine kinase mediated phosphorylation and normal carbohydrate utilization by magnesium dependent enzymes. Calcium controls the glycemic status by affecting the biosynthesis and release of insulin from the beta cells of the pancreas. LDH is a glycolytic enzyme predominantly found normally in heart, liver and muscle tissues. Adenosine deaminase is a key enzyme involved in purine metabolism that irreversibly deaminates adenosine and deoxyadenosine to inosine and deoxyinosine.

This study revealed no significant correlation between serum magnesium, calcium, lactate dehydrogenase and adenosine deaminase with HbA1c among type 2 diabetic mellitus patients.

To conclude among the four parameters chosen for study serum magnesium, calcium, lactate dehydrogenase and adenosine deaminase showed no statistically significant association with glycemic status of diabetic cases.

We propose for future studies with increased sample size and to compare diabetic males and female gender individuals for assessing the complication. We also need to assess these parameters with duration of diabetes.

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