Original Research Article

The Relation between Estradiol Levels and Body Mass Index with Fasting Blood Glucose Levels in Premenopausal Women in Padang in 2017

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ABSTRACT

Premenopause is a transitional period that occurs due to decreased generative or endocrine function of the ovaries. In premenopausal women, there is a decrease in estrogen hormone levels and an increase in Body Mass Index (BMI) so that it will increase the risk of diabetes mellitus which is one of the four priority non-communicable diseases. The incidence of diabetes mellitus in women is much higher when compared to men.

The research was conducted in the city of Padang, with an observational, cross-sectional design. The sampling technique used was multistage random sampling with a sample of 99 premenopausal women. The estradiol level was assessed by ELISA method, BMI was assessed by weight (kg) divided by height (m) squared, fasting blood glucose level was assessed by the enzymatic photometric method. The correlation between estradiol levels and fasting blood glucose levels was analyzed by using the Pearson Correlation test. The correlation between BMI and fasting blood glucose levels was analyzed by using the Pearson Correlation test.

The mean of estradiol level was (148,689±49,417) pg/ml. Average Body Mass Index (BMI) was included in the Obese category I (26.5 kg/m^2). The mean fasting blood glucose level was (98,766±6,549) mg/dL. There is a correlation between estradiol levels and fasting blood glucose levels (p value = 0.007 and r value = 0.270). In addition, there is a correlation between BMI and fasting blood glucose levels (p value = 0.023).

The conclusion of this study is that there is a significant correlation between estradiol levels and fasting blood glucose. There is a significant correlation between BMI and fasting blood glucose

Keywords: Estradiol Levels, Body Mass Index, Fasting Blood Glucose Levels, Premenopause

INTRODUCTION

Diabetes mellitus is one of the four priority non-infectious diseases. Eighty percent (80%) of the incidence of diabetes can be prevented or delayed with optimal treatment management[1]. The prevalence of diabetes in Indonesia according to the characteristics shows an increase in the prevalence of diabetes in the premenopausal group (45-54 years) by 3.3% when compared to the productive group (35-44 years) which is 1.1%. Women have a higher percentage of having diabetes when compared to men, namely 1.7% (men 1.4%)[2]. The climacteric period is a period of transition from the reproductive phase to the old phase (senium) which occurs due to decreased generative or endocrine functions of the ovaries. According to Sastrawinata (2004), one of the climacteric phases is the premenopausal phase, which is the period of 4-5 years before menopause, around the age of 40 years with the start of irregular, prolonged, few or many menstrual cycles, which are sometimes accompanied by a feeling of pain[4]. Women with

premenopausal age have a risk of experiencing abnormalities in body metabolism, one of which is increased blood glucose levels[5]. There are several predisposing factors for an increase in blood glucose, namely lack of exercise, increased amount of food consumed, increased stress and emotional factors, weight gain and age, and the effects of treatment from drugs, eg steroids[6]. High blood glucose levels that occur in premenopausal women can significantly increase the risk of developing diabetes mellitus[5].

One of the biggest risk factors for diabetes that is continuously increasing is the prevalence of overweight (13.5%) and obesity (15.4%) and the presentation of obesity in women, which is 20%7. A study supported by the National Institute of Diabetes and Digestive and Kidney Disease states that there is a significant relation among the main female hormone, 17β-estradiol (E2), and the risk of type 2 diabetes in postmenopausal women. Estrogen therapy given to postmenopausal women shows a decrease in fasting glucose levels, which means that estrogen levels can affect blood glucose [8] . Other studies state that high estrogen levels can increase sensitivity to insulin, so blood glucose levels can be lower than normal. Conversely, low estrogen levels will reduce sensitivity to insulin so that blood glucose levels will increase, this is related to the presence of estrogen receptors (ER) found in cells that affect insulin sensitivity [9]. Other studies state that high estrogen levels can increase sensitivity to insulin, so blood glucose levels can be lower than normal. Conversely, low estrogen levels will reduce sensitivity to insulin so that blood glucose levels will increase, this is related to the presence of estrogen receptors (ER) found in cells that affect insulin sensitivity.\ (Pranita et al., 2011)[11].

LITERATURE REVIEW

Premenopause is a transitional phase from the fertile period to the time of no fertilization (anovulatoir). Premenopausal women are women who experience premenopausal symptoms which generally occur around the age of 40 and peak at the age of 50 years, namely the occurrence of menopause where at this menopause women do not experience menstruation anymore [5].

In the premenopausal phase, there will be a decrease in estrogen levels which causes symptoms (premenopausal syndrome) including hot flashes (hot flashes from the chest to the face), night sweat (sweating at night), dryness vaginal (dry vagina), memory loss, insomnia, depression, fatigue (tired easily), decreased libido, drypareunia (pain during sexual intercourse) and urinary incontinence[5]. Plasma estradiol in blood and intestinal fluids is bound to Sex Hormone Binding Globulin (SHBG), from Sex Hormone Binding Globulin (SHBG) estradiol dissociates to enter cells and binds to their receptors. There are genes that code for two isoforms of the estrogen receptor: α and β. Both receptors are members of the steroid, retinoic, and thyroid receptor superfamily. Estrogen is a steroid hormone that regulates growth, differentiation, and various functions in the tissues of the human body. As one of the main sex hormones in women, estrogen is tremendously important in the control of the menstrual cycle, reproduction and development of female secondary sexual characteristics. In addition to their important function in the reproductive system, estrogens play an important role in the regulation of cardiovascular, immune, bone growth and the central nervous system as well as in metabolic processes [12]. Body mass index is determined by the equation of body weight in kilograms (kg) divided by height in meters squared (m²).

Classification of body mass index starting from underweight, normoweight, and overweight [13]. Glucose is the most important carbohydrate for the body because glucose acts as the main metabolic fuel. It also serves as a precursor for the synthesis of other carbohydrates, such as glycogen, galactose, ribose, and deoxyribose. It is the most end product of

carbohydrate metabolism. Most carbohydrates are absorbed into the blood in the form of glucose, while other monosaccharides such as fructose and galactose are converted to glucose in the liver. Therefore, glucose is the most abundant monosaccharide in the blood [14]. In human metabolic disease, estradiol has an important role in the presence of Estrogen Receptor (ER). ERs will perform a good intracellular signal if the estrogen supply is sufficient. On the other hand, in the presence of estrogen deficiency or in the case of a damaged ER, there will be an increase in the prevalence of metabolic syndrome, type 2 diabetes mellitus [15]. One of the high risk groups of diabetes mellitus is overweight or obesity (BMI $\geq$ 25) [16]. When body weight increases, the risk of insulin resistance will also increase, this is due to a decrease in the ability of insulin to move glucose into cells and to inhibit the release of glucose from the liver. Circulating chemicals such as leptin, adiponectin, resistin, TNFα which are produced by adipocytes (especially in the stomach) increase the risk of developing insulin resistance. [17].

MATERIALS & METHODS

This research is an observational study with a cross sectional study design, where the dependent variable and the independent variable are studied at the same time [18]. This research was conducted in the city of Padang. Anthropometric measurements were carried out at the time the research was carried out. The examination of estradiol levels was carried out at the Biomedical Laboratory of the Faculty of Medicine, Andalas University and blood glucose examinations were carried out at the Biochemistry Laboratory of the Faculty of Medicine, Andalas University, the minimum number of samples in this study was 62 people.

Statistical Analysis

The research data were analyzed with the Kolmogorov Smirnov normality test on numerical data (fasting blood glucose levels and estradiol levels) to see whether the data were normally distributed or not). Then, the analysis used to see the correlation beyweem estradiol level variable (independent variable) and fasting blood glucose (dependent variable) was Pearson correlation statistical test.

RESULT

1. Estradiol Level

Table 1. Average Estradiol Levels in Premenopausal Women in Padang in 2017

Variable	Mean	SD	Minimum	Maximum
Estradiol Level (pg/ml)	148,689	49,417	63,14	310,04

The results of the analysis showed that the average level of estradiol in premenopausal women was 148,689 pg/ml. The lowest estradiol level was 63.14 pg/ml and the highest estradiol level was 310.04 pg/ml**.**

2. Body Mass Index

Table 2. Average Body Mass Index (BMI) of Premenopausal Women in Padang in 2017

Variable	Mean	SD	Minimum	Maximum
Body Mass Index (kg/m^2)	26.5	4.9	16.44	43.76

The results of the analysis showed that the average Body Mass Index (BMI) in premenopausal women in Padang in 2017 was 26.5 kg/m2, which means that the average BMI of premenopausal women in Padang in 2017 was categorized as obese I.

3. Fasting Blood Glucose Level

Table 3. Average Fasting Blood Glucose Levels in Premenopausal Women in Padang in 2017

Variable	Mean	SD	Minimum	Maximum
Fasting Blood Glucose Level (mg/dL)	98,766	6,549	80,00	113,10

Based on the results of the data analysis above, the average value is 98.766 mg/dL. The lowest fasting blood glucose level is 80.00 mg/dL and the highest level is 113.10 mg/dL.

4. The Relation between Estradiol Levels and Fasting Blood Glucose Levels

Table 4. Relation between Estradiol Levels and Fasting Blood Glucose Levels in Premenopausal Women in Padang in 2017

Variable	p value
Estradiol Level (pq/ml)	0,007
Blood Glucose Level (mg/dL)	

Based on the table above, the p value = 0.007 is obtained. From this value, it can be concluded that there is a correlation between estradiol levels and fasting blood glucose levels in premenopausal women in Padang.
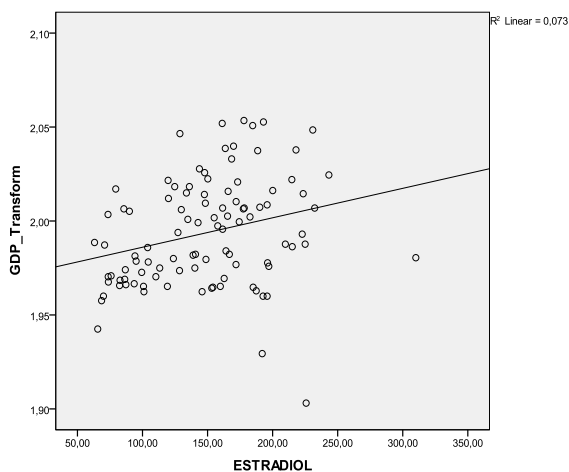

Figure 1. Scatter Plot Linearity Correlation of Estradiol Levels with Fasting Blood Glucose Levels in Premenopausal Women

5. Relation between Body Mass Index (BMI) and Fasting Blood Glucose Level

Table 5. Correlation between Body Mass Index (BMI) and Fasting Blood Glucose Levels in Premenopausal Women in Padang in 2017

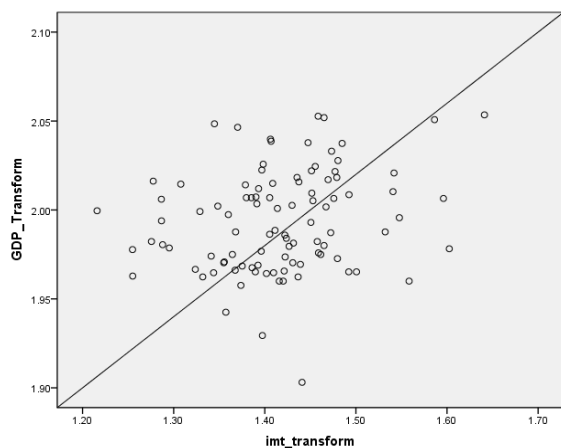| Variable	p value
Body Mass Index (kg/m^2)	0,023
Blood Glucose Level (mg/dL)	

Figure 2. Scatter Plot Linearity of BMI Correlation with Fasting Blood Glucose Levels in Premenopausal Women

Based on the table above, the p value = 0.023 is obtained. From this value, it can be concluded that there is a significant correlation between BMI and fasting blood glucose levels in premenopausal women in Padang.

DISCUSSION
1. Estradiol Level

The results of this study indicate that the average estradiol level is (148.689±49.417) pg/ml, when compared with the normal value of estradiol levels in premenopausal women, which is 50-250 pg/ml [19]. Then the average estradiol level for premenopausal women in Padang in 2017 within the normal range. It is in line with the results of research by Jose` L. Cuadrosusia (2011) finding a decrease in estradiol levels at premenopausal age. The decrease in estradiol hormone levels occurs in the premenopause period, so that the estradiol levels from the results of this study are extremely varied with the lowest range of 63.14 pg/ml and the highest level of 310.04 pg/ml 20. David and Dolores (2007) mentioned that during the reproductive period estradiol levels, the highest level in the blood at the peak of mid-cycle ranges from 150-750 pg/ml, however, this study did not indicate the estradiol levels of the samples during the reproductive period, so the assessment of the decrease in estradiol levels individually cannot be ascertained 19. The decrease in estradiol levels in this phase is indicated by the presence of menstrual disorders such as irregular menstrual cycles, prolonged menstrual cycles, shortened menstrual cycles, sleep disturbances, hot flushes [5].

2. Body Mass Index

The results of the analysis in this study showed that the average BMI of premenopausal women in Padang was in the obesity category (with a result of 26.5 kg/m^2). The high risk group for diabetes mellitus is obesity (BMI 25) (Nadjib, 2015). These results are comparable to the Basic Health Research (2013) which states that the

prevalence of obesity in Indonesia has increased in the premenopausal group (45-54 years) (3.3%) [2]. Obesity that occurs in premenopausal women is influenced by menstrual cycle disorders, namely fluctuations [19]. In comparison with the results of this study, Bose, Olivan, and Laferrere (2009) conducted research on premenopausal women and found that hormonal fluctuations that occur in premenopausal women can cause gradual weight gain to the level of obesity. This is related to the function of Estrogen Receptors (ER) which begins to decrease as a result of decreased levels of estradiol [21].

3. Fasting Blood Glucose Level

In the analysis of the average value, it is found that fasting blood glucose levels in this study is (98,766±6,549) mg/dL and this result is included in the normal category (American Diabetes Association, 2015)[23]. In line with the to the research conducted by Pranita (2011) in India with a total sample of 300 premenopausal women, it was obtained that the average blood glucose level in premenopausal women was (81.12±6.34) mg/dL [22]. Glucose levels in the circulation are affected by several factors such as carbohydrate consumption, physical activity, use of drugs containing steroids, illness, stress, and the menstrual cycle23. Examination of fasting blood glucose levels is one of the ways of early detection of the risk of diabetes mellitus.

4. Correlation between Estradiol Levels and Fasting Blood Glucose Levels in Premenopausal Women in Padang in 2017

In the results of the correlation analysis between estradiol levels and fasting blood glucose levels in premenopausal women in Padang in 2017, the p value = 0.007 is obtained which means that there is a correlation between estradiol levels and fasting blood glucose levels in premenopausal women in Padang in 2017.

This result is in line with the results of research conducted by Mauvais & Jarvis (2017) which states that there is a significant relation between 17β-estradiol (E2) and blood glucose in premenopausal women[24]. Other studies also mention that high estrogen levels can increase insulin sensitivity so that blood glucose levels can be lower [25]. This is influenced because estrogen has receptors (ER) that can affect insulin sensitivity, so that glucose in the blood circulation can enter the pathway of body metabolism [25].

There are many things that affect blood glucose levels besides estradiol levels, such as food intake such as carbohydrates, physical activity, lifestyle, including other hormones that can increase blood glucose levels such as glucagon, asprosin, epinephrine, cortisol, thyroxine, and so forth. In this study, the tendency of estradiol levels to affect fasting blood glucose levels in premenopausal women was only 7.3% (R2 = 0.073) meaning that estradiol levels only affected fasting blood glucose levels by 7.3%. which is able to increase fasting blood glucose levels which was not studied in this study.

5. Relation between Body Mass Index and Fasting Blood Glucose Levels in Premenopausal Women in Padang in 2017

In the results of the analysis of differences in the mean blood glucose levels based on Body Mass Index (BMI), the p value = 0.183 is obtained. With p≥ 0.05, it means that there is no significant difference in the average blood glucose level based on BMI in premenopausal women in Padang in 2017. This study is not in line with the research conducted by Josiah (2013), there is an increase in blood glucose levels and risk type 2 diabetes in obese women (higher BMI), and there is no difference in fasting blood glucose levels in obese and non-obese [26].

Research conducted by Asil E et al., (2014) concluded that BMI is one of the anthropometric methods used in measuring body composition. There are many things that can affect BMI such as age, gender,

genetics, diet and physical activity[27]. Groups that have a high risk of developing diabetes mellitus are those who are overweight and obese [16]. In theory, when body weight increases, the risk of developing insulin resistance will also increase. This is because there is a decrease in the function of insulin in moving glucose from the circulation into the cells. People who are obese will find many chemicals circulating in the blood circulation in high concentrations such as leptin, adiponectin, resistin, TNFα which are produced by adipocytes. This will disrupt insulin function and work so that it can contribute to insulin resistance[17]. Diabetes mellitus can occur as a result of an increased risk of insulin resistance, decreased insulin receptor sensitivity caused by weight gain.

CONCLUSION

Estradiol levels, sugar levels in premenopausal women in Padang in 2017 are in the normal range, Body Mass Index (BMI) of premenopausal women is included in the obese category I. There is a significant correlation between estradiol levels and fasting blood glucose in premenopausal women in Padang in 2017.

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