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Original Research Article

PREDICTORS OF WEIGHT CHANGE DURING METFORMIN THERAPY IN ADULTS WITH TYPE 2 DIABETES : AN OBSERVATIONAL COHORT STUDY

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ABSTRACT

Background: Metformin is the most prescribed first-line medication for people with type 2 diabetes mellitus (T2DM). In addition to its blood sugar-lowering effect, metformin is known to be associated with weight stabilisation or even slight weight reduction. However, the amount and type of weight changes are highly variable with metformin. This study aims to determine the weight-reducing potential of the antihyperglycemic agent. Understanding other factors causing weight changes could help improve treatment plans and metabolic outcomes.

Materials and Methods: This prospective observational cohort study was conducted on an outpatient basis. We used consecutive sampling during routine outpatient visits to enrol 300 adult patients with type 2 diabetes mellitus who had been on metformin for at least six months.

We gathered demographic, clinical, and metabolic information of the participants at baseline. For three months, we conducted follow-ups and recorded their body weight. Data was analysed using paired t-tests and regression modelling to assess weight changes and identify variables that may contribute to weight loss.

Results: The participants had an average age of 52.4 years, with a standard deviation of 9.3 years. The group was made up of 54% men and 46% women. At the beginning of the study, the average body mass index (BMI) was 28.3 kg/m², with a standard deviation of 4.2 kg/m².

During the follow-up period, 42% of patients lost weight, 36% maintained their weight, and 22% gained weight. A higher baseline BMI and a shorter duration of diabetes were strongly correlated with weight loss with metformin medication. Age showed a substantial correlation with weight change, whereas gender did not.

Conclusion: Metformin medication is linked to moderate weight loss in a significant number of individuals with type 2 diabetes. Baseline BMI and diabetes duration appear to be major predictors of weight change. This shows how vital it is to analyse each patient individually when managing diabetes. With appropriate lifestyle changes, we can postulate that the treatment results can be further optimised.

Keywords: Metformin, Type 2 Diabetes Mellitus, Weight Change, Body Mass Index, Predictors, Glycemic Control.

INTRODUCTION

Metformin is often considered the first-line pharmacological therapy for type 2 diabetes mellitus (T2DM) because it is safe, lowers blood glucose levels, and offers additional metabolic benefits. What distinguishes metformin from many other diabetes medicines is that therapy can alter body weight. Metformin is typically considered weight-neutral, or slightly weight-reducing. This is unlike insulin, sulfonylureas, and other glucose-lowering medications, which are associated with weight gain.

Nonetheless, research and clinical experience indicate that the amount and direction of weight change from metformin therapy are highly individualised. While most individuals experience little or no weight loss, some patients may lose significant weight. This implies that a wide range of physiological, behavioural, and metabolic factors may influence weight during this treatment. So, it is critical to understand the factors involved in metformin therapy to improve diabetes control and achieve better overall metabolic health outcomes.[1]

Management of type 2 diabetes requires attention to body weight, as weight gain, particularly abdominal adipose tissue, promotes insulin resistance and worsens metabolic dysregulation. Furthermore, blood glucose control, diabetes medication effectiveness, and heart disease risk all benefit from seemingly insignificant weight reductions. Metformin is an antidiabetic agent that reduces blood glucose levels, in part, by inhibiting hepatic gluconeogenesis. As such, it increases insulin sensitivity and glucose uptake by skeletal muscle. Additional weight-related effects from Metformin may include appetite suppression, changes in gastric hormone secretion, alterations in gut microbiome composition, and increased caloric expenditure. The cumulative effects described make Metformin an appropriate agent in the management of diabetes for patients who are overweight or obese.[2]

Many patients enrolled in Metformin studies tend to either maintain or lose weight. However, the degree of weight change differs markedly. Numerous studies have investigated the effects of Metformin on body weight and have characterised weight change by demographic, clinical, or biochemical attributes. The weight-reducing effects of Metformin vary according to patients' body mass index (BMI), age, sex, diabetes duration, and certain modifiable lifestyle factors such as dietary habits and exercise. Individuals with a higher baseline BMI tend to lose more weight during treatment than those with a lower baseline BMI do.

Similarly, younger patients and those recently diagnosed with diabetes might behave differently than patients who have had diabetes for an extended period, due to variations in insulin resistance and metabolic flexibility.[3]

Weight loss is heterogeneous because several metabolic variables, such as glycaemic control, insulin resistance, lipids, and hormones, vary among individuals. For example, among those who are less insulin-sensitive, metformin could promote significant weight loss by improving insulin sensitivity and decreasing hyperinsulinemia, which is associated with fat tissue development. Interestingly, some individuals may lose weight without actively trying to do so, as metformin can induce appetite suppression and reduced eating as a common side effect. These changes tend to be temporary and likely constitute only a small portion of the differences between the groups.[4]

Various physiological and genetic factors may explain weight loss or weight gain in individuals taking metformin. Some genes, including the organic cation transporters (OCTs), are involved in the transport, metabolism, and utilisation of energy for drugs. These genes could be of relevance to the actions of metformin and its effects on metabolism. A study published this year has identified potential genetic factors that may account for differences in weight loss or gain associated with a given drug. Lastly, an important aspect of metformin's effect on weight reduction and the treatment of other metabolic disorders is its effect on the gut microbiome.[5]

Extending consideration to lifestyle modifications and various modalities of psychotherapy, alongside pharmacologic treatment, is equally important. Patients on metformin are routinely counselled to adopt dietary modifications and engage in physical activity of the order of the recommended level of intensity to achieve a meaningful reduction in body weight. For this reason, in clinical studies, disentangling the impact of metformin from lifestyle modifications is a tedious process. Furthermore, this prescription, when combined with other antidiabetic agents, can influence the dynamics of body weight change. Depending on the pharmacokinetic properties of the concurrent agent, it may induce greater weight loss, attenuate weight loss, or promote weight gain.[6]

A healthcare provider is responsible for understanding the factors that may influence a patient's body weight while receiving metformin. By establishing these factors, the clinician can construct a more optimised management plan, provide more precise direction to the patient, and set a more realistic aim for psychotherapy. Furthermore, identifying such patients may facilitate the implementation of earlier lifestyle modifications or pharmacologic interventions to improve metabolic equilibrium.

Considering the ongoing global rise of obesity and type 2 diabetes, understanding the influence of individual characteristics on weight response during metformin therapy is important to improve long-term management of the disease and its associated complications.[7–10]

This study aims to identify individual characteristics associated with weight change among persons with type 2 diabetes on metformin therapy. Specific objectives include quantifying weight change during treatment and identifying the demographic, clinical, and metabolic characteristics associated with weight gain, weight loss, or no change in weight among patients.

MATERIALS AND METHODS

Research Design: Prospective observational cohort research.

Study setting and Population: Adults with type 2 diabetes who were scheduled for regular outpatient visits.

Sample Size: The study included 300 patients.

Method of Sampling: Consecutive sampling was utilized, which means that eligible patients who came in for routine outpatient appointments were enrolled one after the other until the sample size was reached after obtaining informed consent.

Inclusion Criteria:

- Adults with type 2 diabetes mellitus.
- Patients who have been taking metformin for at least the last six months.
- Patients who are willing to take part in the study and give their informed consent.

Exclusion Criteria:

- Patients with illnesses that alter body weight, including chronic systemic illness, cancer, or endocrine abnormalities.
- Patients taking drugs that are known to affect body weight.
- Women who are pregnant or breastfeeding.

Study Duration / Follow-up: Patients were assessed throughout a 3-month observation period.

Data entry into spreadsheets was performed using Microsoft Excel, while subsequent analyses were conducted using SPSS version 27.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Continuous variables were presented as mean ± standard deviation, while categorical variables were presented as counts and percentages. The unpaired t-test was used for between-group comparisons of continuous variables, whereas the paired t-test was used for within-group comparisons. The chi-square test or Fisher's exact test was used for analyses of categorical variables. Statistical significance was set at $p < 0.05$.

RESULTS

Table 1: Baseline Demographic Characteristics of Study Participants (n = 300)

Variable		Number (n)	Percentage (%)
Age Group (years)	30–40	48	16
	41–50	96	32
	51–60	102	34
	>60	54	18
Gender	Male	162	54
	Female	138	46
Mean Age (years)		52.4 ± 9.3	

Table 2: Baseline Clinical and Metabolic Characteristics

Parameter	Mean ± SD
Body Weight (kg)	76.5 ± 11.2
Body Mass Index (kg/m²)	28.3 ± 4.2
Duration of Diabetes (years)	6.1 ± 3.4
Fasting Blood Sugar (mg/dL)	152.6 ± 38.4
HbA1c (%)	8.2 ± 1.3

Table 3: Weight Change After Follow-up

Weight Change Category	Number (n)	Percentage (%)
Weight Loss (>2 kg)	126	42
Weight Neutral (±2 kg)	108	36
Weight Gain (>2 kg)	66	22
Mean Weight Change:	1.8 ± 3.1 kg	

Table 4. Association Between Baseline BMI and Weight Change

BMI Category	Weight Loss (n=126)	Neutral (n=108)	Weight Gain (n=66)	P value
Normal (<25)	18	39	30	0.003
Overweight (25–29.9)	54	45	21	
Obese (≥30)	54	24	15	

Table 5. Association of Age and Gender with Weight Change

Variable		Weight Loss (n=126)	Neutral (n=108)	Weight Gain (n=66)	P value
Age (years)	≤50	60	39	18	0.021
	>50	66	69	48	
Gender	Male	72	57	33	0.48
	Female	54	51	33	

Table 6: Predictors of Weight Loss During Metformin Therapy

Variable	Odds Ratio (OR)	95% CI	P value
Higher BMI (≥30 kg/m²)	1.92	1.18 – 3.12	0.008
Shorter duration of diabetes (<5 yrs)	1.64	1.01 – 2.68	0.041
Baseline HbA1c >8%	1.53	0.95 – 2.46	0.07
Age <50 years	1.44	0.89 – 2.32	0.11

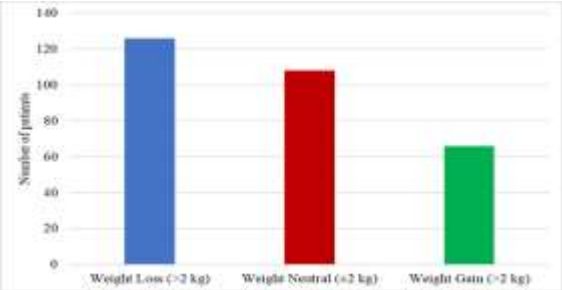

Figure 1: Weight Change After Follow-up

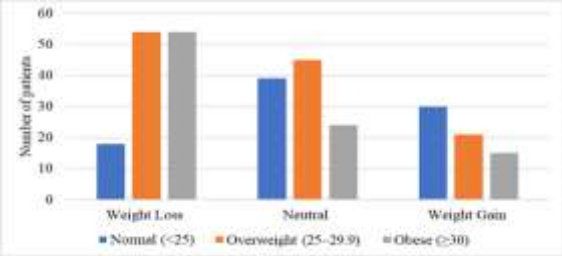

Figure 2: Association of Age and Gender with Weight Change

[Table 1] Initial Demographic Characteristics

The research included 300 adults diagnosed with type 2 diabetes mellitus. Most participants were between 51 and 60 (34%), followed by those between 41 and 50 (32%). The group was composed of 16% of people aged 30-40 and 18% aged 60+. The subjects in the study were, on average, 52.4 years old, with a range of 9.3 years. There were 162 men (54%) and 138 women (46%) among the patients. This suggests that there were a few more male than female patients on metformin.

[Table 2] Initial Clinical and Metabolic Characteristics

The participants' initial clinical data indicated that the mean body weight was 76.5 ± 11.2 kg and the mean body mass index (BMI) was 28.3 ± 4.2 kg/m². This suggests that many of the patients were either overweight or obese. People with diabetes had it for an average of 6.1 years. The mean fasting blood sugar level was 152.6 ± 38.4 mg/dL, while the mean HbA1c level was 8.2 ± 1.3%. This indicates that numerous individuals exhibited inadequate glycemic control prior to the commencement of the trial.

[Table 3] Weight Change After Follow-up

During the study period, 42% of patients (n=126) lost more than 2 kg of weight, whereas 36% (n=108) maintained their weight with only minor fluctuations of ±2 kg. A smaller number, 22% (n=66), gained more than 2 kg. The average weight change during the study was −1.8 ± 3.1 kg, suggesting that participants who used metformin were slightly more likely to lose weight.

[Table 4] Relationship Between Initial BMI and Weight Change

A significant association was observed between baseline BMI and weight fluctuations after metformin administration. More people with a normal BMI either maintained their weight or gained weight. People who were overweight or obese, on the other hand, were more likely to lose weight. For instance, 54 overweight people lost weight, whereas 15 gained weight. Statistical analysis indicated a strong correlation between baseline BMI and weight change ($p = 0.003$). This suggests that people who took metformin and had a higher BMI were more likely to lose weight.

[Table 5] The relationship between age, gender, and weight changes

We also looked at how changes in age, gender, and weight were linked. Patients aged 50 years or younger (n=60) exhibited greater weight loss than those aged 50 years or older (n=66). Conversely, older individuals were more prone to maintain or increase their weight. There was a statistically significant correlation between age and weight change ($p = 0.021$). But gender didn't have a major effect on weight change ($p = 0.48$) because men and women lost, stayed the same, or gained about the same amount of weight.

[Table 6] Factors causing weightloss while on metformin

We employed logistic regression to identify independent predictors of weight loss among individuals on metformin. A higher baseline BMI (≥30 kg/m²) was a robust predictor of weight loss, with an odds ratio (OR) of 1.92 (95% CI: 1.18–3.12, $p = 0.008$). Moreover, having diabetes for fewer than five years was significantly associated with weight loss (OR = 1.64, $p = 0.041$). Even though people with a baseline HbA1c level above 8% and younger than 50 years tended to lose more weight, these characteristics did not reach statistical significance. These data show that the patient's starting BMI and how long they have had diabetes are important factors that affect their weight when they are taking metformin.

DISCUSSION

[Table 1] Basic Information About the Participants

Most of the people who answered this study were between the ages of 51 and 60. The average age was 52.4 years, and there were a few more men (54%) than women (46%). This demographic trend corresponds with the epidemiological profile of type 2 diabetes mellitus in developing countries, where the ailment is primarily seen in middle-aged and older adults. Mohan et al. observed a similar age pattern: most people with type 2 diabetes in their South Indian sample were aged 50-60. This demonstrates that insulin resistance and metabolic dysfunction exacerbate with advancing age.[11] Wild et al. have observed that the incidence of type 2 diabetes markedly increases after age 45, especially in regions experiencing rapidurbanisation and lifestyle changes.[12] Our study found that men were slightly more likely to be affected than women, which is consistent with Hu et al.'s findings. They found that men were more likely to get diabetes because of differences in their lifestyles, such as being inactive,

eating poorly, and having too much fat around their stomachs,[13] Because these groups are so similar, it's likely that the subjects in this study are similar to most people taking metformin in terms of demographics.

[Table 2] Baseline Clinical and Metabolic Characteristics

The average BMI of 28.3 ± 4.2 kg/m² in this study demonstrates that many of the patients were overweight or obese, which is a known risk factor for type 2 diabetes. Knowler et al. found the same results in the Diabetes Prevention Program, which showed that people with higher BMIs were more likely to have insulin resistance and poor glucose metabolism.[14] The mean HbA1c level of 8.2 ± 1.3% in our study indicates that some patients had difficulty regulating their blood glucose at the outset. Turner et al. found something similar in the UK Prospective Diabetes Study: patients who started metformin therapy had baseline HbA1c levels above 8%.[15] People with type 2 diabetes who have recently started treatment or are not getting the right care have high levels of fasting blood sugar and HbA1c. This shows that beta-cell dysfunction worsens over time. These studies show how important it is to use drugs like metformin and to make lifestyle changes to achieve better glycaemic and metabolic outcomes.

[Table 3] Change in Weight After Follow-Up

The study found that 42% of patients lost weight, 36% remained the same, and 22% gained weight during follow-up. Aroda et al. reported that patients in the Diabetes Prevention Program who used metformin lost an average of 2-3 kg over time.[16] Golay et al. also reported that metformin caused small but significant weight loss by reducing hunger and improving insulin sensitivity.[17] The different weight changes observed in this study are similar to those reported in other studies, which show that metabolic and behavioural factors determine the extent of weight change following therapy.

[Table 4] The Link Between Baseline BMI and Weight Loss

In this experiment, there was a statistically significant link between baseline BMI and weight loss ($p = 0.003$). People who were overweight or obese were more likely to lose weight than people who were not overweight or obese. This finding is in line with the study by Seifarth et al., which found that those with a higher baseline BMI lost more weight after taking metformin because their insulin sensitivity increased and their liver's glucose production decreased.[18] Glueck et al. found that obese patients who were given metformin lost a lot of weight and visceral fat compared to people with a normal BMI.[19] The medicine may help overweight people lose more weight because it speeds up their metabolism and lowers hyperinsulinemia, which is a primary reason why people retain fat. It seems that baseline BMI is a key factor in how much weight changes after taking metformin.

[Table 5] Age and Gender Influencing Weight Change with Metformin.

The current investigation demonstrated a robust connection between age and weight change ($p = 0.021$). Younger people were more likely to lose weight than older people. This conclusion aligns with Nathan et al.'s finding that younger patients tend to have better metabolic responses to antidiabetic drugs because their pancreatic beta-cell function is still mostly intact and they are better able to respond to lifestyle changes.[20] On the other hand, gender did not have a statistically significant effect on weight change in this study. Numerous clinical studies demonstrated similar outcomes, indicating that weight reduction following metformin administration was not influenced by gender differences. These results suggest that while age-related metabolic factors may influence therapy response, gender alone may not be a significant predictor of weight change.

[Table 6] Factors affecting weight loss while on metformin

This study used logistic regression to find that higher baseline BMI and shorter diabetes duration were two critical characteristics that predicted weight loss after taking metformin. Individuals with a BMI of 30 kg/m² or more were nearly twice as likely to experience weight loss compared to those with a lower BMI. These results are in line with previous research showing that obese people derive greater metabolic benefits from metformin because it affects insulin signalling and hepatic glucose production. People who had diabetes for a shorter time also lost more weight. This is likely because their insulin sensitivity and pancreatic beta-cell function were still strong. Previous research has also shown that starting metformin early may aid with weight loss and better metabolic control. Our research showed that higher HbA1c levels and younger age were associated with greater weight loss, although these differences were not statistically significant. This means that many metabolic factors work together to determine how much weight patients lose during treatment.

CONCLUSION

In summary, this study showed that metformin can help many individuals with type 2 diabetes mellitus achieve modest weight loss, although responses may vary. Around 42% of participants lost a lot of weight, while the rest either maintained their weight or gained a little. The results demonstrate that a person's baseline body mass index and the duration of diabetes are very important forthe weight they lose after taking metformin. Individuals with a higher BMI at the commencement of the trial and a shorter duration of diabetes were more inclined to experience weight loss. This means that starting metformin medication early and treating people who are overweight or obese may help their metabolism work better. Age was substantially correlated with weight change; gender did not significantly affect weight response. These results demonstrate the importance of considering each patient's distinct clinical and

metabolic characteristics when evaluating therapeutic efficacy. Moreover, these findings offer practical evidence for the ongoing endorsement of metformin as first-line therapy for most people with type 2 diabetes.

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