RESEARCH ARTICLE

Association of rs10830963 *MTNR1B* and rs841853 *SLC2A1* Polymorphism with Obesity on Type 2 Diabetes Patients: An Overview of Melatonin Receptor and Transporter

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Received date: Dec 30, 2020; Revised date: Mar 1, 2021; Accepted date: Mar 4, 2021

Abstract

BACKGROUND: One of the hormones that plays a role in glucose metabolism of Type 2 Diabetes Mellitus (T2DM) is melatonin. Its genetic variation is believed to play a significant role in the pathophysiology of obese and non-obese T2DM. The role of *MTNR1B* (melatonin receptor coding gene) and *SLC2A1* (Glucose transporter 1/GLUT 1 transporter coding gene) on the risk of obese and non-obese T2DM patients is controversial. This study aims to analyze the association between the rs10830963 *MTNR1B* and rs841853 *SLC2A1* polymorphism to the risk of Javanese obese T2DM.

METHODS: This was a cross-sectional study that involved 107 Javanese T2DM patients from primary heath care in Semarang. Furthermore, obese T2DM was defined by a body mass index (BMI) more than 25 kg/m^2. The genetic variations examined were rs10830963 *MTNR1B* and rs841853 *SLC2A1* polymorphism by PCR-RFLP methods. Blood biochemistry parameters were also examined. Allele and genotype frequencies of rs10830963 *MTNR1B* and rs841853 *SLC2A1* polymorphisms were analyzed using the x^2 test with $p \leq 0.05$ and 95% CI.

RESULTS: There was a significant association between rs10830963 *MTNR1B* polymorphisms in obese and non-obese T2DM (p=0.044) and the CG genotype increased the risk of obese T2DM. Furthermore, the allele and genotype frequency of rs841853 *SLC2A1* polymorphism in both group had no significant difference, with a p=0.756 and p=0.802, respectively. There was also no significant difference in the biochemical parameters' in both groups of the two genetic variants studied.

CONCLUSION: The rs10830963 *MTNR1B* polymorphism is associated with the risk of obesity in Javanese T2DM patients but not for the rs841853 *SLC2A1* polymorphism.

KEYWORDS: polymorphism, *MTNR1B*, *SLC2A1*, obese, diabetes mellitus

Indones Biomed J. 2021; 13(2): 155-62

Introduction

Diabetes mellitus (DM), which is characterized by chronic hyperglycemia is a non communicable disease and becomes major problem in Indonesia. According to data, the total number of DM patients in 2019 was around 120,835 people, these include those that received health services by a standard of around 2,066 or 1.71%.(1) Patients with type 2 DM (T2DM) experience abnormalities of blood glucose level homeostasis characterized by an increase of fasting plasma glucose (FPG).

Melatonin is one of the hormones that play a role in the metabolism of carbohydrate and regulates plasma glucose. Moreover, a decrease in the level of melatonin and an increase of insulin in Goto Kakizaki rats was found in T2DM.(2) The melatonin hormone works according to its target organ by binding to melatonin receptors, namely MT1, which is coded for MTNR1A and MT2 and encoded by *MTNR1B* gene. Furthermore, melatonin works across

the plasma membrane in cells mediated by a transporter, namely Glucose transporter 1 (GLUT 1) coded by the *SLC2A1* gene.(3,4)

Genome-wide Association Studies (GWAS) proved that there is a relationship between *MTNR1B* polymorphisms and FPG, insulin secretion, and the T2DM incidence.(5,6) This polymorphism occurs when C allele of the intron on of chromosome 11q21-q22 changes to G, which correlates with the risk of T2DM. The rs10830963 *MTNR1B* polymorphism was reported to be associated with increased FPG and T2DM in Caucasians, Chinese, Japanese, and Sri Lanka.(7,8,9) Another genetic variation regarding the role of melatonin in DM is the rs841853 *SLC2A1* polymorphism (XbaI G>T) which has been shown to double the risk of T2DM in Asia and Tunisian populations.(10)

The characteristics of T2DM patients vary widely. Classic T2DM patients usually have an obese condition. However, T2DM currently occurs in individuals with thin or normal body mass index (BMI). Lean T2DM patients show a faster loss of pancreatic beta-cell function than obese and therefore require earlier insulin treatment.(11,12) Studies in East Asia have shown that the onset of T2DM events is faster in individuals with lower BMI than in Caucasian. (11) Genetic involvement is believed to play a role in the T2DM pathogenesis of obese and non-obese patients. The genetic variations related to insulin secretion such as single-nucleotide polymorphism (SNP) *TCF7L2* are at risk of normal (lean) T2DM BMI. However, those related to insulin sensitivity such as SNP fat mass obesity (FTO) are at risk of T2DM obesity.(13-15) SNP *CDKN2BAS*, *CDKAL1* was associated with the risk of T2DM incidence in normal (lean) people.

Melatonin deficiency plays a role in obesity pathophysiology by regulating energy balance. It regulates energy intake, storage, and expenditure from adipose tissue, which determines a person's body weight. When the intake exceeds energy expenditure, it becomes overweight or obese.(16,17) Obesity is a risk factor for DM incidence. A study involving obese subjects proved that GG genotype of polymorphism rs10830963 *MTNR1B* gene was associated with an increase in fasting glucose levels.(18) There was an association between XbaI restriction fragment length polymorphism (RFLP) GLUT 1 in T2DM obese women. This indicates that gene plays a role in the incidence of T2DM in obese people.(19)

The involvement of rs10830963 *MTNR1B* polymorphisms and rs841853 *SLC2A1* in the risk of T2DM or obesity have been reported. However, there are no reports on the association of these genetic variations in obese and non-obese T2DM individuals. This study aims to analyze the relationship between rs10830963 *MTNR1B* and the rs841853 *SLC2A1* polymorphism to the risk of obese and non-obese T2DM individuals of Javanese ethnicity, which is the largest ethnic group in Indonesia and the underlying clinical chemical parameters. The results will provide an overview of the contribution of genetic variation to the T2DM patients' heterogeneity based on BMI.

Methods

Subject Collection

This was an analytic observational study with a cross-sectional approach involved 107 T2DM patients from 3 health care centers in Semarang. T2DM patients that met the inclusion criteria were consecutively sampled, including Javanese T2DM patients, aged 30-70 years and had signed informed consent. The exclusion criteria include a history of cardiovascular disorders such as stroke, heart failure, and acute myocardial infarction. Obese T2DM was defined by a BMI of more than 25 kg/m^2, according to the BMI classification of the Asia Pacific population. Ethical permission was obtained from the Ethics Commission of the Faculty of Medicine, the Muhammadiyah University of Semarang with Number 040/EC/FK/2019.

Data Collection

The weight and height of the samples were measured to calculate the BMI. Blood pressure was measured at rest and classifed into 5 classes, Normal: Systolic Blood Pressure (SBP) <120 mmHg or Diastolic Blood Pressure (DBP) <80 mmHg; Prehypertension: SBP 120-139 mmHg or DBP 80-89 mmHg; Hypertension grrade 1: SBP 140-159 mmHg or DBP 90-99 mmHg; Hypertension grade 2: SBP ≥160 mmHg or DBP ≥100 mmHg, according to The Seventh Report of The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Presurre (JNC VII).(20) Venous samples were collected on ethylenediaminetetraacetic acid (EDTA) and plain tubes for the examination of gene polymorphisms and biochemical parameters, respectively, such as fasting blood sugar, cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), Cholesterol/HDL ratio (Chol/HDL), urea, and creatinine. Microalbumin examination was carried out using the subject's urine sample.

Biochemical Profile Examination

Respondents had fasted for 8 hours before collecting their venous blood to be examined for guanosine-diphosphatase (GDP) by an enzymatic method (GOD-PAP), ureum by Urease-glutamate dehydrogenase (GLDH), creatinine using the Jaffe, total cholesterol using CHOD-PAP, triglycerides using a GPO-PAP, HDL-C, and LDL-C by direct enzymatic method. Microalbumin was examined using respondents' urine samples with the immunoturbidimetric assay method and measured using a Cobas c311 autoanalyzer (Roche, Basel, Switzerland) at a wavelength of 340 nm.

Genotyping of *MTNR1B* Gene and *SLC2A1* Polymorphism

DNA was isolated from the blood using GeneJETTM Genomic DNA Purification Kit. Amplification of the *MTNR1B* gene was done using Primer forward 5'-ATG CTA AGA ATT CAC ACC AGC T-3 ', reverse 5'-CAC AGT GCA GAC TGT TTT CTA ATC. Polymerase chain reaction (PCR) with predenaturation of 95°C, 7 minutes, 33 cycles: 95°C denaturation, 30 seconds, 60°C annealing, 30 seconds, 72°C elongation, 1 minute. The final extension was at 72°C for 3 minutes. RFLP method with PvuII enzyme was used to digest PCR product and visualized at 4% agarose gel. The electrophoresis results showed the C allele of 125 bp and G at 105 bp and 20 bp.

Amplification of *SLC2A1* was done using Primer forward 5'-TGC AAC CCA TGA GCT AAC AA-3 'and reverse 5'-GAA CCC AGC ACT CTG TAG CC -3'. PCR with predenaturation at 95°C, 5 minutes, 33 cycles: 95°C denaturation, 30 seconds, 60°C annealing, 30 seconds, 72°C elongation, 1 minute. The final extension was at 72°C for 3 minutes. Then, PCR product was digested with XbaI enzyme and visualized at 2% agarose gel. Electrophoresis results showed the T allele of 305 bp and G at 232 bp and 73 bp.

Data Analysis

The data for the existence of rs10830963 *MTNR1B* and rs841853 *SLC2A1* polymorphisms in the form of allele and genotype frequencies were analyzed by x^2 test with $p<0.05$ and CI=95%. The differences in the numerical characteristics of variables between groups were determined by the independent t-test.

Results

A total of 107 T2DM subjects, which consist of 45 obese and 62 non-obese were involved in the study. In the obese group, the majority of the sample was ≥60 years old (46.7%), female (82.2%), uncontrolled blood sugar levels

Table 1. Characteristic data of T2DM subjects in obese and non-obese groups.

Characteristics	n (%)		*p*-value*
	Obese (n=45)	Non-Obese (n=62)	
Age (year)			
30-34	1 (2.2%)	0 (0%)	0.660
35-39	0 (0%)	0 (0%)	
40-44	2 (4.4%)	1 (1.6%)	
45-49	3 (6.7%)	4 (6.5%)	
50-54	7 (15.6%)	7 (11.3%)	
55-59	11 (24.4%)	21 (33.9%)	
≥60	21 (46.7%)	29 (46.8%)	
Gender			
Male	8 (17.8%)	17 (27.4%)	0.245
Female	37 (82.2%)	45 (72.6%)	
Fasting Plasma Glucose Controlling			
Uncontrolled (<90 or >130 mg/dL)	29 (64.4%)	47 (75.8%)	0.201
Controlled (90-130 mg/dL)	16 (35.6%)	15 (24.2%)	
Hypertension			
Normal	3 (6.7%)	7 (11.3%)	0.585
Prehypertension	20 (44.4%)	28 (45.2%)	
Hypertension grade 1	18 (40.0%)	18 (29.0%	
Hypertension grade 2	4 (8.9%)	9 (14.5%)	

* Tested with Chi square test, $p<0.05$ as significant result.

Table 2. Biochemical profile of T2DM subjects in obese and non-obese.

Biochemical Profile	Obese		Non-Obese		*p*-value*
	Mean±SD	Median (Min-Max)	Mean	Median (Min-Max)	
FPG (mg/dL)	155.02±9.94	139 (63-332)	164.24±10.63	141 (60-418)	0.752
HbA1c (mmol/mol)	7.82±0.27	7.2 (5.5-12.5)	7.88±0.26	7.45 (4.9-15.4)	0.847
Cholesterol (mg/dL)	165.09±8.99	160 (41-266)	194.08±5.99	199.5 (58-314)	0.018*
Triglycerides (mg/dL)	209.96±11.86	194 (78-402)	202.34±21.78	164 (61-1340)	0.060
HDL (mg/dL)	58.62±2.24	58 (33-97)	61.65±2.32	61 (33-113)	0.456
LDL (mg/dL)	201.31±8.47	199 (87-343)	196.50±6.96	204 (88-311)	0.786
Chol/HDL ratio	4.91±0.21	4.6 (2.8-9.7)	4.78±0.17	4.6 (2.6-9.2)	0.645
Ureum (mg/dL)	28.87±1.70	25 (15-61)	30.40±1.48	28 (15-80)	0.441
Creatinine (mg/dL)	0.88±0.06	0.76 (0.44-2.49)	0.96±0.63	0.89 (0.38-3.41)	0.362
Microalbumin (mg/dL)	241.89±54.93	50.2 (5-1582)	281.27±132.03	40.6 (4.2-8087.2)	0.202

* Tested with Mann Whitney U test, $p<0.05$ as significant result.

(64.4%), and prehypertension (44.4%). Meanwhile, in the non-obese, the majority was ≥60 years old (46.8%), female (72.6%), uncontrolled blood sugar levels (75.8%), and prehypertension (45.2%) as shown in Table 1.

Based on the comparison results of the biochemical profile in Table 2, there was a significant difference between the obese and non-obese groups in cholesterol levels with *p*-values of 0.018. However,there was no significant differences in FPG, HbA1c, Triglycerides, HDL, LDL Chol/HDL ratio, Ureum, creatinine, and microalbumin with $p>0.05$.

Table 3 shows that in both groups, the majority of respondents with rs10830963 *MTNR1B* polymorphism had the C allele which was the wild type allele. Furthermore, 84.8% had CG genotype in the obese and 62.9% in the non-obese group. There was no significant difference between C and G alleles in both groups. However, the number of individuals with CG genotype was significantly higher than the CC in both groups with a *p*-value of 0.044. There was also a significant relationship between rs10830963 *MTNR1B* polymorphisms with obese and non-obese T2DM types where the CG genotype increased the risk of obesity. Meanwhile, in the rs841853 *SLC2A1* polymorphism, most of the allele was G (wild type) and the most genotype was TT (45.2%) in the non-obese group. Moreover, the obese group found the same number in the TG and TT genotypes. There were no significant differences in the allele frequency and genotype of rs841853 *SLC2A1* polymorphism in the

Table 3. Allele distribution of rs10830963 *MTNR1B* and rs841853 *SLC2A1* polymorphisms.

		n (%)		*p*-value*
		Obese (n= 45)	Non-Obese (n=62)	
rs10830963 *MTNR1B*				
Allele	C	52 (57.8%)	83 (66.9%)	0.171
	G	38 (42.2%)	41 (33.1%)	
Genotype	CC	7 (15.6%)	22 (35.5%)	0.044*
	CG	38 (84.4%)	39 (62.9%)	
	GG	0 (0%)	1 (1.6%)	
rs841853 *SLC2A1*				
Allele	G	54 (60.0%)	77 (62.1%)	0.756
	T	36 (40.0%)	47 (37.9%)	
Genotype	GG	9 (20.0%)	13 (21.0%)	0.802
	TG	18 (40.0%)	21 (33.9%)	
	TT	18 (40.0%)	28 (45.2%)	

* Tested with Chi square test, $p<0.05$ as significant result.

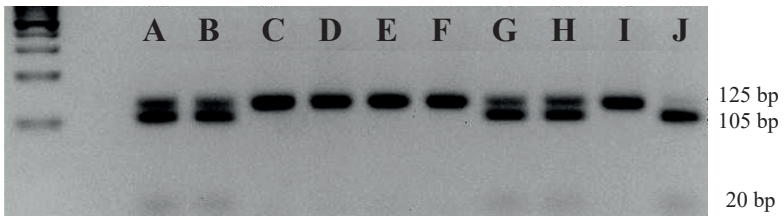

Figure 1. PCR-RFLP electrophoresis result of rs10830963 *MTNR1B* polymorphism. A, B, G, and H were CG heterozygotes; C, D, E, F, and I were CC homozygotes, while J was GG homozygotes.

obese and non-obese groups, with a *p*-value of 0.756 and 0.802 respectively.

The electrophoresis results of PCR-RFLP were shown in Figure 1 and Figure 2 for the *MTNR1B* and *SLC2A1* gene, respectively. In Figure 1, it is seen that the letters A, B, G, and H had 125, 105 and 20 bp, respectively which were the CG (heterozygote) genotypes. C, D, E, F, and I had 125 bp (genotype CC) which were wild type alleles. J was GG homozygotes (105 and 20 bp). Meanwhile, in Figure 2, A, F, H, and I had 232 and 73 bp (genotype GG), B, C, E, G had 305,232 and 73 bp (genotype TG) and D had 305 bp which was the TT genotype (homozygote risk allele T).

When comparing the biochemical profile results based on genotype on rs10830963 *MTNR1B* polymorphism between the obese and non-obese groups, it was found that there was no significant difference in biochemical parameters. However, there were higher but insignificant levels in the CG + GG genotype for FPG, HbA1c, Cholesterol, Chol/HDL ratio, ureum, and microalbumin in the obese group. Likewise, with the non-obese group, levels of FPG, HbA1c, Cholesterol, HDL-C, LDL-C, ureum, creatinine, and microalbumin were higher in the CG + GG genotype (Table 4).

Table 5 showed the comparation of biochemical profile parameters based on the genotype of the rs841853 SLC2A1 polymorphism and shows that there was no significant difference between the values of the GG and TG + TT parameters in both groups.

Discussion

The clinical characteristics of T2DM patients may vary between obese and non-obese. This study analyzed the rs10830963 *MTNR1B* polymorphism in obese and non-obese T2DM individuals. The results indicate a significant relationship between rs10830963 *MTNR1B* polymorphisms in obese T2DM where the CG genotype increases the risk of T2DM obesity. Thus, this is contrary to research which identified the gene variations among T2DM obese and lean Han Chinese populations where this polymorphism was not associated with the risk of BMI in T2DM patients.(13) GG genotype, which has the risk of G allele is associated with a decreased beta-cell function (HOMA-B) and an increased insulin resistance (HOMA-IR) in adults.(18) Although there is a study showing that there is no correlation between HOMA-IR as a marker of insulin resistance and obesity.(21) Various genomic loci associated with the risk of predisposing the clinical characteristics of obese and non-obese T2DM have been identified. A study conducted in Medan, Indonesia proved that the genetic variations such as FTO rs9939609 is associated with the risk of Chinese children obese subjects. (22) The pathophysiology in obese patients is more towards insulin resistance, whereas in lean patients or non-obese it is caused by defective-insulin release or impaired insulin secretion. Meanwhile, the genetic variations that regulate insulin secretion (CDC123/CAMK1D, CDKAL1, TCF7L2,

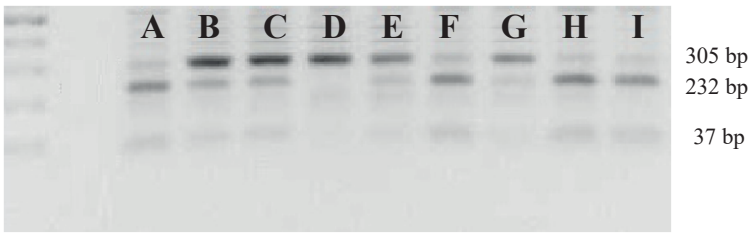

Figure 2. PCR-RFLP electrophoresis results of rs841853 *SLC2A1* polymorphism. A, F, H, I are the GG genotypes; B, C, E, G are the TG genotypes and D was the TT genotypes (homozygote risk allele T).

Table 4. The comparison of biochemical profile based on the genotype of rs10830963 *MTNR1B* polymorphism.

Biochemical Profile	Mean±SD Obese (n=45)		*p*-value	Mean±SD Non-Obese (n=62)		*p*-value
	CC	(CG) + (GG)		CC	(CG) + (GG)	
FPG (mg/dL)	123.43±16.49	160.84±11.19	0.167	146.86±15.03	173.80±14.17	0.219
HbA1c (mmol/mol)	6.94±0.47	7.99±0.31	0.177	7.29±0.35	8.21 ±0.35	0.053
Cholesterol (mg/dL)	160.86±25.49	165.87±9.71	0.795	186.18±11.97	198.43±6.59	0.365
Triglycerides (mg/dL)	211.43±20.62	209.68±13.62	0.725	209.68±54.77	198.30±16.14	0.151
HDL (mg/dL)	63.14±7.36	57.79±2.30	0.529	59.91±4.00	62.60±2.87	0.410
LDL (mg/dL)	224.57±29.48	197.03±8.48	0.415	189.18±11.34	200.53±8.85	0.431
Chol/HDL ratio	4.74±0.54	4.94±0.23	0.702	4.54±0.29	4.92±0.21	0.131
Ureum (mg/dL)	27.00±4.73	29.21±1.84	0.509	26.86±2.09	32.35±1.94	0.061
Creatinin (mg/dL)	0.95±0.26	0.87±0.06	0.635	0.90±0.09	0.99±0.08	0.556
Microalbumin (mg/dL)	97.61±46.98	268.46±63.72	0.347	112.96±47.11	373.84±202.45	0.332

HHEX, CDKN2BAS, TCF7L2,KCNJ11) are associated with T2DM risk in lean or non-obese subjects.(14,23-25) Another study which examined the SNP-19 Calpain-10 (CAPN10) polymorphisms proved that this polymorphism is associated with Javanese ethnic vulnerability to T2DM. (26) Abnormalities in CAPN10 can reduce secretion in pancreatic cells which according to research plays a role in the pathophysiology of T2DM in non-obese patients.

The results showed that those with CG genotype were significantly higher than CC in both groups. Obesity and insulin sensitivity have a modulatory effect on the prediction of genetic susceptibility in the T2DM incidence. (27) A cohort study among obese respondents demonstrated that there was a significant relationship between SNP rs10830963 *MTNR1B* and the prevalence of prediabetes or Impaired Glucose Tolerance (IGT).(28) Therefore, it is presumed that this polymorphism is significantly associated with T2DM-induced obesity.

Other results of this study prove that there is no significant difference of allele and genotype frequency of rs841853 *SLC2A1* polymorphism between 2 groups. The insignificant results in this study is due to ethnic differences, considering that the *SLC2A1* polymorphism is also influenced by ethnicity.(29) Allele 1 of GLUT 1 is associated with T2DM especially in overweight/obese women.(19) There is an increase in proinflammatory in the obese, while proinflammatory increases the GLUT1 (*SLC2A1*) expression in macrophages. This increases glucose uptake as well as metabolism and ultimately causing hyperinflammatory conditions.(30) Other studies have also shown a correlation between inflammatory markers such as high sensitivity C-reactive protein (hsCRP) in central obese elderly men.(31)

Other results also proved that the risk allele G contained in the CG + GG genotype increases the levels of FPG, HbA1c, cholesterol, ureum, and microalbumin in

Table 4. The comparison of biochemical profile based on the genotype of rs841853 *SLC2A1* polymorphism.

Biochemical Profile	Mean±SD Obese (n=45)		*p*-value	Mean±SD Non-Obese (n=62)		*p*-value
	GG	(TG) + (TT)		GG	(TG) + (TT)	
FPG (mg/dl)	159.22±14.86	152.22±13.48	0.677	161.39±17.55	166.59±13.17	0.515
HbA1c	8.09±0.42	7.65±0.37	0.215	7.61±0.39	8.11±0.36	0.520
Cholesterol (mg/dl)	174.50±12.42	158.81±12.52	0.292	194.14±8.88	194.03±8.26	0.832
Triglycerides (mg/dl)	215.72±20.16	206.11±14.77	0.719	199.00±17.82	211.68±37.13	0.904
HDL (mg/dl)	56.28±3.41	60.19±2.97	0.501	61.54±3.57	61.74±3.09	0.944
LDL(mg/dl)	199.28±14.88	202.67±10.28	0.899	203.75±10.23	190.53±9.51	0.380
Chol/HDL ratio	4.76±0.27	5.02±0.30	0.898	4.95±0.28	4.64±0.22	0.308
Ureum (mg/dl)	26.61±2.18	30.37±2.43	0.313	32.82±2.57	28.41±1.64	0.183
Creatinin (mg/dl)	0.76±0.06	0.96±0.09	0.211	1.00±0.11	0.92±0.07	0.529
Microalbumin (mg/dl)	197.45±89.48	271.511±70.25	0.271	162.53±43.54	379.06±238.41	0.651

both groups, although not significant. The risk allele G, which increases FPG is consistent with previous study. (18) In addition, the expression of the *MTNR1B* gene in pancreatic beta islet cells has a direct effect on regulating FPG levels. Therefore, when polymorphisms occur in this gene, it directly affects FPG. Furthermore, individuals at risk of allele G experience hepatic insulin resistance due to a decrease in suppression of hepatic glucose production during euglycemic hyperinsulinemia. This is also due to an increase in the hepatic glucose production rate, which increases gluconeogenesis.(8) In non-obese T2DM patients, there was also an increase in basal production of hepatic glucose, which resulted in an increase in FPG levels. In the obese group, cholesterol and LDL levels were higher in the allele G risk group. Other studies that analyze *MTNR1B* polymorphisms in relation to lipid profiles, stated that cholesteol and LDL have a relationship with the rs3781637 *MTNR1B* polymorphism. (32)

Furthermore, there is no significant difference in the biochemical parameters between GG and TG + TT of rs841853 *SLC2A1* polymorphism. However, the values of FPG, HbA1c, triglycerides, HDL, and microalbumin are higher in the TG + TT group. A high microalbumin levels in T2DM patients indicate a complication of DM nephropathy. The diagnosis of DM nephropathy is carried out when the urinary albumin level is >300 mg/24 hours with or without an increase in serum creatinine (>1.3 mg/dL). In the non-obese group, a mean microalbumin >300 mg/dL was found, which indicates the risk of nephropathy. (33) Furthermore, several studies have shown a relationship between the rs841853 *SLC2A1* polymorphism and the risk of DN which is marked by an increase in microalbumin.(34) TT haplotype was found in nephropathy patients as reported by previous study.(35) However, this is not proven by the results of this study.

Conclusion

There is a significant relationship between rs10830963 *MTNR1B* polymorphism in obese and non-obese T2DM, where the CG genotype increases the risk of obese T2DM. Furthermore, there is no differences in the allele and genotype frequency of rs841853 *SLC2A1* polymorphism in the obese and non-obese groups. There is also no significant difference in the biochemical parameters in obese and non-obese groups on the two genetic variants studied. In addition, rs10830963 *MTNR1B* polymorphism is associated with the risk of obesity in Javanese T2DM patients but not for the rs841853 *SLC2A1* polymorphism.

Acknowledgements

The authors are grateful to the Central Laboratory of Diponegoro University Semarang (Cebior), the Laboratory of the Mathematics and Natural Sciences Faculty, CITO laboratory and the Public Health Center that helped with the data collection. The authors are also grateful to the Directorate of Research and Community Services, Directorate General of Research and Development, Ministry of Research, Technology, and Higher Education, under the scheme of Research on Inter-University Collaboration for funding this study.

Authors Contribution

YT, AK, AY and RS carried out the research; YT organized research data, performed data analysis, interpretation, wrote the manuscript and prepared final version for publication; AK performed data analysis and interpretation of data; AY and RS helped review the data analysis and reviewed the manuscript.

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