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Glycated Hemoglobin (Hba1c), Blood Glucose, and Chromium Levels among Type 2 Diabetic Patients: A Cross-Sectional Study in Denpasar, Bali

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Abstract

Results of Basic Health Research (Riskesdas) in 2013 showed that the prevalence of diabetes in Indonesia was 2.1%, and the highest prevalence was found among the age group of over 55 years in urban areas. Poor blood glucose control remains an issue among patients with type 2 diabetes mellitus (T2DM) and they are predicted to have micronutrients deficiency.

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This study aimed to describe HbA1c, blood glucose and serum chromium levels among T2DM patients. It was conducted from July 2015 to January 2016 in six public health centers (Puskesmas) in City of Denpasar. It was a cross sectional study with 165 subjects selected randomly from those who met the inclusion and exclusion criteria in each PHC. The data collected were HbA1c, blood sugar and chromium levels. HbA1c was measured by using HPLC method and blood glucose level was determined using GOD-PAP enzymatic colorimetric method, while chromium level in serum was measured by AAS method. Median of HbA1c level was 7.1%, median of fasting blood glucose level was 140 mg/dL, and mean of serum chromium level was 42.3 µg/L with an SD of 16.0 µg/L. Although T2DM patients have been getting medical treatment, they have poor glycemic control and lower chromium level compared to non-diabetic subjects in the same area.

Keywords: blood glucose; chromium; diabetes; HbA1c.

1. Introduction

International Diabetes Federation (IDF) reported that Indonesia ranked 7th of the ten countries in terms of the total numbers of people with diabetes, with 8.5 million cases [1]. The report also shows that incidence of diabetes is expected to reach 382 million in 2035, and 46% cases are undiagnosed. Indonesia is expected to rank 6th in 2035, in terms of the highest number of diabetes case in the world. Based on the results of Basic Health Survey (BHS) in 2013, the prevalence of diabetes in Indonesia was reported to have increased by 1% to 2.1%. In general, it increased from 2007 to 2013 in all provinces in Indonesia [2].

National Institute of Health Research and Development (NIHRD) also stated that the prevalence of diabetes was higher among women above 55 years, and the highest number of diabetes case was found in urban areas [2]. In 2007 BHS report, Denpasar had the highest prevalence of diabetes among other cities and regencies in Bali Province, with a prevalence of 2.0% [3].

Diabetes mellitus is a chronic disease that may lead to fatal conditions and even cause death if not managed properly [4]. Improper management of type 2 diabetes mellitus (T2DM) can lead to a surge in blood glucose levels and poor glycemic control [5]. This condition is a global problem that occurs among all people with diabetes worldwide [5]. Besides blood glucose, glycated hemoglobin (HbA1c) level can also become a parameter in assessing the glycemic control of T2DM patients. Long-term poor glycemic control can make T2DM patients have various complications (e.g. diabetic neuropathy, diabetic nephropathy and blindness) and affect their quality of life [6].

People with diabetes are considered to have micronutrient deficiencies, one of which is chromium, although there has not been a lot of supporting data [7]. Chromium is an essential mineral that is required to help the regulation of carbohydrate metabolism, affect insulin function, and the regulation of blood glucose [8]. Several previous studies showed that people with diabetes might have chromium deficiency. It was evidenced by serum chromium levels of the diabetic subjects, which were lower than non-diabetic subjects [8]. Previous study showed that serum chromium was a reflection of the chromium deposits in the body. Chromium status in the blood can be increased significantly by taking chromium supplements.

This study was conducted to describe the profile of Hb1Ac, blood glucose, and chromium levels of patients with T2DM in Denpasar.

2. Material and Methods

2.1. Ethical approval

This study was conducted after having an approval from Research Ethics Committee of Faculty of Medicine, Udayana University/Sanglah Central Public Hospital (RSUP) No. 1439/UN.14.2/Litbang/2015. The subjects had read, got the explanation, and agreed to sign the informed consent.

2.2. Study design and subject selection

This study was conducted from July 2015 to January 2016 in six community health centers (Puskesmas) in Denpasar. It was conducted on patients with T2DM, who were members of diabetes community (*paguyuban*) and/or Chronic Disease Management Program (PROLANIS) at Puskesmas level. Puskesmas's PROLANIS was integrated with Healthcare Social Security Agency (BPJS).

A total of 165 patients with T2DM from six Puskesmas in Denpasar participated in this study; i.e. Puskesmas III in North Denpasar, Puskesmas I in East Denpasar, Puskesmas I in West Denpasar, Puskesmas II in East Denpasar, Puskesmas II in West Denpasar, and Puskesmas IV in South Denpasar. The subjects were selected by simple random sampling method, and they had to meet the inclusion and exclusion criteria. The inclusion criteria were as follows: subjects were diagnosed with T2DM by a doctor, registered in Puskesmas's PROLANIS data, aged 50-70 years, undergoing diabetic diet and antidiabetic drug therapies, and resided in Denpasar. The exclusion criteria were as follows: the ones who used insulin, and had complications based on the doctor's diagnosis.

2.3. Types of data and data collection method

The data collected included characteristics of subjects (name, age which are cross-checked with ID card, sex, complete address, and phone number); nutritional status; blood glucose, serum chromium, and HbA1c levels.

Nutritional status of subjects was assessed based on body mass index (BMI) and waist circumference (WC). BMI was calculated by dividing body weight (kg) with the square of body height (m^2). Body weight was measured by Camry digital scale with a 0.1 kg precision, while body height was measured by *microtoise*with a 0.1 cm precision.

The subjects were requested to fast for 10-12 hours, one day before blood sampling. A 10 ml blood sample was collected and filled into red-top tube and purple-top tube (containing EDTA) in equal amount (5 ml for each tube). The blood samples in red-top tubes were centrifuged to obtain the sera, which were used to measure blood glucose and chromium levels. Meanwhile, the blood samples in EDTA tubes were used to measure HbA1c levels.

Blood glucose levels were measured by enzymatic colorimetric procedure (GOD-PAP method) in Regional Technical Implementation Unit (UPTD) Regional Health Laboratory, located in Bali Province. Serum chromium levels were measured by flame atomic absorption spectrometry (FAAS) method using Shimadzu's instruments in the Laboratory of Faculty of Agricultural Technology, Udayana University in Denpasar. HbA1c levels were measured by high performance liquid chromatography (HPLC) method, conducted in Prodia Clinical Laboratory, Denpasar Branch.

2.4. Statistical analyses

Univariate and bivariate analyses of blood glucose, serum chromium, and HbA1c data were performed using Microsoft Excel program and SPSS Inc. software. Bivariate analysis was performed to analyze the relation of HbA1c to serum chromium and blood glucose and the association between blood glucose and serum chromium. Association between variables was considered significant if $p<\alpha$ ($\alpha = 0.05$). The results were presented in tables, graphs, and narration.

3. Results

Based on our findings, most of the subjects were men (55.8%) and the rest were women. Subjects' mean age was 60.76±5.773 years. Men's and women's age were not significantly different. Table 1 presented the data concerning subjects' characteristics (age, WC, and BMI), as well as HbA1c, blood glucose, and chromium levels.

Table 1 showed that median HbA1c and fasting blood glucose (FBG) were 7.1% and 140.0 mg/dL, respectively. Meanwhile, the mean serum chromium level was 42.3±16.0 µg/L.

Table 1: Subjects' characteristics based on sex†

Variables	Men (n=92)	Women (n=73)	Total (n=165)	Range
Age (years)	60.98±6.3	60.49±5.1	60.76±5.8	50.0-70.0
BMI (kg/m2)	23.80±3.5	24.99±4.1	24.33±3.78	16.79-38.54
WC	89.7±9.7	91.2±9.4	90.36±9.66	66.8-122.0
HbA1c (%)	6.9	7.3	7.1	5.3-15.5
FBG (mg/dL)	136.0	150.0	140.0	75.0-493.0
Chromium (µg/L)	42.0±17.0	43.0±16.0	42.3±0.016	1.49-83.9

† Presented as mean±standard deviation (SD); *presented as median

Table 2 showed WC-based nutritional status. Most of the subjects (67.3%) had central obesity and the rest

(32.7%) had normal nutritional status. However, based on BMI, we found that most of the subjects (55.2%) had normal nutritional status and 39.4% of them were overweight and obese.

Table 2: Distribution of nutritional status based on sex

Sex	WC		BMI			
	Normal	Central Obesity	Underweight	Normal	Overweight	Obese
Men (n=92)	45 (51.1%)	47 (48.9%)	4 (4.3%)	56(60.9%)	27(29.3%)	5 (5.4%)
Women (n=73)	9 (12.3%)	64 (87.7%)	5 (6.8%)	35 (47.9%)	27 (37.0%)	6 (8.2%)
Total (n=165)	54 (32.7%)	111 (67.3%)	9 (100%)	91 (55.2%)	54 (32.7%)	11 (6.7%)

Based on HbA1c levels, we found that half of the total subjects (50.3%) had more than 7.0% HbA1c levels, and the highest level was found in women (53.4%) (Table 3).

Table 3: Distribution of HbA1c levels based on sex

Sex	HbA1c	
	≤7.0%	>7.0%
Men (n=92)	48 (52.2%)	52 (47.8%)
Women (n=73)	34 (46.6%)	39 (53.4%)
Total (n=165)	82 (49.7%)	83 (50.3%)

Three scatter plots were presented below, which described the association between variables (Figure 1-3). Figure 1 showed the inverse relationship between subjects' HbA1c and serum chromium levels (r = -0.015), although it was not significant (p=0.869; p>0.05). Figure 2 showed a significant positive correlation between subjects' HbA1c and blood glucose levels (r=0.593, p<0.05). It showed that HbA1c levels would increase if the subjects had high blood glucose levels.

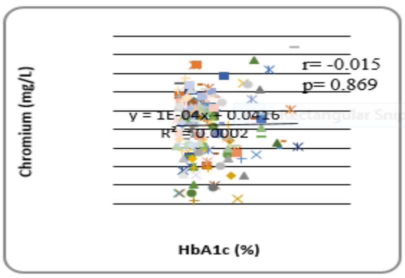

Figure 1: Association between HbA1c and serum chromium

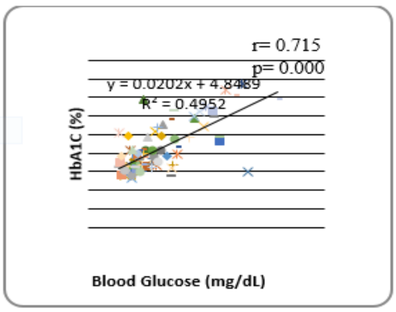

Figure 2: Association between HbA1c and blood glucose

Negative correlation was also found between blood glucose and serum chromium levels, as presented in Figure 3. It was statistically significant, with a correlation coefficient (r) of -0.528 and p<0.05 (p=0.003).

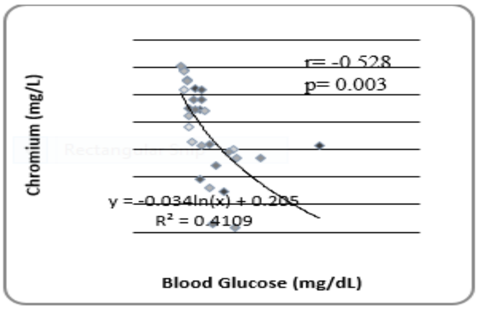

Figure 3: Association between blood glucose and serum chromium

4. Discussion

4.1. Nutritional Status

Most of the subjects had central obesity (WC >90 cm for men, and >80 cm for women), and had BMIs within the normal range (18.5-24.9 kg/m^2). Previous study stated that based on BMI, the prevalence of overweight and obese in Asia were relatively low compared to the Western countries or populations [9]. Another study added that the prevalence of obesity was not directly proportional to the prevalence of diabetes [10]. Asian countries had higher prevalence of diabetes than American countries, even though they had lower obesity rate or BMI values [9-11].

4.2. HbA1c, serum chromium and blood glucose levels

Half of the total subjects had poor glycemic control (HbA1c >7.0%). Previous review stated that diabetes population in South Asia significantly had worse glycemic control than Caucasians[11]. Previous study found that 65.1% of the subjects had poor glycemic control (HbA1c >7.0%)[12]. Variance of HbA1c levels in our study was wide, in a range of 5.3%-15.5%. There was not much difference found in subjects' HbA1c levels between our study and the previous studies [13,14]. However, our findings were in contrast to the study results by previous researchers [8,15]. Our study showed that serum chromium levels of the diabetic subjects (0.0423±0.016 mg/L) were half of the levels found in nondiabetic subjects (0.094±0.005 mg/L) in the same study site. The chromium levels were lower than the previous study [14], but higher than the ones among diabetic patients in India [8]. Several studies on blood chromium levels found varying results with one another. It may be caused by different chromium analysis method they use (type and specification of the instruments). It may also be affected by the subjects' chromium intake, because the type of food or food sources of chromium they consume may vary. Our subjects were patients with T2DM in Denpasar City, who got diabetes treatments with diet therapy and oral antidiabetic drugs (OADs). Although they had been getting diabetes therapy, the serum chromium levels were lower than nondiabetic subjects. This finding was similar to the results of previous studies [8,14,16-18].The low levels of serum chromium in diabetic people might be caused by the increased chromium excretion due to hyperglycemia and high levels of insulin [19]. Insulin resistance might be regarded as the central pathogenesis of T2DM, as the consequences of chromium deficiency [20]. Severe chromium deficiency in human is rarely reported [21]. However, previous researchers reported that older age groups in general might have subclinical chromium deficiency, because their chromium intakes were lower than chromium adequacy recommendation according to age groups [22]. Other researchers added that chromium concentrations in the body decreased by 25%-40% with the advancing age [23]. The concentrations tended to decrease at age above 40 years [18]. Nevertheless, there were no studies explaining the association between age and decreased chromium levels in the body through metabolic processes [21]. The subjects still had high FBG (a median of 140 mg/dl).The United Kingdom Prospective Diabetes Study (UKPDS) in 1998stated that duration of diabetes might contribute to the progressive decrease in insulin secretion, and it might eventually lead to beta-cell failure. The failure might affect the response to diet therapy or OADs, thereby disrupting the glycemic control of people with diabetes. The focus in glycemic control was not only to decrease the risk of cardiovascular disease [24]. Therefore, therapies for treating diabetes not only aim to lower the blood glucose, but also to observe their effects on body weight, blood pressure, lipid profile, cardiovascular protection, and to prevent hypoglycemia [6].T2DM therapy should focus on diet, regular physical activity, and OADs.

4.3. Relation of chromium levels to HbA1c and blood glucose levels

The subjects' chromium serum levels had negative correlations with HbA1c and blood glucose levels. These results were similar with the findings of previous studies [14,18,25]. Previous study reported that patients with well-controlled T2DM had low serum chromium levels [18]. Moreover, patients with uncontrolled T2DM had an extremely low serum chromium. The results found in our study and previous studies showed that chromium effect appeared when there were insulin resistance and poor glycemic control [21]. Chromium is a cofactor in insulin action, which may improve blood glucose levels among diabetic patients who tend to have unstable glucose levels [14]. Micronutrients, one of which is chromium, are being explored for their potential and benefits as medium of therapy for T2DM patients and to prevent complications in patients with diabetes [7].

4.4. Association between HbA1c and blood glucose levels

There was a linear relationship between subjects' blood glucose and HbA1c levels. Our finding did not differ from other studies [26-28]. Based on a systematic review, fasting plasma glucose (FPG) had a correlation with HbA1c[29]. An extremely strong correlation was found between postprandial glucose (PPG) and HbA1c levels among T2DM patients. A strong correlation between FPG and HbA1c levels among T2DM patients was found if the FPG was within the range of 5.6-9.0 mmol/L [30]. HbA1c levels appeared different due to geographic areas and ethnic groups. Its levels increased slightly, as well as FPG per unit, either in patients who underwent OADs therapy or those without OADs. Previous researchers suggested that impaired insulin secretion and increased glucagon secretion might contribute to excessive glucose production [14]. Therefore, some T2DM patients might have elevated blood glucose due to excessive glucagon and abnormal hepatic glucose production. This research has been done with well-planned methods, but we feel our study still has limitations. The limitation is not to estimate the effect of OHO consumed by subject and duration of diabetes diagnosis, so that factor may influence correlation result.

5. Conclusion

Most of the T2DM patients in Denpasar aged 50-70 years, had poor glycemic control (HbA1c levels >7.0% and blood glucose levels >130 mg/dL). Our study also suggested an inverse association between serum chromium and HbA1c levels, a significant correlation between HbA1c and blood glucose levels, and a strong negative correlation between serum chromium and blood glucose levels among patients with T2DM.

6. Recommendation

The patients should monitor their blood glucose levels and check their HbA1c levels twice a year, and continue the diabetes therapy. Although patients with T2DM in Denpasar had already received therapy, their serum chromium levels were lower than nondiabetic subjects in the same area. On the basis of these conditions, they may need chromium supplements in accordance with the required dose.

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