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Association of Family History, Body Mass Index, and Exercise Regularity with HbA1c Status in Type 2 Diabetes Mellitus Patients

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Abstract

Background: Urban life, especially in Surakarta, is easy to access and full of high-carbohydrate food and drink. This has increased unhealthy behavior and diets. The prevalence of diabetes Mellitus (DM) in Surakarta is growing, reaching 24% in 2021. Physical exercise and poor diet are important risk factors for DM, coupled with genetics, causing obesity. HbA1c levels periodically assess DM patients' glycemic management.

Objective: This study aims to determine the association between family history, body mass index, and regular exercise with HbA1c status in type 2 DM patients at UNS Surakarta Hospital.

Methods: The research was an observational study; 24 patients diagnosed with type 2 DM were recruited from the outpatient clinic of Universitas Sebelas Maret Hospital, Surakarta, Indonesia, in October 2021. Measurements were conducted to determine their HbA1c level by enzymatic methods and body mass index by measuring body weight and height, and they were questioned regarding their physical exercise and family history of diabetes. The data collected were analyzed using multiple logistic regression to ascertain the association between family history, body mass index, and exercise regularity with HbA1c status.

Results: The findings indicated no statistically significant association between genetic background, body mass index, and exercise frequency with HbA1c status ($p>0.05$).

Conclusion: This research shows that genetic history, body mass index, and exercise regularity are not associated with HbA1c status in type 2 DM in included subjects.

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INTRODUCTION

The World Health Organization (WHO) states that in 2019, diabetes was the leading cause of 1.5 million deaths, and 48% of deaths occurred under the age of 70 years[1]. According to Riskesdas 2018 data, the prevalence of DM nationally is 8.5%, or around 20.4 million Indonesians have been diagnosed with DM. The prevalence of diabetes in Central Java province, as determined by specialists' diagnoses, is 91,161 people, with most of them being within the age range of 35-44 years. In Surakarta, the prevalence is 1,370 people[2]. The internal medicine polyclinic of the Sebelas Maret University Hospital in Surakarta handles the most outpatient visits (19,539 patients), with a large percentage of diabetes mellitus cases and hemodialysis polyclinic visits. This polyclinic is classified as level 1 severity of the hospital[3].

Humans are a collection of genes and behaviors, so it can be understood why genetic elements impact the likelihood of becoming obese. The protein-coding gene PPARG produces the nuclear ligand-dependent transcription factor in adipocytes. The PPARG gene is a critical metabolic regulator that helps control adipogenesis, fat storage and metabolism, thermogenesis, and insulin sensitivity[4]. The potential for an increased risk of diabetes is also experienced by people with a family history of diabetes, with an increase of 40%[5]. Research by Rudi and Kwureh shows a meaningful relationship between family history and fasting blood sugar levels[6].

Estimation by WHO that globally, 422 million people have diabetes Mellitus (most of whom are type 2 DM), mainly in low-and middle-income countries[1]. The prevalence of type II DM is in line with the increasing prevalence of obesity; about 80% of people with type II DM are obese. People with obesity have a greater risk of diabetes Mellitus than other diseases[7].

Obesity is the "abnormal or excessive accumulation of fat that poses a health risk" and a body mass index (BMI) of over 30. Global obesity rates continue to rise due to the long-term imbalance between energy intake and expenditure[8]. Diabetes Mellitus (DM), as well as obesity, due to its increased incidence, are recognized as epidemics by the World Health Organization. The frequency of type 2 diabetes among overweight and obese people increased from 6.4 people per 100,000 in 1994–1998 to 33.2 in 2009–2013. In Asia, 56.1% to 69.2% of people with type 2 diabetes are obese[9]. Extensive research cites several hypotheses linking obesity to the chronic condition of Diabetes. The most prominent and recent hypotheses are the inflammation, lipid overflow, and adipokine hypothesis[10]. Compared with healthy, thin people, people with obesity have increased basal and postprandial plasma insulin concentrations. People with obesity and type 2 diabetes have lower postprandial insulin than those without type 2 diabetes, and relative insulin insufficiency is responsible for noticeable hyperglycemia in people with type 2 diabetes[11].

In addition to central obesity, low physical activity is also one of the risk factors for type 2 diabetes mellitus (DM)[12]. Along with the times, there have been lifestyle changes with minimal physical activity (sitting for a long time in front of a laptop/computer/smartphone, all needs are readily available, lots of leisure time). Lack of exercise causes a decrease in the availability

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of insulin receptors, and receptors become more passive due to decreased blood flow[13]. A sedentary lifestyle (lack of physical activity) and poor diet cause overweight and lead to obesity[14]. Previous studies have shown a significant relationship between exercise and blood sugar levels[15].

Glycosylated hemoglobin (HbA1c) is a protein fraction due to the reaction between glucose and haemoglobin[16]. HbA1c indicates glucose content that binds to hemoglobin in the blood[17]. Higher levels of uncontrolled HbA1c are associated with an increased risk of complications in diabetes Mellitus, including both macrovascular and microvascular[18]. In addition to fasting blood glucose tests, WHO, ADA, and PERKENI determine that the criteria for establishing the diagnosis of diabetes Mellitus can be done by examining hemoglobin late (HbA1c) as a protein fraction resulting from the reaction between hemoglobin and glucose. HbA1c measures the glucose level that binds to the blood's hemoglobin. This test measures glucose levels in the blood over three months or 120 days. If HbA1c increases, there is also an increased risk of complications in people with DM[17]. An increase in HbA1c levels of 1% is equivalent to an average increase in plasma glucose of 35 mg/dL. According to the ADA, HbA1c levels below 6.5% are a marker of controlled blood glucose. A decrease in HbA1c levels indicates reasonable glucose control, so HbA1c becomes the gold standard for treating DM patients. This is important based on evaluating the patient's glycemic control in the last three months. A 1% reduction in HbA1c levels reduces the risk of microvascular complications by 40%[16].

Recently, no studies have identified any associations between family history, BMI, exercise regularity, and HBA1C status as a periodic glycemic control for DM patients. This information is crucial for issuing public warnings regarding the necessity of maintaining optimal body weight and engaging in regular physical activity to prevent and manage the occurrence of diabetes mellitus in individuals, regardless of whether they have a family history of the condition or not.

METHODS

Study design

This observational study assesses the correlation between family history, body mass index, and exercise regularity with HbA1c status in type 2 DM patients.

The subjects and sample size

The participation of research subjects was carried out by consecutive sampling. Sampling is carried out using a purposive sampling method. A total of 24 patients who came to the internal medicine clinic of Sebelas Maret University Hospital diagnosed with type 2 DM and willing to participate in research were included as research subjects by signing an informed consent. The criteria for inclusion were patients who were diagnosed with type 2 DM by internal medicine specialists at the internal medicine clinic, following the criteria established by the WHO, American Diabetes Association (ADA), Indonesian Ministry of Health, and PERKENI. Exclusion criteria were patients with serum creatinine levels >1.1 mg/dL, patients with a fever in the last week, patients with a history of systemic infectious

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diseases (COVID-19, tuberculosis, and autoimmune), and those who use wheelchairs.

Research variables

Data was collected by assessing the patient's obesity state by measuring their BMI value and directly inquiring about their family history of diabetes and the regularity of exercise. The BMI was calculated by measuring the patient's weight and height and dividing the weight by the square of the height in meters. In line with the guidelines established by the World Health Organization (WHO), a body mass index (BMI) above 25 is classified as obesity. Patients were directly asked about their family history of diabetes (is there a grandfather/grandmother/father/mother/uncle/aunt who suffers from DM or not). Patients were also directly interviewed about regular physical activity during the past 5 years. Exercise performed regularly for a minimum of 3 days per week, with a minimum duration of 1 to 1.5 hours per day, is considered regular exercise, whereas if it is less than this frequency and duration, it is classified as irregular exercise or not exercising regularly. The HbA1c data provided was obtained from the HbA1c examination conducted at the Clinical Pathology Laboratory of UNS Surakarta Hospital using the kit for HbA1c assay based on enzymatic methods. HbA1c status was determined by two categories: hba1c levels<6.5% and hba1c>= 6.5%.

Statistical analysis

The collected data were then analyzed to determine the association between the independent variable (BMI, genetic/family history, and exercise regularity) and the dependent variable (HbA1c) using multiple logistic regression analysis at a statistical significance of 0.05.

RESULTS

Characteristics of the patients

This study was conducted on 24 subjects. Based on **Table 1**, it is stated that the most significant number of subjects are women. The majority of subjects are over 50 years old, and most of the subjects are not working. Based on **Tables 2** and **Table 3**, it is stated that most of the study subjects had a family history of diabetes with HbA1c levels above 6.5%. However, a small percentage of subjects were obese. The logistic regression results in **Table 4** showed no significant relationship between family history of diabetes, BMI, and exercise regularity with HbA1c status.

Table 1. Characteristics of the patients

Profile	Frequency (*n*=24)	Percentage (%)
Gender		
Man	10	41.7
Woman	14	58.3
Age		
<50 years	3	12.5
≥50 years	21	87.5
Duration of diabetes		
≤5 years	15	62.5
>5 years	9	37.5
Working state		
Work	9	37.5

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Does not work	15	62.5

Table 2. Distribution of subjects based on family history, body mass index, and exercise regularity

Profile	Frequency (*n*=24)	Percentage (%)
Family history		
DM	15	62.5
Not DM	9	37.5
Body mass index		
Obesity	6	25.0
Not Obesity	18	75.0
Exercise		
Routine	14	58.3
Not routine	10	41.7

Table 3. Distribution of family history, body mass index (BMI), and exercise regularity of research subjects based on HbA1c status

Variable	HbA1c (%)	
	<6,5	≥6,5
Family history		
DM	3	12
Not DM	1	8
Body mass index		
Obesity	2	4
Not obesity	2	16
Exercise regularity		
Routine	2	12
Not routine	2	8

Table 4. Association of family history, body mass index, and exercise regularity with HbA1c status

Variable	p-value*	OR
Family history	0.568	2.1
Body mass index	0.243	0.2
Exercise regularity	0.869	1.2

*significance value of multiple logistic regression test

DISCUSSION

The high prevalence of DM, mainly categorized as type 2 DM, is caused by the interaction between genetic factors and environmental exposures. People with a family history of DM are more at risk than people with no history of DM in their family. The results of a study in the Japanese population that included 159 families with 359 people with type 2 DM stated that type 2 DM is associated with chromosomes 3q, 15q, and 20q, which are assumed to be a genetic risk for type 2 DM. Other studies say that a history of diabetes in the family will increase the risk of DM by 2–6 times[19]. The present study indicates a family history of diabetes does not correlate significantly with HbA1c levels. This is because DM is the result of interaction between genetic factors and the environment; genetic factors alone, without being accompanied by environmental exposure, are not enough to modify susceptibility to DM. Lifestyle factors such as nutritional status, food abundance,

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physical activity, and other environmental factors can trigger epigenetic modifications, affecting genomic changes in a person's body and disrupting metabolic balance. Such factors can also modify the physiology of an organism through transgenerational epigenetic inheritance, where exposure to the father's or mother's environment can affect metabolism and manifest traits related to obesity or type 2 diabetes in the offspring [20]. Changes in nutritional status, food supply, physical activity/exercise, thermal stress, toxins, or other environmental disturbances can trigger epigenetic modifications and cause genomic changes in somatic cells in individuals that directly disrupt metabolic homeostasis[21,22].

The increase in the prevalence of obesity results from the interaction between genetic and environmental factors (epigenetics), which are a strong trigger in the emergence of diabetes. The genes in the body are programmed to store fat or all the excess energy exposed to the body as much as possible. The rising standard of living worldwide and the abundance of fast food and other high-energy sources make our bodies adapt to new environments[22]. Obesity is the most important cause of insulin resistance, which appears early in the disease and is mainly compensated by hyperinsulinemia. An increased ratio of new-onset type 2 DM is associated with obesity. Obesity is the most common trigger of insulin resistance associated with receptor degradation and post-receptor failure to activate tyrosine kinase as a β subunit of the insulin receptor activated when insulin binds to the α subunit [23]. Excess weight causes a decrease in the reaction of pancreatic beta cells to increases in blood glucose, and insulin receptors in body cells, especially muscle cells, become less sensitive. Insulin resistance, along with obesity, limits glucose intake into muscles and fat cells so that blood sugar levels increase. Being overweight is associated with a monotonous diet and lifestyle[24]. Foods with high carbohydrate and fat content are still popular. Obesity arises if this habit is not balanced with regular exercise[25].

This study found that family history of diabetes, BMI, and exercise routine were not significantly related to HbA1c. A survey conducted by Nugroho and Wijayanti reveals that obese people have a chance of developing diabetes Mellitus 3.378 times compared to people who do not suffer from obesity[26]. Contrasting results are shown by a study performed by Putri and Larasati that indicates no significant association between obesity and HbA1c level27 and is in line with the results of research by Permatasari et al. that there is no correlation between HbA1c levels and CRP in people with type 2 diabetes Mellitus and obesity[25]. A possible explanation for the absence of a significant association between obesity and HbA1c is that patients have well-controlled blood sugar levels. In addition, elderly factors also influence the tendency to obesity because they are less exposed to other risk factors such as ready-to-eat foods, sugary drinks, and awareness of physical activity than the age group below. A systematic study conducted by Regina found that 25 studies (83%) showed an influence of obesity on the incidence of type 2 DM complications[28]. If there are complications of obesity, such as high cholesterol and triglyceride levels in people with DM, the insulin produced by the pancreas, which was supposed to maintain blood glucose levels at normal levels, cannot

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optimally help the body's cells absorb glucose[24].

Exercise in this study is not partially related to HbA1c levels. Since the leading risk factor for type 2 diabetes is obesity, the most critical prevention of this disease is to prevent excessive weight gain. Knowledge of sedimentation diet, physical activity, and lifestyle is vital[29]. Lack of physical activity and poor diet result in excess weight and trigger obesity[30]. Weight gain is also considered one of the side effects of intensive insulin treatment. Increasing insulin doses to maintain optimal glycemic control despite excessive caloric intake will promote adipose tissue growth, increasing insulin resistance and insulin requirements[31]. This is possible because the measurement of HbA1c levels was done sometime before. In contrast, the measurement of blood glucose levels showed the DM category. Another factor is that activities included in exercise do not include daily activities that require sufficient energy, such as intense up and down stairs at work or home, walking to the market or the mosque, household activities such as mopping, etc. Good exercise will increase insulin sensitivity to control blood sugar by increasing cell glucose uptake. Obesity significantly impacts tissue insulin sensitivity, impacting systemic glucose homeostasis. Obesity is prone to various diseases and has been considered a contributing factor to many obesity-related diseases, including insulin resistance and type 2 DM[32].

CONCLUSION

Based on the analysis of the study results, it can be concluded that there is no significant association between family history of diabetes, body mass index, and exercise regularity with HbA1c status in included subjects.

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