Bulletin of the National Research Centre

REVIEW

Open Access

Genetic and nutrient interactions in the escalating global burden of obesity and metabolic disorders: a comprehensive review

Muhammad Ajmal Dina[1,5*], Asif Hanif[2,5], Asifa Karamat[3,5], Muhammad Shakeel Basit[3,5], Muhammad Khalil Ahmed[4,5], Shazia Siddique[3,5] and Muhammad Akram Bhutta[4,5]

Abstract

Background Obesity appeared as one of the most urgent public health issues globally. It markedly upraises the likelihood of disease and early mortality, contributing to various chronic ailments including diabetes (DM), cardiovascular disorders (CVD) and some specific types of cancer. Obesity onset of is not attributable to a one cause. it is a multifaceted interaction among genetic predispositions, environmental factors and lifestyle adoptions. Between these elements, dietary habits stand out as one of the most important influences, determining how the body manages and expends energy. Unhealthy food patterns, coupled inactive lifestyles can progressively disturb metabolic equilibrium. Then result in excessive fat accumulation and enduring health challenges.

Objective This research examines the interplay between genetic factors associated with obesity and nutrient consumption, as well as the implications of these interactions for the regulation of body weight. Additionally, it delves into how these gene-nutrient connections play a role in the onset of obesity and elevate the likelihood of metabolic disorders, such as type 2 diabetes, dyslipidemia, and hypertension.

Methods A comprehensive literature review was performed, focused on research published in the last twenty years. This review investigated significant genetic variants associated with obesity including *FTO*, *MC4R* and *LEPR*. The interactions with various dietary components. Particular emphasis was placed on how certain nutrients can affect gene expression and modify obesity risk. Also, the review observed how metabolic disorders like type 2 diabetes and osteoporosis might influence these gene-diet interactions. Furthermore, it evaluated the role of epigenetic modifications especially those influenced with long-term dietary patterns to the development of obesity and related metabolic issues.

Conclusions This research highlights the complex interplay between genetic components, diet and onset of obesity. It highlights the importance of modified nutrition as a feasible approach for the management and prevention of obesity. Grasping both genetic tendency and environmental factors is essential for developing effective, tailored

*Correspondence:
Muhammad Ajmal Dina
ajmaljhl@gmail.com

Full list of author information is available at the end of the article

interventions. These inclusive strategies can improve treatment results, encourage healthier habits and enhance long-term health across various populations.

Key points

- 1)Obesity arises from a multifactorial interplay among genetic, dietary, and environmental factors regulating metabolism and energy balance.
- 2)Specific nutrients influence gene expression, impacting obesity risk and metabolic health outcomes.
- 3)Long-term dietary habits induce epigenetic changes that modulate obesity-related genes and fat metabolism.
- 4)Personalized nutrition based on genetic variants offers an effective strategy for obesity prevention and management.
- 5)Diverse genetic forms of obesity syndromic, monogenic and polygenic showed the need for targeted interventions.

Keywords Genetic, Nutrient, Epigenomics, Obesity, Metabolic diseases

Introduction

In 1975 World Health Organization (WHO) recognizes obesity as one of the most significant global health issues (Khusainova et al. 2025), from 2016 over 1.9 billion adults were classified as overweight with more than 650 million of these individuals were obese (Górczyńska-Kosiorz et al. 2024). Now approximately 39% of adults globally are overweight and 13% almost obese. The increasing trend was exaggerated in recent years, mostly in the COVID-19 pandemic. Obesity rises from a combination of unhealthy diet, inadequate physical activity and genetic predisposition (Das et al. 2025). While the patterns can differ regionally.

The developed countries frequently report elevated obesity rates due to high-calorie diets and lifestyles issues but developing nations are also experiencing a swift rise in obesity as urbanization and Western dietary practices are more prevalent (Arshad et al. 2025). Obesity is a chronic form that emerges as a mixture of biological and lifestyle influences. It disturbs normal lipid and glucose metabolism, diminishes insulin sensitivity and increase abnormal inflammatory and oxidative responses (Razi et al. 2025). In result the fat accumulation and modify the secretion of adipocytokines can further disrupt metabolic equilibrium.

The aim of this narrative review was to examine the association between genetic factors and nutrient consumption in the obesity and associated metabolic disorders. Emphasizes important obesity-related genes which play a role in appetite control, energy homeostasis, lipid metabolism and insulin sensitivity. It examines how dietary habits and particular nutrients affect gene expression via epigenetic processes. The consolidates existing evidence regarding gene-nutrient interactions and their contribution to various obesity phenotypes. It including syndromic, monogenic and polygenic types.

The review was conducted with used structured literature search. Relevant peer-reviewed published studies, last two decades. That's were identified from scientific databases using predefined keywords related to genetics, nutrition and obesity. Included were original research observational and experimental studies, clinical trials, epigenetic studies, relevant systematic reviews and meta-analyses focusing on gene–nutrient interactions and metabolic outcomes. Non-peer-reviewed articles, case reports, duplicate publications, studies not directly related to obesity gene diet interactions and papers without available full text were excluded. The review is innovative as it integrates genetic variants, nutrient gene interactions and epigenetic mechanisms into a consistent framework explaining obesity development. But distinctly contrasting syndromic, monogenic and polygenic obesity forms and their phenotype-specific nutritional responses.

Bad dietary habits particularly the high in saturated fats with refined sugar and processed foods can alter adipokine function (Abdolla et al. 2025). That diets frequently elevate pro-inflammatory adipokines like leptin and tumor necrosis factor-alpha (TNF-α) but lessening anti-inflammatory ones like adiponectin (Błażejewska et al. 2025). This disruption raises chronic low-grade inflammation, insulin resistance and other metabolic disturbances which can crucial in the onset of obesity (Wang et al. 2025). The accumulation of visceral fat may refer to as abdominal obesity, significantly heightens the risk of cardiometabolic diseases. These cover high blood pressure, type 2 diabetes and abnormal blood lipid levels. After these conditions can may change into severe complications like atherosclerosis, heart attack, stroke, peripheral artery disease and certain cancer types, here bellow explained the various causes of obesity in (Fig.1).

Updated prevalence data on obesity

The incidence of adult obesity has significantly increased worldwide. Nations from 1990 to 2021, indicating a continuous and increasing public health emergency. In 2021,

Fig. 1 Biological, genetic, dietary and lifestyle pathways which contributing to development of obesity and related cardiometabolic complications

about 2.11 billion adults worldwide were classified as overweight or obese, 1.00 billion men and 1.11 billion women. Since 1990 the worldwide prevalence of obesity surged with over 155% in males and 105% in females. The most rapid growth observed in the North Africa and Middle East region. China, India and the United States represented the largest absolute numbers of affected adults. Highlighting the combined effects of population size and increasing prevalence.

The forecasts suggest that if current patterns persist, the number of adults with overweight and obesity could reach about 3.8 billion till 2050. Accounting for more than half of the worldwide adult population with mostly increases anticipated in sub-Saharan Africa and certain areas of Asia. The statistics shows the extensive and escalating nature of obesity and indicate a urgent requirement for effective, region-specific prevention and control measures. In (Fig. 1) explained that how obesity it effects on body with different complications.

Pathways linking obesity, abdominal obesity and cardiometabolic complications

Obesity induced with diet results from the excessive collection of adipose tissue. It is primarily caused of diets high in fat and sugar, as well as the consumption of processed foods, leading to a disruption in the secretion of adipocytokines. The genetic factors and epigenetic changes play a role in determining an individual's vulnerability to fat accumulation. The environmental influences like the quality of diet, the composition of the microbiome, fetal programming, nutrient intake and stress levels further affect the risk of developing obesity. Thus, abdominal obesity contributes to various metabolic complications, including atherosclerosis, dyslipidemia, diabetes and hypertension as explained in (Fig. 1).

Various biological and lifestyle factors that cause obesity

The illustration shows the various interconnected elements that can contribute to the initiation and advancement of obesity (Fig. 1). These factors work in concert and interact insistently over time. Key elements include poor dietary habits, chronic low-grade inflammation and disrupted metabolic regulation(Fic and Polak-Szczybyło 2025). They facilitate extra fat accumulation, particularly in the abdominal region. Obesity subsequently raises the risk of developing metabolic conditions like insulin resistance and abnormal lipid profiles(Razi et al. 2025).

Association between diet and obesity

Obesity rises with a multifaceted interplay between genetic predispositions and environmental influences (Chermon and Birk 2024). An important component of that phenomenon is epigenetics. It refers to modifications in gene expression that do not involve alterations to the DNA sequence itself (Agrawal et al. 2024). The changes may can affect to metabolism, fat accumulation and the regulation of overall body weight.

Diet as instrumental in influencing the epigenetic modifications (Suleiman et al. 2025). Specific nutrients have a capacity to activate or inhibit genes that are relevant to energy balance and fat metabolism like carbohydrates can affect the gut microbiota that subsequently influences genes linked to obesity (Mansour et al. 2024). Prebiotic carbohydrates encourage the proliferation of beneficial gut bacteria that mitigate inflammation and enhance metabolic health and proteins can play a role in gene expression with modulating appetite, energy expenditure and hormonal functions (Yoo et al. 2024). That proteins can activate genes that facilitate fat breakdown but others may suppress the expression of genes that contribute to fat storage.

Role of trace elements and gene regulation in obesity

A deficiency in trace elements has associated to increased fat accumulation and changes in the expression of genes related to obesity (Li et al. 2025). These minerals are important for numerous metabolic functions, including energy production, lipid metabolism and antioxidant defense mechanisms (Agrawal et al. 2024). Important antioxidant enzymes like superoxide dismutase, catalase, peroxidase, glutathione transferase and glutathione reductase rely on trace minerals for their optimal functioning(Lupu et al. 2024). When the enzymes operate effectively, they can increase the expression of genes that facilitate energy usage and inhibit excessive fat storage (Yarahmadi et al. 2024).

The enzymatic antioxidants various non-enzymatic substances also engage with genes associated with obesity(Olivares-Vicente and Herranz-López 2025). These substances encompass glutathione, vitamins A, C and E, as well as carotenoids, tocopherols and tocotrienols (Młynarska et al. 2024). All they assist in mitigating oxidative stress and may affect gene activity related to fat metabolism and storage (Cheng et al. 2025). Although environmental factors like diet, physical activity and lifestyle significantly influence the risk of obesity, genetic factors also play a vital role. Numerous genes have been identified that govern appetite, energy balance and fat distribution, so contributing to individual variations in body weight and metabolic health (Górczyńska-Kosiorz et al. 2024).

Genetic factors of obesity

Several genes are intricately linked with obesity due to the influence on appetite regulation, metabolic processes and energy management, these under.

1) *FTO*: Variants of this gene correlate with heightened appetite and an elevated body mass index(Górczyńska-Kosiorz et al. 2024).
2) *MC4R*: This gene is instrumental in regulating energy consumption, appetite and metabolic rate(Fansa and Acosta 2024).
3) *LEPR*: It encodes the leptin receptor and is vital for managing food intake and sustaining energy equilibrium(Sharma et al. 2025).
4) *PPARG*: This gene is crucial for the formation of fat cells and the overall regulation of metabolism(Górczyńska-Kosiorz et al. 2024; Sharma et al. 2025).
5) *TAS2R*: These genes related to taste receptors may impact food preferences and consequently affect the risk of obesity(Górczyńska-Kosiorz et al. 2024; Ponnusamy et al. 2022).

The interplay between nutrient consumption, genetic predispositions and weight gain is vital for enhancing obesity prevention and treatment strategies(Mansour et al. 2024). The environmental factors and genetic makeup influence how the body accumulates and utilizes energy. Nutrients can alter gene expression but genetic factors can dictate the body's response to particular foods(Priyadarshini et al. 2025).

Genetic, epigenetic and environmental interaction in obesity

The selection of genes concentrated on those recognized for their significant roles in obesity research (Brandolino et al. 2025). The genes like*FTO*, *MC4R*, *LEPR* and *PPARG* (Table 1) were emphasized due to their contributions to appetite regulation, energy metabolism and fat storage (Siddiqui et al. 2025). The second approach investigated the genetic variability associated with obesity (Pratiwi et al. 2025). Genes linked to syndromic, monogenic and polygenic forms were analyzed to guide potential therapeutic strategies. The third approach focused on genes that influence dietary behaviors.

The TAS2R gene family was combined due to its impact on taste perception that effects on food preferences and can raised the risk of obesity (Sternini and Rozengurt 2025). The fourth approach examined epigenetic factors that could modify treatment outcomes. Genes like*PLIN1* and the *SIRT1–SIRT7*family were chosen to shed light on the interaction between genetic and dietary factors and their influence on obesity-related comorbidities (Rana and Nawaz 2025). In Fig.2, the relationship between nutrient intake, gene expression and the obesity phenotype and their relationships.

Associated factors in obesity

Figure 2shows the intricate interactions between genetic predisposition, environmental influences, dietary habits and the gut microbiota concerning obesity and associated metabolic disorders. Genetic factors have a significant role to determining both the likelihood of obesity and personal dietary choices but environmental aspects, including lifestyle and physical activity, have a direct effect on obesity outcomes (Danesh Doost et al. 2025).

The gut microbiota has as a crucial regulator of metabolic health, can influence the likelihood of comorbidities such as type 2 diabetes and osteoporosis (Armutcu and McCloskey 2025). Diet can alter gene expression in both beneficial and detrimental manners and specific nutritional interventions may enhance body weight, microbiota diversity and overall metabolic performance (Ma et al. 2025). Epigenetic mechanisms have more influence on gene activity, intensifying the effects of environmental and dietary factors. In Table1 genes associated with obesity and metabolic disorders explained bellow.

Syndromic forms of obesity

Syndromic forms of obesity that shows as part of a genetic syndrome which shows the presence of excess body weight is merely one characteristic among various other medical or developmental issues (Farzand et al. 2025). This condition may emerge in early life and it is often linked to additional complications like intellectual disabilities, unique facial or physical features and disorders affecting organs or behavior (Wyszyńska et al. 2025). The origins of this form of obesity can maybe traced in multiple genetic anomalies. It included chromosomal alterations, microdeletions or variations in copy number.

Table 1 Genes associated with obesity and metabolic disorders

Gene	Gene symbol	Associated metabolic disorder	Function	References
Leptin	*LEP*	Obesity, Leptin deficiency	Regulates energy balance by inhibiting hunger; promotes energy expenditure. Involved in appetite control.	Ahima and Flier 2025
Leptin receptor	*LEPR*	Obesity, Leptin resistance	Mediates the effects of leptin on appetite and energy expenditure. Key in regulating food intake and energy balance.	Durak et al. 2025
Pro-opiomelanocortin	*POMC*	Obesity, POMC deficiency	Involved in melanocortin signaling for energy homeostasis, regulating hunger and fat metabolism.	Yanik and Durhan 2025
Melanocortin 4 receptor	*MC4R*	Obesity, MC4R mutations	Regulates food intake and energy expenditure; mutations lead to severe obesity.	Imangaliyeva et al. 2025
FTO (Fat Mass and obesity-associated gene)	*FTO*	Obesity, Type 2 Diabetes	Regulates fat storage and body weight; involved in the regulation of energy expenditure and appetite.	Jamali et al. 2025
Adiponectin	*ADIPOQ*	Obesity, Insulin resistance	Modulates glucose regulation and fatty acid oxidation; has anti-inflammatory effects and regulates fat metabolism.	Vuković et al. 2025
Peroxisome proliferator-activated receptor gamma	*PPARγ*	Obesity, Insulin resistance, Type 2 Diabetes	Regulates adipogenesis, glucose metabolism, and insulin sensitivity; crucial for fat storage and energy balance.	Kounatidis et al. 2025
Insulin receptor	*INSR*	Type 2 Diabetes, Obesity	Mediates the effects of insulin on glucose uptake and metabolism; mutations lead to insulin resistance.	Coelho et al. 2025
Uncoupling protein 1	*UCP1*	Obesity, Metabolic disorders	Involved in thermogenesis and energy expenditure; helps regulate heat production in brown adipose tissue.	Klein 2025
PPAR alpha	*PPARA*	Obesity, Hyperlipidemia	Regulates fatty acid oxidation and lipid metabolism; has a role in maintaining energy balance.	Koppen 2025
Cysteine-rich protein 2	*CRP2*	Obesity, Metabolic syndrome	Involved in regulation of adipocyte differentiation and fat accumulation.	Milanović et al. 2025
Fibrillin 1	*FBN1*	Marfan Syndrome, Obesity	Involved in connective tissue formation and energy homeostasis; mutations may contribute to metabolic disorders.	Marsan et al. 2025
MC3R (Melanocortin 3 Receptor)	*MC3R*	Obesity, Insulin resistance	Regulates food intake and energy expenditure; mutations cause excessive weight gain.	Yanik and Durhan 2025
Fatty acid synthase	*FASN*	Obesity, Hyperlipidemia	Key enzyme in the synthesis of fatty acids; excessive activity leads to fat accumulation.	Banaszak et al. 2025
Apolipoprotein E	*APOE*	Alzheimer's, Obesity, Dyslipidemia	Plays a role in lipid metabolism and energy homeostasis; has been implicated in both metabolic diseases and neurodegeneration.	Solanke 2025
UCP2 (Uncoupling protein 2)	*UCP2*	Obesity, Diabetes	Regulates energy expenditure and mitochondrial proton leak; plays a role in metabolic flexibility.	Kelany et al. 2025
Thyroid hormone receptor beta	*THRB*	Hypothyroidism, Obesity	Regulates metabolism and thermogenesis; mutations lead to obesity and metabolic dysregulation.	Tulp et al. 2025
TNF-alpha	*TNF*	Obesity, Insulin resistance	A pro-inflammatory cytokine that affects insulin sensitivity, lipid metabolism, and fat accumulation.	Sierra-Ruelas et al. 2025
CART (Cocaine- and Amphetamine-regulated transcript)	*CARTPT*	Obesity, Eating disorders	Involved in regulating appetite and energy balance; regulates feeding behavior.	Tonin et al. 2025
Ghrelin	*GHRL*	Obesity, Prader-Willi Syndrome	Stimulates appetite, growth hormone release, and energy balance.	Doğan and Bülbül 2025

The researchers have recognized about 140 genetic syndromes that are associated with syndromic obesity, with Prader–Willi syndrome being among the most well-known (Guillon 2025).

The patterns of inheritance can vary, manifesting as autosomal dominant, autosomal recessive, or X-linked traits (Nagral and Mallakmir 2025). A exact diagnosis generally necessitates a collaborative effort among geneticists, endocrinologists and other medical professionals to ascertain the underlying genetic factors. The most common genetic syndromes associated to syndromic obesity encompass Prader–Willi (Table2), Bardet–Biedl, Alström and Cohen syndromes (Table 2) (Argente et al. 2025). The weight gain observed in these syndromes is attributed to disruptions in energy balance, it can be caused with excessive appetite (hyperphagia), insulin resistance or hormonal imbalances like hypothyroidism (Dharia et al. 2025).

Hyperphagia and obesity in Prader–Willi syndrome

The diagnosing Prader–Willi syndrome (PWS) in children in the early stages of infancy are characterized with

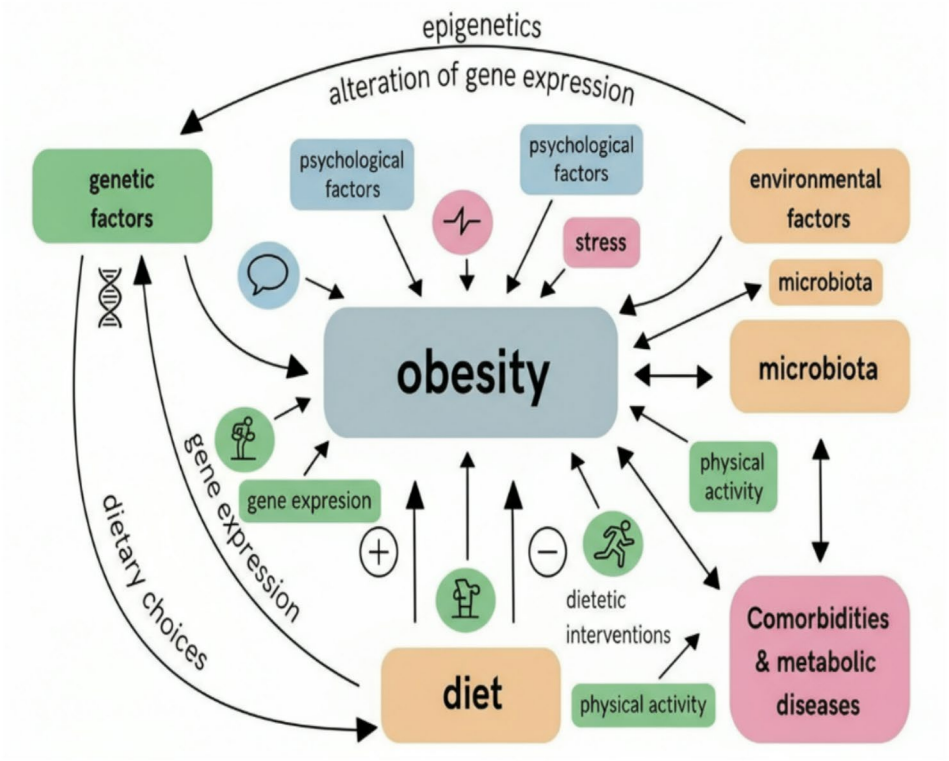

Fig. 2 Integrated framework showing gene–nutrient–environment interactions in obesity and metabolic disorders

a lack of appetite but between the ages of 4 and 8 (Höybye and Petersson 2025) here is a notable increased in appetite, and the results in significant weight gain, this phenomenon attributed to a conceded sense of satiety (Table3). Meals tend to were extended and feelings of hunger frequently re-emerge within 30 min post-consumption (Cassidy 2019).

The behavioral issues related to food and less or no physical activity further can facilitate weight gain. Hyperphagia in PWS is linked with irregular neurotransmitter signaling within the hypothalamus and it is responsible for regulating hunger and satiety (Muscogiuri et al. 2021). The gene SNORD-116 that encodes small nucleolar RNA (snoRNA) which identified as a significant contributor to this dysfunction(Salles et al. 2021). In addressing obesity in PWS necessitates a structured dietary regimen which restricted access food and regular physical activity. A customized nutritional plan like: (1) 6–8 servings of vegetables (2) 4 servings of fruit (3) 3–5 servings of cereal products (4) 2 servings of protein (5) 2 servings of dairy (6) A daily caloric intake should not exceed 1200 kcal(San Miguel et al. 2025).

Monogenic obesity rises by the mutations in individual genes that disrupt energy regulation. The mutations frequently influence the leptin–melanocortin pathway in the hypothalamus that governs appetite and metabolism (Zhang et al. 2025). The genes concerned included*LEP*, *LEPR*, *POMC*, *SIM1*, *PCSK1*, *MC4R*, *BDNF* and *NTRK2* (Minniakhmetov et al. 2025). This type of obesity mostly shows in early childhood and is linked to severe weight gain, endocrine irregularities and disordered eating patterns. Inheritance may follow autosomal dominant or recessive patterns (Alrohaimi 2025).

Polygenic forms of obesity

It is common obesity which results that the combination of various genetic variants (Semenova et al. 2025). These variants include both mutations and polymorphisms found in multiple genes. The genetic arrangement intensifies susceptibility to environmental influences like dietary habits and levels of physical activity. In contrast to monogenic obesity, polygenic obesity typically manifests later in life and tends to be less severe (Ali et al. 2025).

The recent progresses in the next-generation sequencing (NGS) and genome-wide association studies (GWAS) have exposed more than 600 genes which associated with obesity (Zhang et al. 2025). Approximately 30 neuroendocrine peptides which are known to affects eating behaviors with ghrelin being a key player in the regulation of appetite (Mitoiu et al. 2024) (table 3). The genes associated to polygenic obesity can be categorized into three distinct groups: (1) Genes that regulate food intake (Agrawal et al. 2024). (2) Genes that participate

Table 2 The clinical features, syndromic obesity, genes and inheritance

Obesity-related syndrome	Gene	Inheritance pattern Clinical features	Obesity features	References
Prader-Willi Syndrome (PWS)	Chromosome 15q11-q13 (deletion or imprinting defect)	Autosomal dominant (de novo) Hypotonia, developmental delay, intellectual disability, hyperphagia, small hands/feet, hypogonadism	Severe hyperphagia, insatiable appetite leading to extreme obesity in childhood	Chen et al. 2021
Bardet-Biedl Syndrome (BBS)	*BBS1*, *BBS10* (multiple genes, 21 loci)	Autosomal recessive Retinal degeneration, polydactyly, renal abnormalities, developmental delay, heart defects	Early onset obesity, reduced energy expenditure, slow metabolism	Zhang 2025
Alström syndrome	*ALMS1* (Chromosome 2p13)	Autosomal recessive Progressive sensorineural hearing loss, dilated cardiomyopathy, retinal degeneration	Progressive obesity starting in early childhood, adiposity accumulation	Qi et al. 2025
Cohen syndrome	*COH1* (Chromosome 8q22)	Autosomal recessive Intellectual disability, hypotonia, microcephaly, cataracts, facial dysmorphism	Progressive obesity in early childhood, truncal adiposity	Wang et al. 2025
Rasopathies (e.g., Noonan Syndrome)	*PTPN11*, *KRAS*, *SOS1* (multiple genes)	Autosomal dominant Short stature, congenital heart defects, characteristic facial features, developmental delay	Mild to moderate obesity, reduced growth, low muscle mass	Rodríguez 2025
MC4R deficiency	*MC4R* (Chromosome 18q22)	Autosomal dominant Hyperphagia, decreased satiety, early onset obesity, some cognitive delay	Severe obesity starting in early childhood, hyperphagia	Imangaliyeva et al. 2025
Silver-Russell syndrome	Chromosome 11p15	Autosomal dominant (de novo) Short stature, triangular face, asymmetry, developmental delay, feeding difficulties	Growth restriction and obesity at different stages of life, especially in early childhood	Begemann et al. 2025
Congenital leptin deficiency	*LEP* (Chromosome 7q32)	Autosomal recessive Severe early onset obesity, hypogonadotropic hypogonadism, high levels of circulating leptin	Severe obesity beginning in infancy, hyperphagia despite high leptin	Golounina et al. 2025
McCune-Albright syndrome	*GNAS* (Chromosome 20q13)	Mosaic (post-zygotic mutation) Café-au-lait spots, fibrous dysplasia of bone, precocious puberty, endocrine abnormalities	Early onset obesity, particularly due to endocrine dysfunction	Tsintavis and Stathopoulos 2025
Mosaic Trisomy 8 Syndrome	Chromosome 8 (Mosaic trisomy)	De novo (mosaicism) Developmental delay, dysmorphic features, learning disabilities, heart defects	Obesity observed in early childhood, poor motor coordination	Ehn et al. 2025
Smith-magenis syndrome	*RAI1* (Chromosome 17p11.2)	Autosomal dominant (de novo) Intellectual disability, sleep disturbances, behavior problems, craniofacial abnormalities	Increased appetite and obesity, impulsive eating behaviors	Covarelli et al. 2025
Leprechaunism (Donohue Syndrome)	*INSR* (Chromosome 19p13.2)	Autosomal recessive Severe insulin resistance, growth retardation, microcephaly, profound developmental delay	Early onset, severe obesity due to insulin resistance, hyperglycemia	Pliszka and Szablewski 2025

in adipogenesis and triglyceride storage(Takeda and Dai 2024)(3) Genes that manage energy expenditure (Hong et al. 2024). Bellow the table 3 have showed Genes Linked with Obesity, Functional Roles in the Metabolic Regulation.

The dietary interventions interact to genetic variants to affect obesity and metabolic health every method targets unique phenotypic traits which based on the relationships among genes and nutrients. The Low-Carbohydrate Diet (LCD) which may effective for individuals possessing the *FTO* (T-allele) (Table 3) and *MC4R*(C-allele) variants (Gorini and Tonacci 2025). The genetic factors are associated with increase appetite and diminished satiety and low-carbohydrate intake aids in weight reduce and enhances metabolic control.

The mediterranean diet have advantage for the carrying the APOA2 (T-allele) and SIRT1 (G-allele) variants these are linked to compromised lipid metabolism and fat storage (Xiao et al. 2024). The anti-inflammatory and antioxidant characteristics of diet encourage metabolic health and ease obesity associated risks. The high protein diet is recommended for individuals who are with the*LEP (A-allele) and FTO (T-allele)*variants (Vranceanu et al. 2024).

The low-glycemic diet is suitable for individuals with the *TCF7L2 (T-allele)* and *GCKR (C-allele)* variants that are associated with insulin resistance (Table 4) (Gorini and Tonacci 2025). Foods with a low glycemic index assist in stabilizing blood glucose levels and enhancing metabolic outcomes (Saidaiah et al. 2024). The ketogenic diet is effective for those with the*IRX3 (A-allele) and MC4R*

Table 3 Genes linked with obesity, functional roles in the metabolic regulation

Function	Gene name	Phenotypic traits	References
Appetite regulation	*MC4R* (Melanocortin 4 Receptor)	Hyperphagia, early-onset obesity, insulin resistance, metabolic syndrome	Abuzzahab et al. 2025
Fat storage and metabolism	*FTO* (Fat mass and obesity-associated gene)	Increased fat mass, elevated BMI, susceptibility to metabolic diseases	Taneera et al. 2024
Leptin regulation	*LEP* (Leptin)	Hyperphagia, severe early-onset obesity, hypogonadotropic hypogonadism	Mondal et al. 2024
Glucose homeostasis	*INS* (Insulin)	Insulin resistance, early obesity, type 2 diabetes risk	Sajiir et al. 2024
Energy expenditure	*UCP1* (Uncoupling Protein 1)	Reduced thermogenesis, increased adiposity, impaired cold-induced thermogenesis	Gong et al. 2024
Fatty acid oxidation	*PPAR-γ* (Peroxisome proliferator-activated receptor gamma)	Increased adipogenesis, fat storage, insulin sensitivity impairment	Mohajan and Mohajan 2024
Adipocyte differentiation	*KLF6* (Kruppel-like factor 6)	Altered adipocyte differentiation, fat storage, reduced metabolic activity	Abbas Raza et al. 2024
Adipogenesis and fat deposition	*ADIPOQ* (Adiponectin)	Decreased adiponectin levels, impaired fat metabolism, obesity-associated metabolic dysfunction	Błażejewska et al. 2025
Glucose metabolism	*GCKR* (Glucokinase Regulatory Protein)	Insulin resistance, hyperglycemia, obesity with metabolic risk	Paliwal et al. 2024
Cholesterol and lipid metabolism	*APOA2* (Apolipoprotein A2)	Altered lipid profile, obesity-associated dyslipidemia	Kakafoni et al. 2025
Mitochondrial biogenesis	*TOMM40* (Translocase of the outer mitochondrial membrane 40)	Impaired mitochondrial function, low energy expenditure, increased fat accumulation	Yang 2024
Thermogenesis regulation	*IRX3* (Iroquois homeobox 3)	Reduced thermogenic activity, susceptibility to obesity under high-calorie conditions	Hahn 2024
Appetite and reward pathways	*BDNF* (Brain-Derived Neurotrophic Factor)	Reduced satiety, hyperphagia, emotional eating behaviors, obesity susceptibility	Cao 2024
Nutrient sensing and metabolism	*MTOR* (Mechanistic Target of Rapamycin)	Increased adipogenesis, altered fat metabolism, insulin resistance	Liu et al. 2025
Adipocyte metabolism	*CPT1A* (Carnitine palmitoyltransferase 1 A)	Impaired fatty acid oxidation, fat accumulation, metabolic dysfunction	Dong et al. 2024
Inflammation and obesity	*TNF-α* (Tumor necrosis factor-alpha)	Chronic low-grade inflammation, obesity-related insulin resistance, metabolic syndrome	Eswar et al. 2024
Oxidative stress	*SOD2* (Superoxide dismutase 2)	Impaired oxidative stress response, increased adiposity, obesity-associated metabolic disorders	Tamagawa et al. 2024
Neuropeptide regulation	*NPY* (Neuropeptide Y)	Increased appetite, hyperphagia, obesity, stress-induced eating	Sigorski et al. 2025

*(T-allele)*variants, related to decreased thermogenesis and appetite regulation (Voros et al. 2025). Bellow the Table 4 show a clear picture of association of gene, diet and Influence on obesity and metabolic health.

Epigenetic, diet and obesity

Dietary patterns have a important impact on gene expression (Zhang et al. 2024). Diets that are high in processed foods and with saturated fats have a tendency to promote inflammation, glucose intolerance and lipid accumulation (Mann et al. 2024). while diets rich in fruits, vegetables and whole grains are linked with supportive anti-inflammatory gene profiles (Yu et al. 2024). The bioactive compounds like apple polyphenols, resveratrol and Epigallocatechin gallate (EGCG) derived from green tea showed potential in modulating genes which is crucial for fat metabolism, lipolysis and adipogenesis (Capasso et al. 2025). The compound enhances metabolic efficiency and provide protective benefits similar with those achieved by calorie restriction or physical exercise. Furthermore, soy isoflavones and sulforaphane showed anti-obesity properties with altering gene activity and inhibiting the formation of fat cells (Table 4).

The micronutrients like vitamin D, B12 and folate are vital in the regulation of adipogenesis and energy metabolism (Samavat et al. 2025). Vitamin D plays a role in gene expression within adipose tissue and may prevent the differentiation of fat cells, with its receptor (VDR) being critical for metabolic regulation (Sekar et al. 2025) and exposure with endocrine disruptors like Bisphenol A (BPA) can undermine these useful effects with encouraging adipocyte formation (García García et al. 2024). These insights underscore the importance of implementing targeted nutritional strategies for prevent and manage obesity through the modulation of epigenetic factors (Table 4).

Table 4 Association of gene, diet and influence on obesity and metabolic health

Type of diet	Variant, Gene, Allele	Phenotypic effect	References
Low-carbohydrate diet	*FTO (rs9939609, T-allele)*	Increased obesity risk; greater weight loss response with low-carb diet	Hajira et al. 2025
	MC4R (rs17782313, C-allele)	Hyperphagia and obesity risk; improved weight reduction with low-carb intake	Hajira et al. 2025
	GIPR (rs1800437, T-allele)	Increased body fat; low-carb diet enhances metabolic outcomes	Paul et al. 2024
Mediterranean diet	*APOA2 (rs5082, T-allele)*	Impaired lipid metabolism; better outcomes with Mediterranean diet	Abaj et al. 2025
	SIRT1 (rs2273954, G-allele)	Fat accumulation risk; antioxidant-rich Mediterranean diet improves metabolism	Tao et al. 2022
High-protein diet	*LEP (rs7799039, A-allele)*	Reduced leptin signaling; protein diet improves satiety and weight control	Vranceanu et al. 2024
	FTO (rs9939609, T-allele)	Increased fat mass risk; high-protein diet promotes fat loss	Merritt et al. 2018
Low-glycemic diet	*TCF7L2 (rs7903146, T-allele)*	Insulin resistance and diabetes risk; improved glucose control	Hosseinpour-Niazi et al. 2022
	GCKR (rs780094, C-allele)	Higher BMI and T2D risk; low-GI diet stabilizes glucose	Gorini and Tonacci 2025
Ketogenic diet	*MC4R (rs17782313, T-allele)*	Reduced caloric restriction response; better weight loss on ketogenic diet	Abd Ali 2022
	IRX3 (rs16829729, A-allele)	Reduced thermogenesis; ketogenic diet enhances fat oxidation	Rodriguez-Cortes 2025
Low-fat diet	*PPAR-γ (rs1801282, Pro12Ala)*	Fat accumulation tendency; low-fat diet more effective	Duarte et al. 2025
High-fiber diet	*SLC30A8 (rs13266634, A-allele)*	T2D and obesity risk; fiber improves insulin sensitivity	Gupta et al. 2024
Plant-based diet	*BDNF (rs6265, Val66Met)*	Emotional eating tendency; micronutrient-rich plant diet improves outcomes	Zhang and Park 2025
Intermittent fasting	*ADIPOQ (rs1501299, C-allele)*	Low adiponectin levels; fasting improves fat metabolism and insulin sensitivity	Błażejewska et al. 2025
High-fat diet	*CPT1A (rs2835926, T-allele)*	Impaired fat oxidation; high-fat diet worsens obesity risk	Galmés et al. 2020

Limitations

This research has limitations like it based on data that has been published which may lead to slight publication bias. The variations in study populations, dietary evaluations and genetic methodologies may influence the consistency of the results. The scarcity of longitudinal studies limits the ability to interpret causality. However, the results provide valuable insights into the interactions between genes and nutrients in the context of obesity.

Conclusion

To addressing obesity requires a comprehensive approach that incorporates genetic, dietary and environmental factors. Obesity influenced with various elements and making personalized treatment strategies essential for effective management. The need of data that tracks long-term outcomes and methods that support sustainable lifestyle changes. These efforts should involve not only healthcare professionals as well as the general public, aiding in the creation of environments that foster healthier habits. Working together, researchers, healthcare providers and policymakers can develop targeted strategies to reduce obesity and improve public health as a whole.

Abreactions

ADIPOQ	Adiponectin Gene
BMI	Body Mass Index
CVD	cardiovascular disease
DNA	Deoxyribonucleic Acid
DM	Diabetes Mellitus
FTO	Fat Mass and Obesity-Associated Gene
GWAS	Genome-Wide Association Studies
MC4R	Melanocortin 4 Receptor
LEPR	Leptin Receptor
PPARG	Peroxisome Proliferator-Activated Receptor Gamma
TNF-α	Tumor Necrosis Factor Alpha

Author contributions

M.A.D, A.H., A.K., M.S.B., M. K. A., were involved in conceptualization, editing and original manuscript writing, S.S., M.A.B. were in language, language editing, all authors approved the final version of the manuscript.

Funding

No external funding was received for this study.

Data availability

Not applicable.

Declarations

Ethics approval and consent to participate

This review did not require ethical approval or consent for participation.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Biostatistics and Epidemiology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
[2]Department of Biostatistics, Faculty of medicine, Sakarya University, Sakarya, Türkiye
[3]Al Aleem Medical College, Gulab Devi Hospital, Lahore, Pakistan
[4]Institute of agriculture Sciences, University of the Punjab, Lahore, Pakistan
[5]Quaid-e-Azam Medical College, Bahawal Victoria Hospital Bahawalpur, Bahawalpur city, Pakistan

Received: 30 October 2025 / Accepted: 27 January 2026
Published online: 10 February 2026

References

Abaj F, Aali Y, Najafi F, Koohdani F (2025) The relationship of genetic signature for cardiometabolic risk with biomarkers of inflammatory and oxidative stress in diabetic patients. BMC Endocr Disord 25(1):148

Abbas Raza SH, Zhong R, Wei X, Zhao G, Zan L, Pant SD et al (2024) Investigating the role of KLF6 in the growth of bovine preadipocytes: using transcriptomic analyses to understand beef quality. J Agric Food Chem 72(17):9656–68

Abd Ali AH (2022) The common gene MC4R rs17782313 polymorphism associated with obesity: a meta-analysis. Human Gene 33:201035

Abdolla N, Narmuratova G, Abdusattarova Y, Kali A, Perfilyeva Y, Ostapchuk Y et al (2025) The impact of High-Fat diet and circadian disruptions on obesity and immune system dysfunction. ES Food Agrofor 20:1591

Abuzzahab MJ, Dubern B, Goldstone AP, Haqq AM, Heymsfield SB, Miller JL et al (2025) Improving the diagnosis of hyperphagia in melanocortin-4 receptor pathway diseases. Obesity. https://doi.org/10.1002/oby.24287

Agrawal P, Kaur J, Singh J, Rasane P, Sharma K, Bhadariya V et al (2024) Genetics, nutrition, and health: a new frontier in disease prevention. Journal of the american nutrition association 43(4):326–38

Ahima RS, Flier JS (2025) Leptin: 30 Years Later. Annu Rev Physiol. https://doi.org/10.1146/annurev-physiol-042324-100259

Ali F, Ganie MA, Jan S, Rashid F (2025) Interactions Between Genetic and Environmental Risk Factors in Lifestyle Diseases. Environmental Toxicants and Lifestyle Diseases. Springer, pp 377–96

Alrohaimi Y (2025) Genetic syndromes as a cause of obesity in Saudi paediatric population-a narrative review. Journal of Pioneering Medical Sciences. https://doi.org/10.47310/jpms202514S0136

Rodríguez Martín M. Analysis of PTPN11 variants identified in pediatric patients diagnosed with Noonan syndrome. 2025.

Argente J, Farooqi IS, Chowen JA, Kühnen P, López M, Morselli E et al (2025) Hypothalamic obesity: from basic mechanisms to clinical perspectives. The Lancet Diabetes & Endocrinology 13(1):57–68

Armutcu F, McCloskey E (2025) Dysbiosis as a driving force for the relationship between obesity and secondary osteoporosis. Obes Med. https://doi.org/10.1016/j.obmed.2025.100637

Arshad MT, Ali M, Maqsood S, Ikram A, Ahmed F, Aljameel A et al (2025) Personalized nutrition in the era of digital health: a new frontier for managing diabetes and obesity. Food Sci Nutr 13(10):e71006

Banaszak M, Górna I, Drzymała-Czyż S (2025) Fatty acid profile and desaturase activity in obesity: roles, mechanisms, and clinical relevance. Metabolites 15(9):595

Begemann M, Lengyel A, Pinti E, Kovács ÁF, Fekete G, Stratmann S et al (2025) Maternal uniparental disomy of chromosome 7: how chromosome 7-encoded imprinted genes contribute to the Silver–Russell phenotype. Clin Epigenetics 17(1):70

Błażejewska W, Dąbrowska J, Michałowska J, Bogdański P (2025) The role of adiponectin and ADIPOQ variation in metabolic syndrome: a narrative review. Genes 16(6):699

Brandolino S, Franzago M, Murmura G, Ricci F, Gatta V, Stuppia L et al (2025) Nutrition, Environment, and genetics in colorectal Cancer. Epigenetics and possible future perspective. Curr Nutr Rep 14(1):1–14

Capasso L, De Masi L, Sirignano C, Maresca V, Basile A, Nebbioso A et al (2025) Epigallocatechin gallate (EGCG): pharmacological properties, biological activities and therapeutic potential. Molecules 30(3):654

Cao J. Brain-Derived neurotrophic factor (BDNF) as a diagnostic and prognostic biomarker in anorexia nervosa. Université Paris Cité. 2024.

Cassidy C, Celebi S, Savard M, Chamoun M, Tardif C, Rosa-Neto P (2019) ACNP 58th Annual Meeting: Poster Session II

Chen C-P, Lin M-H, Chen Y-Y, Chern S-R, Wu P-S, Chen S-W et al (2021) Prenatal diagnosis of a 15q11. 2-q14 deletion of paternal origin associated with increased nuchal translucency, mosaicism for de novo multiple unbalanced translocations involving 15q11-q14, 5qter, 15qter, 17pter and 3qter and Prader–Willi syndrome. Taiwan J Obstet Gynecol 60(2):335–40

Cheng M, Ding F, Li L, Dai C, Sun X, Xu J et al (2025) Exploring the role of curcumin in mitigating oxidative stress to alleviate lipid metabolism disorders. Front Pharmacol 16:1517174

Chermon D, Birk R (2024) Deciphering the interplay between genetic risk scores and lifestyle factors on individual obesity predisposition. Nutrients 16(9):1296

Zhang P, Wang Y, Chai Y, Zang W. Clinical and genetic analysis of a compound heterozygous mutation in the BBS10 gene in Chinese people with Bardet Biedl syndrome. 2025.

Coelho R, Cruz ÁA, Lima L, Melo AP, Belitardo E, Machado C et al (2025) Genetic variants in insulin, leptin, and their receptors are associated with overweight in a Brazilian asthma cohort. Nutr Res 136:28–38

Covarelli J, Vinciarelli E, Mirarchi A, Prontera P, Arcuri C (2025) Retinoic Acid Induced 1 and Smith–Magenis Syndrome: from genetics to biology and possible therapeutic strategies. Int J Mol Sci 26(14):6667

Danesh Doost H, Jounaghani MN, Riahi R, Heidari-Beni M, Hosseini M, Sharifiazi F et al (2025) Association of genetic, environmental, and nutritional factors with metabolic phenotypes of obesity: a scoping review. J Obes 2025(1):8472196

Das A, Mohsin FM, Urmi BR, Islam S, Hasan M, Mostafa SM et al (2025) How obesity increases the risk of developing type 2 diabetes and some cancers. Eur J Sci Innov Technol 5(3):13–20

Dharia A, Desai D, Desai K (2025) Exploring the link between thyroid disorders and obesity: mechanisms, impacts, and clinical implications. Endocr Pract. https://doi.org/10.1016/j.eprac.2025.02.005

Doğan G, Bülbül A (2025) Genetic disease behind obesity and its nutritional treatment; Prader-Willi syndrome. Acta Med Nicomedia 8(2):240–246

Dong J, Li M, Peng R, Zhang Y, Qiao Z, Sun N (2024) ACACA reduces lipid accumulation through dual regulation of lipid metabolism and mitochondrial function via AMPK-PPARα-CPT1A axis. J Transl Med 22(1):196

Duarte GBS, Pascoal G, Rogero MM (2025) Polymorphisms involved in insulin resistance and metabolic inflammation: influence of nutrients and dietary interventions. Metabolites 15(4):245

Durak S, Aksoyer Sezgin SB, Celik F, Diramali M, Yaylim I, Gurol AO et al (2025) The investigation of leptin (LEP) and leptin receptor (LEPR) gene variations in obese patients. Clin Translational Metabolism 23(1):6

Ehn E, Eisfeldt J, Laffita-Mesa JM, Thonberg H, Schoumans J, Portaankorva AM et al (2025) A de novo, mosaic and complex chromosome 21 rearrangement causes APP triplication and Familial autosomal dominant early onset alzheimer disease. Sci Rep 15(1):2912

Eswar S, Rajagopalan B, Ete K, Gattem SNR (2024) Serum tumor necrosis factor alpha (TNF-α) levels in obese and overweight adults: correlations with metabolic syndrome and inflammatory markers. Cureus. https://doi.org/10.7759/cureus.64619

Fansa S, Acosta A (2024) The melanocortin-4 receptor pathway and the emergence of precision medicine in obesity management. Diabetes Obes Metab 26:46–63

Farzand A, Rohin MAK, Awan SJ, Sharif Z, Yaseen A, Ahmad AMR (2025) A review of syndromic forms of obesity: genetic etiology, clinical features, and molecular diagnosis. Curr Issues Mol Biol 47(9):718

Fic W, Polak-Szczybyło E (2025) Dietary factors influencing the intensity of low-grade inflammation in obesity. Obesities 5(1):12

Galmés S, Palou A, Serra F (2020) Increased risk of high body fat and altered lipid metabolism associated to suboptimal consumption of vitamin A is modulated by genetic variants rs5888 (SCARB1), rs1800629 (UCP1) and rs659366 (UCP2). Nutrients 12(9):2588

García García M, Picó Y, Morales-Suárez-Varela M (2024) Effects of bisphenol A on the risk of developing obesity. Nutrients 16(21):3740

Golounina O, Minniakhmetov I, Salakhov R, Khusainova R, Zakharova E, Bychkov I et al (2025) Pathogenetic therapeutic approaches for endocrine diseases based on antisense oligonucleotides and RNA-interference. Front Endocrinol 16:1525373

Gong D, Lei J, He X, Hao J, Zhang F, Huang X et al (2024) Keys to the switch of fat burning: stimuli that trigger the uncoupling protein 1 (UCP1) activation in adipose tissue. Lipids Health Dis 23(1):322

Górczyńska-Kosiorz S, Kosiorz M, Dzięgielewska-Gęsiak S (2024) Exploring the interplay of genetics and nutrition in the rising epidemic of obesity and metabolic diseases. Nutrients 16(20):3562

Gorini F, Tonacci A (2025) The complex gene–carbohydrate interaction in type 2 diabetes: between current knowledge and future perspectives. Nutrients 17(14):2350

Guillon E, Dubern B, Clément K, Poitou C. Multidimensional characterisation of eating behaviour in genetic Obesity–A systematic review. Obes Facts. 2025.

Gupta MK, Gouda G, Vadde R (2024) Relation between obesity and type 2 diabetes: evolutionary insights, perspectives and controversies. Curr Obes Rep 13(3):475–495

Hahn NA. Irx3 and Irx5 function in adipose tissue. University of Toronto (Canada). 2024.

Hajira B, Sehar B, Fakhrunisa, Siraj S, Malik MO, Naqeeb H et al (2025) Impact of high-protein, low-calorie diet on anthropometric indices, glycation, and

inflammation associated with the fat mass and obesity (FTO) gene among individuals with overweight/obesity. Front Nutr 12:1619543
Hong E, Yang G, Oh S, Kim E (2024) *Lactiplantibacillus plantarum* L67 reduces diet-induced obesity by stimulating gene programming for adipose lipolysis and energy expenditure. J Funct Foods 113:106028
Hosseinpour-Niazi S, Mirmiran P, Hadaegh F, Daneshpour MS, Hedayati M, Azizi F (2022) The effect of TCF7L2 polymorphisms on inflammatory markers after 16 weeks of legume-based dietary approach to stop hypertension (DASH) diet versus a standard DASH diet: a randomised controlled trial. Nutr Metab 19(1):35
Höybye C, Petersson M (2025) The role of the arcuate nucleus in regulating hunger and satiety in Prader-Willi syndrome. Curr Issues Mol Biol 47(3):192
Imangaliyeva A, Sikhayeva N, Bolatov A, Utupov T, Romanova A, Akhmetollayev I et al (2025) Genetic insights into severe obesity: A case study of MC4R variant identification and clinical implications. Genes 16(5):508
Jamali MA, Abdeen SM, Mathew TC, Abdeen AS (2025) Association of Fat Mass and Obesity (FTO) rs9939609 Single Nucleotide Polymorphism (SNP) With Obesity and Type 2 Diabetes (T2D) in Healthy Young Adults in Kuwait. Cureus 17(1):2–15
Kakafoni G, Zvintzou E, Fenyo M, Dimitrescu M, Mparnia V, Gafencu AV et al (2025) The functional interaction of apolipoprotein A2 with the metabolic system of apolipoprotein E-rich-lipoproteins in the regulation of the lipid profile. Atherosclerosis. https://doi.org/10.1016/j.atherosclerosis.2025.119602
Kelany MM, Afify M, Abdelmaksoud MD, Mahdy ES, El Mezyen H, Hamimy WI et al (2025) Association of AMP-activated protein kinase and uncoupling protein-2 gene expressions with hypertension in obese patients. Egypt Pharm J 24(1):69–77
Khusainova R, Minniakhmetov I, Vasyukova O, Yalaev B, Salakhov R, Kopytina D et al (2025) Genetic landscape of obesity in children: research advances and prospects. J Obes 2025(1):9186826
Klein Hazebroek M Cellular mechanisms enhancing white fat metabolism and their impact on obesity: Department of Molecular Biosciences, The Wenner-Gren Institute, Stockholm &#8230. 2025.
Koppen A. Effect of synthetic dietary triglycerides: A novel research paradigm for nutrigenomics. PLoS ONE. 2025.
Kounatidis D, Vallianou NG, Rebelos E, Kouveletsou M, Kontrafouri P, Eleftheriadou I et al (2025) The many facets of PPAR-γ agonism in obesity and associated comorbidities: benefits, risks, challenges, and future directions. Curr Obes Rep 14(1):19
Li X, Wang T, Wang W, Wang Z, Wang H, Fan K et al (2025) Gene dynamics in maternal nutrition: the role of chromium in mitigating offspring obesity. Biol Trace Elem Res. https://doi.org/10.1007/s12011-025-04711-0
Liu Y, Mai K, Zhang W (2025) mTOR signaling in aquaculture animals: a central nutrient-sensing hub orchestrating growth, metabolism, health and quality. Rev Aquacult 17(4):e70068
Lupu A, Fotea S, Jechel E, Starcea IM, Ioniuc I, Knieling A et al (2024) Is oxidative stress-antioxidants imbalance the physiopathogenic core in pediatric obesity? Front Immunol 15:1394869
Ma X, Jiang J, Qian H, Li Y, Fan M, Wang L (2025) Nutritional heterogeneity of dietary proteins: mechanisms of gut microbiota-mediated metabolic regulation and health implications. Compr Rev Food Sci Food Saf 24(5):e70274
Mann V, Sundaresan A, Shishodia S (2024) Overnutrition and lipotoxicity: impaired efferocytosis and chronic inflammation as precursors to multifaceted disease pathogenesis. Biology 13(4):241
Mansour S, Alkhaaldi SM, Sammanasunathan AF, Ibrahim S, Farhat J, Al-Omari B (2024) Precision nutrition unveiled: gene–nutrient interactions, microbiota dynamics, and lifestyle factors in obesity management. Nutrients 16(5):581
Marsan M, Brutti M, Meloni F, Marica M, Soddu C, Lai F et al (2025) A novel missense variant of FBN1 gene in a Sardinian family with Marfan syndrome: a case report. Front Pediatr 13:1549504
Merritt DC, Jamnik J, El-Sohemy A (2018) FTO genotype, dietary protein intake, and body weight in a multiethnic population of young adults: a cross-sectional study. Genes Nutr 13(1):4
Milanović M, Milošević N, Ružić M, Abenavoli L, Milić N (2025) Whey proteins and metabolic dysfunction-associated steatotic liver disease features: evolving the current knowledge and future trends. Metabolites 15(8):516
Minniakhmetov IR, Khusainova RI, Vasyukova OV, Kopytina DA, Yalaev BI, Salakhov RR et al (2025) Molecular genetic architecture of morbid obesity in Russian children. Biomedicines 13(3):756
Mitoiu BI, Nartea R, Miclaus RS (2024) Impact of resistance and endurance training on ghrelin and plasma leptin levels in overweight and obese subjects. Int J Mol Sci 25(15):8067
Młynarska E, Biskup L, Możdżan M, Grygorcewicz O, Możdżan Z, Semeradt J et al (2024) The role of oxidative stress in hypertension: the insight into antihypertensive properties of vitamins A, C and E. Antioxidants 13(7):848
Mohajan D, Mohajan HK (2024) Peroxisome proliferator-activated receptor γ (PPAR γ): a systemic insulin sensitizer associated with decreased risk of type 2 diabetes. J Innovations Med Res 3(2):18–24
Mondal S, Rathor R, Singh SN, Suryakumar G (2024) miRNA and leptin signaling in metabolic diseases and at extreme environments. Pharmacol Res Perspect 12(4):e1248
Muscogiuri G, Barrea L, Faggiano F, Maiorino M, Parrillo M, Pugliese G et al (2021) Obesity in Prader–Willi syndrome: physiopathological mechanisms, nutritional and Pharmacological approaches. J Endocrinol Investig 44(10):2057–2070
Nagral A, Mallakmir S (2025) Inherited and metabolic disorders of the liver. Hepatology. Elsevier, pp 1385–415
Siddiqui I, Khan NA, Haider Z (2025) Obesity-associated genetic variants and AMPK signaling in cardiovascular disease: a systematic review of mechanisms and clinical implications. medRxiv. 2025. 10. 04.25337310.
Olivares-Vicente M, Herranz-López M (2025) The interplay between oxidative stress and lipid composition in obesity-induced inflammation: antioxidants as therapeutic agents in metabolic diseases. Int J Mol Sci 26(17):8544
Paliwal A, Paliwal V, Jain S, Paliwal S, Sharma S (2024) Current insight on the role of glucokinase and glucokinase regulatory protein in diabetes. Mini Rev Med Chem 24(7):674–688
Paul J, Jani R, Thorning S, Obucina M, Davoren P, Knight-Agarwal C (2024) Low carbohydrate diets, glycaemic control, enablers, and barriers in the management of type 1 diabetes: a mixed methods systematic review. Diabetol Metab Syndr 16(1):261
Pliszka M, Szablewski L (2025) Severe Insulin Resistance Syndromes: clinical spectrum and management. Int J Mol Sci 26(12):5669
Ponnusamy V, Subramanian G, Muthuswamy K, Shanmugamprema D, Krishnan V, Velusamy T et al (2022) Genetic variation in sweet taste receptors and a mechanistic perspective on sweet and fat taste sensation in the context of obesity. Obes Rev 23(12):e13512
Pratiwi D, Sidartha M, Wiyarta E, Agustinus Harimawan IW, Lestari NMDA, Kim B et al (2025) Comparison of the risk of obesity in the FTO rs9939609 genotype in a multiethnic group in Asia systematic review and meta-analysis. Front Med 12:1522318
Priyadarshini R, Nair P, Nandan K (2025) Nutritional Genomics and Nutrigenomics: Personalized Nutrition for Disease Prevention and Health Optimization. J Food Process Nutritional Sci 3(1):1–20
Qi Y, Lu J, Sun N, Wang Z, Wang Y, Zhou J et al (2025) Alström syndrome: a rare cause of dilated cardiomyopathy in five Chinese children. Gene 944:149285
Rana S, Nawaz H (2025) Exploring the association of FTO rs9939609 and SIRT1 rs7069102 genetic variants with obesity: a case–control study in a sample of Pakistani population. Nucleus 68(2):299–311
Razi O, de Moraes C, Zamani N, Saeidi A, Hadjicharalambous M, Hackney AC et al (2025) From obesity to muscle insulin resistance: the mediating roles of intramyocellular lipids, inflammation, and oxidative stress. Diabetes Metab Res Rev 41(7):e70094
Saidaiah P, Banu Z, Geetha A, Khan AA (2024) Glyceric index and Covid-19 management: a comprehensive review of low, medium and high glycermic index foods. Ann Phytomed 13(1):56–69
Sajiir H, Wong KY, Müller A, Keshvari S, Burr L, Aiello E et al (2024) Pancreatic beta-cell IL-22 receptor deficiency induces age-dependent dysregulation of insulin biosynthesis and systemic glucose homeostasis. Nat Commun 15(1):4527
Salles J, Lacassagne E, Eddiry S, Franchitto N, Salles J-P, Tauber M (2021) What can we learn from PWS and SNORD116 genes about the pathophysiology of addictive disorders? Mol Psychiatry 26(1):51–59
Samavat J, Boachie J, McTernan PG, Christian M, Saravanan P, Adaikalakoteswari A (2025) Maternal B12 deficiency during pregnancy dysregulates fatty acid metabolism and induces inflammation in human adipose tissue. BMC Med 23(1):232
San Miguel GPT, González M, Ramírez EL, López MFF, López LV (2025) Effect of a Mediterranean diet adapted to the Mexican population on indicators of metabolic risk in patients with obstructive sleep apnea: protocol for a randomized controlled trial. JMIR Res Protoc 14(1):e72513
Sekar AK, Josephine A, Tamilselvan J, Sureka V, Rajendran P, Moovendhan M (2025) Dysregulation and gene polymorphisms of vitamin D receptor: its implications in lipid metabolic disorders. Mol Biol Rep 52(1):630
Semenova E, Guo A, Liang H, Hernandez CJ, John EB, Thaker VV (2025) The expanding landscape of genetic causes of obesity. Pediatr Res 97(4):1358–1369

Sharma I, Bakshi K, Mahajan R, Kapoor N (2025) The LEPR gene: a multifaceted regulator of energy homeostasis, obesity pathogenesis, and metabolic health. Human Gene. https://doi.org/10.1016/j.humgen.2025.201486
Sierra-Ruelas E, Vizmanos B, López Gómez JJ, Rico D, Martínez JA, Luis DAD (2025) Mutual impact of dietary antioxidants and TNF-α rs1800629 on insulin levels in adults with obesity. Nutrients 17(14):2345
Sigorski D, Sejda A, Abualsaud N, Krawczyk E, Izycka-Swieszewska E, Kitlinska J (2025) Neuropeptide Y in cancer—biological functions and potential clinical implications. Cancer Metastasis Rev 44(1):21
Solanke OO. Multi-phenotype associations of apolipoprotein E (APOE) genotypes with cardiometabolic risk factors for Alzheimer's disease in the Finnish population. OO Solanke. 2025.
Sternini C, Rozengurt E (2025) Bitter taste receptors as sensors of gut luminal contents. Nat Rev Gastroenterol Hepatol 22(1):39–53
Suleiman KY, Jimoh AG, Afisu B, Onimajesin AO, Saadudeen MA, Lawal MO (2025) A new frontier in precision nutrition–a systematic review. Gastroenterol and Hepatol from Bed to Bench 18(3):270
Takeda Y, Dai P (2024) Functional roles of pantothenic acid, riboflavin, thiamine, and choline in adipocyte browning in chemically induced human brown adipocytes. Sci Rep 14(1):18252
Tamagawa S, Sakai D, Nojiri H, Nakamura Y, Warita T, Matsushita E et al (2024) SOD2 orchestrates redox homeostasis in intervertebral discs: a novel insight into oxidative stress-mediated degeneration and therapeutic potential. Redox Biol 71:103091
Taneera J, Khalique A, Abdrabh S, Mohammed AK, Bouzid A, El-Huneidi W et al (2024) Fat mass and obesity-associated (FTO) gene is essential for insulin secretion and β-cell function: in vitro studies using INS-1 cells and human pancreatic islets. Life Sci 339:122421
Rodriguez-Cortes B, Gomez-Martínez R, Spenle R, Schwaninger M, Nogueiras R, Rasika S et al (2025) Tanycytes: bloodhounds of the metabolic brain. Trends in Endocrinology & Metabolism
Tao T, Lin X, Tang S, Gui W, Zhu W, Li H (2022) Association of genetic variants in the Sirt1 and Nrf2 genes with the risk of metabolic syndrome in a Chinese Han population. BMC Endocr Disord 22(1):84
Tonin G, Eržen S, Mlinarič Z, Eržen DJ, Horvat S, Kunej T et al (2025) The genetic blueprint of obesity: from pathogenesis to novel therapies. Obes Rev. https://doi.org/10.1111/obr.13978
Tsintavis P, Stathopoulos K (2025) McCune-Albright syndrome and long bone fractures: incidence and methods of treatment. Journal of Research and Practice on the Musculoskeletal System. https://doi.org/10.22540/JRPMS-09-090
Tulp OL, Obidi O, Oyesile T, Sainvil F, Branly R, Sciranka A et al (2025) Mechanistic Contributors to Subclinical Hypothyroidism in obesity: Review of Molecular Evidence for Impaired Thyroid Hormone Receptor Affinity and Actions from Rat Studies. Med Sci: Trends and Innov 13:158
Voros C, Sapantzoglou I, Koulakmanidis A-M, Athanasiou D, Mavrogianni D, Bananis K et al (2025) Impact of bariatric surgery on the expression of fertility-related genes in obese women: a systematic review of LEP, LEPR, MC4R, FTO, and POMC. Int J Mol Sci 26(21):10333
Vranceanu M, Filip L, Hegheș S-C, de Lorenzo D, Cozma-Petruț A, Ghitea TC et al (2024) Genes involved in susceptibility to obesity and emotional eating behavior in a Romanian population. Nutrients 16(16):2652
Vuković M, Maksimović M, Ristić S, Kulić M, Mijović B, Milić M et al (2025) Association of adiponectin and resistin gene polymorphisms with undernutrition risk among type 2 diabetes patients in Bosnia and Herzegovina. Iran J Public Health 54(4):810
Wang L, Wang Q, Xiong Y, Shi W, Qi X (2025) Obesity and its comorbidities: current treatment options, emerging biological mechanisms, future perspectives and challenges. Diabetes, Metab Syndr and Obes 18:3427–3445
Wang Y, Meng K, Chen H, Jin X, Yang G, Ma G et al (2025) Multiple problems: a case of Cohen syndrome VPS13B mutation causing bilateral spherical lenses combined with retinitis pigmentosa. BMC Ophthalmol 25(1):345
Wyszyńska J, Łuszczki E, Seeman T, Simonetti GD, Nyankovska O, Wójcik M et al (2025) Hypertension in children with intellectual disabilities: a population not to be overseen. J Hypertens. https://doi.org/10.1097/HJH.0000000000004052
Xiao Q, Wang J, Wang L, Ding H (2024) APOA1/C3/A4/A5 gene cluster at 11q23. 3 and lipid metabolism disorders: from epigenetic mechanisms to clinical practices. Biomedicines 12(6):1224
Yang NV. TOMM40: bridging mitochondrial and lipid metabolism. University of California, Berkeley. 2024.
Yanik T, Durhan ST (2025) Pro-opiomelanocortin and melanocortin receptor 3 and 4 mutations in genetic obesity. Biomolecules 15(2):209
Yarahmadi A, Afkhami H, Javadi A, Kashfi M (2024) Understanding the complex function of gut microbiota: its impact on the pathogenesis of obesity and beyond: a comprehensive review. Diabetol Metab Syndr 16(1):308
Yoo S, Jung S-C, Kwak K, Kim J-S (2024) The role of prebiotics in modulating gut microbiota: implications for human health. Int J Mol Sci 25(9):4834
Yu X, Pu H, Voss M (2024) Overview of anti-inflammatory diets and their promising effects on non-communicable diseases. Br J Nutr 132(7):898–918
Zhang X, Yang J, Li Y, Li Y, Li G (2025) Role of hypothalamus function in metabolic diseases and its potential mechanisms. PeerJ 13:e19532
Zhang W, Koslowski S, Benzaki M, Lee CJM, Zhu Y, Mak MC et al (2025) Deconstructing the GWAS library-next generation GWAS. Physiol Rev. https://doi.org/10.1152/physrev.00025.2024
Zhang T, Park S (2025) Energy intake-dependent genetic associations with obesity risk: BDNF Val66Met polymorphism and interactions with dietary bioactive compounds. Antioxidants 14(2):170
Zhang R, Zhang B, Shen C, Sahakian BJ, Li Z, Zhang W et al (2024) Associations of dietary patterns with brain health from behavioral, neuroimaging, biochemical and genetic analyses. Nature Mental Health 2(5):535–52

Publisher's Note