

Title :The effect of vitamin D and Physical exercise on glycaemic control in patients with Type 2 Diabetes Mellitus.

mehwish jan¹, shaheena bhat¹, tauseef nazir², and adil shah³

¹GMC Srinagar

²GMC,Srinagar

³GMC

March 07, 2024

Abstract

Background and purpose:The purpose of this study was to find correlation between vitamin D,Physical exercise on glycaemic control in patients of type2DM.**Experimental approach:**The study was conducted from November 2019 to December 2020 among subjects above 40 years of age at sub-district hospital Sopore,North Kashmir.Total 400 patients diagnosed with diabetes were registered for the study.Questionnaire containing relevant patient information was collected at regular intervals.Statistical analysis were performed.**Results:** Biochemistry values in the studied subjects with Type2DM compared to healthy controls in the study revealed that fasting glucose level,HbA1c,LDL,triglycerides,uric acid were higher inT2DM group compared to the control group.The results of our study showed that Vitamin D deficiency,lack of physical exercise,family history of T2DM,hypertension and smoking were significant predictors of diabetes.In Type2DM patients,mean vitamin D value was 21.45ng/ml opposed to 40ng/ml in the control group.Also physical activity was found to be higher in control group when compared to cases with p -value less than 0.00001.Also family history of DM was significantly higher in cases when compared to control group with p-value of 0.044.There was also statistically significant difference when parameters like HTN and smoking were compared (both higher in cases as against the control group) between two groups with p value 0.044 and 0.029 respectively. **Conclusion and implications:** Vit D,physical exercise,family history of diabetes may be contributing factors for the rising burden of diabetes globally and in India.We need to take cognisance of factors leading to the rising global burden of DM and take appropriate and necessary measures to stop this growing menace

Title : The effect of vitamin D and Physical exercise on glycaemic control in patients with Type 2 Diabetes Mellitus(DM).

Running title: Relationship between Vitamin D, physical exercise and DM.

Data citation: No data have been shared.

Author 1: Dr Mehwish Majeed*, GMC Srinagar,Kashmir.

Author 2: Dr Shaheena Rasool,Gmc Srinagar,Kashmir.

Author 3: Dr Tauseef Nazir,Gmc Srinagar, Kashmir.

Author 4: Dr Mohd.Adil,Gmc Srinagar,Kashmir.

Address for correspondence: Mehwish Majeed

Email: mehwishmajeed10@gmail.com

Conflict of interest

There was no conflict of interest among authors

Abstract

Background and purpose: The purpose of this study was to find correlation between vitamin D, Physical exercise on glycaemic control in patients of type2DM. **Experimental approach:** The study was conducted from November 2019 to December 2020 among subjects above 40 years of age at sub-district hospital Sore, North Kashmir. Total 400 patients diagnosed with diabetes were registered for the study. Questionnaire containing relevant patient information was collected at regular intervals. Statistical analysis were performed. **Results:** Biochemistry values in the studied subjects with Type2DM compared to healthy controls in the study revealed that fasting glucose level, HbA1c, LDL, triglycerides, uric acid were higher in T2DM group compared to the control group. The results of our study showed that Vitamin D deficiency, lack of physical exercise, family history of T2DM, hypertension and smoking were significant predictors of diabetes. In Type2DM patients, mean vitamin D value was 21.45ng/ml opposed to 40ng/ml in the control group. Also physical activity was found to be higher in control group when compared to cases with p-value less than 0.00001. Also family history of DM was significantly higher in cases when compared to control group with p-value of 0.044. There was also statistically significant difference when parameters like HTN and smoking were compared (both higher in cases as against the control group) between two groups with p value 0.044 and 0.029 respectively. **Conclusion and implications:** Vit D, physical exercise, family history of diabetes may be contributing factors for the rising burden of diabetes globally and in India. We need to take cognisance of the factors leading to the rising global burden of DM and take appropriate and necessary measures to stop this growing menace.

Key Words:

Diabetes Mellitus(DM), Vitamin D, Insulin deficiency, Physical activity.

Introduction:

Diabetes mellitus is a heterogeneous disorder characterised by hyperglycaemia, insulin deficiency and insulin resistance is increasing economic and health burden throughout the world. American diabetes association defines diabetes as a metabolic disease characterised by hyperglycaemia resulting from defects in insulin secretion, insulin action or both. (1) People with diabetes spend up to 8000 hours per year managing their diabetes outside medical setting (2). This disease often requires various daily tasks such as checking blood glucose levels as well as coherence to many complicated medical regimens (3). Diabetes is often accompanied by risk factors such as obesity, hypertension, hypercoagulability, systemic inflammation and dyslipidaemia, which increases CVD death rates. (4). India is the epicentre of diabetes mellitus and in 2017 it was found that India is the second largest country having 73 million diabetic patients after china. (5). An average Indian exhausts around 5-30% of his house hold earnings on the management of diabetes alone which increases the burden of the nation. (6-8). There is a strong evidence shown by various randomised trials that lifestyle interventions like healthy diet, physical activity and weight loss decreases risk of developing type 2 diabetes (9-12). Recently it has been postulated that dietary modification can preserve B cell mass thereby reversing the progression of type 2 diabetes mellitus. (13-15). It has been shown that inspite of maintaining blood glucose levels below a threshold for diabetes treatment some people develop micro and macro vascular complications from prediabetes even before onset of type 2 diabetes mellitus. (16,17). Around 10% prediabetic subjects develop type 2 diabetes each year. (18)

The aim of our study was to determine the relationship between vitamin D and physical exercise on glycaemic control in type 2 DM patients.

Subjects and Methods:

This is an observational cohort study which was conducted at SDH Hospital Sore during November 2019 to December 2020 among diabetic patients aged 40 years and above. A total of 450 patients were registered for the study who agreed and gave consent to take part in this study of which 50 lost follow up and finally 400 were assessed. (200 cases and 200 control subjects). Subjects were screened and randomised by schedule of

permuted block randomisation with block size 4 was used drug allotment. Subjects diagnosed with DM and taking oral anti diabetics were considered to have DM. Type2 DM diagnosis was made in accordance with the world health organisation criteria where patients having fasting blood glucose level greater than 126mg/dl and post prandial glucose greater than 200mg/dl were considered to be diabetic. (19) The inclusion criteria were: (1)subjects diagnosed with T2DM (2) taking oral medications for around 1 year. (3) [?] 40 years old (4) formal written informed consent.

Serum measurement of vitamin D

Trained expertise collected blood samples and measured vitamin D levels . using kit (DXI kit Beckman Coulter machine) and the samples were then assayed using radioimmunoassay (RIA) technique.

Questionnaire

The questionnaire comprise information about socio-demographic profile including age, sex,, education level, BMI, and, family history of diabetes, type of diabetes, co-morbid hypertension, and diabetic complications. Information on physical activity, and smoking habits were also collected.

Statistical analysis

Categorical variables were summarised as percentages. Continuous variables were summarised as mean and standard deviation. Unpaired t-test was used to analyse the difference of two means. Chi-square test was used to analyse the relationship between two categorical variables. Two-sided p-values were reported and p-value < 0.05 was considered statistically significant.

Results:

Table 1 shows the comparison of socio-demographic characteristics between diabetic and control subjects. There was significant difference between patients of diabetes and control group vis - a -vis vitamin D levels, physical activity, smoking, family history and hypertension. The difference was statistically significant also. Neither educational status nor monthly income seemed to play any significant role in the genesis of DM.

Table 2 shows the biochemistry values of the 2 groups. Vitamin D levels were lower in the of Diabetic group when compared to the control group. Mean vitamin D levels being 20ng/ml in the diabetic patients when compared to 50ng/ml in the control groups (p < 0.0000001). In participants with T2DM, BMI, fasting glucose level , HbA1c, LDL, triglycerides, uric acid and blood pressure were higher when compared to the control group.

Discussion:

Growing burden of diabetes is a major concern in Indian population. With an alarming increase in diabetes cases India will be labelled as diabetes hub of the world. With the changing trend in lifestyle vis -a vis lack of physical exercise , sedentary life style, urbanisation, advancing age, dietary habits etc will result in increasing incidence of DM. A large portion of health care expenditure by the patients effect the health care infra structure because of financial burden.(20) In India it is largely the private sector which spends approximately 68% of financial cost for delivering health care services for diseases in both rural and urban population.(21).Type 2 DM accounts for around more than 90% of all diabetes. This type includes individuals who have relative insulin deficiency and peripheral insulin resistance. Sometimes initially and lately throughout their life time they become dependent on insulin therapy to survive. There are many etiologies of type 2 DM, although the specific ones are unknown. Most of the patients with type 2 DM are obese or overweight. Type 2 DM is mostly missed on diagnosis for many years because symptoms develop gradually and are not severe enough initially and go unnoticed by the patient. Even though not severe in the beginning micro and macrovascular complications do start commencing from the initial stages of disease. Diabetic ketoacidosis ,one of the serious complications rarely occurs in association with stress, like infection or with some drugs like steroids, antipsychotics etc.(22,23)

In our study vitamin D levels were low in diabetic mellitus group when compared to control group. There

are many studies which relate occurrence of diabetes mellitus type 2 with vitamin D deficiency.(24-31).As postulated by meta-analysis done by Pittas et al. suggest that binding of vitamin D to beta cell receptors facilitated by calcium causes regulation of insulin secretion.(32).Thus deficiency of vitamin D can cause impaired insulin secretion in patients with type 2 DM. Vitamin D also stimulates the insulin receptor expression so its deficiency can cause insulin resistance(33,34). Vitamin D also acts as a hormone and regulates many gene functions directly or indirectly which influence large number of physiological functions. In our study there was negative correlation between Vitamin D and HbA1c levels. Previous studies have shown same results.(35) There is increasing risk of developing type 2 DM with increase in age, inadequate physical activity and obesity. It also occurs frequently in those with dyslipidaemia and hypertension. In our study subjects with type 2 DM had higher levels of triglycerides and LDL when compared to control group. Also blood pressure was slightly higher in DM group. In a longitudinal study contrary to association of vitamin D with type 2 DM no correlation was found between vitamin D levels and type I DM.(36).

BMI ≥ 25 kg/m² is a risk factor type 2 DM.(37). In our study physical activity was seen less in type 2 DM patients when compared to control group. Moderate physical activity like brisk walking showed beneficial results in subjects with pre diabetes.(38).Moderate intensity physical activity decreases insulin resistance and reduces abdominal fat in children and adults.(39,40).Besides aerobic activity, resistance training can be included in regular physical activity which can help to prevent diabetes.

Conclusion

Vitamin D , physical activity, smoking, family history of DM may be contributing factors to the rising burden of DM in Indian population. Therefore there is a dire need to recognize causative factors responsible for the rising incidence of this disease which eventually escalates the economic burden on individual level and by and large the global burden of this disease.

References:

- 1.American diabetes association. Diagnosis and classification of diabetes mellitus. Diabetes care2013;36(Supplement 1):S67-74
- 2.Hilliard Me, Sparling KM, Hitchcock J, Oser Tk, Hood KK. The emerging diabetes online community. Curr Diabetes Rev.2015;11(4):261-72.
- 3.Atkinson MA, Eisenbarth GS, Michels AW.Type 1 diabetes.Lancet.2014;383(9911):69-82.
- 4.Stamler J, Vaccaro O, Neaton JD, Wentworth D, Group MRFITR. Diabetes, other risk factors and 12 -yr cardiovascular mortality for men screened in the multiple risk factor intervention trial. Diabetes Care.1993;16(2):434-44.
- 5.International Diabetes federation: IDF Diabetes Atlas(2017)<http://www.idf.org/idf-diabetes-atlas-eight-edition>.Accessed Jan 2018.
- 6.CharlesAK,Grepstad M, VisintinE, FerrarioA. The economic burden of diabetes in India: a review of the literature. Glob health.2014;10(8):2-18.
- 7.Holla R, Prabhu S, Shetty, Deshpande S, Balla S, Hegde S,et al. Awareness about diabetes among adolescents of Mangalore, South India.NUJHS.2014;4(2):118-20.
- 8.Kansra P. Economic burden of diabetes among women: a comparison of out patient and inpatient care. J Health Manag.2018;20(3):401-9.
- 9.Knowler Wc, Barrett-Connor-E, Fowler SE, Hamman RF, Lachin JM, Walker EA,etal. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med.2002;346(6):393-403.
- 10.Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, etal. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and diabetes study. Diabetes care.1997;20(4):537-44.

11. Ramachandran A, Snehalatha C, Mary S, Mukesh b, Bhaskar AD, VijY V,etal. The indian diabetes prevention programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance(IDPP-1). *Diabetologia* 2006;49(2):289-97.
12. Tuomilehto J, Lindstorm J, Eriksson JG, Valle TT, Hamalainen H, Ilanne Parikka P etal. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med.*2001;344(18):1343-50.
13. Ajala O, English P, Pinkney J. Systemic review and meta analysis of different dietary approaches to the management of type 2 diabetes. *Am J Clin Nutr.*2013;97(3):505-16.
14. N.D Guess, " Dietary interventions for the prevention of type 2 diabetes in high risk groups: current state of evidence and future research needs," *Nutrients*, vol.10, no. 9, 2018
15. S. Furmli, R. Elmasry, M. Ramos, and J. Fung, " therapeutic use of intermittent fasting for people with type 2 diabetes as an alternative to insulin," *BMJ Case Rep* ., p.ber-2017:2218 -54.
16. Ford ES, Zhao G, Li C. Prediabetes and the risk for cardiovascular disease: a systematic review of the evidence. *J Am Coll Cardiol.*2010;55(13):1310-7.
17. Tabak AG, Herder C, Rathmann W, Brunner EJ, Kivimaki M. Prediabetes: a high risk state for diabetes development. *Lancet.*2012;379(9833):2279-90.
18. Warren B, Pankow JS, Matsushita K, Punjabi NM, Dava NR, Grams M, etal. Comparative prognostic performance of definitions of prediabetes: a prospective cohort analysis of the atherosclerosis risk in communities (ARIC) study. *Lancet diabetes endocrinol.*2017;5(1):34-42.
19. World health O, International diabetes F. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: report of a WHO/IDF consultation. Geneva: world health organisation; 2006.
20. Yesudian CA, Grepstad M, Visintin E, Ferrario A. The economic burden of DM in india: a review of the literature. *Glob Health.* 2014;10(1):80.
21. Tripathy JP, Prasad BM. Cost of diabetic care in india : An inequitable picture. *Diabetes Metab Syndr Clin Res Rev.*2018;12(3):251-5.
22. Umpierrez G, Korythowski M. Diabetic emergencies -ketoacidosis, hyperglycaemic hyperosmolar state and hypoglycaemia. *Nat Rev Endocrinol* 2016;12:222-232.
23. Fadini GP, Bonora BM, Avogaro A. SGLT2 inhibitors and diabetic ketoacidosis: data from the FDA adverse event reporting system. *Diabetologia* 2017;60:1385-1389
24. Hurskainen A, Virtanen J, Tuomainen T, Nurmi T, Voutilainen S. Association of serum 25-hydroxy vitamin D with type 2 Diabetes and markers of insulin resistance in a general older population in Finland. *Diabetes Metab Res Rev* 2012;28:418-23.
25. Pittas, A., Nelson, J., Mitri, J., Hillmann, W., Garganta, C., Nathan, D. et al Plasma 25-hydroxyvitamin D and progression to diabetes in patients at risk for diabetes: an ancillary analysis in the Diabetes Prevention Program. *Diabetes Care.* 2012;35: 565–573.
26. Kostoglou-Athanassiou I, Athanassiou P, Gkountouvas A, Kaldrymides P. Vitamin D and glycaemic control in Diabetes Mellitus Type 2 . *Ther Adv Endocrinol Metab.*2013;4(4):122-8.
27. Need, A., O'Loughlin, P., Horowitz, M. and Nordin, B. Relationship between fasting serum glucose, age, body mass index and serum 25 hydroxyvitamin D in postmenopausal women. *Clin Endocrinol (Oxford)* 2005; 62: 738–41.
28. Lim, S., Kim, M., Choi, S., Shin, C., Park, K., Jang, H. et al. Association of vitamin D deficiency with incidence of Type 2 Diabetes in high-risk Asian subjects. *Am J Clin Nutr* 2013; 97: 524–530.

- 29.Cavalier E, Delanaye P, Souberbielle JC, Radermecker RP. Vitamin D and Type 2 Diabetes Mellitus: where do we stand? *Diabetes Metab.* 2011 Sep;37(4):265-72.
- 30.Li YX, Zhou L. Vitamin D Deficiency, Obesity and Diabetes. *Cell Mol Biol (Noisy-le- grand).* 2015 Jun 10;61(3):35-8
31. Mezza T, Muscogiuri G, Sorice GP, Priolella A, Salomone E, Pontecorvi A, Giaccari A. Vitamin D deficiency:a new risk factor for Type 2 diabetes? *Ann Nutr Metab* 2012;61:337-48.
32. Pittas, A., Lau, J., Hu, F. and Dawson-Hughes, B. The role of vitamin D and calcium in Type 2 diabetes. A systematic review and meta-analysis. *J Clin Endoc Metab.* 2007: 92: 2017–29.
33. Maestro B, Canpion J, Davila N,Calle C.(2000) Stimulation by 1, 21-dihydroxy vitamin- D3 of insulin receptor expression and insulin responsiveness for glucose transport in U-937 human promonocytic cells. *Endocr J* 47: 383-391.
- 34.Talaei A, Mohamadi M, Adgi Z.(2013)The effect of vitamin D on insulin resistance in patients with type 2 Diabetes. *Diabetol Metab syndr* 5:8.
- 35.Cimbek A, Gursoy G, Kilic Z, Acar Y,D emirbas B,Bayram M,et al. Serum 25 hydroxy vitamin D3 levels in type 2 diabetic patients. *Med BullHaseki.*2013;51:89-94.
- 36.Simpson M,Brady H, Yin X, Seifert J, Barriga K, Hoffman M,et al.No association of vitamin D intake or 25-hydroxy vitamin D levels in childhood with risk of islet autoimmunity and type 1 Diabetes: the diabetes autoimmunity study in the young (DAISY). *Diabetologia* 2011;54(11):2779-88.
- 37.Araneta MRG, Kanaya A, Fugimoto W, et al.Optimum BMI cut points to screen Asian Americans for type 2 diabetes: The UCSD Filipino health study and the North Kohala study[Abstract].*Diabetes* 2014;63(Suppl. 1):A20.
- 38.Knowler WC, Barrett-Connor E, Fowler SE et al; Diabetes prevention programme research group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;346:393-403.
- 39.Fedewa MV, Gist NH, Evans EM, Dishman RK. Exercise and insulin resistance in youth: a metanalysis. *Pediatrics* 2014;133:e163 e174.
- 40.Davis CL, Pollock NK, Waller JL,et al. Exercise dose and diabetes risk in overweight and obese children: a randomised controlled trial. *JAMA* 2012;308:1103 1112.

Table 1:Comparison of socio-demographic and clinical characteristics between case and control groups.

Parameters	Total (n=400)	Cases n= 200	Control n= 200	P -value
Age 40-49 50-59 60-69	50 100 250	30 50 120	20 50 130	0.49
Gender Male Female	150 250	80 120	70 130	0.30
Education status. Illiterate Intermediate College	120 230 50	55 125 20	65 105 30	0.318
BMI(kg/m ²) Normal Overweight Obese	80 210 110	30 110 60	50 100 50	0.041

Parameters	Total (n=400)	Cases n= 200	Control n= 200	P -value
Physical activity.	130 270	60 140	70 130	<0.000001
Yes No				
Smoking Yes No	120 280	70 130	50 150	0.029
Family history of	220 180	120 80	100 100	0.044
DM. Yes No				
Hypertension(mmHg)	180 220	100 100	80 120	0.044
Yes No				
Monthly income < 15000 >15000	150 250	70 130	80 120	0.30

Table 2:Comparison of biochemical values of subjects with type 2 DM and control subjects.

Parameters	Case(n=200) Mean \pm SD	Control(n=200 Mean \pm SD	P-value
Blood glucose(Fasting)	177mg/dl \pm SD 353	93. \pm SD 12.77	0.00001
HbA1c	5.93%	5.86%	0.0001
Triglycerides	240.3mg/dl	134.5mg/dl	0.00001
HDL	19.75mg/dl	44.5mg/dl	0.025
LDL	154.5mg/dl	85.5mg/dl	0.026
Vit D	15ng/ml	43.95ng/ml	0.0000001
Calcium	6.02mg/dl	8.42mg/dl	0.155
Creatinine	0.96mg/dl	0.41mg/dl	0.04
Urea	30mg/dl	35mg/dl	0.59
Uric acid	4.25mg/dl	3.65mg/dl	0.75