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Correlations between glycaemic control and serum chromium levels among type 2 diabetic patients in Denpasar, Bali

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ABSTRACT

Introduction: The National Basic Health Research (Riskesdas) in 2013 showed 6.9% diabetes prevalence in Indonesia with the highest among aged 55 years and above in urban areas. Poor glycaemic control is reported to be related to low chromium levels in type 2 diabetes mellitus (T2DM). This study aimed to determine the correlation between serum chromium and glycaemic control in T2DM patients. **Methods:** A cross-sectional study was conducted at six community health centres (Puskesmas) in Denpasar, Bali in July 2015-Jan 2016. A total of 165 T2DM patients who met the inclusion criteria were included. The subjects were aged 50-70 years, registered in the Chronic Diseases Management Programme (Prolanis), members of diabetic health clubs in the Puskesmas, and were taking oral hypoglycaemic medication. Anthropometric measurements were taken, including weight, height and waist circumference. Fasting blood samples were collected for determination of glycated haemoglobin (HbA1c) using HPLC, blood glucose (FBG) by tipyrine (GOD-PAP) enzymatic colorimetric method, and serum chromium using atomic absorption spectrophotometry (AAS). Correlations between HbA1c and FBG with serum chromium were determined using Spearman Correlation test (95% CI). **Results:** There was a significant negative correlation between FBG levels and serum chromium (r=-0.813; p<0.001); while no significant correlation was found between HbA1c and serum chromium (r=-0.059; p>0.05). **Conclusion:** Serum chromium levels of T2DM patients in this study were low, while their FBG levels correlated negatively with serum chromium status. Studies on a larger sample of T2DM patients should be undertaken to verify this finding for nutritional care of diabetic patients.

Keywords: Diabetes mellitus, fasting blood glucose, HbA1c, serum chromium

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is caused by a combination of genetic and lifestyle factors, such as sedentary lifestyle, high intake in carbohydrate and fat, and lack of physical activity (Hu, 2011). According to the International Diabetes Federation (IDF), Indonesia ranked seventh of the ten countries with the highest number of diabetes cases (8.5 million cases) in 2013 (IDF, 2013). The report also

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predicts that diabetes cases will reach 382 million cases globally by the year 2035. Within that figure, Indonesia will move into the sixth rank for the highest diabetes cases in the world (IDF, 2013). Based on Indonesian National Basic Health Research (RISKESDAS) in 2013, the prevalence of diabetes in Indonesia increased steadily from 5.7% in 2007 to 6.9% in 2013 with all provinces showing the same trend of increase (Balitbangkes, 2013). The prevalence was higher among women over the age of 55 years and in urban areas (Balitbangkes, 2007; Balitbangkes, 2013).

Based on the American Diabetes Association (ADA) and Indonesian Endocrinology Association (PERKENI) guidelines, there are four pillars of T2DM care; i.e. education, diet, physical activity and hypoglycaemic agent and/or insulin where necessary (ADA, 2011; PERKENI, 2015). Without proper management, patients with T2DM may suffer from repeated surge of blood glucose levels or having poor glycaemic control (Khunty*et al.*, 2012). Chronic poor glycaemic control may lead to various complications such as neuropathy, nephropathy, stroke, and retinopathy, which in turn affect the patient's quality of life (ADA, 2015).

Increasing evidence suggests that micronutrients (e.g. vitamin B3, vitamin D, magnesium, zinc, and chromium) play a role in glucose control and prevention of microvascular or macrovascular complications (Kelly & Dyson, 2011; Kaur & Henry, 2014). In the case of chromium, several studies have shown that T2DM patients have lower serum chromium compared to non-diabetic patients or the healthy population (Elabid & Ahmed, 2014; Hajra *et al.*, 2016; Nurohmi, 2017). Chromium is considered as a trace mineral that may help regulate carbohydrate metabolism, improve insulin action and help regulate blood glucose level (Bhanderi *et al.*, 2016; Bai *et al.*, 2015), as well as able to increase glucose uptake in diabetic patients by improving the regulation of glucose transporter 4 (GLUT4) (Hoffman *et al.*, 2014). However, there is limiting evidence associating diabetes and chromium status (Costello, Dwyer & Bailey, 2016).

This study was conducted to determine the correlation between serum chromium and glucose control in Indonesian T2DM patients in Bali.

MATERIALS AND METHODS

This cross-sectional study was undertaken in six community health centres (Puskesmas) in Denpasar, Bali. These sites were chosen purposively considering several factors, including that the Puskesmas has a diabetic club and agreed to provide its register of patients with T2DM. This registry was an integrated dataset of the Chronic Diseases Management Programme (Prolanis) and the National Health Insurance (BPJS Kesehatan). The study was conducted for six months in July 2015-January 2016.

The inclusion criteria for the study included patients aged 50-70 years, registered in the Prolanis registry in each Puskesmas, engaged in the diabetes club each week, taking diabetic medication (diet and anti-diabetic agent), and willing to participate in the study by signing the informed consent. The exclusion criteria were patients with complications (macrovascular and microvascular diseases) at the time of data collection based on medical diagnosis, and receiving insulin therapy. A total of 165 patients out of a total of 178 met the inclusion criteria. All were contacted by phone or door-to-door visits.

Body weight was measured with digital Camry step on weighing device with 0.1 kg precision, body height was measured with a microtoise tape with 0.1 cm precision, while waist circumference

was taken using a measuring tape with 0.1 cm precision.

Venous blood samples were taken after 10-12 hours fasting. HbA1c levels were measured by high performance liquid chromatography (HPLC) at the Prodia clinical laboratory, fasting blood glucose (FBG) was determined by GOD-PAP enzymatic colorimetric method in the Provincial Government Health Laboratory, while serum chromium was determined using atomic absorption spectrophotometer (AAS) in the Integrated Chemistry Laboratory of Udayana University in Denpasar.

Data were processed using Microsoft Excel and SPSS software. Correlations between glycaemic control and serum chromium were adetermined using Spearman correlation (95% CI, α=0.05). Analysis of covariance (ANCOVA) was performed to determine the association between serum chromium levels and glycaemic control variables (HbA1c and FBG). Chi-square test was employed to analyse the relationship between sex and the degree of glycaemic control.

Ethical clearance for the study was granted by Ethical Commission for Research of Faculty of Medicine, Udayana University/ Sanglah Hospital number 1439/UN.14.2/Litbang/2015.

RESULTS

Just over half of the subjects were male (55.8%) and the average age was 60 years (Table 1). The median duration of being

Table 1. Characteristics of subjects and nutritional status based on sex

Variable	*Male (n=92)*	*Female (n=73)*	*p-value*[†]	*All (n=165)*
Age (year), mean±SD	60.98±6.3	60.49±5.1	0.585	60.76±5.8
Diabetes duration, median (range)	2.0 (0.5-31.0)	4.0 (0.5-19.0)	0.344	3.0 (0.5-31.0)
≤5.0 years, *n* (%)	74 (80.4)	57 (78.1)		131 (79.4)
5.1-10 years, *n* (%)	12 (13.0)	10 (13.7)		22 (13.3)
>10 years, *n* (%)	6 (6.6)	6 (8.2)		12 (7.3)
BMI (kg/m^2), mean±SD	23.8±3.5	25.0±4.1	0. 043[*]	24.33±3.8
WC (cm), mean±SD	89.7±9.8	91.2±9.4	0.321	90.4±9.7

SD: Standard Deviation; BMI: Body Mass Index; WC: Waist Circumference
[†]Based on Independent samples *t*-test between male and female
[*]Significant at $p<0.05$

Table 2. HbA1c, blood glucose and serum chromium levels based on the degree of glycaemic control

Variable	*Good glycaemic control (n=81)*	*Poor glycaemic control (n=84)*
Sex		
Female, *n* (%)	34 (46.6)	39 (53.4)
Male, *n* (%)	47 (51.1)	45 (48.9)
HbA1c (%), median (range)	6.4 (5.3-6.9)	8.5 (7.0-15.5)
FBG (mg/dL), median (range)	119 (75-404)	185 (76-493)
Chromium (µg/L), median (range)	45.0 (1.0-75.0)	43.0 (3.0-84.0)

FBG: Fasting Blood Glucose; Good glycaemic control: HbA1c <7.0%; Poor glycaemic control: HbA1c ≥7.0%

Table 3. Bivariate analysis on subjects' serum chromium and glycaemic control†

Variable	*r-value*	*95% Confidence Interval (mean)*		*p-value*
		Lower	*Upper*	
HbA1c (%)	-0.059	7.5	8.2	0.454
FBG (mg/dL)	-0.813	158.0	183.6	0.000

†Glycaemic control: HbA1c and FBG levels; FBG: Fasting Blood Glucose

diagnosed with T2DM was three years, and most of the subjects were diagnosed of diabetes for less than five years. Based on BMI, 40% were overweight or obese and both sexes also showed central obesity.

The median of HbA1c and FBG were 8.5% and 185 mg/dL, respectively (Table 2). The median chromium level of patients with poor glycaemic control was lower than those with better glycaemic control (43.0 µg/L vs 45.0 µg/L).

No significant findings were found between glycaemic control (HbA1c level and FBG) and serum chromium concentrations (Table 3). Based on ANCOVA performed to determine the correlations between serum chromium levels to HbA1c and FBG levels, controlling for age, sex, WC and BMI values, a significant association between serum chromium and FBG levels was found (p=0.032; p<0.05), while no significant association was found between serum chromium and HbA1c levels (p=0.369).

DISCUSSION

Most of the subjects in this study showed high fasting glucose level (a median of 140 mg/dL), indicating that they had poor glycaemic control. Patients were defined as having poor glycaemic control if their HbA1c levels were higher than 7% or their FBG levels were higher than 130 mg/dL (ADA, 2015). Inadequate insulin secretion and high level of glucagon contributed to the increase in blood glucose. Therefore, some patients with T2DM might have impairment in their glucagon level, thereby increasing the hepatic glucose production which caused an increase in blood glucose level (Hædersdal *et al.*, 2018). Blood glucose surge could also be linked to the duration of diabetes (Chacko, 2016). Leibowitz, Kaiser & Cerasi (2011) stated that the duration of DM might progressively affect insulin secretion and would eventually cause β cell failure. What happened to the β cell might impair the response to diet and oral hypoglycaemic drug and cause impairment in glycaemic control. However, T2DM care should not only focus on managing glycaemic control to lower cardiovascular risk but also to manage weight, blood pressure, lipid profile and prevent hypoglycaemia (Fox *et al.*, 2015; ADA, 2015).

Subjects in this study were 50-70 years with the mean age of 60.8 years. RISKESDAS (2013) reported that the highest prevalence of diabetes in Indonesia was among 55 years and above (Balitbangkes, 2013). Likewise in the United States, the prevalence of diabetes increased with age (Kirkman *et al.*, 2012). Other studies reported prevalence of diabetes increased after the age of 60 years (Kirkman *et al.*, 2012; Kamuhabwa & Charles, 2014; Mihardja *et al.*, 2014). Elderly population has a higher risk of glucose tolerance impairment and diabetes mellitus, due to the decline in pancreatic function and the reduction in insulin sensitivity (Kirkman *et al.*, 2012).

Most of the subjects were found to have central obesity despite having

normal BMIs (18.5-24.9 kg/m^2). Hu (2011) stated that the prevalence of obesity based on BMI in Asia was relatively lower compared to Western populations. The prevalence of diabetes in Asia is higher compared to that in the US, although obesity prevalence based on the BMI in Asia is lower compared to the US (Yoon *et al.*, 2006; Hu, 2011). A review by Misra *et al.* (2014) reported that diabetic population in South Asia significantly had poorer glycaemic control compared to Caucasians.

Half of the subjects in this study had poor glycaemic control (HbA1c >7.0%). This proportion was lower than the result of Khattab *et al.* (2010), who reported that 65.1% of T2DM patients had poor glycaemic control. This study also showed that there was a wide range of HbA1c levels among the subjects (5.3-15.5%), which meant that there were patients who had very high HbA1c levels. Female subjects tend to show poor glycaemic control and this finding was in line with the finding of Kamuhabwa & Charles (2014). The duration of diabetes also linked to poor glycaemic control. The longer someone suffers from DM, the faster the progression of the β cell destructions and impairment of insulin secretion, which are related to impairment in insulin action (Kamuhabwa & Charles, 2014).

The median value of serum chromium of the study subjects was 45.0 μg/L. The mean serum chromium level of patients with poor glycaemic control was slightly lower than that of those with good glycaemic control (43.0 μg/L vs. 45.0 μg/L). The serum chromium levels of the subjects were not much different from our previous study on serum chromium levels of T2DM patients and non-diabetic patients in Denpasar City. The study indicated that serum chromium levels of T2DM patients were lower than non-diabetic patients (42.0 μg/L vs 93.0 μg/L) (Sutiari *et al.*, 2017). This finding was in agreement with various other studies (Hasan, Ismail & Aziz, 2012; Elabid & Ahmed, 2014; Rajendran *et al.*, 2015; Hajra *et al.*, 2016). Each of these studies presented a different range of serum chromium levels in T2DM patients. The result variation might be affected by the method used to analyse the serum chromium level and by dietary chromium intake.

The low chromium status of the subjects might be caused by an inadequate intake, based on the recommended intake by age. There has not been any suitable or appropriate reference that we can use to determine the criteria for low, normal, and high serum chromium status of the subjects. Thus, the low chromium status of the subjects was assessed based on the ratio of subjects' serum chromium levels to serum chromium levels of non-diabetic patients. Most of the subjects were elderly, thus the low chromium status might be the result of low intake and absorption of chromium from diets. Therefore, it is recommended to have a high intake of chromium from food and take chromium supplement in order to fulfil the body's chromium requirement. The chromium concentration tends to decrease at the age of 40 (Rajendran *et al.*, 2015). However, there are still no studies confirming the correlation between age and the decrease in chromium levels through the metabolism (Wang & Cefalu, 2010).

The finding here of a negative correlation between serum chromium and the subjects' FBG levels was in line with result of Rajendran *et al.* (2015), who also reported that well-controlled T2DM patients had low serum chromium levels. Serum chromium levels of diabetic patients were lower than non-diabetic patients and healthy population. The negative correlation indicate that chromium might have a positive impact in improving insulin

resistance and glycaemic control in T2DM (Wang & Cefalu, 2010). There was no association found between HbA1c and serum chromium levels, but there was an association between FBG and chromium levels. It can be explained that HbA1c is a reflection of long-term glycaemic control; i.e. reflection of mean FBG levels 8-12 weeks before (Pujar *et al.*, 2014). HbA1c level does not depend on fasting condition. It is different from the FBG level, which is the short-term glycaemic control factor that can be accurately measured when examined under fasting condition.

Correlation analysis showed that patients with poor glycaemic control tended to have low BMI but suffered from central obesity. This tendency can be explained as follows: when the patients have poor glycaemic control, it is easy for them to lose weight; however, they will gain weight if their glycaemic control improve. As for central obesity, it may cause insulin resistant; thereby worsening the glycaemic control (Kamuhabwa & Charles, 2014).

CONCLUSION

The main finding of this study was the negative correlation between serum chromium concentration and FBG levels among T2DM patients with reportedly good glycaemic control. Further research on a larger sample size should be undertaken to verify these results.

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Authors' contributions

Sutiari NK was in charge of data analysis and writing the manuscript; Rimbawan R and Purwantyastuti A contributed in writing the Discussion and Recommendations; Kusharto CM contributed in writing the Results; Effendi AT contributed in making the Discussion.

Conflict of interest

All authors contribute equally to this work and declare that there is no conflict of interest in the study and its results.

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