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# Preventing Diabetes and Diabetic Cardiovascular Diseases with Dietary Zinc

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### Introduction

The importance of zinc for our health is well known. It is well known for the importance of zinc for our health. As stated by Rosalie Marion Bliss on September 23, 2016, USDA website (https://www.ars. usda.gov/news-events/news/research-news/2016/adequate-zinc-vitalto-healthy-immune-response/): "As cold and flu season nears, now is a good time to take stock of zinc intake, because adequate zinc is essential to immune response". It is true that zinc is an essential mineral and is involved in numerous aspects of cellular metabolism. It is required for the catalytic activity of hundreds of enzymes, plays a role in immune function, protein synthesis, wound healing, DNA synthesis, and cell division. Zinc also supports normal growth and development during pregnancy, childhood, and adolescence and is required for proper sense of taste and smell. A daily intake of zinc is required to maintain a steady state because the body has no specialized zinc storage system (NIH website: https://ods.od.nih.gov/factsheets/Zinc-HealthProfessional/). In this editorial, I would like to specially emphasize the preventive effects of zinc on diabetes and diabetic complications since both are big public health threats worldwide.

It is known that pancreatic B cells, which are the only cells that can produce insulin in our body, contain large amount of zinc, where one of the major roles of zinc is the binding of insulin in hexamers, a crystalline structure comprising two zinc ions and six insulin molecules, which are stored in the secretory granules. The indispensable role of zinc for insulin structure makes it a requirement when insulin analog was prepared to ensure its activity and stabilization [1]. Low levels of zinc in drinking water has been associated with high risk of type 1 diabetes [T1D] in children in Finland and England, which was supported by the data from Sardinia Island [2-4]. In line with these findings, the presence of an antibody against Zn-transport 8 has been well documented as a diagnostic consideration for T1D [5-7]. This may explain the importance of zinc dyshomeostasis, resulting from insufficient dietary intake or genetic causes, in the development of T1D. Zinc has insulin like effects on cells by promotion of lipogenesis and promotion of glucose transport. This suggests that zinc may stimulate tissues to: enhance insulin signaling, use glucose, maintain normal lipid metabolism and maintain normal cellular functions [8].

Zinc plays important roles in attenuating oxidative stress, partially by including metallothionein and zinc-copper superoxide dismutase [1]. Hyperglycemia increases free radicals, which have been implicated as a cause of complications from diabetes [1,9]. This is supported by the earlier study showing an increased risk of diabetes related complications in adults with zinc deficiency [10]. For instance, in this large cohort of patients with type 2 diabetes [T2D], low serum zinc level was an independent risk factor for coronary heart disease [CHD] events [10]. In this study, 1,050 patients with T2D with serum zinc values available were followed up for 7 years for their CHD mortality. During the follow-up, 156 patients died from CHD and 254 patients had a fatal or nonfatal MI. Patients with low serum zinc concentration had a higher risk for death from CHD than patients with high serum zinc level (Figure 1). More recent studies diabetic patients from Iraq, China and Japan also confirmed that lower serum zinc level in T2D patients was related to higher prevalence of diabetic microvascular complications, and represented as an independent risk factor for diabetic nephropathy [11-13]. Patients with lower zinc level were more likely to have a longer duration of diabetes, poorer glucose control and worse  $\beta$  cell function [12]. Advancing diabetic nephropathy represented by decreasing GFR and increasing microalbuminuria is associated with lower serum zinc levels [11]. Low serum zinc to copper ratio was positively associated with renal dysfunction in all subjects and poor glycemic control in patients with T2D [13].

To support the important role of zinc in the control of hyperglycemia and the prevention of diabetic complications,Kahn et al. [14] did a study with T2D patents with microalbuminuria who were on oral hypoglycemic agents[OHA] and angiotensin converting enzyme inhibitors. Patients were divided into 2 groups: One group (n=27) continued on OHA alone and the second group (n=27) continued on OHA with 50 mg elemental zinc, given as zinc sulphate supplement, for 12 weeks. Supplementation of zinc improved the effectiveness of OHA that is beneficial in decreasing blood glucose, triglyceride, urinary albumin excretion and inflammation in diabetic nephropathy patients and thus reducing the risk of complications. An earlier systematical evaluation of the literature and meta-analysis of the effects of zinc supplementation on diabetes reported that zinc supplementation has beneficial effects on glycemic control and promotes healthy lipid parameters [15]. This was further confirmed by subsequent systemic review, showed that zinc supplementation in T2D patients has improved glycemic control, since the %HbA1c significantly reduced in these individuals [16]. In addition, a recent randomized, doubleblind, placebo-controlled trial confirmed that zinc supplementation for 12 weeks among diabetic foot ulcer patients had beneficial effects on parameters of ulcer size and metabolic profiles [17].

The above studies have clearly indicated that zinc deficiency is a significant potential risk for the development of T1D in children and also for the development of various complications in the diabetic patients. Do we have enough zinc in our body with the current model life style? A recent summary of the National Risk of Zinc Deficiency as estimated by national surveys, included 19 countries that assessed plasma zinc concentration in young children and 14 countries in women of reproductive age, demonstrated that the prevalence of low

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**Figure 1:** In T2D patients, low serum zinc level is an independent risk factor for CHD events. Among 1,050 T2D patients serum zinc levels and CHD mortality were assessed in a 7 years follow-up. T2D Patients with serum zinc concentration  $\leq$  14.1 µmol/l at baseline had a higher risk for death from CHD (156/1050, 20.8%) than T2D patients with serum zinc level >14.1 µmol/l (254/1050, 12.8%), respectively (P=0.001). Graph was made by the author based on published data [10].

Age	Male	Female	Pregnancy	Lactation
0-6 months	2 mg*	2 mg*		
7-12 months	3 mg	3 mg		
1-3 Years	3 mg	3 mg		
4-8 Years	5 mg	5 mg		
9-13 Years	8 mg	8 mg		
14-18 Years	11 mg	9 mg	12 mg	13 mg
19+ Years	11 mg	8 mg	11 mg	12 mg

AL: Adequate Intake

Table 1: Recommended dietary allowances (RDAs) for zinc.

plasma zinc concentrate in children was >20% in 13 of the 19 surveys. Only Afghanistan, Azerbaijan, Nigeria, the Republic of Maldives, Sri Lanka, and China found a low prevalence of inadequate plasma zinc concentrations among children. Similarly in 13 of 14 surveys, the prevalence of low plasma zinc concentrations in women was >20%. Estimates of percentage population with inadequate dietary zinc intake based on food balance sheets underestimate the risk of zinc deficiency. Therefore, the results from 20 countries suggest that zinc deficiency remains a public health concern in the majority of these countries [18]. Of course, this is not the only report of its kind. The study was carried out in schools in Altindag, the district of Ankara, Turkey, which was not included in the above report, including a total of 1063 healthy children, 585 girls and 478 boys, aged 5-16 years were included in the study. Serum zinc levels with other biochemical assays were

Age	Male	Female	Pregnancy	Lactating
0-6 months	4 mg	4mg		
7-12 months	5 mg	5 mg		
1-3 Years	7 mg	7 mg		
4-8 Years	12 mg	12 mg		
9-13 Years	23 mg	23 mg		
14-18 Years	34 mg	34 mg	34 mg	34 mg
19+ Years	40 mg	40 mg	40 mg	40 mg

Interaction with medications

Table 2: Tolerable upper intake levels (ULs) for zinc.

The RDAs and Uls recommended by NIH. The tables were directly copied from NIH online page without modification

measured: a serum zinc level <65 µg/dL was considered as subclinical zinc deficiency for children <10 years of age. For children  $\geq$  10 years of age the cutoffs for serum zinc concentration were set at 66 µg/dL for females and 70 µg/dL for males. The prevalence of subclinical zinc deficiency in children attending the study was detected to be 27.8%. This high ratio showed zinc deficiency was an important health problem in the Altindag district of Ankara, Turkey, too. Therefore, the above two studies reveal the high prevalence of subclinical zinc deficiency and indicates that zinc deficiency is a public health concern for the children and adults [19].

## In closing, I want to clarify

Nowadays we remain having the risk of zinc deficiency in several

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countries, particularly in children; Prediabetic and diabetic patients need to watch their status of blood and urine zinc levels to avoid zinc deficiency [1,2]. If their blood zinc level or zinc to copper ratio is low, they need to consult a doctor or nutrition advisor to look forward to taking zinc supplement or zinc-rich foods; Zinc is not only relatively safe but also excess zinc is readily removed from the body via excretion in feces or removed from the blood by the pancreas or liver [3]. Here I provide, in Tables 1 and 2, the current NIH recommendations for the Dietary Allowances [RDAs] and the Tolerable Upper Intake Levels [ULs] for zinc. The future clinical implications for zinc in treating diabetes and diabetes complications is very exciting, as well as showing great promise for future success. I look forward to seeing more and new research in this exciting field.

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