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Vitamin D levels and incident type 2 diabetes**Anil Batta**

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Low vitamin D status is prevalent in many populations and has become a common public health problem worldwide. Vitamin D is well-known for its essential role in calcium homeostasis and bone health. Emerging evidence from both in vitro and in vivo studies has suggested extraskeletal effects of vitamin D, including on insulin action and secretion. Population studies have provided further support to the hypothesis that low vitamin D status, as assessed by circulating 25-hydroxy vitamin D [25(OH) D] levels, is associated with impaired β -cell function, insulin resistance, and impaired glucose intolerance and thereby may be associated with higher risk of type 2 diabetes. An inverse association between 25(OH) D levels and prevalent type 2 diabetes has been shown; however, a temporal relationship cannot be established from such cross-sectional studies that are subject to bias due to the possibility of reverse causation. Recently, several prospective observational studies have reported a significant association between high circulating levels of 25(OH) D and lower incidence of type 2 diabetes. However, no association was observed in other studies. In addition, individual studies have been underpowered to examine this relation across a broad range of circulating 25(OH) D levels. As highlighted by the recent report on vitamin D from the Institute of Medicine (IOM), available evidence on the relation between vitamin D status and type 2 diabetes remains inconsistent and inconclusive, and there is a need for further research to clarify the optimal levels of 25(OH) D for nonskeletal outcomes, including type 2 diabetes, and to assess whether there is a nonlinear relationship between 25(OH)D and diabetes risk. Assessment of possible threshold levels of 25(OH) D will greatly advance our understanding of the magnitude and shape of the association of vitamin D with incidence of type 2 diabetes.

Objective: Quantitatively assess the strength and shape of the association between blood 25-hydroxy vitamin D [25(OH) D] levels with incident risk of type 2 diabetes.

Research Design and Methods: A systematic search of the MEDLINE and Embase databases and a hand search of references from original reports were conducted up to 31 October 2012. Prospective observational studies that assessed the association between blood levels of 25(OH) D and risk of incident type 2 diabetes were included for meta-analysis. Der-Simonian and Laird's random-effects model was used. A quadratic spline regression analysis was used to examine the shape of the association with a generalized least-squares trend test performed for the dose-response relation.

Results: A total of 21 prospective studies involving 76,220 participants and 4,996 incident type 2 diabetes cases were included for meta-analysis. Comparing the highest to the lowest category of 25(OH)D levels, the summary relative risk for type 2 diabetes was 0.62 (95% CI 0.54–0.70). A spline regression model showed that higher 25(OH) D levels were monotonically associated with a lower diabetes risk. This inverse association did not differ by sex, duration of follow-up, study sample size, diabetes diagnostic criteria, or 25(OH) D assay method. A linear trend analysis showed that each 10 nmol/L increment in 25(OH)D levels was associated with a 4% lower risk of type 2 diabetes (95% CI 3–6; P for linear trend < 0.0001).

Conclusions: Our meta-analysis showed an inverse and significant association between circulating 25(OH) D levels and risk of type 2 diabetes across a broad range of blood 25(OH) D levels in diverse populations.