

Research Article

Insulin Resistance in Obese Women: Does it Affect Fertility ?***Resistensi Insulin pada Perempuan Obesitas:
Apakah Mempengaruhi Kesuburan?*****Satrio B. Purnomo, Bobby I. Utama, Yusrawati, Ori John, Muhammad Iqbal***Department of Obstetrics and Gynecology
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Dr. M. Djamil General Hospital, Padang***Abstract**

Objective: To know the correlation of insulin resistance with body mass index in obesity women infertility.

Methods: This research used a cross-sectional study design. This study was conducted on February 2017 until January 2019 at Obstetric and Gynecology Division of RSUP Dr. M. Djamil and Ibnu Sina Hospital in Padang. The population of the study were all patients were obese in women of reproductive age with infertility complaints with a total sample of 27 people. The sampling technique was consecutive sampling. Data analysis was done by univariate and bivariate using Pearson correlation test.

Results: We found that less than half of the respondents experienced insulin resistance with HOMA-IR values > 2,5 (22.2%) and more than half of respondents did not experience insulin resistance with HOMA-IR values < 2,5 (77.8%). There was a correlation of insulin resistance with body mass index in obese female infertility ($p < 0,05$) with strong relationship strength.

Conclusions: There was a correlation of insulin resistance with body mass index in obese female infertility.

Keywords: infertility, insulin resistance, obesity.

Abstrak

Tujuan: Mengetahui korelasi resistensi insulin dengan indeks massa tubuh pada infertilitas perempuan obesitas.

Metode: Penelitian ini menggunakan desain potong lintang. Penelitian dilakukan di Poliklinik Bagian Obstetri dan Ginekologi RSUP Dr. M. Djamil Padang dan RS Islam Ibnu Sina Padang sejak bulan Februari 2017 – Januari 2019. Populasi pada penelitian ini adalah semua pasien yang mengalami obesitas pada perempuan usia reproduksi dengan keluhan infertilitas dengan jumlah sampel sebanyak 27 orang. Teknik pengambilan sampel dengan consecutive sampling. Analisis data dilakukan secara univariat dan bivariat dengan menggunakan uji korelasi pearson.

Hasil: Hasil penelitian diketahui kurang dari separuh responden mengalami resistensi insulin dengan nilai HOMA-IR > 2,5 (22,2%) dan lebih dari separuh responden tidak mengalami resistensi insulin dengan nilai HOMA-IR < 2,5 (77,8%). Terdapat korelasi resistensi insulin dengan indeks massa tubuh pada infertilitas perempuan obesitas ($p < 0,05$) dengan kekuatan hubungan kuat.

Kesimpulan: Terdapat korelasi resistensi insulin dengan indeks massa tubuh pada infertilitas perempuan obesitas.

Kata kunci: infertilitas, obesitas, resistensi Insulin.

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INTRODUCTION

About 61% of complaints found are related to infertility. The study found that the causes of infertility were fallopian tube dysfunction (27.4%), menstrual disorders (20%), uterine disorders (9.1%), sexual disorders (2.7%), age-related factors (2.7%), and other unknown causes (24.5%).¹ Infertility can also be influenced by a person's unhealthy lifestyle which affects fertility. Infertility can also be affected by body mass index where a person who is obese 9.9% to 16% has infertility.²

The occurrence of disorders of the female reproductive system causing infertility can be affected by excessive weight or obesity. In the body of a person who is obese, there is fat storage in the liver and muscles caused by rising levels of fatty acids and other fats. Patients with insulin resistance have a chance of accumulating fat in their bodies due to triglyceride turnover and the production of essential molecules of fatty acid derivatives, or activation in dangerous cells such as Reactive Oxygen Species (ROS), mitochondrial dysfunction or endoplasmic reticulum stress.²

Insulin resistance can affect the ovulation cycle in women of reproductive age. That women with gestational diabetes had higher HOMA-IR values compared to normal pregnant women. In this study, 271 pregnant women with 10-14 weeks of gestation were involved and the HOMA-IR cut-off value was 2.6.³ In 1.854 pregnant women who were examined by HOMA-IR found that the cut-off value for identifying patients who experienced insulin resistance was > 3.8 .⁴

Anthropometric measurement is one way to assess the nutritional status of pregnant women. With these measurements, the measurement result obtained is weight (kilogram) and height (meters) that can be used to determine the Body Mass Index (BMI).⁵ Women who are obese have a risk of suffering from infertility three times greater than women with a normal BMI. Both natural and fertility disorders that are assisted are experienced by women with BMI above normal.⁶

The result of the study of patients with Polycystic Ovary Syndrome (PCOS) where the presence of endocrine and metabolic abnormalities carried out revealed that 33.3% of patients with PCOS had insulin resistance. Clinically it is known that 72.04% have infertility and 50.5% with obesity. The result of the study show obesity and infertility can be affected by insulin resistance.⁷

Based on this background the researcher wanted to find out how the description of insulin resistance and BMI and the correlation of insulin resistance with BMI in obese female infertility.

METHODS

This study was an analytical study using a cross-sectional study design to determine the correlation of insulin resistance with BMI in female infertility.

The study was conducted from February 2017 until the number of samples was fulfilled at the Obstetrics and Gynecology Polyclinic of RSUP Dr. M. Djamil and Ibnu Sina Hospital in Padang.

The population of this study were all patients who were obese in women of reproductive age with infertility and were willing to be the study sample. The number of samples was 27 people. Sampling technique was consecutive sampling.

Each sample would explain the information of study (information for consent) and sign an informed consent.

To determine the correlation of insulin resistance with body mass index in obese female infertility, Pearson correlation test was used with 95% CI ($p \leq 0.05$). Data were analyzed using a computer program.

RESULTS

Table 1. Characteristics of Respondents

Variables	Mean \pm SD	Min-Max
Age (year)	29.78 \pm 4.51	21.17 – 39.42
Body Mass Index	33.54 \pm 3.50	30.20 – 38.81
Fasting glucose (mmol/L)	5.83 \pm 0.80	4.72 – 7.66
Insulin (μ U/mL)	7.43 \pm 2.45	3.42 – 14.00

Based on Table 1 it is known that the mean age of respondents is 29.78 \pm 4.51 years, Body Mass Index (BMI) is 33.54 \pm 3.50 kg/m², fasting glucose is 5.83 \pm 0.80 mmol/L and insulin level is 7.43 \pm 2.45 μ U/mL.

Table 2. Description of Insulin Resistance

Variables	Mean \pm SD	Min-Max
HOMA-IR	1.93 \pm 0.76	0.81 – 4.60

Table 2 shows that mean of HOMA-IR value of respondents is 1.93 \pm 0.76. The minimum and maximum value are 0.81 and 4.60. Based on the categorization to determine insulin resistance using the HOMA-IR value with a cut-off point > 2.50 .

Table 3. Insulin Resistance Category with HOMA-IR value

Variables	f	%
Insulin resistance (> 2.5)	6	22.2
No insulin resistance (≤ 2.5)	21	77.8

Table 3 summarizes that less than half of the respondents experienced insulin resistance with HOMA-IR values > 2.5 (22.2%) and more than half of respondents did not experience insulin resistance with HOMA-IR values ≤ 2.5 (77.8%).

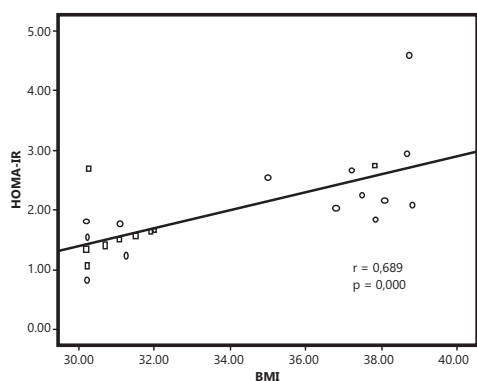


Figure 1. Correlation of insulin resistance and BMI

Based on Figure 1 it can be concluded that the correlation of insulin resistance with the Body Mass Index (BMI) in obese female infertility has a positive direction, meaning that if there is an increase in HOMA-IR value there will be an increase in infertility in obese women. Based on the results of the Pearson correlation test, it was found that there was a correlation of insulin resistance with body mass index in infertility of obese women with a value of $p=0.000$ ($p<0.05$) with a strong relationship strength, namely $r = 0.689$.

DISCUSSION

Based on the results of the study it was found that the mean HOMA-IR values of respondents were 1.93 ± 0.76 . In determining whether respondents experienced insulin resistance the cut-off point value >2.5 was used so that less than half of the respondents experienced insulin resistance where the HOMA-IR value was >2.5 (22.2%) and more than half of the respondents did not experience insulin resistance with HOMA-IR value <2.5 (77.8%).

The results of previous studies stated that the percentage of obesity in the incidence of infertility was 9.9 to 16%. Research found by researcher is slightly different stating the prevalence of infertility in obese women is 9.9% - 16%, the difference in the results of this study can be caused by the average Body Mass Index (BMI) in this study, namely, 33.54 ± 3.50 kg/m² while Aristizabal 31.4 kg/m², the average difference in Body Mass Index (BMI) can be a difference in prevalence found by researchers a little higher than that obtained, because the higher the Body Mass Index (BMI) the higher the risk to experience infertility.⁸

Insulin resistance is also associated with an increased prevalence of different clinical features of PCOS cases. Franks (1989) study found that 300 women with PCOS experienced amenorrhea of 52%, 28% with oligomenorrhea, 64% experienced hirsutism, 35% obese, 27% with acne, 3% with alopecia, <1% with symptoms acanthosis nigricans, and 42% experienced infertility.⁹

The results of the study revealed that the average BMI of respondents was 33.54 ± 3.50 . The results of this study indicate the average BMI in the obese group. Obese women suffer from infertility 3 times more than women with normal BMI. Women with body weight above normal experience interference with both natural fertility and the conception cycle with help.⁶

Women with underweight (<18.5 kg / m²) BMI and overweight BMI (≥ 25 kg / m²) had a greater risk of infertility than women with normal BMI. The results of this study are in accordance with other studies which found that obesity in women is associated with no occurrence of ovulation which has a negative effect on female sexual function. Infertility associated with ovulation factors as much as 12% is caused by underweight and 25% due to overweight. Decreased weight increases the probability of conception.¹⁰

Insulin resistance and hyperinsulinemia experienced by obese women results in a decrease in sex hormone production. While androgen hormones increase and suppress FSH produced by the pituitary gland, which results in follicle formation and ovulation is inhibited, not even ovulation. The situation that is often experienced by obese women is irregular menstrual cycles. Ovulation can occur again if the bodyweight is lowered by 10.2 kg (on average) so that it also allows for pregnancy to occur, lowering insulin and testosterone levels, increasing sex hormones that bind globulins. But increasing weight can increase the risk of infertility.⁸

Based on the analysis of the researchers, the occurrence of insulin resistance is associated with an increase in body mass index, this is due to women with obesity having problems with fertility due to disruption of the conception cycle. This condition triggers the disruption of the ovulation process and has an impact on infertility.

The results of the study show that the correlation of insulin resistance with BMI in obese women who have infertility has a positive direction, meaning that if there is an increase in HOMA-IR value there will be an increase in infertility in obese women. Based on the results of statistical tests it is known that there is a correlation of insulin resistance with body mass index in obese female infertility.

The results of previous studies conducted on patients with Polycystic Ovary Syndrome (PCOS) where endocrine and metabolic abnormalities occur in women of reproductive age with a sample of 105 people in cases from 2009 to 2011. Based on the study results it was found 33.3% people with PCOS experience insulin resistance. Clinical features showed 72.04% experienced infertility and as much as 50.5% with obesity. From the results of the statistical test, it was concluded that there was a significant relationship between insulin resistance and obesity ($p < 0.05$) and there was a significant relationship between insulin resistance and infertility ($p < 0.05$).⁷

The prevalence of insulin resistance for the normal BMI group (18.5–24.9 kg / m²), overweight (25–29.9 kg / m²) and obesity (≥ 30 kg / m²) is 19.3%, 56.2% and 78.2%, respectively. Being overweight and obese increases insulin resistance by OR 5.3 in overweight and OR 14.9 in obesity. The results of the analysis found an association between insulin resistance and infertility in obese women ($p < 0.05$).¹¹

Research conducted was found in patients with polycystic ovary syndrome in the four most common phenotypes, namely type I (50.3%), with type III (29.6%), type II (14.5 %) and type IV (5.7%). Type I had the highest fasting insulin value (median = 12.98 mU / mL) and found differences in IR HOMA values in all four phenotypes and found an association of insulin resistance with infertility in obese women ($p < 0.05$).¹²

There is a correlation between the incidence of infertility with obesity, diabetes mellitus and polycystic ovary syndrome (PCOS). PCOS patients had higher fasting glucose levels than controls ($p < 0.001$, 101.18 vs 90.17 mg / dL), fasting plasma insulin ($p < 0.01$, 41.52 ± 29.45 vs 24.64 ± 16 , 39 μ IU / mL), fasting insulin resistance ($p < 0.001$, 169.63 vs 91.85), HOMA index ($p < 0.001$, $10.25 \pm$

7.5 vs 6.04 ± 4.4). The results of this study found an association of insulin resistance with infertility in obese women ($p < 0.05$).¹³

Insulin resistance can affect the ovulatory cycle of women of reproductive age. Insulin resistance causes high levels of insulin in the blood (hyperinsulinemia). Menstrual cycle disorders that are increasingly rare in women are a result of higher insulin levels. This can be attributed to high androgen levels which are the effects of high insulin levels. The high levels of androgens result in barriers to the aromatization and work of FSH which influence the immaturity of follicles which has an impact on the lack of estrogen produced. If there is a situation like this, there will be no positive feedback on Luteinizing Hormone (LH) so that ovulation does not occur.⁹ This ovulation disorder initially manifested clinically into oligomenorrhea and amenorrhea. If this continues, it will cause infertility.¹⁴

Obesity can be a trigger factor for the occurrence of polycystic ovary syndrome. This is because obesity can cause insulin resistance by increasing the production of free fatty acids so that insulin sensitivity decreases and hyperinsulinemia occurs.¹⁵ High insulin levels associated with insulin resistance can stimulate the ovaries to produce excessive androgen levels. Obesity can cause cholesterol levels to increase and stimulate steroid pathways that will turn cholesterol into androstenedione. Furthermore, androstenedione will be converted to estrogen. High androgen levels can cause the androstenedione conversion process to be disrupted. As a result, androgen levels increase and polycystic ovary syndrome occurs which affects infertility in obese women.⁹

Based on the analysis of the researcher, there is a correlation between insulin resistance and the Body Mass Index (BMI) in obese female infertility associated with ovulatory dysfunction, hyperandrogenemia, and the occurrence of PCOS. Apart from that insulin resistance can also affect the ovulatory cycle of women of reproductive age. Insulin resistance causes high levels of insulin in the blood (hyperinsulinemia). This has an impact on the disruption of ovulation and has an impact on infertility. Therefore there is a need for efforts to control BMI by controlling body weight in women of childbearing age to be in the normal category, other than that it is necessary to

make regular checks of blood sugar levels per six months as an effort to prevent insulin resistance.

CONCLUSION

The results showed that less than half of the respondents (22.2%) experienced insulin resistance in obese women, the average body mass index of respondents was 33.54 ± 3.50 kg/m². There is a correlation between insulin resistance and body mass index in infertility of obese women who have a positive direction and have strong relationship strength.

In identifying the incidence of infertility in obese women there is a need to calculate HOMA-IR. Women of childbearing age should control their weight so that they are in the normal category. Periodic check of blood sugar and insulin levels are needed to prevent insulin resistance.

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