

RESEARCH ARTICLE

Evaluation of Serum Ghrelin Level in Patients with Type 2 Diabetes Mellitus Before and After Supplementation of 5000 IU of Vitamin D

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ABSTRACT

Background: Throughout the twenty-first century, type 2 diabetes mellitus (T2DM) has emerged as a severe worldwide public health concern, with the incidence of the disease growing on an annual basis. T2DM has been linked to abnormalities in glucose, lipid, and protein metabolism, among other things. Diabetes has been related to low vitamin D levels, as have the preventive effects of sufficient vitamin D consumption on the risk of microvascular and macrovascular problems in people with T2DM. In addition to regulating hunger, energy balance, and glucose homeostasis, ghrelin is known to be involved in many other biological functions as well.

Aim of the Study: One of the goals of this study is to compare the levels of the hormone ghrelin in patients with type 2 diabetes mellitus before and after they have taken an oral vitamin D supplement of 500 IU.

Patients & Methods: From January 1st to March 31st, 2021, a follow-up case study was conducted in Kirkuk Governorate. The study comprised 60 diabetes type 2 patients who were given 5000 IU of vitamin D for two months and then had their serum ghrelin levels checked before and after treatment. The SPSS application was used to examine all of the data.

Results: In this study, the mean level of ghrelin was elevated significantly in type two diabetes mellitus before administered vitamin D treatment as compared with type two diabetes mellitus after administered vitamin D treatment at p-value <0.01

Conclusions: It was concluded that vitamin D was an important treatment protocol in management of type two diabetes mellitus

Keywords: Ghrelin, Type 2 Diabetes Mellitus, Vitamin D.

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INTRODUCTION

Type 2 diabetes Mellitus (T2DM) is a physiological disorder characterized by high blood glucose levels. Primary causes of diabetes include endocrinopathies such as hypothyroidism, chronic steroid use, and certain medications. Secondary causes of diabetes include gestational diabetes, maturity-onset diabetes of the young (MODY), neonatal diabetes, and gestational diabetes.¹ Insulin production from pancreatic beta-cells declines over time, leading in elevated blood glucose levels in patients. This may lead to long-term effects in the form of eye, nerve, and kidney damage in patients with type 2 diabetes (T2D). Pancreatic-cell fatigue is commonly recognized because of increased insulin production resulting from unsustainable demands on the pancreas.² Vitamin D supplementation decreased the risk of developing diabetes in those with prediabetes who were not at risk for vitamin

D deficiency by 10 to 13% in those who were not at risk for it.³ Vitamin D supplementation has been shown to have an influence on circulating ghrelin hormone levels, resulting in enhanced insulin sensitivity and, as a consequence, improved hunger hormone control in certain individuals.⁴ Because food limitation causes ghrelin levels to rise, it's plausible that ghrelin is engaged in the food-mediated longevity process, which would be beneficial.⁵ In blood glucose control, both ghrelin and insulin secretion are involved, and it is possible that there is a negative feedback loop between the two hormones.⁶ Ghrelin is an orexigenic hormone that may activate the hunger region in the brain, causing it to become more active.⁷ Because of a variety of beneficial effects on system metabolism, pharmacological targeting of the endogenous ghrelin system is generally regarded as a valuable strategy for treating metabolic issues such as chronic inflammation, gastroparesis,

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or cancer-associated anorexia and cachexia, among other conditions.⁸ Exactly how ghrelin influences insulin secretion in T2D patients' islets remains a mystery, as does whether islet ghrelin expression differs from circulating ghrelin levels in T2D patients. In this study, we wanted to understand more about how ghrelin controls insulin production in human islets, as well as how T2D affects circulating ghrelin levels and islet ghrelin cells in humans.⁹ Grin is an orexigenic hormone that may activate the hunger region in the brain, causing it to become more active.¹⁰ Ghrelin is mostly generated in the stomach, although it may move to the central nervous system (CNS) across the blood-brain barrier (BBB). When ghrelin is present in the central nervous system, it can influence food intake in the hypothalamus.¹¹ Ghrelin-stimulating drugs may be a promising pharmacological solution for increasing food intake while preventing hypoglycemia, body weight loss, depression and anxiety, and even death during acute nutritional and psychological challenges such as severe caloric restriction, cachexia, and psychosocial stress.¹²

PATIENTS AND METHOD

From January 1st to March 31st, 2021, a case control research was conducted in Kirkuk Governorate. The study included 60 diabetic type 2 patients, with information on the patients obtained directly from the patients. Diabetic patients were identified using FBS and HbA1c tests, as well as clinical examinations by their specialists. All diabetes patients were between the ages of 38 and 78, and their weight ranged from 61 to 128, with a BMI of 20.6 to 47.09 kg/m². BMI before and after vitamin D supplementation (mean SE) (30.13 ± 0.69) (29.72 ± 0.67), respectively. Renal impairment, hepatic impairment, and hyper or hypoparathyroidism were the exclusion criteria. About five milliliters of blood were collected from patients' antecubital veins in simple tubes without any anticoagulant and allowed to clot at room temperature for 10–15 minutes. The tube was then centrifuged for 15 minutes at 3000 rpm.

RESULTS

In this study, the mean level of ghrelin was elevated significantly in type two diabetes mellitus before administered vitamin D treatment as compared with T2DM after administered vitamin D treatment at p-value <0.01 as evidenced by the Table 1.

Correlation between Ghrelin and Vitamin D in T2DM

As shown in Figure 1, the study discovered a negative correlation between ghrelin and vitamin D in diabetic patients before and after taking vitamin D supplementation (r: -0.092 and r: -0.168, respectively), as shown in the Figures 1 and 2.^{1,2}

DISCUSSION

In this study, the mean level of ghrelin was elevated significantly in type two diabetes mellitus before administered vitamin D treatment as compared with type two diabetes mellitus after administered vitamin D treatment at p-value <0.01. In agreement, a recent study¹³ showed that improved insulin sensitivity associated with higher vitamin D levels may be beneficial in the management of appetite hormones. Jawed

and colleagues.¹⁴ An investigation has shown that high glucose lowers ghrelin levels in T2D and obese persons, with serum ghrelin levels in T2DM and obesity being lower as a result of high glucose. This protein is an crucial controllers of balance of energy and breakdown of fat in the central nervous system as well as a range of peripheral organs, including the pancreas and adipose tissue.¹⁵ Gastrointestinal hormone (ghrelin) regulates lipid metabolism and acts as a connective tissue between the brain and the rest of the body.¹⁶ Ghrelin levels may be affected by a variety of variables, including food composition, activity, climate, and way of life.¹⁷ Ghrelin levels in individuals with T2DM were significantly lowered by a high-whey protein diet.¹⁸ Hypocaloric diets, polyunsaturated fat-rich diets, and fructose supplements may all be beneficial in suppressing ghrelin production.¹⁹ In individuals with T2D, a decreased meal frequency is more effective at increasing fasting plasma ghrelin

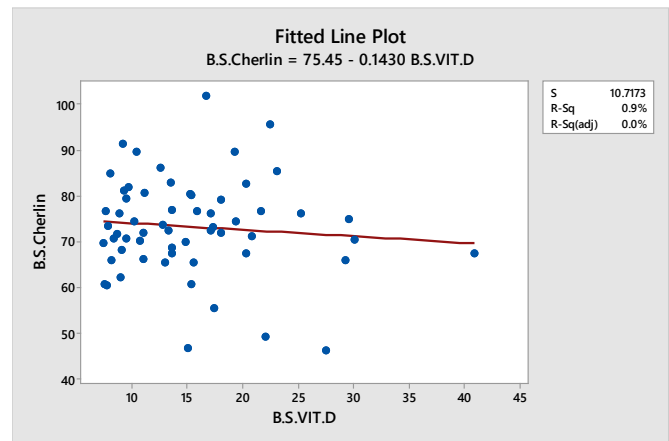


Figure 1: Correlation between ghrelin and vitamin D before vitamin D supplementation

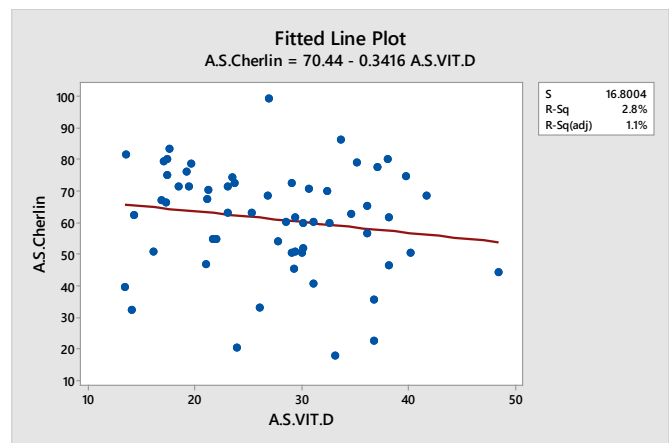


Figure 2: Correlation between ghrelin and vitamin D after vitamin D supplementation

Table 1: Levels of ghrelin before and after vitamin D supplementation are shown

Ghrelin (pg/dL)			
Group	Mean	SD	p-value
ghrelin before taking vit D	73.3	± 10.7	< 0.01
ghrelin after taking vit D	61.1	± 12.9	

levels than a six-meal calorie restriction.²⁰ It is possible that elevated ghrelin levels, which occur during sleep deprivation and are associated with increased calorie consumption which have recently been proven to have an effect on the production of hunger hormones in both animals and humans. Increased colonic SCFAs have been shown to reduce ghrelin hormone levels in the short term.²¹ Before a meal, ghrelin content increases by about threefold, and then rapidly decreases thereafter. Recent research found that both normal-weight and obese guys saw a temporary increase in AG concentration after a meal, which then declined.²² Various additional brain networks integrate environmental and emotional inputs to alter the hypothalamic-controlled 'hedonic' driving force.²³ The researchers discovered a negative relationship between ghrelin and vitamin D in patients with T2D before treatment with vitamin D ($r: -0.167$), as well as a negative relationship between ghrelin and vitamin D in individuals with type 2 diabetes after treatment with vitamin D. ($r: -0.194$). Churm and colleagues²⁴ Acrylghrelin has been shown to have an influence on blood sugar uptake. Among those who have contributed to this work are Zhang *et al.*,²⁵ It has been shown that the relationship between circulating ghrelin levels and insulin resistance in obesity is equivocal. Although circulating ghrelin levels in obese patients with normal fasting blood glucose were found to be much lower, they were shown to be highly associated with insulin resistance. Ghrelin is a hormone that influences glucose and lipid metabolism in obese persons. A rise in insulin, glucagon, and leptin levels in the blood has been shown to be associated with ghrelin, according to Skuratovskaia *et al.*²⁶ Specific activation of receptors and posttranslational modifications of ghrelin have been shown to be effective in controlling the development of IR in obese individuals. According to Stoica and colleagues²⁷ study, the metabolism of all adipokines is significantly dysregulated in obese people. According to study conducted by Mehdar *et al.*,²⁸ the hormone ghrelin is implicated in the etiology of obesity and T2DM. The presence or absence of ghrelin cells in three key stomach locations in obese people may be influenced by their diabetes status. Similarly, Ahmed *et al.*²⁹ says that a variety of physiological conditions, including as obesity and diabetes mellitus, are hypothesized to be responsible for fluctuations in ghrelin concentrations.

CONCLUSIONS

It was concluded that vitamin D was an important treatment protocol in management of T2DM.

REFERENCE

- Rajaei E, Jalali MT, Shahrabi S, Asnafi AA, Pezeshki S. HLAs in autoimmune diseases: dependable diagnostic biomarkers?. *Current Rheumatology Reviews*. 2019 Nov 1;15(4):269-76.
- Butler AE, Dargham SR, Latif A, Mokhtar HR, Robay A, Chidiac OM, Jayyousi A, Al Suwaidi J, Crystal RG, Abi Khalil C, Atkin SL. Association of vitamin D3 and its metabolites in patients with and without type 2 diabetes and their relationship to diabetes complications. *Therapeutic advances in chronic disease*. 2020 Sep;11:2040622320924159.
- Hajimohammadi M, Shab-Bidar S, Neyestani TR. Consumption of vitamin D-fortified yogurt drink increased leptin and ghrelin levels but reduced leptin to ghrelin ratio in type 2 diabetes patients: a single blind randomized controlled trial. *European journal of nutrition*. 2017 Sep;56(6):2029-36.
- Amitani M, Amitani H, Cheng KC, Kairupan TS, Sameshima N, Shimoshikiryo I, Mizuma K, Rokot NT, Nerome Y, Owaki T, Asakawa A. The role of ghrelin and ghrelin signaling in aging. *International Journal of Molecular Sciences*. 2017 Jul;18(7):1511.
- Kumar V, Gill KD. *Basic concepts in clinical biochemistry: a practical guide*. Singapore: Springer; 2018 Mar 30.
- Urbanovych AM, Laniush FV. The role of ghrelin and serotonin in the control of eating behavior in patients with obesity and diabetes mellitus type 2. *INTERNATIONAL JOURNAL OF ENDOCRINOLOGY (Ukraine)*. 2020 Mar 1;16(2):145-51.
- Colldén G, Tschöp MH, Müller TD. Therapeutic potential of targeting the ghrelin pathway. *International Journal of Molecular Sciences*. 2017 Apr;18(4):798.
- Khorgami Z, Shoar S, Saber AA, Howard CA, Danaei G, Sclabas GM. Outcomes of bariatric surgery versus medical management for type 2 diabetes mellitus: a meta-analysis of randomized controlled trials. *Obesity surgery*. 2019 Mar;29(3):964-74.
- Cervone DT, Lovell AJ, Dyck DJ. Regulation of adipose tissue and skeletal muscle substrate metabolism by the stomach-derived hormone, ghrelin. *Current Opinion in Pharmacology*. 2020 Jun 1;52:25-32.
- Colldén G, Tschöp MH, Müller TD. Therapeutic potential of targeting the ghrelin pathway. *International Journal of Molecular Sciences*. 2017 Apr;18(4):798.
- Mani BK, Zigman JM. Ghrelin as a survival hormone. *Trends in Endocrinology & Metabolism*. 2017 Dec 1;28(12):843-54.
- Cornejo MP, Castrogiovanni D, Schiöth HB, Reynaldo M, Marie J, Fehrentz JA, Perello M. Growth hormone secretagogue receptor signalling affects high-fat intake independently of plasma levels of ghrelin and LEAP 2, in a 4-day binge eating model. *Journal of neuroendocrinology*. 2019 Oct;31(10):e12785.
- Jawed M, Saeed MS, Shahid A, Jawed S. Ghrelin level in type 2 diabetes mellitus and obesity. *Annals of King Edward Medical University*. 2017 Dec 5;23(3).
- Rejeski JJ, Fanning J, Nicklas BJ, Rejeski WJ. Six-month changes in ghrelin and glucagon-like peptide-1 with weight loss are unrelated to long-term weight regain in obese older adults. *International Journal of Obesity*. 2021 Apr;45(4):888-94.
- Stoica L, Gadea R, Navolan DB, Lazar F, Duta C, Stoian D, Tarta C, Oлару F, Isaac A, Dobrescu A. Plasma ghrelin, adiponectin and leptin levels in obese rats with type 2 diabetes mellitus after sleeve gastrectomy and gastric plication. *Experimental and Therapeutic Medicine*. 2021 Mar 1;21(3):1-.
- Jakubowicz D, Wainstein J, Landau Z, Ahren B, Barnea M, Bar-Dayana Y, Froy O. High-energy breakfast based on whey protein reduces body weight, postprandial glycemia and HbA1C in Type 2 diabetes. *The Journal of nutritional biochemistry*. 2017 Nov 1;49:1-7.
- Giezenaar C, Trahair LG, Luscombe-Marsh ND, Hausken T, Standfield S, Jones KL, Lange K, Horowitz M, Chapman I, Soenen S. Effects of randomized whey-protein loads on energy intake, appetite, gastric emptying, and plasma gut-hormone concentrations in older men and women. *The American journal of clinical nutrition*. 2017 Sep 1;106(3):865-77.
- Yau AM, McLaughlin J, Maughan RJ, Gilmore W, Evans GH. The effect of short-term dietary fructose supplementation on

- gastric emptying rate and gastrointestinal hormone responses in healthy men. *Nutrients*. 2017 Mar;9(3):258.
19. Belinova L, Kahleova H, Malinska H, Topolcan O, Windrichova J, Oliyarnyk O, Kazdova L, Hill M, Pelikanova T. The effect of meal frequency in a reduced-energy regimen on the gastrointestinal and appetite hormones in patients with type 2 diabetes: A randomised crossover study. *PLoS One*. 2017 Apr 3;12(4):e0174820.
 20. Rahat-Rozenbloom S, Fernandes J, Cheng J, Wolever TM. Acute increases in serum colonic short-chain fatty acids elicited by inulin do not increase GLP-1 or PYY responses but may reduce ghrelin in lean and overweight humans. *European journal of clinical nutrition*. 2017 Aug;71(8):953-8.
 21. Faure C, Charlot K, Henri S, Hardy-Dessources MD, Hue O, Antoine-Jonville S. Effect of heat exposure and exercise on food intake regulation: a randomized crossover study in young healthy men. *Metabolism*. 2016 Oct 1;65(10):1541-9.
 22. Ralevski E, Horvath TL, Shanabrough M, Hayden R, Newcomb J, Petrakis I. Ghrelin is suppressed by intravenous alcohol and is related to stimulant and sedative effects of alcohol. *Alcohol and Alcoholism*. 2017 Jul 1;52(4):431-8.
 23. Donato J, Wasinski F, Furigo IC, Metzger M, Frazão R. Central regulation of metabolism by growth hormone. *Cells*. 2021 Jan;10(1):129.
 24. Churm, R., Davies, J. S., Stephens, J. W., & Prior, S. L. (2017). Ghrelin function in human obesity and type 2 diabetes: a concise review. *Obesity reviews*, 18(2), 140-148.
 25. Zhang CS, Wang LX, Wang R, Liu Y, Song LM, Yuan JH, Wang B, Dong J. The correlation between circulating ghrelin and insulin resistance in obesity: a meta-analysis. *Frontiers in physiology*. 2018:1308.
 26. Skuratovskaia D, Vulf M, Chasovskikh N, Komar A, Kirienkova E, Shunkin E, Zatolokin P, Litvinova L. The links of ghrelin to incretins, insulin, glucagon, and leptin after bariatric surgery. *Frontiers in genetics*. 2021;12.
 27. Stoica L, Gadea R, Navolan DB, Lazar F, Duta C, Stoian D, Tarta C, Olaru F, Isaic A, Dobrescu A. Plasma ghrelin, adiponectin and leptin levels in obese rats with type 2 diabetes mellitus after sleeve gastrectomy and gastric plication. *Experimental and Therapeutic Medicine*. 2021 Mar 1;21(3):1-.
 28. Mehdar KM, Alsareii SA, Alshafie SE, Al-Rafiah AR, Alamri AM. Ghrelin gastric tissue expression in patients with morbid obesity and type 2 diabetes submitted to laparoscopic sleeve gastrectomy: immunohistochemical and biochemical study. *Folia Histochemica et Cytobiologica*. 2020;58(4): 235-46.
 29. Ahmed HS, Hammadi MH, Al-Sheakh MA. Assessment Of Serum Ghrelin And Cytokines Profiling Levels In Type-2 Diabetic Iraqi Patients. *Plant Archives*. 2020;20(1):3426-30.