Serum Calcium, Inorganic Phosphate and Serum Alkaline Phosphatase levels in Type 2 Diabetes Mellitus

*Afrin S,[1] Sarker A,[2] Anwar M,[3] Sarkar CR,[4] Sarker PC,[5] Zahid AR[6]

In type 2 diabetes mellitus, a metabolic disorder causes disturbances of different metabolic processes of the body including electrolyte and minerals imbalance. Therefore changes in serum level of total calcium, ionized calcium, inorganic phosphate and alkaline phosphatase in patients with type 2 diabetes mellitus . So, this cross sectional study was conducted to observe serum total calcium, ionized calcium, inorganic phosphate and alkaline phosphatase levels in Type 2 diabetes mellitus patients from July 2014 to June 2015 in the Department of Physiology, Rangpur Medical College, Rangpur. For this study, total number of 100 subjects aged 30 – 50 years of both sex were selected. Subjects were also sex and socio-economical condition matched. Among them 50 non-diabetic subjects were included in group-A (Control) and 50 Type 2 diabetes mellitus patients included in group-B (Experimental). The subjects of group-A were selected from surrounding community of Rangpur district and subjects of Group-B were selected from Diabetic Association and from Outdoor of Endocrinology Department, Rangpur Medical College and Hospital. For statistical analysis independent sample "t" test was performed by computer based software SPSS-17.0 version for windows. Serum total calcium, ionized calcium, inorganic phosphate levels are significantly lower ($p<0.001$) and serum alkaline Phosphatase level significantly higher ($p<0.001$) in Type 2 diabetes mellitus patients. Early evaluations of these parameters are helpful to control blood glucose level and prevent complications in diabetic patients.

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Key words: Type 2 Diabetes Mellitus, serum total and ionized calcium, inorganic phosphate, alkaline phosphatase

Introduction

Diabetes mellitus is a syndrome of impaired carbohydrate, fat and protein metabolism caused by either lack of insulin secretion or decreased sensitivity of the tissues to insulin.[1] WHO estimation of global diabetes prevalence for all aged group was 2.8% in 2000 and will be 4.8% in 2030.[2] In 2010 an estimated 285 million people worldwide had diabetes, according to the International Diabetes Federation. The federation predicts as many as 438 million will have diabetes by 2030.[3] Type 2 diabetes is more common than Type 1 accounting for about 90-95% of all cases of Type 2 Diabetes mellitus.[1] Type 2 Diabetes Mellitus poses a major global health threat, both in the developed and developing countries. Researchers observed that type 2 diabetes mellitus in Bangladesh ranging from 1.0 to 3.8% in rural population and 1.5 to 8% in urban population.[4]

1. *Dr. Sajeda Afrin, Lecturer, Department of Physiology, Rangpur Medical College, Rangpur. sajedaafrin82@gmail.com.
2. Dr. Anupam Sarker, BIRDEM Hospital, Dhaka.anupam.imc@gmail.com
3. Dr. Mahfuj-ul-Anwar, Medical Officer, Department of Medicine, Rangpur Medical College Hospital, Rangpur.
4. Professor Dr. Chandra Rani Sarkar, Head of the Department of Physiology, Rangpur Medical College, Rangpur.
5. Professor Dr. Parimal Chandra Sarker, Head of the Department of Microbiology, Rangpur Medical College, Rangpur
6. Dr. A.T.M Zoadur Rahim Zahid, Associate Professor, Department of Physiology, Rangpur Medical College, Rangpur.

*For correspondence

High intake of calcium and vitamin D, particularly from supplements may lower the risk of diabetes by 33%. Calcium have been suspected as modifiers of diabetes risk. Disturbance in mineral metabolism in diabetes is well-known for the last three decades. Calcium ion plays an important role in glycemic control by influencing the biosynthesis and release of insulin from the beta cells of the pancreas. Recently there is enough evidence to suggest that altered calcium homeostasis may also play a role in the development of type 2 diabetes.[5] A metabolic imbalance in inorganic phosphate occurs from the early onset of diabetes mellitus and may lead to a reduction of high energy phosphates and tissue hypoxia. These changes take place in the cells and tissues in which the entry of glucose is not controlled by insulin. Changes in serum phosphate level is related with severity of diabetes mellitus.[6]

In type 2 diabetes mellitus, hyperinsulinemia in combination with a high free fatty acid (FFA) influx and hyperglycemia are known to up-regulate lipogenic transcription factors. The fatty acids overload the hepatic mitochondrial-oxidation system, leading to accumulation of fatty acids in the liver.[5] These mechanisms finally lead to non-alcoholic fatty liver disease (NAFLD) in type 2 Diabetes Mellitus patients.[7] In the majority of cases, non-alcoholic fatty liver disease causes asymptomatic abnormality of alkaline phosphatase (ALP). It has been reported that diabetes mellitus lead to alteration in bone metabolism. Changes in bone metabolism in patients with type 2 have been reported. [8] Alteration in bone formation, impaired quality of bones and disturbances in bone micro and macro architecture have also been observed. This lead to changes in serum alkaline phosphatase.[9]

So this study will be helpful for proper management, prevent complications, improving health and reduce morbidity of type 2 diabetes mellitus patients.

Methods

This is a cross sectional analytical study was conducted in Department of Physiology, Rangpur Medical College, Rangpur from July, 2014 to June, 2015. A total number of 100 subjects with age ranging from 30 to 50 years were included in this study. Among them 50 were apparently healthy control subjects and 50 were newly diagnosed untreated Type 2 diabetes Mellitus experimental subjects. All subjects were age, sex and socio-economical condition matched. Type 2 diabetes mellitus patients were selected from outpatient department of Endocrinology, Rangpur Medical College and Diabetic Association, Rangpur. The objectives, nature, purpose and benefit of the study were explained to the subjects in details. Informed written consents were taken from all participants. Subjects of known Type 2 Diabetes Mellitus with complications like retinopathy, nephropathy, neuropathy, hypertensive and alcoholic or smokers diabetic patients were excluded from the study.

The subjects were advised to be overnight (8-10 hrs) in fasting state. Fasting venous blood sample was collected from the subjects next day at 8.00 am. Five ml of venous blood was collected from antecubital vein from each subject under all aseptic precaution by a disposable syringe. The needle detached from the nozzle and blood was immediately transferred into a de-ionized test tube with a gentle push to avoid hemolysis. Test tubes were kept in standing position till formation of clot. Serum was separated by centrifuging the blood at 3000 rpm for 5 minutes. The clear supernatant was taken and kept in an ependorfs. Tests were carried out as early as possible. Tests were done for serum total calcium, inorganic phosphate, serum alkaline phosphatase, serum fasting blood sugar. Serum total protein was done for the calculation of ionized serum calcium.[10] For collection of next sample 75 gm. glucose was ingested to the subjects. Just after 2 hours 5 ml blood again collected and centrifuge prepared for serum glucose. All tests were done by Auto Analyzer

in the Department of Biochemistry, Rangpur Medical College, Rangpur.

All data were recorded systematically in a preformed history sheet and all statistical analysis was done by computer using the software SPSS 17.0 version for windows. Comparison of serum total and ionized calcium, inorganic phosphate, serum alkaline phosphatase levels in apparently healthy non-diabetic subjects and diabetic patients done by unpaired 't' test. In the interpretation of results, < 0.05 level of probability (p) was accepted as significance.

Results

The mean ±SD level of fasting serum glucose and serum glucose level 2 hours after ingestion of 75 gm glucose in type 2 diabetes mellitus patients were statistically significant (p< 0.001) than that of control group (Table-I).

Table I: Showing mean ± SD serum glucose and serum 2 hours after 75 gm glucose ingestion in non-diabetic and diabetic subjects

Variables	Non diabetes N=50 Mean ± SD	Type 2 Diabetes mellitus N=50 Mean ± SD	p value
Fasting serum glucose (mmol/L)	3.45 ± .287	9.388 ± 1.452	0.000***
Serum glucose level 2 hours after ingestion of 75 gm glucose (mmol/L)	5.54 ± .240	17.52 ± 1.66	0.000***

Data were expressed as mean ± SD. Statistical analysis was done by Unpaired student's 't' test to compare between two groups. *** = P< 0.001.

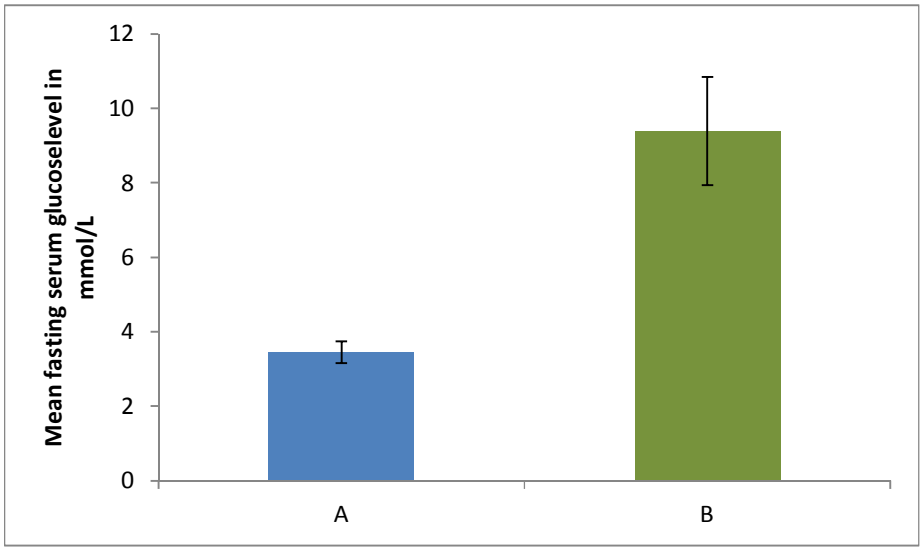

Figure 1. Mean ± SD serum fasting glucose level in group A (Control) and group B (Experimental).
*** = p< 0.001.

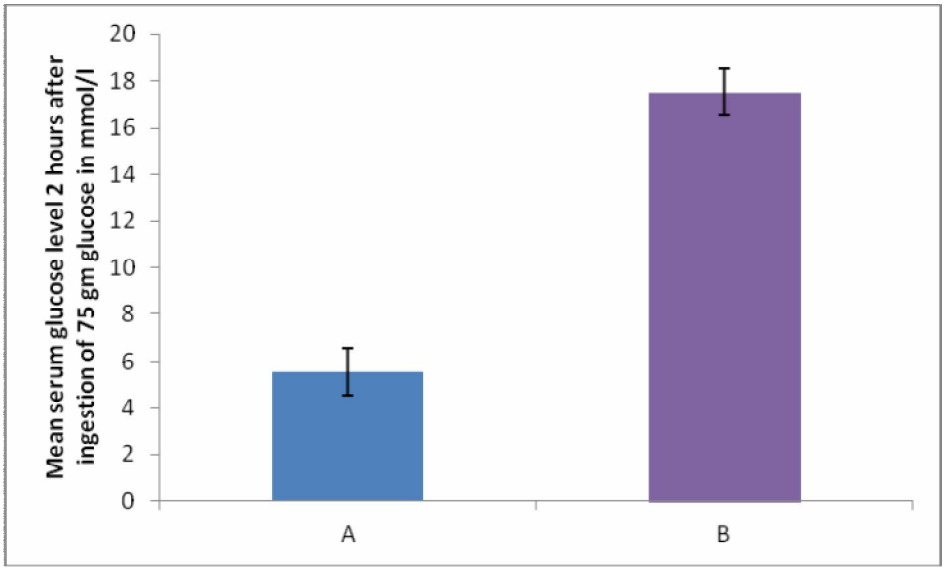

Figure 1. Mean ± SD serum glucose level 2 hours after ingestion of 75 gm glucose in group A (Control) and group B (Experimental). *** = p< 0.001.

The mean ±SD levels of serum total calcium , serum ionized calcium, serum inorganic phosphate and serum alkaline phosphatase (ALP) in type 2 diabetes mellitus patients were statistically significant (p< 0.001) than that of control group (Table-II)

Table II: Showing mean ± SD serum total Calcium, ionized Calcium, serum inorganic phosphate and serum alkaline phosphatase (ALP) levels in study subjects

Variables	Non diabetes N=50 Mean ± SD	Type 2 diabetes mellitus N=50 Mean ± SD	p value
Serum total calcium (mmol/L)	2.30 ± 0.02	2.12 ± 0.03	0.000**
Serum ionized calcium (mmol/L)	1.08 ±0.009	1.02 ± 0.007	0.000***
Serum inorganic Phosphate (mmol/L)	1.32 ±0.03	1.07 ± 0.01	0.000***
Serum Alkaline phosphatase level(IU/L)	124.68 ± 9.496	152.41 ± 23.31	0.000***

Data were expressed as mean ± SD. Statistical analysis was done by Unpaired student's 't' test to compare between two groups. *** = P< 0.001.

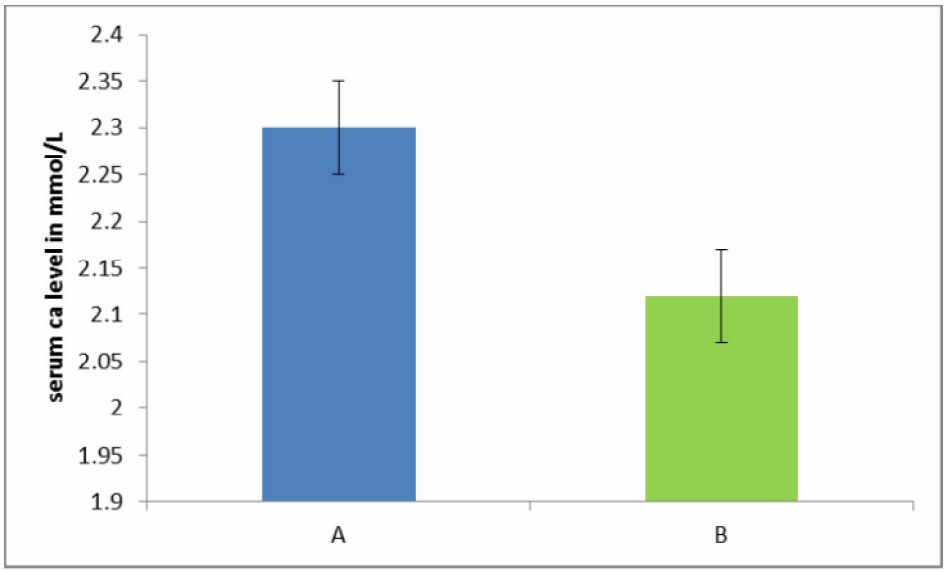

Figure 2. Mean ± SD serum total calcium levels in group A (Control) and group B (Experimental). *** = p< 0.001

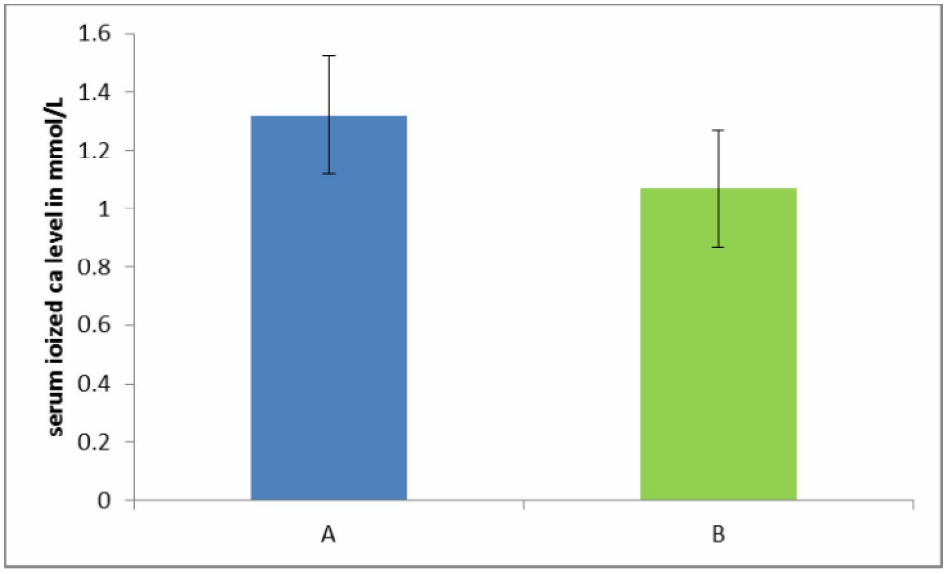

Figure 3. Mean ± SD serum ionized calcium levels in group A (Control) and group B (Experimental). *** = p< 0.001

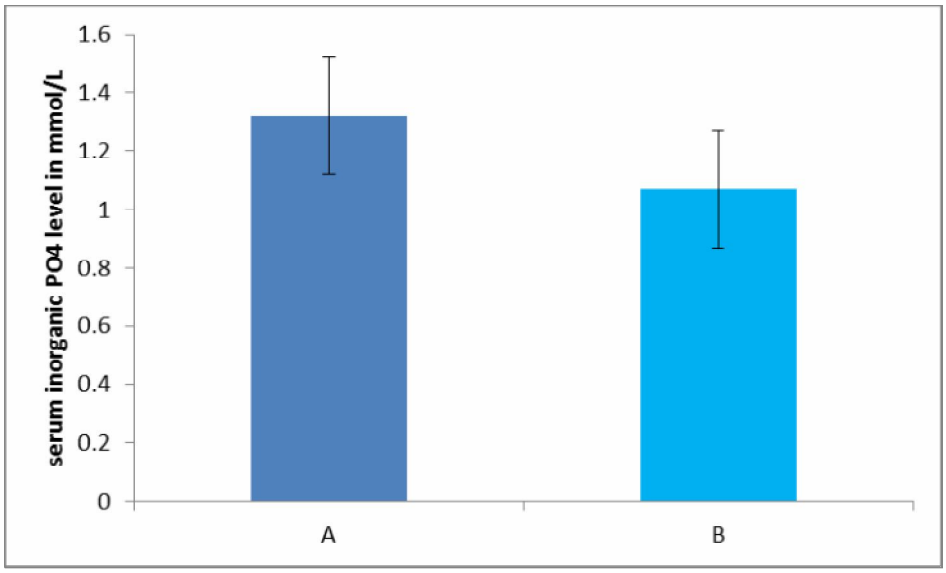

Figure 4. Mean ± SD serum inorganic phosphate levels in group A (Control) and group B (Experimental).. *** = p< 0.001

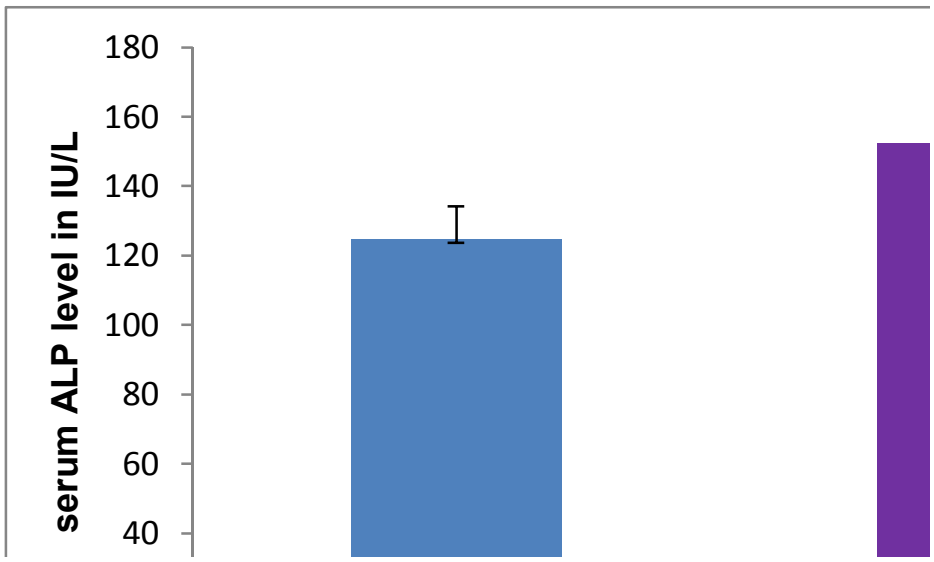

Figure 5. Mean ± SD serum alkaline phosphatase levels in group A (Control) and group B (Experimental). *** = p<0 .001

Discussion

In the present study, serum total and ionized calcium, inorganic phosphate levels were significantly lower and serum alkaline phosphate level was significantly higher in Type 2 diabetes mellitus patients than that of control subjects. This finding is consistent with that of some other investigators.[3,8,9,11] In contrast some studies found no change in level of serum calcium and decreased alkaline phosphatase level.[12] Other studies also found

increase level of serum calcium level in type 2 diabetes mellitus patients.[13]

This present study showed lower levels of serum calcium in diabetic as compared to non-diabetic subjects. From thisfindings of the present study in diabetes mellitus, increased urinary loss of calcium due to osmotic diuresis may be the common and most important cause of lower level of serum total calcium, ionized calcium. Altered calcium homeostasis may play a role in the development of type 2 diabetes. For this reasons calcium supplements rather than diet were associated with a lower risk of type 2 diabetes. Therefore this indicating that calcium is essential in normalizing glucose intolerance.

Maximal capacity of renal tubular reabsorption of phosphate was significantly suppressed in diabetic patients. Urinary phosphate excretion was also higher in diabetic patients . This is in concordance with our study showing lower inorganic phosphate level in diagnosed diabetic patients.

Type 2 diabetes mellitus is also associated with altered bone metabolism and osteolysis. This leads to increased level of alkaline phosphatase in Type 2 diabetes mellitus patients. In Type 2 diabetes, hyperinsulinemia in combination with a high free fatty acid (FFA) influx affecting mitochondrial-oxidation system, leading to accumulation of fatty acids in the liver. These possible mechanisms finally lead to increase level of alkaline phosphatase (ALP).

Conclusion

Our present study may be concluded that there is lower serum total calcium, ionized calcium, inorganic phosphate and higher alkaline phosphatase levels in Type-2 diabetes mellitus. All these minerals play important role in the regulation of glucose level in the blood. Hence oral supplementations of all these minerals are recommended for prevention of altered mineral metabolism as common complication in Type-2 diabetes mellitus.

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