



A Prospective Assessment Of Clinical Association Of Vit D, Serum Calcium And Pth In Diabetes Patients

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Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Background: Vitamin d levels are related to glucose concentrations. studies suggest role of vit d in maintaining normal insulin synthesis and secretion. Vitamin D and PTH are both responsible for maintaining extracellular calcium homeostasis. Vitamin D increases the efficiency of intestinal calcium absorption, and PTH is secreted in response to low-circulating calcium concentrations. Elevated PTH secondary to low vitamin D increases calcium resorption from the skeleton at the expense of an increased risk of fracture. Secondary hyperparathyroidism may also increase the risk of developing diabetes .This study aims at studying the association between vit d, pth and calcium in diabetes patients

Methods: This study was done in tertiary care hospital from May 2021 to December 2021. A total of 200 patients were selected based on inclusion and exclusion criteria. All patients with diabetes were done routine investigations and sent special investigations like pth and vit d.

Inclusion criteria:1.all patients with diabetes 2.

Exclusion criteria:1.patients less than 12 years 2.pregnant women 3.patients with previous hypocalcemic disorders.4.patients with previous hormonal disorders 5.any previous liver disorders.

Results: A total of 200 patients were studied during the period. out of which 114 were male 86 were female. Out of which 12 were in the 12-30 year age group,90 were in the 31-50 year age group,70 were in the 50-70 year age group, 28 were in the greater than 70 year age group. Vit d levels considerably decreased in all diabetic patients.50 were newly detected diabetics,62 were diabetics with greater than 5 years ,84 were diabetics with greater than 10 year history. pth levels also varied in diabetics. the levels were increased in patients with longer diabetes history. serum calcium levels were decreased in diabetics with longer history

Conclusions: it was observed in our study that indeed there is an inverse association between diabetics and vit d. While low vitamin D induces secondary hyperparathyroidism, increased PTH levels are also associated with diabetes. serum calcium levels were decreased more in patients with longer diabetes history.

Keywords: vit d,pth,calcium,insulin

Introduction

Non-communicable diseases (NCDs) are becoming major health challenges with continually increasing burden¹

Diabetes mellitus is a group of metabolic diseases characterized by chronic hyperglycemia resulting

from defects in insulin secretion, insulin action, or both. Metabolic abnormalities in carbohydrates, lipids, and proteins result from the importance of insulin as an anabolic hormone. Low levels of insulin to achieve adequate response and/or insulin resistance of target tissues, mainly skeletal muscles, adipose tissue, and to a lesser extent, liver, at the

level of insulin receptors, signal transduction system, and/or effector enzymes or genes are responsible for these metabolic abnormalities.²⁻⁵

DM has several categories, including type 1, type 2, maturity-onset diabetes of the young (MODY), gestational diabetes, neonatal diabetes, and secondary causes due to endocrinopathies, steroid use, etc.

Type 1 DM

Type 1 DM is caused by a complex autoimmune destruction of pancreatic islet β - cells, leading to absolute insulin deficiency. The autoimmune nature of type 1 DM has been clarified with the detection of auto-antibodies against islet β -cells and their infiltration by T cells, B cells, and macrophages⁶

Type 2 DM

Insulin resistance frequently precedes type 2 DM,^{7,8} and it is characterized by a decreased response of the target tissues to the normal levels of circulating insulin. These target tissues require higher-than-normal levels of insulin for an adequate response (for example, glucose uptake in muscles or suppression of fatty acid release in fat) to occur, thereby creating a state of hyperinsulinemia.

Vitamin D deficiency is also recognized as a worldwide health problem⁹ and is associated with rickets and fracture. In addition, hypovitamin D has recently been considered a responsible factor in the onset and progression of DM has been increasing evidence suggesting that an inverse vitamin D status is prevalent in patients with DM or CKD¹⁰

Vitamin D has been shown to have immunomodulatory properties as many autoimmune diseases have association with vitamin D deficiency.¹¹Type 1 DM is also said to be related to vitamin D deficiency¹² As VDR are expressed in human T and B lymphocytes, vitamin D is thought to modify the Th1/Th2 cytokine profile¹³ In addition, vitamin D is also thought to be associated with the immune system via its inhibition of lymphocyte proliferation¹⁴

As VDRs in pancreatic β -cells play an important role in the progression of type 2 DM¹⁵ vitamin D deficiency is related to insulin secretion, insulin resistance, and β -cell dysfunction in the pancreas¹⁶

The secretion of pancreatic insulin is inhibited by vitamin D deficiency in the diabetics.^{17,18}

Administration of vitamin D restores glucose-stimulated insulin secretion and promotes β -cell survival by modulating the generation and effects of cytokines^{19,20}

By stimulating the expression of insulin receptors, vitamin D regulates insulin sensitivity^{21,22}. In addition, vitamin D enhances insulin sensitivity by promoting the expression of peroxisome proliferator-activated receptor (PPAR) delta,regulates fatty acids in skeletal muscle and adipose tissue²³

The indirect effect of vitamin D is exerted by regulating calcium flux through the cell membrane and intracellular calcium.

Vitamin D affects insulin resistance through the RAAS.Furthermore, low levels of 1,25(OH)2D increased renal renin production and activated the RAAS system²⁴. Finally, angiotensin II inhibited the action of insulin in vascular and skeletal muscle tissues, leading to impaired glucose uptake²⁵.

Systemic inflammation has an important role in insulin resistance and cardiovascular events in patients with type 2 DM²⁶ β -cells in the pancreas are affected via cytokine-induced apoptosis.. Vitamin D could decrease the effects of systemic inflammation and protect against β -cell cytokine-induced apoptosis by directly modulating the expression and activity of cytokines^{27,28}.

Insulin secretion is also influenced by calcium concentration and flux through the β -cells²⁹. Vitamin D regulates the function of calbindin, a systolic calcium-binding protein found in pancreatic β -cells, and acts as a modulator of depolarization-stimulated insulin secretion via regulation of intracellular calcium³⁰⁻³².

Calcium is essential for insulin-mediated intracellular processes in insulin-responsive tissues such as skeletal muscle and adipose tissue with a very narrow range of $[Ca^{2+}]_i$ needed for optimal insulin-mediated functions . Changes in $[Ca^{2+}]_i$ in primary insulin target tissues may contribute to peripheral insulin resistance via impaired insulin signal transduction leading to decreased GLUT-4 activity³³⁻³⁶.

Parathyroid hormone (PTH) helps to regulate circulating calcium concentrations by promoting bone resorption, suppressing urinary calcium loss, and enhancing the formation of calcitriol, the active

metabolite of vitamin D. PTH levels are elevated in primary hyperparathyroidism and secondarily in vitamin D deficiency, chronic kidney disease, and other conditions.

Recent evidence has linked elevated PTH concentrations with insulin resistance, beta cell dysfunction, and dysglycemia which may eventually lead to the development of diabetes^{37,38}.

While low vitamin D induces secondary hyperparathyroidism, increased PTH levels are also associated with diabetes Hypovitamin D levels with increased PTH levels were an independent predictor of β -cell dysfunction, insulin resistance, and glycemia³⁹.

Methods

The present Prospective observational study was done in Department of general medicine in tertiary care hospital from June 2021 to December 2021. A total of 200 cases of diabetics were studied during the period based on inclusion and exclusion criteria. All patients were done routine investigations like CBP, Lipid profile, serum electrolytes. Special investigations like PTH and Vit D were done in all enrolled patients.

Inclusion criteria: 1.all patients with diabetes 2.

Exclusion criteria: 1.patients less than 12 years 2.pregnant women 3.patients with previous hypocalcemic disorders. 4.patients with previous hormonal disorders 5.any previous liver disorders.

The statistical software SPASS was used to analyse the data and Microsoft word and excel have been used to generate graphs, figure etc.

Results

Of all the patients 114[57%] were males and 86[43%] were females with male preponderance. . Out of which 12[6%] were in the 12-30 year age group, 90[45%] were in the 31-50 year age group, 70[35%] were in the 50-70 year age group, 28[14%] were in the greater than 70 year age group. Vit d levels considerably decreased in all diabetic patients. 54 were newly detected diabetics, 62 were diabetics with greater than 5 years, 84 were diabetics with greater than 10 year history. pth levels also varied in diabetics. the levels were increased in patients with longer diabetes history. serum calcium levels were decreased in diabetics with longer history

Table 1 Gender Distribution

In Table 1 there is a depiction of male preponderance with males 114 vs females 86 in the ratio M:F [1.3:1]

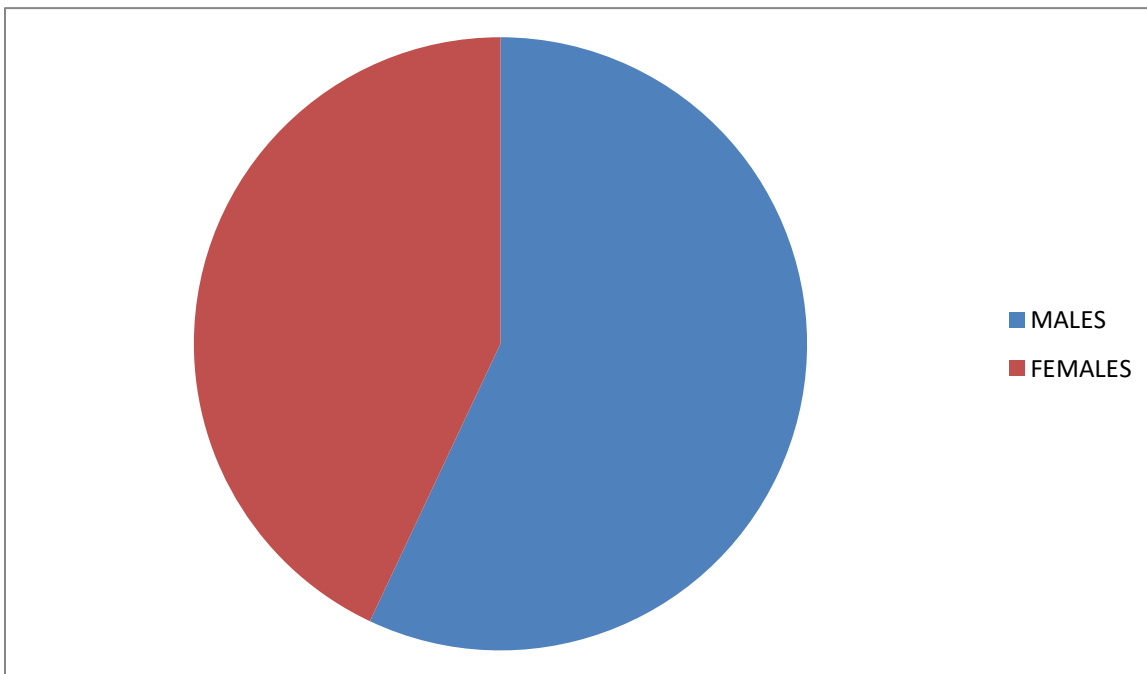


Table 2 Age Group

In table 2 the diabetics were more in the age group 31-50yrs followed by patients in the age group between 51-70 years.

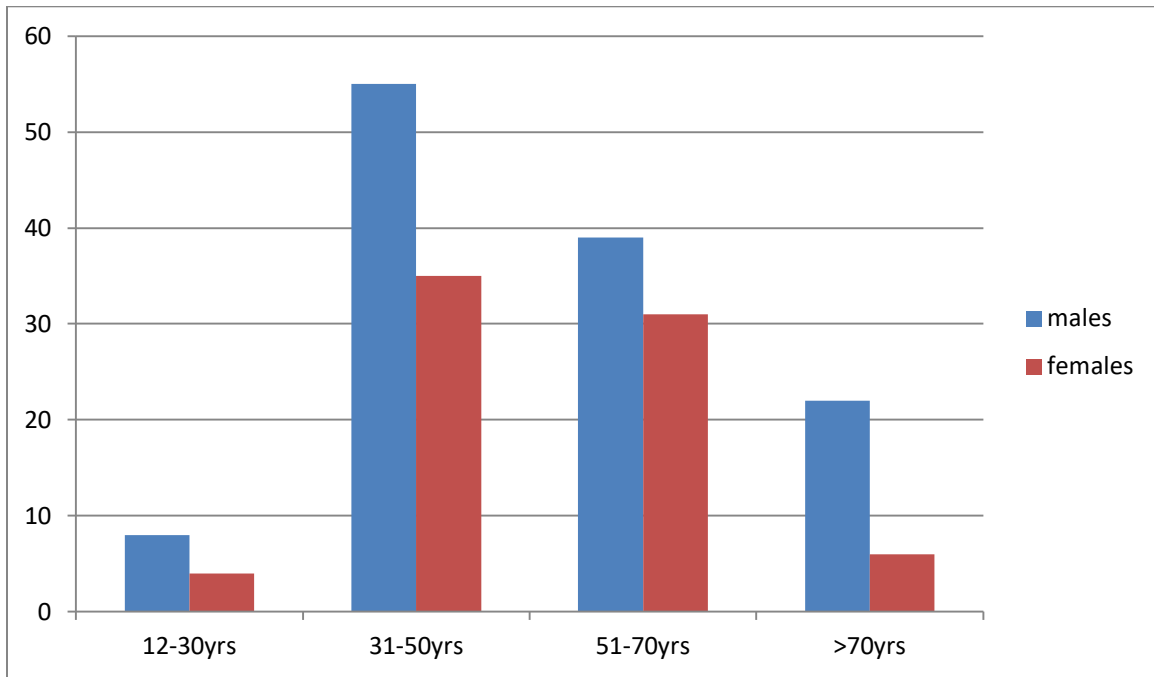


Table 3 In Table 3 the patients with dm and low vit d levels noted

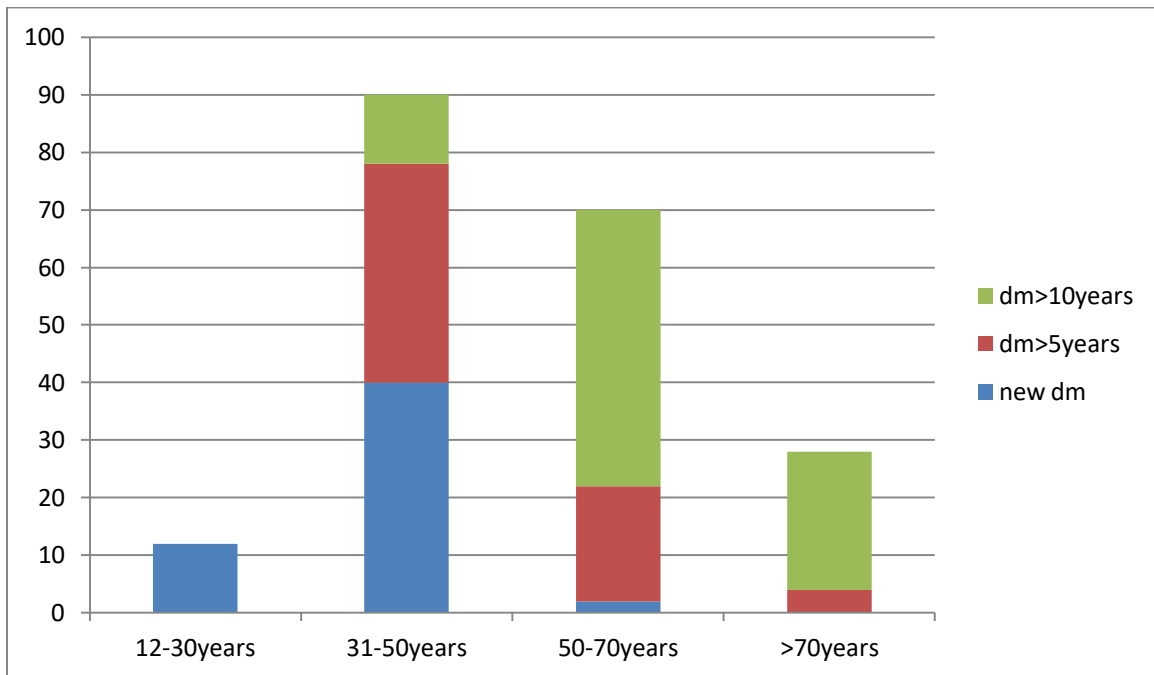


Table 4 pth levels In this table the patients with increase in pth were depicted.

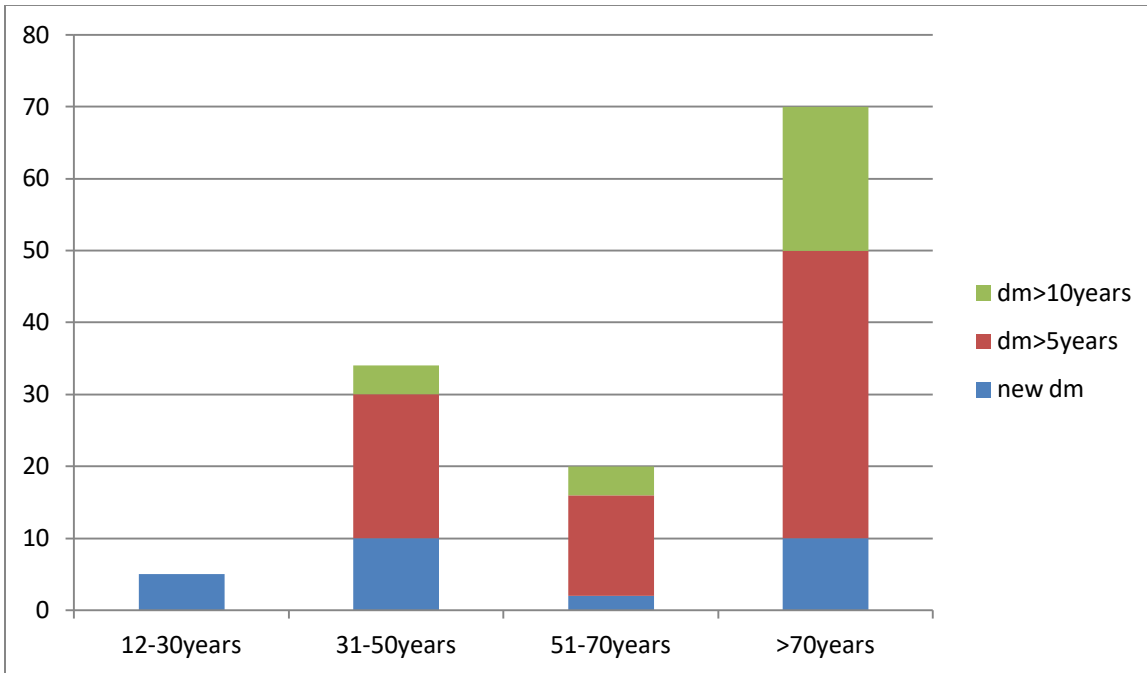
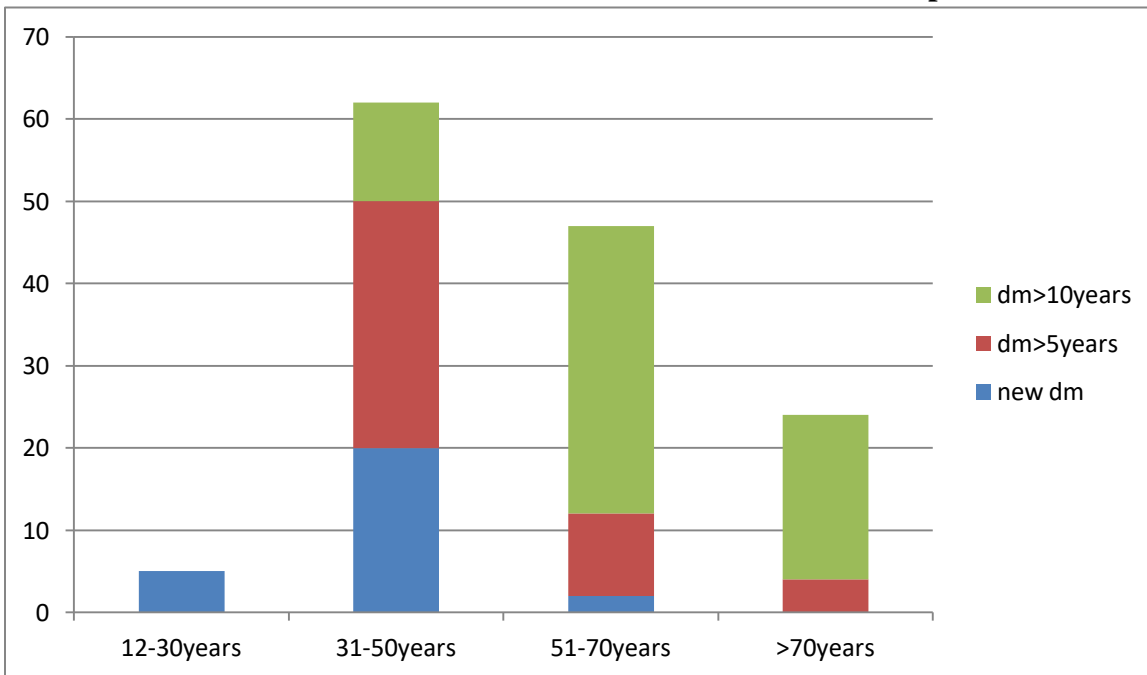


Table 5 In Table 5 the calcium levels in diabetics were depicted.



Discussion :

In our study there was male preponderance with 114 males and 86 females in the ratio 1.3:1. this was in concordance with the studies by Mattila *et al*³⁹ there were more number of patients in the age group 31-50 [90] followed by age group 51-70 [70] greater than 70 years were 28. this was in concordance with the studies done by Lieu *et al*⁴⁰. in our study we observed

low levels of vit d in all patients. the levels were low in older patients with longer diabetic history. these findings were in concordance with studies done by Anderson *et al*⁴². in our study we observed serum pth levels were increased in some patients. the levels were increased in patients with longer diabetic history. these results were in concordance with studies by Stanley *et al*⁴³ and Hamed *et al*⁴⁴. we

observed serum calcium levels were decreased in diabetic patients. In patients with $dm > 10$ years 67 patients had low calcium levels. In patients with $dm > 5$ years 44 patients had low calcium levels. In newly detected dm 27 patients had low calcium levels. These results were in concordance with Anastassios *et al*⁴⁵

Conclusion:

Our study concludes that indeed there is an inverse association between diabetics and vit d. Vitamin D deficiency may be linked to onset and progression of DM. There are two main forms of vitamin D: vitamin D₂ and vitamin D₃. Vitamin D₂ is synthesized by plants whereas vitamin D₃ is synthesized in skin when it is exposed to ultraviolet B rays from sunlight. Vitamin D has been shown to have immunomodulatory properties as many autoimmune diseases have association with vitamin D deficiency. Type 1 DM is also said to be related to vitamin D deficiency. As VDRs are expressed in human T and B lymphocytes, vitamin D is thought to modify the Th1/Th2 cytokine profile. In addition, vitamin D is also thought to be associated with the immune system via its inhibition of lymphocyte proliferation.

As VDRs in pancreatic β -cells play an important role in the progression of type 2 DM. Vitamin D deficiency is related to insulin secretion, insulin resistance, and β -cell dysfunction in the pancreas. Vitamin D deficiency leads to reduced insulin secretion and its supplementation restores insulin secretion in animals; predictive of the future development of type 2 diabetes. Serum calcium levels were decreased in diabetics with longer duration than with newly detected diabetes. Calcium is essential for insulin-mediated intracellular processes in insulin-responsive tissues such as skeletal muscle and adipose tissue with a very narrow range of $[Ca^{2+}]_i$ needed for optimal insulin-mediated functions. Changes in $[Ca^{2+}]_i$ in primary insulin target tissues may contribute to peripheral insulin resistance via impaired insulin signal transduction leading to decreased GLUT-4 activity. Parathyroid hormone levels were increased in diabetics with longer duration. Primary and secondary hyperparathyroidism are suspected to be involved in glucose metabolism and diabetes. Clinical investigations consistently show a two- to fourfold elevated risk of diabetes among individuals with

hyperparathyroidism. While low vitamin D induces secondary hyperparathyroidism, increased PTH levels are also associated with diabetes. Hypovitamin D levels with increased PTH levels were an independent predictor of β -cell dysfunction, insulin resistance, and glycemia. Our observation results were more in the females than males. Though limitations in our study with sample size and duration if done on a larger scale we could get encouraging results.

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