

Vitamin D receptor and type 2 diabetes mellitus: Growing therapeutic opportunities

Parmeet Kaur Manchanda, Hemant K. Bid¹

Department of Radiation Oncology, James Cancer Center, The Ohio State University, Columbus, OH, USA 43210,
¹Center for Childhood Cancer, Nationwide Children's Hospital, Columbus, Ohio, USA 43205

Type 2 diabetes mellitus (T2DM) is a complex, polygenic, and multi-factorial disease. Both genetic predisposition and environmental factors contribute in the development and pathogenesis of T2DM. Several reports in literature have already been shown that Vitamin D deficiency may persuade to glucose intolerance, tainted insulin secretion, and finally results T2DM, suggesting the role for vitamin D in the pathogenesis of T2DM.^[1] Expression and nuclear activation of the Vitamin D receptor (VDR) are necessary for the effects of vitamin D. Vitamin D plays an important role in insulin secretion. Pancreatic tissue (exclusively the insulin-producing beta-cells) expresses the VDR and allelic variations are involved in vitamin D metabolism and are associated with glucose intolerance and insulin sensitivity.^[2] Interestingly, T2DM patients also have a higher incidence of hypovitaminosis D.^[3] Till date, numerous genetic variations have been identified in the *VDR* gene and variations in this receptor have been linked to several diseases, including T2DM.^[4-9] Previously, we reported that the frequency and distribution of *VDR* gene variants is substantially different in diverse populations and ethnic groups.^[10] Genetic studies with respect to *VDR* gene will definitely offer exceptional opportunities to connect molecular insights with epidemiological data and

may reveal reticent and subtle but true biological effects. Collective evidences from few decades have indicated the association of many polymorphisms that exist in the *VDR* gene with T2DM including ours.^[9] But there is no concrete conclusion or insight from the available literature that we can use the VDR variants as diagnostic tools or as a marker in future in case of T2DM. This is a big question and still a matter of debate. Additional attempts have to be initiated for better understanding of the molecular and cellular variations exaggerated by *VDR* gene variants including multi cohort studies; in bigger populations, special attention should be paid to correlate the effects of all the risk factors for the better understanding of the role of *VDR* gene variants with T2DM risk. Furthermore, the study of the different haplotypes, instead of single variant study, could eliminate some of the discrepancy found so far. Also, there is a need of more randomized clinical trial to explore the effect of Vitamin D and/or calcium supplementation with conciliator endpoints (like glucose tolerance, insulin secretion, and insulin sensitivity) and eventually with the incident of T2DM. One more prospect for better understanding of the physiological role of the vitamin-D system in diabetes is not only the insulin secretion, but also insulin resistance, which needs to be further investigated. This will increase the attention in its budding function in prevention and management of T2DM.

Access this article online

Quick Response Code:



Website:

www.ijhg.com

DOI:

10.4103/0971-6866.107975

References

1. Palomer X, González-Clemente JM, Blanco-Vaca F, Mauricio D. Role of vitamin D in the pathogenesis of type 2 diabetes mellitus. *Diabetes Obes Metab* 2008;10:185-97.

Address for correspondence: Dr. Hemant Kumar Bid, Center for Childhood Cancer, The Research Institute, Nationwide Children's Hospital, 700 Children's Drive, Columbus, OH 43205 USA. E-mail: hemant.bid@nationwidechildrens.org

2. Bland R, Markovic D, Hills CE, Hughes SV, Chan SL, Squires PE, *et al.* Expression of 25-hydroxyvitamin D3-1alpha-hydroxylase in pancreatic islets. *J Steroid Biochem Mol Biol* 2004;89:121-5.
3. Isaia G, Giorgino R, Adami S. High prevalence of hypovitaminosis D in female type 2 diabetic population. *Diabetes Care* 2001;24:1496.
4. Manchanda PK, Konwar R, Nayak VL, Singh V, Bid HK. Association of genetic variants of the vitamin D receptor (VDR) gene (Fok-I, Taq-I and Bsm-I) with susceptibility of benign prostatic hyperplasia in a North Indian population. *Asian Pac J Cancer Prev* 2010;11:1005-8.
5. Mittal RD, Manchanda PK, Bhat S, Bid HK. Association of vitamin-D receptor (Fok-I) gene polymorphism with bladder cancer in an Indian population. *BJU Int* 2007;99:933-7.
6. Mishra DK, Bid HK, Srivastava DS, Mandhani A, Mittal RD. Association of vitamin D receptor gene polymorphism and risk of prostate cancer in India. *Urol Int* 2005;74:315-8.
7. Bid HK, Chaudhary H, Mittal RD. Association of vitamin-D and calcitonin receptor gene polymorphism in paediatric nephrolithiasis. *Pediatr Nephrol* 2005;20:773-6.
8. Bid HK, Konwar R, Saxena M, Chaudhari P, Agrawal CG, Banerjee M. Association of glutathione S-transferase (GSTM1, T1 and P1) gene polymorphisms with type 2 diabetes mellitus in north Indian population. *J Postgrad Med* 2009;56:176-81.
9. Bid HK, Konwar R, Aggarwal CG, Gautam S, Saxena M, Nayak VL, *et al.* Vitamin D receptor (FokI, BsmI and TaqI) gene polymorphisms and type 2 diabetes mellitus: A North Indian study. *Indian J Med Sci* 2009;63:187-94.
10. Bid HK, Mishra DK, Mittal RD. Vitamin-D receptor (VDR) gene (Fok-I, Taq-I and Apa-I) polymorphisms in healthy individuals from north Indian population. *Asian Pac J Cancer Prev* 2005;6:147-52.

Announcement



2nd International Conference on Primary Immunodeficiency Diseases

2nd - 4th February, 2013

Venue: Hyatt Regency Hotel, Mumbai-India

Recent advances in the following areas will be covered during the conference.

- Basic mechanisms of immune response
- Diagnosis of PIDs
- Molecular mechanisms of PIDs
- PID in India
- Therapy of PID

For more details please visit the Website: <http://www.niih.org.in>

Conference Secretariat : Dr .Manisha Madkaikar

National Institute of Immunohaematology, 13th Floor, New Multistoreyed Building, KEM Hospital Campus, Parel, Mumbai – 400 012. India
Email Id: madkaikarmanisha@gmail.com pidcon2013@gmail.com