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OVERVIEW OF METABOLIC SYNDROME DIAGNOSIS AND MANAGEMENT

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Abstract:

Background: MetS patients has an increased risk of atherosclerosis, cardiovascular disease, and mortality rate overall due to a combination of aberrant laboratory and physical findings, including dyslipidemia, hypertension, glucose intolerance, proinflammatory state, and diabetes that effect body system. Worldwide, there are a few minor variations in how different organizations define metabolic syndrome. Appropriate identification of patients exhibiting symptoms of metabolic syndrome is crucial to ensure appropriate care and treatment, as well as reduce the likelihood of comorbidities.

Objective: In this review, we aim to investigate the biology of metabolic syndrome development as well as management strategies.

Methods: this review conducted using a comprehensive search of PubMed and google scholar from 1990 to 2023.

Conclusion: MetS is a complex disorder with various definitions and underlying mechanisms. Early detection and management are essential to prevent further complications. Lifestyle modifications, pharmacotherapy, and surgical interventions play critical roles in managing MetS and reducing associated health risks.

Keywords: MetS, diabetes mellitus, dyslipidemia, insulin resistance, obesity, CV mortality, pro-inflammatory state

INTRODUCTION:

MetS is a collection of disorders that increase the risk of developing DM 2 , CVD, and several malignancies. It is diagnosed by the co-occurrence of three out of five medical conditions: abdominal obesity, elevated BP, elevated FBG, high serum TG, and LDL-C levels. The underlying component of the syndrome is intraabdominal or visceral obesity, which leads to the development of various

metabolic abnormalities such as dyslipidemia, insulin resistance, endothelial dysfunction, hypertension, and a proinflammatory state[1]. The definition of MetS has minimal differences between organizations such as the WHO, AACE, NCEP ATP III, IDF, and EGIR (Table1). The diagnostic criteria of MetS suggested by WHO, AACE, and EGIR depend mainly on insulin resistance, oral glucose tolerance test, and/or hyperinsulinemia-euglycemic clamp, which is not practically used in the clinical setting. On the other hand, the NCEP ATPIII uses more practical, more reliable measures that do not apply to different ethnicities. Moreover, the limitations of the IDF criteria to diagnose MetS include the reliance on WC as a surrogate marker for abdominal obesity, defined based on national cutoff points. In addition, The IDF criteria also require additional diagnostic tests, such as 2-hour postprandial plasma glucose test, which may not be practical or feasible in all settings. Furthermore, the IDF criteria may not capture all individuals with MetS, as other factors, such as adipose tissue inflammation, are fundamental mechanisms of metabolic derangements. The multiple differences in definitions of MetS may lead to significant uncertainty on whether they refer to the same people and impact health. Another research study proposes a new definition of MetS to be the presence of obesity with two of the three criteria: impaired glucose metabolism, high BP, and elevated non-HDL-C (Figure 1)[2,3]. Besides that, it is implicated by other medical conditions such as obstructive sleep apnea, heart failure, impaired kidney function tests, polycystic ovarian syndrome, hyperuricemia, sympathetic activation, and chronic inflammations.

WHO	Insulin Resistance DM 2 Impaired FBG Impaired glucose tolerance If FG <110 mg/dl, hyperinsulinemia, euglycemic clamp-glucose uptake in the lowest 25%. Plus 2 of the following: BMI > 30kg/m^2 or waist to hip ration > 0.9 (male) and 0.85 (female). TG ≥ 150 mg/dl (1.7 mmol/l). HDL-c < 35 mg/dl (0.9 mmol/l) for male and < 39 mg/dl (1mmol/l) for female. BP ≥ 140/90 mmHg or on medication. Urinary albumin excretion ≥ 20 µg/min or albumin/creatinine ratio ≥ 30 mg/g.
AACE	TG ≥ 150 mg/dl (1.7 mmol/l). HDL-c < 40 mg/dl (1 mmol/L) for male or < 50 mg/dl (1.3 mmol/l) for female. BP ≥ 130/85 mmHg or on medications. 2 hours post OGTT-glycemia > 140mg/dl (7.8mmol/l) and > 200 mg/dl (mmol/l).
NCEP ATP III	Three or more of the following: Abdominal obesity: WC > 102 cm for males and 88 cm for females. TG ≥ 150 mg/dl (1.7 mmol/l). HDL-c < 40 mg/dl (1 mmol/L) for male or < 50 mg/dl (1.3 mmol/l) for female. BP ≥ 130/85 mmHg or on medications. FBG ≥ 110 mg/dl (6.1 mmol/l).
EGIR	insulin resistance- hyperinsulinemia: top 25% of fasting insulin values from non-diabetic population. Plus 2 or more of the following: WC ≥ 94 cm for males and 80 cm for females or BMI > 30 kg/m^2. FBG ≥ 110 mg/dl (6.1 mmol/l) and < 126 mg/dl (7mmol/l). TG≥ 180 mg/dl (2 mmol/l) or HDL-c ≤ 40 mg/dl (1 mmol/l). BP ≥ 140/90 mmHg or on medication.
IDF	Central obesity (WC ≥ 94 cm for Europid men and ≥ 80 cm for Europid women). Plus any 2 of the following: TG ≥ 150 mg/dl (1.7 mmol/l) or on medication. HDL-c < 40 mg/dl (1 mmol/L) for male or < 50 mg/dl (1.3 mmol/l) for female or on medication. Systolic BP ≥ 130 or diastolic BP ≥ 85 mmHg or on medication. FBG ≥ 100 mg/dl (5.6 mmol/l) or previously diagnosed DM 2.
Table (1): Definition of MetS according to WHO[1], AACE[2], NCEP ATP III[4], IDF[5], and EGIR[6].	

PATHOPHYSIOLOGY:

The pathophysiology of MetS involves a combination of risk factors and metabolic defects, including overnutrition and a sedentary lifestyle that contribute to elevated TG, decreased HDL-C, increased BP, and FBG. Also, imbalance between oxidants and antioxidants and low-grade inflammation play key roles in the manifestations. These increase insulin resistance, chronic inflammation, and neurohormonal disturbances [7].

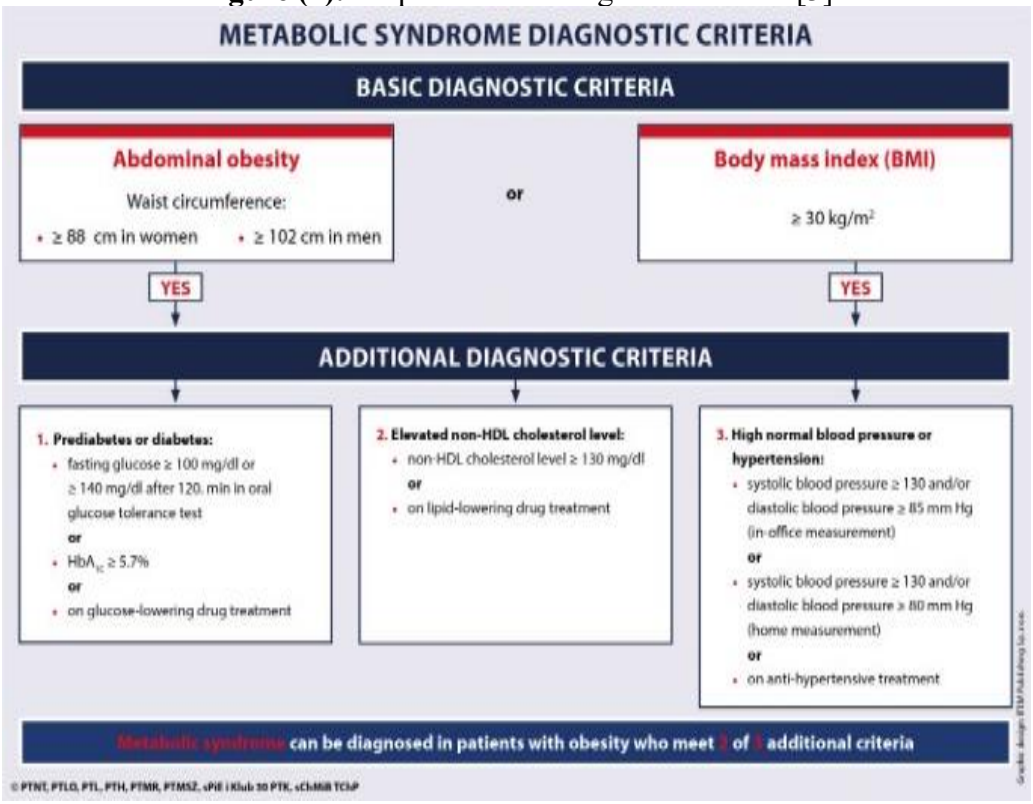
Obesity:
Obesity is considered one of the key elements of MetS and is influenced by several factors, like genetic, environmental, socioeconomic, and behavioral influences. The molecular interactions between white adipose tissue, the gastrointestinal tract, the gut microbiome, and immune cells contribute to the development of metabolic disease. Also, Abdominal fat synthesizes pro-inflammatory cytokines and adipokines, which contribute to insulin resistance and affect carbohydrate and fat metabolism; they play a crucial role in various metabolic abnormalities, including elevated FBG, TG, TC, and LDL-C, as well as decreased HDL-C levels [8,9]. Obesity can be diagnosed using various methods. One approach is to use anthropometric measurements such as BMI, HC, WC, and skin fold thickness, which may not accurately assess body fat percentage [1]. Another method involves measuring TG concentration in the blood. Other diagnostic elements, such as VFA and body composition parameters, must be considered for a comprehensive obesity evaluation [10]. BIA is a method that can be used to measure body fat percentage and provide a more accurate assessment of obesity [11]. Therefore, it is important to consider multiple diagnostic elements, including body fat percentage, when diagnosing obesity.

Insulin Resistance:
Insulin resistance is a complex syndrome that disrupts the normal cyclical pattern of insulin secretion, leading to decreased receptor availability and relative hyperinsulinemia. This disruption is associated with a reduction in β-cell mass and asynchronous insulin secretion in DM 2 [12]. Insulin resistance is the primary cause of DM 2, increasing insulin secretion, beta-cell exhaustion, and islet cell destruction. The dysregulation of neuro-humoral and neuro-immune systems and chronic low-grade inflammation play a role in insulin resistance. Molecular abnormalities, such as defects in insulin receptor structure, number, binding affinity, and signaling capacity, contribute to insulin resistance. Additionally, hyperglycemia and other mechanisms impair insulin signaling, including the degradation of insulin receptor substrates and phosphorylation of insulin receptors and receptor substrates. Insulin resistance also plays a role in the pathogenesis and progression of hypertension-induced target organ damage.

Prediabetes and diabetes:
Prediabetes is closely related to MetS, and several studies have shown a high prevalence of prediabetes in individuals with MetS [13,14]. Prediabetes is characterized by impaired fasting glucose or elevated HbA1c levels, and it is considered a risk factor for CVD. Individuals with prediabetes and MetS have higher WC, BP, FBG, serum TG levels, and lower serum HDL-C. Obesity and low serum HDL-C have been identified as independent risk factors for prediabetes.

The altered levels of FBG and lipid profiles observed in individuals with MetS and prediabetes suggest an association between prediabetes and CVD. Concurrently, Several studies have shown a high prevalence of MetS in patients with diabetes, including both type 1 and DM2. [15,16]. In patients with type 1 diabetes (DM 1), MetS has been associated with an increased risk of microvascular complications such as diabetic kidney disease and diabetic retinopathy. Still, in DM 2 patients, MetS is associated with an increased risk of chronic complications and mortality. Overall, these findings highlight the importance of early detection and management of prediabetes in individuals with MetS to prevent the progression of CVD.

Figure (1): Proposed MetS diagnostic criteria [3]



Hypertension:

The pathogenesis of hypertension in MetS is multifactorial. High salt intake, vasoconstriction, impaired vasodilation, extracellular volume expansion, inflammation, and increased sympathetic nervous system activity are mechanisms involved in developing hypertension in MetS [17,18]. Gut dysbiosis, short-chain fatty acid-producing bacteria reduction, and increased trimethylamine N-oxide and lipopolysaccharides contribute to salt and water retention, chronic inflammation, and endothelial dysfunction, further increasing BP. The renin-angiotensin-aldosterone system, insulin resistance, hyperinsulinemia, and endothelial dysfunction also play a role in the development of hypertension in MetS.

Dyslipidemia

Dyslipidemia in MetS is characterized by increased levels of LDL-C and TG, along with decreased levels of HDL-C [19]. This dyslipidemia results from alterations in lipoprotein metabolism, including overproduction of potentially atherogenic lipoproteins, reduced levels of HDL particles, and an increase in small, dense LDL-C particles. The pathogenesis of dyslipidemia in MetS is also influenced by insulin resistance and insulin deficiency, which play important roles in lipid metabolism. Additionally, dyslipidemia in MetS is associated with oxidative stress, inflammation, and adipokine dysregulation, further contributing to the development of lipid abnormalities [20].

Genetics:

Genetic variations, including single-nucleotide polymorphisms, have been associated with MetS and related traits. Epigenetic factors, such as DNA methylation and histone modification, are also likely to play important roles in MetS, which is non-modifiable. Several cholesterol-related genes, such as apolipoprotein, lipoprotein lipase , cholesteryl ester transfer protein, and adiponectin, have been identified as being associated with MetS. Additionally, the fat mass and FTO has been found to significantly contribute to the early onset of MetS in children and adolescents. Mechanistic studies have shown that FTO polymorphisms lead to aberrant expressions of FTO and adjacent genes, promoting adipogenesis and appetite while reducing satiety and energy expenditure [21,22]

Treatment of MetS:

The main mechanism of Mets is the chronic proinflammatory state that leads to systemic symptoms; hence, to achieve the appropriate management and treatment and reduce the risk of subsequent disease, correct diagnosis of symptomatic patients with MetS is crucial. Lifestyle modifications are central to treatment and have been shown to have positive effects, including negative energy balance with increased physical activity and a balanced diet, considering anthropometric measurements and atherogenic lipid profiles, BP, and glycemic index of nutrients [23]. Lifestyle interventions, including fasting, diet, and exercise, have improved quality of life and psychological parameters in patients with MetS. Adherence to lifestyle interventions is crucial for their effectiveness, and factors such as individualized education, regular follow-ups, and interpersonal support can facilitate adherence. Additionally, incorporating lifestyle modifications into daily life is key to maintaining compliance.

Weight Reduction Pharmacological and Surgical:

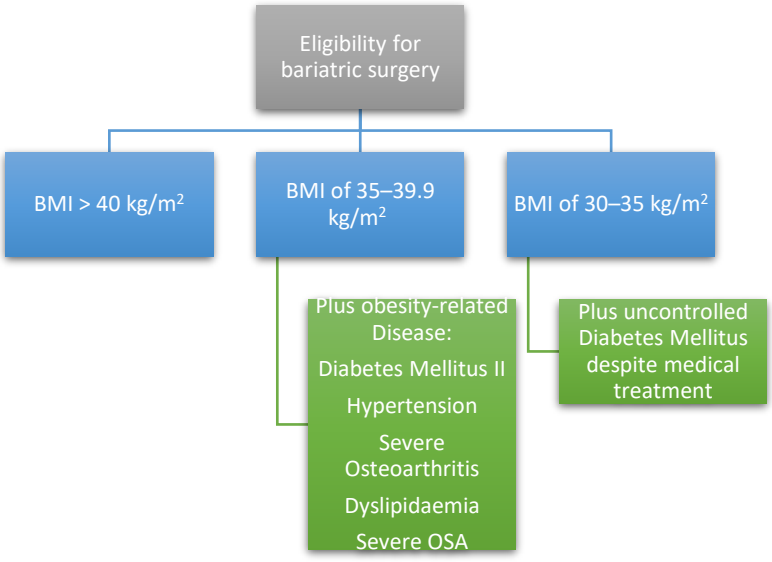
Pharmacotherapy is recommended for All patients with a BMI over 30 kg/m^2 and those with a BMI of 27 kg/m^2 or higher associated with other comorbidities for at least a year [24]. The following medications are currently authorized and accessible in Saudi Arabia for the treatment of obesity[25]:

- GLP-1RA like Liraglutide and Semaglutide
- Lipase inhibitors like Orlistat
- Phentermine-topiramate and naltrexone-bupropion.

Moreover, GLP-1RA are the classical medication used to treat DM 2 and obesity [26]. They have been shown to have antihyperglycemic effects, reduce body weight, and improve CV risk factors such as BP and lipid levels. They also have potential renal protective and beneficial effects on nonalcoholic fatty liver disease. The only medication whose effectiveness and safety in obese patients have been demonstrated, either before or following bariatric surgery, is Liraglutide. Conversely, Patients with obesity who also have depression should be the primary targets for Naltrexone/Bupropion in fixed-dose combination therapy [24]. Other candidates include people who have quit smoking and whose weight has increased since quitting. Patients who snack excessively and become obese should also take this into account [27].

Bariatric surgery, such as laparoscopic sleeve gastrectomy, is considered the most effective and long-term treatment for obesity and remission of obesity-related disorders, such as DM 2, hypertension, dyslipidemia, and MetS [28,29]. There is evidence that conversion of adjustable gastric band to laparoscopic sleeve gastrectomy is a safe and effective option for patients who experience weight regain or band intolerance [30]. The patient's eligibility for bariatric surgery is based on their BMI (Figure 2).

Figure (2): Eligibility for bariatric surgery based on their BMI[3].



Pharmacological Treatment:

Medical treatment is part of a complex treatment approach when non-medical therapies fail. As is the situation with patients who fail to apply suitable therapies for chronic conditions, including hypertension, diabetes, hypercholesterolemia, and others. For hypertensive patients, WHO recommends initiation of pharmacological antihypertensive treatment within four weeks following diagnosis of hypertension; systolic BP ≥ 140 mmHg or a diastolic BP ≥ 90 mmHg, systolic BP 130–139 mmHg with existing CVD, or high CV risks like diabetes, or chronic kidney disease. Treatment must start immediately if systolic ≥160 mmHg or diastolic ≥100 mmHg [31]. As an initiative treatment, WHO recommends three classes: thiazide, angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers, and long-acting dihydropyridine calcium channel blockers. Also, they strongly recommend Single-pill combination therapy from the same three drug classes if BP ≥20/10 mmHg higher than the target for long-term control and maintain adherence.

According to the latest update of new guidelines for the treatment of diabetes in Saudi Arabia[32], Metformin therapy is recommended for prediabetic patients to prevent diabetes II. On the contrary, multiple daily injections of insulin are the first of choice for DM 1, whether continuous subcutaneous insulin infusion or Mixed insulin. However, the preferred initial for DM 2is Metformin plus insulin therapy should be considered if patients presented with weight loss or hyperglycemia symptoms or when HA1C >10% (86 mmol/mol) or blood glucose ≥300 mg/dL (16.7 mmol/L). For patients with DM 2with CVD, kidney disease, or heart failure, a sodium-glucose cotransporter 2 inhibitor (Empagliflozin) or glucagon-like peptide 1 receptor agonist (Dulaglutide) is recommended as part of the glucose-lowering agents.

As regards dyslipidemia treatment; intensive statin therapy is recommended in all patients with CV symptoms irrespective of the baseline LDL-C values and to be combined with ezetimibe high-risk patients [33]. Furthermore, intensive therapy also encouraged if any potential risk of diabetes or in case of genetic causes abnormal lipoproteins levels. The treatment goals of Pharmacological interventions is to control serum LDL-C, serum TGs or non-HDL-C and LP (A) (Table 2).

PHARMACOLOGICAL INTERVENTION	MODE OF ACTION	DRUGS USED	THERAPEUTIC INDICATIONS
Moderate or high-intensity HMG-CoA reductase inhibitors (statins)	Reduce LDL-C	Simvastatin Pitavastatin Rosuvastatin	Primary Hypercholesterolemia Mixed dyslipidemia Familial hypercholesterolemia CV symptoms DM
Cholesterol absorption inhibitors	Reduce LDL-C Reduce APO-B	Ezetimibe	Primary hypercholesterolemia Familial hypercholesterolemia Phytosterolemia Prevention of cv events
Fibrates	Reduce serum LDL-C, TC, TGS, and Apo-B. Increase HDL-C.	Fenofibrate Gemfibrozil	Hypertriglyceridemia Mixed hyperlipidemia High CV risk
PCSK9 Monoclonal antibodies	Reduce LDL-C, Apo-B, LP (a), TGS. Increase HDL-C, Apoprotein A1	Alirocumab Evolocumab	Primary hypercholesterolemia Mixed dyslipidemia Reduce CV risk
Eicosapentaenoic acid ethyl	Reduces LDL-c, APO-b, TC.	Icosapent ethyl	Hypertriglyceridemia
Small interfering RNA molecule	Reduces LDL-C, LP (A), Apo-B, non-HDL-C	Inclisiran	Primary hypercholesterolemia Mixed dyslipidemia
Microsomal TGtransfer protein inhibitor	Reduce LDL-C, Apo-B	Lomitapide	Familial hypercholesterolemia Other forms of primary hyperlipoproteinemia Secondary causes of hypercholesterolemia
Bempedoic acid	Reduces LDL-C		
Olpasiran	Reduce LP (A)		

Table (2): Lipid modifying drugsand approved indications [33].

CONCLUSION:

MetS is a complex disorder with various definitions and underlying mechanisms. Early detection and management are essential to prevent further complications. Lifestyle modifications, pharmacotherapy, and surgical interventions play critical roles in managing MetS and reducing associated health risks.

Abbreviations:

American Association of Clinical Endocrinologists	AACE
Apolipoprotein B	Apo-B
Bioelectrical Impedance Analysis	BIA
Blood Pressure	BP
Body Mass Index	BMI
Cardiovascular	CV
Cardiovascular Disease	CVD
European Group For The Study Of Insulin Resistance	EGIR
Fasting Plasma Glucose	FBG
Glucagon-Like Peptide-1 Receptor Agonists	GLP-1RA
Glycated Hemoglobin	HbA1C
High-Density Lipoprotein Cholesterol	HDL-C
Hip Circumference	HC
Hydroxymethylglutaryl-Coenzyme A	HMG-CoA
International Diabetes Federation	IDF
Lipoprotein (A)	LP (A)
Low-Density Lipoprotein Cholesterol	LDL-C
Metabolic Syndrome	MetS
National Cholesterol Education Program Adult Treatment Panel Iii	NCEP ATP III
Non-High-Density Lipoprotein Cholesterol	non-HDL-C
Obesity-Associated Gene	FTO
Obstructive Sleep Apnea	OSA
Proprotein Convertase Subtilisin/Kexin Type 9	PCSK9
Total Cholesterol	TC
Triglycerides	TG
Type 2 Diabetes	DM 2
Visceral Fat Area	VFA
Waist Circumference	WC
World Health Organization	WHO

REFERENCES:

1. Compés CC: Nutrition in Metabolic Syndrome. 2006.
2. Einhorn D, Reaven GM, Cobin RH, et al.: American College of Endocrinology position statement on the insulin resistance syndrome. Endocr Pract. 2003, 9:237-252.
3. Dobrowolski P, Prejbisz A, Kuryłowicz A, et al.: Metabolic syndrome - a new definition and management guidelines: A joint position paper by the Polish Society of Hypertension, Polish Society for the Treatment of Obesity, Polish Lipid Association, Polish Association for Study of Liver, Polish Society of Family Medicine, Polish Society of Lifestyle Medicine, Division of Prevention and Epidemiology Polish Cardiac Society, "Club 30" Polish Cardiac Society, and Division of Metabolic and Bariatric Surgery Society of Polish Surgeons. Arch Med Sci. 2022, 18:1133-1156. 10.5114/aoms/152921
4. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). Jama. 2001, 285:2486-2497. 10.1001/jama.285.19.2486
5. Alberti KG, Zimmet P, Shaw J: Metabolic syndrome--a new world-wide definition. A Consensus Statement from the International Diabetes Federation. Diabet Med. 2006, 23:469-480. 10.1111/j.1464-5491.2006.01858.x
6. Balkau B, Charles MA: Comment on the provisional report from the WHO consultation. European Group for the Study of Insulin Resistance (EGIR). Diabet Med. 1999, 16:442-443. 10.1046/j.1464-5491.1999.00059.x
7. Jha BK, Sherpa ML, Imran M, et al.: Progress in Understanding Metabolic Syndrome and Knowledge of Its Complex Pathophysiology. Diabetology. 2023, 4:134-159. 10.3390/diabetology4020015
8. Kumar B, Kumari S, Khandelwal N, Kumar D, Dhaked S, Bhatt R: Obesity: An important predictor of metabolic syndrome. Scripta Medica. 2023, 54:81-85. 10.5937/scriptamed54-40389

9. Gopalan C, Kirk E: Chapter 4 - Obesity and metabolic syndrome. Biology of Cardiovascular and Metabolic Diseases. Gopalan C, Kirk E (eds): Academic Press; 2022. 67-83. https://doi.org/10.1016/B978-0-12-823421-1.00001-9
10. Haam J-H, Kim BT, Kim EM, et al.: Diagnosis of obesity: 2022 update of clinical practice guidelines for obesity by the Korean Society for the Study of Obesity. Journal of obesity & metabolic syndrome. 2023, 32:121.
11. Salman H, Koca TG, Dereci S, Akçam M: Comparison of Body Composition and Body Mass Index in the Determination of Obesity in Schoolchildren. Turkish Archives of Pediatrics. 2022, 57:506.
12. Gupta A: Chapter 8 - Etiopathogenesis of insulin resistance. Understanding Insulin and Insulin Resistance. Gupta A (ed): Elsevier; 2022. 231-273. https://doi.org/10.1016/B978-0-12-820234-0.00010-X
13. Davidson MB: The Role of Prediabetes in the Metabolic Syndrome: Guilt by Association. Metabolic Syndrome and Related Disorders. 2023, 21:197-204.
14. Tangjittipokin W, Srisawat L, Teerawattanapong N, Narkdontri T, Homsanit M, Plengvidhya N: Prevalence and Characteristics of Prediabetes and Metabolic Syndrome in Seemingly Healthy Persons at a Health Check-Up Clinic. Journal of Multidisciplinary Healthcare. 2022, Volume 15:1585-1594. 10.2147/jmdh.s374164
15. Essafi MA, Bouabdellaoui L, Aynaou H, Salhi H, El Ouahabi H: Metabolic Syndrome in Patients With Diabetes Mellitus. Cureus. 2022. 10.7759/cureus.24469
16. Kim G: Association between Metabolic Syndrome and Microvascular Complications in Chinese Adults with Type 1 Diabetes Mellitus (Diabetes Metab J 2022;46:93-103). Diabetes & Metabolism Journal. 2022, 46:512-514. 10.4093/dmj.2022.0134
17. Katsimardou A, Imprialos K, Stavropoulos K, Sachinidis A, Doumas M, Athyros V: Hypertension in metabolic syndrome: novel insights. Current Hypertension Reviews. 2020, 16:12-18.
18. Stanciu S, Rusu E, Miricescu D, et al.: Links between Metabolic Syndrome and Hypertension: The Relationship with the Current Antidiabetic Drugs. Metabolites. 2023, 13:87. 10.3390/metabo13010087
19. Su X, Cheng Y, Zhang G, Wang B: Novel insights into the pathological mechanisms of metabolic related dyslipidemia. Molecular Biology Reports. 2021, 48:5675-5687. 10.1007/s11033-021-06529-0
20. Hurza V, Vatashchuk M, Bayliak M: Pathogenesis and Biomarkers of Metabolic Syndrome. Journal of Vasyl Stefanyk Precarpathian National University. 2022, 8:7-19. 10.15330/jpnu.8.4.7-19
21. Rana S, Ali S, Wani HA, Mushtaq QD, Sharma S, Rehman MU: Metabolic syndrome and underlying genetic determinants-A systematic review. Journal of Diabetes & Metabolic Disorders. 2022, 21:1095-1104. 10.1007/s40200-022-01009-z
22. Zafar U, Khaliq S, Ahmad HU, Manzoor S, Lone KP: Metabolic syndrome: an update on diagnostic criteria, pathogenesis, and genetic links. Hormones. 2018, 17:299-313. 10.1007/s42000-018-0051-3
23. Wang Q, Chair SY, Wong EML, Qiu X: Actively incorporating lifestyle modifications into daily life: The key to adherence in a lifestyle intervention programme for metabolic syndrome. Frontiers in Public Health. 2022, 10. 10.3389/fpubh.2022.929043
24. Wharton S, Lau DC, Vallis M, et al.: Obesity in adults: a clinical practice guideline. Cmaj. 2020, 192:E875-E891.
25. Almughais ES, Alshehri MH, Alsatti M, et al.: Awareness and Perception of Anti-obesity Medications Among Al-Ahsaa, Riyadh, and Hail in Saudi Arabia Populations. Cureus. 2023. 10.7759/cureus.40425
26. Jeon JY, Kim HJ: Glucagon-like Peptide-1 Receptor Agonists. Stroke Revisited: Diabetes in Stroke. Lee S-H, Kang D-W (eds): Springer Singapore, Singapore; 2021. 167-177. 10.1007/978-981-16-5123-6_14

27. Grilo CM, Lydecker JA, Gueorguieva R: Naltrexone plus bupropion combination medication maintenance treatment for binge-eating disorder following successful acute treatments: randomized double-blind placebo-controlled trial. Psychological Medicine. 2023, 53:7775-7784. 10.1017/s0033291723001800
28. Alqahtani SJ, Alfawaz HA, Moubayed NMS, et al.: Bariatric Surgery as Treatment Strategy of Obesity in Saudi People: Effects of Gut Microbiota. Nutrients. 2023, 15:361. 10.3390/nu15020361
29. Mahfouz MEM, Alsuwat MAM, Almnjwami RFM, Sarriyah AFA: Patient preferences for bariatric surgery in Saudi Arabia. International Journal of Medicine in Developing Countries. 2021, 5:1469-1469.
30. Almayouf M, Alqahtani A: Should adjustable gastric band be abandoned as a bariatric surgery option? Private center's experience with adjustable gastric band conversion. Research Square Platform LLC; 2023.
31. Guideline for the pharmacological treatment of hypertension in adults . World Health Organization; 2021.
32. Diabetes Pharmacotherapy Clinic Guidelines. Edited by Departments CP. Menistry of Health, Saudi Arabia; 2021.
33. AlRahimi J, AlSaif S, Alasnag M, et al.: 022 Saudi Guidelines for the Management of Dyslipidemia. Heart Views. 2023, 24:67-92. 10.4103/heartviews.heartviews_102_22