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The Significance and Importance of Vitamin D and Zinc in Type2 Diabetes Mellitus

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Abstract: *Vitamin D is an essential nutrient for both humans and animals. Although vitamin D was previously considered to be involved in bone metabolism, epidemiological studies have demonstrated its deficiency linked to Type 2 Diabetes Mellitus (T2DM) and is closely related to obesity. It is also involved in altering Insulin synthesis and modulating its activities. Vitamin D is said to exert its action on Insulin through regulation of calcium levels. Extensive research have been done in the area to link its acceptance in regulating obesity induced DM. The trace elements zinc has historically been linked to a record number of about 300 functional enzymes and its clinical useful in DM has recently been extensively studied. This review article highlight the research work done during the last two decades on the diagnostic usefulness and importance of Vitamin D and zinc in T2DM. More research in this field will bring about awareness and importance of making the measurement of Vitamin D and zinc as routine laboratory tests for the diagnosis T2DM .*

Keywords: *Vitamin D, Zinc, Diabetes, Pancreas.*

1. INTRODUCTION

Vitamin D is a necessary nutrient for humans. People usually do not pay attention to supplementing vitamin D, since vitamin D can be produced when their skin is exposed to the sunlight. Vitamin D deficiency has been shown to alter insulin synthesis and secretion in both humans and animal models may predispose to glucose intolerance, altered insulin secretion and T2DM. Modulatory role of vitamin D in insulin secretion and action is especially relevant for Gestational Diabetes Mellitus (GDM). Diabetes was shown to be associated with a considerable lowering of 25(OH)D3 in blood serum of mice. The vitamin D endocrine system is now recognized as sub serving a wide range of fundamental biological functions in cell differentiation, inhibition of cell growth as well as immunomodulation. Vitamin D is involved in the pathogenesis of pancreatic β-cell dysfunction, insulin resistance, and systemic inflammation, conditions that contribute to the development of T2DM. Zinc is an essential trace element crucial for the function of more than 300 enzymes and it is important for cellular processes like cell division and apoptosis. Furthermore, zinc might play a role in the development of diabetes, since genetic polymorphisms in the gene of zinc transporter 8 and in metallothionein (MT)-encoding genes could be demonstrated to be associated with T2DM. The disturbance in the zinc micronutrient and increased oxidative stress in T2DM may bring about insulin resistance and the creation of diabetic complications. Zinc is required for normal immune function and taste acuity and enhances the in vitro effectiveness of insulin. The relationship between diabetes, insulin and zinc is complex with no clear cause and effect relationships. The role of zinc in islet function has recently achieved new attention as a consequence of the identification of zinc transporter 8 (ZNT8) in islets. Understanding the molecular events in the pathogenesis of DM with regards to regulation of zinc uptake would be critical to the evaluation of the natural history of diabetes in humans and especially in various racial groups.

2. VITAMIN D AND T2DM

Diabetes mellitus (DM) has been increasing rapidly worldwide, making it a huge health pressure on society in both the developed and developing countries. During the last thirty years, DM, a chronic

metabolic disease characterized by hyperglycemia is proving itself to be fatal. Periodontitis was considered as one of the main, oral health problems encountered in patients with DM. There exists a direct relation between the risk of complications of diabetes and periodontitis over time [1].Type 2 diabetes mellitus (T2DM) has become a significant global health care problem and its reported incidence is increasing at an alarming rate. Despite the improvement in therapy and development of new drugs, treatment is still not optimal especially with the associated adverse effects of most of the available drugs. New efforts are shifting toward disease prevention and a search for safer drugs. New mounting evidence is the association of low vitamin D to DM and as such many studies were conducted to test the effect of vitamin D replacement on incidence of diabetes complications and control. Although these studies present several limitations, vitamin D replacement seems to have beneficial effect on all aspects of diabetes, incidence, complications and control [2].

Obesity associatedT2DM are main chronic disease harming human health. Although the association between obesity and T2DM is well established, the molecular mechanism is still unclear. Accumulating evidence suggests that vitamin D plays a role in the development of these diseases. Vitamin D deficiency is a global problem. Vitamin D deficiency has previously been considered only to influence bone metabolism. In Vivo studies it has been revealed that vitamin D deficiency reduces insulin secretion capacity of the islet beta cells in pancreas. Moreover, epidemiological studies have demonstrated that vitamin D deficiency is closely related to obesity and increased risk of T2DM [3]. Vitamin D replenishment improves glycaemia and insulin secretion in patients with T2DM and hypovitaminosis D. The presence of vitamin D receptors (VDR) and vitamin D-binding proteins (DBP) in pancreatic tissue and the relationship between certain allelic variations in the VDR and DBP genes with glucose tolerance and insulin secretion have further supported this hypothesis. The mechanism of action of vitamin D in T2DM is thought to be mediated not only through regulation of plasma calcium levels, which regulate insulin synthesis and secretion, but also through a direct action on pancreatic beta-cell function [4].

Cardiovascular disease is the leading cause of morbidity and mortality in patients with DM, and patients with DM frequently develop diabetic cardiomyopathy. Currently, effective treatments for diabetic cardiomyopathy are limited. Vitamin D exerts pleiotropic effects on the cardiovascular system and is associated with DM. Some evidence suggests that vitamin D may improve cardiovascular outcomes in diabetes through anti-inflammatory, antioxidative, anti-hypertrophic, antifibrotic, antiatherosclerotic activities and by regulating advanced glycation end-product signaling, the renin-angiotensin system, cardiac metabolism, and hence vitamin D may be a potential agent in treating diabetic cardiomyopathy[5].Vitamins and minerals play an important role in glucose metabolism, so understanding the impact of vitamin and mineral deficiencies and the potential utility of supplementation is relevant to the prevention and or management T2DM. In order to prevent deficiencies and maintain health, the majority of diabetic individuals should receive daily vitamins and minerals within the ranges of recommended values from consumption of natural food sources and/or fortified foods [6]. 25-Hydroxy-vitamin D3 (25(OH)D) and vitamin D deficiencies were associated with the presence of diabetic retinopathy, and patients with more advanced stages of retinopathy (grades 2-4) had lower concentrations of 25(OH)D and were more frequently vitamin D deficient as compared with patients not carrying this eye complication[7].

Vitamin D was not significantly decreased in Gestational Diabetes Melliyus(GDM) compared to controls during pregnancy; however, pregnant women exhibited high prevalence of vitamin D deficiency. Prevalence of postpartum 25(OH) D deficiency in post-GDM women remained significantly higher and their postpartum 25(OH)D levels were significantly lower compared to non-GDM counterparts. Oral Glucose Tolerance Test (oGTT) repeated early postpartum persistent glucose abnormality was ascertained in 15% of post-GDM women, and neither midgestational nor postpartum 25(OH)D levels significantly differed between subjects with GDM history and persistent postpartum glucose intolerance and those with normal glucose tolerance after delivery[8].The potential beneficial effects of supplementing vitamin D or treatment with pharmacological doses of vitamin D in the prevention or cure of both form of DM remains the subject of debate. Data from epidemiological and association studies clearly indicate a correlation between vitamin D deficiency and a higher prevalence of both forms of diabetes. In animal models, vitamin D deficiency predisposes to T1DM and T2DM, whereas high doses of vitamin D or its active hormonal form, 1, 25-dihydroxyvitamin D, prevent disease. Large scale, randomized, blinded prospective studies however, remain lacking [9].

Vitamin D3 deficiency was correlated with impaired mineral metabolism in bone tissue, indicating the development of secondary osteoporosis. A decrease in weight, length and diameter (diaphysis, proximal metaepiphysis) of tibia in diabetic animals was observed as compared with control. Diabetes caused hypocalcemia, hypophosphatemia and increased enzymatic activity of alkaline phosphatase (ALP) and its isoenzymes in serum. This changes were accompanied by the impairments of vitamin D3 25-hydroxylase isoforms (CYP27A1 and CYP2R1) expression, which are the main enzymes of cholecalciferol biotransformation to 25(OH) D3 - precursor of hormonally active form of vitamin D3. A decrease in bone resorption processes was established after vitamin D3 administration as it is evident from normalization of bone morphometrical parameters and mineral metabolism in diabetic mice. Vitamin D3 ability to counter diabetes-induced alterations in bone tissue can be ascribed, at least in part, to its positive effects on the formation of vitamin D3 hormonally active forms [10].

The highest prevalence of low vitamin D levels are among Hispanics and non-Hispanic Blacks. Evidence suggests that low vitamin D levels may contribute to increased risk for diabetes and its complications. Hispanics are at greater risk for vitamin D deficiency. Evidence supports an association between low vitamin D and risk for diabetes, but there remains insufficient evidence to suggest whether treatment of low vitamin D can prevent or improve diabetes. In addition, there is limited research regarding vitamin D deficiency in the Hispanic population. Factors such as obesity, dark skin pigmentation, northern geographical latitude, and prevalence of renal insufficiency may place Hispanics at greater risk for low vitamin D levels. Nurses need to understand the signs and symptoms of vitamin D deficiency and treatment recommendation guidelines, which are also described. This information will allow nurses to improve the health outcomes and decrease the disparities amongst adult Hispanics with diabetes [11].

Both forms of immunity, namely adaptive and innate, are regulated by 1, 25(OH) 2D3. The immune-modulatory properties of vitamin D suggest that it could play a potential therapeutic role in prevention of T1DM. It is postulated that large doses of vitamin D supplementation may influence the pattern of immune regulation and subsequent progression to T1DM in a genetically susceptible individual. More studies are required to substantiate the relation between T1DM and vitamin D/vitamin D analogues in the pattern of immune regulations in susceptible individuals. In T2DM, vitamin D may influence both insulin secretion and sensitivity. An inverse relationship between T2DM and vitamin D is postulated from cross-sectional and prospective studies, though conclusive proof is as yet lacking. Available studies differ in their design and in the recommended daily allowances of vitamin D in non-skeletal diseases and β-cell function. Large, well designed, controlled, randomized interventional studies on the potential role of vitamin D and calcium in prevention and management of T2DM are required to clarify the relationship between vitamin D and glucose homeostasis in T2DM[12].Based on increasing evidence from animal and human studies, vitamin D deficiency is now regarded as a potential risk factor for T2DM. Vitamin D can affect the progress of this disease directly through the activation of its own receptor, and indirectly via the regulation of calcium homeostasis. Observational studies have revealed the association between vitamin D deficiency and incident T2DM. More double-blind randomized control studies that investigate the effects of vitamin D supplementation on insulin sensitivity, insulin secretion, and the occurrence of T2DM are needed [13].

Recent compelling evidence suggests a role of vitamin D deficiency in the pathogenesis of insulin resistance and insulin secretion derangements, with a consequent possible interference with T2DM. The mechanism of this link is incompletely understood. In fact, vitamin D deficiency is usually detected in obesity in which insulin resistance is also a common finding. The coexistence of insulin resistance and vitamin D deficiency has generated several hypotheses. Some cross-sectional and prospective studies have suggested that vitamin D deficiency may play a role in worsening insulin resistance; others have identified obesity as a risk factor predisposing individuals to exhibit both vitamin D deficiency and insulin resistance. The available data from intervention studies are largely confounded, and inadequate considerations of seasonal effects on 25(OH)D concentrations are also a common design flaw in many studies. On the contrary, there is strong evidence that obesity might cause both vitamin D deficiency and insulin resistance, leaving open the possibility that vitamin D and diabetes are not related at all. It might seem premature to draw firm conclusions on the role of vitamin D supplementation in reducing insulin resistance and preventing T2DM(14)

Calcium is necessary for insulin secretion, suggesting vitamin D may contribute to maintaining insulin secretion. Vitamin D, formed in skin in bright sunshine, is scarce in foodstuffs. Data linking

hypovitaminosis D to hyperglycemia, T2DM and metabolic disorders increasing cardiovascular risk [metabolic 'syndrome'] has accumulated over 40 years. Many mechanisms are known whereby hypovitaminosis D could be causal, e.g. by increasing insulin resistance, reducing insulin secretion and increasing autoimmune or inflammatory damage to pancreatic islets. Major questions still to be answered are whether increasing vitamin D status to the maximum seen in healthy people would reduce the risk of diabetes, the severity of the disease or of its complications, including cardiovascular disease. These questions urgently require answers. In on-going planned RCTs confirm maintenance of adequate vitamin D status at the population level by food-fortification or supplementation would be cost-effective measures likely to reduce the burden and costs of diabetes to individuals and health services. Additionally, vitamin D(2/3) supplementation is cheap but whether some non-hypercalcemia-inducing analogue may prove safer has not yet been addressed at the population level[15].

The initial observations linking vitamin D to T2DM in humans came from studies showing that both healthy and diabetic subjects had a seasonal variation of glycemic control. Currently, there is evidence supporting that vitamin D status is important to regulate some pathways related to T2DM development. Since the activation of inflammatory pathways interferes with normal metabolism and disrupts proper insulin signaling, it is hypothesized that vitamin D could influence glucose homeostasis by modulating inflammatory response. Human studies investigating the impact of vitamin D supplementation on inflammatory biomarkers of subjects with or at high risk of developing T2DM are scarce and have generated conflicting results. Based on available clinical and epidemiological data, the positive effects of vitamin D seem to be primarily related to its action on insulin secretion and sensitivity and secondary to its action on inflammation. Future studies specifically designed to investigate the role of vitamin D on T2DM using inflammation as the main outcome are urgently needed in order to provide a more robust link between vitamin D, inflammation and T2DM[16].

The prevalence of T2DM continues to climb in many parts of the globe in association with the rise in obesity. Although the latter is clearly a predominant factor in the pathogenesis of T2DM, other modifiable lifestyle factors such as exercise, alcohol consumption, smoking, and certain nutritional factors, such as vitamin D deficiency, are also believed to play a role. In contrast to the findings of observational studies, information pooled from vitamin D intervention trials lack conclusive evidence in support of vitamin D supplementation and changes in diabetes risk or measures of glucose intolerance, although an effect on insulin resistance may exist. Well-designed trials that focus on intermediate biomarkers of diabetes risk in response to increased vitamin D intake are still needed. It will be important to include in the design of these studies selection of insulin-resistant study subjects who have a low (< 50 nmol/L) initial serum vitamin D (25-hydroxyvitamin D) status and administration of sufficient vitamin D to adequately increase their vitamin D status to > 75 nmol/L serum 25-hydroxyvitamin D[17].

Vitamin D deficiency is mainly a consequence of insufficient sunlight induced vitamin D production in the skin and has been associated with various chronic diseases including T2DM. Experimental data have shown that vitamin D is important for glucose induced insulin secretion, improves insulin resistance, and exerts anti-inflammatory actions. Epidemiological studies have largely documented that a poor vitamin D status is associated with higher risk of insulin resistance and T2DM. The majority of randomized controlled trials (RCTs) in healthy or prediabetic individuals have, however, failed to demonstrate relevant vitamin D effects on insulin resistance or diabetes incidence. In patients with T2DM, a few RCTs reported some moderate effects of vitamin D on glycemic control and insulin resistance. While these findings warrant further in-depth studies, the current evidence is insufficient to recommend vitamin D supplementation for the prevention or treatment of T2DM [18].

Experimental evidence indicates that vitamin D may play a role in the defense against T1DM as well as T2DM. Epidemiological data have established a link between vitamin D deficiency and an increased incidence of both T1DM and T2DM, whereas early and long-term vitamin D supplementation may decrease the risk of these disorders. The protective effects of vitamin D are mediated through the regulation of several components such as the immune system and calcium homeostasis. However, an increasing amount of evidence suggests that vitamin D also affects beta cells directly thereby rendering them more resistant to the types of cellular stress encountered during T1DM and T2DM. This review evaluates the role of vitamin D signaling in the pathogenesis of

T1DM and T2DM with a special emphasis on the direct effects of vitamin D on pancreatic beta cells [19].

3. ROLE OF ZINC IN DIABETES

The concentration of zinc in the human body is tightly regulated and disturbances of zinc homeostasis have been associated with several diseases including DM, a disease characterized by high blood glucose concentrations as a consequence of decreased secretion or action of insulin. Zinc supplementation of animals and humans has been shown to ameliorate glycemic control in T1DM and T2DM, the two major forms of diabetes mellitus, but the underlying molecular mechanisms have only slowly been elucidated. Zinc seems to exert insulin-like effects by supporting the signal transduction of insulin and by reducing the production of cytokines, which lead to beta-cell death during the inflammatory process in the pancreas in the course of the disease. The fact that antibodies against this zinc transporter have been detected in type 1 diabetic patients offers new diagnostic possibilities (20).

The progression of diabetes mellitus may bring about perturbation in micronutrient metabolism and status. Zinc is an essential trace element that plays a vital role in maintaining many biological processes and cellular homeostasis. Dysfunctional zinc signaling is associated with a number of chronic disease states including cancer, cardiovascular disease, Alzheimer's disease, and diabetes. Cellular homeostasis requires mechanisms that tightly control the uptake, storage, and distribution of zinc. This is achieved through the coordinated actions of zinc transporters and metallothioneins. Evidence on the role of these proteins in T2DM is now emerging. Zinc plays a key role in the synthesis, secretion and action of insulin in both physiological and pathophysiological states. Moreover, recent studies highlight zinc's dynamic role as a "cellular second messenger" in the control of insulin signaling and glucose homeostasis. This suggests that zinc plays an unidentified role as a novel second messenger that augments insulin activity. This previously unexplored concept would raise a whole new area of research into the pathophysiology of insulin resistance and introduce a new class of drug target with utility for diabetes pharmacotherapy [1] & [21].

Impaired immune function and taste have been reported in diabetic subjects, and decreased serum zinc levels and hyperzincuria occur in some diabetic subjects and animals. In an earlier study, the subjects with T2DM were examined to determine whether the similar effects of zinc depletion and diabetes are causally related. Low serum zinc levels were found in 16 of 180 subjects (9 percent). There was no correlation between serum zinc and glycosylated hemoglobin levels. Natural killer cell activity did not differ between diabetic and control subjects and did not correlate with serum zinc levels. T lymphocyte response to phytohemagglutinin was lower in diabetic subjects than in control subjects but was not lowest in those with the lowest zinc levels. Taste thresholds for hydrochloric acid, sucrose, sodium chloride, and urea were elevated in diabetic subjects versus control subjects, but thresholds did not correlate with glycosylated hemoglobin or serum zinc levels. Zinc supplementation in diabetic subjects had no effect on the glycosylated hemoglobin level, natural killer cell activity, or taste thresholds, but it did increase mitogen activity in those with the lowest initial phytohemagglutinin responses.Zinc deficiency occurs in a subset of subjects with T2DM but is not related to diabetes control and does not explain decreased taste acuity. Zinc deficiency may play a role in abnormal immune function in T2DM [22].

Chronic hyperglycemia statue noticed in DM favors the manifestation of oxidative stress by increasing the production of reactive oxygen species and/or by reducing the antioxidant defense system activity. Zinc plays an important role in antioxidant defense in T2DM patients by notably acting as a cofactor of the superoxide dismutase enzyme, by modulating the glutathione metabolism and metallothionein expression, by competing with iron and copper in the cell membrane and by inhibiting nicotinamide adenine dinucleotide phosphate-oxidase enzyme. Zinc also improves the oxidative stress in these patients by reducing chronic hyperglycemia. It indeed promotes phosphorylation of insulin receptors by enhancing transport of glucose into cells. However, several studies reveal changes in zinc metabolism in individuals with T2DM and controversies remain regarding the effect of zinc supplementation in the improvement of oxidative stress in these patients. Faced with the serious challenge of the metabolic disorders related to oxidative stress in diabetes along with the importance of antioxidant nutrients in the control of this disease, new studies may contribute to improve our understanding of the role played by zinc against oxidative stress and its connection with T2DM prognosis [23].

This could serve as a prelude to the development of prevention strategies and treatment of disorders associated with this chronic disease. Pancreatic β cells contain the highest amount of zinc among cells within the human body, and hence, the relationship between zinc and diabetes has been of great interest. To date, many studies of zinc and diabetes have been reported, including studies demonstrating that diabetic patients and mice have a decreased amount of zinc in the pancreas. Zinc may counteract the deleterious effects of oxidative stress, which contributes to reduced insulin resistance, and may also protect pancreatic β cells from glucolipotoxicity. Recently, it has been shown that SLC30A8/zinc transporter 8, which is a transporter expressed on the surface of insulin granules, plays a key role in zinc transport into insulin granules and in the regulation of hepatic insulin clearance [24].

DM results from defects in insulin secretion or action, or both. In pancreatic islets, insulin production is linked with zinc transport mediated by zinc transporter ZnT-8, a product of the SLC30A8 gene. Therefore, altered activity of ZnT-8 is expected to be associated with impaired glucose-induced insulin response and promote progression from glucose intolerance to diabetes. Recent findings do emerge with a role of SLC30A8 in diabetes. Genome-wide association scans for T2DM susceptibility loci revealed and then replicated a highly significant association between the R allele of the R325W variant of SLC30A8 in and susceptibility to T2DM in Caucasians. A role of ZnT-8 as a new major self-antigenic determinant in T1DM was found. Marker rs13266634 was also shown to modulate anti-ZnT-8 self-antibody specificity in islet autoimmunity. Hence, these findings suggest for a dual role of SLC30A8 in diabetes, which is consisted in conferring genetic susceptibility to T2DM and being a major islet self-antigen in T1DM as well. Here we characterize an emerging role of ZnT-8 in diabetes and discuss potential mechanisms of its involvement in the etiology of both forms of diabetes [25].

In T1DM there is a lack of insulin production, in T2DM resistance to the effects of insulin are predominant. Both T1DM and T2DM have the same long-term complications. Diabetes effects zinc homeostasis in many ways, although it is most probably the hyperglycemia, rather than any primary lesion related to diabetes, which is responsible for the increased urinary loss and decreases in total body zinc. The role of Zn deficiency, which could, at least potentially, exacerbate the cytokine-induced damage in the autoimmune attack which destroys the islet cell in T1DM, is unclear. Since Zn plays a clear role in the synthesis, storage and secretion of insulin as well as conformational integrity of insulin in the hexameric form, the decreased Zn, which affects the ability of the islet cell to produce and secrete insulin, might then compound the problem, particularly in T2DM. Several of the complications of diabetes may be related to increased intracellular oxidants and free radicals associated with decreases in intracellular Zn and in Zn dependent antioxidant enzymes. There appears to be a complex interrelationship between Zn and both T1DM and T2DM. The role of Zn in the clinical management of diabetes, its complications, or in its prevention is, at best, unclear [26].

The association of mutations in the gene for this zinc transporter with glucose intolerance and T2DM. ZNT8 is also an autoantigen associated with the appearance of T1DM. A number of experimental models have been employed to suggest how ZNT8 and other zinc transporters regulate beta cell insulin processing and possibly secretion. An additional role for the zinc transporters in regulating alpha cell function has been suggested. In this issue of Diabetologia, Wijesekara and colleagues, using a cell-specific Znt8 (also known as Slc30a8) knockout model, demonstrate that beta cell insulin processing and glucose tolerance is negatively affected after beta cell knock out of Znt8, whereas Znt8 knockout in alpha cells seems to have little effect on glucagon secretion or glucose tolerance. Although we are yet to see the therapeutic potential of these new findings, the area represents a field through which manipulation of islet function may eventually be possible [27].

Of note, the content of zinc in pancreatic beta gells is among the highest in the body; however, very little is known about the uptake and storage of zinc inside these cells. One of the major reason suffer from DM (as well as some other illnesses like prostate cancer, CVD and hypertension) is due to their inherent inability to transport appropriate amount of zinc in the crucial cell types that require relatively higher amount of zinc than the other cell types. In both normal healthy individuals and diabetic patients. The hZIPs play an important role in the development of diabetes, and the main other illnesses like prostate and pancreatic cancers, hypertension, and CVD) as compared to low degree of expressions of the critical zinc transporters in the beta cells. If a direct link between zinc transport and diabetes can be established, then a special nutritional formula, medication or other intervention

might be especially designed to test the ability to decrease the incidence of this disease in DM susceptible groups [28].

Zinc is an essential element crucial for growth and development, and also plays a role in cell signaling for cellular processes like cell division and apoptosis. In the mammalian pancreas, Zinc is essential for the correct processing, storage, secretion, and action of insulin in beta (β)-cells. Insulin is stored inside secretory vesicles or granules, where two Zinc ions coordinate six insulin monomers to form the hexameric-structure on which maturated insulin crystals are based. The total Zinc content of the mammalian pancreas is among the highest in the body, and Zinc concentration reach millimolar levels in the interior of the dense-core granule. Changes in Zinc levels in the pancreas have been found to be associated with diabetes. Hence, the relationship between co-stored Zinc and insulin undoubtedly is critical to normal β-cell function. The advances in the field of Zinc biology over the last decade have facilitated our understanding of Zinc trafficking, its intracellular distribution and its storage. When exocytosis of insulin occurs, insulin granules fuse with the β-cell plasma membrane and release their contents, i.e., insulin as well as substantial amount of free Zinc, into the extracellular space and the local circulation. Studies increasingly indicate that secreted Zinc has autocrine or paracrine signaling in β-cells or the neighboring cells. This review discusses the Zinc homeostasis in β-cells with emphasis on the potential signaling role of Zinc to islet biology [29]

Zinc is an essential trace element, involved in many different cellular processes. A relationship between Zinc, pancreatic function and diabetes was suggested almost 70 years ago. Zinc signaling in the pancreatic islet, the redox functions of Zinc and its target genes. The recent association of two 'Zn genes', metallothionein (MT) and Zinc transporter 8 (SLC 30A8), with T2DM at the genetic level and with insulin secretion in clinical studies offers a potential new way to identify new drug targets to modulate Zinc homeostasis directly in β-cells. The action of Zn for insulin action in its target organs, as Zinc signaling in other pancreatic islet cells, will be addressed. Therapeutic Zinc-insulin preparations and the influence of Zinc transporters in T1DM will also be discussed. An extensive review of the literature on the clinical studies using Zinc supplementation in the prevention and treatment of both types of diabetes, including complications of the disease, will evaluate the overall beneficial effects of Zinc supplementation on blood glucose control, suggesting that Zinc might be a candidate ion for diabetes prevention and therapy [30].

4. CONCLUSION

The review article is a compilation of research findings done on the role of vitamin D and zinc in the pathogenesis of T2DM. Experimental studies have clearly demonstrated that both vitamin D and zinc are directly controlling the synthesis, release and modulating the action of Insulin as vitamin D is said to affect beta cells directly. Zinc along with its role as modulator of many enzymes and organ functions plays a major role in T2DM compared to other trace metals. Deficiency of both vitamin and Zinc equally affect insulin secretion, its action and controlling Insulin resistance. Hence both vitamin D and zins is said to play a major role in controlling T2DM. The contents found in this review article will help research scholars to undertake more explorative research, especially supplementation studies with both Vitamin D & Zinc T2DM and based on the outcome recommend the measurement of both as routine tests for all T2DM.

Conflict of Interest: None

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