Analysis of Serum Selenium and Zinc Level Among Type 2 Diabetes Mellitus Patient and their Correlation with Glycemic Control

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Abstract

Background: Diabetes mellitus (DM) is a noncommunicable disease that stills being a burden in health system. Some trace minerals such as selenium and zinc was postulated having role in blood and insulin regulation in Type 2 Diabetes Mellitus. The objective of this study is conducted to determine the level of selenoium and zinc serum in Type 2 Diabetes Mellitus patient, and its correlation with glycemic control parameter. Methods: A cross sectional study was conducted at Abdul Moeloek and Hasan Sadikin Hospital from endocrinology outpatient clinic from october to december 2022 with random sampling. Patient was tested for glycated albumin, fasting blood glucose, and glycated hemoglobin as marker od glycemic control Data then analyzed descriptively and underwent bivariate analysis with Spearman Rank Correlation. Results: Low level of Zinc, but with normal level of selenium was found among research subject. Bivariate analysis between the variables showed that there is positive, weak, and insignificant correlation of zinc and selenium with fasting blood glucose, HbA1C, and glycated albumin. (Selenium with HbA1C: r:0,131, p:0.099, Selenium with FBG: r:0,135, p:0.092, Selenium with glycated albumin: r: 0.084, p:0,223, Zinc with HbA1C: r:0.069, p:0,389, Zinc with FBG: r:0,084, r:0,544, Zinc with glycated albumin: r:0.007, p:0,920) Conclusion: There is a positive, weak, and insignificant correlation of serum selenium and zinc with glycemic control parameters.

Keywords: Diabetes Mellitus, Glycemic Control, Selenium, Zinc.

Diabetes mellitus (DM) is a noncommunicable disease that stills being a burden in health system, since the complication of DM could increase the mortality among the

patient. Impaired glucose regulation, hyperglicemia, and stress oxidant could precipitate the damage of microvascular, and destroy target organ. Some microminerals has the role to prevent the damage, such as Selenium (Se) and Zinc (Zn). Previous research already stated that the microminerals has cardioprotective and insulin regulation role. There is accumulating evidence that the metabolism of several trace elements is altered in DM and that these nutrients might have specific roles in the pathogenesis and progress of this disease.1

As previously discussed, both Selenium (Se) and Zinc (Zn) are already well-known in some physiological process. Selenium is a component of selenoproteins, which were critical elements of several anti-oxidative enzymes. Previous studies on the associations between Se and glycemic parameters were inconclusive. Some researchers found that high Se was positively associated with glucose, Hemoglobin A1c (HbA1c), insulin resistance, and risk of diabetes, while others did not find any significance correlations between them. Another RCTs show that supplementation of Seleniumn could regulate blood glucose level alongside with glycated hemoglobin (HbA1C) level, it is proposed that Selenium could increase the production of insulin, by mediating kalium-gated-channel in islet of Langerhans. 1,2

Zinc takes roles in the pathogenesis and progress of this disease. Zinc (Zn) is an essential trace metal that is directly involved in the synthesis, storage, secretion, and conformational integrity of insulin monomers and that Zn assembles to a dimeric form for storage and secretion as crystalline insulin. Lower levels of Zn may affect the ability of pancreatic islet cells responsible for the production and secretion of insulin, such as in type 2 diabetes.3 Epidemiological studies have reported decreased plasma and intracellular Zn concentrations in conjunction with increased urinary Zn excretion in diabetic patients. In subjects with type 2 DM with low Zn intake, the risk of coronary heart disease increases by a factor of two to four times and is a major cause of mortality among diabetic patients.4,5

This research was conducted to understand the correlation between some trace minerals levels (Selenium and Zinc) with glycemic control parameter (fasting plasma glucose, glycated hemoglobin, and glycated albumin) in Type 2 Diabetes Mellitus patient.

METHODS

Study Design and Population

The study was conducted over a period of three months (September to November 2022), from patient visiting Hasan Sadikin Hospital in Bandung, and Abdul Moeloek Hospital in Bandar Lampung. Subject of this research is T2DM patient that visits Internal Medicine Polyclinic. The study population consists of 220 ales and females T2DM patient from outpatient department. Informed consent was signed and obtained from individuals before enrollment into the study. Clearance was obtained from the institutional ethical committee.

Inclusion criteria in this research is patient aged >17 years; known as type 2 diabetic patients for the past five years, meanwhile the exclusion criteria in this research was patients who had diabetes other than type 2 DM, diabetic patients who had been treated with insulin, patients had taken hypotensive diuretics, subjects who had acute complications such as severe infections, major operations, trauma, GI disorders, severe cardiovascular/respiratory disease, patients who were presenting with ketoacidosis, subjects on any concomitant medication such as antioxidant vitamins, minerals, herbal treatment that may interact with glycemic status and oxidative stress parameters, cigarette smokers, and alcoholics were excluded from the study.

Ethical Approval

This research was ethically approved from Ethical Committee Faculty of Medicine Universitas Lampung No: 2000/UN26.18/PP05.02.00/2022

Sample Collection and Preparation

Fasting blood samples were collected into labeled centrifuge tubes, after an 8–12 h overnight fast, from the subjects by venipuncture. The blood samples were centrifuged at 2000 rpm for 10 min using a desktop centrifuge and the serum separated and kept in labeled sample bottles at −70°C until further analysis. The sera were analyzed for HbA1c and FBG using an autoanalyzer (HbA1C: D-100 Biorad, and FBG: Abbott Alinity). The concentration of trace elements of each sample was measured by ICP-MS (Inductively Coupling Plasma-Mass Spectrometry) using calibration method. The accuracy of determination was evaluated by measuring the metal contents of certified biological reference materials (Seronorm Trace Elements Serum; Nycomed Pharma, Oslo, Norway).

Statistical Analysis

Statistical analysis in this study were performed with SPSS for Windows (ver 24.0, Chicago, Illinois, USA). All quantitative variables were evaluated with the Kolgomorov-Smirnov test for normality measurement. The quantitative data were expressed with mean with standard deviation, and expressed as median with interquartile rage, if the data were not normally distributed, meanwhile the Qualitative variables were expressed as amount and percentages.

Bivariate analysis in this paper was conducted with nonparametric statistics with Spearman rank's correlation between the Zinc and Selenium with glycemic control variable. If r value is more than 0.6 was considered good correlation, and meanwhile a p-value < 0.05 was considered statistically significant.

RESULT

Baseline Characteristics

Baseline data characteristics in this research was collected by interview methods in case report form, the characteristics of research subject could be seen in the following table:

Table 1. Baseline Characteristics of This Research

Variable	N
Age (N=220)	
Mean±Std	58.43±10.805
Median	58.50
Range (min-max)	20.00-82.00
Ethnicity (N=220)	
Sundanese	124(56.36%)
Javanese	60(27.27%)
Betawinese	12(5.45%)
Sulawesi	10(4.54%)
Sumateran	9(4.09%)
Mix	5(2.29%)
Family History (N=220)	
Yes	112(50.9%)
No	108(49.1%)
Other Comorbidities (N=220)	
Yes	26(16.4%)
No	133(83.6%)
Other Medication History (N=220)	
Yes	151(95.0%)
No	8(5.0%)
Body Weight (N=220)	
Mean±Std	67.07±13.669
Median	64.60
Range (min-max)	42.95-118.00
Body Height (N=220)	
Mean±Std	159.61±8.674
Median	160.00
Range (min-max)	140.00-190.00
Body Mass Index (N=220)	
Mean±Std	26.25±4.408
Median	25.50
Range (min-max)	18.61-42.91

Baseline characteristic of research variable that was measured could be seen in the following table:

Table 2. Desciptive Analysis of Research Parameter

Variabel	N	Normal or Target Value
FPG (mg/dL)		<140
Mean±Std	145.03±57.861	
Median	125.50	
Range (min-max)	72.00-366.00	
HbA1C (%)		<7
Mean±Std	8.34±1.965	
Median	8.10	
Range (min-max)	3.20-14.50	
Glycated albumin (µmol/L)		121-300
Mean±Std	821.58±284.249	
Median	828.33	
Range (min-max)	312.06-3536.69	
Zinc (µg/dL)		60 – 120
Mean±Std	47.89±40.692	
Median	37.50	
Range (min-max)	2.00-241.00	
Selenium (µg/L)		110-170
Mean±Std	123.95±67.833	
Median	117.50	
Range (min-max)	9.00-422.00	

In this research glycemic control was measured by glycated hemoglobin (HbA1C), glycated albumin, and fasting blood glucose. Meanwhile, the correlation of zinc and selenium level in T2DM with glycemic control parameters in research subject could be seen in the following table:

Tabel 2 Analysis Correlation of Glycemic Control Parameters with Zinc and Selenium Level

Variable	**Correlation**	**R**	**p-value**
HbA1C with Selenium	*Spearman*	**0.131**	**0.099**
HbA1C with Zinc	*Spearman*	**0.069**	**0.389**
FBG with Selenium	*Spearman*	**0.135**	**0.092**
FBG with Zinc	*Spearman*	**0.044**	**0.584**
Glycated Albumin with Selenium	*Spearman*	**0.084**	**0.223**
Glycated Albumin with Zinc	*Spearman*	0.007	**0.920**

DISCUSSION

Interest in the biochemical and clinical consequence of trace element metabolism has been steadily increasing. Trace elements have important physiological effects when present at concentrations other than those associated with classical toxicity or with extreme deficiency. There is accumulating evidence that the metabolism of several trace elements is altered in diabetes mellitus. Some trace elements has negative correlation to glycemic control, meanwhile other elements give positive correlation to glycemic control.6

Selenium also was suggested to have insulin-mimetic properties and was an important regulator in insulin secretion. Several large-scale cross-sectional studies indicated that Selenium supplementation increased the risk of developing type 2 diabetes. However, in RCTs, unequivocal results were reported on the effect of Se on glucose metabolism. A recent meta-analysis of RCTs found that Selenium supplementation increased the risk of diabetes by 11 % compared with the placebo control. While in contrast to this

study, a six-week Se supplementation trial demonstrated that Selenium supplementation could decrease serum HbA1C levels, but not decreasing FPG levels. The Denmark PRECISE study demonstrated that supplementation with 100, 200 or 300 μg selenium-enriched yeast per day did not significantly affect the HbA1c levels in T2DM subjects.7,8

Several prior studies suggested that the synthesis of selenoprotein was varied after consumption selenomethionine or selenium yeast. In addition, the associations of Selenium with glycemic parameters also were in relation to its baseline levels. A cross-sectional study in China found that serum Se was positively correlated with glucose in the Se deficient population (median, 58ug/L), and no relationship of Se with glucose was detected in the non-deficient population (median, 103ug/L).8

Selenium is an essential trace element in nutrition for the prevention of disease in humans, since it has antioxidant activity. Epidemiological studies indicate an association between low nutritional Selenium status and increased risks of cardiomyopathy, cardiovascular disease, and carcinogenesis, and metabolic disorder in various sites of the body. In this research it was found that Selenium has weak and insignificant correlation with any glycemic control parameter (HbA1C, Glycated albumin, and fasting blood glucose). The possible reasons why the result of research was different with others were difference in the characteristics of the population and the intervention agents, and the duration time of disease. There were also unclear mechanisms about absorption, mechanism of action, metabolism, and clearance of selenium in vivo.9

The role of Zn on the lipid and carbohydrate metabolism has been widely documented. Zinc plays a clear role in the synthesis, storage and secretion of insulin, as well as conformational integrity of insulin in the hexameric form. It has the ability to regulate insulin receptor intracellular events that determine glucose tolerance and the ability to support a normal pancreatic reaction to a glucose load. It has a protective effect against β cell destruction and it has well known antiviral effects.

In a meta-analysis involved in 20 RCTs, zinc supplementation showed beneficial effects on multiple cardiometabolic risk factors in patients with metabolic disorders, particularly in improving lipid profile and glycemic indices. On the other hand, Zn also is an important mediator of insulin storage and secretion from the pancreas, which can promote the insulin stimulated glucose transport and the phosphorylation of insulin-receptor substrates to activate a series of signal transduction, improving insulin sensitivity, but we did not find causal effects of Zn on glucose measurements. The beneficial effects of Zn supplementation on glucose metabolism in patients of T2D or other metabolic abnormalities have been well established. However, when stratified by health status, distinct effects of Zn were observed, , suggesting that the effect of Zinc on metabolism may be corelated with the health status of the population.10-12

In those with pathological conditions like T2D, Zn homeostasis has been interfered. Hyperglycaemia has been postulated to interfere with the active transport of zinc back in to the tubular. Other possible causes may be disturbed metabolisms of zinc metalloenzymes and an abnormal binding of zinc to tissue proteins, which cause hyperzincuria. Zinc has been found to enhance the effectiveness of insulin in–vitro and hence, a zinc deficiency may aggravate the insulin resistance in type II diabetes. This may cause complications. Antioxidant enzymes such as oxide desmutase, catalase and peroxidase require zinc. Future studies are warranted to examine the beneficial effect of Zn supplementation on metabolism in general population.13

In this research, we found that there were weak and unsignificant correlation of Zn and glycemic control in this research population. Furthermore, this research could be different to other research should be because the difference of research population, and daily dietary intake

of Zinc in Indonesian's population. European and American could eat more redmeat compared to Indonesian, and this could make their serum Zn level higher than Indonesian, and contribute to differences of research result.14

Poor control of glucose in blood will increase HbA1C level. In this research, it was found that mean of Zinc level in research subject is lower than normal groups. Zinc helps in the utilization of glucose by muscle and fat cells. It is required as a cofactor for the function of intracellular enzymes that may be involved in protein, lipid, and glucose metabolism. The zinc may be involved in the regulation of insulin receptor-initiated signal transudation mechanism and insulin receptor synthesis These two elements, zinc and selenium have positive correlations with those glycemic control parameters, even the correlation was weak and insignificant. Weak and insignificant correlation between Zinc and any glycaemic control parameters could be caused by some factors, such as the influence of nutritional intake status of the trace elements, and also inflammation status that was not assesed quantitavely in this research.14

Hence, these trace element deficiencies appear to be an additional risk factor in the development and progress of disease and they contribute to the pathogenesis of diabetes mellitus and its complications. Zinc and Selenium also have positive correlation with HbA1C and fasting blood glucose eventhough weak and not significant. Their repletion may be an effective therapeutic intervention in prevention of the progression of the diabetes and its complications, along with glycaemic control and control of other risk factors. Clinician with dietitian could consider Zinc and Selenium as additional therapy for T2DM to reduce HbA1C level, lowering fasting plasma glucose, and improve glycemic status of the patient, and increase the sensitivity of body cell to insulin.15

This present study had certain limitations. The sample size of the present study was small, so the generalization of results cannot be recommended. Secondly, lipid levels, nutritional assesment, and inflammation status of the research subjects were not quantitatively assesed, also with dyslipidemia and nephropathy as consequences and complications of DM.

CONCLUSION

There is positive correlation of Zinc and Selenium to glycemic control parameters in Type 2 Diabetes Mellitus patient, but the correlation is weak and insignificant. Further studies with larger sample and assess other clinical features could be conducted.

CONFLICT OF INTEREST

All writers declare no conflict of interest related to this study

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