RESEARCH ARTICLE

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IGF-1 Levels in Patients with Type 2 Diabetes Mellitus

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Abstract

Type 2 Diabetes Mellitus (Type 2 DM) is a metabolic disorder group with mechanisms that include hyperglycemia, insulin resistance and hyperinsulinemia. Type 2 DM has a close association with IGF-1, where the active form of the IGF-1 becomes elevated by reason of the fact that hyperinsulinemia inhibits the production of IGF-binding proteins (IGFBP) 1/IGFBP 2. The active form of IGF-1 has the ability to promote cell proliferation and inhibit apoptosis, hence becomes one of the risk factors for cancer cell growth. This was an analytical study conducted in August at the Harapan Bunda Clinic, Medan, Indonesia to determine the difference between the IGF-1 level and blood glucose level in type 2 DM patients in different age groups. Twenty subjects with Type 2 DM participated in this study and were divided based on their age into 35–50 years old or Group 1 (n=10) and 51–65 year old group or Group 2 (n=10). The IGF-1 levels in both groups were compared and analyzed using the T-test dependent method. Results showed that the IGF-1 and blood glucose levels were higher in Group 1 (35-50 years old) when compared to Group 2 and the difference was significant. The change in the IGF-1 level in diabetic patients cannot be determined only by the blood sugar level.

Keywords: Blood glucose level, IGF-1 level, type 2 diabetes mellitus

Kadar IGF-1 pada Pasien dengan Diabetes Melitus Tipe 2

Abstrak

Diabetes Melitus Tipe 2 (DM Tipe 2) merupakan suatu kelompok gangguan metabolik dengan mekanisme penyebab seperti hiperglikemia, resistensi insulin dan hiperinsulinemia. DM tipe 2 memiliki kaitan yang erat dengan IGF-1, bentuk aktif IGF-1 meningkat karena fakta bahwa hiperinsulinemia menghambat produksi protein pengikat IGF (IGFBP) 1/IGFBP 2. Kemampuan yang dimiliki bentuk aktif IGF-1 dalam hal proliferasi sel dan menghambat apoptosis sehingga menjadi salah satu faktor resiko pertumbuhan sel kanker. Penelitian ini dilakukan pada bulan Agustus di Klinik Harapan Bunda Medan untuk menentukan perbedaan kadar IGF-1 dengan kadar glukosa darah pada pasien DM tipe 2 berdasarkan kelompok umur yang berbeda. Penelitian menggunakan 20 sampel pasien DM tipe 2 yang dibagi dalam 2 kelompok, dimana 10 sampel berusia 35–50 tahun (kelompok 1), dan 10 sampel berusia 51–65 tahun (kelompok 2). Desain penelitian yang digunakan adalah penelitian analitik yang membandingkan kadar IGF-1 pada dua kelompok umur yang berbeda. Hasil penelitian dianalisis dengan metode *t-test dependent* dan didapati bahwa kadar IGF-1 pada kelompok umur 35–50 tahun (kelompok 1) lebih tinggi daripada kelompok umur 51–65 tahun (kelompok 2). Simpulan, terdapat perbedaan yang signifikan pada kadar IGF-1 kelompok umur 1 dan 2. Naik-turunnya kadar IGF-1 pada kedua kelompok umur pasien DM tipe 2 tidak hanya dapat ditentukan oleh kadar gula darah.

Kata kunci: Diabetes melitus tipe 2, kadar IGF-1, kadar glukosa darah

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Introduction

Type 2 Diabetes Mellitus (type 2 DM) is one of the major health problems. In the Diabetes Atlas 2019 (International Diabetes Federation), it was noted that sufferers of type 2 diabetes in the world in 2019 amounted to 463 million people and that number will continue to increase and is estimated in 2045 to be 629 million people. The disease ranks seventh in terms of death-related diseases in developing countries and Indonesia ranks sixth out of 10 developing countries with the highest number of people with type 2 diabetes.[1] Estimates from the World Health Organization (WHO), an increase in the number of people with type 2 DM in Indonesia from 8.4 million in 2000 to around 21.3 million in 2030. This report shows an increase in the number of people with type 2 DM by 2–3 fold in 2035.[2]

Type 2 DM is closely related to IGF-1, where the active form of IGF-1 is increased due to the fact that hyperinsulinemia inhibits the production of IGF-binding protein (IGFBP) 1 / IGFBP 2. The ability of the active form of IGF-1 along with its receptors is stronger in terms of proliferation cells and inhibits apoptosis. Therefore, the risk of cancer cell growth more easily occur. A study from the National Center for Biotechnology Information 2010 found that low serum IGF-1 was positively related to Diabetes Mellitus in younger subjects, then high IGF-1 serum was associated with older subjects.[3,4] The study is in line with the journal from Joel Furman which states that a high serum IGF-1 is seen with age.[5]

Based on the study from Swapnil and his team also found the fact that in addition to IGF-1, there is also IGFBP-1/Insulin Growth Factor Binding Protein-1 plays an important role in type 2 DM. High IGFBP-1 has been shown to cause a decrease in IGF-1 and circulating glucose levels which means IGFBP-1 is a component of IGF-1 regulation.[6] Along with age, insulin which that contribute to IGFBP-1 and IGF-1 regulation can be disrupted and cause unstable effects on IGFBP-1 production.[7]

Age and Diabetes Mellitus have a bond. A study showed that IGF-1 serum level increases in children with age, reaching its peak during puberty, followed by a subsequent decline in adulthood. A similar pattern with age has been found in individuals with diabetes.[8] Patient with Diabetes Mellitus also decreased functional status and loss of muscle mass increasing with age. All of these things have a major impact on the ability to manage diabetes independently, thus making Diabetes Melitus increasingly out of control. As a result, strategies to improve management in older adults are chosen. The risk of overtreatment of hyperglycemia in older adults also can cause hypoglycemia.[9] Therefore, this study was designed to evaluate the total serum levels of IGF-I in type 2 diabetic patients aged 35–65 years.

Methods

This research is analytic cross sectional that to assess the correlation of IGF-1 levels in two different age groups of type 2 Diabetes Mellitus patients, conducted in August 2019 at Harapan Bunda Clinic, Medan, Indonesia. It approved by Ethic Committee (020/KEPK/UNPRI/XI/2020). Inclusion criteria were controlled type 2 Diabetes Mellitus patient, female or male, aged 35–65 years, and willing to participate in the study. While the exclusion criteria are type 2 diabetes mellitus patients with other comorbidities.

Sampling was done incidentally from patients who met the criteria for acceptance of the sample until the number of samples were met, as many as 20 samples. Anamnesis is performed on type 2 diabetes mellitus patients at Harapan Bunda Clinic. Then the patient is given information for informed consent about the study. If the patient agrees and has signed an informed consent. Venous blood sampling is carried out in the morning from 8–9 after the patient is fasting for 10–12 hours. Blood samples were put in an edta vacutainer, centrifuged, and then examined fasting blood sugar levels and IGF-1 levels in the Indonesian Laboratory (PATHLAB) Medan. The results of the examination of fasting blood sugar levels and IGF-1 levels are recorded on the data collection sheet and then carried out data processing according to age group.

All statistical analyzes were performed using SPSS version 17.0. The limit of significance test (p) used in this study was 0.05. To determine the normality of data distribution, the Kolmogorov-Smirnov test was used. Data that have a normal distribution, to assess differences in the mean of two variables that are numerically used t-independent test. To assess the relationship between the independent variable and the dependent variable used correlation test. The independent t-test was used to differentiate the glucose and IGF-1 levels among two groups and the Pearson correlation test was used to analyze the correlation between IGF-1 and glucose levels.

Table 1 Characteristics of Type 2 DM Patient

Age (years)	Gender	
	Male	Female
	(n=6)	(n=14)
35–50	5	5
51–65	1	9

Results

The subjects of this study were 20 women with type 2 diabetes mellitus, where there were more people at the age of 46–50 years as many as 14 of 20 people and the remaining 6 of 20 people aged 40–45 years (Table 1).

Comparison of fasting blood sugar levels of patients with type 2 diabetes mellitus against age groups there was no statistically significant difference (p=0.219; Tabel 2). The average blood sugar level of subjects from the age group of 35-50 years was 177.0±29.70 and 176.1±53.15 from the older age group (51–65 years).

Table 3 shows the statistically significant differences between IGF-1 levels in the two age groups (p=0.047). Where the average IGF-1 level of subjects from the age group of 35–50 years (140.60±16.91) is higher than the age group 51–65 years (126.50±42.76).

After knowing the effect of age on blood sugar levels and IGF-1 subjects, then the analysis continued with the correlation analysis between blood sugar levels and IGF-1 levels of subjects. There were no statistically significant correlation between blood sugar level (176.55±41.91) and IGF-1 level (133.55±32.46) on the whole subject of the research, which is reflected in the value of p=0.209. Although the correlation coefficient is 0.293 which means that there is a very weak correlation between blood sugar level and IGF-1 level, but the correlation is not statistically significant because the P value >0.05.

Table 2 Blood Sugar Level of Age Group of Type 2 DM Patient

Age (years)	Level of IGF-1 (ng/mL) [Mean ± SD]	p-value
35–50	177.0 ± 29.70	0.219
51–65	176.1 ± 53.15	

Table 3 IGF-1 Level in the Age Group of Type 2 DM Patient

Age (years)	Level of IGF-1 (ng/mL) [Mean ± SD]	p-value
35–50	140.60 ± 16.91	0.047
51–65	126.50 ± 42.76	

Discussion

Rony, in his research at RSUP Adam Malik Medan which obtained the proportion of patients with type 2 DM more women (51%) compared to men (49%).[10] This is consistent with research that has been done in table 1 shows the type 2 diabetes mellitus patients are more women (70%) than men (30%). Similar to the theory is that women are more at risk for type 2 diabetes because they have a greater chance of increasing their BMI (Body Mass Index). Monthly cycle syndrome (premenstrual syndrome) or post menopause that can make body fat distribution easily accumulate can also increase the risk of women suffering from type 2 diabetes.[11]

In addition to gender, according Liyanage., age is not the only reason for the increase in type 2 diabetes because it contributes indirectly to the glucose tolerance. Direct contribution depends on BMI and physical activity. This is consistent with the theory which says that as we age, muscle mass decreases universally. This condition results in loss of muscle strength and an indirect contribution to the inability of individuals to carry out daily tasks. Reduced muscle mass and reduced physical activity that contribute to increased body fat and insulin resistance make individuals become obese. The presence of obesity changes the levels of plasma glucose, insulin and glucagon. Because of this, the development of insulin resistance and diabetes is more caused by changes in body composition than aging.[12] This theory is also related to the results of the study in table 2 which shows no significant difference in blood sugar levels of the two age groups.

Insulin like Growth Factor-1 (IGF-1) has a close relationship with type 2 DM. In the case of type 2 DM, the IGF-1 component has an important role. It was found that the young age group (35–50 years) had higher levels of IGF-1, which is higher than the old age group (51–65 years). The results of this study were not in line with the study of Garg et al. which obtained results that were inversely proportional to this study.[3] However, these results are in accordance with research conducted by Gong et al., which

states that decreasing IGF-1 levels is associated with osteoporosis in old age. IGF-1 levels have decreased associated with the development of lean bones/slender bones. This characteristic of slender bones develops at an early age of puberty and lasts up to 52 weeks, which affects most bone growth. This condition causes an effect on the peak bone mass resulting in IGF-1 need to provide a role as a protective and more optimal repair, and when bone loss becomes more common where there is a decrease in IGF-1.[13]

Rising and decreasing of IGF-1 can not only be determined by blood sugar levels. According to a study conducted by Clemmons, the variable that also regulates IGF-1 levels is nutrient intake. Either calorie or protein intake is an important variable. If calorie intake is reduced by about 50%, there is a significant reduction in IGF-1 secretion. The effects of protein are more graded so that even a small reduction results in changes in IGF-1. For every 25% reduction in protein intake, there is also an equivalent reduction in IGF-1. The majority of IGF-1 comes from liver synthesis. Both protein and calories participate in the regulation of liver synthesis with calories that regulate IGF-1 transcription and proteins that function primarily to regulate stability and translation.[14,15] The results of IGF-1 usually cause changes and the results are inversely proportional to IGFBP in type 2 DM, so that the active form of IGF-1 also undergoes changes. In pre-diabetes, IGFBP-1 is initially lower. This is caused by hyperinsulinemia which occurs in the pre-diabetes phase. This condition results in an increase in the active form of IGF-1, but as insulin resistance develops, production of IGFBP-1 is inhibited and causes an active form of IGF-1 to increase.

In reducing IGF-1 levels, a combination of good nutrition and physical activity is needed. Physical activity can avoid obesity which can cause changes in IGF-1 secretion.[16,17] Without balance in lifestyle, it is possible for IGF-1 levels to increase. Elevated levels of IGF-1 are always associated with cancer risk, such as breast, prostate and colorectal cancer.[18,19,20,21] Some of these studies further support the results achieved in this study that there is no close relationship between blood sugar levels with a decrease or increase in IGF-1.

Correlation between age and IGF-1 in patients with type 2 Diabetes Mellitus in Harapan Bunda Clinic Medan has been conducted with the following conclusions; there were no statistically significant differences in blood sugar levels in the age group; average IGF-1 levels in the age group (35–50 years) are higher than the age group (51–65 years); rising and decreasing of IGF-1 levels in each age group cannot only be determined by blood sugar level; and there is no close relationship between type 2 diabetes and IGF-1 levels.

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