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Assessment of Zinc Level in Type 2 Diabetic patients in Sana'a City, Yemen. Uni-center Experience. Cross-Sectional Study

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Abstract

Introduction: Diabetes mellitus (DM) is a common public health problem with high morbidity and mortality which may be affected by zinc level. This study assessed the relationship between zinc level and diabetic control and its complications.

Methods: A cross-sectional study was conducted from December 2021 to June 2022 involving 149 diabetic patients at the main diabetic center in Sana'a, Yemen (Dr. Zayed Atef center). Data contained patients' characters, diabetic history and their zinc level. Serum zinc level was tested using BIO SYSTEMS BTS-350 spectrophotometer using ZINC solution. Data were analyzed by SPSS with significance on p-value<0.05.

Results: Out of 149 participants, the majority were female (51.7%), aged less than 50 years (50.3%), had low income (61.7%), were overweight (58.4%), had DM for>5 years (51.7%), used oral anti-diabetic drugs (78.5%). Zinc deficiency was seen in the majority of patients (51%), aged over 50 years (51.3%), females (56.6%) and among overweight patients (53.9%). The majority of patients were nonsmokers. Nutritional status didn't show a relationship with zinc level (Vegetable intake (p = 0.218), fish (p-value = 0.096), beans (p = 0.465) and ginger (p = 0.645)). There was no relation between zinc and diabetic complications (hospitalization, ischemic heart disease, diabetic foot and other systemic diseases) with non-significant p-value. Glycemic control determined by HbA1C showed no statistical significance with serum zinc (p = 0.207), as lipid profile, liver and renal function tests.

Conclusions: Low zinc level is observed among diabetic females, aged over 50 years and overweight patients. Negative relation is noted between zinc and all variables. We recommend further study for evaluation of relation with taking a large sample.

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1. INTRODUCTION

Diabetes mellitus (DM) was considered as the seventh major causes of death. According to data published by World Health Organization (WHO) in 2022, 14% of adults aged 18 years and older were living with diabetes, an increase from 7% in 1990, and the prevalence of diabetes in Yemen is 7.7% in 2016. It is due to insulinopenia or insulin resistance. It had a high morbidity and mortality [1, 2, 3, 4, 5, 6, 7]. There are two types of diabetes mellitus disease. Type 1 DM occurs as a result of complete damage of pancreatic islets of Langerhans by autoimmunity whereas type 2 is related to decreased release of insulin and low action on target organ. It can sometimes occur due to hereditary or environmental factors that affect insulin action. This type of diabetes is multifactorial and genetic related [2, 3, 5, 8, 9]. According to information released by International Diabetes Federation in their fifth edition of Diabetes Atlas, people with diabetes are expected to increase from 366 million in 2011 to 577 million by 2030. In 2017, the global prevalence of diabetes mellitus among people aged 20-79 years was 8.8%. more than 90% of people have type 2 diabetes mellitus whereas 490,100 children below age 15 have type 1 diabetes mellitus [2, 3, 4, 5, 9]. Diabetes mellitus is a chronic disease that can't be cured but patient's life can be improved by using oral anti-diabetic agents, zinc supplementation, insulin therapy and changes in lifestyle [2, 6]. Zinc plays an important role in reducing sugar levels by maintaining normal functioning of islet cells of pancreas. It also maintains glucose use by muscle and fat cells [1, 2, 3, 4, 5, 6, 7, 9, 10]. Zinc is an essential element found in trace amounts in body and is needed for the functioning of more than 300 enzymes and for cellular processes such as cell division. It regulates growth, immunity, glucose and whole body metabolism [5, 6, 8, 9]. Zinc is distributed in body tissues in various amounts. It is found in bones and muscles, skin and liver, blood and blood vessels about 85% , 11% and 3% respectively. It is found in foods of animal origin such as meat and in foods of plant origin such as cereals and legumes. Serum zinc level ranges from 70-120 µg/dl. [5, 7, 8, 9]. Zinc plays an important role in human body as it provides structural stability to cell membranes, regulates expression of genes, reverses cardiac morphology impairment, synthesis DNA and RNA, helps in physiologic functioning of immunity, normal growth, reproductive functioning and reduces cholesterol, low density lipoprotein (LDL) and triglycerides (TG) levels. Zinc plays an important role in insulin synthesis, storage and secretion. It also maintains structural integrity of insulin, regulates insulin signaling, inhibits cytokines which cause death of insulin cells, reduces oxidative stress so prevents nerve damage and reduces levels of fasting blood sugar (FBS), 2 hours post prandial (2 hr PPBS) blood sugar and glycated hemoglobin (HbA1C) level [10]. Low serum zinc level (or Hypozincemia) was seen in diabetic population due to low gastrointestinal absorption and high secretion of zinc in urine. [4] In the other hand, higher total and dietary zinc consumption lowers the risk of type 2 diabetes mellitus in subsequent years [5, 9]. To the best of our knowledge, there are no previous studies assessed the association between zinc level and the diabetes mellitus in Yemen. This study aimed to assess serum zinc level among type 2 diabetic patients in Yemen.

2. SUBJECTS AND METHODS

2.1. Study design, setting and population

A prospective cross-sectional study was conducted at the main specialized center in endocrinology in Yemen (Zayed Atef's Diabetes Center) in Sana'a, Yemen, which was chosen due to its referral situation in Yemen, from December 2021 to June 2022.

2.2. Sampling method

Random selection of patients.

2.3. Inclusion criteria

All diabetic patients attending the Center.

2.4. Exclusion criteria

Pregnant women and children below 18 years were excluded.

2.5. Sample size

The sample size calculated on the study of Al-maroof; (zinc supplementation on glycemic control) [9], (133 diabetic patients) was considered as a near-reference of our sample size (149) due to the similarity of objectives of both studies.

2.6. Ethical considerations

This study was approved by the Research Ethics Committee of the Faculty of Medicine and Health Sciences, University of Science and Technology, Sana'a (N.:1446/0051/UREC/UST). Permission was also obtained from the authority of the Diabetes Center. Written informed consent was obtained from participants.

2.7. Data collection

Data were collected on a pre-designed checklist including demographic data (age, gender, income, BMI), diabetes mellites characteristics (duration of DM, type of treatment oral or insulin or both), DM complications (hospitalization, ischemic heart disease, diabetic foot, renal

disease (urinary tract infection and renal failure), hepatic diseases (hepatitis and fatty liver), lung disease (chronic cough), neurological diseases (loss of consciousness, cerebral vascular accident CVA), ophthalmic disease (cataract, retinal detachment, blindness)) , hematological and biochemical parameters (HbA1C, lipid, renal and liver function tests and serum zinc).

2.8. Sample collection

About 3-5 ml of blood was collected from each patient under aseptic method. Sample was analyzed for Hb, RBS, FBS, HBA1C, TG, HDL, LDL, Cholesterol, total proteins, creatinine, TSH, T4, SGPT, SGOT, total bilirubin, direct bilirubin and zinc. Glucose tests (HBA1C, RBS, and FBS) were tested by COBAS INTEGRA400 PLUS using Glucose HK Gen.3 solution and Tina-quant HemoglobinA1C Gen.3 solution. Both are trademarks of Roche. Creatinine, TG, HDL and LDL were all tested by COBAS INTEGRA 400 PLUS as well. Zinc was tested by BIO SYSTEMS BTS-350 spectrophotometer using ZINC solution (colorimetric test with 5-BromoPAPS).

2.9. Data analysis

Data were analyzed using IBM SPSS Statistics, Version 26 (IBM Corp., Armonk, NY, USA). Qualitative variables were described as frequency and percentage, and quantitative variables were expressed as mean and standard deviation (SD). Chi-square and Fisher's exact tests were used to study the significance of association between qualitative variables. Statistical significance was considered at p-values < 0.05.

3. RESULTS

Table (1) shows the sociodemographic characteristics, anthropometric measurement and diabetic history of diabetic patients. It was shown that the majority of patients were females 77(51.7%), aged less than 50 years 75(50.3%) and had income of 50.000 Yemeni Rial (Y.R.) or less or unknown 92(61.7%). The mean (± SD) of weight was (67.6 ± 11.3 kg), of height was (160.1 ± 7.3 cm), while Body Mass Index (BMI) was (26.4 ± 4.2 kg/m2). The majority of patients had overweight (BMI: 25-29.9) 87(58.4%), diagnosed as having DM for more than 5 years 77(51.7%) and used oral anti-diabetic drugs 117(78.5%).

Table (2) shows the HbA1c and zinc level of diabetic patients. It was shown that the majority of patients had an uncontrolled DM with an HbA1C more than (6.5) 124 (91%). Zinc level was low in 76 (51%) patients.

Table (3) shows the association of socio-demographic characteristics and habits of diabetic patients with low serum zinc level. It was shown that there was no significant relationship was observed between low zinc level

Table 1. Sociodemographic and anthropometric characteristics of diabetic patients

Variable	Mean (SD)	n (%)
Gender		
Male		72 (48.3)
Female		77 (51.7)
Age (Years)*	53.2 (14.5)	
< 50		75 (50.3)
≥50		74 (49.7)
Income (Y.R.)		
≤50,000 or unknown		92 (61.7)
>50,000		57 (38.3)
Weight (Kg)	67.6 (11.3)	
Height (cm)	160.0 (7.3)	
BMI (Kg/m^2)**	26.4 (4.2)	
Underweight (< 18.5)		3 (2.0)
Normal weight (18.5–24.9)		38 (25.5)
Overweight (25–29.9)		87 (58.4)
Obese (≥30)		21 (14.1)
Duration of DM (Years)		
< 1		19 (12.8)
1–5		53 (35.6)
>5		77 (51.7)
Type of antidiabetic drug		
Oral		117 (78.5)
Insulin		25 (16.8)
Oral & insulin		7 (4.7)

*source: Minimum = 18 years, Maximum = 90 years
** source: WHO Global Database on Body Mass Index. World Health Organization; 2006. BMI classification.

Table 2. HbA1c and zinc level of diabetic patients.

Variable	n	(%)
HbA1c level (%)		
Controlled (< 6.5)	12	(9)
Uncontrolled (≥ 6.5)	124	(91)
Zinc level (μg/dl)		
Normal (50–150 μg/dl)	73	(49)
Low (< 50 μg/dl)	76	(51)

Table 3. Association of socio-demographic characteristics of diabetic patients with low serum zinc level

Variable	N	Low Serum Zinc Level (N=76)		P-value
		n	(%)	
Age (Years)				0.681
< 50	75	37	(49.3)	
≥50	74	39	(52.7)	
Gender				0.222
Male	72	33	(45.8)	
Female	77	43	(55.8)	
Income (YR)				0.516
≤50,000 or unknown	92	45	(48.9)	
>50,000	57	31	(54.3)	
Body Mass Index (Kg/m^2)				0.669
Underweight (<18.5)	3	2	(66.6)	
Normal weight (18.5–24.9)	38	22	(57.9)	
Overweight (25–29.9)	87	41	(47.1)	
Obese (≥30)	21	11	(52.4)	
Smoking				0.142
Yes	32	20	(62.5)	
No	117	56	(47.8)	
Vegetable intake				0.486
<1 /month	60	30	(50.0)	
≥2/month	89	46	(51.7)	
Meat intake				0.321
<1/month	59	27	(45.7)	
≥2/month	90	49	(54.4)	
Fish intake				0.096
<1/month	80	41	(51.25)	
≥2/month	69	35	(50.7)	
Beans intake				0.465
< 1/month	31	18	(58.0)	
≥2/month	118	58	(49.0)	
Ginger intake				0.645
<1/month	35	20	(57.0)	
≥2/month	114	56	(49.0)	

and age(p = 0.681), gender (p = 0.222), income (p = 0.516), BMI (p = 0.669) and all type of intake (tobacco (p = 0.142), vegetable (p = 0.486), meat (p = 0.321), fish (p = 0.096), beans (p = 0.465) and ginger (p = 0.645)). Table (4) shows the association of zinc level and diabetic complications. It was shown that there was no significant relation between low zinc level and diabetic complications (hospitalization (p = 0.299), ischemic heart disease (p = 0.304), diabetic foot (p = 0.230), renal (p = 0.763), hepatic (p = 0.500), pulmonary (p = 0.154), thyroid (p = 0.734), neurological (p = 0.743) or ophthalmological diseases (p = 0.456)).

Table (5) shows the association of laboratory results and low zinc level. It was shown that the majority of patients had high HbA1c (91%) in both group with unsignificant p-value. Both groups had a non-significant p-value regarding all laboratory investigations (hemoglobin, cholesterol, triglycerides, LDL, HDL, glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), urea and creatinine).

4. DISCUSSION

Diabetes mellitus is a chronic disease that has shown to be a major cause of death worldwide. In our study we aimed to assess the relationship between serum zinc and glycemic control. The study was conducted on 149 diabetic patients with an average age of 53.2 years, and slight female dominance. Oral antidiabetic drugs represented the main used drug (78.5%) compared to insulin use (16.8%), Gradinaru et al and Perez A. Found similar results [11, 12]; that shows the wide and easy use of oral antidiabetic drugs with an optimal diabetic control. Low serum zinc was presented in the majority of all participants patients (51%), with similar result found by Gradinaru et al and others [11, 13, 14, 15, 16, 17, 18, 19, 20, 21] but different in studies conducted by Marjan Jeddi et al and others who found an increase in serum zinc level [22, 12, 23, 24, 25, 26]. Our finding may be expained by the nutrtional status of the majority of Yemeni people. The income had an impact on the decrease of zinc level as we found out in our study that the income of most patients was low (61.7%) and this may explaine the lack of meat, fish and vegetable intake by the patients involved in our study. Overweight had an influence on decreasing the serm level in (58.4%) of patienits. Hivi M. Mahmoud et al and others agreed to this in their studies [13, 14, 12, 21, 25] and this can be attrebuted to the negative effect of obesity of absorption of zinc and the unhealthy food that contributes to the obesity. Our study didn't find any relation between the serum zinc level and the glycmic control despite the

Table 4. Distribution of complications at diabetic patients according to low zinc level.

Variable	N	Low Serum Zinc Level (N=76)		P-value
		n	(%)	
Hospitalization				0.299
Yes	34	20	(58.8)	
No	115	56	(48.7)	
Ischemic heart disease				0.304
Yes	23	14	(60.8)	
No	126	62	(49.2)	
Diabetic foot				0.230
Yes	17	11	(64.7)	
No	132	65	(49.2)	
Renal disease				0.763
Yes	28	15	(53.5)	
No	121	61	(50.4)	
Liver disease				0.500
Yes	12	5	(41.6)	
No	137	71	(51.8)	
Lung disease				0.154
Yes	25	16	(64.0)	
No	124	60	(48.3)	
Thyroid disease				0.734
Yes	19	9	(47.3)	
No	130	67	(51.5)	
Neurological disease				0.743
Yes	29	14	(48.2)	
No	120	62	(51.6)	
Ophthalmological disease				0.456
Yes	77	37	(48.0)	
No	72	39	(54.1)	

Table 5. Association of laboratory test and low Zinc level of diabetic patients.

Test	N	Low Serum Zinc Level (N=76)		P-value
		n	(%)	
HbA1c (%)				0.207
Normal (< 6.5)	12	8	(66.6)	
High (≥ 6.5)	124	59	(47.5)	
Hemoglobin level (mg/dl)				0.924
Normal (12–18 mg/dl)	115	54	(46.9)	
Low (<12 mg/dl)	11	5	(45.4)	
Cholesterol (mg/dl)				0.259
Normal (< 200 mg/dl)	92	48	(52.1)	
High (>200 mg/dl)	14	5	(35.7)	
Triglycerides (mg/dl)				0.588
Normal (150–200 mg/dl)	77	40	(51.9)	
High (> 200 mg/dl)	12	6	(50.0)	
LDL (mg/dl)				0.326
Normal (< 159 mg/dl)	52	29	(55.7)	
High (> 159 mg/dl)	33	14	(42.2)	
HDL (mg/dl)				0.345
Normal (40–60 mg/dl)	81	40	(49.3)	
Low (< 40 mg/dl)	4	3	(75.0)	
SGOT (U/L)				0.572
Normal (9–40 U/L)	93	51	(54.8)	
High (> 40 U/L)	6	4	(66.6)	
SGPT (U/L)				0.607
Normal (10–55 U/L)	98	52	(53.0)	
High (> 55 U/L)	8	5	(62.5)	
Urea mg/dl)				0.937
Normal (7–20 mg/dl)	94	54	(57.4)	
High (>20 mg/dl)	3	2	(66.6)	
Creatinine (mg/dl)				0.349
Normal (0.6–1.4 mg/dl)	130	71	(54.6)	
High (>1.4 mg/dl)	6	2	(33.3)	

high HbA1c level in the majority of pateints (94.2%); p-value was 0.207. High HbA1c was also seen in studies conducted by Marjan Jeddi et al and others [22, 14, 16, 23, 17, 18, 27] but this increase wasn't seen in the studies of Hivi M. Mahmoud et al and others [13, 12, 24]. This finding reflects the diminshed level of awarness and carfullness of diabetic patients about their health status. Liver funciton tests were not related to the zinc level in our study as found by Perez A. et al. [12] this can be expalaind by the fact that the metabolism of zinc which not influenced by the liver function. Renal function tests had no relation to the zinc level in our study as concluded by Gradinaru et al. and others [11, 15, 25], that's may be due to the non-renal metabolism cycle of zinc. Lipid profile was found to be in a normal range in our study and not influenced by the level of serum zinc as found by Dhedhi M. Farooq et al and Ying Ying Luo [16, 17]. Our results were on contrary with the studies of Gradinaru et al for HDL [11], and Muhammad Farooq for LDL [27]. This result may be explained by the rural nature of the majority of Yemeni people with a presereved physical activity and traditional food.

5. CONCLUSION AND RECOMMENDATION

In conclusion, despite the finding of this study of low serum zinc level in many diabetic patients but it didn't find a significant relation with all studied variables; gender, age, BMI, lifestyle, habits, complications and laboratory investigations. We recommend more studies in this topic to highlight the effect of zinc on general health status and its effect on mortality and morbidity of chronic diseases. We recommend further study for evaluation of this relation in considering a different study design as case-control study with a larger sample size to overcome the limitation of this study. Suggestion of more dietary consumption (types and details) and cooking mode with their zinc content.

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COMPETING INTERESTS

The authors declare that they have no competing interests associated with this article.

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