The Association Between Parents History of Type 2 Diabetes with Metabolic Syndrome Component and Insulin Resistance in Non-Diabetic Young Adult Male

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ABSTRAK

Latar belakang: *sifat kekeluargaan diabetes tipe 2 dimanifestasi oleh adanya resistensi insulin pada keturunan pertama keluarga non-diabetes. Sebagian besar penelitian ini telah dilakukan pada usia menengah dan hanya beberapa penelitian yang dilakukan pada usia muda dan remaja. Penelitian ini bertujuan untuk menganalis hubungan antara riwayat orang tua yang memiliki diabetes melitus (DM) tipe 2 dengan komponen sindroma metabolik dan kejadian resistensi insulin pada subyek dewasa muda non-diabetes.* ***Metode:*** *studi ini merupakan penelitian potong lintang pada pria dewasa muda non-diabetes (usia 16-24 tahun) dengan riwayat satu atau kedua orang tua DM tipe 2. Sebagai pembanding adalah subyek yang tidak mempunyai riwayat orang tua DM tipe 2. Dilakukan pemeriksaan anamnesis, pemeriksaan fisis, dan pemeriksaan laboratorium glukosa darah puasa, profil lipid, insulin puasa dan resistensi insulin dengan menggunakan rumus HOMA-IR.* ***Hasil:*** *profil metabolik yang abnormal lebih banyak ditemukan pada subyek dengan riwayat orang tua menderita DM tipe 2, khususnya dalam hal lingkar pinggang, glukosa darah puasa, trigliserida, insulin puasa dan HOMA-IR (p=0.000). Subyek dewasa muda non-diabetes dengan riwayat orang tua DM tipe 2 beresiko untuk menglami obesitas sentral sebesar 19.3 kali (95%CI 2.46-151.07) dan juga beresiko terhadap terjadinya resistensi insulin sebesar 10.3 kali (95%CI 3.89-27.23). Hasil uji regresi logistik menunjukkan bahwa faktor orang tua menderita DM tipe 2 bersama–sama dengan komponen sindroma metabolik yaitu lingkar pinggang >90 cm dan kadar trigliserida ≥150 mg/dl merupakan faktor determinan kuat untuk terjadinya resistensi insulin (R2=50.7%).* ***Kesimpulan:*** *pada Subyek dewasa muda non-diabetes dengan riwayat orang tua menderita DM tipe 2 sudah dapat ditemukan abnormalitas metabolik yang multipel. Kluster dari komponen sindoma metabolik pada populasi tersebut merupakan faktor determinan kuat untuk terjadinya resistensi insulin.*

Kata kunci: *riwayat orang tua DM tipe 2, sindrom metabolik, resistensi insulin.*

ABSTRACT

Background: *the familial nature of type 2 diabetes is manifested by the presence of insulin resistance in non-diabetic first degree relatives. Most of these studies have been performed in middle-aged and there is only few published studies in young age individuals and adolescents. This study aimed to determine the relationship between parents history of type 2 diabetes with metabolic syndrome component and insulin resistance in adolescent non-diabetic subjects.* ***Methods:*** *this was a cross sectional study comparing the metabolic profile, risk of metabolic syndrome and insulin resistance in non-diabetic male adolescents (17-24 years old) whose one or both parents were with type 2 diabetes. We performed anamnesis, physical examination, fasting plasma glucose, lipid profile,*

fasting insulin level and insulin resistance based on HOMA-IR. ***Results:*** *metabolic abnormalities were more prevalent in subjects whose parents were with history of type 2 diabetes, especially their waist circumference, fasting plasma glucose, triglyceride, fasting insulin and HOMA-IR (p=0.000). There was increased risk of developing central obesity in adolescents with parental history of 19.3 fold (95%CI 2.46-151.07) and insulin resistance of 10.3 fold (95%CI 3.89-27.23). Parental history of type 2 diabetes together with metabolic syndrome component ie. waist circumference >90 cm and triglyceride ≥150 mg/dl were strong determinat factors for insulin resistance (R^2=50.7%).* ***Conclusion:*** *the early multiple metabolic defect can be detected in non-diabetes adolescents with parental history of type 2 diabetes. Cluster of metabolic syndrome component in these subject become a powerful determinat factor for insulin resistance.*

Keywords: *parent history of type 2 diabetes, metabolic syndrome, insulin resistance.*

INTRODUCTION

The rapid rise of the global prevalence of type 2 diabetes in the last two decades constitutes a health threat to the individual and represents a major socioeconomic burden in health.[1,2] Type 2 diabetes is a predictable and preventable disease, therefore it is crucial to identify specific risk groups, targeting them for preventive strategies. Primary prevention strategies on high-risk populations have been shown to be cost-effective in model studies.[3,4] One of the high-risk groups is the children of people with type 2 diabetes, since this is a heritable pathologic condition. Offsprings of one parent with type 2 diabetes mellitus have a two to fourfold relative risk of developing the disease, equivalent to a 20-40% absolute risk.[5,6]

The pathophysiology of type 2 diabetes involves impairment in both insulin sensitivity and insulin secretion.[2,7] Insulin resistance and compensatory hyperinsulinenmia have been associated with obesity, hypertension, increased level of serum triglyceride, small dense LDL particle and decreased level of HDL-cholesterol. These multiple metabolic abnormalities also known as metabolic syndrome are more commonly found in the relatives of diabetic patients.[8,9]

Some studies have shown that the familial nature of type 2 diabetes is manifested as the precence of insulin resistance in non-diabetic first degree relatives.[10-12] Most of these studies were performed in middle-age individuals and only few published studies were done in young age individuals and adolescents.

Therefore, in this study we examined and identified insulin resistance and diabetic risk factors in non-diabetic adolescents with parent history of type 2 diabetes and compared with subject without parental history of type 2 diabetes.

METHODS

This was a comparative observational study with a cross sectional design performed at several teaching hospitals in Makassar, South Sulawesi. A total of 128 healthy male adolescents (17-24 years old), including 64 subjects with and 64 without parental history of type 2 diabetes were studied. All subjects were in good health condition. History taking and physical examinations (i.e. blood pressure and waist circumference) were performed. Following 10-12 hours overnight fasting, blood samples were taken for the measurement of fasting plasma glucose, fasting insulin level and lipid profile. This study had been approved by the Ethics Committee of the Faculty of Medicine, Hasanuddin University with a reference number 0273/H04.8.4.5.31/PP36-KOMETIK/2016.

Parental history of type 2 diabetes was defined as one or both parents having from type 2 diabetes. Metabolic syndrome components based on Asia Pasific modification from The National Cholesterol Education Program–Adult Treatment Panel III (NCEP-ATP III) were waist circumference >90 cm, HDL-cholesterol <40 mg/dl, triglyseride ≥150 mg/dl, blood pressure ≥130/85 mmHg and fasting plasma glucose ≥100 mg/dl.[13,14] Insulin resistance was estimated from fasting plasma glucose and insulin using Homeostasis Model Assesment–Insulin Resistance (HOMA-IR) formula.[15] HOMA-IR is divided in tertiles, whereas insulin resistance is confirmed if HOMA-IR in the 3rd tertile.

To evaluate the difference in characteristic

between the two groups, we used independent t test and Mann Whitney U test. We also performed multiple regression analysis and calculated the odd ratio to determine factors that influence the incidence of insulin resistance.

RESULTS

Waist circumference, fasting plasma glucose, triglyceride, fasting insulin and HOMA-IR were significantly higher in adolescent with parental history of type-2 diabetes (p=0.000). HDL-cholesterol was significantly lower in adolescent with parental history of type-2 diabetes (p=0.030). (**Table 1**)

Adolescents with parental history of type-2 diabetes showed increased of central obesity (OR =19.3, 95%CI 2.46–151.07), hypertrygliseridemia (OR=2.5, 95% CI 0.87–6.96) and also hypo-HDL-emia (OR=1.2, 95%CI 0.51–2.88), although the last two results were not statistically significant. Parental history of type 2 diabetes also showed correlation with other metabolic syndrome components but the odd ratio could not be determined in this study since result of FPG ≥100 mg/dl and blood pressure ≥130/85 mmHg was only found in subject with parental history of type 2 diabetes (**Table 2**). This study also found that adolescent with parental history of type-2 diabetes showed correlation with insulin resistance with odds ratio of 10.3 (95%CI 3.89–27.23). (**Table 3**)

A multiple logistic regression analysis was performed to evaluate the correlation between

Table 1. Characteristic of subjects with and without parent history of type 2 diabetes

Variables	Parent with history of type 2 diabetes (n=64)	Parent without history of type 2 diabetes (n=64)	p
WC (cm)	0.1 (12.8)	69.5 (6.3)	0.000
SBP (mmHg)	112.5 (13.0)	113.3 (6.9)	0.672
DBP (mmHg)	74.7 (10.1)	74.9 (5.0)	0.868
FPG (mg/dl)	85.9 (8.3)	79.4 (7.2)	0.000
HDL-chol (mg/dl)	45.1 (8.6)	47.6 (9.1)	0.030
Triglyceride (mg/dl)	120.9 (110)	93.1 (38.8)	0.000
Fasting Insulin (µIU/ml)	11.7 (10.5)	6.0 (4.1)	0.000
HOMA-IR	2.7 (2.9)	1.2 (0.9)	0.000

WC = waist circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure; FPG = fasting plasma glucose; HDL-chol = HDL-cholesterol

Table 2. Distribution of metabolic syndrome component in subject with and without parent history of type 2 diabetes

Variables	Groups		OR (95% CI)
	Parent with history of type 2 diabetes (n=64)	Parent without history of type 2 diabetes (n=64)	
W.Circumference			
- >90 cm	15	1	19.3 (2.46–151.07)
- ≤90 cm	49	63	
FPG			
- ≥100 mg/dl	3	0	
- <100 mg/dl	61	64	
HDL-cholesterol			
- <40 mg/dl	14	12	1.2 (0.51–2.88)
- ≥40 mg/dl	50	52	
Triglyceride			
- ≥150 mg/dl	13	6	2.5 (0.87–6.96)
- <150 mg/dl	51	58	
Blood Pressure			
- ≥130/85 mmHg	4	0	
- <130/85 mmHg	60	64	

Table 3. Correlation between parent history of type 2 diabetes with insulin resistance (n=64)

Insulin resistance	Parent history of type 2 Diabetes		OR (95% CI)
	With	Without	
Positif	33 (51.6)	6 (9.4)	10.3 (3.89–27.23)
Negatif	31 (48.4)	58 (90.6)	

Table 4. Multiple logistic regression analysis between parent history of type 2 diabetes and metabolic syndrome component with insulin resistance

Variables	OR (95% CI)	Determinant (R^2)
Parent history of type 2 diabetes	13.4 (2.68–49.07)	26.3%
Waist circumference >90 cm	8.2 (1.59–42.25)	14.0%
Triglyceride ≥150 mg/dl	6.3 (1.52–26.96)	8.7%

Determinan (R2) model = 50.7%

parental history of type 2 diabetes and metabolic syndrome components that may influence insulin resistance (e.g. Waist circumference and hypertriglyceridemia). We found that the three variables together increased the accumulative risk of insulin resistance incidence with a determinant factor of 50.7%. (**Table 4**)

DISCUSSION

Type 2 diabetes is a multi-factorial disease in which an individuals risk is defined by complex interplay between genetic and environmental factors. Parental history of type 2 diabetes also increases the risk of developing type-2 diabetes in children and adolescent. Meanwhile, the clustering of diabetes risk factors, known as metabolic syndrome is asssociated with insulin resistance, a key factor in pathogenesis for type- 2 diabetes. Results from The Bogalusa Heart Study[15] had identified that metabolic abnormalities in childhood with parental history of type-2 diabetes were associated with an increased risk of developing diabetes in adulthood.

This study showed that waist circumference, fasting plasma glucose, hypertriglyceridemia, and HOMA-IR were higher in adolescent with parental history of type-2 diabetes, whereas HDL-cholesterol was lower. It was postulated that the lower insulin sensitivity in adolescent with parental history of type-2 diabetes was associated with lower insulin clearance, wich could be an early compensation for the insulin resistance.[16] Our data also showed that healthy adolescent with parental history of type-2 diabetes was associated with higher level of fasting insulin plasma and hyperinsulinemia. This is consistent with epidemiologic findings as a reported by Veldes et al[17] which showed that people with family history of diabetes might have early signs of defective insulin actions, glucose intolerance, lipid abnormalities, high blood pressure, large weight gains, reduced β-cell function, impaired endothelial function, and altered energy metabolism, even childhood and youth. American Diabetes Association (ADA) consensus and Indonesian Diabetes Association (PEKENI), recomended that parental history of type-2 diabetes should be included as a screening component for type 2 diabetes.[18,19]

As shown in **Table 3**, parental history of type 2 diabetes had positive correlation with insulin resistance. Previous studies had also found that healthy subjects with parental history of type 2 diabetes were less insulin sensitive.[6,20,21]

The present study also demonstrated the metabolic syndrome component that influences the risk of insulin resistance in subjects with parental history of type 2 diabetes were body weight (waist circumference) and higher blood triglyceride level. Jeong et al[22] also reported the similar result, whereas systolic and diastolic blood pressure and HDL-cholesterol were not different between the two groups. The association of metabolic syndrome component in adolescent with parental history of type 2 diabetes probably reflects the pleiotropic effects of genes that are transmitted from affected persons to their offsprings.

CONCLUSION

Healthy adolescents with parental history of type 2 diabetes have a higher incidence of insulin resistance and abnormality of metabolic profile, especially waist circumference and elevated level of triglyceride. Detection of metabolic disturbance and risk of insulin resistance in healthy adolescent with parental history of type-2 diabetes in our study suggest that screening for

metabolic risk factors are strongly recommended in this population.

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