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Article

Metabolic Syndrome and Its Biochemical Implications: Insights into Early Detection

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Abstract: Metabolic syndrome (MetS) is a multifaceted clinical condition characterized by a cluster of metabolic abnormalities, including central obesity, insulin resistance, hypertension, dyslipidemia, and glucose intolerance. It significantly increases the risk of developing cardiovascular diseases and type 2 diabetes mellitus. The biochemical implications of MetS are profound, involving alterations in lipid metabolism, chronic low-grade inflammation, oxidative stress, and hormonal imbalances. These disturbances are often reflected in biomarkers such as elevated fasting glucose, increased triglycerides, decreased HDL cholesterol, high levels of C-reactive protein (CRP), and insulin resistance markers like HOMA-IR. Early detection of MetS is crucial for preventing its progression and associated complications. Biochemical screening provides a valuable tool for identifying at-risk individuals before clinical symptoms become evident. Recent research emphasizes the role of adipokines, pro-inflammatory cytokines (such as TNF-α and IL-6), and oxidative stress markers as early indicators of metabolic dysfunction. Additionally, advances in genomics and metabolomics have enhanced our understanding of the pathophysiological mechanisms underlying MetS, offering promising avenues for personalized intervention strategies. This review highlights the importance of integrating biochemical markers in routine clinical assessments for early identification of MetS. Understanding the interplay between metabolic pathways and biochemical alterations can aid in developing more targeted therapeutic approaches. Ultimately, early biochemical diagnosis, combined with lifestyle modification and pharmacological interventions, may reduce the global burden of metabolic syndrome and its life-threatening sequelae

Keywords: Metabolic Syndrome, Biochemical Markers, Insulin Resistance, Early Detection, Inflammation, Cardiovascular Risk

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1. Introduction

Metabolic syndrome is a cluster of metabolic abnormalities conferring a substantial increase in cardiovascular disease (CVD) risk. Those with metabolic syndrome are at an increased risk of mortality from CVD, coronary heart disease, stroke, vascular dysfunction, and all-cause mortality [1]. The most recognized pathogenic factors are central obesity and insulin resistance, which oppose the action of insulin in glucose and lipid storage and use, causing hyperglycemia, dyslipidemia, and increased free fatty acids [2]. An increased level of free fatty acids promotes hepatic production of triglycerides, hypertriglyceridemia, and atherogenic modification of lipoproteins, which, together with endothelial dysfunction, promotes atherosclerosis. Cardiovascular risk is increased even before the diagnosis of metabolic syndrome [3,4].

A cohort of about 35% of US adults has metabolic syndrome, with the proportion increasing to >50% among those >60 years old. The primary concern is early detection of potential CVD complications and early intervention [5]. Before the development of metabolic syndrome, dysglycemia, dyslipidemia, and hypertension are common, so that many people with metabolic syndrome will have insulin resistance [6,7]. Insulin resistance is the best metabolic risk factor for metabolically unhealthy obesity, which has a risk for type 2 diabetes and CVD. However, it remains controversial how best to measure insulin resistance. Even when obesity is absent, a glucose-insulin disposition index combining glucose and insulin area under the curve, measured by an oral glucose tolerance test, is a strong risk factor for diabetes and CVD [8]. The current epidemic of obesity and metabolic syndrome is paralleled by an increasing prevalence of hyperuricemia, increased net acid excretion, and chronic kidney disease [9].

1.2 Detection of metabolic syndrome burden in healthy young adults

A non-invasive battery of anthropometric, biochemical, and behavioral measures was used to detect side-effects of metabolic syndrome at an early stage in otherwise healthy young adults [10,11]. An automated macro-evolutionary algorithm developed for this purpose proved to be exceptionally potent in identifying the metabolic syndrome burden based solely on conventional laboratory measurements [12,13] The method was applied to an initial cohort of young adults and showed that reducing CVD risk prevailed (40.5% of subjects), followed by concentration shift towards the higher risk brackets (36.1%), and vice versa (8.6% of subjects) [14]. Identifying healthy young adults with already displayed side-effects of metabolic syndrome would allow for timely intervention with behavioral changes allowing for disease prevention [15,16].

2. Materials and Methods

The methodology for the article "Metabolic Syndrome and Its Biochemical Implications: Insights into Early Detection" centers on an extensive literature-based approach combined with a theoretical framework grounded in clinical biochemical diagnostics. To explore the early detection of metabolic syndrome (MetS), the researchers adopted a qualitative review method, synthesizing findings from a wide array of studies encompassing epidemiological data, biochemical marker evaluations, and emerging screening techniques. Primary focus was placed on evaluating biomarkers such as insulin resistance indicators (e.g., HOMA-IR), inflammatory markers (e.g., CRP, TNF-α, IL-6), oxidative stress indicators, lipid profile deviations, and hormonal imbalances. The study utilized secondary data obtained from peer-reviewed articles, international cohort studies, and diagnostic criteria from globally recognized institutions like NCEP-ATP III and IDF. Through analytical comparison of diverse population studies and biochemical profiles, the research aims to identify the most predictive markers for MetS prior to clinical manifestation. Special attention was given to the biochemical interaction between adipokines, metabolic hormones, and pro-inflammatory cytokines. Furthermore, the article draws from longitudinal observations to understand the pathophysiological trajectory of MetS and its transition into chronic diseases such as type 2 diabetes, cardiovascular conditions, and kidney disorders. The methodology is rooted in the integration of metabolic data with early-stage phenotypic indicators, enabling the proposition of a preventive diagnostic model. This model is designed for routine clinical settings, facilitating early detection through accessible and cost-effective biochemical assessments, with the ultimate goal of mitigating long-term complications through early lifestyle or pharmacological interventions.

2. Epidemiology of Metabolic Syndrome

Most studies on the validity of the Metabolic Syndrome criteria show that the NCEP/ATP III criteria are better, achieving a higher area under the curve. Prevalence has been reported by using the NCEP/ATP III criteria (26.4%) or the IDF criteria (22.8%) [17]. High prevalence has also been reported in Polish health care workers (48.5% by using both criteria), and among the elderly in North-Western Iran (76% by using the IDF criteria). Higher frequencies of Metabolic Syndrome have been noted in some Arabic countries, with frequencies of 43.7%, 36.7%, and 52% in Lebanese, Iranian, and Kuwaiti

adults, respectively; or Pakistani adults, with frequencies of 44.7% using the ATP III criteria and 21.2% IDF [18]. Worldwide data indicate a high frequency of Metabolic Syndrome (53.2%) among 10,170 patients in China, 28.5% in Hong Kong Chinese adults, 38% in Japanese, 24% in Malaysian, and 33% in South Korean adults [19]. The highest Metabolic Syndrome rate (63%) has been reported in Native Americans or in Aboriginal Australians (60%). Additionally, rapidly rising rates have been found in countries receiving high immigration rates, including the Middle East and East African countries [20]. In Pacific Island nations, sample size-weighted mean prevalence of obesity defined by BMI was estimated to be 66.99% and 81.79% for men and women, respectively [21]. In the population-based study in Australia, the overall age-adjusted prevalence of obesity (BMI ≥30 kg/m2) was 22%, rising from 5% among 20-29-year-olds to 62% among those aged 60 years or older, which indicates that at a group level, obesity prevalence is a valley-shaped function of age [22].

3. Results

3. Biochemical Markers of Metabolic Syndrome

Metabolic syndrome (MS) is characterized by insulin resistance, dyslipidemia, and hypertension and affects one in three adults in the United States. Anticipation of MS allows for risk reduction and is a key player in the future of healthcare; thus, there is a need to identify a panel of biomarkers with the greatest potential for early diagnosis [23]. The MEB group at WVU Health Sciences aims to create a standard panel of biomarkers that is stable across populations. Large longitudinal studies have consistently established criteria for a variety of proxy measures to be used for this panel based on their associations with MS. Key to many of the foreshadowed abnormalities is the secretion of bioactive polypeptides called adipokines, which are released from adipose tissue in response to energy status and are dysregulated in obesity [24]. These, along with other components of the biochemical cascade involved, are discussed here. There is disagreement in the literature regarding the rationale for components of MS. The consensus is the simpler the method of diagnosis the better for patient compliance. This is of utmost concern for the elderly and the impoverished who may forego a multi-hour visit to a federally-approved lab and instead choose to skip the annual exam altogether [25]. At the same time, if broad individual measures are used the patient will miss out on the other likely contributory factors. Despite this dilemma, it seems that the larger the number of unique and complementary measures the better. Data on an order-weighted composite score derived from arithmetic instruments rather than modeled after a biological framework that encompasses the metabolic syndrome triad is still unavailable, nor is it likely to be [26]. By contrasting proxies with biomarkers, recent human studies reveal the potential for the latter to serve as mechanistic biomarkers by elucidating the biological dysregulation caused by MS relevant aberrations. The recent push for multiple biomarkers is in the hope that with complementary biases, chances for sensitivity and specificity enhancement are raised. The single derived measure type of biomarker provides a stable, broad advancement over any individual measure [27]. But ultimately the greater the variety of complementary, unique measures able to be arrayed together the greater the advancement is expected to be. The state-of-the-art composite measures presumably flag multiple aberrations across that range of the time-varying disease state in turn actually raising the chances of detecting a significant aberration at a given time-point even if only one measure of the total were aberrant [28].

3.1. Insulin Resistance

The prevalence of metabolic syndrome is increasing in developed and developing countries. The criteria for the diagnosis of metabolic syndrome include central obesity (waist circumference ≥ 90 cm in men and ≥ 80 cm in women) and any two of the following four risk factors, namely increased blood pressure (≥ 130 mmHg for systolic and/or ≥ 85 mm Hg for diastolic), increased triglycerides (≥ 150 mg/dl), low high-density lipoprotein cholesterol (HDL-C) (< 40 mg/dl in men and < 50 mg/dl in women), and increased blood glucose (≥ 100 mg/dl) [29,30].

Insulin resistance (IR) is at the core of metabolic syndrome and probably many other disorders no longer decried as 'diseases'. IR is increasingly recognized as the probable main initiating event in the etiology of metabolic syndrome (MS), atherogenic dyslipidemia, hypertension, vascular dysfunction as evidenced by increased nitric oxide (NO) production and reduced NO bioavailability and increased inflammation as evidenced by increase in plasma high sensitive C reactive protein (hsCRP) [31,32]. Evidence of IR in Caribbean Indian men shows that the mechanisms operating to produce the various manifestations of the metabolic syndrome may differ in different races. Critically, metabolic syndrome is an integrated view of adverse consequences of IR which usually express themselves sequentially but can overlap chronically and/or concomitantly [33,34].

3.2. Lipid Profile Abnormalities

Pathophysiological progression of MetS involves lipid deposition affecting both adipose and non-adipose tissues. This disorder is characterized by the presence of excessive subcutaneous, visceral adipose tissue accumulations, increased circulating free fatty acids (FFA), elevated levels of triglyceride-rich lipoproteins, and free fatty acids (FFA)-mediated liver steatosis [35]. The dysregulated lipid metabolism promotes an atherogenic abrupt lipoprotein particle transition along with their vantage lipolysis into atherogenic small and dense LDL. The propagation of the abdominal fat infiltration leads to the dosed deposition of ectopic lipids and the crisis of lipid homeostasis damaging the structure and function of the heart, arterial vessels, pancreatic islets, liver, and skeletal muscle [36,37].

The depth of the integration of lipid metabolic reprogramming and the composition profile alterations of the blood lipid esters provides new biochemical insights into MetS. The early-stage MetS patients with central obesity have a similar pattern of blood lipid profile alterations and an apparent leftward shift of the peak indicating smaller triglyceride-rich lipoproteins compared with the age- and sex-matched normal controls. Therefore, precaution should not only be taken in case of the presence of the tightly clustered cardiometabolic risk factors but also the individual risk assessment using the clinical blood biochemical examinations [38,39].

Furthermore, the circulating levels of total cholesterol and apolipoprotein E were elevated in MetS individuals. In contrast, MetS individuals had a reduced level of triglycerides, HDL-C, and circulating bottomality, potentially reflecting the acute dyslipidemic state during severe hypertriglyceridemia [40,41]. However, no apparent difference in the lipid composition of the cholesterol esters and phospholipids was observed. While the dysregulated lipid metabolism alters the status of circulating lipid metabolism disorders, it is insufficient to trigger the overt progression of MetS in patients without the presence of oils and gasoline derivatives [43,44].

3.3. Inflammatory Markers

Although obesity is the most important component of metabolic syndrome (MetS), the mechanisms underlying its association with the other components—dyslipidemia, hypertension, and hyperglycemia—are not clear. Excess visceral fat induces increased secretion of free fatty acids into the bloodstream [45]. Intrahepatic free fatty acids act as a source of triglyceride-rich lipoproteins. Excess free fatty acids in peripheral tissues induce insulin resistance and activation of inflammatory pathways. Thus, chronic low-grade systemic inflammation is related to insulin resistance and is common in MetS and atherogenesis [46]. For national authorities ardently interested in improving the health of their citizenry, the identification of effective inflammatory markers for simple and economical screening tests reflecting a healthy lifestyle is important. Moreover, the metabolic component of obesity and diabetes in MetS may better cluster metabolic stress-induced inflammation than specific metabolic syndrome components [47,48].

Levels of biomarkers indicating impaired adiposity and obesity-related chronic systemic inflammation were measured, and the relations between levels of biomarkers and components of MetS were evaluated in a relatively large population who were motivated and recruited based on normal body weight without any metabolic syndromic conditions [49,50]. Of the fifteen adiposity-related putative metabolic markers, four

biomarkers of obesity/overweight status—waist circumference (WC), body mass index (BMI), fat mass index (FMI), and blood HDL—were components of MetS. Of the fifteen systemic inflammation-related metabolic markers, three biomarkers of obesity-related chronic inflammation—leptin, resistin, and TNF-α—were significantly higher in the metabolic syndrome (MetS) group than in the control group [51]. Correlations of BMI, FMI, lepti, and TNF-α were statistically higher than all other pairs of components. Both inflammation and adiposity anomalies were the most significantly clustered in subjects with MetS or obesity/overweight, respectively [52]. However, either inflammation or adiposity anomaly was significantly clustered, conflicting with the respective criteria of MetS or obesity. These findings indicate that inflammation-induced metabolic stress is the most important but not solely inducing condition determining the consequent obesity-related complications in MetS [53,54].

4. Pathophysiology of Metabolic Syndrome

The metabolic syndrome (MetS) is a global epidemic with hereditary or acquired causes that lead to an increase in cardiovascular disease (CVD) consequences [1]. MetS encompasses a constellation of prevalent cardiovascular risk factors, including central obesity, hyperglycemia, dyslipidaemia, and hypertension [55]. The metabolic syndrome has become an epidemic, along with the rising prevalence of obesity during the previous two decades. Consistent federal and regional data reveal that the total obesity percentage exceeds 40% in all states and persists above 35% in 34 states, notwithstanding efforts by the US Government to mitigate obesity[56].

The region with the highest obesity rates (40% and above) along with the highest rates of CVD events, sub-optimal CVD risk factor control, and non-compliance with treatment is located within the Appalachian region of the eastern United States. Appalachian Kentucky and West Virginia are also associated with high facilities for the management of obesity programs. According to reports, a geographic concentration of CVD deaths is concentrated in Kentucky, West Virginia, and Ohio. Focusing on the modality of choice, regional counties were reported to have the highest mean CHD (Coronary Heart Disease) death rates followed by Appalachian and non-Appalachian locations [57,58].

In West Virginia, this increased CVD mortality incidence rate for ischemic heart disease was ranked first in the nation with 248.5 deaths per 100,000 population. Because MetS causes primarily associated risk factors in this population, it is often misdiagnosed and has been recognized as a separate syndrome only relatively recently [59]. Identifying people with MetS is often overlooked in clinical settings resulting in increased morbidity and mortality from CVD alone. Many health systems manage to treat weight changes based on various factors, including bioethics issues and healthcare costs [60,61].

4.1. Genetic Factors

In the last decades, small interfering RNA (siRNA) technology emerged as a highly sophisticated and versatile tool in biological and clinical research. Following the discovery of the phenomenon of RNA interference (RNAi), there is a surge of interest in siRNA and RNAi. Their functional biology opened up novel research opportunities for biology and medicine and has posed special challenges in advancing siRNA as a therapeutic agent [62]. Generating various types and formats of RNAi as tools and drugs, therefore, became a hot area of research. Considering the rapid and broad advances generated with siRNA technology in a relatively short period, it is an opportune time to provide a comprehensive overview of siRNA and RNAi as tools and drugs for researchers and clinicians working in various fields [63,64]. There are three functional types of RNAi: siRNA, shRNA, and miRNA. Synthetic or vector-derived siRNA initiates the cytoplasmic processing of the long double-stranded RNA (dsRNA) precursors into small interfering RNAs (siRNAs) followed by their incorporation into RISC. The RISC complex containing the guide strand then binds to a complementary \$3 ϱγ_1@Οιξυ\$ of the target mRNA and carries out the degradation of the substrate through the action of one or more nucleases [65]. ShRNAs are synthetically assembled or expressed vector-derived long hairpin dsRNA that triggers RNAi. ShRNAs are processed into siRNA-like duplexes by Dicer in the cytoplasm followed by incorporation into the RISC. miRNA, like shRNA, is processed into a ~22 nt small RNA by Dicer, but its biogenesis differs from shRNA in that the precursor is single-

stranded and much longer [66]. It is co-transcriptionally processed by Drosha to a ~70 nt hairpin miRNA followed by an export from the nucleus and processing by Dicer to a mature ~22 nt miRNA. miRNA directs posttranscriptional regulation of a set of target mRNAs with imperfect base pairing in the 3' UTRs via inhibition of translation and/or degradation [67,68].

4.2. Environmental Influences

Most of the environmental factors that program MetS have their origins in adversity during early life, including maternal undernutrition or overnutrition, maternal diabetes, maternal exposure to environmental toxicants, and disruptions of early-life psychosocial environment [69]. These factors produce structural, functional, and behavioral changes in offspring, which increase vulnerability to MetS later in life [70,71]. Specifically, these metabolic physical manifestations include increased body size and weight, increased adiposity and fat mass, increased hepatic steatosis, dyslipidemia, endoplasmic reticulum (ER) stress, inflammation, muscle swap from slow to fast-twitch fibers, altered neural activation, insulin resistance, and hypertension. Some of the programming actions are sex-dependent, with male- and female-biased programming of obesity, insulin resistance, and hypertension [72,73].

Considerable evidences have emerged indicating that multiple environmental factors may drive the onset of MetS, the factors targeting common cellular machineries, and the biochemical events that take root through cell-signaling cascades and gene regulation, underlie the origins of different risk factors. Extensive offspring impact data gathered in a variety of animal and human longitudinal studies documenting the early-life antecedents of later adulthood MetS traits and behaviors have paved the way for targeted research into preventive strategies [74,75]. Epidemiological studies of various birth churches and cohort studies, with almost all of offspring outcomes fitting into increased risk of MetS-driven baccalaureate events, adulthood MetS traits, and behaviors. Mismatch and toxicants are among commonly investigated but underutilized factors driving MetS. Continuing works involve an investigation to fill in gaps in knowledge in these areas [76].

Non-exposition remains a government concern in lower- and middle-income countries for burthening millions of unseen, deleterious energy imbalance with unmet fat and sugar energy densities, and hence, among the undernourished. Persisting altitude discrepancies in the initial environments, housing conditions and capabilities to catch up regarding nutrition finer still appear [77]. The government is to facilitate the establishment of environmental standard, with continuous proxies of prevention and schooling against under-nutrition-induced sequelae in cutter-up and cutter-down situations [78,79].

4.3. Hormonal Imbalances

In the past, metabolic syndrome was considered a risk marker but not a clinical entity. However, recent findings demonstrate that the biochemical and hormonal alterations caused by insulin resistance will lead to the development of symptoms at the level of the cardiovascular system, liver, and other organs and systems. These symptoms are a group of risk factors for cardiovascular disease and diabetes, whose early detection and treatment represents a profound change of current medical practice [80].

Functional alterations related to insulin resistance may precede the establishment of abnormalities in glucose metabolism, plasma lipids, and blood pressure by years. Inflammation, proinflammatory chemokines and cytokines, alterations in adipocytokine secretion, dysregulation of blood pressure control, and autonomic dysfunction are some of the biochemical and hormonal disturbances associated with metabolic syndrome, which can be detected before the development of symptoms. As has been recently reviewed [81,82], metabolically “healthy” obese and women with polycystic ovary syndrome, both data point to the common existence of underlying, still undetected metabolic disorder leading to alterations at the cardiac, vascular, liver, and other organ levels[83].

Metabolic syndrome is a clinical entity whose early detection is possible by measuring hormonal and biochemical alterations that result from insulin resistance. The presence of these alterations even when clinical symptoms have not yet developed is indicative of a high risk of developing complications [84,85]. New pharmacological preparations for the

treatment of diabetes and the cardiovascular disease bear the hope of reversing these alterations early enough to avoid the onset of disease. If the elaboration of mass screening methods allows for an easier and less expensive detection of the biochemical and hormonal risk factors for metabolic syndrome, it should be widely spread [86,87].

5. Diagnostic Criteria for Metabolic Syndrome

The metabolic syndrome has become a prominent concern this decade due to the substantial increase in cardiovascular risk associated with a combination of risk factors. The risk factors associated with this syndrome are primarily acknowledged: hypertension, dyslipidaemia (elevated triglycerides and diminished HDL), increased fasting blood glucose, and central obesity [88,90]. The American Heart Association currently categorises individuals as having this syndrome if they display three out of five anomalous outcomes. The incidence of metabolic syndrome, as delineated by the Adult Treatment Panel III criteria, rose by more than 70%. This is especially alarming due to the linkage with type 2 diabetes, over 80% of which is linked to metabolic syndrome [91]. Insulin resistance is strongly connected with most risk factors linked to metabolic syndrome [92].

Insulin resistance is unequivocally associated with obesity. The inquiry posed is whether insulin resistance constitutes the fundamental mechanism of the entire condition. Three more components must be incorporated into the assessment of metabolic syndrome [93,94]. The primary factor is genetic predisposition. The expression of each metabolic risk factor is likely partially governed by its own genetic regulation, which subsequently affects the response to various environmental exposures. Obesity and insulin resistance have grown increasingly prevalent in global populations due to westernisation, characterised by dietary changes and physical inactivity [95].

Certain populations with a genetic pre-disposition to obesity at an early age often develop insulin resistance but without significant obesity at later stages. On the other hand, there are some overweight peoples with absence of significant metabolic complication like type 2 diabetes and cardiovascular disease [96]. These individuals usually belong to has an E-allele or high efficiency variant of arginine form of beta 3 adrenergic receptor which is involved in lipolysis with disadvantaged decrease in apple shape fat distribution [97,98].

5.1. IDF Criteria

Metabolic syndrome is a globally prevalent health condition. The main aim of this study is to evaluate the prevalence of metabolic syndrome in the population using the accepted criteria. Numerous previously neglected conditions have recently garnered notice. The rural population has systemic inflammation and displays sluggish conduct [99]. Sedentary conduct significantly contributes to metabolic syndrome. Metabolic syndrome has essential elements like abdominal obesity, hypertension, elevated blood triglycerides, and diminished high-density lipoproteins [100]. Contributing variables may encompass reduced insulin sensitivity, compromised glucose tolerance, and inflammation. The likelihood of encountering complications, including Type 2 Diabetes Mellitus and cardiovascular disease, increases when multiple conditions are present. Metabolic syndrome can negatively affect health and healthcare expenditures [101]. The principal variables contributing to the onset include excess body weight, obesity, inadequate physical activity, and genetic predisposition. It has been recommended that ethnic groups be assigned specific cut-off points for waist circumference. The proposal aims to establish standards to enable uniform global epidemiological examinations of metabolic syndrome symptoms. [102,103].

The criteria led to an increased proportion of metabolic syndrome diagnoses, which is more suitable. The global lifestyle has undergone a noticeable transformation due to the rising sedentary tendencies of contemporary living and inadequate food habits. Activity levels have significantly declined, and a rising prevalence of obesity has been observed globally [104]. The lifestyle changes have coincided with significant increases in the prevalence of type two diabetes mellitus and cardiovascular disease globally, rendering metabolic syndrome a priority issue. Individuals with metabolic syndrome face an elevated risk of acquiring severe health disorders, including diabetes, cardiovascular

disease, and stroke [105]. A multitude of research have been undertaken worldwide to examine the frequency of metabolic syndrome in diabetic and non-diabetic populations. Numerous research investigations conducted in Pakistan have indicated a significant frequency of metabolic syndrome [106,107].

5.2. NCEP ATP III Criteria

The metabolic syndrome (MetS) was identified as a multifaceted risk factor for cardiovascular disease (CVD) that warrants increased therapeutic attention in the Adult Treatment Panel III (ATP III) report of the National Cholesterol Education Program (NCEP). The MetS's ATP III requirements are different from those of other organisations [108].

- CVD as the primary clinical outcome. The criteria for the MetS were developed mainly with diabetes as the primary clinical outcome [109].

- MetS components related to CVD. Criteria for the MetS include several components that are not known to relate to CVD adverse outcomes, such as elevated insulin [110].

- ATP III recommendations for simple screening of the MetS (early detection) based on only three components: obesity, dyslipidemia, and hypertension. Because insulin resistance, glucose intolerance, and inflammation/phlebotic state are difficult to quantify, simple screening can be recommended based on fatness, fat distribution, and atherogenic dyslipidemia [111].

In light of the ATP III criteria, many epidemiological studies, clinical studies, or interventional studies have been conducted, leading to a better understanding of the MetS [112]. Nevertheless, important questions remain regarding the key character, underlying mechanism, and the determinants or implications of the MetS, which are unmet even by the ATP III criteria [113].

5.3. Other Proposed Criteria

With the increasing test performance and reliability, there is ongoing interest in evaluating and establishing other new criteria for MS [114,115]. Overall, additional 18 prevention and intervention target proteins reflecting different disorders underpinning MS were proposed for the early detection, risk stratification, and treatment stratagem to why and how to restore the metabolic balance remain questions worthy of further exploration [116,117].

6. Clinical Implications of Metabolic Syndrome

It has been reported that among metabolic syndrome patients, only 5% may be eligible to receive drug therapy in accordance with the National Cholesterol Education Program (NCEP) ATP III guidelines. Since most reports are based on Asian data, it is unclear whether the findings are applicable to Western populations [118]. A study recruited subjects with metabolic syndrome from the Massachusetts General Hospital's general medicine clinic and compared them with a control group [119]. Medical records and clinical characteristics were used to categorize subjects as either opportunity or new metabolic syndrome candidates. Biochemical characteristics were compared between subjects with and without new onset metabolic syndrome. To identify inclusive metabolic syndrome components, stepwise regression analysis was performed on subjects without treatment and with individualized cut-offs for at least one glucose variable [120,121]. Metabolic syndrome components and alternative definitions that may reduce patient misclassification were provided. Improved identification of treatment eligible patients and improved patient cardiovascular risk management are warranted. Activity/non-activity ratios were compared between groups using repeated measures ANOVA [122]. Spearman rho was used to correlate activity percent change with waist circumference and BMI percent change. A semi-structured focus group interview with a random selection of 15 participants was conducted. Besides dietary recommendations and physical activity advice, teams and competitions were suggested. The use of electronic health record documentation templates has the potential to ensure intervention fidelity and facilitate future translational research [123].

While every definition may identify those at increased cardiovascular risk, only the NCEP ATP III guidelines identify drug therapy eligible individuals. Moreover, the components comprising metabolic syndrome differ greatly across definitions [124]. For

example, the 80-88th percentile cut-offs for waist circumference developed using data from a well-cited sample of Mexican-American adults in San Antonio in the late 1970's-early 1980's are recommended by NCEP ATP III to identify "opportunity" candidates for treatment. These "cut-offs" may lack applicability to more recent cohorts from different populations, who may have greater heights and body dimensions [125].

6.1. Cardiovascular Risks

Cardiovascular disease-related complications are a global issue of growing concern. Recent statistics estimate that coronary heart disease causes 7.3 million deaths a year, whereas strokes cause 5.5 million. Approximately 70 million people in the United States, constituting 29% of the adult population, are affected by cardiovascular disease. Its prevalence is on the rise in low- and middle-income countries, particularly in Eastern Europe and in Central and South America [126]. Economic tolls are an important incentive for cardiologic research, though admittedly the industry grows in size every year. Nevertheless, the enactment of public policy to address the CVD epidemic must be informed by gathering the best possible data to illustrate those most at risk. For example, countries with lower national income experience a dual burden of malnutrition and rising obesity. Rapidly changing diets and reduced levels of physical activity are causing disproportionately high rates of obesity/diabetes and subsequent cardiovascular disease [127]. A lack of research and government awareness perpetuates this trend. Unlike their higher-income counterparts, screening guidelines are rarely implemented, and clinicians have little knowledge about metabolic syndrome and its implications, including cardiovascular disease. Common across varied etiologies, metabolic syndrome is recognized as a clinical manifestation which is indicative of future cardiovascular death [128]. Although the underlying biological mechanisms associated with its clustering remain to be fully elucidated, it is believed that factors such as central obesity, dyslipidemia, and hypertension are all associated with the onset of both metabolic syndrome and cardiovascular disease. These metabolic derangements work in concert to heighten the risk of cardiovascular events by promoting and sustaining atherogenic processes. Whatever the case, it is clear that a better understanding of biological mechanisms involved in metabolic syndrome progression and subsequent CVD may assist in further research endeavors [129].

6.2. Diabetes Mellitus

Type 2 diabetes mellitus is the most common form of diabetes in all countries from all populations studied. It is defined as a disorder of glucose metabolism with particular reference to the anabolic condition known as insulin resistance. Diabetes mellitus is a serious progressive metabolic condition in which plasma glucose concentrations are affected by an imbalance between the insulin secreted by the pancreatic β-cells, the sensitivity of target tissues to insulin, and the rate of hepatic glucose removal from the blood [130,131]. All these levels together represent an operational definition of diabetes originally devised by the American Diabetes Association. New knowledge has been accrued concerning the pathophysiology of type 1 and 2 diabetes; i.e. glucotoxicity, lipotoxicity and apoptosis of β-cells, and also α-cells have been recognized as new mechanisms involved in hyperglycemia in both diabetic conditions [132]. Eventually, the excessive secretion of pro-inflammatory cytokines from adipose tissue, hepatic steatosis and dyslipidemic liver have been noticed as key events inducing insulin resistance and vascular disorders in obesity-associated type 2 diabetes [133].

The widespread endocrine condition known as metabolic syndrome is typified by central (visceral) obesity, dyslipidaemia, hypertension, and impaired glucose tolerance. It is believed to be the cause of the higher prevalence of physical impairment and microvascular and macrovascular problems [134]. A considerable percentage of people with type 2 diabetes have metabolic syndrome (+/- 25% in Caucasian populations, +/- 50% in Asian populations), and this number is probably rising. Numerous centres' efforts have focused on determining the prevalence and elements of metabolic syndrome in individuals with type 2 diabetes and whether it can be used to forecast the baseline severity or the emergence of additional diabetic complications that would support a more intensive treatment plan [135,136].

6.3. Chronic Kidney Disease

Cardiovascular diseases and end-stage renal disease represent the primary causes of mortality among individuals eligible for kidney transplantation as well as those who are not candidates for the procedure. Hypertension represents the most common risk factor for heart disease in individuals with chronic kidney disease (CKD), whereas CKD is recognised as a significant risk factor for cardiovascular disease (CVD) [137]. Cardiovascular disease and chronic kidney disease exhibit numerous shared risk factors and harmful pathophysiological alterations. Chronic kidney disease (CKD) is significantly linked to cardiovascular events, even in individuals with earlier stages of the condition. Diabetes represents the primary risk factor for cardiovascular disease in patients with chronic kidney disease, particularly in those eligible for kidney transplantation [138]. Metabolic syndrome (MetS) is the predominant clinical definition utilised to identify individuals at heightened risk for cardiovascular disease (CVD) and diabetes across both genders and all member nations. The condition consists of five components: abdominal obesity, elevated triglycerides, decreased high-density lipoprotein cholesterol, increased blood pressure, and elevated fasting plasma glucose levels [139]. Among these five components, the measurement of central obesity via waist circumference demonstrates high sensitivity and specificity, especially in Asian populations. The progression of diabetic kidney disease significantly influences mortality rates compared to cardiovascular disease, as both conditions are components of the metabolic syndrome spectrum. The relationship between MetS and its components and renal injury, as evidenced by decreased estimated glomerular filtration rate (eGFR) and elevated urine albumin excretion (UAE), has been documented, utilising laboratory tests that may not be easily accessible in community environments [140]. Chronic kidney disease (CKD) is identified through elevated serum creatinine levels, a laboratory assessment that is generally not feasible given that most contemporary screening techniques for metabolic syndrome (MetS) rely on anthropometric measurements. Furthermore, prior research was exclusively performed in clinical or hospital settings, which may have resulted in the selection of patients with greater disease severity and associated risks [141]. The incremental rise in the total number of MetS components correlated with a decline in eGFR and a corresponding increase in CKD prevalence, with the most severe renal function noted in participants exhibiting MetS. Additionally, incremental increases in the number of MetS components were linked to higher odds of CKD [142].

7. Early Detection Strategies

Prevention of the metabolic syndrome, its associations and consequences, is of broad interest as it is a health problem of global challenge. High caloric intake and sedentary lifestyle have been statistically most significantly associated with changes of metabolic pathways, leading to a cluster of metabolic syndrome features [143]. Therefore, the final aim of the Prevention of Metabolic Syndrome Project was to identify the cluster of fasting biochemical parameters that best describes the metabolic profile of incipient obesity and its association with overweight in early adulthood, when lifestyle modifications can have most impact on future health [144]. Early detection of metabolic syndrome (MetSy) and its components in populations without or only with mild obesity is of major preventive importance to enhance target preventive approaches [145]. Methods involved a comprehensive analyses of clinically routinely available metabolic and inflammatory parameters with regards to their sensitivity, specificity, and association with anthropometrics and body fat mass in defining high MetSy burden in young health individuals [146]. Moreover, the proposed procedure for MetSy burden estimation was designed to be implemented in clinical practice and to enable automatic classification of tested individuals to either the low or high burden. Clustering of fasting metabolic parameters into the three highest risk scores of association with body fat mass, overweight, visceral fat and waist circumference was achieved [147]. If these parameters are elevated, individuals have an increased risk for the same metabolic perturbations over the time course. The cut-offs were chosen as a point on the receiver operating characteristics curve that enables best discrimination with a low number of false

discovery. High classification specificity was the motivation to choose the cut-off of a less substantial change in accuracy and to propose a single cut-off of MetSy burden present on entering the MetSy stage of low obesity category [148,149].

7.1. Screening Guidelines

The National Cholesterol Education Program Adult Treatment Panel III criteria, with the modification of phosphorus, described the MS syndrome with inclusion of obesity. Screening the increased caution of a patient to have MS is very easy, and nearly all cases of MS have been early detected with a simple initial assess risk table in clinical approach [150]. Guidelines recommend routine test determine separately each MS component should begin as early as 20 years old since indicators of cardiovascular diseases. However, in a community-based population of female aged over 35, only 4.5% had ever checked waist circumference at least once [151]. The VO2 peak cutoff of 40 ml/kg/min found under the specific condition of this study in early detection of basal metabolic rate was incorrect approach since fitness cannot be independent of age in consideration [152,153]. Although there are variety of endurance exercise training(s), this study preferred confirm the commonly nutritional pathophysiology. Serum cholesterol is the most preventive risk factor among MS components in all mathematical models with detection cutoff not requiring complex laboratory usage. Immediate nutritional approach according to small change in practice also required with low chance of effort and return [154,155].

7.2. Role of Biomarkers

Currently, the wide range of pathophysiologies involved in metabolic syndrome has hampered discovery of high accuracy biomarkers. Traditionally, risk factors of metabolic syndrome have been considered as biomarkers [156]. However, independently of abdominal obesity (waist circumference/waist-to-height ratio), serum levels of high sensitivity C-reactive protein (hs-CRP), triglycerides (TG), uric acid (UA), total cholesterol (TC), and lipoprotein associated phospholipase A2 (Lp-PLA2) activity have been suggested as candidates for being used in a panel of biomarkers [157]. Sensitivity and specificity of screening methods such as the triglyceride-glucose index, waist circumference-to-height ratio, and aesculins have shown moderate results. Thus so far, methods for early detection of metabolic syndrome that combine good specificity and sensitivity are lacking [158]. The aim of this study to provide a review of existing and proposed biochemical biomarkers of metabolic syndrome that can potential for being used in early detection of metabolic syndrome, and also provide new insights into metabolic syndrome pathophysiology. A systematic review of existing studies was conducted to group biomarkers according to biological functions. As well, validity of biomarkers as indicators of metabolic syndrome was reviewed [159,160].

The label "metabolic syndrome" arose from the awareness that abdominal obesity was a key driver of insulin resistance, type 2 diabetes, and cardiovascular diseases. The systemic oxidative stress and altered lipid metabolism are other key drivers of metabolic syndrome [161]. Systemic oxidative stress is an imbalance between the body’s production of reactive oxygen species (ROS) and its ability to eliminate them. The source of ROS are thought to be mainly hypertrophied adipocytes [162]. Excessive and dysfunctional adipose tissue is linked to chronic low-grade inflammation marked by infiltration of a combination of M1 macrophages and other immune cells secreting inflammatory cytokines that promote systemic insulin resistance, pancreatic beta-cell dysfunction, and -cell cytotoxicity [163,164].

7.3. Patient Education

Management of metabolic syndrome is challenging, and thus, intervention is needed at an early stage before progression to diabetes or overt cardiovascular disease. With people living longer and still being able to maintain a good quality of life, there is an insistent need to investigate metabolic syndrome at a younger age [165]. Metabolic syndrome at a younger age might mean much longer health issues and life deprivation. Therefore, there is a need to continually assess and detect early biochemical changes in long-term healthy young individuals. Specific attention should be given to assessing their lifestyle, physical activity, and behaviour. Not every individual who develops a biochemical change will remain unhealthy; some will remain healthy [166,167].

With early detection of biochemical changes that indicate the burden of metabolic syndrome in the frame of lifestyle, behaviour, stress, and psychological status, preventive lifestyle modifications could be timely introduced. Transitioning to age-independent group values with inherent colour code risk assessment and description behaviour responses might improve the engagement of the younger public to the survey [168]. Blank areas and missing information in some included criteria of metabolic syndrome could be acknowledged as errors of observation evidenced by countless outputs confirming hypertriglyceridemiae and hypertension. Gradient quantification of individual metabolic syndrome risk could provide unique information for the affected individuals, allowing valuable insight into future lifestyle and behaviour that are simultaneously possible to act and change [169,170].

Relying only on the severity of each metabolic syndrome definition component could diminish the intensity of information indicating metabolic change detection. Healthy screening assessment appointments for somewhat unhealthy young people could be important opportunities to transfer in-depth individual information that cannot be obtained at mass level [171]. Inviting the affected public and personal engagement could provide much newer involvement in generated public health issues at a population level, such as increasing consumption of hidden sugars in food obtained outside of restaurants [172]. With early detection of metabolic syndrome changes in the lifestyle frame and prevention potentials, public action could generate much niched public attention and study results with the capacity of catching major account of consideration [173,174].

8. Lifestyle Interventions

A comprehensive understanding of the connections between lifestyle exposures and biochemical alterations is essential for identifying early metabolic changes that could result in metabolic syndrome (MS). This may facilitate the identification of individuals with early multiple sclerosis and address the epidemic of its complications [175,176]. Metabolic syndrome comprises a collection of risk factors that increase the likelihood of cardiovascular disease and diabetes. It is widely prevalent worldwide and significantly increases the risk of complications for a substantial portion of the population. The metabolic syndrome and its related conditions, including cardiovascular disease (CVD) and diabetes, impose a significant burden on global health [177,178]. They are widely prevalent globally and are anticipated to rise further, while existing health care systems appear inadequate in fully addressing the impact of their complications. The early identification of metabolic syndrome and its associated biochemical abnormalities is crucial for the timely implementation of preventive lifestyle measures to halt its progression [179,180].

Lifestyle promotion is an accepted, low-cost, and relatively simple approach to improving physical activity and dietary habits and reducing the prevalence of metabolic syndrome and its components [181]. The vast majority of studies aimed at healthy lifestyle promotion have focused on the effects on clinical parameters; however, it is vital to better understand how such interventions affect the biochemical background [182]. Healthy promotion programs related to preventive goals are scarce in young adults despite having a relevant preventive potential given a high prevalence of premature metabolic syndrome origins in this high-risk group. The promotion of healthy eating and active living program resulted in significant changes in life habits that have been associated with altered serum metabolite profiles in middle-aged individuals [183,184].

8.1. Dietary Modifications

The metabolic syndrome (MetS) comprises a cluster of metabolic disorders that elevate the risk for cardiovascular disease, type 2 diabetes, and various other chronic conditions. MetS is characterised by the presence of three or more cardiovascular disease (CVD) risk factors, including abdominal obesity, dyslipidaemia, hypertension, and insulin resistance [185,186]. Although advancements in pharmacological development have been made, modifications in lifestyle habits remain the primary therapeutic approach. Dietary habits are critical factors influencing the progression of metabolic syndrome. Recent studies indicate that strong adherence to certain dietary patterns is associated with a reduced prevalence of MetS [187,188]. The Mediterranean diet (MD) is

linked to a reduced prevalence of Metabolic Syndrome (MetS) across various populations. Comparable protective effects against metabolic syndrome were noted with other identified healthy dietary patterns, such as the Dietary Approaches to Stop Hypertension (DASH), the alternative healthy eating index score (AHEI), and the Root Vegetable Consumption Index (RVCI) [1189,190].

In recent years, many factors affecting energetic balance among the population, including changes in physical activity levels and dietary habits together with other aspects related to social behavior and lifestyle habits, have contributed toward an increasing prevalence of metabolic syndrome in developed and developing countries [191]. This scenario has provoked an increase in metabolic syndrome prevalence to 20–25% in adults. Complementarily, and as a consequence of a complex pathological cascade, other non-communicable chronic diseases (NCDs) related to unhealthy dietary habits have expanded, leading to significant morbidity and mortality. Between them, cardiovascular diseases (CVD) and type 2 diabetes mellitus (T2DM) are the most public health priorities [192,193]. A remarkable expansion in type 2 diabetes incidence has occurred in recent years, which has almost doubled the prevalence in many countries. In parallel with that increase, MetS prevalence has also risen to 20–25% of the adult population in developed countries, and this incidence continues to increase [194,195]. The recently published guidelines on cardiovascular disease prevention point out that CVD risk factors can be treated with analysis and algorithms similar to those for metabolic abnormalities linked to diabetes or metabolic syndrome. This issue highlights how a recent and previously underestimated risk factor—MetS—contributes to CVD [196,197].

8.2. Physical Activity Recommendations

Adults of all ages are advised to engage in a minimum of 150 minutes of moderate-intensity aerobic physical activity per week. This can be accomplished by engaging in 30-60 minutes of moderate-intensity physical activity on five or more days per week, or 20-60 minutes of vigorous-intensity physical exercise on three or more days per week, or a combination of both activities. To attain further and more significant benefits, individuals should participate in physical exercise for over 300 minutes weekly [198]. It is also encouraged to engage in muscle strength and resistance training for all main muscle groups on two or more days per week. The advised weekly amount of moderate to vigorous physical activity can be achieved in sessions lasting at least 10 minutes each or accumulated in shorter intervals throughout the day. To improve or sustain balance and avert falls, older persons should engage in balance activities at least three times per week [199].

Adhering to these activity recommendations can enhance physical and mental health and well-being, as well as prevent and/or manage chronic conditions, including metabolic syndrome. A significant section of the population fails to adhere to the physical activity guidelines, which stipulate a minimum of 150 minutes of moderate to vigorous physical activity each week in sessions lasting at least 10 minutes each. Metabolic syndrome is among the most common chronic disorders, with its prevalence on the rise. Numerous prospective cohort studies have investigated the relationship between physical activity and the onset or occurrence of metabolic syndrome [201].

Leisure time physical activity is characterised as exercise conducted outside of occupational duties. Each study examined the correlations between total leisure time physical activity, often evaluated using questionnaires, and/or its subcategories and the onset or prevalence of metabolic syndrome and its components. In the majority of research, the metabolic syndrome was delineated based on the criteria set forth by ATP III, IDF, WHO, or a combination of these entities [202]. The studies indicated that increased leisure time physical activity throughout midlife or at baseline correlated with a reduced risk or incidence of metabolic syndrome. These studies and the molecular processes connecting physical activity to metabolic syndrome indicate that leisure time physical activity has preventive effects against the onset or occurrence of metabolic syndrome in midlife [203,204].

8.3. Behavioral Therapy

Mind-body therapies have been shown to positively affect loneliness, perplexity, and rage. Given the interrelation between psychosocial factors and metabolic syndrome—where psychosocial elements may foster insulin resistance and vice versa—it is probable that mind-body therapies would affect variables associated with metabolic syndrome [205,206]. The metabolic syndrome comprises a collection of risk factors for cardiovascular disease and diabetes, including increased waist circumference, raised triglycerides, diminished high-density lipoprotein cholesterol, hypertension, and elevated fasting blood glucose. Approximately one in three persons in the United States is thought to have metabolic syndrome. Due to the unfavourable prognosis for persons with these risk factors, there is an immediate necessity to discover cost-effective preventative and care solutions [208]. Lifestyle adjustments are presently advised as the exclusive treatment for prehypertension and any isolated symptoms of metabolic syndrome. Simultaneously, numerous community, faith-based, and commercial organisations in the United States provide instruction in mind-body therapies, which are typically cost-effective [209].

Given that the metabolic syndrome is expected to be increasingly prevalent, it is essential that healthcare practitioners help patients find suitable, acceptable, and cost-effective self-care. The main objective of the current paper is to provide healthcare practitioners with information that could be used in decision-making about recommendations for mind-body practices to influence individuals with the metabolic syndrome [210]. Reacting to the metabolic syndrome with behaviors that unfavorably influence its components has been described as losing the metabolic battle, and evidence indicates that mind-body therapies may favorably influence interactions among psychosocial factors and metabolic syndrome-related risk factors. In addition to providing information that may be useful in decision-making about recommendations for mind-body therapies, an overview of two of the metabolic syndrome components is presented, along with a brief description of mind-body components that may synergistically influence psychosocial factors and other related constructs [211].

4. Discussion.

9. Pharmacological Management

In 2005, the pharmacological treatment with statins, prescribed until the goal of LDL-C levels ≥100 mg/dL is achieved, was regarded the standard approach [212]. For recent-onset diabetic patients aged <40 years, with 10-year cardiovascular disease risk of 20% or above, combination of LDL-C lowering agent with lifestyle modification for compliance of triglycerides diet <150 mg/dL while HDL-C ≥40 mg/dL was regarded an adviced strategy. With the rapid growth of herbal formula containing flavonoids nowadays, such formula have drawn attention in the area of biochemical and clinical investigations and merits of further investigations for widely uses have been recommended [213]. Furthermore, in the diabetes-prevention field, more large dose, long-term treatment by large scale RCT studies are warranted for potential availability of large-scale applications. The MetS concept is a valuable tool in medical education. It provides an overview of the complex mechanisms by which chronic exposure to a positive caloric balance or lipotoxicity causes long-term complications [214]. The role of excess free fatty acids and adipokines secreted by adipose tissue in the genesis of systemic insulin resistance is particularly well stated. In this context, the metabolic involvement of other organs such as the liver, pancreas, and skeletal muscle is discussed. It should be noted, however, that despite the escalating pandemic of obesity and the MetS, there is still considerable heterogeneity in the knowledge of clinicians regarding this condition, especially among experts who are perceived as not being up to date with the field. The literature on the complex and intricate influences on weight gain/maintenance is vast [215]. Moreover, these issues are even more complicated in the context of the public health implications regarding the critical period in childhood and the obesity epidemic. A personalized approach should be applied in the adoption of a healthy lifestyle and in the prescription of drug therapy. However, it is difficult to convince patients, particularly in their teens and twenties, regarding the difficulties, implications, and long-term consequences of

obesity [216]. One caution is that the MetS concept may lead to over-prescription of pharmacotherapy unless it is coupled with a concerted campaign to deal with the pandemic of obesity and pro-obesity environments, as well as social and cultural pressures through educational campaigns [217].

9.1. Insulin Sensitizers

The efficacy of insulin sensitizers for the treatment of dyslipidemia is inconsistent, but its derivatives such as PPAR γ are frequently employed to enhance insulin usage in peripheral tissues, such as muscle and fat. However, it is essential to consider its undesirable side effects like weight gain, edema, or exacerbation of congestive heart failure. The glucose-lowering effect of the drug was utilized to determine the possible source of insulin resistance by administering 35 mg/day and 105 mg/day, respectively [218]. Incremental insulin dose (μU/mL) curves were checked for different times of fasting. SLE and TMP-002 appear to be safe drugs which could provide inferences to manage the metabolic syndrome from pre-diabetes to dyslipidemia [219]. At 07:00 and 19:00, blood was drawn from fingertip capillaries to assess plasma glucose concentrations with a glucose monitor. The abnormal plasma glucose concentration was considered from 2 h plasma glucose 140 mg/dL. All computed tomography scans were performed on a 64-row multislice computed tomography scanner [220]. Epicardial fat area and abdominal visceral adipose tissue area were measured through the assessment of volumetric computed tomography images. Meta-analysis studies with at least four cohorts, adult subjects, examinations using FAMT, and the publication year before 2022 were included [221]. In the first experiment group involving glucose monitoring, dietary records and exercise diary were assessed [220]. After dietary and activity adjustments, METSU 30 (22.68 ± 9.23) significantly decreased to METSU 20 (18.08 ± 6.92) at follow-up 1 but METSU 40 at follow-up 2 (28.08 ± 3.50) was not significantly different from METSU at baseline. After interventions, ANCOVA indicated that follow-up 1 METSU, metabolic syndrome and NCD risk factors were significantly associated accounting age scaling at < 65 years and sex scaling in WH Ratio [222].

9.2. Statins

Statins inhibit cellular cholesterol synthesis by blocking HMG-CoA reductase, the rate-limiting enzyme in the mevalonate pathway. Statins have pleiotropic effects beyond lipid-lowering, such as increased endothelial nitric oxide synthetase (eNOS) expression, nitric oxide (NO) release from endothelial cells, enhanced NO specificity, and the consequent inhibition of myocyte apoptosis, smooth muscle cell migration, and thrombosis [223]. In addition to improving endothelial function, statins build plaque stability by decreasing inflammatory cell infiltration, reducing the release of pro-inflammatory cytokines by foam cells and macrophages, decreasing matrix metalloproteinases and tissue factor release, decreasing tissue factor release from the endothelium, and decreasing prothrombotic lipid and microparticle release from activated platelets [224].

Statin treatment is associated with improved symptoms and functional capacity in heart failure patients. In ischemic heart failure patients, atorvastatin treatment has been reported to improve endothelial function. Statins have also been found to improve the decline in microvascular density and diastolic dysfunction associated with myocardial air deprivation. Statin treatment also increases patients' symptom domains and 6-minute walk distance, and these beneficial effects are consistent with decreased left ventricular systolic wall motion score [225]. The positive treatment effect on functional capacity is consistent with previous findings that statin use is associated with a lower incidence of heart failure hospitalization and improved symptoms. In addition to the direct effects of statins on cardiomyocytes and plaque stabilization, indirect effects such as improved endothelial function and decreased pro-thrombotic tissue factor release from activated platelets, leading to decreased thrombus size, may also play a role [226].

9.3. Antihypertensives

Considering that MetS comprises a series of disorders, including hypertension, its management involves antihypertensive medications. Lifestyle modifications are crucial for those with Metabolic Syndrome. Diets such as DASH and Mediterranean, along with

other weight loss regimens that encourage physical activity (exceeding 300 kcal/day), should be advocated and reinforced by familial and social environments [227]. Secondly, improved adherence and reevaluation of initial antihypertensive medication, including triple or quadruple fixed combinations that address various processes in the pathophysiology of hypertension, are also crucial. This novel methodology plays a significant role in attaining improved blood pressure regulation [228]. Every hypertensive patient (untreated) with a blood pressure exceeding 160/100 mmHg should first be administered at least a dual fixed combination of an ACE inhibitor, Angiotensin II receptor antagonist, or calcium channel blocker. This will facilitate the attainment of a blood pressure goal of less than 140/90 mmHg in a reduced timeframe, with minimal hospitalisations and diminished adverse effects [229]. An approach for first-line antihypertensive medication should be advocated based on clinical and laboratory parameters. Timely detection and intervention for cardiometabolic variables, including dyslipidaemia, glucose intolerance, metabolic syndrome, and obstructive sleep apnoea syndrome, correlate with a positive effect on mortality and morbidity [230,231].

5. Conclusion

The metabolic syndrome is a growing public health problem that is increasingly affecting adolescents and young adults. Its prevalence is often underestimated, as this age group rarely undergoes screening or laboratory testing. Therefore, it is important to look for more direct and simple indicators of this condition that could alert physicians to its potential presence in a broader age group. The main biochemical indicators related to the classic clusters forming the metabolic syndrome are blood glucose, triglycerides, and cholesterol. Other important parameters signaling early modification and potential progression of the metabolic syndrome are insulin, PAI-1, and the adipokines leptin and adiponectin. It is generally accepted that obesity is strongly correlated with diabetes and hypertension due to physiological dysfunctions associated with ectopic fat storage and fatty liver. Growing evidence shows that glucose metabolism modifications are correlated with atherosclerosis progression, but most measurements related to glucose metabolism are currently not broadly assessable in health-care settings. The same is the case for chronic inflammation and oxidative stress. Hypertension is well defined as a cluster of diseases that include dyslipidemia, but no emerging pathways beyond cholesterol–atherosclerosis have led to novel risk indicators. In fact, total cholesterol and LDL cholesterol have decreased in individuals eligible for medical therapy, while non-HDL cholesterol managed indirectly through lifestyle modification is instead showing a rise. Inexpensive and broadly compatible parameters related to an excessively prothrombotic environment may indicate early disease stages. Persistent early morning blood plasminogen activator inhibitor may provide a more global risk indicator of cardiovascular disease in clonal growths or further artherogenic or atheroprotective adjusters of large artery structure or function. Obesity-related deviations in the metabolic milieu around a high-calorie lifestyle, sedentary daily habits, and low levels of physical activity stimulate the excessive secretion of leptin and other hormones. At least for leptin, excessive secretion advances to its accumulation-derived resistance, which eventually pairs with the depletion of the counterregulatory adipokines over decades of a non-resolving low-grade immune response, oxidative stress, and endoplasmic reticulum stress. This is related to the clustering of multi-organ diseases characterizing metabolic syndrome. Anti-inflammatory and adipogenic mechanisms may empower adiponectin and the Natriuretic peptide system, while pro-inflammatory cytokines from ectopic fat deposits may inhibit insulin signaling. Dyslipidemia clustering these metabolic disorders is of great clinical and preventive interest due to its contribution to the greater burden of cardiovascular disease. The primary treatment strategy needs to better understand the time-related biochemical alterations. Aside for weight loss, no approved pharmacological interventions are focused on the metabolic syndrome. Biomarkers such as proinflammatory cytokines (IL-6, TNF-α), pro-oxidant status, or prothrombic factors (PAI-1) are elevated. Soon upon reaching a certain threshold, the changes cluster into

distinct, time separable disorders as the secretion of leptin and other hormones switch to resistance.

REFERENCES

[1] K. Srikanthan, A. Feyh, H. Visweshwar, J. I MD Shapiro et al., "Systematic Review of Metabolic Syndrome Biomarkers: A Panel for Early Detection, Management, and Risk Stratification in the West Virginian Population," 2016.

[2] X. Liang, B. Or, M. F. Tsoi, and C. L. Cheung, "Prevalence of metabolic syndrome in the United States national health and nutrition examination survey 2011–18," Postgraduate Medical Journal, 2023.

[3] H. Chen, X. Zheng, X. Zong, Z. Li, N. Li, J. Hur, and C. D. L. Fritz, "Metabolic syndrome, metabolic comorbid conditions and risk of early-onset colorectal cancer," *Gut*, vol. 70, no. 4, pp. 678-685, 2021.

[4] C. Yang, X. Jia, Y. Wang, J. Fan et al., "Trends and influence factors in the prevalence, intervention, and control of metabolic syndrome among US adults, 1999–2018," BMC geriatrics, 2022.

[5] P. Rattan, D. D. Penrice, J. C. Ahn, A. Ferrer, et al., "Inverse association of telomere length with liver disease and mortality in the US population," Hepatology, vol. 76, no. 4, pp. 1002-1012, 2022.

[6] C. W. Hicks, D. Wang, K. Matsushita, et al., "Peripheral neuropathy and all-cause and cardiovascular mortality in US adults: a prospective cohort study," *Annals of Internal Medicine*, vol. 2021.

[7] S. Lim, J. W. Kim, and G. Targher, "Links between metabolic syndrome and metabolic dysfunction-associated fatty liver disease," Trends in Endocrinology & Metabolism, 2021.

[8] N. Ahluwalia, R. Raghavan, G. Zhang, et al., "Vitamin D status and prevalence of metabolic syndrome by race and Hispanic origin in US adults: findings from the 2007–2014 NHANES," The American Journal of Clinical Nutrition, 2023.

[9] J. Hong, R. Zhang, H. Tang, S. Wu, and Y. Chen, "... in predicting cardiovascular diseases incidence among populations with cardiovascular-kidney-metabolic syndrome stages 0–3: a nationwide prospective cohort," Cardiovascular, vol. 2025, Springer.

[10] A. Šoštarič, B. Jenko, N. Rotovnik Kozjek, D. Ovijač et al., "Detection of metabolic syndrome burden in healthy young adults may enable timely introduction of disease prevention," 2019.

[11] K. Shin, Y. M. Bae, and H. Kweon, "Non-Invasive Multichannel Vagus Nerve Stimulator With Heart Rate Measurement for Closed-Loop Control," 2025 International Conference on …, 2025.

[12] W. K. Chan, K. H. Chuah, R. B. Rajaram, et al., "Metabolic dysfunction-associated steatotic liver disease (MASLD): a state-of-the-art review," *Journal of Metabolic Syndrome*, 2023.

[13] S. Alfihed, M. Majrashi, M. Ansary, N. Alshamrani, "Non-invasive brain sensing technologies for modulation of neurological disorders," Biosensors, 2024.

[14] K. Wang, S. Margolis, J. M. Cho, S. Wang, et al., "Non-Invasive Detection of Early-Stage Fatty Liver Disease via an On-Skin Impedance Sensor and Attention-Based Deep Learning," *Advanced*, vol. 2024, Wiley Online Library.

[15] Y. Shi and W. Wu, "Multimodal non-invasive non-pharmacological therapies for chronic pain: mechanisms and progress," BMC medicine, 2023.

[16] A. Kandwal, Y. D. Sharma, R. Jasrotia, C. C. Kit, "A comprehensive review on electromagnetic wave based non-invasive glucose monitoring in microwave frequencies," Heliyon, 2024.

[17] S. Kumari, D. K Kataria, S. Kumari, R. Rani et al., "Metabolic Syndrome Frequency in Type 2 Diabetics Using International Diabetes Federation (IDF) Criteria Analysis," 2024.

[18] M. Nwankwo, C. J. Okamkpa, and B. Danborno, "Comparison of diagnostic criteria and prevalence of metabolic syndrome using WHO, NCEP-ATP III, IDF and harmonized criteria: A case study from urban southeast …," Diabetes & Metabolic Syndrome, vol. XX, no. XX, pp. XX-XX, 2022.

[19] E. Rivadeneyra-Domínguez and J. J. Díaz-Vallejo, "A Comparative Study of Metabolic Syndrome Using NCEP—ATP III and IDF Criteria in Children and Its Relationship with Biochemical Indicators in Huatusco, Veracruz," Children, 2023.

[20] S. O. Adil, K. I. Musa, F. Uddin, A. Khan, I. Khan, "Prevalence of undiagnosed metabolic syndrome using three different definitions and identifying associated risk factors among apparently healthy adults in Karachi," Archives of Public Health, vol. 2024, Springer, 2024.

[21] Y. Huang, L. Zhang, Z. Wang, X. Wang, Z. Chen, and L. Shao, "The prevalence and characteristics of metabolic syndrome according to different definitions in China: a nationwide cross-sectional study, 2012–2015," BMC Public Health, vol. 22, no. 1, 2022.

[22] Z. Jamali, F. Ayoobi, Z. Jalali, R. Bidaki, and M. A. Lotfi, "Metabolic syndrome: a population-based study of prevalence and risk factors," *Scientific Reports*, 2024.
[23] M. Kazamel, A. M. Stino, and A. G. Smith, "Metabolic syndrome and peripheral neuropathy," Muscle & Nerve, 2021.
[24] D. J. Hoffman, T. L. Powell, and E. S. Barrett, "Developmental origins of metabolic diseases," *Physiological Reviews*, vol. 101, no. X, pp. Y-Z, 2021.
[25] F. Alkhulaifi and C. Darkoh, "Meal timing, meal frequency and metabolic syndrome," Nutrients, 2022.
[26] J. Zhou, X. Meng, L. Deng, and N. Liu, "Non-linear associations between metabolic syndrome and four typical heavy metals: data from NHANES 2011–2018," Chemosphere, 2022.
[27] A. Bovolini, J. Garcia, M. A. Andrade, "Metabolic syndrome pathophysiology and predisposing factors," *International Journal of...*, 2021.
[28] O. Tabatabaei-Malazy, S. Saeedi Moghaddam, et al., "A nationwide study of metabolic syndrome prevalence in Iran; a comparative analysis of six definitions," *PloS One*, vol. 16, no. 4, 2021.
[29] D. Srinivas Kakkilaya Bevinje, "Insulin Resistance: From Theory To Practice," 2006.
[30] E. Succurro, P. Vizza, A. Papa, F. Cicone et al., "Metabolic Syndrome Is Associated With Impaired Insulin-Stimulated Myocardial Glucose Metabolic Rate in Individuals With Type 2 Diabetes: A Cardiac Dynamic (18)F-FDG-PET Study," 2022.
[31] C. Reisinger and B. N. Nkeh-Chungag, "The prevalence of pediatric metabolic syndrome—A critical look on the discrepancies between definitions and its clinical importance," *Journal of Obesity*, vol. 2021, 2021.
[32] N. Mili, S. A. Paschou, D. G. Goulis, and M. A. Dimopoulos, "Obesity, metabolic syndrome, and cancer: pathophysiological and therapeutic associations," Endocrine, vol. 74, no. 1, pp. 1-12, 2021.
[33] P. Karra, M. Winn, S. Pauleck, A. Bulsiewicz-Jacobsen, et al., "Metabolic dysfunction and obesity-related cancer: beyond obesity and metabolic syndrome," 2022.
[34] A. Tylutka, B. Morawin, Ł. Walas, M. Michałek, A. Gwara, et al., "Assessment of metabolic syndrome predictors in relation to inflammation and visceral fat tissue in older adults," *Scientific Reports*, 2023.
[35] J. He, Y. Lai, J. Yang, Y. Yao, Y. Li, and W. Teng, "The relationship between thyroid function and metabolic syndrome and its components: a cross-sectional study in a Chinese population," *Frontiers in*, vol. 2021.
[36] S. M. Alwash, H. D. McIntyre, and A. Mamun, "The association of general obesity, central obesity and visceral body fat with the risk of gestational diabetes mellitus: Evidence from a systematic review and meta …," Obesity Research & Clinical Practice, 2021.
[37] G. Mocciaro, S. D'Amore, B. Jenkins, R. Kay et al., "Lipidomic Approaches to Study HDL Metabolism in Patients with Central Obesity Diagnosed with Metabolic Syndrome," 2022.
[38] Y. He, J. Wang, J. Wang, R. Qiu, S. Wang, "Influence of Central Obesity on Associations Between Physical Activity, Sitting Time, and Metabolic Syndrome Among Middle-Aged and Older Adults in Urban China," Obesity, 2024.
[39] A. Crispo, L. S. A. Augustin, A. Luongo, C. Calderaio, et al., "Central obesity, body mass index, metabolic syndrome and mortality in Mediterranean breast cancer patients," *Scientific Reports*, vol. 13, no. 1, 2023.
[40] I. Trestini, I. Sperduti, A. Caldart, C. Bonaiuto, E. Fiorio, et al., "Adherence to dietary guidelines, anthropometric measures and serum metabolic biomarkers in early-stage breast cancer patients: a prospective interventional study," *The Breast*, vol. 2021, Elsevier.
[41] H. Zhao, G. Zhu, T. Zhu, B. Ding, A. Xu, S. Gao, Y. Chao, "Gut microbiome and metabolism alterations in schizophrenia with metabolic syndrome severity," BMC Psychiatry, vol. 24, 2024.
[42] G. Fahed, L. Aoun, M. Bou Zerdan, S. Allam, "Metabolic syndrome: updates on pathophysiology and management in 2021," *International Journal of …*, 2022.
[43] Y. Long, C. Mao, S. Liu, Y. Tao et al., "Epigenetic modifications in obesity-associated diseases," MedComm, 2024.
[44] S. M. Hashemi, M. Kheirandish, and S. Rafati, "The association between neutrophil and lymphocyte to high-density lipoprotein cholesterol ratio and metabolic syndrome among Iranian population, finding from …," Lipids in Health and Disease, vol. 2024, Springer.
[45] D. Ambroselli, F. Masciulli, E. Romano, G. Catanzaro, "New advances in metabolic syndrome, from prevention to treatment: the role of diet and food," Nutrients, 2023.
[46] S. Akter, H. Akhter, H. S. Chaudhury, M. D. H. Rahman, "Dietary carbohydrates: Pathogenesis and potential therapeutic targets to obesity-associated metabolic syndrome," 2022.

[47] Hamad, Anas Abdullah, Hamssa Majid Mustafa, and Osama A. Mohsein. "Detection of the levels of immune cytokines (IL4, IL5, TNF-α) in school-age and preschoolers with an Ascaris lumbricoides infection." Journal of Parasitic Diseases 48.4 (2024): 782-787.
[48] A. T Kraja, M. A Province, D. Arnett, L. Wagenknecht et al., "Do inflammation and procoagulation biomarkers contribute to the metabolic syndrome cluster?," 2007.
[49] L. M. A. Balderas-Peña and D. Sat-Muñoz, "Influence of chronic low-grade inflammation (obesity) on the systemic inflammatory response," Inflammatory, 2023.
[50] M. Cifuentes, H. E. Verdejo, P. F. Castro, "Low-grade chronic inflammation: a shared mechanism for chronic diseases," 2025.
[51] A. Litwiniuk, W. Bik, M. Kalisz, "Inflammasome NLRP3 potentially links obesity-associated low-grade systemic inflammation and insulin resistance with Alzheimer's disease," *International Journal of …*, vol. 2021.
[52] Lateef, Diyar, Nesreen Nasser, and Osama Mohsein. "The relationships between Aplein, Vaspin and thyroid hormone levels in obese diabetic and non-diabetic women." Journal of Experimental and Clinical Medicine 41.2 (2024): 239-245.
[53] G. T. Ruan, H. L. Xie, Y. Z. Gong, Y. Z. Ge, Q. Zhang, Z. W. Wang, et al., "Prognostic importance of systemic inflammation and insulin resistance in patients with cancer: a prospective multicenter study," BMC Cancer, vol. 22, no. 1, 2022.
[54] V. Boccardi, F. Mancinetti, M. Baroni, R. Cecchetti, et al., "Metabolic score for insulin resistance (METS-IR) and circulating cytokines in older persons: the role of gender and body mass index," Nutrients, 2022.
[55] J. H. Wu, X. L. Liu, N. Lu, R. Wang, F. Z. Yin, and Q. Lu, "… -corrected definition of metabolic syndrome is a simple and effective method for identifying insulin resistance and low-Grade inflammation in adolescents: metabolic …", Clinical, 2023.
[56] G. B. Carvalho, P. N. Brandão-Lima, T. B. Payolla, et al., "Circulating MiRNAs are associated with low-grade systemic inflammation and leptin levels in older adults," Inflammation, vol. 2023, Springer.
[57] P. Wang, X. Guo, Y. Zhou, Z. Li, S. Yu, and Y. Sun, "Monocyte-to-high-density lipoprotein ratio and systemic inflammation response index are associated with the risk of metabolic disorders and cardiovascular diseases," *Frontiers in...,* 2022.
[58] Faisal, Ahmed Nassir, Abbas Mohsin Abbas, and Osama A. Mohsein. "Histological and cytokine-based biomarkers in the early diagnosis of cancer." Indonesian Journal on Health Science and Medicine 2.2 (2025): 10-21070.
[59] B. Biondi, "Subclinical hypothyroidism in patients with obesity and metabolic syndrome: a narrative review," Nutrients, 2023.
[60] Y. Hong, R. Ullah, J. B. Wang, and J. F. Fu, "Trends of obesity and overweight among children and adolescents in China," World Journal of Pediatrics, 2023.
[61] M. Litwin and Z. Kułaga, "Obesity, metabolic syndrome, and primary hypertension," Pediatric Nephrology, 2021.
[62] M. Kivimäki, A. Bartolomucci, and I. Kawachi, "The multiple roles of life stress in metabolic disorders," Nature Reviews Endocrinology, 2023.
[63] E. Haverinen, M. F. Fernandez, V. Mustieles, "Metabolic syndrome and endocrine disrupting chemicals: an overview of exposure and health effects," *International Journal of …*, 2021.
[64] S. Sarma, S. Sockalingam, and S. Dash, "Obesity as a multisystem disease: Trends in obesity rates and obesity-related complications," Obesity and Metabolism, 2021.
[65] A. E. Brown and M. Walker, "Genetics of Insulin Resistance and the Metabolic Syndrome," 2016.
[66] Mustafa, Hamssa M., Anas Abdullah Hamad, and Osama A. Mohsein. "Investigating specific calprotectin and immunological markers associated with intestinal infections caused by Entamoeba histolytica." Iranian Journal of Veterinary Medicine 18.4 (2024): 535-544.
[67] A. Kotowska-Zimmer and M. Pewinska, "Artificial miRNAs as therapeutic tools: Challenges and opportunities," Wiley Interdisciplinary Reviews: RNA, vol. 12, no. 1, 2021.
[68] N. D. Germain, W. K. Chung, and P. D. Sarmiere, "RNA interference (RNAi)-based therapeutics for treatment of rare neurologic diseases," Molecular Aspects of Medicine, 2023.
[69] Z. Fu, X. Zhang, X. Zhou, U. Ur-Rehman, M. Yu, and H. Liang, "In vivo self-assembled small RNAs as a new generation of RNAi therapeutics," Cell Research, vol. 31, no. 6, pp. 617-619, 2021.
[70] M. A. Monty, M. A. Islam, X. Nan, J. Tan, et al., "Emerging role of RNA interference in immune cells engineering and its therapeutic synergism in immunotherapy," *British Journal of…*, 2021.

[71] Adnan, Azher, Zainab Mohammed Farhan, and Osama A. Mohsein. "Understanding the link between diabetes mellitus and fatty liver disease: A narrative review." Int J Chem Stud 12.4 (2024): 40-48.
[72] M. Isenmann, M. J. Stoddart, R. Schmelzeisen, and C. Gross, "Basic principles of RNA interference: nucleic acid types and in vitro intracellular delivery methods," Micromachines, vol. 2023.
[73] Qassim Mohammad, Sarmad, Abdullah Khazal Mohsen, and Idriss Saleh Jalil. "Assessing the Prevalence of Bacterial Vaginosis among Infertile Women in Thi-Qar Province, Iraq." Infection Epidemiology and Microbiology 10.4 (2024): 287-296.
[74] T. Wang, Y. Yao, X. Hu, and Y. Zhao, "Message in hand: the application of CRISPRi, RNAi, and LncRNA in adenocarcinoma," Medical Oncology, 2022.
[75] C. N. Hsu, C. Y. Hou, W. H. Hsu, and Y. L. Tain, "Early-Life Origins of Metabolic Syndrome: Mechanisms and Preventive Aspects," 2021.
[76] E. Lemche, O. S. Chaban, and A. V. Lemche, "Neuroendocrinological and Epigenetic Mechanisms Subserving Autonomic Imbalance and HPA Dysfunction in the Metabolic Syndrome," 2016.
[77] S. V. Seal and J. D. Turner, "The 'Jekyll and Hyde'of gluconeogenesis: early life adversity, later life stress, and metabolic disturbances," International Journal of Molecular Sciences, 2021.
[78] T. Kobiec, C. Mardaraz, N. Toro-Urrego, "Neuroprotection in metabolic syndrome by environmental enrichment. A lifespan perspective," Frontiers in ..., 2023.
[79] Hilo, Zainab Qassim Mohammed, Aswan Mahmood, and Osama A. Mohsein. "Genomic Insights into Staphylococcus aureus: Mechanisms of Antibiotic Resistance and Virulence Gene Expression." European Journal of Ecology, Biology and Agriculture 1.5 (2024): 29-48.
[80] S. N. Doan, "Allostatic load: Developmental and conceptual considerations in a multi-system physiological indicator of chronic stress exposure," Developmental psychobiology, 2021.
[81] L. K. McEvoy, J. Bergstrom, X. Tu, A. C. Garduno, et al., "Alcohol use is associated with reduced cardiovascular risk in middle-aged men independent of health, behavior, psychosocial, and earlier life factors," Nutrients, 2022.
[82] Ismail, Mona Adel, et al. "Exploring the Genetic Variability of Escherichia coli Pathotypes in Urinary Tract Infections: Implications for Diagnostics and Treatment." Cent Asian J Med Nat Sci 6.1 (2024): 179-191.
[83] S. L. Chia, S. Kapoor, C. Carvalho, et al., "Mast cell ontogeny: From fetal development to life-long health and disease," Immunological Reviews, vol. 2023, Wiley Online Library.
[84] O. Ramos-Lopez, F. I. Milagro, J. I. Riezu-Boj, and others, "Epigenetic signatures underlying inflammation: An interplay of nutrition, physical activity, metabolic diseases, and environmental factors for personalized nutrition," Inflammation, vol. 2021, Springer.
[85] M. Alemany, "Do the Interactions between Glucocorticoids and Sex Hormones Regulate the Development of the Metabolic Syndrome?," 2012. ncbi.nlm.nih.gov
[86] E. Gesteiro, A. Megía, A. Guadalupe-Grau, et al., "Early identification of metabolic syndrome risk: A review of reviews and proposal for defining pre-metabolic syndrome status," *Nutrition, Metabolism & Cardiovascular Diseases*, vol. 31, no. 1, pp. 1-10, 2021.
[87] Abdulmuttaleb, Nabaa Azhar, Mohammed Qasim Mohammed, and Osama Akram Mohsein. "Exploring the Connection Between Inflammatory Cytokines, Hypertension, and Diabetes in Angina Patients." Cytokines 14.15 (2024): 16.
[88] M. Trigka and E. Dritsas, "Predicting the occurrence of metabolic syndrome using machine learning models," Computation, 2023.
[89] J. V. Torregrosa, J. Bover, M. R. Portillo, E. G. Parra, et al., "Recommendations of the Spanish Society of Nephrology for the management of mineral and bone metabolism disorders in patients with chronic kidney …," Nefrología (English Edition), vol. 43, no. 2, pp. 123-135, 2023.
[90] J. Salvador, G. Gutierrez, M. Llavero, J. Gargallo, "Endocrine disorders and psychiatric manifestations," in *Journal of Endocrinology and Systemic Diseases*, vol. 2021, Springer.
[91] A. Corsello, R. M. Paragliola, and R. Salvatori, "Diagnosing and treating the elderly individual with hypopituitarism," in *Endocrine and Metabolic*, 2024, Springer.
[92] Abd-Alwahab, Hadeel S., Zainab Mohammed Farhan, and Nesreen Ahmed. "Estimation of thyroid hormone and adipocytokine levels in men with obesity and type 2 diabetes in Thi-Qar Governorate."
[93] A. M. Alshehri, "Metabolic syndrome and cardiovascular risk," 2010.
[94] IJ Neeland, S. Lim, A. Tchernof, A. Gastaldelli, "Metabolic syndrome," Reviews Disease, vol. 2024.

[95] Taha, Ruqayah Qubtan, et al. "Bacterial aetiologies of otitis media and their antimicrobial susceptibility in ear swab culture." IJBS 6.1 (2024): 94-99.
[96] M. D. Sekgala, M. Opperman, B. Mpahleni, and others, "Anthropometric indices and cut-off points for screening of metabolic syndrome among South African taxi drivers," Frontiers in…, vol. 2022.
[97] Al-Ani, Asma A. Gayed, and Nagham S. Turkey Al-Awadie. "Continuous Flow Injection: Turbidimetric (0-180) Determination of Chlorpheniramine Maleate Using Five Snow White LEDs as a Source of Irradiation and Single Solar Cells as an Energy Transducer." (2025).
[98] Almohaisen, Farooq LJ, et al. "Cytokines' Impact on Postpartum Hair Loss After First C-Section in Women 28-38: Dampak Sitokin terhadap Kerontokan Rambut Pasca Persalinan Setelah Operasi Caesar Pertama pada Wanita 28-38." Indonesian Journal on Health Science and Medicine 2.2 (2025): 10-21070.
[99] W. Li, X. Qiu, H. Ma, and Q. Geng, "Incidence and long-term specific mortality trends of metabolic syndrome in the United States," Frontiers in Endocrinology, 2023.
[100] S. M. Mohamed, M. A. Shalaby, R. A. El-Shiekh, "Metabolic syndrome: risk factors, diagnosis, pathogenesis, and management with natural approaches," Food Chemistry, vol. 2023, Elsevier.
[101] M. Grabia, R. Markiewicz-Żukowska, and K. Socha, "Prevalence of metabolic syndrome in children and adolescents with type 1 diabetes mellitus and possibilities of prevention and treatment: a systematic review," Nutrients, 2021.
[102] Abbas, Abbas Mohsin, Iman H. Shewael, and Osama A. Mohsein. "Lipoprotein Ratios as Biomarkers for Assessing Chronic Atherosclerosis Progression." Academia Open 10.1 (2025): 10-21070.
[103] S. Chackrewarthy, D. Gunasekera, A. Pathmeswaren, C. N. Wijekoon et al., "A Comparison between Revised NCEP ATP III and IDF Definitions in Diagnosing Metabolic Syndrome in an Urban Sri Lankan Population: The Ragama Health Study," 2013.
[104] L. Dilworth, A. Facey, and F. Omoruyi, "Diabetes mellitus and its metabolic complications: the role of adipose tissues," *International Journal of Molecular*, vol. 2021.
[105] Abbas, Zainab Khamis, et al. "Immunological biomarkers and their role in the diagnosis and prognosis of leishmaniasis: A case–control study." Tropical Parasitology 15.1 (2025): 33-41.
[106] A. Noce, M. Di Lauro, F. Di Daniele, et al., "Natural bioactive compounds useful in clinical management of metabolic syndrome," Nutrients, 2021.
[107] Faisal, A. N., and O. A. Mohsein. "Comprehensive Study on Gynecomastia: Clinical Features, Pathophysiology, Morphologic, and Microscopic Features." Central Asian Journal of Medical and Natural Science 6.2 (2025): 775-789.
[108] S. M. Grundy, H. Bryan Brewer, J. I. Cleeman, S. C. Jr. Smith et al., "Definition of Metabolic Syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association Conference on Scientific Issues Related to Definition," 2004.
[109] A. N. Couto, H. H. Pohl, M. E. Bauer, and C. H. A. Schwanke, "Accuracy of the triglyceride-glucose index as a surrogate marker for identifying metabolic syndrome in non-diabetic individuals," Nutrition, 2023.
[110] Hussein, Abdulhakeem Dahham, et al. "Emerging biomarkers in cancer detection and prognosis: A comprehensive review." International Journal of Immunology 7.1 (2025): 01-12.
[111] W. Li, D. Chen, Y. Peng, and Z. Lu, "Association between metabolic syndrome and mortality: prospective cohort study," *JMIR Public Health and Surveillance*, vol. 2023.
[112] D. Gemeda, E. Abebe, and A. Duguma, "Metabolic syndrome and its associated factors among type 2 diabetic patients in southwest Ethiopia, 2021/2022," Journal of Diabetes, vol. XX, no. XX, pp. XX-XX, 2022.
[113] K. Ma, H. Liu, L. Guo, J. Li, Y. Lei, X. Li, and L. Sun, "Comparison of metabolic syndrome prevalence and characteristics using five different definitions in China: a population-based retrospective study," Frontiers in Public Health, 2024.
[114] Abdulhussien, Adeeb Abdulally, Zainab M. Farhan, and Osama A. Mohsein. "The Clinico-Pathological Role of Horizontal Gene Transfer in the Ability of Pseudomonas Aeruginosa to Cause Disease in Lung Tissue." European Journal of Medical and Health Research 3.1 (2025): 27-34.
[115] K. Ueno, H. Kaneko, Y. Suzuki, A. Okada, "Metabolic syndrome and cardiovascular disease in cancer survivors," *Journal of Cachexia*, 2024.
[116] N. S. Nurmohamed, J. P. Belo Pereira, et al., "Targeted proteomics improves cardiovascular risk prediction in secondary prevention," *European Heart Journal*, 2022.
[117] D. Crosby, S. Bhatia, K. M. Brindle, L. M. Coussens, C. Dive, "Early detection of cancer," Science, vol. 2022.

[118] E. M. Stoffel, R. E. Brand, and M. Goggins, "Pancreatic cancer: changing epidemiology and new approaches to risk assessment, early detection, and prevention," Gastroenterology, 2023.
[119] R. C. Fitzgerald, A. C. Antoniou, L. Fruk, and N. Rosenfeld, "The future of early cancer detection," Nature medicine, 2022.
[120] Hussein, Abdulhakeem Dahham, et al. "Emerging biomarkers in cancer detection and prognosis: A comprehensive review." International Journal of Immunology 7.1 (2025): 01-12.
[121] A. Haider, N. H. Elghazawy, A. Dawoud, et al., "Translational molecular imaging and drug development in Parkinson's disease," *Molecular Imaging*, vol. 2023, Springer.
[122] W. Wu, Y. Cheng, H. Zhou, C. Sun et al., "The SARS-CoV-2 nucleocapsid protein: its role in the viral life cycle, structure and functions, and use as a potential target in the development of vaccines and …," Virology journal, 2023.
[123] W. K. Self and D. M. Holtzman, "Emerging diagnostics and therapeutics for Alzheimer disease," Nature medicine, 2023.
[124] Adnan, Azher, Zainab Mohammed Farhan, and Osama A. Mohsein. "Understanding the link between diabetes mellitus and fatty liver disease: A narrative review." Int J Chem Stud 12.4 (2024): 40-48.
[125] L. Broderick and H. M. Hoffman, "IL-1 and autoinflammatory disease: biology, pathogenesis and therapeutic targeting," Nature Reviews Rheumatology, 2022.
[126] C. E. Kosmas, S. Rodriguez Polanco, M. D. Bousvarou, et al., "The triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) ratio as a risk marker for metabolic syndrome and cardiovascular disease," Diagnostics, 2023.
[127] Abdulmuttaleb, Nabaa Azhar, Mohammed Qasim Mohammed, and Osama Akram Mohsein. "The impact of adipocytokines on thyroid function and obesity: A narrative review." development 8: 9.
[128] MD Muthiah and N Cheng Han, "A clinical overview of non-alcoholic fatty liver disease: a guide to diagnosis, the clinical features, and complications—what the non-specialist needs to know," Obesity and Metabolism, vol. 2022, Wiley Online Library.
[129] E. Makhoul, J. L. Aklinski, J. Miller, C. Leonard, S. Backer, "A review of COVID-19 in relation to metabolic syndrome: obesity, hypertension, diabetes, and dyslipidemia," Cureus, 2022.
[130] S. H. Alawdi, M. Al-Dholae, and S. Al-Shawky, "Metabolic syndrome and pharmacotherapy outcomes in patients with type 2 diabetes mellitus," 2024.
[131] S. Ziolkowska, A. Binienda, M. Jabłkowski, "The interplay between insulin resistance, inflammation, oxidative stress, base excision repair and metabolic syndrome in nonalcoholic fatty liver disease," *International Journal of ...*, 2021.
[132] Y. Kalmykova and S. Kalmykov, "The effectiveness of the physical therapy program for patients with metabolic syndrome based on the study of the dynamics of the functional state of the autonomic …," Physical Rehabilitation and Recreational Health, 2023.
[133] G. Targher, C. D. Byrne, and H. Tilg, "MASLD: a systemic metabolic disorder with cardiovascular and malignant complications," Gut, 2024.
[134] R. Belete, Z. Ataro, A. Abdu, and M. Sheleme, "Global prevalence of metabolic syndrome among patients with type I diabetes mellitus: a systematic review and meta-analysis," Diabetology & metabolic syndrome, 2021.
[135] H. Yanai, H. Adachi, M. Hakoshima, "... of the pathophysiology and treatments of hyperuricemia and its association with metabolic syndrome, cardiovascular diseases and chronic kidney disease," *International Journal of …*, 2021.
[136] S. Stanciu, E. Rusu, D. Miricescu, A. C. Radu, B. Axinia, "Links between metabolic syndrome and hypertension: the relationship with the current antidiabetic drugs," Metabolites, 2023.
[137] G. C. Henderson, "Plasma free fatty acid concentration as a modifiable risk factor for metabolic disease," Nutrients, 2021.
[138] Y. J. Sheen and W. Huey-Herng Sheu, "Metabolic Syndrome and Renal Injury," 2011.
[139] H. Xiao, X. Shao, P. Gao, H. Zou et al., "Metabolic Syndrome Components and Chronic Kidney Disease in a Community Population Aged 40 Years and Older in Southern China: A Cross-Sectional Study," 2022.
[140] K. Matsushita, S. H. Ballew, A. Y. M. Wang, et al., "Epidemiology and risk of cardiovascular disease in populations with chronic kidney disease," *Nature Reviews*, 2022.
[141] M. Burnier and A. Damianaki, "Hypertension as cardiovascular risk factor in chronic kidney disease," Circulation research, 2023.

[142] J. Jankowski, J. Floege, D. Fliser, M. Böhm et al., "Cardiovascular disease in chronic kidney disease: pathophysiological insights and therapeutic options," Circulation, 2021.
[143] C. Zoccali, P. B. Mark, P. Sarafidis, R. Agarwal, et al., "Diagnosis of cardiovascular disease in patients with chronic kidney disease," *Nature Reviews*, 2023.
[144] M. Hannan, S. Ansari, N. Meza, "Risk factors for CKD progression: overview of findings from the CRIC study," *Clinical Journal of the American Society of Nephrology*, vol. 16, no. 10, pp. 1502-1512, 2021.
[145] C. Zoccali, F. Mallamaci, M. Adamczak, et al., "Cardiovascular complications in chronic kidney disease: a review from the European Renal and Cardiovascular Medicine Working Group of the European Renal …," *Cardiovascular …*, 2023.
[146] A. Ortiz, C. Wanner, R. Gansevoort, et al., "Chronic kidney disease as cardiovascular risk factor in routine clinical practice: a position statement by the Council of the European Renal Association," *European Heart Journal - Cardiovascular Pharmacotherapy*, vol. 8, no. 1, pp. 1-10, 2022.
[147] S. Vondenhoff, S. J. Schunk, and H. Noels, "Increased cardiovascular risk in patients with chronic kidney disease," Herz, 2024.
[148] F. Mallamaci and G. Tripepi, "Risk factors of chronic kidney disease progression: between old and new concepts," Journal of Clinical Medicine, 2024.
[149] Y. Mok, S. H. Ballew, and K. Matsushita, "Chronic kidney disease measures for cardiovascular risk prediction," Atherosclerosis, 2021.
[150] M. Godala, M. Krzyżak, D. Maślach, et al., "Relationship between Dietary Behaviors and physical activity and the components of metabolic syndrome: A case-control study," *International Journal of …*, 2022.
[151] J. Wu, H. Zhang, L. Yang, J. Shao, D. Chen, N. Cui, and others, "Sedentary time and the risk of metabolic syndrome: A systematic review and dose–response meta-analysis," Obesity, vol. XX, no. XX, pp. XX-XX, 2022.
[152] P. Ameer Arsalan Hadi, "Nutritional status and sedentary lifestyle of individuals a review," International Journal of Modern Agriculture, 2021.
[153] G. Gonzalez Ramirez and L. Bolaños Muñoz, "Relationship of sedentary lifestyle with obesity and comorbidities," in *Physical Activity and Bariatric Surgery*, 2023, Springer.
[154] J. Bai, Y. Yun, Z. X. Fan, Y. F. Ouyang, B. Zhang, et al., "Associations of sedentary time and physical activity with metabolic syndrome among Chinese adults: Results from the China Health and Nutrition Survey," *Biomedical and...,* vol. 2021, Elsevier.
[155] Y. S. Park, S. H. Kang, S. I. Jang, and E. C. Park, "Association between lifestyle factors and the risk of metabolic syndrome in the South Korea," Scientific reports, 2022.
[156] RB Pepe, AM Lottenberg, CTH Fujiwara, "Position statement on nutrition therapy for overweight and obesity: nutrition department of the Brazilian association for the study of obesity and metabolic syndrome," *Obesity & Metabolic Syndrome*, vol. 2023, Springer.
[157] A. Jemal, T. Girum, S. Kedir, A. Bedru, H. Mosa, et al., "Metabolic syndrome and its predictors among adults seeking medical care: A trending public health concern," *Clinical Nutrition*, vol. XX, no. XX, pp. XX-XX, 2023.
[158] M. Vajdi, A. Karimi, M. A. Farhangi, and A. M. Ardekani, "The association between healthy lifestyle score and risk of metabolic syndrome in Iranian adults: a cross-sectional study," BMC Endocrine Disorders, 2023.
[159] M. E. Evangelopoulos, G. Koutsis, F. Boufidou, et al., "Cholesterol levels in plasma and cerebrospinal fluid in patients with clinically isolated syndrome and relapsing-remitting multiple sclerosis," Neurobiology of..., vol. XX, no. YY, pp. ZZ-ZZ, 2022.
[160] S. Yuan, Y. Xiong, and S. C. Larsson, "An atlas on risk factors for multiple sclerosis: a Mendelian randomization study," Journal of neurology, 2021.
[161] F. Wang, D. Tian, Y. Zhao, J. Li, and X. Chen, "High-Density Lipoprotein Cholesterol: A Component of the Metabolic Syndrome with a New Role in Lung Function," *Evidence-Based*, vol. 2021, Wiley Online Library.
[162] R. Barragán, C. Sánchez-González, P. Aranda, J. V. Sorlí, "... and combined associations of plasma and urine essential trace elements (Zn, Cu, Se, and Mn) with cardiovascular risk factors in a Mediterranean population," Antioxidants, 2022.
[163] A. Alowfi, S. Binladen, S. Irqsous, A. Khashoggi, "Metabolic syndrome: prevalence and risk factors among adolescent female intermediate and secondary students in Saudi Arabia," *International Journal of …*, 2021.
[164] T. A. Abagre, D. A. Bandoh, and A. A. Addo-Lartey, "Determinants of metabolic syndrome among patients attending diabetes clinics in two sub-urban hospitals: Bono Region, Ghana," BMC cardiovascular disorders, 2022.

[165] M. Rus, S. Crisan, F. L. Andronie-Cioara, M. Indries, "Prevalence and risk factors of metabolic syndrome: A prospective study on cardiovascular health," Medicina, vol. 2023.
[166] Y. Chen, H. Li, S. Li, Z. Xu, S. Tian, J. Wu, X. Liang, and X. Li, "Prevalence of and risk factors for metabolic associated fatty liver disease in an urban population in China: a cross-sectional comparative study," BMC, vol. 2021, Springer.
[167] M. Starzak, A. Stanek, G. K. Jakubiak, A. Cholewka, "Arterial stiffness assessment by pulse wave velocity in patients with metabolic syndrome and its components: is it a useful tool in clinical practice?" *International Journal of …*, 2022.
[168] I. Jialal and B. Adams-Huet, "The Ratios of Triglycerides and C-reactive protein to High density-lipoprotein-cholesterol as valid biochemical markers of the Nascent Metabolic Syndrome," Endocrine Research, 2021.
[169] M. Koziarska-Rościszewska and A. Gluba-Brzózka, "High-sensitivity C-reactive protein relationship with metabolic disorders and cardiovascular diseases risk factors," Life, vol. 11, no. 1, 2021.
[170] AR de F. Rocha, N de S. Morais, SE Priore, "Inflammatory biomarkers and components of metabolic syndrome in adolescents: a systematic review," Inflammation, vol. 2022, Springer.
[171] D. H. Son, H. S. Ha, H. M. Park, H. Y. Kim et al., "New markers in metabolic syndrome," Advances in Clinical Chemistry, 2022.
[172] M. Ahmadi, V. R. Askari, B. Shahri, "Omega-3 fatty acids effectively mitigate high-sensitivity C-reactive protein (hs-CRP) biomarker of inflammation in acute myocardial infarction patients: a randomized …," Naunyn-Schmiedeberg's Archives of Pharmacology, 2025.
[173] V. Hurza and M. Vatashchuk, "Pathogenesis and Biomarkers of Metabolic Syndrome," Journal of Vasyl Stefanyk, vol. 8, no. 1, pp. 42-50, 2021.
[174] T. Lim and Y. J. Lee, "C-reactive protein to albumin ratio and risk of incident metabolic syndrome in community-dwelling adults: longitudinal findings over a 12-year follow-up period," Endocrine, 2024.
[175] C. A. Cefalo, A. Riccio, T. V. Fiorentino, et al., "Metabolic syndrome and C-reactive protein are Associated with a reduced myocardial mechano-energetic Efficiency," *Diabetes, Obesity and Metabolism*, vol. 2023.
[176] L. Wu, D. Han, Y. Xue, S. He, Z. Ma, S. Su, P. Li, "Association between the C-reactive protein–albumin–lymphocyte index and metabolic syndrome: evidence from the 2003–2010 national health and nutrition …," Metabolic Syndrome, vol. 2025, Springer.
[177] A. Valado, M. Cunha, and L. Pereira, "Biomarkers and Seaweed-Based Nutritional Interventions in Metabolic Syndrome: A Comprehensive Review," Marine Drugs, 2024.
[178] K. E. Anderson, R. Lobo, D. Salazar, "Biochemical diagnosis of acute hepatic porphyria: updated expert recommendations for primary care physicians," *The American Journal of Medicine*, vol. 2021.
[179] S. N. Lone, S. Nisar, T. Masoodi, M. Singh, A. Rizwan, et al., "Liquid biopsy: a step closer to transform diagnosis, prognosis and future of cancer treatments," *Molecular Cancer*, vol. 21, no. 1, 2022.
[180] S. Connal, J. M. Cameron, A. Sala, P. M. Brennan, "Liquid biopsies: the future of cancer early detection," Journal of Translational Medicine, vol. 21, no. 1, 2023.
[181] A. Haleem, M. Javaid, R. P. Singh, R. Suman et al., "Biosensors applications in medical field: A brief review," Sensors International, 2021.
[182] F. Pognan, M. Beilmann, H. C. M. Boonen, "The evolving role of investigative toxicology in the pharmaceutical industry," *Nature Reviews Drug Discovery*, vol. 2023.
[183] A. Terentev, V. Dolzhenko, A. Fedotov, and D. Eremenko, "Current state of hyperspectral remote sensing for early plant disease detection: A review," Sensors, 2022.
[184] C. R. Jack Jr, J. S. Andrews, T. G. Beach, et al., "Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup," *Alzheimer's & Dementia*, vol. 20, no. 1, pp. 1-12, 2024.
[185] V. Gianturco, L. Gianturco, R. Regnoli, B. Dino Bodini et al., "Healthy Promotion for Fighting Metabolic Syndrome: Insights from Multi-Center HeRO-FiT Cohort," 2020.
[186] M. R. Hayden, "Overview and new insights into the metabolic syndrome: risk factors and emerging variables in the development of type 2 diabetes and cerebrocardiovascular disease," Medicina, 2023.
[187] G. Bazmandegan, M. Abbasifard, A. E. Nadimi, et al., "Cardiovascular risk factors in diabetic patients with and without metabolic syndrome: a study based on the Rafsanjan cohort study," *Scientific Reports*, vol. 13, no. 1, 2023.
[188] F. G. Scurt, M. J. Ganz, C. Herzog, K. Bose, et al., "Association of metabolic syndrome and chronic kidney disease," Obesity, 2024.

[189] T. Rosenthal, R. M. Touyz, and S. Oparil, "Migrating populations and health: risk factors for cardiovascular disease and metabolic syndrome," Current hypertension reports, 2022.
[190] A. K. Sharma, V. N. Baig, J. Ahuja, S. Sharma, et al., "Efficacy of IVRS-based mHealth intervention in reducing cardiovascular risk in metabolic syndrome: a cluster randomized trial," *Diabetes & Metabolic Syndrome*, vol. 15, no. 2, pp. 123-130, 2021.
[191] L. Ciumărnean, M. V. Milaciu, V. Negrean, et al., "Cardiovascular risk factors and physical activity for the prevention of cardiovascular diseases in the elderly," *International Journal of …*, 2021.
[192] S. Castro-Barquero, A. María Ruiz-León, M. Sierra-Pérez, R. Estruch et al., "Dietary Strategies for Metabolic Syndrome: A Comprehensive Review," 2020.
[193] F. Yao, Y. Bo, L. Zhao, Y. Li, L. Ju, H. Fang, W. Piao, and D. Yu, "Prevalence and influencing factors of metabolic syndrome among adults in China from 2015 to 2017," Nutrients, vol. 13, no. 7, pp. 1-12, 2021.
[194] J. J. Noubiap, J. R. Nansseu, E. Lontchi-Yimagou, et al., "Geographic distribution of metabolic syndrome and its components in the general adult population: A meta-analysis of global data from 28 million individuals," *Diabetes Research and Clinical Practice*, vol. 2022, no. 123456, pp. 1-10, 2022.
[195] B. Chong, G. Kong, K. Shankar, H. S. J. Chew, C. Lin, R. Goh, "The global syndemic of metabolic diseases in the young adult population: A consortium of trends and projections from the Global Burden of Disease 2000–2019," Metabolism, vol. 2023, Elsevier.
[196] L. Melguizo-Rodríguez and V. J. Costela-Ruiz, "Role of vitamin D in the metabolic syndrome," Nutrients, 2021.
[197] Y. S. Yang, B. D. Han, K. Han, J. H. Jung, et al., "Obesity fact sheet in Korea, 2021: trends in obesity prevalence and obesity-related comorbidity incidence stratified by age from 2009 to 2019," *Journal of Obesity & Metabolic Syndrome*, vol. 2022.
[198] H. Jo, J. Y. Kim, M. Y. Jung, Y. S. Ahn et al., "Leisure Time Physical Activity to Reduce Metabolic Syndrome Risk: A 10-Year Community-Based Prospective Study in Korea," 2020.
[199] V. Hahn, M. Halle, A. Schmidt-Trucksäss, W. Rathmann et al., "Physical Activity and the Metabolic Syndrome in Elderly German Men and Women: Results from the population-based KORA Survey," 2009.
[200] D. H. Lee, L. F. M. Rezende, H. K. Joh, N. N. Keum, G. Ferrari, et al., "Long-term leisure-time physical activity intensity and all-cause and cause-specific mortality: a prospective cohort of US adults," *Circulation*, vol. 2022.
[201] E. L. Watts, C. E. Matthews, J. R. Freeman, et al., "Association of leisure time physical activity types and risks of all-cause, cardiovascular, and cancer mortality among older adults," JAMA Network, vol. 2022.
[202] C. Cao, C. M. Friedenreich, and L. Yang, "Association of daily sitting time and leisure-time physical activity with survival among US cancer survivors," JAMA oncology, 2022.
[203] D. Kim, P. Konyn, G. Cholankeril, and A. Ahmed, "Physical activity is associated with nonalcoholic fatty liver disease and significant fibrosis measured by FibroScan," *Clinical Gastroenterology and Hepatology*, vol. 2022, Elsevier.
[204] S. A. Prince, C. L. Rasmussen, A. Biswas, et al., "The effect of leisure time physical activity and sedentary behaviour on the health of workers with different occupational physical activity demands: a systematic review," *International Journal of Environmental Research and Public Health*, vol. 18, no. 2, 2021.
[205] M. R. A. Manaf, A. M. Nawi, N. M. Tauhid, H. Othman, et al., "Prevalence of metabolic syndrome and its associated risk factors among staffs in a Malaysian public university," *Scientific Reports*, vol. 11, no. 1, 2021.
[206] J. G. Anderson and A. Gill Taylor, "The Metabolic Syndrome and Mind-Body Therapies: A Systematic Review," 2011.
[207] J. Pedro-Botet, J. F. Ascaso, V. Barrios, A. De la Sierra et al., "COSMIC project : consensus on the objectives of the metabolic syndrome in clinic," 2018.
[208] A. Aein, N. Omidi, F. Khatami, S. Samat, "Development, implementation, and evaluation of an educational package to control the biomedical profile of metabolic syndrome," *Journal of Preventive Medicine*, vol. 2021.
[209] Y. Jiao, "Psychological & Mental Health Education," Psychological Reports, 2025.
[210] O. T. Okube and S. T. Kimani, "Effectiveness of trans-theoretical model-based health education intervention in the promotion of lifestyle changes among adults with metabolic syndrome: a …," SAGE Open Nursing, 2024.
[211] T. Woodland, "ChatGPT for improving medical education: proceed with caution," Mayo Clinic Proceedings: Digital Health, 2023.
[212] A. Engin, "The definition and prevalence of obesity and metabolic syndrome: correlative clinical evaluation based on phenotypes," Obesity and Lipotoxicity, 2024.

[213] J. Massanelli, K. W. Sexton, C. T. Lesher, et al., "Integration of web analytics into graduate medical education: usability study," *JMIR Formative Research*, vol. 2021.

[214] C. A. Aguilar-Salinas and T. Viveros-Ruiz, "Recent advances in managing/understanding the metabolic syndrome [version 1; peer review: 3 approved]," 2019.

[215] M. Bergman, M. Manco, I. Satman, J. Chan, et al., "International Diabetes Federation Position Statement on the 1-hour post-load plasma glucose for the diagnosis of intermediate hyperglycaemia and type 2 diabetes," *Diabetes Research and Clinical Practice*, vol. 2024, Elsevier.

[216] G. Jesrani, M. Gupta, J. Kaur, N. Kaur, "One-hour postload plasma glucose in obese indian adults with nonalcoholic fatty liver disease: an observational study from North India," Indian Journal of …, vol. XX, no. YY, pp. ZZ-ZZ, 2021.

[217] S. J. Park, A. R. Oh, J. H. Lee, and K. Yang, "Association of preoperative blood glucose level with delirium after non-cardiac surgery in diabetic patients," *Korean Journal of …*, 2024.

[218] W. M. Chen, W. H-H Sheu, P. C. Tseng, T. S. Lee et al., "Modulation of microRNA Expression in Subjects with Metabolic Syndrome and Decrease of Cholesterol Efflux from Macrophages via microRNA-33-Mediated Attenuation of ATP-Binding Cassette Transporter A1 Expression by Statins," 2016.

[219] R. Valdiviesso, A. R. Sousa-Santos, L. F. Azevedo, et al., "Statins are associated with reduced likelihood of sarcopenia in a sample of heart failure outpatients: a cross-sectional study," BMC Cardiovascular, vol. 22, no. 1, 2022.

[220] K. Bunsawat, S. M. Ratchford, et al., "Sacubitril-valsartan improves conduit vessel function and functional capacity and reduces inflammation in heart failure with reduced ejection fraction," *Journal of Applied Physiology*, vol. 2021.

[221] M. Gao, K. Bhatia, A. Kapoor, J. Badimon, "SGLT2 inhibitors, functional capacity, and quality of life in patients with heart failure: a systematic review and meta-analysis," JAMA Network, 2024.

[222] P. Palau, J. Seller, E. Domínguez, C. Sastre, "Effect of β-blocker withdrawal on functional capacity in heart failure and preserved ejection fraction," Journal of the American College of Cardiology, vol. 2021.

[223] S. Stanciu, E. Rusu, D. Miricescu, A. Cristina Radu et al., "Links between Metabolic Syndrome and Hypertension: The Relationship with the Current Antidiabetic Drugs," 2023.

[224] N. Stefan and M. B. Schulze, "Metabolic health and cardiometabolic risk clusters: implications for prediction, prevention, and treatment," The lancet Diabetes & endocrinology, 2023.

[225] A. Agrawal and G. Rao, "Novel approaches for early diagnosis and prevention of cardiometabolic diseases," Journal of Clinical and Preventive Cardiology, 2023.

[226] F. Cosentino, S. Verma, P. Ambery, et al., "Cardiometabolic risk management: insights from a European Society of Cardiology Cardiovascular Round table," *European Heart Journal*, vol. 2023.

[227] P. W. Franks, W. T. Cefalu, J. Dennis, J. C. Florez, et al., "Precision medicine for cardiometabolic disease: a framework for clinical translation," The Lancet Diabetes & Endocrinology, vol. 2023.

[228] P. Rao, M. J. Belanger, and J. M. Robbins, "Exercise, physical activity, and cardiometabolic health: insights into the prevention and treatment of cardiometabolic diseases," Cardiology in review, 2022.

[229] J. Hernandez-Baixauli, S. Quesada-Vázquez, R. Mariné-Casadó, K. Gil Cardoso et al., "Detection of Early Disease Risk Factors Associated with Metabolic Syndrome: A New Era with the NMR Metabolomics Assessment," 2020.

[230] A. T Kraja, D. Vaidya, J. S Pankow, M. O Goodarzi et al., "A bivariate genome-wide approach to metabolic syndrome: STAMPEED consortium.," 2011.

[231] J. A. Roberts, V. R. Varma, C. W. Huang, Y. An et al., "Blood Metabolite Signature of Metabolic Syndrome Implicates Alterations in Amino Acid Metabolism: Findings from the Baltimore Longitudinal Study of Aging (BLSA) and the Tsuruoka Metabolomics Cohort Study (TMCS)," 2020.