ORIGINAL ARTICLE

Investigating body composition and body mass index using oral hypoglycemic agents and insulin therapy in type 2 diabetes mellitus

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ABSTRACT

Background and aim: Type 2 diabetes mellitus (T2DM) is increasingly prevalent worldwide, and pharmacological therapy is essential for glycemic control. Insulin therapy (IT) and oral hypoglycemic agents (OHA) are commonly used, but they may have different effects on body composition. This study aimed to compare body composition between patients with T2DM receiving IT and those receiving OHA.

Methods: A comparative cross-sectional study was conducted among 314 patients with T2DM at a tertiary hospital in Banda Aceh, Indonesia. Participants were divided equally into IT and OHA groups (n=157 each). Body composition was assessed using bioelectrical impedance analysis, and data were analyzed using independent t-tests, and multiple linear regression.

Results: Patients treated with IT had significantly higher body weight, BMI, body fat, muscle mass, bone mass, muscle quality score, physique rating, and visceral fat compared with those on OHA (all $p<0.05$). No significant differences were observed in basal metabolic rate, metabolic age, total body water, or body height. Regression analysis showed that BMI and gender were the strongest predictors of body fat, muscle mass, and visceral fat, while age was associated with muscle quality and metabolic age.

Conclusion: Insulin therapy in patients with T2DM was associated with higher adiposity and altered body composition compared with OHA use. Routine monitoring of body composition and targeted lifestyle interventions should be integrated into the management of T2DM patients receiving insulin. (www.actabiomedica.it)

Key words: diabetes mellitus, insulin therapy, oral hypoglycemic agents, body composition, BMI

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Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by hyperglycemia resulting from impaired insulin secretion, insulin resistance, or both. Its global prevalence continues to rise, with an estimated 537 million adults affected in 2021, projected to reach 783 million by 2045 (1). Indonesia ranks among the countries with the highest burden of T2DM in Southeast Asia and globally. The 2023 National Health Survey (Survei Kesehatan Indonesia/SKI) reported a diabetes prevalence of 11.7% among individuals aged ≥15 years, reflecting a steady increase from the RISKESDAS 2018 findings (2). According to the International Diabetes Federation, Indonesia ranked fifth worldwide in 2021, with approximately 19.5 million adults (aged 20–79 years) living with diabetes (3). Despite this high burden, substantial care gaps remain: nearly 70% of cases are undiagnosed, only about two-thirds of diagnosed patients receive treatment, and less than one-third achieve adequate glycemic control (4). This uncontrolled state contributes to the high prevalence of microvascular complications (retinopathy, neuropathy, nephropathy) and macrovascular complications (coronary heart disease, stroke, peripheral arterial disease) in the Indonesian population (5,6). Pharmacological therapy is a cornerstone of management for T2DM, comprising a range of treatments from traditional oral hypoglycemic agents (OHAs) to newer classes such as sodium-glucose cotransporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists (7). Metformin remains the most widely recommended first-line therapy due to its efficacy in improving glycemic control and its relatively favourable safety profile, including weight neutrality or modest weight loss benefits (8), compared to other agents (e.g, sulfonylureas and thiazolidinedione), which can sometimes be associated with weight gain or other metabolic complications (7). OHAs like sulfonylureas and thiazolidinediones (TZDs) are still frequently utilized, although they carry risks; sulfonylureas can lead to hypoglycemia, and TZDs are associated with weight gain (7). Sulfonylureas, specifically glibenclamide, are associated with a high risk of hypoglycemia, weight gain, skin rashes, and concerns regarding cardiovascular outcomes. This risk condition causes oral food intake to be disrupted and insufficient for body needs, leading to changes and a reduction in the composition of body fat and weight of patients (9). The introduction of SGLT2 inhibitors, such as empagliflozin and canagliflozin, has transformed the treatment landscape by offering dual benefits of glycemic control and weight reduction while also positively impacting cardiovascular endpoints, particularly in patients with concurrent heart failure or chronic kidney disease. For instance, studies have illustrated that SGLT2 inhibitors result in a significant reduction in body weight due to increased urinary glucose excretion (10). Additionally, sodium-glucose cotransporter 2 (SGLT2) inhibitors and glucagon-like peptide 1 receptor agonists (GLP1-RA) can provide cardiovascular and renal protection to maintain glycemic control effects (11,12). Previous studies have shown that OHAs and IT may have distinct effects on body weight and body composition. Metformin is often weight-neutral or associated with modest weight loss (8), while insulin is typically associated with weight gain and increased fat mass (13). The use of IT is associated with weight gain relative to the level of dose administered (14). However, the impact of long-term OHA and IT use on detailed body composition parameters, such as fat mass, muscle mass, visceral fat, and bone mass, remains less well established, particularly in Southeast Asian populations. Therefore, this study aimed to compare the body composition of T2DM patients receiving insulin therapy and those receiving oral hypoglycemic agents in a tertiary hospital in Banda Aceh, Indonesia. Understanding these differences may provide insight into optimizing treatment strategies and mitigating therapy-related metabolic risks.

Methods and Materials

Study design

This was a comparative cross-sectional study conducted at Dr. Zainoel Abidin Regional General Hospital, Banda Aceh, Indonesia. The study was approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Syiah Kuala (No.035/EA/FK-RSUDZA/2023). Written informed consent was obtained from all participants.

Population, sample, and setting

A total of 314 patients with T2DM were recruited using purposive sampling and divided into two groups: 157 patients receiving insulin therapy (IT) and 157 patients receiving oral hypoglycemic agents (OHA). Inclusion criteria were T2DM patient receiving either IT or OHA for at least six months. Exclusion criteria were the presence of diabetic foot ulcers or other acute complications and incomplete clinical or demographic data.

Data collection and measurement

Sociodemographic and clinical data were obtained using a structured questionnaire and medical records, including age, sex, education level, occupation, duration of T2DM, and duration of therapy. Body composition was measured using a validated Bioelectrical Impedance Analysis (BIA). The parameters assessed were body weight and height, body mass index (BMI), muscle mass, body fat, body water content, visceral fat, basal metabolic rate (BMR), and bone mass. All measurements were conducted by trained research assistants following standardized protocols.

Outcomes

The primary outcome was the difference in body composition parameters between the IT and OHA groups. Secondary outcomes included the association of sociodemographic and clinical factors with body composition.

Data analysis

Data were analyzed using SPSS version 16. Continuous variables were expressed as mean ± standard deviation (SD) and compared using independent t-tests. Categorical variables were expressed as frequencies and percentages, analyzed using chi-square tests. Multiple linear regression analyses were performed to identify independent sociodemographic and clinical predictors of body composition parameters. A p-value <0.05 was considered statistically significant.

Results

Demographic data

A total of 314 patients with T2DM were included, with 157 in the insulin therapy (IT) group and 157 in the oral hypoglycemic agent (OHA) group. The mean age was 60 ± 9.5 years in the IT group and 59 ± 9.5 years in the OHA group. The gender distribution was comparable between groups (IT: 43.3% male, 56.6% female; OHA: 45.8% male, 54.1% female). The mean duration of diabetes was significantly longer in the IT group compared to the OHA group (11.2 ± 7.1 vs. 8.3 ± 6.7 years, p<0.001). Education and occupational status were similar between groups. Detailed sociodemographic and clinical characteristics are presented in Table 1.

Body composition measurements

Table 2 shows the differences in body composition between IT and OHA groups. Patients treated with insulin had higher values for most body composition measures compared with those receiving OHA, except for body height, BMR, metabolic age, and total body water (TBW). Significant differences were observed in body weight (p<0.001), body mass index (BMI) (p<0.001), body fat (p<0.001), muscle mass (p<0.001), muscle quality score (p=0.001), physique rating (<0.001), bone mass (p=0.007), and visceral fat rating (p=0.047) between both groups. No significant differences were found in body height (p=0.256), BMR (p=0.154), metabolic age (p=0.122), or total body water (p=0.330). The detail of the difference in body composition of the respondents is presented in Table 2.

BMI classification differed significantly between groups (p=0.001). In the OHA group, most patients were in the normal weight category (59.9%), whereas in the IT group a larger proportion were overweight (42.0%) or obese (24.8%). Only 0.6% of IT patients were underweight, compared with 7.0% in the OHA group. Detailed distributions are shown in Table 3.

Multiple regression analysis

Multiple linear regression identified several independent predictors of body composition in the IT group (Table 4). Key findings are as follow. Body fat

Table 1. Sociodemographic and clinical characteristics of respondents.

Characteristics	Total (%)	IT n (%)	OHA n (%)	*X2 or t*	*p-value*
Age (M±SD)	59 + 9.5	60 + 9.5	59 + 9.5	0.858	0.392
Gender Male Female	140 (44.4) 174 (55.4)	68 (43.3) 89 (56.6)	72 (45.8) 85 (54.1)	0.000	1.000
Education Elementary High school University	39 (12.4) 143 (45.5) 132 (42)	16 (10.1) 67 (42.6) 74(47.1)	23 (14.6) 76 (48.4) 56 (35.6)	6.163	0.187
Occupation Not working Irregular job Formal job Retired	118 (37.5) 69 (21.9) 46 (14.6) 81 (25.7)	59 (37.5) 31 (19.7) 23 (14.6) 44 (28)	59 (37.5) 38 (24.2) 23 (14.6) 37 (23.5)	10.512	0.311
Having DM (year)	9.80 + 7.01	11.2 + 7.06	8.32 + 6.66	3.797	0.000

Table 2. The difference in body composition between OHA and IT groups.

Body composition	Range score (unit)	IT (n=157)	OHA (n=157)	t-test	*p-value*
Body height	cm	158 (7.79)	159 (7.39)	-1.13	0.256
Body weight	kg	68.9 (12.2)	61.2 (12.3)	4.72	<0.001
Body mass index	kg/m^2	27.3 (4.62)	24.0 (4.47)	6.47	<0.001
Body fat	%	32.9 (9.77)	27.7 (9.95)	4.62	<0.001
Muscle mass	kg	43.1 (8.98)	39. 4 (8.70)	3.75	<0.001
Muscle quality score	point	42.9 (10.6)	38.5 (12.8)	3.32	0.001
Physique rating	1-9*	3.19 (1.53)	4.04 (1.52)	-4.94	<0.001
Bone mass	kg	2.81 (2.85)	2.18 (0.51)	2.72	0.007
Visceral fat rating	1-59*	11.6 (4.30)	2.18 (2.85)	1.99	0.047
Basal metabolic rate	kcal	1307 (267.6)	1267 (221.5)	1.430	0.154
Metabolic age	year	58.5 (10.3)	60.4 (11.6)	-1.55	0.122
Total body water	%	45.07 (35.9)	38.7 (7.56)	2.14	0.330

Abbreviations: IT: Insulin therapy; OHA: Oral hypoglycemic agents.

Table 3. The difference in BMI between OHA and IT in T2DM.

Body mass index	Total (%)	IT n (%)	OHA n (%)	X^2	*p*
Underweight	12 (3.8)	1 (0.64)	11 (7.01)	39.25	0.001
Normal	145 (46.2)	51 (32.48)	94 (59.87)		
Overweight	101 (32.2)	66 (42.04)	35 (22.29)		
Obese	56 (17.8)	39 (24.84)	17 (10.83)		

Table 4. Multiple regression analysis for the detailed body composition of IT respondents.

Variable	β-Coefficient	*p-value*
Body fat		
Gender	0.405	<0.001
BMI	0.571	<0.001
Muscle mass		
Gender	0.038	<0.001
Length of therapy	0.078	0.067
Height	0.061	<0.001
Weight	0.044	0.003
BMI	0.117	<0.001
Muscle quality		
Age	0.080	<0.001
Physique rating		
Age	0.011	0.083
Having DM	-0.177	0.027
Length of therapy	0.207	0.009
BMI	-0.218	0.350
Visceral fat		
Age	0.190	<0.001
Gender	-0.585	<0.001
Having DM	-0.131	0.002
Length of therapy	0.113	0.008
BMI	0.542	<0.001
Basal metabolic rate		
Gender	-0.142	0.001
Having DM	-0.125	0.005
Body height	0.461	<0.001
Body weight	0.220	<0.001
BMI	0.468	<0.001
Metabolic age		
Age	0.512	<0.001
BMI	0.448	<0.001
Total body water		
Length of therapy	-0.206	0.011
BMI	-0.200	0.056

was significantly associated with gender (β=0.405, p<0.001) and BMI (β=0.571, p<0.001). Muscle mass was associated with gender (β=0.038, p<0.001), height (β=0.061, p<0.001), weight (β=0.044, p=0.003), and BMI (β=0.117, p<0.001). Muscle quality score was associated with age (β=0.080, p<0.001). Visceral fat rating was influenced by age, gender, duration of diabetes, therapy duration, and BMI (all p<0.01). BMR was associated with gender, duration of diabetes, body height, weight, and BMI (all p<0.01). Metabolic age was associated with age (β=0.512, p<0.001) and BMI (β=0.448, p<0.001). Total body water was influenced by therapy duration (β=−0.206, p=0.011).

Discussion

Body composition and growth are major components of personal and community health status. Body composition is defined as the nutritional assessment of body components (15). Body composition plays a crucial role in assessing the health status of a person (16), and affected by age, weight, height, waist circumference, serum creatinine levels, alcohol consumption status, physical activity, and smoking history (14). This study compared body composition in patients with T2DM treated with insulin therapy (IT) versus oral hypoglycemic agents (OHA). The main findings were that patients receiving IT had significantly higher body weight, BMI, body fat, muscle mass, bone mass, muscle quality score, physique rating, and visceral fat compared with those treated with OHA. Regression analysis further showed that BMI and gender were the strongest predictors of body fat, muscle mass, and visceral fat, while age was a key determinant of muscle quality and metabolic age. Our findings are consistent with prior research showing that insulin therapy is commonly associated with weight gain and increased fat mass (17). The mechanisms are related to insulin's anabolic effects, including enhanced glucose storage as glycogen and fat deposition. In contrast, metformin and other OHAs such as SGLT2 inhibitors and GLP-1 receptor agonists are weight-neutral or promote weight loss through reduced appetite, increased urinary glucose excretion, or improved energy expenditure (18,19). SGLT2 inhibitors may improve body composition in T2DM, including weight, BMI, waist circumference, visceral fat area, subcutaneous fat area, percentage body fat, and fat mass reduction, and reducing muscle mass should be considered (20). There are various side effects of administering OHA, particularly biguanides, followed by dipeptidyl peptidase-4 inhibitors and thiazolidinediones. These include gastrointestinal disturbances as the most prevalent, followed by weakness and tiredness, which can interfere with the dietary needs of T2DM (21). These pharmacological differences may explain the more favourable

body composition profile observed in the OHA group. The association between insulin therapy and increased visceral fat is clinically relevant, as visceral adiposity is strongly linked with insulin resistance, cardiovascular disease, and metabolic complications regardless of BMI (22). Previous studies have also demonstrated gender-related differences in body composition among patients with T2DM, with women generally having higher fat mass and men greater lean mass (23). In general, females have a higher BMI at diagnosis of T2DM and a greater amount of total body fat. Biological differences between genders contribute to the excess of diabetes-related cardiovascular risk in females, body fat and appendicular fat was observed in female patients (21,24). Our regression results confirmed that gender was a significant determinant of several body composition parameters. Prolonged exposure to insulin may promote adipogenesis, while also reducing lipolysis, contributing to fat accumulation (25). The connection of IT to weight gain in T2DM is inversely related to changes in HbA1c, with patients experiencing weight loss and increased HbA1c before IT. Monitoring for excessive weight gain after IT, or weight loss before the administration, with increased HbA1c is emphasized. Initiation of IT improves glycaemic control and reduces the risk of microvascular complications. Increase in weight gain in the first year after the initiation of IT, and should be considered by both patients and healthcare providers to control body weight (26). IT caused changes in body composition and weight, while increased fat mass and other components could predict health-related risks (27). Impacts weight gain and is correlated with insulin metabolism, low physical activity, dietary habits, and unhealthy nutrition (28). On the other hand, OHA such as metformin may counteract weight gain by reducing hepatic gluconeogenesis and improving peripheral insulin sensitivity. SGLT2 inhibitors and GLP-1 receptor agonists provide additional cardiovascular and renal protection beyond glucose lowering, partly through their favourable effects on body composition (10). Age-related changes also contributed to our results. Consistent with earlier reports, older patients had reduced muscle quality and higher visceral fat, reflecting sarcopenic obesity commonly observed in T2DM (29). Age-related changes in body composition and glucose metabolism, and gender (30), and appropriate changes in body composition can help prevent new-onset DM (14). These findings emphasize the importance of monitoring both fat and lean mass in addition to BMI. Age patterns and changes in body composition may be related to gender, ethnicity, physical activity level, and caloric intake. An increase in unhealthy body composition not only increases the risk of developing diabetes but also increases the risk of developing various diseases. Age affects functional status and quality of life in T2DM patients (14). This study provides valuable local data on the impact of different T2DM therapies on body composition in an Indonesian population. The relatively large sample size (n=314) strengthens the validity of the findings. However, several limitations should be acknowledged. First, the cross-sectional design precludes conclusions about causality. Second, bioelectrical impedance analysis (BIA), while practical and non-invasive, is less precise than gold-standard methods such as dual-energy X-ray absorptiometry (DXA). Third, the study was conducted in a single center, which may limit generalizability. Finally, potential confounders such as diet, physical activity, and socioeconomic factors were not fully controlled. Despite these limitations, our findings have practical relevance. Clinicians should be aware of the potential for insulin therapy to increase body fat and visceral adiposity, and incorporate regular monitoring of body composition into diabetes management. Lifestyle interventions such as dietary counselling and exercise should be emphasized in patients receiving insulin to mitigate adverse changes. Where feasible, combination therapy with OHAs that have favourable effects on weight and adiposity should be considered.

Conclusion

In this cross-sectional study, patients with T2DM receiving insulin therapy had higher body weight, BMI, body fat, muscle mass, bone mass, and visceral fat compared with those receiving oral hypoglycemic agents. BMI and gender were the most consistent determinants of body composition across groups. These findings highlight the need for routine monitoring of body composition in patients treated with insulin, alongside lifestyle and therapeutic strategies to

minimize excess weight and adiposity. Future longitudinal studies using more precise body composition measures are warranted to clarify causal relationships and long-term clinical implications.

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Declaration on the Use of AI: None

Authors' Contributions: CH, DW, and SF designed the study protocol and supervised data collection. AY and IN collected the data and assisted with statistical analysis. CH and SF conducted the primary data analysis and drafted the initial manuscript. DW and SF provided critical revisions for intellectual content. All authors read and approved the final manuscript.

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