Section: Physiology

Original Research Article

CORRELATION BETWEEN BONE TURNOVER MARKERS IN OBESE TYPE 2 DIABETIC SUBJECTS

Rubeena Shakeel[1], S Aijaz A. Rizvi[2], Sangeeta Singhal[3], Sheelu S. Siddiqi[4]

[1]*Assistant Professor, Department of Physiology, Rohilkhand Medical College & Hospital Bareilly, Uttar Pradesh, India*
[2]*Associate Professor, Department of Physiology JNMCH, A.M.U., Aligarh, Uttar Pradesh, India3*
[3]*Professor, Department of Physiology JNMCH, A.M.U., Aligarh, Uttar Pradesh, India*
[4]*Professor, Rajiv Gandhi Centre for Diabetes and Endocrinology, JNMCH, A.M.U., Aligarh, Uttar Pradesh, India*

Received *: 02/02/2026*
Received in revised form *: 10/02/2026*
Accepted *: 16/02/2026*

Corresponding Author:
Dr. Rubeena Shakeel,
Assistant Professor, Dept of Physiology, Rohilkhand Medical College & Hospital Bareilly, Uttar Pradesh, India.
Email: drrubeenashakeel@gmail.com

DOI: 10.70034/ijmedph.2026.1.280

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (1); 1604-1608

ABSTRACT

Background: Diabetes mellitus (DM) is a group of common metabolic disorders which shares the features of hyperglycemia. Complex interaction between environmental factors and genetics causes several distinct types of DM. The objective is to Assess the association between bone turn over markers in obese diabetic and healthy adults.

Materials and Methods: This hospital based analytical Cross-sectional study was conducted in OPD of Rajiv Gandhi Centre for Diabetes and Endocrinology and Department of Physiology, JNMCH, A.M.U., Aligarh on patients of Type 2 Diabetes Mellitus(T2DM) who were obese as well, having BMI more than 30 Kg/m². The period of study was from 2018 to 2020.

Results: Obesity is a modifiable risk factor for development of diabetes. Obese diabetic individuals are at greater risk of various types of fractures as compared to healthy individuals because of decreased bone strength as serum calcium, phosphorus and vitamin D decreases and Parathormone and alkaline phosphatase increases in diabetes as well as in obesity.

Conclusion: Data obtained from the current study shows how diabetes and obesity is associated with bone turn over markers.

Keywords: Bone Turnover Markers, Obese, Type 2 Diabetic, BMI, Calcium, Phosphorus, Alkaline Phosphatase, Parathormone, Vitamin D.

INTRODUCTION

Insulin resistance and abnormal insulin secretion are central to the development of type 2 DM. Although the primary defect is controversial, most studies support the view that insulin resistance precedes an insulin secretory defect but that diabetes develops only when insulin secretion becomes inadequate. Type 2 DM likely encompasses a range of disorders with common phenotype of hyperglycemia. It is becoming increasing.

American has a different, but yet undefined, pathophysiology. In these groups, DM that is ketosisprone (often obese) or ketosis-resistant (often lean) is commonly seen.[1]

Obesity is defined as a state of excess adipose tissue mass. Although it is often considered as equivalent to increased body weight, this is not always the case. A person can be lean but overweight due to increased muscularity without having increased adiposity. Obesity is therefore more effectively defined by assessing its linkage to morbidity or mortality.[2]

The distribution of different adipose tissue in different anatomic depots also has substantial implications for morbidity. Specifically abdominal and intra-abdominal subcutaneous fat are more significant than subcutaneous fat present in the lower extremities and gluteal region. Clinically distinction is easily made by determining the waist to hip ratio, with a ratio > 1.0 in men and > 0.9 in women being abnormal. Intra- abdominal and central obesity is more strongly linked to many of the important complications of obesity such as diabetes mellitus, insulin resistance, hypertension, hyperlipidemia and PCOS in women than overall adiposity.[2]

How Obesity and type 2 DM are related

There is a close association between obesity and type 2 diabetes. The likelihood and severity of type 2 diabetes are closely linked with body mass index (BMI). There is a seven times greater risk of

diabetes in obese people compared to those of healthy weight, with a threefold increase in risk for overweight people. Whilst it is known that body fat distribution is an important determinant of increased risk of diabetes, the precise mechanism of association remains unclear. It is also uncertain why not all people who are obese develop type 2 diabetes and why not all people with type 2 diabetes are obese.

Linkage mechanisms

Theories of why obesity may lead to type 2 diabetes include:

- Abdominal obesity may cause fat cells to release pro-inflammatory chemicals. These chemicals can make the body less sensitive to the insulin it produces by disrupting the function of insulin responsive cells and their ability to respond to insulin.
- Obesity may trigger changes to the body's metabolism that cause adipose (fat) tissue to release increased amounts of fatty acids, glycerol, hormones, pro-inflammatory cytokines and other factors that are involved in the development of insulin resistance. When insulin resistance is accompanied by dysfunction of pancreatic islet beta-cells (the cells that release insulin) it leads to failure to control blood glucose levels.[3]

Bone Turnover Markers are a series of protein or protein derivative biomarkers which are released during bone remodelling by osteoblasts or osteoclasts (Calcium, Phosphorus, Alkaline Phosphatase, Parathormone, Vitamin D).[4]

Physiology of Bone Turnover Markers

Bone is a metabolically active structure that undergoes continuous remodelling throughout the life. After attaining peak bone mass, bone undergoes constant remodelling through bone resorption followed by formation sequentially at basic multicellular unit of bone which is called as ―Bone remodelling unit. Various biomolecules that are released into the circulation during bone formation and resorption are called Bone Turn over Markers. Under optimal physiological conditions, bone formation takes about 3 months while bone resorption takes around 10 days. Every year, up to 20% of the skeleton may be replaced by remodelling.[5]

MATERIALS AND METHODS

This hospital based analytical Cross-sectional study was conducted in OPD of Rajiv Gandhi Centre for Diabetes and Endocrinology and Department of Physiology, JNMCH, A.M.U., Aligarh on patients of Type 2 Diabetes Mellitus(T2DM) who were obese as well, having BMI more than 30 Kg/m². The period of study was from 2018 to 2020. Total 60 subjects were taken. Out of which 30 were selected as cases for further study, who met the inclusion and exclusion criteria and gave the valid consent after explaining the procedure to the subject prior to entering for further investigations. After approval from the ethical committee of JNMCH, A.M.U., Aligarh, Informed consent was taken from each of the patients in writing after explaining the procedure to the subject prior to entering the study.30 healthy controls were taken who went through same investigations as of the cases.

Selected cases of T2DM with obesity having age between 29 to 69 years were assessed for Bone turn over markers.

Inclusion Criteria

- Subjects (male/female) with a diagnosis of diabetes and obesity, patients who have given informed consent.
- Type 2 DM patients aged 29 – 69 years.

Criteria for diagnosing diabetes mellitus:

- Symptoms of diabetes plus Random blood glucose concentration >200 mg/dl
- Fasting plasma glucose > 126 mg/dl or
- HbA1C > 6.5%.

Exclusion Criteria

- Patients aged < 29 years and > 69 years.
- Previous history of systemic condition related to diabetes (Trauma, alcoholic neuropathy, renal failure).
- Patients taking calcium, Vitamin D/ Mineral supplements (including herbal drugs) within past 4 weeks.
- Post-menopausal women on hormone replacement therapy.
- Malignancies or history of chemotherapy or radiotherapy within past 1 year.
- Patients on any inflammatory drugs.
- Patient with any other autoimmune & rheumatic disease or cancer.
- Patients with recent venous thromboembolism episode.
- Patients already known for:-
  - Inflammatory bowel disease
  - Malabsorption Syndrome
  - Gastric bypass surgery
  - Hyerphosphatemia
  - AIDS Patients
  - Patients taking Corticosteroids within past 4 weeks

Procedure: Only those patients were selected whose BMI > 30 Kg/m². Clinical assessment was done after taking valid consent. Estimation of Bone turnover markers was done in cases of Obese Diabetic Patients (study group) and healthy controls. Blood for fasting and post prandial glucose estimation was collected on the same day. Investigation for HbA1C was also done. Venous blood samples were taken. Serum was separated from blood and then it was analyzed for following Bone turn over markers:

- Serum Calcium
- Serum Phosphorus
- Alkaline Phosphatase
- Parathormone
- Vitamin D

Statistical Analysis: All the data was compiled on Microsoft Office Excel 2015.Analysis was performed using SPSS version 20.0 statistical package for windows (SPSS,Chicago,IL).Continuous variables were expressed as mean + Standard Deviation (S.D.) and qualitative data was expressed in percentages. Unpaired —t tests for independent samples were used for comparison of means between two groups. All tests were two tailed and were calculated and a p-value of <0.05 was considered statistically significant.

RESULTS

The mean age of subjects in cases were 51.93 years and in controls were 38.73 years. There were 6 male subjects and 24 female subjects out of total 30 cases. There were 24 male subjects and 6 female subjects out of total 30 controls.

Mean of age in case were 51.93 ± 8.43 years and in control were 38.73 ± 8.01 years. Unpaired t-test was applied and p-value <0.001.

Mean of BMI in case was 35.03 ± 4.41 kg/m2 and in control was 22.38 ± 2.25 kg/m2 .Unpaired t-test was applied and p-value <0.001.

Mean value of fasting blood sugar level in female cases was found to be 175.46 ± 57.00 mg/dl and in male cases was found to be 224.50 ± 105 mg/dl. Unpaired t-test was applied and p-value<0.126.

Mean value of HbA1C in female cases was found to be 9.63 ± 1.86% and in male cases was 9.83 ± 2.32% and p-value<0.817.

Table 1: Glycemic parameters in cases

	N	Mean	Std. Deviation
Fasting Blood Sugar(mg/dl)	30	185.27	69.90
HbA1C(%)	30	9.67	1.92

Mean value of fasting blood sugar was 185.27 ± 69.90 mg/dl and HbA1C was 9.67 ± 1.92% amongst cases.

Table 2: Distribution of Calcium levels in case and control

	Group	N	Mean	Std. Deviation
Calcium(mg/dl)	Case	30	6.90	1.58
	Control	30	9.77	0.69

(Unpaired t- test for Calcium, p- value <0.001)

Mean level of serum Calcium amongst cases was 6.90 ± 1.58 mg/dl and amongst control was found to be 9.77 ± 0.69 mg/dl. Unpaired t-test was applied and p-value <0.001 is statistically significant.

Table 3: Distribution of Alkaline Phosphatase levels in case and control

	Group	N	Mean	Std. Deviation
Alkaline Phosphatase (IU/L)	Case	30	194.67	42.54
	Control	30	85.73	22.94

(Unpaired t- test for Alkaline Phosphatase, p- value <0.001)

Mean level of serum Alkaline Phosphatase amongst cases was found to be 194.67 ± 42.54 IU/L and amongst control was found to be 85.73 ± 22.94 IU/L. Unpaired t-test was applied and p-value <0.001 is statistically significant.

Table 4: Distribution of Phosphorous levels in case and control

	Group	N	Mean	Std. Deviation
Phosphorus (mg/dl)	Case	30	3.13	0.63
	Control	30	3.92	0.43

(Unpaired t- test for Phosphorus, p- value <0.001)

Mean level of serum Phosphorous amongst cases was found to be 3.13 ± 0.63 mg/dl and amongst control was found to be 3.92 ± 0.43 mg/dl. Unpaired t-test was applied and p-value <0.001 is statistically significant.

Table 5: Distribution of Parathormone levels in case and control

	Group	N	Mean	Std. Deviation
Parathormone (pg/ml)	Case	30	82.30	24.03
	Control	30	30.50	10.11

(Unpaired t- test for Parathormone, p -value <0.001)

Mean level of Parathormone amongst cases was found to be 82.30 ± 24.03 pg/ml and amongst control was found to be 30.50 ± 10.11 pg/ml. Unpaired t-test was applied and p-value <0.001 is statistically significant.

Table 6: Distribution of Vitamin D levels in case and control

	Group	N	Mean	Std. Deviation
Vitamin D (ng/ml)	Case	30	9.00	3.86
	Control	30	39.40	13.62

(Unpaired t- test for Vitamin D, p- value <0.001)

Mean level of Vitamin D amongst cases was found to be 9.00 ± 3.86 ng/ml and amongst control was found to be 39.40 ± 13.62 ng/ml. Unpaired t-test was applied and p-value <0.001 is statistically significant.

DISCUSSION

Overweight and obesity is associated with insulin resistance. Abdominal obesity is more strongly correlated with metabolic risk. Increase in BMI is associated with increase in prevalence of diabetes mellitus. Obesity and type – 2 diabetes mellitus are very closely associated. With increasing BMI there is increase in severity of diabetes. Because of the impact of obesity on type 2 diabetes, the rising prevalence of obesity has led, and will continue to lead, to a rise in the prevalence of diabetes.

Diabetic subjects have higher Body Mass Index (BMI). This was further confirmed by the study done by Daousi C et al. where they had 86% of diabetics obese. 84% diabetic patients were obese in Mayur Patel et al. Eric and John and NHANES report indicates that most adults with diagnosed diabetes were overweight or obese.

Diabetes mellitus is associated with an increased risk of fractures. Bone turnover Markers are found to be decreased in diabetes patients, markers of bone formation and resorption seem to be lower whereas alkaline phosphatase, which is an enzyme of mineralization, is found to be increased which suggest that the matrix is hypermineralised in diabetics. This explain the reason behind the low bone strength. Some bone turnover markers may help in predicting the risk of fractures in diabetic patients.[6]

Serum Calcium: In this study, Mean level of serum calcium was found to be lowered in the cases (6.90 ± 1.58 mg/dl) as compared to the controls which has mean level of (9.77 ± 0.69 mg/dl). The finding in the present study is in consonance with the study made by khanna M. et. al. and Moyad J. et. al.

Vitamin D: In this study, Mean level of vitamin D was found to be lowered in the cases (9.00 ± 3.86 ng/ml) as compared to that of the controls which has mean level of (39.40 ± 13.62 ng/ml). The findings in the present study were similar to the findings by khanna M. et. al. . and Moyad J. et. al.[7,8] Khanna et. al. study suggests that Vit D and calcium may be playing role in development of diabetes. Vit D and Calcium is needed for release of insulin from the β cells of islet of Langerhans of pancreas and also for proper action of insulin is mediated if S. vit D levels are optimal. S. Calcium level is maintained by S. Vit D levels. Moyad et. al. study shows that obese individuals were observed to have lower serum calcium levels; similarly, association between abdominal obesity and serum calcium levels were found, where the abdominal obese subjects were more likely to have low serum calcium levels. The same pattern of the results was reported for vitamin D homeostasis, a significant association was observed between the serum vitamin D level and abdominal obesity with lower serum vitamin D level for the abdominal obese participants, it is unlikely to be due to inadequate absorption or low intake of vitamin D. One of the reasons can be a result of reduced sunlight exposure in the morbid obese individuals compared to that in the normal subjects. Another explanation could be that 25-hydroxy vitamin D is stored in fat tissue; hence having less bioavailability, resulting in lower levels of 25-hydroxy vitamin D.

In the present study the mean levels of vitamin D were found to be lower in cases as compared to controls. Contradictory reports have been suggested as far as levels of Vitamin D are concerned. Studies have reported both lower and higher levels of Vitamin D in diabetics.[9]

Nevertheless, low levels of Vitamin D are associated with deranged beta cell function and insulin resistance. Studies have reported reduced risk of diabetes and better glucose homeostasis with calcium and vitamin D supplements.[10]

Parathormone: In this study, Mean level of Parathormone was found to be increased in the cases (82.30 ± 24.03 pg/ml) as compared to that of the controls which has mean level of (30.50 ± 10.11 pg/ml)

The findings in the present study were similar to the findings by Ioannis Legakis et. al and Nahid Hamoui et al.[11,12] Ioannis Legakis et. al study shows that elevated Parathormone levels might play a compensatory role in calcium homeostasis in diabetic patients.

The results of present study show that the serum levels of calcium and PTH were significantly lower and higher in cases as compared to controls respectively. The results are in accordance with earlier reported studies. Higher levels of PTH appear to predispose an individual to diabetes. The possible explanation could be that PTH interferes with signalling of insulin in the adipocytes. The mechanism appear to be manifold including decreased insulin induced glucose transport and decrease in the expressions of GLUT 4 and insulin receptor substrate 1 (IRS 1) by elevated levels of PTH.[13]

Similarly, studies have shown that the low levels of calcium due to Vitamin D deficiency effects the release of the insulin from the beta cells of pancreas. The results of our study assume significant in the background of the reports that suggest possible links between hyperparathyroidism, serum calcium and insulin resistance. Resistance to insulin may in turn effect the requirements of insulin in diabetics.[14]

Increase in the levels of PTH in our study could also possibly be due to vitamin D deficiency. Similar, results have been reported in earlier studies.[15]

Phosphorus: In this study, Mean level of serum phosphorus was found to be lowered in the cases (3.13 ± 0.63 mg/dl) as compared to that of the controls which has mean level of (3.92 ± 0.43

mg/dl). The findings in the present study was similar to the findings by khanna M. et. al., Obeid O. et. al.[7,16] study suggests that the ability of phosphate depletion to simulate glucose intolerance, probably through the stimulation of hepatic glucose production and reduced insulin level that requires ATP for its release by pancreatic β-cells, is supported by several observations. For example, increased serum phosphate and phosphorus intake of non-diabetic subjects were reported to be synergistically related to improvement in glucose tolerance and insulin sensitivity. Thus, reduced phosphorus status would favour the development of obesity, as postprandial glycaemia is known to be implicated in the development of chronic metabolic diseases such as obesity, type 2 diabetes mellitus and cardiovascular disease. Such a process can be further aggravated by the development of obesity that is characterized by insulin resistance, which predisposes to the development of impaired glucose tolerance that is known to decrease peripheral uptake of both glucose and phosphorus.

Alkaline Phosphatase: In this study, Mean level of ALP was found to be increased in the cases (194.67 ± 42.54 IU/L) as compared to that of the controls which has mean level of (85.73 ± 22.94 IU/L).

The findings in the present study were similar to the findings by Tibi. L. et. al. Ali AT. et. al,[17,18] study shows that the higher level of liver ALP in obese than in lean subjects is a result of ALP release from adipose tissue. Liver ALP is a TNALP isoenzyme (as are bone and kidney ALP), and it is known that TNALP is present in human preadipocytes and in the murine preadipocyte cell, 3T3- L1. Therefore, the association of liver but not bone serum ALP levels with obesity suggests that the TNALP isoform in adipose tissue may be the liver form. The function of ALP in adipose tissue has been studied. Thus, it has been demonstrated in human and 3T3-L1 preadipocytes that inhibition of ALP activity blocks intracellular lipid accumulation and that ALP is localized to the lipid containing droplets of preadipocytes. It, therefore, has been hypothesized that ALP may be involved in the control of lipid accumulation during the maturation of preadipocytes into adipocytes.

CONCLUSION

Obesity is a modifiable risk factor for development of diabetes. Obese diabetic individuals are at greater risk of various types of fractures as compared to healthy individuals because of decreased bone strength as serum calcium, phosphorus and vitamin D decreases and Parathormone and alkaline phosphatase increases in diabetes as well as in obesity. Both diabetes and obesity are strongly associated with unhealthy diet and sedentary lifestyle.

Lifestyle modification could help in overcoming these problems and a person can lead a better and healthy life. Eating a balanced, healthy diet and increased physical activity can be of great help. Regular self- monitoring of blood glucose level should be done in known diabetics. Weight can be maintained with incorporation of healthy eating habits and exercise.

REFERENCES

1. Harrison's Principles of Internal Medicine, Volume-2, 18th Edition, Published by McGraw Hill, P 2974.
2. Harrison's Principles of Internal Medicine, Volume-1, 18th Edition, Published by McGraw Hill, P 622.
3. Gatineau M, Hancock C, Holman N, Outhwaite H, Oldridge L, Christie A, Ells L. Adult obesity and type 2 diabetes. Oxford: Public Health England, 2014.
4. Matthew B. Greenblat, Joy N. Tsai, Marc N. Wein, Bone turn over markers in the diagnosis & monitoring of metabolic bone disease, DOI: 10.1373/clinchem.2016.259085 Published Jan 2017.
5. Lian JB, Stein GS. The cells of bone. In: Seibel MJ, Robins SP, Bilezikian JP, editors. Dynamics of Bone and Cartilage Metabolism. San Diego: Academic Press; 1999. pp. 165–86.
6. Jakob starup linde, peter vestergaard, Biochemical bone turnover markers in diabetis mellitus – A systematic review, Bone (2015), http://dx.doi.org/10.1016/j.bone.2015.02.019.
7. Khanna M., Mahajan M, Sharma A, Khanna R, Correlation Of Vitamin D And Serum Calcium Levels With Type 2 Diabetes Mellitus In North Indian Punjabi Population; International Journal of Recent Scientific Research Vol. 5, Issue, 10, pp.1949-1954, October, 2014.
8. Moyad J. Shahwan , Mohammed H. Khattab , Ammar A. Jairoun, Association of Serum Calcium Level with Waist Circumference and Other Biochemical Health-care Predictors among Patients with Type 2 Diabetes; Journal of Pharmacy and Bioallied Sciences, Volume 11, Issue 3, July-September 2019.
9. Paula, F.J.A., Lanna, C.M.M., Shuhama, T., & Foss, M.C.. (2001). Effect of metabolic control on parathyroid hormone secretion in diabetic patients. Brazilian Journal of Medical and Biological Research, 34(9), 1139-1145.
10. Martin T and R. Keith Campbell. Vitamin D and Diabetes. Diabetes Spectrum .2011; 24(2): 113-118.
11. Ioannis Legakis and TimosMantzouridis, Positive Correlation of PTH-Related Peptide with Glucose in Type 2 Diabetes; Hindawi Publishing Corporation Experimental Diabetes Research Volume 2009, Article ID 291027, doi:10.1155/2009/291027
12. Nahid Hamoui , Gary Anthone, Peter F Crookes, Calcium metabolism in the morbidly obese; obes surg. 2004 Jan;14(1):9-12. doi: 10.1381/096089204772787211.
13. Rahimi Z. Parathyroid hormone, glucose metabolism and diabetes mellitus J Parathyr Dis 2014; 2(1): 55-56.
14. Ahn C, Kang JH, Jeung EB. Calcium homeostasis in diabetes mellitus. J Vet Sci. 2017;18(3):261-266.
15. Nakashima A, Yokoyama K, Yokoo T, Urashima M. Role of vitamin D in diabetes mellitus and chronic kidney disease. World J Diabetes. 2016;7(5):89-100.
16. Obeid O. Low phosphorus status might contribute to the onset of obesity. Obes Rev 2013; 14: 659–664.
17. Tibi, L., Collier, A., Patrick, A. W., Clarke, B. F. & Smith, A. F. Plasma alkaline phosphatase isoenzymes in diabetes mellitus. ClinChimActa 177, 147–155 (1988).
18. Ali AT, Paiker JE, Crowther NJ. The relationship between anthropometry and serum concentrations of alkaline phosphatase isoenzymes, liver enzymes, albumin, and bilirubin. Am J Clin Pathol.2006; 126:437-42.