# Effect of Metformin on Fasting Insulin Levels in Non-Diabetic Obese Patients Over 8 Weeks of Time

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## ABSTRACT

**Objective:** To determine the effect of metformin on fasting insulin levels in non-diabetic obese patients over 8 weeks of time.

**Study Design:** Prospective Interventional Study

**Place and Duration of Study:** This study was conducted at the Department of Medicine of Al-Nafees Medical College and Hospital, Islamabad from November, 2020 to May, 2021.

**Materials and Methods:** The study was conducted after the hospital's ethical committee approval, and informed written consent was taken. Patients with obesity having BMI equal to or more than 25 without diabetes mellitus were selected after fulfilling inclusion criteria and sub-categorized on the basis of gender and age. HBA1C and fasting insulin levels were performed. Metformin 1000mg was given to these subjects twice a day for 8 weeks. The fasting insulin levels were repeated after 8 weeks. Collected information was analyzed by using SPSS 23 version

**Results:** A total of 50 random individuals were selected of which 26 (52%) were males and 24 (48%) were females. The mean age of males and females in the study is 32.640 and 36.250. The mean HBA1C of males and females is 5.464 and 5.308 respectively. The mean weight of males and females before drug use is 88.280 kg and 83.458 kg respectively. The mean weight of males and females after drug use is 85.080 kg and 80.208 kg respectively. The average reduction in fasting insulin levels in individuals from 9.112mIU/mL to 7.215mIU/mL during the period of 8 weeks.

**Conclusion:** It has been concluded from this study that metformin significantly lowers fasting insulin levels in obese non-diabetic patients. Early detection and therapy of the obese adolescent with a family history of type 2 diabetes may interrupt the cycle of weight gain and insulin resistance that leads to glucose intolerance in adulthood.

**Key Words:** Non-diabetic Obese, Metformin, Fasting Insulin, Insulin Resistance

## INTRODUCTION

The weight gain is a major concern for all adults. The deleterious effect of obesity are diverse and include an increased risk of premature death, decreased quality of life and as well as diseases. There is a surge in the number of young adults with obesity and a marked increase in the incidence of T2DM.

Obesity was traditionally defined as an increase in body weight that was greater than 20% of an individual's ideal body weight.

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Today obesity is based primarily on measures of height, weight and BMI. Recently, the WHO proposed guidelines for classifying weight status by BMI. BMI represents the relationship between weight and height and is calculated as (weight in kg/height in m2) or as (weight in pounds x 704 / height in inches)[1]. The definition of obesity and its classification has been varying globally. There is much importance on waist circumference and BMI in European guidelines and waist circumference of more than 94 cm in men and 80 cm in women is related to increased visceral fat and increase risk of cardiac diseases. The increased BMI is classified as a BMI of 25 to 29.9 being overweight, 30 to 34.9 is class 1 obesity, 35 to 39.9 is class 2 obesity, and greater than 40 is class 3 according to the U.S. Preventive Services Task Force (USPSTF)[2]. The increase of insulin resistance by obesity is a major risk factor for T2DM and pancreatic fat contents increase proportionally with obesity[3]. It is clear from numerous investigations that intensive lifestyle interventions through diet and exercise can promote weight loss and insulin sensitivity and reduce the risk of developing T2DM. Thus, diet and exercise represent the foundation

of care for all obese individuals and critical components of the approach to therapy[4]. Unfortunately, in clinical practice the long-term success of lifestyle intervention alone is sometimes disappointing and T2DM continues to increase. This has stimulated the search for a potential pharmacological approach to prevent diabetes with obesity[5].

In the treatment, metformin has become a popular choice since its effectiveness, safety and multiple metabolic and cardiovascular benefits[6]. Metformin 1, dimethyl biguanide hydrochloride is a biguanide currently used as an oral anti-hyperglycemic agent. Its primary action appears to be in the inhibition of hepatic glucose production. And the increase in peripheral insulin sensitivity which result in a reduction of circulating insulin levels and reduce fatty acid oxidation. Metformin also reported to improve dyslipidemias in obese and overweight patients. Metformin has potential benefits with regards to dyslipidemias and insulin resistance which in turn can reduce cardiovascular disease. Being overweight or obese increase the chance of Type-2 diabetes. In this disease body makes enough insulin but the cells in the body have become resistant to the salutary action of insulin. Metformin does not increase insulin level in the body but instead the less the amount of sugar the body produces and absorbs as it lowers glucose production in the liver. Metformin also lowers blood sugar by increasing in the body sensitivity to insulin[7].

Rationale of this study is to see the effect metformin on fasting insulin level in obese non-diabetic patients because they showed significant degree of insulin resistance. The hypothesis is that metformin would decrease body weight, BMI and fat mass, improve insulin sensitivity and ameliorate effect of metabolic syndrome. The objective is to determine whether metformin treatment causes decreasing fasting insulin level over 8 week period in obese non-diabetic patients.

## MATERIALS AND METHODS

This prospective study was conducted at the outpatient department, Department of Medicine, Al- Nafees Medical College, and Hospital Islamabad for six months from 15th November 2020 to 15th May 2021 after approval from the hospital's ethical committee. The sample size was calculated (n=50) with a mean in population was 9, variance was 5, confidence level was 95 % and power test was 80 %.

Detailed history regarding the illness was obtained from each patient. A complete clinical examination was performed by the trainee researcher. Informed consent was taken from the patients. 50 patients were included in this study. According to inclusive criteria, patients HBA1C and fasting insulin levels were done. Then metformin 1000mg twice a day was given for 8 weeks period. The fasting insulin levels were repeated after 8 week period. Patients with obesity having BMI equal to

or more than 25 without diabetes mellitus were selected after fulfilling inclusion criteria and subcategorized on the basis of gender and age. HBA1C and fasting insulin levels were performed. The metformin 1000mg was given to these subjects twice a day for 8 weeks period. The fasting insulin levels were repeated after 8 weeks period.

Data were analyzed by SPSS version 23. Quantitative variables like age, gender, mean and SD were calculated. Following the therapy by metformin, fasting insulin levels were documented at the start of study and 8 weeks were compared for statistical significance with the help of chi-square, p value of less than or equal to 0.05 was considered statistically significant.

## RESULTS

A total of 50 patients were selected of which 26 (52%) were male and 24 (48%) were male in our study as shown in Figure-1. The mean age of males and females in the study is 32.640 and 36.250. The mean HBA1C of males and females is 5.464 and 5.308 respectively as shown in Table 1.
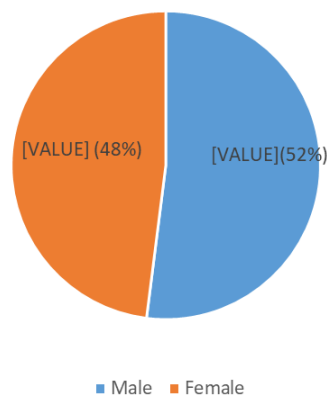


■ Male ■ Female

**Figure No.1: Frequency distribution of Gender (n=50)**

**Table No.1: Results of HbA1c in study group (n=50)**

| Sex | Size | Mean | Std. Dev | Std. Error | C.I. of Mean |
|-----|------|------|----------|-----------|--------------|
| Male | 26 | 5.464 | 0.549 | 0.110 | 0.227 |
| Female | 24 | 5.308 | 0.419 | 0.0855 | 0.177 |

The mean weight of males and females before drug use is 88.280 kg and 83.458 kg respectively and the mean weight of males and females after drug use at 8 weeks is 85.080 kg and 80.208 kg respectively as shown in Table -2. In this study, the weight loss in patients have been evident and the estimated average weight loss in both male and female is about 3.2 kg under treatment with 1000mg metformin twice daily for a period of 8 weeks in obese non-diabetic individuals. The average reduction in Fasting Insulin levels in individuals from 9.112mIU/mL to 7.215mIU/mL during the period of 8 weeks is shown in Table -3.

**Table No.2: Comparison of weight of patients before treatment and at 8 week with metformin use (n=50)**

| Weight of patients before treatment | | | | | |
|---|---|---|---|---|---|
| Sex | Size | Mean | Std. Dev | Std. Error | C.I. of Mean |
| Male | 26 | 88.280 | 16.552 | 3.310 | 6.832 |
| Female | 24 | 83.458 | 13.756 | 2.808 | 5.808 |
| Weight of patients at 8 weeks with metformin use | | | | | |
| Sex | Size | Mean | Std. Dev | Std. Error | C.I. of Mean |
| Male | 26 | 85.080 | 16.938 | 3.388 | 6.992 |
| Female | 24 | 80.208 | 13.733 | 2.803 | 5.799 |

**Table No.3: Comparison of fasting insulin level of patients before treatment and at 8 week with metformin use (n=50)**

| Fasting insulin level | Size | Mean | STD dev | STD error | CI of mean | p value |
|---|---|---|---|---|---|---|
| Before treatment | 50 | 9.112 | 6.546 | 0.945 | 1.901 | 0.001 |
| At 8 week | 50 | 7.215 | 6.414 | 0.926 | 1.863 | |

# DISCUSSION

In developing and developed countries, the common occurrence of overweight and obesity is increasing.[8] Obesity is related to chronic diseases including diabetes, hypertension and metabolic syndrome. These are accompanying metabolic abnormalities of insulin resistance. Insulin resistance is a condition in which a given amount of insulin produces a subnormal biological response. It is characterized to suppress hepatic glucose production and output by decreasing the ability of insulin to stimulate the use of glucose by muscles and adipose tissues[9].

Fasting insulin predicts insulin resistance with accuracy. If a person loses a considerable amount of weight, insulin resistance can be further reduced[10]. Fasting insulin level is between 3-8 mIU/ml (18-48 pmol/L). It is a test to measure the amount of insulin in the human body and to monitor insulin[11].

In this study, the weight loss in patients have been evident and the estimated average weight loss in both male and female is about 3.2 kg under treatment with 1000mg metformin twice daily for a period of 8 weeks in obese non-diabetic individuals. Similarly, in another study, the mean weight loss in the metformin-treated group was 5.8±7.0 kg (5.6±6.5%) [12].

Another study was done in Regensburg, Germany in Endocrinology Department in outpatients. For endocrine patients, they included overweight and obese patients, desiring to lose weight for insulin resistance during the period of 18 months. Patients who chose not to take medication as a means to reduce weight served as a controlled group. In this study average weight loss of 5.8 kg under treatment with metformin for 6 months. Untreated controlled gained weight of about 0.8 kg on average. Patients with severe insulin resistance lose significantly more weight as compared insulin sensitive patients[13].

In this study, non-diabetic obese individuals were chosen for metformin medication for 8 weeks. All patients agreed to refrain from diet programs as well as the change of habits in physical exercise for the time of the study and were regularly questioned on that issue. The mean value of fasting insulin of non-diabetic obese individuals before taking metformin was 9.112mIU/ml. After taking metformin the mean value of fasting insulin turned out to be 7.215mIU/ml. The study was done by Nidhi Sharma, Siriesha and Vineet kaur on polycystic ovarian disease in which the patients were randomized to receive metformin 500mg twice daily or a placebo for a total of 6 months. Reduction in fasting insulin levels from 31.3 to 19.3 mIU/ml. In contrast placebo group in which fasting insulin did not change[14]. A systematic review and meta-analysis in 2018 by Sun, Juan MN, Wang, et al on the effects of metformin on insulin resistance in overweight or obese children and adolescents. Their work shows effectiveness in reducing BMI in obese children and also improving insulin resistance in obese children[15].

Metformin was well tolerated by the majority of patients[16].

# CONCLUSION

In our data suggest that if metformin is administered to obese patients in high doses is a beneficial and cost-effective drug to reduce weight. It has been concluded from this study that metformin significantly lowers fasting insulin levels in obese non-diabetic patients. Early detection and therapy of the obese adolescent with a family history of type 2 diabetes may interrupt the cycle of weight gain and insulin resistance that leads to glucose intolerance in adulthood.

**Limitations and Recommendations:** Our study has the following limitations
1.      The duration of our study was short
2.      The study was single-center study
3.      Sample size limited

We recommend a longer study may be conducted at multiple centers to briefly address the efficacy of metformin as a weight-reducing agent and decreasing fasting insulin level.

**Author's Contribution:**

| | |
|---|---|
| Concept & Design of Study: | Syed Saif Ur Rehman |
| Drafting: | Syed Hur Hussain Hamdani, Safdar Hussain |
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| Revisiting Critically: | Rehan Sarwar |
| Final Approval of version: | Syed Saif Ur Rehman |

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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