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Case report

Unlocking weight loss potential: Investigating the impact of personalized nutrigenetic-based diet in an Indian population

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Abstract: Obesity and its related complications have become a pressing public health issue, requiring personalized nutritional and lifestyle interventions. Nutrigenetic diets utilize genetic information to tailor dietary recommendations based on an individual's genetic variations. This case-control study aimed to evaluate the impact of a nutrigenetic diet on weight loss and clinical parameters. Three groups were included: obese individuals following a nutrigenetic diet (n = 27), obese individuals following a generic diet (n = 23), and a control group of individuals with a normal body mass index (BMI) (n = 19). Based on polygenic risk scoring, personalized diet plans were developed that considered various genetic traits such as the impact of high amounts of protein on weight loss, the impact of low amounts of carbohydrates on weight loss, the risk of a high body fat percentage, the impact of a calorie restriction on weight loss, lactose intolerance, and gluten intolerance. By assessing a subject's risk scores, a personalized diet was created. Measurements taken at baseline and after four months included weight, BMI, body fat, lean mass, fasting blood sugar levels, total cholesterol, triglycerides, thyroid-stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), and uric acid. Results showed significant differences favouring the nutrigenetic group in weight ($p < 0.001$), BMI ($p < 0.001$), and body fat percentage ($p = 0.05$) when compared to the control and the generic diet groups. Additionally, the nutrigenetic group exhibited significant improvements in triglycerides ($p = 0.003$). Moreover, the within-group effect among nutrigenetic subjects showed a significant weight reduction ($p < 0.001$), BMI ($p < 0.001$), body fat percentage ($p < 0.001$), fat mass ($p < 0.001$), fasting blood sugar level ($p = 0.019$), and uric acid ($p = 0.042$). These findings suggest that a nutrigenetic diet may yield more effective

weight loss and improved clinical parameters compared to a generic diet.

Keywords: obesity; personalized nutrition; nutrigenomic-based diet; weight loss

1. Introduction

In a world where obesity has become an escalating concern, recent studies and guidelines have shed light on its prevalence and impact on the Indian population [1]. According to the World Health Organization (WHO) guidelines for the Asian population, obesity is defined as having a body mass index (BMI) equal to or exceeding 25 kg/m^2, while overweight falls within the range of 23.0–24.9 kg/m^2 [2]. In India, the effects of obesity have significantly affected a staggering number of individuals, recently surpassing 135 million [1].

The prevalence rates of obesity and central obesity vary across different demographic factors, including age, sex, geographical environment, and socio-economic status. The Indian Council of Medical Research–India Diabetes (ICMR-INDIAB) study conducted in 2015 revealed crucial insights into the prevalence of obesity in India. The study reported obesity rates ranging from 11.8% to 31.3%, while central obesity rates ranged from 16.9% to 36.3% [1]. Such alarming figures pose significant challenges for the government in terms of healthcare provision and financial implications.

Recognizing the urgency to address obesity-related issues, researchers have delved into the intricate relationship between genetic variations and the efficacy of specific diets in weight loss and metabolic improvements. For instance, the fat mass and obesity-associated protein (FTO) variants have gained attention. Studies have revealed that individuals who carry the risk allele (A allele) experience more favourable outcomes when following a high-protein diet, including weight loss, improved body composition, and positive changes in fat distribution [3].

In addition to FTO, numerous other genetic variants have been associated with obesity. The SH2B adaptor protein 1 (SH2B1), glutaminyl-peptide cyclo transferase-like protein (QPCTL), neuronal growth regulator (NEGR1), Homolog B, endoplasmic reticulum export factor (SEC16B), melanocortin 4 receptor gene (MC4R), potassium channel tetramerization domain containing 15 (KCTD15), transmembrane protein 18 (TMEM18), nudix hydrolase 3 (NUDT3), transcription factor AP2-Beta (TFAP2B), and adrenergic receptor gene (ADRB3) have all been identified as genetic variants associated with obesity [4–12].

With the abundance of research highlighting the connection between genetic variants and obesity and the impact of macronutrients on our bodies, the concept of nutrigenetic diets has gained significant popularity [12]. This approach aims to optimize nutrition and promote better health outcomes by tailoring diets based on an individual's genetic predispositions and dietary needs [1,5].

The implementation of a nutrigenetic diet begins with genetic testing, where an individual's DNA is analyzed to identify either specific genetic variants or single nucleotide polymorphisms (SNPs) related to nutrition and metabolism. Then, these variants are studied to understand how the body processes nutrients such as carbohydrates, fats, vitamins, and minerals. Based on this information, personalized dietary recommendations are formulated based on the individual's genetic profile. For example, individuals with genetic variations affecting carbohydrate metabolism may be advised to follow a lower-carbohydrate diet to effectively manage blood sugar levels [13,14]

Nutrigenetic diets typically include personalized meal plans that provide specific guidelines on

food categories and quantities, thereby considering the influence of genetic variations on nutrient metabolism. Continuous monitoring and feedback are essential to ensure the effectiveness of these diets. Follow-up genetic testing, blood tests, or other diagnostic measures may be employed to evaluate the impact of personalized dietary recommendations and make any necessary adjustments.

2. Materials and methods

2.1. Selection of SNP rsID

To facilitate the selection of SNPs for our study, we conducted extensive secondary research and compiled a list of SNPs that exhibit potential correlations with weight loss. Our selection process ensured that the chosen SNPs demonstrated significant associations with their respective traits in at least two distinct populations and were supported by a minimum sample size of 1000 individuals (Supplementary Table 1). Through our secondary research, we identified specific reference SNP cluster IDs (rsIDs) linked to various factors influencing weight loss, including the impact of protein and carbohydrate intake, calorie restriction, body fat percentage, BMI, lactose intolerance, and gluten intolerance. Considering the impact of lactose and gluten intolerance on the digestive system and metabolism, we incorporated these genes into the formulation of our nutrigenetic diet. By considering the genetic risk associated with the aforementioned factors, we have developed individualized nutrigenetic diets for each subject (Supplementary Table 2). These diets have been tailored to align with the specific genetic profiles of the subjects, taking their unique genetic predispositions for the factors influencing weight loss into account. Upon identifying the relevant rsIDs, we conducted genetic risk scoring to assess the risk.

2.2. Study subjects and sample collection

For the case-control study, we divided the participants into three distinct groups. The first group consisted of individuals classified as obese who followed a nutrigenetic diet. The second group comprised obese individuals who adhered to a generic diet. Lastly, the control group included non-obese individuals. To ensure homogeneity among the obese subjects, specific inclusion criteria were established. These criteria mandated that subjects be 18 years or older, display an interest in weight reduction, and have a BMI of 23 kg/m² or above. We selectively recruited individuals who expressed a keenness to adopt the nutrigenetic diet for the study. A separate group was formed for those not interested in the nutrigenetic approach, and they followed a generic diet. The control group consisted of non-obese individuals with a BMI below 23 kg/m². Additionally, we recruited subjects who were willing to provide pre- and post-clinical laboratory data from laboratories accredited by the National Accreditation Board for Testing and Calibration Laboratories (NABL). The blood samples collected by the respective diagnostic laboratories were sent to a genetic laboratory for further analysis. DNA extraction was performed on the collected samples, followed by genotyping using an Illumina microarray Infinium GSA V3 Chip, specifically designed to detect and analyze specific SNPs selected for the study (Figure 1).

To prioritize the ethical aspects of our research, we obtained informed consent from all subjects, thus ensuring their full understanding and agreement to the utilization of their data for research purposes. Our study was conducted in adherence to the guidelines and regulations set forth by the

Answergenomics Ethical Review Committee Board. The authors, as well as the NABL Accredited Clinical Laboratories Healthians and Molley's Lab, affirm that there are no conflicts of interest. This study was conducted independently, without any external funding or competing interests that could potentially impact the research, analysis, or interpretation of the study's findings.

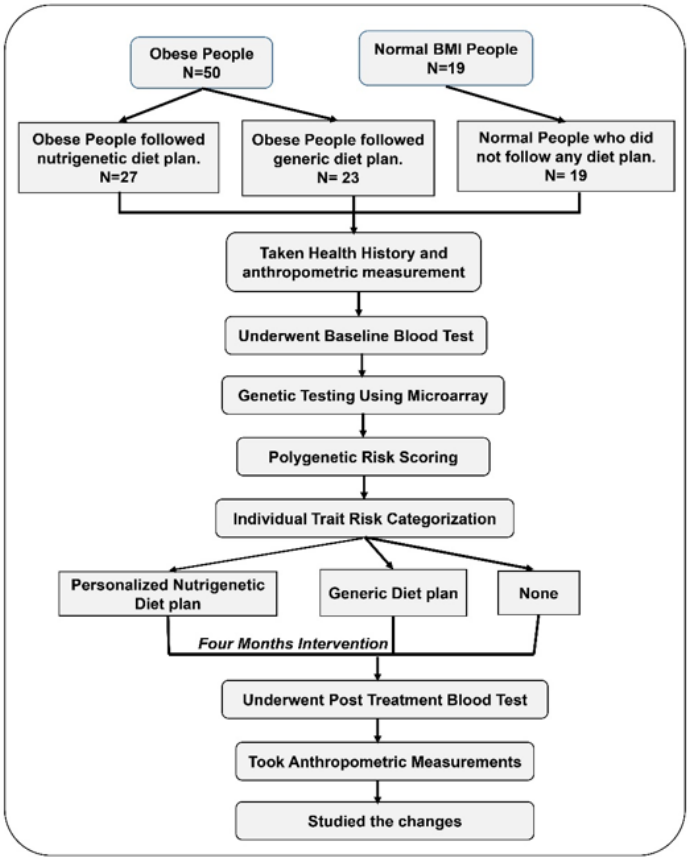

Figure 1. Overview of the methodology of the study.

2.3. Genotype data generation and risk score categorization

The first step in our study involved genotyping a set of SNPs using a genotyping array. This array includes the specific sets of genetic markers relevant to the traits under investigation without the need for genotype imputation. After receiving the RAW genetic data, we performed the genotype calling using GenomeStudio and ensured that all samples had 99.7% call rates. Quality checks, such as sex prediction and missing genotype, and sample checks were performed, and then the filtered data was saved in a tab-delimited Text file.

We relied on existing literature and prior research to assign risk scores to each genotype for a marker. The risk assignment was based on the reported associations between specific genotypes and the traits of interest. For each marker, we used either an additive or dominant model of risk scoring, where specific genotypes were assigned a risk score based on their established impact on trait susceptibility. These risk scores were predetermined using prior knowledge and were specific to each marker.

To calculate personalized genetic risk scores for each trait, we employed a two-step process. First, we obtained beta values for each marker from previously conducted association studies or regression analyses. These beta values represented the effect size or weightage associated with each genotype of a marker for the given trait.

Then, the risk score for an individual was computed by summing the product of the risk score for each genotype and the corresponding beta value across all markers relevant to the trait. Mathematically, the personalized genetic risk score for a trait (PGRS trait) was obtained using the following formula:

$$\text{PGRS trait} = \sum(\text{Risk score genotype} \times \text{Beta value genotype})$$

After calculating the risk score, we applied a normalization procedure to ensure consistency and comparability across different traits. This involved transforming the risk scores to a standardized scale. Then, the normalized risk scores were reported as the final output, thus representing an individual's genetic predisposition for the specific trait under investigation [15,16].

2.4. Trait risk categorization

The process of categorizing the trait into high, medium, and low risk groups is based on a thorough analysis of genotype frequencies within the South Asian population. To begin, we collected the allelic frequencies associated with all the risks relevant to the trait of interest. These allelic frequencies served as a foundation for further calculations.

Using the principles of the Hardy-Weinberg equilibrium, we then derived the genotype frequencies for each marker of the trait. This equilibrium enabled us to determine the expected proportions of homozygous dominant, recessive, and heterozygous genotypes based on the allelic frequencies obtained earlier. By applying this equilibrium, we gained insights into the distribution of genotypes within the population.

Next, we established a connection between the genotypes and their corresponding risk scores by referring to the existing literature on the trait. Each genotype was assigned a specific risk score based on its association with the trait's manifestation or susceptibility. This step allowed us to link genetic information with potential risk levels.

To capture the complexity of the trait and account for multiple markers simultaneously, we conducted permutations and combinations of all the markers involved. This process enabled us to obtain combined risk scores for the population, taking the various possible combinations of genotypes into account.

Through this comprehensive analysis, we arrived at an estimated genotype frequency for specific combinations of markers within the South Asian population. By utilizing this estimated frequency as a reference point, we proceed to categorize the risk into three distinct groups: high, medium, and low. Additionally, we considered the prevalence of the trait to refine the categorization, thereby adjusting the risk levels to reflect the trait's overall impact within the population.

2.5. Designing a personalized nutrigenetic diet

Utilizing the principles of polygenic risk scoring, this study evaluated individual risk factors related to dietary traits, including protein metabolism, carbohydrate intake, body fat percentage, response to calorie restriction, lactose intolerance, and gluten intolerance. In a case analysis, the subject

exhibited a low risk for weight loss associated with high protein intake, a low risk in the context of low carbohydrate intake, a moderate risk for body fat percentage, a high susceptibility to calorie restriction, a significant risk for lactose intolerance, and a minimal risk for gluten intolerance. Leveraging these genetic risk assessments, a tailored nutritional regimen was formulated for the subject, emphasizing a "lactose-free diet with a high protein and low carbohydrate content". Considering the subject's elevated risk profile for calorie restriction, the strategy involved maintaining their total daily energy expenditure (TDEE) without any caloric reduction. Participants were required to document their dietary intake to monitor adherence to the specified nutritional plan. Additionally, weekly telephonic follow-ups were implemented to provide motivational support and evaluate ongoing progress throughout the study period (Supplementary Table 2).

2.6. Designing the generic diet

In the generic diet group of our study, participants were provided with a balanced meal plan based on the dietary recommendations established by the Indian Council of Medical Research (ICMR). The ICMR guidelines serve as a standard for general dietary recommendations for adults in India. To promote weight loss, the meal plan aimed to achieve a reduction of 500 kcal from the participants' TDEE.

The TDEE Formula is as follows:

$$\text{TDEE} = 655.1 + (9.563 \times \text{weight in kilograms}) + (1.85 \times \text{height in centimetres}) - (4.676 \times \text{age in years}) \times \text{Physical Activity Level (PAL)}$$

Physical Activity Level (PAL): Sedentary: 1.2 (little to no exercise), Lightly active: 1.375 (light exercise or sports 1–3 days a week), Moderately active: 1.55 (moderate exercise or sports 3–5, Very active: 1.725 (hard exercise or sports 6-7 days a week), Super active: 1.9 (very hard exercise or daily physical labor)].

2.7. Statistical analysis

The descriptive measures used in this study included medians and interquartile ranges (IQR) for continuous data, and frequencies and percentages (%) for categorical data. The normality of the continuous data was assessed using Q-Q plots and the Shapiro-Wilk test. Bivariate analyses were conducted using appropriate statistical tests based on the nature of the data. The Mann-Whitney U test and the Kruskal-Wallis test were used for independent samples, while either the Wilcoxon signed-rank test or the sign test (if the assumption of symmetrical distribution was violated) were used for paired samples. Effect sizes were calculated using the r-statistic, with values of 0.10 to <0.30 considered as small, 0.30 to <0.50 considered as medium, and ≥0.50 considered as large effects.

For categorical variables, the Chi-square test was used, and Fisher's exact test was employed if any cell had an expected count less than five. To examine the factors influencing the post-test BMI results, a linear regression model was constructed. The dependent variables were the post-test BMI, while the independent variables included age, sex, post-test exercising habits, hydration, macronutrient distribution, and sleeping hours. The goodness of fit was assessed using the R-squared and adjusted R-squared statistical methods, and multi-collinearity was examined using the variance inflation factor (VIF).

Missing data were handled using the pair-wise deletion method under the assumption that it was missing completely at random (MCAR). Statistical significance was determined at a two-sided p-value of ≤ 0.05. Data analyses were performed using the IBM Statistical Package for the Social Sciences (SPSS) software, version 26.0.

2.8. Ethics statement

This study was approved by the Answergenomics Ethical Review Committee Board. We have obtained written consent from all the subjects.

3. Results

The study included a total of 69 subjects, with a median age of 36.0 years. In terms of sex, 52.2% of the subjects were males, while 47.8% were females. Of those study subjects, obese people who followed a nutrigenetic diet constituted 39.1%, obese people who followed a generic diet constituted 33.3%, and people who had a normal BMI (control group) constituted 27.5%. The subjects represented various ethnicities, with the majority being South Indian 28.98%, and notably, a considerable portion of participants (28.98%) identified their ethnicity as 'Others' or 'Don't Know,' which was predominantly comprised of individuals born to inter-state parents. Regarding the macronutrient distribution, the mean percentages were calculated for carbohydrates, proteins, and fats. The participants' average carbohydrate percentage was 53.4%, the mean protein percentage was 15.3%, and the mean fat percentage was 31.3% (Table 1).

Table 1. General Demographics of overall groups.

General Demographics	Overall (N = 69)
Age	
Median (IQR)	36.0 (30.0–43.0)
Sex	
Male	36 (52.2%)
Female	33 (47.8%)
Group	
Obese with Nutrigenetic diet	27 (39.1%)
Obese with Generic diet	23 (33.3%)
Normal BMI	19 (27.5%)
Macronutrient distribution, mean (SD)	
Carbohydrates percentage	53.4 (3.9)
Proteins percentage	15.3 (3.3)
Fat percentage	31.3 (2.1)
Ethnicity	
South Indian	28.98% (20)
North Indian	24.63% (17)
West Indian	17.39% (12)
Others & Don’t Know	28.98% (20)

The bivariate analysis compared the characteristics between the generic diet group and the nutrigenetic diet group. There were no significant differences observed between the two groups for age ($p = 0.33$) or sex ($p = 0.42$). In terms of macronutrient distribution, there were no significant differences between the groups for carbohydrate percentage ($p = 0.16$), protein percentage ($p = 0.53$), or fat percentage ($p = 0.61$). These results suggest that the generic diet group and the nutrigenetic diet group had similar ages, sex distribution, and macronutrient distribution. Furthermore, the bivariate analysis of demographic data across different regions of India within the generic and nutrigenetic groups revealed no significant ethnic differences impacting our study outcomes. These results suggest a uniformity in the influence of ethnic diversity on the primary outcomes of our research, despite the sample's varied ethnic composition (Table 2).

Table 2. Bivariate analysis of the Demographic data between the Generic, and the Nutrigenetic groups.

Variables	Generic diet (N = 23)	Nutrigenetic diet (N = 27)	P-value
Age			
Median (IQR)	40.0 (32.0–52.5)	37.0 (30.5–41.5)	0.33
Sex			
Male	16 (59.3%)	11 (47.8%)	0.42
Female	11 (40.7%)	12 (52.2%)	
Macronutrient distribution, median (IQR)			
Carbohydrates percentage	55.0 (51.0–55.0)	55.0 (54.0–55.5)	0.16
Proteins percentage	15.0 (15.0–15.0)	15.0 (13.5–15.0)	0.53
Fat percentage	30.0 (30.0–33.0)	30.0 (30.0–33.0)	0.61
Ethnicity			
South India	30.43% (7)	29.63% (8)	1
North India	30.43% (7)	18.52% (5)	0.68
West India	21.73% (5)	11.11% (3)	0.61
Others and Don’t Know	17.39% (4)	40.74% (11)	0.44

The bivariate analysis compared the baseline characteristics between the control group, generic diet, and nutrigenetic diet groups. The nutrigenetic diet group had higher median values compared to the control group and the generic diet group for the weight (84.0 kg vs. 63.0 kg and 81.0 kg; $p < 0.001$), BMI (29.2 Kg/m^2 vs. 22.5 Kg/m^2 and 29.0 Kg/m^2; $p < 0.001$), and lean mass (61.0 kg vs. 46.4 kg and 52.4 kg; $p = 0.015$). On the other hand, the generic diet group showed higher median values compared to the control group and nutrigenetic diet group for fat mass (27.0 kg, vs. 14.6 kg and 25.3 kg; $p < 0.001$) and body fat percentage (35.7 kg, vs. 25.0 kg 31.4 kg; $p < 0.001$). The prevalence of a sedentary lifestyle was significantly higher in the nutrigenetic diet group (18.5%) compared to the control group (0.0%) and the generic diet group (17.4%; $p = 0.032$). Furthermore, laboratory results showed significant differences for lower HbA1C levels ($p = 0.004$) and lower fasting insulin levels ($p = 0.001$) among control groups compared to the generic diet and nutrigenetic diet group (Table 3).

Table 3. Bivariate analysis of the baseline characteristics between the Non-obese, Generic, and Nutrigenetic groups.

Variables	Non-obese (Control Group) (N = 19)	Generic diet (N = 23)	Nutrigenetic diet (N = 27)	P-value
Body measurements, median (IQR)				
Weight (kg)	63.0 (54.0–67.0)	81.0 (72.0 – 90.5)	84.0 (73.5–79.5)	**<0.001**
BMI (Kg/m^2)	22.5 (22.0–23.3)	29.0 (27.7 – 33.0)	29.2 (27.4–31.2)	**<0.001**
Body Fat Percentage	25.0 (19.6–28.4)	35.7 (30.6 – 40.6)	31.4 (25.5–37.3)	**<0.001**
Fat mass (kg)	14.6 (13.1–16.3)	27.0 (23.9 – 34.7)	25.3 (21.1–31.9)	**<0.001**
Lean mass (kg)	46.4 (39.7–54.6)	52.4 (46.3 – 61.8)	61.0 (44.8–69.1)	**0.015**
Exercising habits				
Sedentary lifestyle	0 (0.0%)	4 (17.4%)	5 (18.5%)	**0.032**
Slightly active	11 (61.1%)	15 (65.2%)	17 (63.0%)	
Moderately active	7 (38.9%)	1 (4.3%)	3 (11.1%)	
Very active	0 (0.0%)	3 (13.0%)	2 (7.4%)	
Laboratory results, median (IQR)				
HbA1C (%)	5.40 (5.30–5.65)	5.80 (5.65–5.95)	5.60 (5.50–6.10)	**0.004**
Fasting Blood Sugar (mg/dl)	93.50 (87.15–96.68)	98.10 (89.00–101.74)	95.30 (89.30–103.65)	0.296
Fasting Insulin (Miu/L)	6.24 (4.50–8.75)	11.82 (8.36–18.04)	8.98 (6.53–12.49)	**0.001**
Total cholesterol (mg/dl)	189.00 (173.00–213.50)	200.00 (179.00–216.50)	202.00 (169.50–220.00)	0.564
Triglycerides (mg/dl)	93.00 (71.00–121.50)	118.00 (93.21–144.00)	123.00 (83.50–181.50)	0.121
Iron (mcg/dl)	88.80 (64.95–119.10)	83.75 (63.50–107.90)	85.25 (64.10–94.70)	0.659
Uric acid (mg/dl)	5.20 (4.50–6.25)	5.60 (4.25–7.15)	6.00 (4.95–7.00)	0.405
TSH (Miu/ml)	2.55 (1.69–3.14)	2.94 (2.12–4.79)	2.00 (1.76–3.88)	0.176
T3 (ng/dl)	1.06 (0.93–1.23)	1.07 (0.97–1.15)	1.15 (1.02–1.26)	0.391
T4 (ng/dl)	8.00 (7.29–8.87)	8.80 (8.51–9.46)	8.66 (7.50–9.93)	0.121

The bivariate analysis of the post-test characteristics among the three groups revealed several significant differences. The nutrigenetic diet group exhibited noteworthy improvements in body measurements, including reductions in weight, BMI ($p < 0.001$), body fat percentage ($p = 0.002$), and fat mass ($p < 0.001$) compared to the generic diet group. Additionally, the nutrigenetic diet group had higher lean mass (($p = 0.005$). In terms of laboratory parameters, the nutrigenetic diet group showed lower HBA1C levels ($p = 0.029$) and lower fasting insulin levels ($p = 0.021$) compared to the generic diet group. However, no significant differences were observed in other laboratory measures (Table 4).

Table 4. Bivariate analysis of the Post-test characteristics between the Non-obese, Generic, and Nutrigenetic groups.

Variables	Non-obese (Control Group) (N = 19)	Generic diet (N = 23)	Nutrigenetic diet (N = 27)	P-value
Body measurements, median (IQR)				
Weight (kg)	58.5 (54.0–68.0)	85.0 (77.5–93.8)	80.0 (70.8–90.0)	**<0.001**
BMI (Kg/m^2)	22.3 (21.7–23.4)	30.7 (28.2–33.4)	27.9 (25.1–29.7)	**<0.001**
Body Fat Percentage	25.4 (17.2–27.7)	35.6 (26.3–40.9)	29.0 (24.7–34.5)	**0.002**
Fat mass (kg)	13.0 (11.1–15.3)	23.2 (20.0–30.0)	22.3 (19.3–26.7)	**<0.001**
Lean mass (kg)	44.3 (40.7–52.9)	58.7 (51.4–62.3)	57.9 (50.7–63.5)	**0.005**
Exercising habits				
Sedentary lifestyle	0 (0.0%)	3 (13.0%)	0 (0.0%)	**0.004**
Slightly active	9 (33.3%)	12 (52.2%)	9 (47.4%)	
Moderately active	12 (44.4%)	8 (34.8%)	3 (15.8%)	
Very active	6 (22.2%)	0 (0.0%)	7 (36.8%)	
Laboratory results, median (IQR)				
HbA1C (%)	5.70 (5.50–5.75)	5.90 (5.70–6.50)	5.70 (5.50–6.00)	**0.029**
Fasting Blood Sugar (mg/dl)	89.90 (83.60–94.10)	93.02 (89.70–98.90)	87.90 (81.65–96.05)	0.097
Fasting Insulin (Miu/l)	6.63 (5.13–9.60)	10.67 (7.03–16.13)	7.50 (5.90–11.75)	**0.021**
Total cholesterol (mg/dl)	189.00 (182.50–218.50)	198.00 (176.00–214.50)	198.00 (165.00–221.50)	0.963
LDL (mg/dl)	123.90 (99.10–132.70)	105.50 (51.00–125.20)	130.00 (109.05–144.85)	0.067
Triglycerides (mg/dl)	126.00 (88.50–151.00)	139.00 (113.00–180.00)	118.00 (94.00–163.50)	0.251
Iron (mcg/dl)	96.10 (78.31–113.35)	76.45 (65.00–98.60)	84.30 (54.45–95.05)	0.121
Uric acid (mg/dl)	5.40 (4.59–6.05)	5.70 (4.35–6.85)	5.80 (4.70–6.75)	0.656
TSH (mIU/dl)	2.84 (2.09–3.63)	3.22 (2.03–4.38)	2.36 (1.71–3.37)	0.368
T3 (ng/dl)	1.10 (0.99–1.54)	1.02 (0.96–1.18)	1.07 (0.96–1.19)	0.220
T4 (ng/dl)	8.01 (7.15–8.82)	8.65 (8.25 – 9.58)	8.94 (7.97–10.08)	0.143

The nutrigenetic diet group demonstrated significant improvements compared to the non-obese and generic diet groups. Notably, the nutrigenetic diet group exhibited substantial weight reduction (median: 5.00 kg, IQR: 3.25–6.00) and a significant decrease in BMI (median: 1.58, IQR: 1.06–2.19). Additionally, body fat percentage significantly decreased in the nutrigenetic diet group (median: 1.34, IQR: 0.48–3.68). Conversely, the non-obese group experienced a significant reduction in triglyceride levels (median: -22.00, IQR: −47.50–−3.50) compared to the other groups (p = 0.003) (Table 5).

Table 5. Bivariate analysis of the changes in body measurements and laboratory results between the Non-obese, the Generic, and Nutrigenetic groups (Baseline–Post-test).

Variables	Non-obese group (Control Group) (N = 19)	Generic diet (N = 23)	Nutrigenetic diet (N = 27)	P-value
Changes in Body measurements, median (IQR)				
Weight (kg)	0.00 (−0.25–0.00)	0.00 (−0.25–0.00)	5.00 (3.25–6.00)	**<0.001**
BMI (Kg/m^2)	0.00 (−0.02–0.30)	0.00 (0.00–0.04)	1.58 (1.06–2.19)	**<0.001**
Body Fat Percentage	0.23 (−0.46–2.07)	−0.23 (−1.19–2.22)	1.34 (0.48–3.68)	**0.055**
Fat mass (kg)	3.00 (−1.60–5.19)	5.13 (−0.87–8.55)	4.37 (0.32–8.60)	0.435
Lean mass (kg)	−2.99 (−5.19–2.61)	−2.84 (−7.29–2.21)	2.63 (−4.47–5.08)	0.329
Changes in Laboratory results, median (IQR)				
HbA1C (%)	−0.10 (−0.25–0.00)	−0.10 (−0.20–0.00)	0.00 (−0.10–0.10)	0.331
Fasting Blood Sugar (mg/dL)	0.00 (−4.45–5.80)	0.50 (−2.54–8.40)	5.10 (−0.35–13.00)	0.153
Fasting Insulin (Miu/L)	−0.58 (−1.24–0.00)	0.24 (−3.13–3.20)	0.58 (−1.41–3.58)	0.360
Total cholesterol (mg/dL)	−4.30 (−15.00–1.00)	0.00 (−11.38–8.50)	5.00 (−13.00–20.00)	0.221
Triglycerides (mg/dL)	−22.00 (−47.50–−3.50)	−11.00 (−40.50–0.00)	4.00 (−13.00–33.00)	**0.003**
Iron (mcg/dL)	0.00 (−16.35–18.85)	0.00 (−12.90–18.00)	0.45 (−22.00–23.70)	0.923
Uric acid (mg/dL)	0.00 (−0.50–0.42)	0.00 (−0.45–0.30)	0.40 (−0.20–0.80)	0.102
TSH (Miu/mL)	−0.27 (−0.67–0.00)	0.04 (−0.40–0.41)	−0.01 (−0.35–0.33)	0.097
T3 (ng/dL)	0.00 (−0.08–0.07)	0.00 (−0.09–0.13)	0.06 (−0.07–0.11)	0.656
T4 (ng/dL)	0.06 (−0.72–0.57)	0.57 (−0.79–1.05)	0.57 (−0.79–1.05)	0.491

To understand whether the dependent variables such as age, sex, exercise, hydration, and sleep can influence the post-treatment BMI, we performed a multiple linear regression. After controlling for age (coefficient of 0.026 (SE = 0.058, β = 0.068, p = 0.659, 95% CI = −0.092–0.143)), gender (coefficient of 0.311 (SE = 1.278, β = 0.038, p = 0.809, 95% CI = −2.274–2.897)), exercising habits (coefficient of -0.759 (SE = 0.889, β = −0.147, p = 0.398, 95% CI = −2.558–1.039)), hydration (coefficient of −2.127 (SE = 0.865, β = −0.386, **p = 0.018**, 95% CI = −3.876–−0.379)), sleeping hours (coefficient of -0.655 (SE = 1.210, β = −0.079, p = 0.591, 95% CI = −3.101–1.792)), macronutrient distribution (coefficient of 2.371 (SE = 1.320, β = 0.286, p = 0.080, 95% CI = −0.300–5.042)), and TSH levels (coefficient of 0.070 (SE = 1.86, β = 0.056, p = 0.707, 95% CI = −0.305–0.446)), the only variable that showed a statistically significant association with BMI was hydration. The coefficients of the other variables were not statistically significant, indicating that they did not have a significant impact on the BMI (Table 6).

Table 6. Linear regression model, examining the possible factors impacting the post-test BMI value.

Model	Unstandardized coefficients		Standardized coefficients	t	P-value	95% CI for BMI
	B	Std. Error	β			
(Constant)	29.878	3.977		7.512	**<0.001**	21.833–37.992
Age	0.026	0.058	0.068	0.444	0.659	−0.092–0.143
Gender	0.311	1.278	0.038	0.244	0.809	−2.274–2.897
Exercising habits	−0.759	0.889	−0.147	−0.854	0.398	−2.558–1.039
Hydration	−2.127	0.865	−0.386	−2.461	**0.018**	−3.876–−0.379
Sleeping hours	−0.655	1.210	−0.079	−0.541	0.591	−3.101–1.792
TSH levels	0.070	0.186	0.056	0.378	0.707	−0.305–0.446
Macronutrient Distribution	2.371	1.320	0.286	1.795	0.080	−0.300–5.042

Gender, 1: Male, 2: Female. **Exercising habits**, 1: Sedentary lifestyle, 2: Slightly active, 3: Moderately active, 4: Very active. **Water drinking**, 1: Rarely, 2: 3-5 glasses, 3: 5-7 glasses, 4: Elixir of life. **Sleeping hours**, 1: 5-7 hours, 2: 7-9 hours, 3: Most of the day. **Diet type**, 1: Nutrigenetic. 2: Generic.

We also wanted to understand whether there could be differences in the nutrigenetic diet group between the baseline and post-treatment after four months. Significant results were observed, with participants experiencing a reduction in weight ($p < 0.001$, effect size $r = 0.96$), BMI ($p < 0.001$, effect size $r = 0.84$), body fat percentage ($p < 0.001$, effect size $r = 0.68$), and fat mass ($p < 0.001$, effect size $r = 0.71$) after the treatment. The sedentary lifestyle category significantly decreased ($p = 0.001$), indicating a positive shift towards a more active lifestyle. Additionally, the fasting blood sugar ($p = 0.019$, effect size $r = 0.44$) and uric acid levels ($p = 0.042$, effect size $r = 0.39$) showed significant improvements. Moreover, no significant changes were found in lean mass levels or other laboratory measurements (Supplementary Table 3).

The bivariate analysis comparing the baseline characteristics between the generic and nutrigenetic diet groups showed no significant differences in most of the measured variables. Body measurements such as weight, BMI, body fat percentage, fat mass, lean mass, basal metabolic rate, and recommended calories were similar between the groups. The distribution of individuals across different exercise habits was also comparable. Additionally, there were no significant disparities in laboratory results, including HbA1C, fasting blood sugar, total cholesterol, triglycerides, iron, uric acid, triiodothyronine (T3), and thyroxine (T4) levels. However, a trend towards lower fasting insulin levels was observed in the nutrigenetic diet group ($p = 0.079$). These findings suggest that the nutrigenetic diet did not have a significant impact on most baseline characteristics compared to the generic diet (Supplementary Table 4).

The bivariate analysis comparing the post test of subjects in the generic and nutrigenetic diet groups revealed some notable differences. Subjects following the nutrigenetic diet had significantly lower BMIs ($p = 0.009$, effect size $r = 0.81$) compared to those on the generic diet. Moreover, the nutrigenetic diet group has lowered fasting blood sugar ($p = 0.038$, effect size $r = 0.62$) and fasting insulin ($p = 0.047$, effect size $r = 0.59$). However, no significant differences were found for the body weight, body fat percentage, fat mass, and most other laboratory results. These findings suggest that

the nutrigenetic diet may have favorable effects on BMI, blood sugar, and insulin compared to the generic diet (Supplementary Table 5).

The bivariate analysis comparing the changes in body measurements and laboratory results between the generic and nutrigenetic diet groups revealed some significant findings. Subjects following the nutrigenetic diet exhibited significantly lower weight ($p < 0.001$, effect size $r = 0.86$), BMIs ($p < 0.001$, effect size = 0.76) compared to those on the generic diet. Additionally, the nutrigenetic diet group showed a significant decrease in body fat percentage ($p = 0.020$, effect size $r = 0.33$) compared to the generic diet group. No significant differences were observed for the weight, fat mass, and lean mass between the groups. In terms of laboratory results, there were significant improvements in triglyceride levels ($p = 0.008$, effect size $r = 0.37$) and uric acid levels ($p = 0.047$, effect size $r = 0.28$) in the nutrigenetic diet group compared to the generic diet group. However, no significant differences were found for the HbA1C, fasting blood sugar, fasting insulin, total cholesterol, LDL cholesterol, iron, thyroid-stimulating hormone (TSH), T3, and T4 levels between the groups (Supplementary Table 6).

The bivariate analysis of the baseline and post-treatment non-obese group characteristics revealed a significant increase in triglyceride levels ($p = 0.004$, effect size $r = 0.64$) and TSH levels ($p = 0.021$ effect size $r = 0.52$) post-treatment. Meanwhile, the baseline and post-treatment generic diet group showed a significant decrease in fat mass ($p = 0.002$, effect size $r = 0.61$) and a significant increase in triglyceride levels ($p = 0.009$, effect size $r = 0.53$) after the intervention (Supplementary Tables 7 and 8).

4. Discussion

This case-control study aimed to investigate the impact of a personalized nutrigenetic diet on weight loss and its effects on various clinical parameters in an Indian population. The study included three groups: obese individuals following a nutrigenetic diet, obese individuals following a generic diet, and a control group comprised of subjects with a normal BMI who did not follow any specific diet.

The nutrigenetic test utilized in this study examined genetic variations in 18 genes and 25 rsIDs. It should be noted that the test was not originally designed as a weight management tool, but rather as a means to enhance personalization and to optimize overall healthy eating practices. The selection of gene variants was based on established evidence of gene-diet interactions, where the impact of genetic variation can be modified through nutrition or exercise interventions (Supplementary Table 1). In the nutrigenetic diet group, all subjects received specific guidance in terms of nutritional recommendations and meal plans tailored to their genetic makeup and lifestyle. Genotyping data were generated using a microarray chip, and personalized genetic risk scores were calculated for each trait of interest. These risk scores were used to categorize individuals into high-, medium-, and low-risk groups. In the generic diet group, all subjects received specific guidance in terms of nutritional recommendations and meal plans tailored to their lifestyle.

The study sample consisted of 69 subjects, with a median age of 36.0 years. The distribution of sex and age among the three groups was not statistically significant, indicating that any observed differences in the outcomes can be attributed to the dietary interventions rather than initial variations in the participant's characteristics.

The analysis of baseline characteristics revealed some interesting findings. The nutrigenetic diet group had higher values for weight and BMI compared to the control group and the generic diet group, suggesting that individuals in this group had a higher baseline weight and BMI. Conversely, the generic

diet group had higher values for fat mass and body fat percentage compared to the control group and the nutrigenetic diet group, indicating a higher adiposity for this group. These baseline differences may have influenced the outcomes observed in the study.

In our findings, the nutrigenetic diet group showed a notable decrease in fat mass and body fat percentage, aligning them more closely with the metrics observed in the control group and demonstrating the efficacy of personalized dietary approaches. This is corroborated by results from the Nutrigenomics Overweight/Obesity and Weight Management (NOW) Trial, where the group experienced significantly greater reductions in their body fat percentage over a standard group lifestyle balance (GLB), highlighting the impact of nutrigenomic interventions in weight management ($P < 0.05$) [17].

Regarding the laboratory results, the nutrigenetic diet group displayed an improved glycemic control, as indicated by a lower HbA1C level compared to the generic diet group. Although the difference was statistically significant, both groups had HbA1C values within the normal range, thus suggesting that both dietary approaches were generally effective in maintaining glycemic control. Moreover, fasting insulin levels were significantly lower in the nutrigenetic diet group compared to the generic diet group, thus indicating better insulin sensitivity. Most importantly, the within-group effect among the nutrigenetic diet group showed significant reduction in BMI, weight, body fat percentage, fat mass, and triglycerides.

We conducted a multiple linear regression analysis to assess the influence of sex, age, exercise, sleep, and macronutrient distribution on the post-BMI value. The regression model yielded some interesting findings. Among the variables examined, only hydration showed a significant association with the outcome variable (weight loss). Individuals who reported higher hydration levels had a significant decrease in weight compared to those with lower hydration. This suggests that increased hydration may have contributed to the observed weight loss in the study participants. However, the other variables, including age, sex, exercising habits, sleeping hours, TSH levels, and macronutrient distribution, did not show statistically significant associations with weight loss. These results indicate that these factors may not have played a significant role in influencing the effectiveness of the nutrigenetic diet in promoting weight loss in the study population.

A study conducted by Stookey, et al. 2008, found that increasing drinking water intake may positively impact weight loss among overweight women following a diet intervention. Over 12 months, both absolute and relative increases in drinking water were associated with significant reductions in body weight and fat, independent of other factors such as diet group, changes in beverage intake, food consumption, and physical activity. These results provide support for the notion that drinking water could promote weight loss and improve the body composition levels, as we have discovered in our study [18].

Interestingly, our overall study result correlates with the study conducted by Arkadianos et al. [14]. Their study investigated the effectiveness of nutrigenetics based diet in long-term weight management. Patients with a history of unsuccessful weight loss attempts underwent a nutrigenetic test, while a comparison group did not receive the test. After 300 days, the nutrigenetic group showed a better maintenance of weight loss (73% vs. 32% in the comparison group) and a significant average reduction in BMI (1.93 kg/m^2) compared to a gain in the comparison group (0.51 kg/m^2). Additionally, the nutrigenetic group demonstrated improved blood fasting glucose levels, with a higher percentage achieving levels below 100 mg/dL (57% vs. 25% in the non-tested group). Additionally, their findings suggested that incorporating nutrigenetic information into personalized diets could lead to a better compliance, sustained weight loss, and improved glucose levels [14].

Another study conducted by Talib, et al. [19] also aligned to our results. They investigated the effectiveness of a DNA-based customized diet and exercise plan for weight management as compared to a conventional plan. A total of 30 subjects were divided into two groups: Plan A consisted of 15 individuals who followed the DNA-based plan, and Plan B consisted of 15 individuals who adhered to the conventional plan. The results showed that both Plan A and Plan B led to weight loss after three months, although the difference in weight loss between the two groups was not statistically significant at that time. However, after six months, the subjects in Plan A exhibited a significant weight reduction compared to those in Plan B, indicating the potential long-term benefits of the DNA-based approach. Similarly, while the BMI of individuals in Plan A did not show significant differences after three months, it became statistically significant after six months, further supporting the efficacy of the DNA-based plan for sustained weight management. Additionally, the study revealed that subjects in Plan A experienced a significant reduction in waistline measurements compared to those in Plan B after six months, indicating the impact of the DNA-based plan on body composition changes. These findings suggested that incorporating genetic information into personalized weight management strategies could provide a more effective approach to weight loss among obese individuals. Furthermore, the inclusion of a genetically personalized component improved motivation and compliance, thus indicating the potential psychological benefits of tailoring weight management plans to an individual's genetic profile [19].

5. Limitations

A notable challenge in our study was the practicality of modifying participants' diets and subsequently collecting post-intervention data, which resulted in a smaller sample size. This limitation underscores the need for further research to validate our findings. In future studies, it would be feasible to segregate subjects based on their ethnicity with a larger sample size. Such segmentation would enable a more detailed examination of the specific changes and impacts associated with different ethnic groups. This approach could provide deeper insights into the nuanced relationship between diet, genetic background, and health outcomes across diverse ethnicities.

6. Conclusions

The findings of this study suggest that a nutrigenetic diet, along with proper hydration, may have beneficial effects on body weight, body composition, and glucose metabolism compared to a generic diet. Subjects following the nutrigenetic diet exhibited significant reductions in BMI, body fat percentage, and fat mass, thus indicating the potential for weight loss and an improved body composition. Furthermore, the nutrigenetic diet group showed lower fasting blood sugar and fasting insulin levels, suggesting an improved glucose metabolism. However, no significant differences were found in most other laboratory results. These findings highlight the potential advantages of tailoring dietary interventions based on genetic factors for weight management and metabolic health.

It is important to note that individual responses to a nutrigenetic diet may vary, and further research is needed to explore the underlying mechanisms and long-term effects. Future studies with larger sample sizes, longer durations, and more comprehensive assessments of metabolic parameters would provide additional insights into the benefits and limitations of a nutrigenetic approach to diet management. Overall, the present study contributes to the growing body of evidence supporting the

potential of nutrigenetic approaches in personalized nutrition and highlights its role in promoting healthier lifestyles and a metabolic well-being.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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Conflict of interest

The authors declare no conflicts of interest.

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