Unaffected fasting blood glucose levels by micronutrients in diabetes mellitus type 2 patients in Jember regency

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Abstract. Background: Macronutrients have been studied with regard to their relationship with blood glucose, but only a few have examined blood glucose relationship with micronutrients. Consumption of both macro and micronutrients that are right on target can help improve metabolic control, optimize treatment, and reduce the risk of further complications of Diabetes Mellitus (DM). Objectives: To determine whether or not there is a relationship between micronutrient intake and fasting blood glucose (FBG) levels of DM type 2 patients in Jember. Methods: This was a cross-sectional study with 80 samples of type 2 DM patients in Jember by using the consecutive proportionate sampling technique from three hospitals. Measurement of micronutrient intake using the “24-hour food recall” questionnaire, conducted three times, while FBG data were obtained secondary from the patient's medical record. Results: Statistical analysis using the Spearman rho correlation test showed that there was no significant relationship between each intake of micronutrients with FBG levels (p>0.05). Conclusion: The amount of micronutrient intake did not have a significant relationship with the level of FBG in this study. Nevertheless, DM patients still need to pay attention to both macro and micronutrient intake to maintain regulated blood glucose levels.

1. Introduction
The International Diabetes Federation (IDF) predicts an increase in the number of people with Diabetes Mellitus (DM) in Indonesia from 9.1 million in 2014 to 14.1 million in 2035\cite{1}. East Java Province is one of the regions in Indonesia with a prevalence of DM sufferers of 2.1\%, Riskesdas report\cite{2}. In Jember Regency itself, DM ranks third in the population.

Hyperglycemia is a common effect of DM that can be caused by the lack of control in food consumption\cite{3}. Poor control of food intake can lead to long-term complications, both macrovascular and microvascular such as heart disease, peripheral vascular disease, kidney failure, nerve damage,
and blindness[4]. One of the most important things for DM patients is to prevent prolonged complications by controlling blood glucose levels. Control of blood glucose levels in people with DM related to dietary planning factors or eating patterns, this is because excessive food intake will increase blood glucose levels[5,6]. Diabetes control actions to prevent complications are very vital, especially maintaining blood glucose levels to within normal limits[7].

There is a long debate about the relationship of macronutrients (protein, carbohydrates, and fats) and blood glucose levels, but there is only little information about micronutrients (vitamins and minerals) and blood glucose levels. Micronutrients are involved in carbohydrate metabolism, glucose metabolism, insulin release, and insulin sensitivity[8]. The loss of water-soluble vitamins and the elements increase during uncontrolled hyperglycemia and glycosuria in DM patients. The content of copper, manganese, iron, and selenium can be higher in the body tissues of people with DM compared to people without DM. While serum vitamins C, B, and D are often lower in individuals with DM. Targeted micronutrient consumption can help to improve metabolic control, optimize treatment, and reduce the risk of further diabetes complications[9]. Therefore, the purpose of this study was to determine whether there was a relationship between micronutrient consumption and blood glucose levels in patients with DM type 2 in Jember Regency.

2. Method
The study design of this research was a cross-sectional study with a non-experimental analytic epidemiologic study. This research was conducted in November 2018 - December 2018 in three hospitals representing eight hospitals located in Jember Regency. The selection of research locations was based on the hospital area as a reference for the city center, west area and east area of the city. The population was DM type 2 patients aged 18-59 years old who were treated in internal disease outward in all three hospitals. Samples were taken by using consecutive proportionate sampling technique until the acquired number of samples based on the Slovin formula filled, which was 80 peoples with the proportion of 40-25-15 based on the ratio of DM patient visits at the three hospitals. The study was conducted with an interview method of food recall 1x24 hours for 3 days[10].

3. Results
This research involved 80 peoples as research subjects, with majority of female samples i.e., 46 peoples (58%), from the average number of populations of DM type 2 patients every month in internal diseases outward dr. Soebandi Hospital (225 patients), Kaliwates Hospital (75 patients), and Kalisat Hospital (100 patients). The samples were between 19-64 years old, with a mean and standard deviation of 61.6 ± 8.6 years. The highest category of samples in the 50-64 years age group i.e. 50 peoples (75%). Data distribution of subject characteristics in this study can be seen in Table 1.

| Variable | n (%) |
|----------|-------|
| Gender   |       |
| Male     | 34 (42.5%) |
| Female   | 46 (57.5%) |
| Age      |       |
| 19-29 years old | 1 (1.3%) |
| 30-49 years old  | 19 (24%) |
| 50-64 years old   | 50 (75%) |

3.1. Fasting Blood Glucose of Research Subject
The Fasting blood glucose (FBG) in this study was the blood glucose concentration of patients who had fasted for 8-10 hours before the examination, obtained from the medical record data of patients with DM type 2 in the internal disease outward RSD Dr. Soebandi, Kaliwates Hospital and Kalisat
Hospital. Based on the classification of fasting blood glucose, 77.5% had hyperglycemia, while the average of FBG was 179.8 mg/dL. Data distribution of research subjects based on fasting blood glucose can be seen in Table 2.

| Fasting Blood Glucose | Classification  | n (%)   |
|-----------------------|-----------------|---------|
| 80-109 mg/dL          | hypoglycemia    | 5 (6,3%)|
| 110-125 mg/dL         | normal          | 13 (24%)|
| > 126 mg/dL           | hyperglycemia   | 62 (77,5%)|

3.2. Micronutrient Intake of Research Subjects

The micronutrient intake of subjects was the average consumption of each micronutrient daily, obtained from the conversion of all food and beverages consumed by subjects within the last 24 hours. This amount was obtained using a 24-hour food recall interview method which was conducted 3 times in different days randomly and in no order and then converted into a daily calorie needs table using the Indonesian version of Nutrisurvey for Windows software as shown in Figure 1.

3.3. Relation of Micronutrient Intake with Fasting Blood Glucose Levels

Statistical analysis showed that there was no relationship between FBG and consumption of each micronutrient, indicated by p value > 0.05 through the Spearman rho correlation test (because FBG data were not normally distributed). Table 3 shows the correlation coefficient data of each relation, but this could not be used as a reference because the relationship was not significant.

| Micronutrient | Fasting Blood Glucose | Correlation Coefficient | Sig. (2-tailed) |
|---------------|-----------------------|-------------------------|-----------------|
| PUFA          | -0,010                |                         | 0,929           |
Vitamine A   0,054   0,633  
Vitamine B1   0,163   0,150  
Vitamine B2   0,100   0,379  
Vitamine B6   0,087   0,442  
Vitamine C   0,097   0,390  
Kalium       0,024   0,833  
Calcium      0,021   0,851  
Magnesium    -0,054  0,637  
Phosphor     0,120   0,290  
Iron         -0,035  0,756  
Zinc         0,031   0,784  

4. Discussion

This study showed that micronutrient intake did not have a significant relationship with the FBG level of DM patients or it can be interpreted that micronutrients did not affect FBG levels and vice versa. But keep in mind that FBG levels can be influenced by many factors so that although there was no direct relationship proven, micronutrient intake may still have an influence on the progress of DM disease. This situation was pointed out by several research findings showed that supplementation of zinc and magnesium[11–14]could improve DM conditions through improvement of insulin resistance and increased insulin potential. Similarly, supplements of several antioxidants such as vitamins B, C and D could improve the condition of DM.

The relationship between diet and blood glucose levels has been investigated in several prospective observational studies. In the past two decades, substantial information has been collected showing that long-term consumption of carbohydrates with high glycemic levels can affect metabolism and health[15,16]. Specifically, chronic hyperglycemia and hyperinsulinemia, induced by carbohydrates with high glycemic levels can cause a number of hormonal and physiological changes that increase insulin resistance[15,16].Insulin resistance is often referred to as a "disease of civilization"[17], including obesity, coronary heart disease, DM type 2, hypertension, and dyslipidemia (increased serum triacylglycerol serum; cholesterol lipoprotein small density, low density, low fat, and reduced high-density lipoprotein cholesterol).

Some micronutrient intakes in the subjects of this study appear to be less than RDA (Figure 1). This possibly because DM patients undergo a strict diet because patients who seek treatment at a hospital usually, they have complications. This situation made them more attentive to diet and treatment so that they could recover quickly from its complications. Although some evidences showed the positive effect of micronutrient supplementation on glycemic control detected by improvement on FBG, still much remains to be investigated. Additional research is needed to characterize biomarkers better than micronutrient status and the number of micronutrients required by patients with DM type 2. Optimal levels of micronutrient supplementation to achieve glucose homeostasis in patients with DM type 2 are still a challenge[9].

5. Conclusion

The amount of micronutrient intake did not have a significant relationship with the level of FBG in this study. Nevertheless, DM patients still need to pay attention to both macro and micronutrient intake to maintain blood glucose levels regulation. Future studies need to consider the use of dummy food to improve the method of taking food recall data 1x24 hours to make it more standardized or using a food record method.

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References

[1] PERKENI 2015 Konsensus Pengelolaan dan Pencegahan Diabetes Melitus Tipe 2 di Indonesia [in Indonesian] (Jakarta: PB PERKENI)

[2] Ministry of Health of the Republic of Indonesia 2014 Situasi dan Analisis Diabetes [in Indonesian] (Jakarta: Pusat Data dan Informasi Kementerian Kesehatan RI) Available from: http://www.depkes.go.id/resources/download/pusdatin/infodatin/infodatin-diabetes.pdf

[3] World Health Organization 2016 Global Report On Diabetes (Geneva: World Health Organization) Available from: https://apps.who.int/iris/bitstream/handle/10665/204871/9789241565257_eng.pdf;jsessionid=919071F5CA6D2085999797134AD1DBE43?sequence=1

[4] Anani S 2012 Hubungan Antara Perilaku Pengendalian Diabetes dan Kadar Glukosa Darah Pasien Rawat Jalan Diabetes Melitus [in Indonesian] J. Kesehat. Masy. 1246−78. Available from: http://ejournal-s1.undip.ac.id/index.php/jkm/article/view/1136

[5] Forouhi NG, Misra A, Mohan V, Taylor R 2018 Dietary and nutritional approaches for prevention and management of type 2 diabetes BMJ 361 i. Available from: http://dx.doi.org/doi:10.1136/bmj.k2234

[6] Berkat, Saraswati LD, Muniroh M 2018 Faktor-faktor yang Berhubungan dengan Kadar Gula Darah pada Penderita Diabetes Mellitus Tipe 2 di RSUD K.R.M.T Wongsonengoro Semarang [in Indonesian] J. Kesehat. Masy. 6 1200–6. Available from: https://ejournal3.undip.ac.id/index.php/jkm/article/viewFile/19866/18783

[7] Arviani D 2015 Gambaran asupan makan pasien Diabetes Mellitus tipe II dengan kadar glukosa darah pada pasien rawat jalan di RSUD dr. Moewardi Universitas Muhammadiyah Surakarta Available from: http://eprints.ums.ac.id/38292/

[8] Nsonwu-anyanwu AC, Egbe ER, Offor JS, Usoro CAO 2015 Glycemic control, micronutrients and some metabolic enzyme activity in type 2 diabetes International Journal of Research in Medical Sciences 3102757–64

[9] Kaur B, Henry J 2014 Micronutrient status in type 2 diabetes: a review Adv. Food. Nutr. Res. 7155–100

[10] Supariasa I 2002 Penilaian Status Gizi [in Indonesian] (Jakarta: EGC)

[11] Looman M, Geelen A, Samal RAK, Heijligenberg R, Brouwer-brolsma EM, Feskens EJM 2019 Changes in Micronutrient Intake and Status, Diet Quality and Glucose Tolerance from Preconception to the Second Trimester of Pregnancy Nutrients 114601–16

[12] Khanani S 2018 Role of Zinc Supplementation on Diabetes Abstract Rep. Endocr. Disord. 2110–1.

[13] Rodriguez-Moran M, Guerrero-Romero F 2003 Improves Insulin Sensitivity and Metabolic Control in Type 2 Diabetic Diabetes Care 2641147–52.

[14] Masood N, Baloch GH, Ghori RA, Memon IA, Memon MA, Memon MS 2009 Serum Zinc and Magnesium in Type-2 Diabetic Patients J. Coll. Physicians Surg. Pakistan 198483–6

[15] Ludwig DS 2002 The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease JAMA 2882414–23.

[16] Villegas R, Liu S, Gao Y, Yang G, Li H, Zheng W, Shu XO2007 Prospective Study of Dietary Carbohydrates, Glycemic Index, Glycemic Load, and Incidence of Type 2 Diabetes Mellitus in Middle-aged Chinese Women Arch. Intern. Med. 167212310−6 Available from: https://www.ncbi.nlm.nih.gov/pubmed/18039989

[17] Cordain L, Eades MR, Eades EM 2003 Hyperinsulinemic diseases of civilization: more than just syndrome X Comp. Biochem. Physiol. A Mol. Integr. Physiol. 136 1 95–112