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Association between MC4R rs17782313 genotype and body fat percentage as an indicator of obesity among Indonesian adults

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Original Article

ABSTRACT

Background: Obesity is influenced by both environmental and genetic factors, including variation in the melanocortin-4 receptor (MC4R) gene, which plays a role in appetite regulation and energy balance. Identifying genetic risks, particularly whether obesity linked to inherited dysregulation of appetite, is crucial for early intervention and personalized prevention strategies.
Objectives: This study aimed to examine the association between MC4R genotype and body fat percentage as an indicator of obesity among Indonesian adults.
Methods: A cross-sectional study was conducted among 79 Indonesian adults aged 21–56 years in Jakarta. Participants were consecutively recruited and screened based on predefined inclusion and exclusion criteria. Anthropometric data, including height and weight, were obtained using a standardized stadiometer and digital scale to calculate body mass index (BMI). Body fat percentage (BFP) was assessed using bioelectrical impedance analysis (BIA) with an Omron Karada Scan device. Genomic DNA was extracted from venous blood samples, and the MC4R rs17782313 polymorphism was genotyped using the polymerase chain reaction– fragment length polymorphism (PCR-RFLP) method. Statistical analyses were performed to assess the association between genotypes and body fat percentages.
Results: Most participants were classified as overweight (36.1%) or obese (41.7%) based on BMI. The genotypic distribution of rs17782313 was TT (48.1%), CT (39.2%), and CC (12.7%). Higher body fat percentages were significantly more common among individuals carrying the C allele. The CC genotype demonstrated the strongest association with obesity, with an odds ratio (OR) of 4.00 (95% CI: 1.02–15.64, p=0.04) compared to the wild-type TT genotype.
Conclusion: Variations in the MC4R rs17782313 gene are associated with increased body fat percentage and a higher risk of obesity among Indonesian adults. Individuals carrying the risk allele may have greater susceptibility to excess fat accumulation, underscoring the importance of incorporating genetic factors into obesity prevention and management strategies.

INTRODUCTION

Obesity has emerged as a major global public health challenge, with its prevalence continuing to rise worldwide. It is a complex, multifactorial disorder resulting from an imbalance between energy intake and energy expenditure, leading to the excessive accumulation of body fat. This condition is influenced by intricate interactions between genetic, environmental, and behavioral factors.[1] Obesity is associated with a wide range of adverse health outcomes, and contributes substantially to increased morbidity and mortality, particularly through metabolic disorders such as diabetes mellitus, hypertension, dyslipidemia, osteoarthritis, sleep apnea, and various forms of cancer.[2] According to the World Obesity Federation, approximately 800 million people worldwide are currently living with obesity, including roughly 379 million children and adolescents while at least one billion more individuals are considered at risk. Over recent

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decades, substantial advances have elucidated the genetic and molecular mechanisms underlying obesity, revealing that genetic mutations and common polymorphisms strongly influence physical activity levels, eating behaviors, and individual's susceptibility to obesity. The heritability of body mass index (BMI) is estimated to be relatively high, ranging from 30% to 70%.[3,4]

A substantial body of evidence indicates that the leptin-melanocortin signaling pathway in the hypothalamus plays a central role in the regulation of appetite and energy homeostasis. Within this pathway, the *melanocortin-4 receptor* (MC4R) gene, located on chromosome 18q21.3, has been identified as a critical regulator of appetite control.[5] Specifically, the C allele of the single nucleotide polymorphism (SNP) rs17782313, located downstream of the MC4R gene, has been consistently identified as a robust genetic risk factor for obesity, affecting satiety and causing excessive energy accumulation.[6] In obesity, leptin levels are chronically elevated, which may lead to leptin resistance, a condition similar to insulin resistance. Under normal physiological conditions, leptin acts through leptin receptors (LEPRs) in the hypothalamus, particularly within the arcuate nucleus, where it influences two key neuronal populations: pro-opiomelanocortin (POMC) neurons, which suppress food intake, and agouti-related protein (AGRP) neurons, which promote feeding. These neurons regulate downstream *MC4R* signaling to maintain energy balance between hunger and satiety. Disruption of this regulatory system, including through *MC4R* polymorphisms, may impair satiety signaling, resulting in persistent hunger despite adequate energy stores and ultimately leading to increased food intake and adipose tissue accumulation.[7]

Despite the established role of MC4R polymorphisms, previous studies have predominantly used body mass index (BMI) as the primary indicator of obesity,[8] However, BMI has important limitation, as it cannot accurately distinguish between fat mass and lean muscle mass. Therefore, body fat percentage (BFP) is increasingly recognized as a more precise and sensitive indicator of adiposity and metabolic risk. Investigating the association between the MC4R rs17782313 variant and BFP is particularly important, as genetic variants directly influence lipid metabolism and fat distribution (e.g., visceral adiposity), independent of overall body weight.[9,10] Furthermore, although the association between MC4R rs17782313 and obesity-related traits has been widely reported globally, there remains a significant research gap regarding its relationship with BFP in Southeast Asian populations, such as Indonesians. The Indonesian population has unique genetic admixtures, distinct dietary patterns with high refined carbohydrate intake, and phenotypic traits that often include higher body fat percentages at lower BMI thresholds compared to Western populations.[10] Therefore, this study aimed to address this gap by examining the association between the MC4R rs17782313 genotype and body fat percentage as an indicator of obesity among Indonesian adults, thereby providing important localized epidemiological evidence.

METHODS

Study design

This study employed a cross-sectional design. It was an observational, non-experimental study aimed at assessing the statistical association between MC4R genotype and body fat percentage.

Population and sample

This study was conducted among adults 79 adult participants aged 18–50 years living in Jakarta, Indonesia. In this cross-sectional design, data on both potential risk factors and outcomes was collected simultaneously. Each participant was assessed once, and all measurements reflected their condition at the time of data collection. This design enables the evaluation of associations between variables within the study population but does not permit causal inference.

Data collection

Participants were recruited using a consecutive sampling method, whereby all individuals who met the inclusion and exclusion criteria during the study period were invited to participate.

Eligible participants were apparently healthy adults who provided written informed consent. To minimize potential confounding factors affecting body fat accumulation, strict exclusion criteria were applied. Individuals were excluded if they had clinically diagnosed metabolic syndrome; chronic illnesses (e.g., severe renal or hepatic disease); were pregnant or breastfeeding; were taking medications known to influence body weight (e.g., corticosteroids or anti-obesity drugs); or had psychological conditions, such as severe depression or anxiety, that could affect eating behavior.[11] Anthropometric measurements, including height and weight, were obtained using a standardized stadiometer and a calibrated digital scale. Body fat percentage (BFP) was assessed using a validated bioelectrical impedance analysis (BIA) device (Omron Karada Scan).

MC4R genotyping

Approximately 3 mL of whole blood was collected in ethylenediaminetetraacetic acid (EDTA) tubes for genomic DNA extraction using the gSYNC™ DNA Extraction Kit (Geneaid). Polymerase Chain Reaction (PCR) was performed in a volume of 20 µL, each reaction containing 2 µL DNA product, 2 µL 10x buffer, 1.6 µL dNTP, 0.2 µL Taq DNA polymerase, 0.8 µL forward primer, 0.8 µL reverse primer, and 12.6 µL Double Distilled Water (DDW). The specific primers used for amplifying the rs17782313 region were: Forward 5'-AAGGTTTAAACAAGAGAGG-3' and Reverse 5'-AAGCTGACAAGTCGTCACT-3'. PCR conditions were 5 minutes at 94˚C for pre-denaturation and 35 cycles of 30 seconds at 94˚C for denaturation, 30 seconds at 58˚C for annealing, 30 seconds at 72˚C for extension, and 10 minutes at 72˚C for final extension using a Perkin Elmer Thermal Cycler PCR system. The resulting PCR products (approximately 318 bp in length) were visualized on a standard 1.5% agarose gel stained with ethidium bromide. The SNP rs17782313 (C>T) was used for genotyping by the PCR-Restriction Fragment Length Polymorphism (PCR-RFLP) method with the restriction enzyme *HpyCH4IV*. PCR-RFLP was performed in a reaction volume of 20 µL with approximately 15 µL of PCR product, 2 µL of 10x buffer, 0.5 µL of restriction enzyme, and 2.8 µL of DDW. The mixture was incubated at 37°C for proper enzymatic digestion. The digested product was run on a 4% agarose gel.

Data analysis

Statistical analyses were performed using GraphPad software. Data distribution was assessed for normality. For normally distributed data, an independent t-test was used; otherwise, the Mann–Whitney U test was applied. MC4R genotypes were compared with body fat percentage. Statistical significance was defined as a p-value < 0.05.

Ethical statement

Ethical approval was obtained from Ethical unit of the Faculty of Medicine, Trisakti University, Jakarta (Ethical Clearance No.: 001/KER/FK/05/2025). All participants provided written informed consent prior to participation. Participant confidentiality and data privacy of were strictly maintained throughout the study. Participants were informed about the study objectives and were free to withdraw at any time without consequences. All procedures involving human participants and biological samples were conducted in accordance with applicable ethical guidelines and regulations.

RESULTS

This study included 79 participants whose demographic and anthropometric characteristics were evaluated, including age, sex, body weight, and height. The mean age was 41.01 ± 8.92 years, with a median age of 41 years, indicating a relatively symmetrical age distribution. Participants ranged from 21 to 56 years, representing young to middle-aged adults. Females comprised the majority of the sample (53 participants, 67.1%), while males accounted for 26 participants (32.9%). The mean body weight was 74.34 ± 13.95 kg (median: 72.7 kg; ranged from 48.4 kg to 129.0 kg), reflecting substantial variability. The mean height was 161.10 ± 8.20 cm (median: 159.0 cm; range: 143.0 cm to 178.0 cm). These baseline characteristics are summarized in Table 1.

Table 1. Basic Characteristic of Subject (N=79)

Variable	Value
Age (years)	
Mean ± SD	41.01 ± 8.92
Median (min-max)	41.00 (21.00 – 56.00)
Gender, n (%)	
Female	53 (67.1)
Male	26 (32.9)
Weight (kg)	
Mean ± SD	74.34 ± 13.95
Median (min-max)	72.70 (48.40 – 129.00)
Height (cm)	
Mean ± SD	161.10 ± 8.20
Median (min-max)	159.00 (143.00 – 178.00)

The majority of participants in this study fell into the obesity category, with 30 respondents or 41.7% of the total sample. The overweight group ranked second with 26 respondents (36.1%), while the normal BMI group (18.5–25) included 15 respondents (20.8%). Only one respondent (1.4%) was categorized as underweight (BMI <18.5). This distribution indicates that most study participants were overweight or obese (Table 2).

Table 2. Body Mass Index (BMI)

BMI Classification	Frequency	Percentage (%)
Underweigth (< 18,5)	1	1.4
Normal (18,5-25)	15	20.8
Overweight (≥ 25)	26	36.1
Obesity (≥30)	30	41.7

The distribution of body fat percentage classifications among male participants showed that the majority of respondents fell into the obese category, with 17 individuals (65.4%). Meanwhile, 4 respondents (15.4%) were classified as overfat, and 5 individuals (19.2%) fell into the healthy category. No male participants were classified as under fat. Among female participants, the tendency toward excess body fat appeared to be higher compared to males. A total of 42 women (79.2%) were categorized as obese, while 6 individuals (11.3%) were overfat. The remaining 4 respondents (7.5%) were classified as healthy, and only 1 person (1.9%) was under fat (Table 3).

The table 4 presents the distribution of MC4R genotypes among 79 subjects included in the study. Three genotypes were identified: TT (wild type), CT (heterozygous), and CC (homozygous mutant). The TT genotype, representing individuals who carry two normal alleles of the MC4R gene, was observed in 38 participants, accounting for 48.1% of the total sample. This indicates that nearly half of the studied population possesses the non-mutated form of the gene.

Table 3. Body Fat Mass Percentage Data

Variable	Frequency	Percentage (%)
Man		
Under fat	0	0
Healthy	5	19,2
Overfat	4	15,4
Obese	17	65,4
Woman		
Under fat	1	1,9
Healthy	4	7,5
Overfat	6	11,3
Obese	42	79,2

The CT genotype, representing heterozygous individuals who carry one normal allele (A) and one mutant allele (G), was found in 31 subjects, or 39.2% of the total. The relatively high frequency of the heterozygous genotype suggests a considerable presence of the G allele within the population, indicating genetic variability at the MC4R locus. Meanwhile, the CC genotype, in which both alleles carry the mutation, was detected in 10 participants, corresponding to 12.7% of the total sample. Although this percentage is lower than that of the other genotypes, it still reflects a notable proportion of individuals who are homozygous for the variant allele.

Table 4. Genotype Frequency Distribution and Allel of MC4R Gene

Genotipe MC4R	Frequency (n)	Percentage (%)
TT (Wild type)	38	48.1
CT (Heterozygote)	31	39.2
CC (Homozygote mutant)	10	12.7

Table 5 presents the association between MC4R genotypes and the proportion of participants classified as obese based on body fat percentage. The TT genotype, considered the wild-type variant, was used as the reference group. Among individuals carrying the TT genotype, 50% were classified as obese. Participants with the CT genotype showed a higher prevalence of obesity, with 67.7% categorized as obese. This corresponded to an odds ratio of 2.00 (95% CI: 0.81–4.90) and a p-value of 0.15, indicating a higher tendency toward obesity compared with the TT group; however, this association did not reach statistical significance. The highest prevalence of obesity was observed among individuals with the CC genotype, in which 80% were classified as obese. This group demonstrated a significantly increased risk of obesity, with an odds ratio of 4.00 (95% CI: 1.02–15.64) and a p-value of 0.04, suggesting a statistically significant association between the CC genotype and obesity based on body fat percentage.

Table 5. Association between MC4R Gene and Obesity Status Based on Body Fat Percentage

MC4R Genotype	Non-Obese (n, %)	Obese (n, %)	Odds Ratio (95% CI)	p-value
TT (Wild type)	19 (50%)	19 (50%)	1.00 (Ref)	—
CT (Heterozygote)	10 (32.3%)	21 (67.7%)	2.00 (0.81–4.90)	0.15
CC (Homozygote)	2 (20%)	8 (80%)	4.00 (1.02–15.64)	0.04*

* Statistically significant ($p < 0.05$)

These findings suggest a dose-dependent relationship between MC4R genetic variation and obesity risk. As the number of mutant alleles increased from zero (TT) to one (CT) and two (CC), the proportion of obese individuals also increased. This pattern supports the role of the MC4R gene in body fat regulation and indicates that the presence of the mutant allele may contribute to greater adiposity. However, given the multifactorial nature of obesity, this genetic effect is likely to interact with environmental and lifestyle factors in influencing obesity risk.

DISCUSSION

This study provides epidemiological evidence demonstrating a significant association between the *MC4R* rs17782313 polymorphism and adiposity, as measured by body fat percentage (BFP), among Indonesian adults. Our findings reveal that individuals homozygous for the risk allele (CC genotype) have approximately a four-fold higher likelihood of being categorized as obese based on their BFP compared with those carrying the wild-type TT genotype. By evaluating BFP rather than relying exclusively on Body Mass Index (BMI), this study offers a more physiological representation of pathological fat accumulation. BMI is inherently limited because it cannot differentiate between lean muscle mass and adipose tissue. Conversely, adiposity-based measures like BFP and visceral fat are much stronger predictors of metabolic complications, such as insulin resistance, dyslipidemia, and cardiovascular disease. [12] Our

findings demonstrate that individuals carrying the homozygous mutant CC genotype of MC4R rs17782313 have approximately a four fold increased risk of being categorized as obese based on body fat percentage compared with individuals carrying the wild-type TT genotype.

This observation are consistent previous genetic association studies identifying MC4R as one of the most consistently replicated loci related to obesity susceptibility. Genome-wide association studies (GWAS) have repeatedly demonstrated that common polymorphisms located near the MC4R gene are strongly associated with increased adiposity and body weight regulation.[13] Importantly, our results expand this understanding by emphasizing that MC4R variation is associated not only with BMI but also with actual fat mass accumulation, which may better reflect the biological impact of this gene.[8,14] The biological mechanisms underlying this association center heavily on the leptin-melanocortin signaling pathway, where *MC4R* acts as a central node for energy homeostasis in the hypothalamus. *MC4R* is primarily activated by anorexigenic peptides such as α-melanocyte-stimulating hormone (α-MSH) cleaved from POMC, which suppresses appetite and boosts metabolic energy expenditure. Simultaneously, it is antagonized by the agouti-related peptide (AgRP), which promotes feeding.[15]

MC4R signaling is activated by melanocortin peptides such as α-melanocyte-stimulating hormone (α-MSH), which produce anorexigenic effects by suppressing appetite and increasing energy expenditure. Conversely, inhibition of MC4R by agouti-related peptide (AgRP) stimulates appetite and promotes positive energy balance. Disruption of this signaling pathway due to genetic polymorphisms can impair satiety regulation and promote excessive caloric intake, ultimately leading to increased adipose tissue accumulation. Among these genetic variants, the single-nucleotide polymorphism (SNP) rs17782313 located near the MC4R gene has been widely studied and consistently associated with obesity susceptibility across multiple populations. Individuals carrying the C risk allele of rs17782313 tend to show increased adiposity and higher body mass index (BMI), supporting the role of MC4R as one of the most reproducible loci associated with obesity in genome-wide association studies.[16]

Beyond its association with BMI, emerging evidence indicates that MC4R variants may more specifically influence body composition, including body fat percentage (BFP) and fat mass distribution. Studies evaluating body composition using imaging techniques such as dual-energy X-ray absorptiometry (DXA) have demonstrated that polymorphisms near MC4R are associated with increased total body fat and altered fat distribution patterns, suggesting that the genetic influence of MC4R extends beyond body weight to actual adipose tissue accumulation. This finding is important because BMI alone cannot distinguish between lean mass and fat mass, whereas BFP provides a more precise measure of adiposity. Therefore, evaluating the relationship between MC4R polymorphisms and BFP offers a more physiologically relevant understanding of how genetic variation contributes to obesity.[17,4,18] Mechanistically, MC4R regulates both appetite and metabolic energy expenditure through sympathetic nervous system activation and hypothalamic signaling pathways. Variants affecting MC4R function may lead to reduced receptor activity, resulting in impaired satiety signaling, increased food intake, and decreased energy expenditure. Over time, this imbalance promotes the preferential storage of excess energy as adipose tissue, contributing to higher body fat percentage. In addition, MC4R signaling has been implicated in glucose metabolism and insulin sensitivity, indicating that alterations in this pathway may influence not only adiposity but also metabolic health outcomes.[19,20,21]

Recent studies also suggest that the phenotypic expression of MC4R variants may be influenced by environmental factors, particularly dietary patterns and lifestyle behaviors. Gene environment interactions have been observed in which individuals carrying MC4R risk alleles exhibit greater susceptibility to fat accumulation when exposed to energy-dense diets or unfavorable dietary fat profiles. Conversely, healthier dietary patterns may attenuate the metabolic impact of these variants.[22] Collectively, these findings support the concept that MC4R contributes to obesity not only through increased body weight but also through changes in fat mass and body fat percentage. Therefore, investigating the relationship between MC4R polymorphisms and BFP provides important insight into the genetic determinants of adiposity

and may improve the understanding of obesity pathophysiology beyond traditional BMI-based assessments.[23] Experimental studies have shown that the rs17782313 polymorphism located near MC4R may alter receptor signaling or gene expression, resulting in impaired satiety signaling and increased caloric intake.[24] Consequently, individuals carrying the C risk allele may exhibit greater fat accumulation due to both increased appetite and reduced metabolic energy expenditure. Importantly, the impact of MC4R polymorphisms appears to vary across different ethnic populations. Asian populations, including Indonesians, tend to exhibit a distinct metabolic phenotype characterized by higher body fat percentage and greater visceral adiposity at lower BMI values compared with Western populations.[25,26] This condition has been described as the "metabolically obese normal-weight phenotype," in which individuals with relatively normal BMI still possess high levels of body fat and elevated metabolic risk.[27] Because of this characteristic, BMI may underestimate the prevalence of obesity in Asian populations. Therefore, evaluating obesity through BFP becomes particularly relevant in this demographic. The present findings thus provide valuable evidence regarding the role of MC4R polymorphisms in influencing adiposity within Southeast Asian populations, which remain underrepresented in genetic obesity research.[3]

Importantly, the phenotypic expression of the *MC4R* risk allele is deeply intertwined with ethnic contexts and dietary pattern. Research on gene diet interactions illustrates that the metabolic detriment of *MC4R* variants is sharply amplified in obesogenic environments characterized by high-fat and high-carbohydrate diets.[28] The traditional Indonesian dietary pattern, heavily reliant on refined carbohydrates (e.g., white rice) and frequently combined with fat-rich cooking methods, likely creates an environment that triggers and exacerbates the genetic susceptibility carried by the C allele.[21,29,30] Furthermore, Asian populations, including Indonesians, exhibit a distinct "metabolically obese normal-weight" phenotype. Because Asians tend to accumulate a higher percentage of total body fat and visceral adiposity at lower BMI thresholds than Western populations, standard BMI classifications frequently underestimate true obesity in this demographic.[31,17] Conversely, dietary patterns rich in fiber and unsaturated fats may attenuate the genetic susceptibility to obesity.[3] Therefore, individuals carrying the CT or CC genotype in the present cohort may experience greater fat accumulation due to the combined effects of impaired satiety signaling and environmental exposure to high-calorie diets.[15,18,22,32]

Therefore, validating the strong association between the *MC4R* polymorphism and BFP in this study provides highly relevant genetic data for Southeast Asian populations, proving that evaluating actual adiposity is critical for accurate risk assessment.[13,19] Despite the important insights provided by this study, several limitations should be acknowledged. First, the cross-sectional design limits the ability to determine a temporal causal relationship between MC4R genotype and the development of obesity. Second, the relatively small sample size may reduce statistical power and limit the generalizability of the findings to the broader Indonesian population. Third, the present study did not incorporate detailed measurements of lifestyle factors such as daily caloric intake, dietary composition, and physical activity levels, which may act as confounding variables in genetic association studies. Future research should employ larger, multi-center longitudinal designs and incorporate comprehensive lifestyle data and multivariable regression analysis to more precisely quantify the independent contribution of MC4R rs17782313 to adiposity in Indonesian populations.

CONCLUSION

The MC4R rs17782313 polymorphism is significantly associated with increased body fat percentage among Indonesian adults. Individuals carrying the C risk allele, particularly those with the CC genotype, have a higher likelihood of obesity based on body fat percentage. Despite limitations, including the relatively small sample size and the absence of multivariable adjustments, these findings highlight the potential role of genetic factors in modulating lipid metabolism and body fat regulation within this population. These results underscore the potential utility of incorporating genetic screening into targeted, culturally appropriate obesity prevention and precision-management strategies.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest related to this study. The authors have no financial or personal relationships with any organization or entity that could inappropriately influence or bias the content of this manuscript. The authors also confirm that no financial support, commercial funding, or competing interests from any company whose products may be related to the subject of this research influenced the design, analysis, interpretation, or publication of this study. Any potential conflicts of interest, including financial arrangements with organizations whose products are relevant to the submitted manuscript or with companies producing competing products, would be disclosed at the time of revision. Such information will be treated confidentially during the peer-review process and will not influence the editorial decision.

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DATA AVAILABILITY

The data supporting the results of this study are available upon request from the corresponding author. Due to privacy concerns and ethical considerations, the data are not publicly accessible. However, researchers interested in accessing the data may contact the corresponding author directly via email at meutia.atika@trisakti.ac.id.

SUPPLEMENTAL DATA

No additional supplemental data are provided for this study. All relevant data supporting the findings of this research are included within the main article. Additional information is available from the corresponding author upon reasonable request.

AUTHOR CONTRIBUTIONS

M.A.F. contributed to the conceptualization of the study, methodology, and manuscript drafting. Y. provided assistance in data collection and analysis, contributing to the results section. D.Y. supported the analysis and interpretation of the data, especially in statistical modeling. A.H. was responsible for the review and editing of the manuscript, ensuring clarity and cohesion. S. supervised the research and provided critical revisions to the manuscript, particularly in terms of the study design and methodology.

DECLARATION OF USING AI IN THE WRITING PROCESS

The authors affirm that artificial intelligence (AI) tools were used solely to assist in the writing process for language enhancement purposes, including grammar checking, proofreading, paraphrasing, and improving the clarity and readability of the manuscript. No AI tools, including generative AI systems such as ChatGPT, Gemini, or similar platforms, were used to generate original scientific content, perform data analysis, interpret research findings, or draw scientific conclusions. All analyses, interpretations, and scientific arguments presented in this manuscript were conducted entirely by the authors. The authors take full responsibility for the accuracy, integrity, and originality of the manuscript, including all data, interpretations, and conclusions presented.

LIST OF ABBREVIATIONS

In this manuscript, the following abbreviations are used: In this manuscript, the following abbreviations are used: AgRP: Agouti-Related Peptide; AI: Artificial Intelligence; BFP: Body Fat Percentage; BIA: Bioelectrical Impedance Analysis; BMI: Body Mass Index; CI: Confidence Interval; DDW: Double

Distilled Water; DNA: Deoxyribonucleic Acid; DXA: Dual-Energy X-ray Absorptiometry; EDTA: Ethylenediaminetetraacetic Acid; GWAS: Genome-Wide Association Studies; HPLC: High-Performance Liquid Chromatography; LEPRs: Leptin Receptors; MC4R: Melanocortin-4 Receptor; MRI: Magnetic Resonance Imaging; PCR: Polymerase Chain Reaction; PCR-RFLP: Polymerase Chain Reaction-Restriction Fragment Length Polymorphism; POMC: Pro-opiomelanocortin; SD: Standard Deviation; SNP: Single Nucleotide Polymorphism; α-MSH: α-Melanocyte-Stimulating Hormone.

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