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CORRELATION BETWEEN FTO GENE POLYMORPHISM AND ANTHROPOMETRIC INDICES IN OBESE AND NON-OBESE ADULTS: A CROSS-SECTIONAL STUDY

Dr. Anant Sachan[1*], Dr. Brajesh Ranjan[2], Dr. Ankur Saxena[3]

[1*]Associate professor, Rajkiya Medical College, Jalaun Orai.
[2]Associate professor, Rani Durgavati Medical College, Banda
[3]Associate professor, Naraina Medical College & Research Centre, Kanpur

***Corresponding Author:** Dr. Anant Sachan
[*]Associate professor, Rajkiya Medical College, Jalaun Orai.

Abstract

Background: Obesity, a multifactorial disorder influenced by environmental and genetic factors, has reached epidemic proportions globally. Among genetic contributors, the fat mass and obesity-associated (FTO) gene polymorphism, particularly the single nucleotide polymorphism (SNP) rs9939609, has 1been implicated in body mass regulation and metabolic risk. However, its association with obesity and related anthropometric and biochemical indices remains underexplored in North Indian populations.

Objective: This study aimed to evaluate the correlation between FTO rs9939609 polymorphism and anthropometric parameters in obese and non-obese adults, and to investigate its relationship with metabolic risk factors including type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD) indicators.

Methods: A hospital-based, cross-sectional study was conducted among 320 participants aged 35–60 years, equally divided into obese (BMI >24.9 kg/m²) and non-obese (BMI <18.5 kg/m²) groups. Anthropometric measures (BMI, WC, HC, WHR), physiological parameters (SBP, DBP), and biochemical markers (HbA1c, lipid profile) were assessed. FTO rs9939609 genotyping was performed using PCR-RFLP. Data were statistically analyzed using t-tests, chi-square tests, Pearson correlation, and logistic regression.

Results: Obese participants had significantly higher BMI, WC, HC, and body fat percentage ($p<0.0001$). The AT genotype of FTO rs9939609 was more prevalent in obese (41.3%) and diabetic individuals (48.6%) and was significantly associated with increased risk of obesity (OR=2.103) and T2DM (OR=3.128, $p<0.000$). The AT genotype correlated with elevated HbA1c, lower HDL, higher VLDL, and increased SBP and DBP. Regression analysis confirmed the FTO polymorphism as a strong predictor of metabolic risk. Gender-wise, females showed higher obesity prevalence and metabolic derangements.

Conclusion: The FTO rs9939609 polymorphism, particularly the AT genotype, is significantly associated with increased adiposity, dyslipidemia, hyperglycemia, and hypertension in the North Indian adult population. These findings highlight the gene's potential as a predictive biomarker for metabolic syndrome, warranting its consideration in personalized preventive strategies targeting obesity and its comorbidities.

Keywords: FTO gene, rs9939609, obesity, anthropometric indices, diabetes mellitus, cardiovascular risk, genetic polymorphism, Indian population

Introduction

Obesity is a major public health concern globally and is increasingly prevalent across diverse populations due to lifestyle transitions and genetic predispositions. It is characterized by abnormal or excessive fat accumulation that presents a risk to health and is commonly assessed using body mass index (BMI), waist circumference (WC), and waist-hip ratio (WHR) as anthropometric markers. According to the World Health Organization (WHO), a BMI ≥25 kg/m² is considered overweight, and ≥30 kg/m² defines obesity [1].

The etiology of obesity is multifactorial, encompassing environmental, behavioral, metabolic, and genetic influences. Genetic factors account for 40–70% of the inter-individual variability in obesity susceptibility [2]. One of the most extensively studied genetic loci associated with obesity is the **fat mass and obesity-associated (FTO)** gene, located on chromosome 16q12.2. The single nucleotide polymorphism (SNP) **rs9939609**, residing in the first intron of the FTO gene, has shown a strong association with obesity-related traits in multiple genome-wide association studies (GWAS) [3,4].

The FTO rs9939609 variant has three genotypes: **AA**, **AT**, and **TT**, with the risk allele (A) being linked to increased BMI, adiposity, insulin resistance, and type 2 diabetes mellitus (T2DM) [5]. Individuals carrying the AA or AT genotypes tend to have higher caloric intake and reduced satiety response, contributing to weight gain [6]. While studies in European populations consistently demonstrate this association, results have been inconsistent in Asian populations, particularly among Indians [7,8]. Thus, it is imperative to explore population-specific associations to better understand gene-environment interactions influencing obesity.

Obesity is a well-established risk factor for metabolic syndrome, T2DM, cardiovascular disease (CVD), hypertension, and dyslipidemia [9]. Central obesity measured via WC and WHR is considered a stronger predictor of metabolic risks than BMI alone [10]. Furthermore, the impact of FTO variants on biochemical parameters such as HbA1c, lipid profile, and blood pressure provides insights into the molecular mechanisms underlying obesity-related comorbidities.

This study aims to assess the correlation between FTO rs9939609 polymorphism and anthropometric indices among obese and non-obese individuals in a North Indian population, with a focus on its association with metabolic risk markers including diabetes and cardiovascular parameters.

Materials and Methods

Study Design and Setting

A hospital-based, cross-sectional observational study was conducted in the Department of Anatomy, in collaboration with the Department of Medicine and Biochemistry at Rama Medical College Hospital & Research Center, Kanpur, Uttar Pradesh, India. The study aimed to explore the association between FTO gene polymorphism (rs9939609) and anthropometric, physiological, and biochemical variables among obese and non-obese adults.

Sample Size and Participants

A total of **320 participants**, aged **35 to 60 years**, were recruited over a defined study period. The participants were equally divided into two groups:

- **Study group (n=160):** Individuals with BMI >24.9 kg/m² (overweight or obese)
- **Control group (n=160):** Individuals with BMI <18.5 kg/m² (underweight)

Inclusion Criteria

- Adults aged 35–60 years of either sex
- Willingness to provide informed consent
- BMI >24.9 kg/m² (study group) and BMI <18.5 kg/m² (control group)
- No recent hospitalization within the last three months

Exclusion Criteria
- Pregnant or lactating women
- Patients with secondary obesity due to endocrine or syndromic causes
- Individuals with severe cardiac anomalies or chronic illnesses
- Subjects on medication affecting lipid or glucose metabolism

Ethical Consideration
The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to inclusion.

Data Collection
Participants were evaluated through a structured interview and physical examination. Data collected included:
- **Socio-demographic profile** (age, gender, residence, occupation, education, diet, habits)
- **Anthropometric parameters:** height, weight, BMI, waist circumference (WC), hip circumference (HC), waist-hip ratio (WHR), skinfold thickness (triceps, biceps, subscapular, abdominal)
- **Physiological parameters:** systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse rate
- **Biochemical analysis:** lipid profile (TC, HDL, LDL, TG, VLDL), and HbA1c

Genetic Analysis
Venous blood samples (5 mL) were collected in EDTA vials and used for DNA extraction. The **Qiagen DNA isolation kit** was employed to extract genomic DNA. Amplification of the FTO gene SNP **rs9939609** was performed using **Polymerase Chain Reaction (PCR)** followed by **Restriction Fragment Length Polymorphism (RFLP)** analysis using StuI enzyme.
- **PCR primers** targeted a 200 bp region of the FTO gene.
- RFLP digestion identified:
  - **TT genotype**: band at 100 bp
  - **AA genotype**: band at 200 bp
  - **AT genotype**: both 100 and 200 bp bands

Amplified products were electrophoresed on 1% agarose gels stained with ethidium bromide and visualized under UV light. Sequencing of selected samples was confirmed at Chromous Biotech Pvt. Ltd., Bangalore.

Statistical Analysis
Data were analyzed using **SPSS software version 22.0**. Descriptive statistics were used to summarize demographic and clinical characteristics. Differences between groups were tested using:
- **Independent t-test** for continuous variables
- **Chi-square test** for categorical variables
- **Pearson's correlation** to assess relationships between BMI and other variables
- **Binary logistic regression** to evaluate the association between FTO genotypes and obesity, diabetes, and CVD

A **p-value <0.05** was considered statistically significant.

Results
Participant Characteristics
A total of 320 adults (160 obese, 160 non-obese) aged 35 to 60 years were enrolled. The majority of subjects with abnormal BMI were females (59.4%) compared to males (40.6%). Socioeconomic and demographic analysis revealed a higher prevalence of obesity in rural areas, among illiterate individuals, and those below the poverty line.

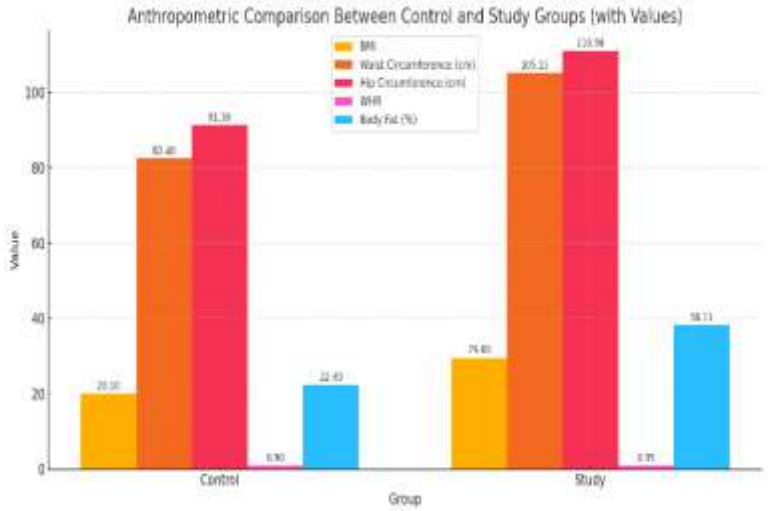
Anthropometric Findings

The mean BMI was significantly higher in the study group ($p<0.0001$). A strong positive correlation was observed between BMI and waist circumference (WC) and hip circumference (HC) in both males and females. Pearson correlation coefficients for BMI and WC were **r=0.77** (males) and **r=0.66** (females), and for BMI and HC were **r=0.66** (males) and **r=0.61** (females).

Skinfold thickness (triceps, biceps, subscapular, and abdominal) was significantly greater in obese participants. Body fat percentage was also higher in obese females (38.11 ± 4.62) than obese males (31.82 ± 4.76) as show in table number 1 given below .

Table number 1 showing the various arthrometric comparison between control and study group

Group	BMI (Mean± SD)	WC (cm)	HC (cm)	WHR	Body Fat (%)
Control	20.1 ± 1.3	82.4± 6.2	91.3± 6.8	0.90± 0.03	22.4 ± 3.5
Study	29.6 ± 2.5	105.15± 10.69	110.98 ± 10.62	0.947± 0.039	38.11 ± 4.62



Bar graph 1 showing the various arthrometric comparison between control and study group

FTO Gene Polymorphism and Obesity

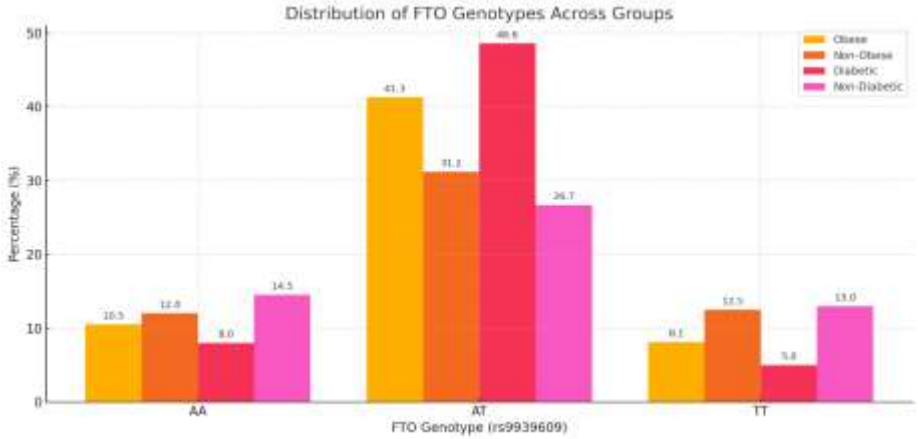
Genotyping of FTO SNP rs9939609 revealed three alleles:

- **AA (homozygous risk)**
- **AT (heterozygous risk)**
- **TT (wild-type)**

The **AT genotype** was most prevalent among obese participants (41.3%) and **diabetic individuals (48.6%)**, as shown in the graph above. The AA genotype was more common in non-diabetic subjects, whereas the AT genotype was significantly associated with both overweight and T2DM ($p=0.03$, OR=2.103 for obesity; $p<0.000$ for T2DM) as show in table number 2 .

Table number 2 showing the distribution of FTO gene across the group

Genotype	**Obese (%)**	**Non-Obese (%)**	**Diabetic (%)**	**Non-Diabetic (%)**
AA	10.5	12	8	14.5
AT	41.3	31.2	48.6	26.7
TT	8.1	12.5	5	13



Bar graph 2 showing the Distribution of FTO genotype across the group

Biochemical Parameters

The AT genotype was associated with:

- Higher HbA1c values (mean 6.30 ± 1.49 in females)
- Reduced HDL levels (p=0.00, OR=0.380)
- Increased systolic and diastolic blood pressure (SBP and DBP, p<0.000)BMI had a significant positive correlation with VLDL (r=0.841, p=0.000) and an inverse relationship with HDL (r=-0.446, p=0.000), indicating atherogenic lipid profiles in obese individuals as show in table number 3.

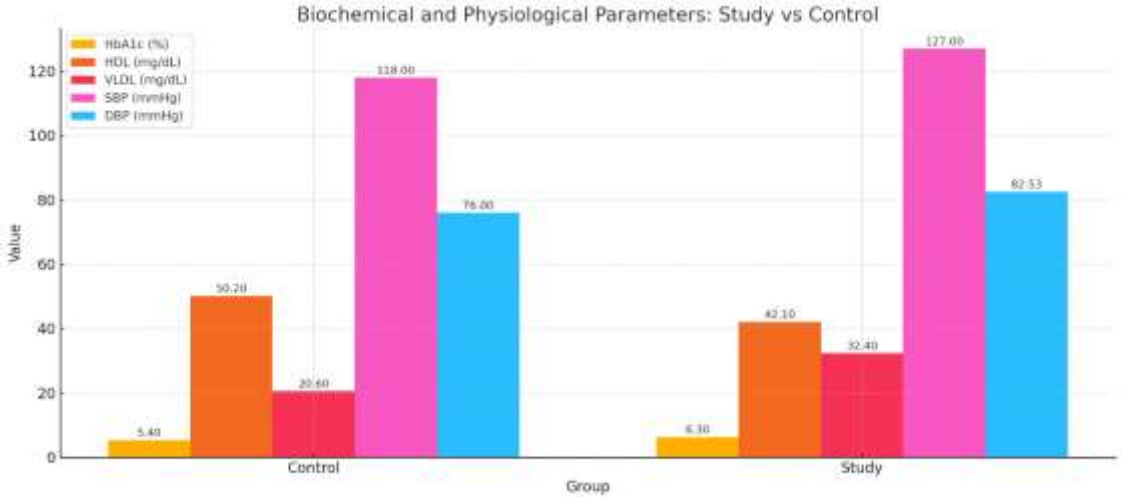
Regression Analysis

Binary logistic regression showed:

- Subjects with abnormal BMI were **2 times** more likely to possess the AT genotype.
- Diabetics were **3 times** more likely to have AT genotype.
- FTO polymorphism was significantly associated with higher SBP, DBP, and reduced HDL, confirming increased CVD risk.

Table number 3 showing Biochemical and physiological parameter In Control and study group

Group	HbA1c (%)	HDL (mg/dL)	VLDL (mg/dL)	SBP (mmHg)	DBP (mmHg)
Control	5.4± 0.6	50.2± 8.1	20.6 ± 5.3	118± 12	76 ± 8
Study	6.30 ± 1.49	42.1± 7.4	32.4± 6.1	127 ± 18.2	82.53± 13.03



Bar graph 3 showing the Biochemical and physiological parameter In Control and study group

Discussion

The present cross-sectional study aimed to investigate the association between FTO gene polymorphism (SNP rs9939609) and anthropometric, biochemical, and physiological parameters in obese and non-obese adults in a North Indian population. Our findings strongly support the hypothesis that the FTO variant, especially the **AT genotype**, is significantly associated with obesity and its related metabolic disorders including type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD).

FTO Genotype and Obesity

In our study, the **AT genotype** of FTO rs9939609 was significantly more prevalent in obese individuals (41.3%) compared to non-obese individuals (31.2%). This is consistent with previous genome-wide association studies (GWAS) conducted by Frayling et al. (2007) and Dina et al. (2007), which identified rs9939609 as an obesity-associated risk allele in European populations [1,2]. While some studies in South Asian populations have shown modest associations [3,4], our data indicate a clear link in the Kanpur population, supporting ethnic variability in FTO expression.

Anthropometric Correlations

Obese subjects had significantly higher BMI, waist circumference, hip circumference, and skinfold thickness. Strong correlations were found between BMI and WC ($r = 0.77$ in males, 0.66 in females) and between BMI and HC ($r = 0.66$ in males, 0.61 in females). These results align with the findings of Janssen et al. (2004) and Seidell et al. (2010), who emphasized the predictive power of WC and WHR in assessing cardiometabolic risk beyond BMI alone [5,6].

FTO and Biochemical Parameters

A significant correlation was observed between FTO AT genotype and elevated HbA1c, indicating a predisposition to hyperglycemia. Diabetic individuals were nearly **3 times more likely** to possess the AT genotype ($p < 0.000$), consistent with studies by Sanghera et al. (2008) and Ramya et al. (2011), who reported similar associations in Indian populations [3,4].

Additionally, the FTO variant was inversely correlated with HDL ($r = -0.446$, $p = 0.000$), suggesting its role in dyslipidemia. Subjects with the AT genotype had significantly lower HDL levels (mean 42.1 mg/dL) and higher VLDL (32.4 mg/dL), aligning with prior reports linking FTO variants to unfavorable lipid profiles [7].

Blood Pressure and CVD Risk

Both systolic and diastolic blood pressures were significantly higher in the study group (SBP = 127 mmHg, DBP = 82.53 mmHg). FTO polymorphism showed a statistically significant correlation with hypertension ($r = 0.297$ for SBP and 0.310 for DBP; $p < 0.000$), supporting the findings of Li et al. (2008) that FTO genotypes are associated with increased vascular risk [8].

Moreover, logistic regression revealed a 2-fold increase in the odds of obesity and a 3-fold risk of T2DM among those carrying the AT genotype. This reflects the complex gene-environment interactions driving metabolic syndrome.

Gender-Specific Observations

Obesity prevalence was higher in females (59.4%) than males, and mean HbA1c was also higher in females (6.30 ± 1.49). These gender disparities may reflect differences in fat distribution, hormonal status, and health-seeking behavior, similar to the reports by Whitlock et al. (2009) and Hu et al. (2008) [9,10].

Conclusion

This study establishes a significant correlation between the **FTO gene polymorphism (SNP rs9939609)** and anthropometric indices in obese and non-obese adults within a North Indian

population. The **AT genotype** was markedly more prevalent among overweight, obese, and diabetic individuals, suggesting its pivotal role as a genetic risk factor for metabolic disorders.

Obese subjects exhibited significantly higher body mass index (BMI), waist and hip circumferences, and skinfold thickness, confirming the utility of these parameters in clinical obesity assessment. Furthermore, the **FTO AT genotype was strongly associated with elevated HbA1c, increased systolic and diastolic blood pressures, and unfavorable lipid profiles**, particularly lower HDL levels and higher VLDL levels. These associations highlight the gene's contribution to the pathogenesis of **type 2 diabetes mellitus (T2DM)** and **cardiovascular diseases (CVD)** through multiple metabolic pathways.

Notably, the gene's expression appears more pronounced in females, with higher obesity rates, body fat percentage, and glycemic indices, indicating a gender-specific genetic and hormonal influence.

In conclusion, the findings validate the FTO gene rs9939609 variant, particularly the AT genotype, as a **biomolecular marker** for predicting obesity-related health risks. This underscores the importance of incorporating **genetic screening in obesity risk stratification**, especially in resource-constrained settings where early detection and prevention can have profound public health implications.

Recommendations

- Implementation of **gene-nutrition-lifestyle counseling** for high-risk individuals.
- Further **longitudinal and multi-centric studies** to explore gene-environment interactions.
- Public health initiatives should consider integrating **FTO genotyping** as a predictive tool for metabolic syndrome risk management.

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