

ORIGINAL ARTICLE

Influence of Family History of Diabetes Mellitus, Menopausal Status, and Physical Activity on Insulin Resistance in Indonesian Non-diabetic Women: A Cross-sectional Study

Yhenti Widjayanti^{1,2}, Budi Santoso³, Purwo Sri Rejeki⁴, Muhammad Putra Ramadhan²

¹ Doctoral Program of Medical Science, Faculty of Medicine, Universitas Airlangga, 60131 Surabaya, East Java, Indonesia

² Department of Nursing, Faculty of Medicine, Universitas Negeri Malang, 65145 Malang, East Java, Indonesia

³ Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Airlangga, 60131 Surabaya, East Java, Indonesia

⁴ Physiology Division, Department of Medical Physiology and Biochemistry, Faculty of Medicine, Universitas Airlangga, 60131 Surabaya, East Java, Indonesia

ABSTRACT

Background: Insulin resistance (IR) is a common complication of type 2 diabetes mellitus (T2DM). Women's risk of IR increases significantly after menopause. This Study aimed to determine the risk of IR and related risk variables in non-diabetic women. **Methods:** This cross-sectional study was conducted in East Java, Indonesia, between June - August 2024. Participants were 196 nondiabetic women selected using consecutive method. This study used a questionnaire and the FINDRISC tool. **Results:** The average FINDRISC score of respondents was 10.4. There were five risk categories for IR: low (24.3%), moderate (15.5%), high (24.3%), slightly increased (33.7%), and extremely high (2.2%). The FINDRISC score was significantly correlated with menopausal status, smoking, history of hypertension, and family history of DM (p-value = 0.000, $p < \alpha$). Multivariate test results showed that age, menopausal status, waist circumference (WC), body mass index (BMI), physical activity, and family history of DM can significantly be used to predict the risk of insulin resistance (p-value = 0.000, $p < \alpha$). Menopausal status (Coef. B = 3.489), lack of physical activity (Coef. B = 1.262), and family history of DM (Coef. B = 3.715) were the three factors that were most significant in predicting the likelihood of IR. **Conclusion:** The risk of IR is projected to increase with age, WC, BMI, and family history of DM and to decrease with increasing physical activity.

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Corresponding Author:

Budi Santoso, Professor

Email: budi.santoso@fk.unair.ac.id

Tel: +62 31 5020251, 5030252-3

it difficult for the body to regulate blood sugar levels. The emergence and advancement of disorders linked to metabolism are significantly influenced by insulin resistance (IR)(3,4).

INTRODUCTION

The rate at which the world's population is aging is unparalleled. The population 65 and older will rise substantially by 2050, surpassing that of children and young adults. This demographic shift is no longer confined to wealthy nations; it is a worldwide issue with far-reaching implications for health, society, and economics(1). As the population ages, there's a growing number of people with chronic, long-term illnesses, which put a heavy burden on healthcare systems and hinder economic growth. One of the most deadly of these diseases is diabetes mellitus. Nearly half a billion individuals globally are currently affected by diabetes, and this figure is expected to rise by a quarter in 2030 and over half by 2045(2). Diabetes is a disorder where the pancreas produces insufficient insulin, making

Insulin resistance is a primary precursor to type 2 diabetes mellitus (T2DM), often preceding the onset of the disease by a decade or more. The global prevalence of insulin resistance exhibits significant geographic variation. IR is notably common in Southeast Asia, with a prevalence rate of 44.3%, surpassing the global average of 15.5% and 46.5%. The prevalence of IR in Indonesia is 42.4 % and be one of the the top 10 nations with the highest prevalence of diabetes in the world(5) (6).

IR is the incapacity of either endogenous or exogenous insulin to carry out its function in a normal population's uptake and utilization of glucose. It is characterized by aberrant lipid buildup, elevated lipid breakdown activities in adipocytes, insulin-mediated blood glucose management abnormalities, and blood glucose utilization disorders(7,8).

Several variables put some people in a higher risk category when it comes to diabetes. Among these include advanced age, obesity, genetics, inactivity, particular ethnic groups, aberrant blood sugar, gestational diabetes, hypertension, unhealthy cholesterol, polycystic ovarian syndrome, and a history of blood vessel issues. Before menopause, IR is more common in males than in women. However, women's risk of IR increases significantly after menopause, reaching levels similar to those of men. A United States study of 4,968 postmenopausal women found that 16% had type 2 diabetes caused by insulin resistance(9). A significant finding from the 2023 Indonesian Health Survey was the prevalence of Diabetes Mellitus among women aged 15 years and above, at 2.7%. Notably, 49.2% of these cases were attributed to type 2 Diabetes Mellitus, a condition characterized by insulin resistance. This change is linked to sex hormones, particularly estrogen, which helps maintain insulin sensitivity in women during their reproductive years(7). Women's insulin resistance has been linked to a number of variables, including body weight, body mass index (BMI), menopausal status, physical activity, and food consumption(10–13). Typical predictors of insulin resistance have been thoroughly studied in the literature, but the most dominant predictors influencing the occurrence of insulin resistance in women, especially non-diabetic women, are still controversial and require further evaluation given the unique dietary habits and body composition profiles among Indonesian women, future research should explore how traditional diets rich in carbohydrates and variations in physical activity patterns may influence the development of insulin resistance in this population

Individuals with IR are at a significantly higher risk of developing heart disease and incur triple healthcare costs than those people without IR(14)It is imperative to identify and treat insulin resistance early in order to stop the disease's progression and the health issues it is connected with. The hyperinsulinemic euglycemic clamp is the gold standard technique for determining insulin sensitivity (HEC). HEC requires a lot of money, time, and resources, though. A quick assessment should be used to pinpoint individuals at high risk. Those identified should undergo more comprehensive blood tests for a definitive diagnosis(15). The FINDRISC is a widely recognized and utilized tool globally for identifying individuals at risk of developing T2DM or insulin resistance. Its effectiveness in screening for T2DM has been established through extensive research, demonstrating sensitivity rates of 78-81% and specificity rates of 76-77%. Due to its consistent performance across diverse populations and robust validation, the International Diabetes Federation has officially endorsed the FINDRISC as a standard screening instrument for T2DM or insulin resistance. This study aimed to identify the risk of IR and identify the best predictors of risk of insulin resistance for early screening of T2DM in women.

MATERIALS AND METHODS

Study Design

The design of this study was a cross-sectional study, which included 196 women. The study's inclusion criteria included women over the age of eighteen, adults, and older women who did not have a diagnosis of diabetes, spoke Bahasa Indonesia fluently, and expressed willingness to participate. Exclusion criteria were having mental illness, chronic metabolic pathologies, and those who did not wish to participate. This study was conducted in East Java, Indonesia, between June and August 2024. All of the women who matched the requirements for inclusion and were willing to take part were included as respondents through the use of consecutive sampling.

The size of the subject is calculated according to the Slovin formula.

$$n = (Z^2 \alpha \cdot p \cdot q) / d^2$$

n = Minimum required sample size

$Z^2 \alpha$ = Confidence level (1.96)

p = Proportion of women with insulin resistance (assumed to be 0.5 since it is unknown)

q = 1-p

d = Margin of error (0.05)

Instruments

The FINDRISC tool was used in this study to predict the likelihood that a person will become insulin resistant and develop diabetes during the following ten years(16,17). The selection of the FINDRISC score as an initial prediction method in this study was based on several key advantages. Firstly, this score was a simple, non-invasive, and easily applicable screening tool in population settings, making it suitable for community-based studies with limited resources. Secondly, the FINDRISC score demonstrated good validity in identifying individuals at risk of type 2 diabetes, which was indirectly associated with insulin resistance risk. Although this score had limitations in directly detecting insulin resistance, its use provided practical value as an initial step in selecting at-risk populations. The decision to use the FINDRISC score also considered its ability to integrate clinical and lifestyle risk factors, such as family history, age, and physical activity. This approach supported a multifactorial analysis that was relevant to the research objectives while minimizing the need for more costly and invasive diagnostic procedures in the initial screening phase.

FINDRISC scoring takes into account the patient's age, weight, waist circumference, exercise routine, food, use of blood pressure medication, history of high blood sugar, and family history of diabetes. The range of the total scores is 0 to 26. Low risk (<7), moderate risk (12–14), high risk (15–20), and very high risk (>20) were the scores assigned.

Every participant had their height, weight, and waist circumference measured as part of an anthropometric assessment. Next, body mass in kilograms divided by height in square meters was used to compute BMI. Physical activity level was assessed using the International Physical Activity Questionnaire (IPAQ) short form. Scoring was conducted based on standard IPAQ guidelines, which categorize respondents into three groups: inactive, minimally active, and health-enhancing physical activity (HEPA) active. With the help of qualified research technicians, a questionnaire was used to ascertain the diabetes family history. Every participant was asked to respond to inquiries regarding any family history of diabetes, the age of a relative's diagnosis, the type of diabetes, and the course of treatment (if any).

Data Analysis

IBM SPSS version 23 was used to analyze the data. Insulin resistance risk variables and insulin resistance risk categories were analyzed using descriptive statistics (frequency and percentage). The Kolmogorov-Smirnov test was used to determine whether the data was normal. The variables age, waist circumference, BMI, and FINDRISC score displayed a non-normal data distribution, according to the findings of the normality test using the Kolmogorov-Smirnov test (p value $> \alpha$; $\alpha = 0.05$). Therefore, bivariate analysis in this study was carried out using non-parametric tests, namely Spearman's Rank, Wilcoxon test, and Friedman test to determine the relationship between variables consisting of age, waist circumference, BMI, menopausal status, smoking, physical activity, history of hypertension, and family history of DM with FINDRISC score. Multivariate analysis in this study was carried out using multiple linear regression to estimate the increased risk of insulin resistance using independent variables and identify the independent variables that most influence it.

RESULT

With the youngest respondent being twenty-six (26) years old and the oldest being eighty-three (83) years old, the analysis's findings revealed that the average age of the respondents was 49.20 years. With the lowest waist circumference of 58.00 cm and the maximum of 120.00 cm, the average waist circumference of the respondents was 86.90 cm. With the lowest BMI being 17.90 kg/m² and the highest being 44.99 kg/m², the respondents' average BMI was 25.61 kg/m². The average FINDRISC score of respondents is 10.40, with the lowest score being 0.00 and the highest being 23.00 (table 1).

Table I: Descriptive statistics of the variables that characterize the sample ($n = 196$)

Parameter	Mean	Min - Max	Std. Dev
Age	49.20	26.00 - 83.00	13.69
Waist Circumference	86.90	58.00 - 120.00	11.55
Body Mass Index	25.61	17.90 - 44.99	5.03
FINDRISC Score	10.40	0.00 - 23.00	4.78

Table 2 showed that the majority of respondents were menopausal (53.6%), did not smoke (98.3%), had inactive physical activity (43.3%), had no history of hypertension (90.6%), and had no family history of DM (74.5%). In this study, bivariate analysis was used to ascertain how the FINDRISC score related to variables like age, waist circumference, BMI, menopausal status, smoking, physical activity, history of hypertension, and family history of diabetes. Apart from that, this analysis was also used to select variables that could be included in modeling in the next analysis, namely multivariate analysis. In this research, a data normality test was carried out to determine the appropriate statistical test. To choose the best statistical test for this study, a data normality test was performed. The Kolmogorov-Smirnov test was used to determine whether the data was normal. The variables age, waist circumference, BMI, and FINDRISC score have a non-normal data distribution, according to the findings of the normality test (p -value $> \alpha$; $\alpha = 0.05$). Therefore, bivariate analysis in this study was carried out using non-parametric tests, namely Rank Spearman, Wilcoxon, and Friedman.

Table II: Distribution of Respondents Based on FINDRISC Categories, Menopausal Status, Smoking, Physical Activity, History of Hypertension, and Family History of Diabetes Mellitus ($n = 196$)

Parameters	n	%
FINDRISC categories		
Low Risk (0-6)	48	24.3
Slightly Elevated Risk (7-11)	66	33.7
Moderate risk (12-14)	30	15.5
High Risk (15-20)	48	24.3
Very High Risk (21-26)	4	2.2
Menopausal status		
Reproductive age	91	46.4
Menopause	105	53.6
Smoking		
No	193	98.3
Yes	3	1.7
Physical activity		
Inactive	85	43.3
Minimally Active	86	43.9
HEPA active	25	12.8
History of Hypertension		
None	178	90.6
Yes	18	9.4
Family History of Diabetes Mellitus		
None	146	74.5
Yes	50	25.5

The FINDRISC score is significantly correlated with age (p-value = 0.000), waist circumference (p-value = 0.000), and BMI (p-value = 0.000), according to the Spearman test results. Apart from that, an r value (correlation coefficient) was obtained of 0.482 for the age variable, 0.693 for the waist circumference variable, and 0.652 for the BMI variable. This means that there is a moderate and positive relationship, where every increase in age, waist circumference, and BMI will be followed by an increase in the FINDRISC score (Table 3). A substantial correlation between the FINDRISC score and menopausal state (p-value = 0.000), smoking (p-value = 0.000), history of hypertension (p-value = 0.000), and family history of diabetes (p-value = 0.000) was also demonstrated by the Wilcoxon test findings, as Table 3 demonstrates. Physical activity and the FINDRISC score were shown to be significantly correlated (p-value = 0.000) in the Friedman test results. Based on the findings of this connection study, it can be said that every variable in multivariate modeling has a link with the FINDRISC score.

Table III: Analysis of the Relationship between Age, Waist Circumference, BMI, Menopausal Status, Smoking, Physical Activity, History of Hypertension, and Family History of DM with FINDRISC Score

Parameter	r	p value
Age	0.482	0.000*
Waist Circumference	0.693	0.000*
Body Mass Index	0.652	0.000*
Menopausal status	-	0.000**
Smoking	-	0.000**
Physical activity	-	0.000***
History of hypertension	-	0.000**
Family History of Diabetes mellitus	-	0.000**

*p value < α ; α = 0.05 with Spearman test. **p value < α ; α = 0.05 with Wilcoxon test. ***p value < α ; α = 0.05 with Friedman test; All p-values are two-tailed unless otherwise indicated

Multiple linear regression was used in this study as the multivariate. Two factors, smoking status and history of hypertension, had a p-value > 0.05, according to the modeling analysis results in the first model. Subsequently, each of these two factors were eliminated from the modeling individually, beginning with the one with the highest p-value—the history of smoking (p-value = 0.839)—and working down to the history of hypertension (p-value = 0.756). In the second modeling, namely eliminating the smoking status variable, it was discovered that there was no change in the r square and Coef values. B that exceeds 10%, so the smoking status variable is excluded from modeling. Then, in the third modeling carried out by eliminating the hypertension history variable, it was found that there was no change in the r square and Coef values. B exceeds 10%, so the hypertension history variable is removed from the modeling, resulting in the final model, namely Model 3 (Table 4).

The results of the analysis showed an r-square value of 0.758, which means that the regression obtained can explain 78.5% of the variation in the FINDRISC variable. Then, the results of the analysis also showed a p-value of 0.000 in the Anova test, which means that the regression model obtained is a fit, or it can be said that these variables can significantly be used to predict FINDRISC variables. The line equation obtained from regression analysis is $\text{FINDRISC} = -12,433 + 0.077 \text{ Age} + 3,489 \text{ Menopausal Status} + 0.081 \text{ Waist Circumference} + 0,267 \text{ Body Mass Indeks} - 1,262 \text{ Physical Activity} + 3,715 \text{ Family history of diabetes mellitus}$. To assess the presence of multicollinearity among predictors, the Variance Inflation Factor (VIF) was calculated for each independent variable. All VIF values were below the threshold of 5, indicating no significant multicollinearity and confirming that each predictor contributed uniquely to the model. The high R value reflects the strong association between the selected predictors and the FINDRISC score. However, external validation using independent datasets is recommended to evaluate the model's robustness and generalizability

DISCUSSION

The findings of this study revealed a spectrum of type 2 diabetes risk among the participants. While the majority fell within the low to slightly elevated risk categories but a considerable proportion exhibited moderate to high risk provides important insights into the potential for diabetes risk within this group. In terms of determining FINDRISC scores in the community, Mula Tarigan's cross-sectional research yielded different results than the findings of this study. The results of Mula Tarigan's research show that more than 50% of women in Indonesia have low FINDRISC scores, while our research shows that the majority of respondents have moderate FINDRISC scores(18). There may be differences in the age characteristics of respondents. In our study, the average age was > 45 years, while in the Tarigan study the majority of respondents were < 45 years old.

The study's conclusions revealed that the average age of respondents was 49.2 years old and that there was a strong positive association ($p = 0.00$, $r = +0.482$) between women's age and their higher risk of developing insulin resistance. This implies that the likelihood of developing insulin resistance rises in proportion to age. Diabetes is more likely to develop as people age. People are often diagnosed between the ages of 45 and 64.

Based on linear regression analysis, for every one-year increase in age, the FINDRISC score increased by 0.077 after controlling for other variables such as menopausal status, waist circumference, physical activity, and family history of diabetes mellitus. Numerous theories have been put out to explain how aging and insulin resistance are related. As individuals age, the function of pancreatic beta cells in producing insulin tends to decline, leading

to an imbalance between insulin supply and demand. Insulin resistance can be somewhat compensated for up to a point when functioning β -cells are present. Ultimately, nevertheless, aging-related gradual loss of β -cell mass and function compromises glucose tolerance and results in hyperglycemia. Mechanistic studies have implicated cellular senescence as a key contributor to the limited proliferative capacity of aged pancreatic β -cells, underscoring its role in insulin resistance pathogenesis(19,20). Simultaneously, aging is frequently linked to alterations in body composition, which are marked by a decline in muscle mass and an increase in fat mass. These changes might impair glucose metabolism and exacerbate insulin resistance. Furthermore, the chronic inflammation commonly observed in the elderly can interfere with insulin signaling, exacerbating the condition. Finally, age-related mitochondrial dysfunction can impair cellular energy metabolism, further promoting insulin resistance(21,22).

There is ongoing discussion over the causal relationship between age and insulin resistance. Research using a variety of techniques (hyperinsulinemic-euglycemic clamp, forearm perfusion, minimum model) has demonstrated that insulin sensitivity declines with advancing age(23). Nevertheless, other studies have failed to establish a clear correlation. Notably, some studies included participants with impaired glucose tolerance, potentially indicating incomplete hepatic glucose suppression, while others neglected to consider body composition. A large-scale study utilizing the hyperinsulinemic-euglycemic clamp technique revealed that the negative impact of age on insulin sensitivity was predominantly observed in lean women(24).

Menopausal status. Over half of the study population was in the menopausal period. Statistical analysis revealed a highly significant correlation between menopausal status and the FINDRISC score. The findings also indicated that the transition to menopause was associated with a substantial increase in the FINDRISC score, which remained significant even after adjusting for potential confounding factors. According to the study's findings, menopause is linked to a noticeably increased risk of insulin resistance. Estrogens exert regulatory influences on metabolic processes governing energy homeostasis and possess the capacity to modulate inflammatory responses. Estrogen activates a wide variety of inflammatory cell types, such as macrophages and monocytes, through the expression of estrogen receptors in these cells. Moreover, a correlation exists between diminished estrogen levels in menopausal women and an augmented inflammatory milieu. Compared to childbearing-age women, menopausal women exhibit elevated lymphocyte and monocyte counts, increased expression of proinflammatory cytokines, and an accumulation of senescent inflammatory cells, indicative of an impaired immune function(25–27). Insulin resistance and other pathological diseases are

linked to the increased production of pro-inflammatory cytokines TNF- α and IL-6 by lymphocytes and macrophages during menopause due to the decreasing of estrogen levels(28,29). TNF- α impairs insulin signaling through multiple mechanisms, including direct inhibition of insulin action, decreased expression of glucose transporters (e.g., Glut4), and disruption of intracellular signaling pathways. Additionally, TNF- α promotes lipolysis, increases free fatty acid levels, and suppresses PPAR- γ activity, contributing to insulin resistance(30,31).

Waist circumference. The anthropometric measurements in this study indicated a considerable prevalence of central obesity among the participants, as defined by waist circumference. Furthermore, our analysis revealed a significant positive correlation between the FINDRISC score, a measure of insulin resistance risk, and waist circumference. This suggests that a larger waist circumference is associated with a higher predicted risk of developing insulin resistance within this population.

Waist circumference is a common measure of visceral adiposity. Greater waist circumference is linked to increased visceral fat accumulation. Pro-inflammatory cytokines produced by visceral fat, such as TNF- α and IL-6, disrupt insulin signaling and worsen insulin resistance. According to earlier research, the strongest indicator of the metabolic risk associated with visceral fat is waist circumference. Visceral abdominal fat is also the factor most strongly linked to insulin resistance. One of the main risk factors for insulin resistance is visceral fat. Compared to BMI, waist circumference is a better indicator of metabolic risk(32). Increased hepatic steatosis and insulin resistance are caused by increased transport of free fatty acids from visceral adipose tissue to the liver. Additionally, dyslipidemia, characterized by low HDL cholesterol, often accompanies insulin resistance(33,34).

Physical activity. Our logistic regression analyses showed that increased intensities of physical activities could significantly reduce the FINDRISC score. Respondents with more physical activity will reduce their FINDRISC score by 1,262 after controlling for the other variables (age, menopausal status, waist circumference, and family history of diabetes mellitus). The primary anabolic hormone that lowers blood sugar and encourages the production of proteins, lipids, and glycogen is insulin. Hyperglycemia is the result of cells being less sensitive to insulin, a condition known as insulin resistance. Research has demonstrated that physical activity can enhance insulin sensitivity and reduce insulin levels, even in the presence of oxidative stress (28,35). AMP-activated protein kinase (AMPK) activation during muscular contraction causes TBC1D1 (a protein that prevents glucose transfer into the cell) to become phosphorylated. Phosphorylation of TBC1D1 inactivates this protein, allowing GLUT4 vesicles

carrying glucose transporter molecules to translocate to the cell membrane and facilitate glucose uptake(36,37). Regular aerobic activity, three to five days a week, at a moderate intensity for at least half an hour, is linked to better glycemic management and insulin sensitivity(38,39). Following a single exercise session, there are immediate changes in insulin sensitivity (duration of 2–72 hours post-exercise), and training trials comprising interventions conducted for a minimum of 8 weeks demonstrate permanent adaptations (40,41) .

Family history. According to earlier research, those with a family history of diabetes mellitus were 2.86 to 6.16 times more likely to develop insulin resistance than people without a family history of the condition (42,43). Other research has consistently demonstrated that a familial history of type 2 diabetes mellitus is an independent predictor of diabetes risk, uninfluenced by body mass index or waist circumference. This association is particularly pronounced in pediatric populations, with over 75% of children diagnosed with type 2 diabetes in the United States reporting affected relatives. Considering the robust correlation between family history and disease susceptibility, a comprehensive assessment of familial diabetes risk may serve as a clinically expedient and efficacious strategy for identifying individuals predisposed to insulin resistance.

Based on the results of multiple regression modeling, the variables that most influence the increase in FINDRISC scores are family history of diabetes mellitus, menopausal status, and physical activity. This shows that it is important for women who have entered menopause to pay attention to their physical activity needs, especially menopausal women who have a family history of diabetes mellitus. Exercise (aerobic, resistance training, or combination) reduces biomarkers of insulin resistance (calprotectin, insulin, glucose, leptin, resistin, lipid profiles, and insulin resistance index (HOMA-IR)) during menopause (38,44).

A family history of diabetes is a critical component in the risk analysis of insulin resistance. In this study, findings indicate that individuals with a family history of diabetes have a higher risk of experiencing insulin resistance, even if they have not been diagnosed with diabetes. This is consistent with previous evidence suggesting that both genetic and familial environmental factors play a significant role in determining insulin sensitivity and glucose metabolism. Genetic factors can influence molecular pathways related to insulin regulation, including insulin receptor function and downstream signaling pathways(45,46). Additionally, lifestyle patterns established within families, such as dietary habits and physical activity, also contribute to increased risk. The impact of family history becomes more pronounced when combined with other factors such as menopausal status and low physical activity, which tend to exacerbate insulin sensitivity. This discussion

underscores the importance of considering family history of diabetes in the prevention and management strategies for insulin resistance, particularly in high-risk populations. Further research exploring the interaction between genetic and environmental factors can provide deeper insights to identify the mechanisms underlying this risk.

Exercise does not appear to be beneficial in preventing insulin resistance or type 2 diabetes in people with a family history of the disease, particularly first-degree (parents and siblings). On the other hand, data indicates that individuals with high levels of physical activity have a lower Primary care physicians ought to encourage menopausal women to engage in regular physical activity, as advised by the World Health Organization (WHO). According to current guidelines, menopausal women should exercise for at least 150 to 300 minutes per week at a moderate to vigorous effort, 75 to 150 minutes per week at a vigorous intensity, or a similar combination of both.

The study's weakness is that no laboratory tests, including HOMA-IR, blood glucose tolerance, insulin levels, or blood glucose tolerance, were run to validate the diagnosis of insulin resistance. This study adopted a non-invasive approach using the FINDRISC score to predict insulin resistance risk. This approach offers the advantage of being easy to implement and not requiring complex laboratory procedures. However, it is acknowledged that FINDRISC has limitations, particularly in sensitivity and specificity for directly detecting insulin resistance. This score is more designed to assess the overall risk of type 2 diabetes, so its use as a predictor of insulin resistance may be less optimal in certain populations. To strengthen the findings and improve predictive accuracy, further research is recommended to combine the FINDRISC score with laboratory tests, such as measuring HbA1c levels. HbA1c not only reflects long-term glucose control but can also provide a deeper understanding of the risk of metabolic disorders. Combining these methods is expected to yield more robust and reliable data in identifying individuals at risk of insulin resistance.

Based on the results of the FINDRISC Score calculation, it can be used as a prediction of insulin resistance in the next 10 years. The FINDRISC tool is easily applicable in daily clinical practice, especially in primary care, as it is simple, non-invasive, and inexpensive. Health workers can provide recommendations to conduct Type 2 diabetes mellitus screening by conducting HbA1C examinations every year (score > 21) and every 3-5 years (score 15-20).

It should be noted that while FINDRISC is a validated tool for predicting T2DM risk, it serves only as an indirect indicator of insulin resistance. Therefore, future studies incorporating direct biomarkers such as HOMA-

IR or fasting insulin levels are recommended to confirm these associations

CONCLUSION & RECOMMENDATIONS

The increased risk of insulin resistance in women is significantly influenced by increasing age, menopausal status, increasing waist circumference, increasing body mass index, family history of diabetes mellitus, and decreased physical activity. The variables that most influence the increased risk of insulin resistance are family history of diabetes mellitus, menopausal status, and decreased physical activity. Advice for women who have a family history of diabetes mellitus is to increase their level of physical activity, especially when entering menopause, to prevent insulin resistance, which can trigger Type 2 diabetes mellitus and other metabolic diseases.

This study provides initial insights into the factors influencing insulin resistance. However, to strengthen the findings, further studies employing a more in-depth approach are needed. A key recommendation is the use of laboratory tests, such as HbA1c, fasting glucose, or HOMA-IR, to directly assess insulin resistance. Combining non-invasive screening methods, such as the FINDRISC score, with laboratory biomarker data can enhance the validity of the results and provide a more comprehensive understanding of insulin resistance risk. Furthermore, the relationship between family history of diabetes and insulin resistance warrants deeper exploration in future studies. Genetic and epigenetic approaches, including the analysis of genotypes or insulin-related gene expression, could help elucidate the biological mechanisms underlying this association. Longitudinal studies examining the interactions between family history, lifestyle factors, and hormonal influences may also yield richer insights into the progression of insulin resistance over time. These recommendations are expected to form a foundation for further research that not only strengthens the validity of findings but also provides more precise guidance for preventing insulin resistance in high-risk populations. Specifically, our findings suggest that targeted interventions—such as promoting physical activity and implementing regular screening—may be particularly beneficial for postmenopausal women with a family history of diabetes, thereby potentially reducing the population burden of type 2 diabetes.

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REFERENCES

1. Rosenberg M, Tomioka S, Barber SL. Research to inform health systems' responses to rapid population ageing: a collection of studies funded by the WHO Centre for Health Development in Kobe, Japan. *Heal Res Policy Syst* [Internet]. 2022;20(1):1–6. Available from: <https://doi.org/10.1186/s12961-022-00917-z>
2. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract* [Internet]. 2019;157:107843. Available from: <https://doi.org/10.1016/j.diabres.2019.107843>
3. Hotta N, Hori A, Okamura Y, Baba R, Watanabe H, Sugawara J, et al. Insulin resistance is associated with an exaggerated blood pressure response to ischemic rhythmic handgrip exercise in nondiabetic older adults. *J Appl Physiol*. 2020;129(1):144–51.
4. Zhao W, Diao H, Chen X, Xu S, Jiang S, Cao H, et al. The serum oestradiol/progesterone ratio on the day of OPU + 7, but not the day of OPU + 5, affects the rates of live birth in fresh blastocyst embryo transfer cycles. *J Ovarian Res* [Internet]. 2023;16(1):1–10. Available from: <https://doi.org/10.1186/s13048-023-01096-3>
5. Magliano D, Boyko E. IDF diabetes atlas [Internet]. 10th editi. International Diabetes Federation; 2021. Available from: <https://diabetesatlas.org/atlas/tenthedition/>
6. Goh LPW, Sani SA, Sabullah MK, Gansau JA. The Prevalence of Insulin Resistance in Malaysia and Indonesia: An Updated Systematic Review and Meta-Analysis. *Med*. 2022;58(6).
7. Ciarambino T, Crispino P, Guarisco G, Giordano M. Gender Differences in Insulin Resistance: New Knowledge and Perspectives. *Curr Issues Mol Biol*. 2023;45(10):7845–61.
8. Lee SH, Park SY, Choi CS. Insulin Resistance: From Mechanisms to Therapeutic Strategies. *Diabetes Metab J*. 2022;46(1):15–37.
9. Sigit FS, Tahapary DL, Trompet S, Sartono E, Willems Van Dijk K, Rosendaal FR, et al. The prevalence of metabolic syndrome and its association with body fat distribution in middle-aged individuals from Indonesia and the Netherlands: A cross-sectional analysis of two population-based studies. *Diabetol Metab Syndr* [Internet]. 2020;12(1):1–11. Available from: <https://doi.org/10.1186/s13098-019-0503-1>
10. Verma A, Malhotra A, Ranjan P, Kumari A, Chopra S, Khan MA, et al. A comprehensive evaluation of predictors of obesity in women during the perimenopausal period: A systematic review and narrative synthesis. *Diabetes Metab Syndr Clin Res Rev* [Internet]. 2024;18(1):102933. Available from:

- <https://doi.org/10.1016/j.dsx.2023.102933>
11. Numao S, Katayama Y, Nakata Y, Matsuo T, Nakagaichi M, Tanaka K. Association of abdominal fat with metabolic syndrome components in overweight women: Effect of menopausal status. *J Physiol Anthropol*. 2020;39(1):1–8.
12. Elsayed MM, El Refaye GE, Rabiee A, Abouzeid S, Elsis HF. Aerobic exercise with diet induces hormonal, metabolic, and psychological changes in postmenopausal obese women. *Heliyon* [Internet]. 2022;8(3):e09165. Available from: <https://doi.org/10.1016/j.heliyon.2022.e09165>
13. Lee SM, Ryu KJ, Son S, Lee YJ, Park H, Kim T. Body fat distribution and insulin resistance among Korean middle-aged women: a Korean National Health and Nutrition Examination Survey. *Obstet Gynecol Sci*. 2022;65(5):468–76.
14. Zhao X, An X, Yang C, Sun W, Ji H, Lian F. The crucial role and mechanism of insulin resistance in metabolic disease. *Front Endocrinol (Lausanne)*. 2023;14(March).
15. Abdallah M, Sharbaji S, Sharbaji M, Daher Z, Faour T, Mansour Z, et al. Diagnostic accuracy of the Finnish Diabetes Risk Score for the prediction of undiagnosed type 2 diabetes, prediabetes, and metabolic syndrome in the Lebanese University. *Diabetol Metab Syndr* [Internet]. 2020;12(1):1–11. Available from: <https://doi.org/10.1186/s13098-020-00590-8>
16. Mohammed Saleem S, Salim Khan SM, Sumaya Jan S. Finnish Diabetic Risk Score- A Tool For Predicting Risk Of Undiagnosed Type 2 Diabetes Mellitus. *Ann Med Heal Sci Res* [Internet]. 2017;9(3):39–42. Available from: <https://www.amhsr.org/articles/finnish-diabetic-risk-score-a-tool-for-predicting-risk-of-undiagnosed-type-2-diabetes-mellitus.pdf>
17. Juille A, Midthjell K, Holmen J, Carlsen SM, Tuomilehto J, Bjørngaard JH, et al. Validity of the FINDRISC as a prediction tool for diabetes in a contemporary Norwegian population: A 10-year follow-up of the HUNT study. *BMJ Open Diabetes Res Care*. 2019;7(1):1–9.
18. Tarigan M, Setiawan, Tarigan R, Imelda F, Jongudomkarn D. Identifying diabetes risks among Indonesians: A cross-sectional study in a community setting. *Belitung Nurs J*. 2024;10(1):41–7.
19. Kehm R, Kluth O, Schürmann A, Grune T, Huhn A. The role of aging and senescence on pancreatic β -cell function and proliferation. *Free Radic Biol Med*. 2017;108:S71.
20. De Tata V. Age-related impairment of pancreatic beta-cell function: Pathophysiological and cellular mechanisms. *Front Endocrinol (Lausanne)*. 2014;5(SEP):1–8.
21. Shou J, Chen PJ, Xiao WH. Mechanism of increased risk of insulin resistance in aging skeletal muscle. *Diabetol Metab Syndr* [Internet]. 2020;12(1):1–10. Available from: <https://doi.org/10.1186/s13098-020-0523-x>
22. Freitas RDS, Maria C, Silva DS, Fratelli CF, Lima LR De, Stival MM, et al. Syndrome : Insights into Older Adults ' Clinical Characteristics. 2024;16(1241):1–13.
23. Zhang Y, Xu L, Liu X, Wang Y. Evaluation of insulin sensitivity by hyperinsulinemic-euglycemic clamps using stable isotope-labeled glucose. *Cell Discov* [Internet]. 2018;4(1):4–7. Available from: <http://dx.doi.org/10.1038/s41421-018-0016-3>
24. Chia CW, Egan JM, Ferrucci L. Age-related changes in glucose metabolism, hyperglycemia, and cardiovascular risk. *Circ Res*. 2018;123(7):886–904.
25. Abildgaard J, Tingstedt J, Zhao Y, Hartling HJ, Pedersen AT, Lindegaard B, et al. Increased systemic inflammation and altered distribution of T-cell subsets in postmenopausal women. *PLoS One*. 2020;15(6).
26. De Paoli M, Zakharia A, Werstuck GH. The Role of Estrogen in Insulin Resistance: A Review of Clinical and Preclinical Data. *Am J Pathol* [Internet]. 2021;191(9):1490–8. Available from: <https://doi.org/10.1016/j.ajpath.2021.05.011>
27. Ntikoudi A, Spyrou A, Evangelou E, Dokoutsidou E, Mastorakos G. The Effect of Menopausal Status, Insulin Resistance and Body Mass Index on the Prevalence of Non-Alcoholic Fatty Liver Disease. *Healthc*. 2024;12(1081):1–17.
28. Biteli P, Barbalho SM, Detregiachi CRP, dos Santos Haber JF, Chagas EFB. Dyslipidemia influences the effect of physical exercise on inflammatory markers on obese women in post-menopause: A randomized clinical trial. *Exp Gerontol*. 2021;150(111355):1–6.
29. Kamińska MS, Lubkowska A, Panczyk M, Walaszek I, Grochans S, Grochans E, et al. Relationships of Body Mass Index, Relative Fat Mass Index, and Waist Circumference with Serum Concentrations of Parameters of Chronic Inflammation. *Nutrients*. 2023;15(2789).
30. Mohallem R, Aryal UK. Regulators of TNF α mediated insulin resistance elucidated by quantitative proteomics. *Sci Rep* [Internet]. 2020;10(1):1–15. Available from: <https://doi.org/10.1038/s41598-020-77914-1>
31. Sethi JK, Hotamisligil GS. Metabolic Messengers: tumour necrosis factor. *Nat Metab*. 2021;3(10):1302–12.
32. Sasaki R, Yano Y, Yasuma T, Onishi Y, Suzuki T, Maruyama-Furuta N, et al. Association of waist circumference and body fat weight with insulin resistance in male subjects with normal body mass index and normal glucose tolerance. *Intern Med*. 2016;55(11):1425–32.
33. Chait A, den Hartigh LJ. Adipose Tissue Distribution, Inflammation and Its Metabolic Consequences, Including Diabetes and Cardiovascular Disease. *Front Cardiovasc Med*. 2020;7(22):1–41.
34. Deusdar6 R, Souza A de M, Szklo M. Association

- between Obesity, Overweight, Elevated Waist Circumference, and Insulin Resistance Markers among Brazilian Adolescent Students. *Nutrients* [Internet]. 2022;14(3487):1–11. Available from: <https://www.mdpi.com/2072-6643/14/17/3487>
35. Lin Y, Fan R, Hao Z, Li J, Yang X, Zhang Y, et al. The Association Between Physical Activity and Insulin Level Under Different Levels of Lipid Indices and Serum Uric Acid. *Front Physiol*. 2022;13(February).
36. Kjøbsted R, Roll JLW, Jørgensen NO, Birk JB, Foretz M, Viollet B, et al. AMPK and TBC1D1 regulate muscle glucose uptake after, but not during, exercise and contraction. *Diabetes*. 2019;68(7):1427–40.
37. Esquejo RM, Albuquerque B, Sher A, Blatnik M, Wald K, Peloquin M, et al. AMPK activation is sufficient to increase skeletal muscle glucose uptake and glycogen synthesis but is not required for contraction-mediated increases in glucose metabolism. *Heliyon* [Internet]. 2022;8(10):e11091. Available from: <https://doi.org/10.1016/j.heliyon.2022.e11091>
38. Friedenreich CM, Neilson HK, Wang Q, Stanczyk FZ, Yasui Y, Brenner DR, et al. Exercise Dose Effects on Insulin Resistance Indicators in Postmenopausal Women: A Randomized Trial. *J Endocrinol Metab*. 2016;6(2):35–45.
39. Lloyd JW, Evans KA, Zerfass KM, Holmstrup ME, Kanaley JA, Keslacy S. Effect of an acute bout of aerobic exercise on chemerin levels in obese adults [Internet]. Vol. 10, *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. Elsevier BV; 2016. p. 37–42. Available from: <http://dx.doi.org/10.1016/j.dsx.2015.04.010>
40. Bird SR, Hawley JA. Update on the effects of physical activity on insulin sensitivity in humans. *BMJ Open Sport Exerc Med*. 2017;2(1):1–26.
41. Syeda USA, Battillo D, Visaria A, Malin SK. The importance of exercise for glycemic control in type 2 diabetes. *Am J Med Open*. 2023;9(April 2022):100031.
42. Bennet L, Franks PW, Zuller B, Groop L. Family history of diabetes and its relationship with insulin secretion and insulin sensitivity in Iraqi immigrants and native Swedes: a population-based cohort study. *Acta Diabetol* [Internet]. 2018;55(3):233–42. Available from: <https://doi.org/10.1007/s00592-017-1088-5>
43. Gościk J, Bauer W, Wawrusiewicz-Kurylonek N, Paczkowska-Abdulsalam M, Niemira M, Citko A, et al. Efficacy of family history, genetic risk score, and physical activity in assessing the prevalence of type 2 diabetes. *Polish Arch Intern Med*. 2019;129(7–8):442–50.
44. Van Gemert WA, Monninkhof EM, May AM, Peeters PH, Schuit AJ. Effect of exercise on insulin sensitivity in healthy postmenopausal women: The SHAPE study. *Cancer Epidemiol Biomarkers Prev*. 2015;24(1):81–7.
45. Tremblay J, Hamet P. Environmental and genetic contributions to diabetes. *Metabolism*. 2019;100:1–6.
46. Brown AE, Walker M. Genetics of Insulin Resistance and the Metabolic Syndrome. *Curr Cardiol Rep* [Internet]. 2016;18(8). Available from: <http://dx.doi.org/10.1007/s11886-016-0755-4>