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Genetic polymorphisms as a predisposition to metabolic syndrome: an integrative review

Polimorfismos genéticos como predisposição à síndrome metabólica: uma revisão integrativa

Polimorfismos genéticos como predisposición al síndrome metabólico: una revisión integrativa

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ABSTRACT
Metabolic syndrome is characterized by a set of metabolic disorders, including abdominal obesity, insulin resistance, dyslipidemia, and hypertension, increasing the risk of cardiovascular diseases and diabetes. Objective: This study aimed to To identify genetic polymorphisms associated with metabolic syndrome and analyze their clinical implications. Methodology: This study was an integrative review conducted an integrative review based on articles published between 2020 and 2024, utilizing the Virtual Health Library and the PubMed database. A total of 19 studies were selected according to eligibility criteria. Results: The findings highlight polymorphisms that influence metabolic risk factors, demonstrating a complex interaction between genetics and lifestyle. Conclusion: Identifying relevant polymorphisms can enhance diagnostic and preventive strategies for metabolic syndrome, particularly in primary care.

Keywords: genetic predisposition, cardiovascular diseases, dyslipidemia, obesity, public health.

RESUMO
A Síndrome Metabólica caracteriza-se por um conjunto de distúrbios metabólicos, incluindo obesidade abdominal, resistência à insulina, dislipidemia e hipertensão, aumentando o risco de doenças cardiovasculares e diabetes. Objetivo: Identificar os polimorfismos genéticos associados à síndrome metabólica a fim de analisar suas implicações clínicas. Metodologia: Revisão integrativa baseada em artigos publicados entre 2020 e 2024, utilizando a Biblioteca Virtual em Saúde e a base de dados PubMed. Foram selecionados 19 estudos conforme critérios de elegibilidade. Resultados: Os achados direcionam

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polimorfismos que influenciam fatores de risco metabólicos, evidenciando uma interação complexa entre a genética e o estilo de vida. Conclusão: A identificação de polimorfismos relevantes pode aprimorar as estratégias diagnósticas e preventivas para a síndrome metabólica, ainda na atenção primária.

Palavras-chave: predisposição genética, doenças cardiovasculares, dislipidemia, obesidade, saúde pública.

RESUMEN
El Síndrome Metabólico se caracteriza por un conjunto de trastornos metabólicos, incluyendo obesidad abdominal, resistencia a la insulina, dislipidemia e hipertensión, lo que aumenta el riesgo de enfermedades cardiovasculares y diabetes. Objetivo: Identificar los polimorfismos genéticos asociados con el síndrome metabólico para analizar sus implicaciones clínicas. Metodología: Revisión integrativa basada en artículos publicados entre 2020 y 2024, utilizando la Biblioteca Virtual en Salud y la base de datos PubMed. Se seleccionaron 19 estudios según criterios de elegibilidad. Resultados: Los hallazgos destacan polimorfismos que influyen en factores de riesgo metabólico, evidenciando una interacción compleja entre la genética y el estilo de vida. Conclusión: La identificación de polimorfismos relevantes puede mejorar las estrategias diagnósticas y preventivas del síndrome metabólico, especialmente en la atención primaria.

Palabras clave: predisposición genética, enfermedades cardiovasculares, dislipidemia, obesidad, salud pública.

1 INTRODUCTION

Metabolic syndrome is a multifactorial condition characterised by interrelated metabolic abnormalities such as abdominal obesity, insulin resistance, dyslipidaemia and hypertension (Martemucci *et. al.,* 2023). These factors increase the risk of cardiovascular disease, diabetes and neurological disorders and are particularly prevalent in industrialised countries.

Its aetiology involves a complex interaction between genetic predisposition (Lin; Sun, 2024), environmental factors, poor diet, sedentary behaviour, stress and ageing (Abdulghani; Al-Fayyadh, 2024). Its progression triggers chronic inflammatory processes that contribute to significant metabolic disturbances such as vascular dysfunction.

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Different organisations, including the American Heart Association (AHA), have adopted different criteria for the syndrome, reflecting its complexity and the evolution of scientific knowledge (Gargari; Chatterjee, 2024).

For this study, the diagnostic reference adopted is based on the criteria of the Adult Treatment Panel III (ATP III) and the International Diabetes Federation (IDF), which consider abdominal obesity, dyslipidaemia, hypertension and hyperglycaemia as core metabolic components (Wilson; Grundy, 2003; Duvnjak; Duvnjak, 2009).

The global rise in metabolic syndrome is associated with increasing rates of obesity, driven by global lifestyle changes, population ageing and demographic shifts (Lameira; Lejeune; Mourad, 2008), which together contribute to one of the greatest public health challenges.

Intra-abdominal fat plays a crucial role in the development of insulin resistance, a condition in which the body's cells have a reduced response to the action of this hormone, which is essential for regulating blood glucose levels (Arantes *et. al.,* 2023a). This impairment of insulin metabolism leads to persistent hyperglycaemia, which promotes progression to type 2 diabetes (Bhat; Santhosh; Sudha, 2023).

Consequently, obesity leads to an increase in systemic blood pressure, contributing to hypertension (Ahmed *et. al.,* 2022). This excess adipose tissue affects blood volume and alters vascular function (Gargari; Chatterjee, 2024).

This includes lipid abnormalities such as elevated triglycerides and low levels of high-density lipoprotein (HDL) cholesterol (Bethell; Brodie, 2023). This lipid abnormality is a significant risk factor for cardiovascular disease (Ahmed *et. al.*, 2022).

Metabolic syndrome has a heterogeneous global distribution, affects approximately 25% of the adult population and is strongly associated with increased cardiovascular mortality (Arantes *et. al.*, 2023). Its increasing prevalence, especially in developing countries, indicates a potential public health crisis and reinforces the need for urgent interventions, including lifestyle changes and more effective therapeutic strategies (Lim; Eckel, 2014).

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In Brazil, it represents a significant public health challenge, with discrepancies in prevalence between different regions, particularly in rural areas. These disparities reflect socioeconomic inequalities and barriers to healthcare access, which affect the prevention and management of the disease (Cremonini *et. al.*, 2023).

Lee *et. al.* (2022) identified a number of genetic polymorphisms associated with metabolic syndrome and categorised them according to the major clinical components of the condition. Polymorphisms in the *COL6A2, FTO, SPARC* and *MTHFR* genes were associated with central obesity, whereas variants in the *APOB, SLC2A2, LPA, ABCG5, ABCG8* and *GCKR* genes were associated with hyperglycaemia. In relation to hypertriglyceridemia, notable polymorphisms were found in the *APOA1, APOC2, APOA4* and *LMF1* genes, while variants in the *ABCA1, CETP, SCARBB* and *LDLR* genes were associated with reduced HDL levels. In addition, the *ADD1* gene was identified as a factor associated with hypertension.

Given the increasing prevalence of metabolic syndrome and its serious health consequences, the development of effective public policies to promote the prevention and control of chronic diseases is essential. Vulnerable populations, such as the elderly and women, require special attention due to their higher susceptibility to metabolic complications (Silva; Nascimento; Braz, 2024; Zanre *et. al.*, 2022).

In this context, the present study aims to identify genetic polymorphisms relevant to the metabolic syndrome, taking into account not only their population frequency, but more importantly, their pathophysiological impact. Understanding the relationship between these variants and the development of the syndrome may contribute to a better understanding of the biological mechanisms involved, allowing advances in diagnosis, clinical management and prevention strategies in primary health care.

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2 METHODOLOGY

The present integrative review adopted the PICO strategy in order to structure the research question and guide the search for evidence (Santos; Pimenta; Nobre, 2007). In this model, **P (Patient)** is used to denote individuals at high risk for or already diagnosed with Metabolic Syndrome; **I (Intervention)** corresponds to the analysis of genetic polymorphisms associated with the condition; and **Co (Context)** encompasses studies investigating the relationship between these genetic variants and Metabolic Syndrome. The study's objective is to provide an answer to the following overarching question: The present study sets out to investigate which genetic polymorphisms are associated with metabolic syndrome in individuals at high risk or with a confirmed diagnosis.

The selection of studies was conducted through the Virtual Health Library (VHL) and the PubMed database, which is maintained by the National Center for Biotechnology Information (NCBI). The search was restricted to English and Portuguese languages and employed a combinatorial strategy using specific descriptors with Boolean operators to refine and narrow the results. The search terms employed were: A search was conducted using the following search terms: *'Genetic polymorphisms'* OR *'Genetic variations'* OR *'Polymorphisms'* OR *'Gene mutations'*. These terms were combined with *'Metabolic syndrome'* OR *'Metabolic disorders'* OR *'Metabolic risk factors'*. The search was then restricted to *'Genetic predisposition'* OR *'Genetic susceptibility'* OR *'Genetic risk factors'*. This combination of search terms was deemed to ensure greater accuracy in retrieving the evidence.

The inclusion criteria defined for the selection of studies were: **(i)** publications in journals/periodicals; **(ii)** full-text articles available online with free access; **(iii)** articles published in portuguese and english; **(iv)** publications addressing the main topic (genetic polymorphisms and metabolic syndrome); and **(v)** studies published between january 2020 and december 2024.

The following articles were excluded from the review: literature review articles; duplicate publications; laboratory studies involving animal models; and

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grey literature, such as clinical case reports, book chapters, books and manuals, due to the lack of methodological standardisation.

The organisation and analysis of the data was facilitated by the utilisation of complimentary software tools, namely Google Sheets and the Rayyan platform. The latter played a pivotal role in the management of the study selection process, enabling the categorisation of articles as *"included," "excluded,"* or *"maybe"*. This approach enhanced screening efficiency, systematic organisation, and standardisation of data analysis.

3 RESULTS

The selection of articles for the construction of this integrative review included the following steps, **(i) identification:** this stage involved selecting articles from the databases, totaling 97 identified articles (39 from PubMed, 58 from VHL). Of these, 28 articles from VHL were excluded based on the eligibility criteria; **(ii) screening:** of the remaining 69 articles, 23 were selected for abstract review. At this stage, 46 articles were excluded after reading the titles. No articles were excluded after the abstract review; **(iii) eligibility:** after full-text reading of the remaining 23 articles, 4 were excluded for not addressing the guiding research question, resulting in 19 articles included in the review, as shown in Figure 1.

The 19 selected articles were published in various scientific journals, including Lifestyle Genomics, Archives of Physiology and Biochemistry, PLOS ONE, Cellular and Molecular Biology, Journal of the Renin-Angiotensin-Aldosterone System, The Journal of Gene Medicine, European Journal of Clinical Investigation, Medicine, Brazilian Archives of Endocrinology and Metabolism, Genes, Prostaglandins, Leukotrienes and Essential Fatty Acids, British Journal of Nutrition, Nutrients, Diabetology & Metabolic Syndrome, BMC Endocrine Disorders, Journal of Physiology and Pharmacology, Scientific Reports, Journal of Clinical Laboratory Analysis, and Immunology and Inflammation Diseases.

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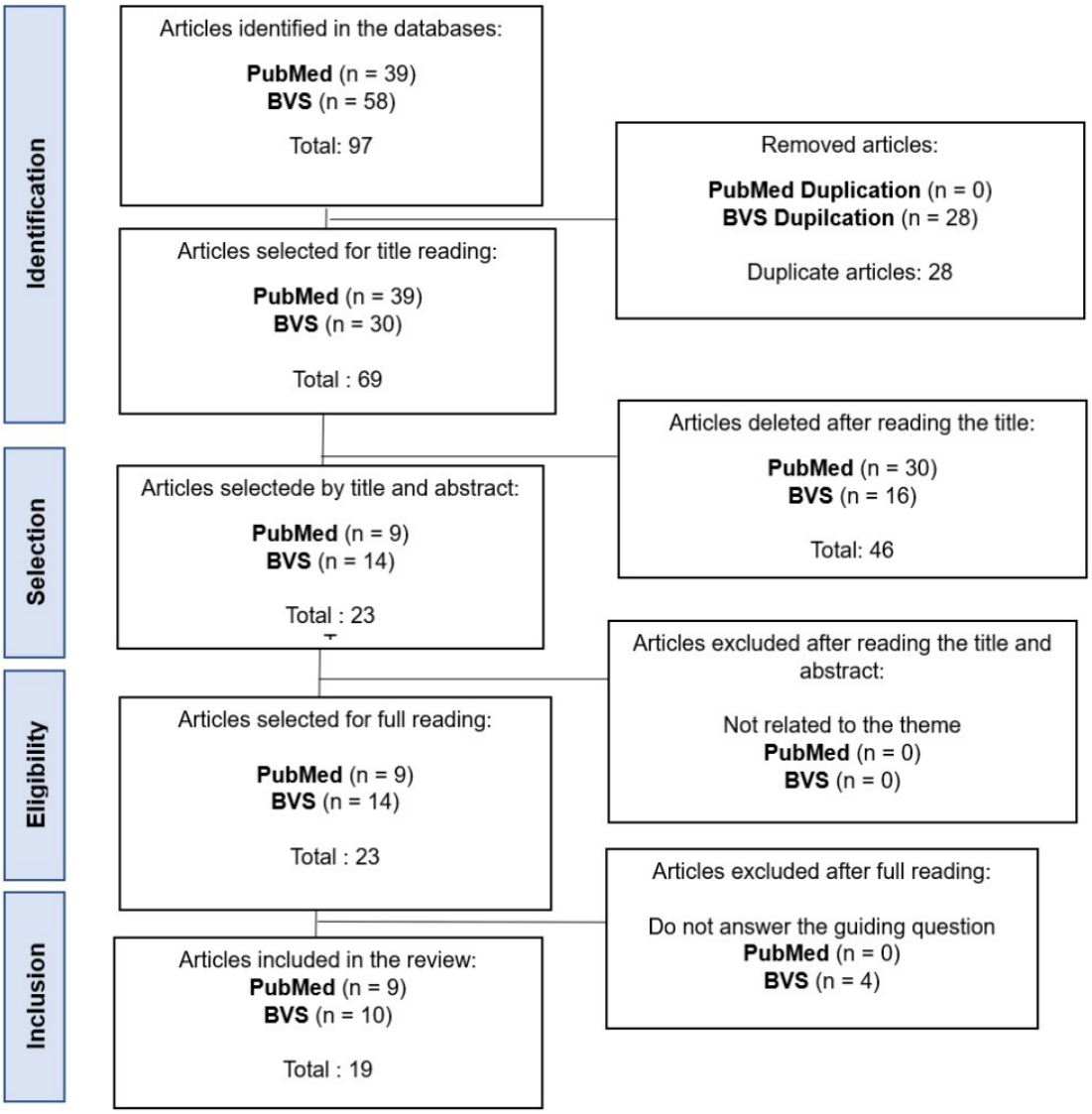
Figure 1: Flowchart of article selection



Source: Costa *et. al.,* 2025.

Table 1 presents a summary of the studies selected for the integrative review, compiled after applying the eligibility criteria. The essential information, including the authors, title, and the overall objective of each study, has been organised in order to provide a comprehensive and structured overview of the selected works. Moreover, the table incorporates the extant evidence that underpins the analysis of the relationship between genetic polymorphisms and metabolic syndrome.

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Table 1: Studies selected after applying the eligibility criteria.

AUTHORS	TITLE	OBJECTIVE	METHOD
Abbasalized Farhangi *et al*. (2020)	Interaction between Vascular Endothelial Growth Factor-A (rs2010963) Gene Polymorphisms and Dietary Diversity Score on Cardiovascular Risk Factors in Patients with Metabolic Syndrom	To Evaluate the interaction between Dietary Diversity Score (DDS) and the rs2010963 polymorphism of the VEGFA gene in the modification of metabolic risk factors in patients with metabolic syndrome.	A cross-sectional study was conducted on 254 patients diagnosed with metabolic syndrome. Measurements of blood pressure, anthropometric parameters, dietary intake and calculation of DDS were performed. Biochemical variables were analyzed by ELISA and colorimetric methods. *VEGFA* gene polymorphisms were determined by *PCR-RFLP.*
Aghajani *et.al. (*2020)	Genetic polymorphisms *−137 (G>C)* (rs187238) and *−607 (C>A)* (rs1946518) and serum level of interleukin 18 in Fars ethnic groups with metabolic syndrome in Northern Iran	To investigate the impact of genetic polymorphisms *−137 (G>C)* and *−607(C>A)* on interleukin 18 levels.	Study conducted at the Center for Research in Metabolic Disorders, with blood samples collected after a 12-hour fast. Interleukin 18 levels were measured by ELISA using commercial kits.
Aly *et al.* (2020)	Gene polymorphisms of Patatin-like phospholipase domain containing 3 (*PNPLA3*), adiponectin, leptin in diabetic obese patients	To evaluate the possible role of irisin, adiponectin, leptin and polymorphisms in the *PNPLA3* gene as predictive markers of diabetes associated with obesity.	Included adult obese diabetic patients, diagnosed by blood glucose levels and BMI. Data collected by blood samples and genetic analyses.
Kermanshahi *et al.* (2020)	Association of a genetic variant in the *AKT* gene locus and cardiovascular risk factors	To examine the association of the genetic polymorphism *AKT*-rs1130233 located on chromosome 14 with cardiovascular risk factors.	Cross-sectional study with 721 individuals from the MASHAD (Mashhad Stroke and Heart Atherosclerotic Disorders) cohort. Data collected included anthropometric, biochemical, demographic information and genotyping by TaqMan real-time PCR.
Khamlaoui *et al.* (2020)	Association of angiotensin-converting enzyme insertion/deletion *(ACE I/D)* and angiotensinogen *(AGT M235T)*	To determine the association between genetics in the *ACE I/D* and *AGT M235T* polymorphisms with overweight, obesity	Case-control study, matched by age and sex, with overweight/obese individuals and normal controls. Collection of blood samples for genetic analysis.

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	polymorphisms with the risk of obesity in a populationTunisian adults with obesity	and body mass index (BMI).	
Narayanasamy *et al. (*2020)	Association of metabolic syndrome and patatin-like phospholipase 3 gene variant (rs738409) with non-alcoholic fatty liver disease in South Indian population	To investigate the relationship between metabolic syndrome and the PNPLA3 genetic variant (rs738409) in patients with nonalcoholic fatty liver disease (NAFLD).	The study included classification of patients based on MS criteria, diagnosis of NAFLD by abdominal ultrasonography, and genetic analysis using PCR and agarose gel electrophoresis.
Pourgholi *et al.* (2020)	The association between *CYBA* gene *C242T* variant and risk of metabolic syndrome	To investigate the association between the *C242T* variant of the *CYBA* gene and the risk of developing MS.	The study used diagnostic criteria for MS based on NCEP ATP-III, with modification for the Iranian population, and included DNA extraction and genetic analysis.
Schneider – Matyka *et al.* (2020)	The Relationship between the *IFNG* (rs2430561) Polymorphism and Metabolic Syndrome in Perimenopausal Women	To investigate the association between the *IFNG* polymorphism (rs2430561) and metabolic syndrome in perimenopausal women.	The study used laboratory and anthropometric measurements to classify participants into subgroups with and without metabolic syndrome, followed by statistical analyses to assess the association between genetic polymorphism and metabolic syndrome.
Faramarzi *et al.* (2021)	*DDAH2* promoter may act as a protective factor against metabolic syndrome in the Azar-Cohort population	To investigate the association between the -499C/G polymorphism of the *DDAH2* gene and the reduced risk of metabolic syndrome.	Case-control study with genotype analysis and evaluation of metabolic syndrome components, including anthropometric measurements and laboratory tests.
Nowak *et al.* (2021)	Adiponectin Gene Polymorphism (rs17300539) Has No Influence on the Occurrence of Metabolic Syndrome in Women with Polycystic Ovary Syndrome	To investigate the influence of the rs17300539 polymorphism of the adiponectin gene on the occurrence of Metabolic Syndrome in women with polycystic ovary syndrome.	The study included gynecological examinations, anthropometric measurements, laboratory tests for biochemical parameters, and genetic testing to identify adiponectin gene polymorphism.
Validity *et al*. (2021)	The association between a Fatty Acid	To evaluate the association	Case-control study with 2737 individuals (2203 with

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	Binding Protein 1 *(FABP1)* gene polymorphism and serum lipid abnormalities in the MASHAD cohort study.	between *FABP1* gene polymorphism and dyslipidemia.	dyslipidemia and 534 controls). Dyslipidemia was defined based on criteria of total cholesterol, triglycerides, LDL-C and HDL-C. The lipid profile was determined with a biochemical analyzer and genotyping performed by PCR.
Abaj F.; Mirzaei K. (2022)	Caveolin-1 genetic polymorphism interacts with PUFA to modulate metabolic syndrome risk	To investigate the interaction between the rs3807992 polymorphism of the *CAV-1* gene, the intake of polyunsaturated (PUFA) and saturated (SFA) fatty acids, and the risk of metabolic syndrome in obese women.	Cross-sectional study that used the food frequency questionnaire (FFQ) to assess dietary intake and the *PCR-RFLP* technique for genotyping *CAV-1* polymorphisms.
Araujo *et al.*(2022)	Association of *CYP2R1* and *VDR* Polymorphisms with Metabolic Syndrome Components in Non-Diabetic Brazilian Adolescents	To investigate the associations between *CYP2R1* and *VDR* genes and metabolic syndrome.	Cross-sectional study with 174 adolescents classified as overweight/obese, using allelic discrimination to identify variants of the *CYP2R1* and *VDR* genes.
Lee *et al*. (2022)	Identification of genetic variants related to metabolic syndrome by next-generation sequencing	To identify genetic variants associated with clinical features of metabolic syndrome.	The research used next-generation sequencing (NGS) to identify genetic variants in individuals with metabolic syndrome.
Khodarahmi *et al*. (2022)	Dietary glycemic index and glycemic load mediate the effect of *CARTPT* rs2239670 gene polymorphism on metabolic syndrome and metabolic risk factors among adults with obesity	To determine the associations between genetic, sociodemographic and dietary factors with metabolic risk factors and metabolic syndrome in obese adults.	Cross-sectional study with 288 healthy adults with obesity, recruited by convenience sampling. Participants were assessed for inclusion and exclusion criteria and data on genetic, socioeconomic factors and dietary habits were collected.
Sajed; Mir; Marjani (2022)	Genetic Polymorphism 415 (T>C) (rs9658635) and + 87 (C > T) (rs7610) and Serum Level of Chromogranin A in Subjects with Metabolic Syndrome in the Fars Ethnic Group.	To investigate the association between genetic polymorphism, chromogranin A (CgA) levels and metabolic syndrome.	The study included 246 individuals, divided into groups with and without Metabolic Syndrome. Blood samples were collected for genetic analysis and evaluation of biochemical parameters. The presence of metabolic syndrome was

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			determined according to the NCEP ATP III criteria.
Bread *et al.* (2024)	Genetic variations in *ACE2* gene associated with metabolic syndrome in southern China	To investigate the relationship between variations in the *ACE2* gene and the risk of metabolic syndrome between genders.	The study used genotyping of SNPs of the *ACE2* gene in a patient population and statistical analyses to determine associations with components of the metabolic syndrome.
Paniri *et al*. (2024)	Genetic variations in *IKZF3, LET7-a2*, and *CDKN2B-AS1*: Exploring associations with metabolic syndrome susceptibility and clinical manifestations	To evaluate the impact of *IKZF3, LET7-a2* and *CDKN2B-AS1* genetic variations on susceptibility to metabolic syndrome.	A genotype-phenotype assessment was performed for the SNPs *IKZF3* (rs907091), microRNA-let-7a-2 (rs1143770) and 333045).
Tang; Yin; Lin (2024)	Association of rs2241766 and rs1501299 polymorphisms in the adiponectin gene with metabolic syndrome	To investigate the association of rs2241766 and rs1501299 polymorphisms with metabolic syndrome.	The study included patients with metabolic syndrome and healthy controls. Blood samples were collected for genetic analysis and biochemical parameters. Diagnosis followed the 2016 guidelines for management of dyslipidemia.

Source: Macedo *et. al.,* 2025.

Table 2 provides a detailed description of the genes involved in the relationship between genetic polymorphisms and the clinical components of metabolic syndrome. This includes the population analysed and the respective references. This structure provides a consistent foundation for understanding and interpreting the scientific evidence.

Table 2: Parameters analyzed in the selected studies.

GENE	POLYMORPHISM	CLINICAL COMPONENT	POPULATION	REFERENCE
AKT	rs1130233	Cardiovascular risk factors and metabolic syndrome	Individuals recruited from the MASHAD cohort study (Iran)	Kermanshahi *et al*. (2020)
ACE	R/D	Obesity risk, BMI	Tunisian adults with obesity	
AGT	M235T			

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PNPLA3	rs738409	Susceptibility to type 2 diabetes and insulin resistance	Egyptian diabetic obese	Aly *et al*. (2020)
ADIPOQ	rs266729	Adiponectin levels and diabetes risk		
LEP	rs2167270	Leptin levels and diabetes risk		
VEGFA	+405 C/G (rs2010963)	VEGF production, risk of metabolic syndrome	Iranian	Abbasalized Farhangi *et al.*(2020)
IFNG	rs2430561	Levels of inflammatory cytokines IL-6	Perimenopausal women	Schneider-Matyka *et al.*(2020)
IL-18	−137 (G > C)	IL-18 levels and metabolic syndrome	Fars ethnic groups	Aghajani *et al*. (2020)
	−607 (C > A)			
CYBA	C242T	Metabolic Syndrome	Iranian Men	Pourgholi *et al*. (2020)
PNPLA3	rs738409	Nonalcoholic Fatty Liver Disease (NAFLD) and Metabolic Syndrome	South Indian adults with NAFLD	Narayanasamy *et al.* (2020)
Adiponectin	rs17300539	Metabolic Syndrome	Women with polycystic ovary syndrome	Nowak *et al*. (2021)
FABP1	rs2241883	Dyslipidemia	Iranian	Valizadeh *et al.* (2021)
DDAH2	rs805304 (- 1151 C/A)	Diabetes and hypertension	From the Azar cohort	Faramarzi *et al.*(2021)
	-449 G/C (rs805305)	Prevalence of hypertension Risk of Metabolic Syndrome		
	rs2272592	Type 2 diabetes		
CAV-1	rs3807992	Abdominal obesity and hypertension	General population	Abaj *et al*. (2021)
LDLR	rs200990725 (c.769C>T, p.(Arg257Trp))	Metabolic Syndrome	EAS (East Asian)	Lee *et al.* (2022)
CHGA	+87 C>T	Chromogranin A (CgA) levels	Fars ethnic group	Sajed *et al*. (2022)
	-415 T>C	Blood glucose levels (FBS)		
IL18	-137 G>C	Interleukin 18 levels		
	-607 C>A			
CARTPT	rs2239670	Obesity and Metabolic Syndrome	Iranian	Khodarahmi *et al.*(2022)
CYP2R1	rs12794714	Metabolic Syndrome		Araujo *et al*. (2022)

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	rs10741657	Hyperglycemia	Brazilian non-diabetic adolescents	
VDR	rs7975232	Hypertension		
IKZF3	rs907091	Increased triglycerides, cholesterol and HOMA index	From Mazandaran	Paniri *et al.*(2024)
microRNA-let-7a-2	rs1143770	Elevated HbA1c levels and BMI		
lncRNA-CDKN2B-AS1	rs1333045	Increased HDL levels and decreased risk of metabolic syndrome		
ADIPOQ	rs2241766	Adiponectin levels and risk of metabolic syndrome	Patients with metabolic syndrome and healthy controls	Tang; Yin; Lin (2024)
	rs1501299			
ACE2	rs2074192	Diabetes	South China	Bread *et al.*(2024)
	rs2106809	Dyslipidemia		

Source: Macedo *et. al.,* 2025.

The genetic polymorphisms under consideration have been demonstrated to be implicated in a variety of metabolic, inflammatory, and cardiovascular processes. This observation underscores the intricate nature of Metabolic Syndrome and its association with particular genetic factors across diverse populations. The analysis of genetic profiles facilitates the identification of polymorphisms that influence susceptibility to the development of the syndrome, thereby contributing to a more comprehensive understanding of the health-disease continuum. Furthermore, this approach is directly conducive to improvements in diagnosis, the implementation of preventive strategies, and the clinical management of Metabolic Syndrome (Kermanshahi *et. al.*, 2020).

4 DISCUSSIONS

The analysis of the studies included in this review reveals the complexity of the relationship between genetic polymorphisms and metabolic syndrome, as well as the diversity of approaches used to investigate this association.

Khamlaoui *et. al.* (2020) examined the relationship between *ACE I/D* and *AGT M235T* gene polymorphisms and obesity risk in a Tunisian population, while

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Aly *et. al.* (2020) analysed variants in the *PNPLA3*, adiponectin, and leptin genes in obese diabetic patients. Despite the disparities in the populations studied, both studies demonstrate that genetic variations influence the predisposition to obesity and metabolic syndrome, and are also impacted by extrinsic factors such as dietary habits and socioeconomic conditions.

In the context of lipid disorders, Valizadeh *et. al.* (2021) examined the association of the *FABP1* gene with dyslipidaemia, while Araújo *et. al.* (2022) explored the *CYP2R1* and *VDR* genes and their relationship with metabolic syndrome. These findings serve to reinforce the influence of genetic polymorphisms on lipid metabolism, thereby contributing to a more complete understanding of the mechanisms involved in the disease. Additionally, Aghajani *et. al.* (2020) investigated the *IL-137 (G>C)* and *-607 (C>A)* polymorphisms of the interleukin-18 gene, highlighting its role in the regulation of inflammatory markers, which are essential to the development of metabolic syndrome.

The genetic influence on metabolic syndrome is also reflected in the presence of comorbidities. Narayanasamy *et. al.* (2020) and Paderina *et. al.* (2021) analysed individuals with pre-existing chronic conditions, including non-alcoholic fatty liver disease (NAFLD) and schizophrenia, emphasising the coexistence of these conditions with metabolic syndrome (see Table 1). This intersection suggests a shared genetic basis between the syndrome and other metabolic and psychiatric disorders.

In the field of gene research, Tang, Yin, and Lin (2024) investigated polymorphisms in the adiponectin gene, while Paniri *et. al.* (2024) analysed variations in the *IKZF3, LET7-a2*, and *CDKN2B-AS1* genes. Despite the heterogeneity in the genes investigated, these studies collectively substantiate the significance of genetic variants in regulating lipid and glucose metabolism. Specifically, Paniri *et. al*. (2024) highlighted that the *TT* genotype for *IKZF3* rs907091 is associated with elevated levels of triglycerides and cholesterol, as well as an increased HOMA index, indicating insulin resistance. Furthermore, the *CDKN2B* rs1333045 polymorphism has been associated with elevated HDL levels, indicating a possible protective effect against cardiovascular diseases.

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The study by Pan *et al.* (2024) focused exclusively on the *ACE2* gene and its relationship with metabolic syndrome in a population from southern China, highlighting its influence on obesity, hypertension, and dyslipidaemia. In contrast, Tang, Yin, and Lin (2024) and Paniri *et al.* (2024) investigated multiple genes and their interactions with different clinical manifestations, thus reinforcing the complexity of the genetic basis of metabolic syndrome.

In the domain of cardiovascular risk factors, Kermanshahi *et. al*. (2020), Abbassalizad Farangi *et. al.* (2020), and Abaj e Mirzaei (2022) analysed genetic variants associated with this group of diseases. Kermanshahi *et. al.* (2020) studied the *AKT* gene in an Iranian population, while Abbassalizad Farangi *et. al.* (2020) investigated the *VEGFA* gene and its interaction with diet in patients with metabolic syndrome. These findings emphasise the interaction between genetics and environmental factors in the development of the syndrome and its associated cardiovascular diseases.

Pourgholi *et. al.* (2020) identified the *C242T* variant of the *CYBA* gene as a risk factor for metabolic syndrome, while Faramarzi *et. al.* (2021) suggested a protective effect of the *DDAH2* gene promoter. Schneider-Matyka *et. al.* (2020) and Nowak *et. al.* (2021) analysed polymorphisms in women with different hormonal conditions, suggesting that certain genetic variants may influence Metabolic Syndrome in distinct ways, such as the *T/T* and *A/T* genotypes of the *IFNG* gene, which may affect *IL-6* levels and metabolism.

Notwithstanding recent advances in the field, the relationship between genetic polymorphisms and metabolic syndrome remains to be fully elucidated, with significant challenges yet to be overcome. A significant number of studies have been found to involve small sample sizes and limited scope, which hinders the generalisation of findings. An exemplar of this can be found in the study by Zdrojowy-Wełna *et al.* (2020), which analysed the rs9939609 polymorphism of the *FTO* gene and its correlation with body mass index (BMI) and blood glucose levels, without identifying significant associations. These discrepancies underscore the necessity for more extensive and varied research endeavours to

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enhance our comprehension of the genetic elements that underpin metabolic syndrome and their clinical ramifications.

5 FINAL CONSIDERATIONS

The analyses presented in this study demonstrate that several polymorphic genetic variants may be associated with an increased risk of developing metabolic syndrome or the pathological condition itself. The relevance of these genetic markers in the predisposition to metabolic disorders is evidenced by the diversity of approaches adopted, encompassing different populations and gene targets.

Furthermore, the investigation of multiple genes and their clinical influences reinforces the complexity and progression of metabolic syndrome, emphasising the importance of an integrated perspective on its genetic determinants.

The findings emphasise the necessity to incorporate genetic studies into preventive and diagnostic strategies, thus contributing to the development of more effective public health policies.

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