PM&DC IP NO. IP/002

ISSN (ISSN-L) 0030-9982

JPMA

Journal of the
Pakistan Medical Association (Centre)

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The Journal of Pakistan Medical Association (JPMA) is published monthly from PMA House, Aga Khan III Road, Karachi-74400, Pakistan.

Price: Rs.1,500.00 (Single Issue)

Annual Subscription: Rs.17,000 in Pakistan and US$500.00 for overseas countries (including air mail postage).

Publication Office: PMA House, Aga Khan III Road, Karachi-74400, Pakistan. Telephone: 92-21-32226443.

E-mail: editor@jpma.org.pk

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Metabesity Guideline: A Pakistan Perspective

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Defining Metabesity has been challenging as it's a complex medical issue. Background of the problem is multifactorial, which differs due epidemiological and differences in genetics among various regions of globe. Hence, it has a different impact for Pakistan due to its unique perspective.

It's about time, that we as a physician community should join hands to fight this epidemic. We should work together to better understand and device guidelines for better management of this unique condition.

Metabesity is a complex medical condition, which has its deep roots in different medical condition. These include, but not limited to, Psychosocial disorders¸ Cardiovascular risk (Dyslipidemia, Hypertension, Stroke - CVA), Metabolic disorders (Diabetes, Liver disease), Risk of cancer, Neurological disorders, Immunity deficiency (Infections) and Fertility issues (Men and Women). This impacts not only Adolescent and children but has deleterious effect on life expectancy of general population.

We need to come to a consensus about how to overall decrease the incidence of Metabesity by preventing it and managing it better for those who already have it. Multidisciplinary approach is needed which include Lifestyle changes, Dietary recommendation, Physical Activity, Psycho - Social - Stress management and medical intervention.

Guidelines for Medical Treatment of Metabesity include Psycho-social intervention, Pharmacotherapy, Surgical intervention (Bariatric Surgery) and Non-Surgical approaches (Embolisation/ Balloon Therapy)

We, as Medical community, need to work together and emphasize the dangers of this Metabesity epidemic and identify limitations of our current screening programmes. These guidelines will be a step forward towards are combined goal.

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Prevention of obesity can go a long way in decreasing the cardiometabolic disease burden and its complications. These metabesity guidelines have been developed with consensus from all the major stakeholders and will provide a much needed initiative in combating and tackling the ongoing obesity pandemic. While preparing these guidelines, a holistic approach has been used to address metabesity with lifestyle modifications, changes in food habits and treatment of any associated comorbidities like hypertension, hyperglycemia or dyslipidemia. Measures to prevent metabesity needs to be introduced at all levels and should begin early in life.

Healthy eating habits and physical activities should be a part of every child and young adult's daily routine.

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Metabesity Project is a great initiative by Getz Pharma and this will definitely have a great impact on the health of the common people. Diabetes, obesity and cardiovascular diseases, joined by neurodegenerative disorders, cancer and even the aging process itself, share metabolic and inflammatory provenances. Targeting the prevention of cardiovascular disease in diabetics could be very challenging since it is the leading cause of morbidity and mortality in people with diabetes. Along with that accompanies significantly increased prevalence of hypertension and dyslipidemia.

In my strong belief, science, clinical practice, medical community and most importantly our people will benefit if we come out of our professional silos and look for opportunities to prevent or reduce the risk of these conditions together. And such is an opening move by Getz Pharma in reducing the overall burden and increasing the healthy lifespan of the people.

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As a neurologist and the president of Pakistan Society of Neurology, I strongly believe that this new combination of multiple diseases is a new center of attention for all the healthcare professionals. Metabesity is an outbreak, and efforts are currently underway to identify therapeutic targets. The high prevalence of T2DM, together with the fact that current treatments are only palliative and do not avoid major secondary complications, reveals the need for novel approaches to treat the cause of this disease.

Metabesity project, in this regard, is an incredible start up by Getz Pharma to unravel the new challenges in treating and managing metabesity. These guidelines will definitely be an important asset to the healthcare system.

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Metabesity is an emerging topic that discusses the root cause of obesity and its related complications. It is a great pleasure for me to be part of this first ever guideline for Metabesity in Pakistan. This guideline will support the physicians of all specialties to help their patients in a holistic way. I am also thankful to Getz Pharma for their support for this academic activity.

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Getz Pharma has always come up with solutions to deteriorating health of our people. And this time again under the banner of Metabesity Project, they are helping to organize, connect, energize and enabling us to contribute to the audacious goals of substantially reducing the burden of chronic disease. There are a number of people diagnosed each year with diabetes and they don't get the recommended standards of care that they should get. A substantial percentage of them don't get any education to empower them to manage disease successfully, thus avoiding pooling complications of stroke, heart disease, blindness, amputation, kidney failure, all very serious and expensive to treat conditions that put huge burden on the patients, their families and healthcare system.

With the right standards of care and education, complications can be avoided and that for me is a bit of a no-brainer. We shouldn't be spending our resources in treating the end stages of complications of diabetes. Therefore, we should be putting more efforts in the early stages enabling people to live healthier and longer through quality of care.

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Obesity has been a significant and independent risk factor for many cardiovascular diseases such as hypertension, heart failure, myocardial infarction, stroke and sudden cardiac death. It has also been a major cause of derangements in metabolic parameters such as dyslipidemia, hyperglycemia and systemic inflammation. Adding to the mix of obesity and diabetes, is a newer and the latest entrant "Metabesity." It has become a debilitating and a crippling disease that needs immediate addressing.

To overcome this challenge, Getz Pharma has been in the spearhead to bring all the Healthcare professionals a solution to the treatment of metabesity through the metabesity management clinics and the guidelines. Early interventions and diagnosis could be a major change in improving the overall quality of life of an individual.

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Metabesity refers to constellation of metabolic diseases that include diabetes, obesity, metabolic syndrome, cardiovascular disease, neurodegenerative disorders and accelerated aging. It is now considered to be one of the major public health problem worldwide with emphasis shifting on a more holistic approach of management. Neurological disorders are on the rise in Pakistan due to high prevalence of risk factors like diabetes, obesity and hypertension in general population. Recent studies have indicated that diabetes is not only caused by failure in β-cells but also by dysfunctions in the central nervous system (CNS), especially in the hypothalamus and brainstem. Stroke is a serious health concern with an annual incidence of 250/100000 population.

The prevalence of depression and anxiety was 34% and dementia was reported to be 3.79% in one study. It's high time now that we break the silos and collaborate among different specialties' to control the risk factors so as to improve patient care.

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Metabesity is a complex interplay of genes, behavioral, environmental and metabolic interactions that influence the development of obesity. Recent data of Pakistan suggests the need for preventive interventions to manage the obesogenic state of the country, which can be achieved with the help of effective practice guidelines and procedures. Diabetes being a systemic disease affects many organ systems, and the GI tract is no exception. As with other complications of diabetes, the duration of the disorder and poor glycemic control seem to be associated with more severe GI problems. Patients with a history of retinopathy, nephropathy, or neuropathy should be presumed to have GI abnormalities until proven otherwise. GI problems in diabetes are common but not commonly recognized in clinical practice. Many patients go undiagnosed and under-treated because the GI tract has not been traditionally associated with diabetes and its complications.

Considering this rising global incidence of obesity, Getz Pharma has set the bar in embarking on the journey in treating Metabesity by colonizing different specialties for better health outcomes and it will serve as a platform to enhance clinical practices of the healthcare professionals.

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Diabetes is becoming a serious threat to the global health and the increasing prevalence of diabetes in Pakistan is a wakeup call for all. Adding to this, obesity is currently playing a major role in health related problems and its association with several chronic diseases.

People with prediabetes have an increased risk of getting diabetes, and studies have shown that about 10% of them develop diabetes every year. Prediabetes has come to be known as the middle stage between normal blood sugar levels and diabetes, with many people camping at this stage for years on end without ever progressing to the next stage. Such patients may develop chronic kidney disease (CKD), which features kidney alterations and dysfunction. Acute forms of CKD manifest as an end-stage renal disease (ESRD). This further complicates the management of their diabetes and increases mortality risk.

However, Getz Pharma has taken a strong lead to overcome the burden of Metabesity by developing clinical insights and aiding medical professionals in their fight against kidney disease and many other chronic disease related to diabetes.

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Metabesity Management Clinics

Metabesity is an impending epidemic which will cause a huge effect on public health. It encompasses most of major chronic diseases of our time. It refers to metabolic problems associated with obesity. Along with genetic component, life style is also very important in consideration of metabesity.

Metabesity is associated with several co-morbidities including an increased risk for cardiovascular conditions, insulin resistance, high blood pressure and sugar levels, visceral adiposity, progressive atherosclerosis, dyslipidemias and fatty liver are common in obese individuals.

Metabesity adversely impacts endocrine balance. Interventions to combat sedentary life style and healthy eating habits should be introduced early in life to prevent onset and progression of obesity.

Getz Pharma has come forward in taking this big initiative of establishment of metabesity management clinics all over Pakistan. They are providing us with HbA1c meters, cholesterol strips, retinal scan devices, biothesiometers and dopplex diabetic foot assessment kit which will help to detect diabetic complications early under a single roof in a very short time. We will collect data to plan our future strategies.

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Metabesity is a relatively newer terminology in Medicine, defined to cover different metabolic diseases under one caption. It includes obesity, metabolic syndrome, diabetes, cardiovascular diseases, neurodegenerative disorders and accelerated aging. The diseases included in 'metabesity' have mechanisms which are both metabolic and inflammatory in nature.

A major hallmark of 'metabesity' is continuous destruction of specialized cells (myocardial cells, neurons, beta cells of pancreas and hepatocytes etc.) which leads to increased fatigue and decreased quality of life in the affected individuals. Evolving data in our country points to the increasing prevalence of this syndrome, like other developed countries.

Understanding the underlying mechanisms of 'metabesity' will guide us to the therapeutic goal of rebuilding the damaged tissues and preventing complications of the disease. Aging itself causes damage to the cells and tissues and worsens the effects of 'metabesity. Therefore, screening of patients in "Metabesity Clinics" is the need of the hour and this will go a long way in the prevention of comorbidities associated with it.

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Obesity is creeping slowly in our community to gain a status of an epidemic. Moreover the disorders under the umbrella of metabesity is again posing a huge burden on health economics.

In this situation prevention is the best strategy to control this epidemic. Getz Pharma has taken an initiative in this regard by establishing metabesity clinics in different centers, which would help to collect the data of obesity and related co-morbid conditions, so better treatment strategies can be employed in tackling this problem.

The focal group would help to design guidelines with local perspective, and create public awareness campaign to cater the ultimate stakeholders.

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METABESITY GUIDELINE: A PAKISTAN PERSPECTIVE

Abstract

Pakistan is among the top ten countries in terms of obesity, with individuals at a higher risk of metabolic disorders or metabesity. Metabesity is a combination of obesity with metabolic disorders such as diabetes, which also increases the risk of cardiovascular and neurovascular disorders, and accelerated ageing. There is a complex interplay of genetic, behavioural and metabolic influences in metabesity, which necessitates the need for comprehensive guidelines for its management, especially in the Pakistani population. For this purpose, rigorous literary evidence was gathered, and standardised guidelines such as the American Association of Clinical Endocrinology (AACE) were explored. The prepared guidelines for metabesity suggest screening tests for hyperglycaemia, dyslipidaemia and coronary disorders at regular intervals, and following a standard diagnostic criteria for metabesity. This involves measurement of waist circumference (Asian-based cut off >90cm in men and >80cm in women), lipid profile (HDL <40mg/dl in men and <50mg/dl in women), blood pressure (>135/85mmHg), and fasting blood glucose (>99mg/dl) to determine the risk.

Treatment protocol involves lifestyle changes including 500-750kcal reduction in diet per day along with 150 minutes of weekly physical activity. Pharmacotherapy is advised for weight loss, hypertension, hyperglycaemia, and dyslipidaemia, along with management of other comorbid conditions if any. In patients with a body mass index (BMI) above 35, surgical options such as bariatric surgery can be considered. Metabesity impacts other comorbid conditions and has individual risks for each age group. A more personalised approach for management should be preferred in persons with polycystic ovary syndrome (PCOS), neurologic disorders, Alzheimer's, stroke and infections, due to significant impact of the disease.

Keywords: Metabesity, Medical nutrition therapy, Diabetes mellitus, Obesity.

Introduction

Metabesity refers to the spectrum of metabolic disorders with metabolic and inflammatory origins, including obesity, metabolic syndrome, diabetes, cardiovascular diseases and neurodegenerative disorders, and accelerated aging (Figure-1).[1] It encompasses various conditions whose aetiology lies within complex relationships between genes in an obesogenic environment.[2] The progression of metabesity involves inflammatory and oxidative damage, due to insensitivity to regulators such as insulin or leptin, which results in cell death due to compromise in the natural regeneration capacity of the tissues.[3]

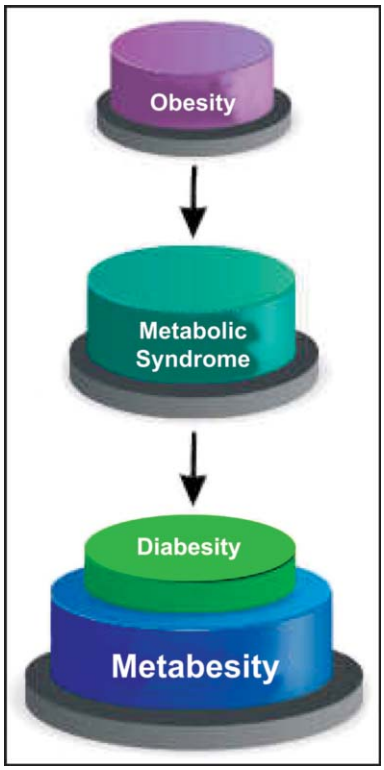

Figure-1: Relationship between obesity and metabesity.

According to the recent statistics from the World Health Organization (WHO), approximately 39% of the adult population is overweight, with 13% being obese.[4] The prevalence of obesity is also on the rise among children, with 42 million being either obese or overweight according to the world statistics. With an increase in the prevalence of obesity, there is also an increase in metabolic complications such as type 2 diabetes and cardiovascular diseases across the world.[2]

In metabesity, a complex interplay of genetic, behavioural, environmental and metabolic interactions influence the development of obesity[5] (Figure-2). Obesity, having a parental influence, has been described as a genetic trait with specific markers for increased body mass index (BMI), variability in fat

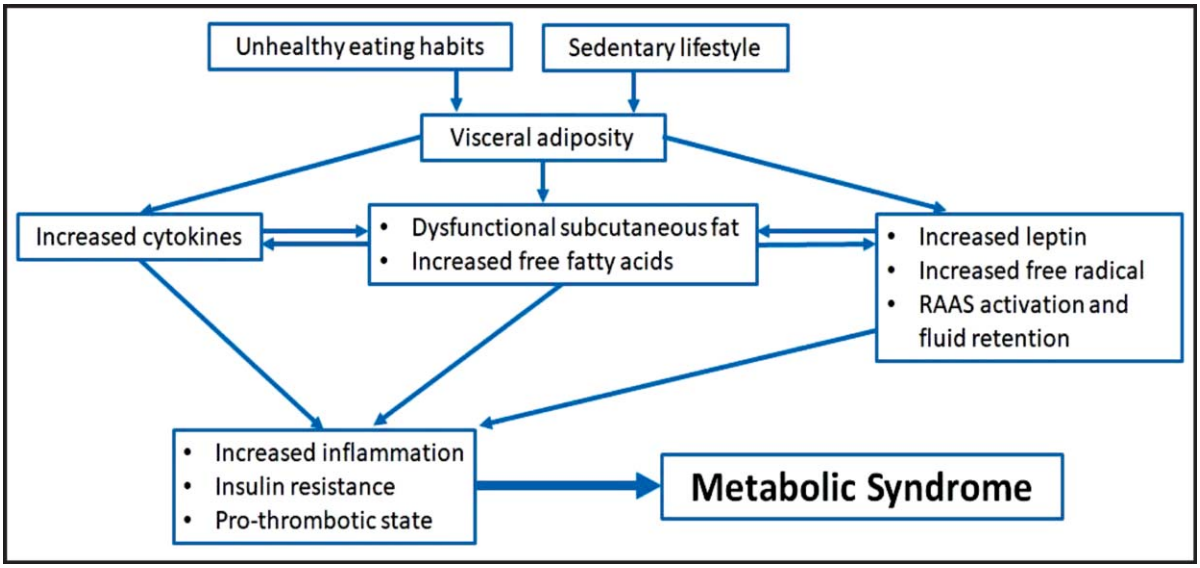

Figure-2: Interlinked aetiologies behind metabesity.

distribution, and association with metabolic syndromes. Genetic determinants of obesity include mutations or polymorphisms in the fat mass and obesity-associated (FTO) gene, melanocortin-4 receptor (MC4R) gene, and the gastric inhibitory polypeptide receptor (GIPR) gene.[6] Genetic variants of fat distribution, affecting waist circumference and waist-hip ratio, include loci near transcription factor AP-2 beta (TFAP2B), methionine sulfoxide reductase A (MSRA), and lysophospholipase-like-1 (LYPLAL1) genes. The FTO and neurexin 3 (NRXN3) genes are also associated with waist circumference and BMI.[7]

Due to a higher metabolic and cardiovascular risk, the BMI range for Asian population differs from the rest of the world.[8,9] It is suggested to be different from its standard values to include low- to moderate-risk categories within the range of normal BMI category of the world's population (Table-1). Table-2 demonstrates the mean BMI of Pakistani population as per data from Dr. Habibullah in the year 1998.[4]

Table-1: Body mass index (BMI) classification according to WHO and Asia-Pacific Guidelines.

	WHO General BMI Classification (kg/m^2)*[8]	Asia-Pacific BMI Classification (kg/m^2)[9]
Underweight	<18.5	<18.5
Normal range	18.5-24.9	18.5-22.9
Overweight	≥25	≥23
Pre-obese / At Risk	25-29.9	23-24.9
Obese class I	30-34.9	25-29.9
Obese class II	35-39.9	≥30
Obese class III	≥40	

* WHO Expert Consultation advises cut-offs for public health action for the Asian population as follows: less than 18.5 kg/m^2 underweight; 18.5-23 kg/m^2 increasing but acceptable risk; 23-27.5 kg/m^2 increased risk; and ≥27.5 kg/m^2 high risk.

In a more recent Diabetes Prevalence Survey of Pakistan (DPS-PAK) of 18,856 eligible participants, the prevalence of pre-diabetes and type 2 diabetes was 10.91% (95% CI 10.46 to 11.36; n=2057) and 16.98% (95% CI 16.44 to 17.51; n=3201), respectively.[10] The prevalence was highest in the age group 51-60 years (26.03%, p<0.001), those with no formal education (17.66%, p<0.001), those with class III obesity (35.09%, p<0.001), and positive family history (31.29%, p<0.001) and in females (17.80%, p=0.009).

It can be noted that a large number of population lies in the category of low-to-moderate risk according to WHO recommendations for Asian population.[8] However, obesity as depicted by calculation of BMI does not appear to reflect the true risk factor for metabesity. This suggests the need for preventive interventions to manage the obesogenic state of the country, which can be achieved with the help of effective practice guidelines and procedures. Further, with the rising global incidence of obesity, it is also eminent that its prevalence must be higher than this estimated value in 2020. According to more recent statistics from 2018, the incidence of obesity among school-going children in Pakistan is almost 14%, indicating the risk of lifetime obesity and metabolic disorders.[11] It has also been determined that the risk of metabolic syndromes is higher among Pakistani population due to the central distribution of obesity or a higher waist circumference.[12]

Table-2: Mean body mass index (BMI) of Pakistani population as per data from Dr. Habibullah in the year 1998.[4]

BMI values	15-29 years	30-44 years	45-59 years	60-69 years	70-79 years
Male	20.7	21.8	21.9	21.6	21.0
Female	21.1	22.5	22.7	22.3	21.3

Pakistan is ranked eighth among the top 10 countries of obese population with a prevalence rate of 46%.[11] It may be attributed to unhealthy eating patterns, including intake of high carbohydrate foods and those high in trans-fats.[13] While the association of obesity with metabolic disorders has been affirmed in the Pakistani population, there exists a dearth of standard recommendation for its management, suggesting the need for clinical practice guidelines for managing metabesity. Metabesity is not only associated with diabetes and cardiovascular disorders, but also has a high risk of cancers (Figure-3) such as renal cancer or that of the prostate.[14]

Figure-3: Underlying risks of metabesity.

This suggests the need for rigorous guidelines that can manage the prevalence of metabesity and reduce the risks of mortality in our population. These guidelines will be instrumental in reducing the prevalence of obesity as well as metabolic disorders in Pakistan while managing its risk and reducing the burden on the existing healthcare systems.[15]

Methodology

Clinical Practice Guideline for the Management of Metabesity in Pakistan was formed on the basis of literary evidence and an overview of existing guidelines. Extensive literature search on the epidemiology of obesity and metabolic conditions was gathered, including global and Pakistani population data, so that guidelines specific to the population could be created. Relevant sources were gathered from PubMed, Journal of Pakistan Medical Association (JPMA), Elsevier and Cochrane after careful assessment and analysis. In addition to literature research, standard guidelines such as the American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) clinical practice guidelines for obesity and metabolic disorders were searched along with WHO framework for the assessment of standard BMI measures. Based on the strength of evidence, grades were awarded to each recommendation, and levels of recommendation were made, as detailed in Table-3 and 4.

The first draft of recommendations was prepared and circulated to gather opinions for review. Suggestions, recommendations and opinions specific to each section of the guideline were collected in a written format. The draft was then revised to address the existing gaps and again forwarded for opinions and review. As all experts approved these recommendations, the second draft of guidelines was finalised and submitted for publication.

Table-3: Levels of evidence.

Level	Type of Evidence
IA	Systematic review (with homogeneity) of RCTs / Existing practice guidelines (AACE) with supporting large-size RCTs
IB	Individual RCT (with narrow CI)
IC	All or none RCT
IIA	Systematic review (with homogeneity) of cohort studies / Small RCTs with unclear results
IIB	Individual cohort study (including low quality RCT e.g. <80% of follow-up)
IIC	'Outcomes' research; Ecological studies
IIIA	Systematic review (with homogeneity) of case-control studies
IIIB	Individual case-control study
IV	Case series (poor quality cohort and case-control study)
V	Expert opinion without explicit critical appraisal or based on physiological bench research or 'first principles'

AACE: American Association of Clinical Endocrinologists; CI: Confidence interval; RCT: randomised controlled trials.

Table-4: Grade practice recommendations.

Grade	Descriptor	Quantifying Evidence	Implications for Practice
A	Strong recommendation	Level I evidence: consistent findings from multiple studies of levels II, III, or IV	Clinicians should follow this recommendation unless a clear and compelling rationale for an alternative approach is present
B	Recommendation	Levels II, III, or IV evidence with consistent findings	Generally, clinicians should follow the recommendation but should remain alert to new published evidence while being sensitive to patient preferences
C	Option	Levels II, III, or IV evidence with inconsistent findings	Clinicians should be flexible in their decision-making approach, although they may set bounds on alternatives; patient preference should have a substantial influencing role
D	Option	Level V evidence: little or no systematic empirical evidence	Clinicians should consider all options in their decision making and be alert to new published evidence that clarifies the benefit versus harm of the selected approach; patient preference should have a substantial influencing role

The Guidelines

Screening and Diagnosis of Metabesity

Cardiovascular Risk / Dyslipidaemia or Hypercholesterolaemia (LDL-cholesterol tests, triglyceride levels and non-HDL-cholesterol)

- Total cholesterol and high-density lipoprotein (HDL) cholesterol must be evaluated in non-fasting or fasting samples at 3 months in persons with a known risk.[16]
- Abnormal screening tests must be confirmed by a repeated sample at 3 months.
- Middle aged adults above 45 years of age must be assessed every 1 to 2 years.[17]
- Older adults above 65 years of age must be screened each year.[18]
- In children between the age of 9 to 11 years, screening tests must be performed every 3 years in the presence of family history.[19]
- Those above 16 years of age must be assessed every 5 years in the presence of family history of obesity.
- Frequency of screening must be compliant with the individual risk profile in compliance with the best judgments of the physician. Higher screening frequency is necessitated for individuals with obesity, insulin resistance and familial risk factors.[2]
- All persons should be assessed for familial hypercholesterolaemia when low-density lipoprotein (LDL) cholesterol levels are elevated above 130mg/dl or triglycerides above 500mg/dl.[17]

Recommendations

Adult patients (20-45 years) must be screened every 5 years for total cholesterol and LDL cholesterol and the tests should be repeated at 3 months in case of an abnormal profile. Annual screening is recommended for older patients. For children and adolescents, these tests must be performed after 3 years.

Grade A

Diabetes Mellitus - Type 2

- Regular screening must be performed in asymptomatic patients with risk factors for diabetes.
- A1c levels between 5.7-6.4% must be assessed for the risk of diabetes.[20,21]
- Fasting blood glucose or oral glucose tolerance tests are used for confirmatory diagnosis along with A1c levels. A random plasma glucose level of >200mg/dl is also a criterion for confirming diagnosis with classic symptoms of hyperglycaemia or hyperglycaemic crises.[21]
- Fasting plasma glucose concentration of 126mg/dl after 8 hours of fasting, or plasma glucose greater than 200mg/dl after 2 hours of 75g oral glucose load is confirmatory of diabetes.[20] In the absence of unequivocal hyperglycaemia, diagnosis requires two abnormal test results from the same sample or in two separate test samples.
- Confirm by either repeating the initial test on another day or performing a different test. Glycohaemoglobin A1c has limitations in our population where anaemia and haemoglobinopathies like thalassemia are prevalent.[22]
- Oral glucose tolerance tests can also be used for screening persons with impaired glucose levels indicative of prediabetes and hence future risk of diabetes.[23]
- Pregnant women must be screened at first antenatal visit with 75g oral glucose tolerance test (OGTT) (0, 1, and 2 hour); if that is negative then rescreen at 24 to 28 weeks of gestation with 75g OGTT. A1c tests must be avoided in pregnant women.[17]
- Screening for diabetic neuropathy must be performed 5 years after the diagnosis of diabetes. This test must then be repeated annually.[20] Screening for neuropathy, nephropathy and retinopathy is recommended at the time of diagnosis of type 2 diabetes.
- Perform comprehensive foot care evaluation at least annually.

Risk Factors for Prediabetes and Type 2 Diabetes

- Age more than 40 years with or without the presence of other risk factors.
- Obese or overweight in terms of BMI.
- Family history of type 2 diabetes or cardiovascular disorders.
- Low HDL cholesterol levels.
- Hypertension with blood pressure higher than 135/85mmHg or patients on antihypertensive medications.
- Impaired glucose tolerance / impaired fasting glucose levels / HbA1c greater than 5.7% from a standardised laboratory.[20]
- Metabolic syndromes such as polycystic ovary syndrome (PCOS), acanthosis nigricans, hypertension or history of gestational diabetes.
- History of delivering a baby of more than 4kg weight at the time of birth.
- Antipsychotic therapy for schizophrenia and/or severe bipolar disease.
- Patients on long-term steroids.
- Patients with endocrinopathies such as Cushing's syndrome, acromegaly etc. and hereditary syndromes such as Prader-Willi syndrome etc.
- Sleep disorders such as obstructive sleep apnoea, chronic sleep deprivation or night-shift occupation in the presence of glucose intolerance.
- Screen children after onset of puberty or after 10 years of age if they are overweight and obese and have additional risk factors for diabetes.

Recommendations

HbA1c is a primary screening tool when done from a standardised laboratory, which must be used in persons with a risk of diabetes. HbA1c levels above 6.5 % must be further confirmed with additional tests such as fasting blood glucose or 2-hour 75-g oral glucose tolerance test.

Grade A

Metabolic Syndrome

- The circumference of waist is $\geq$90cm in men and $\geq$80cm in women.[17]
- Fasting glucose is $\geq$100 mg/dl, or the patient has type 2 diabetes and is receiving drug therapy for hyperglycaemia.

- Patient has a high blood pressure ≥130/85mmHg on two different occasions or has been diagnosed with hypertension and receiving drug therapy.
- The levels of triglycerides are above 150mg/dl or the person is on treatment for high plasma triglycerides value.[24]
- HDL cholesterol is less than 40 mg/dl in men and less than 50 mg/dl in women or if the person is under therapy for reduced HDL cholesterol levels.

Metabesity is diagnosed when three of the above five criteria are met in obese persons.

Recommendations

Tests for fasting blood glucose, blood pressure, triglycerides and HDL levels must be selected for diagnosing metabesity in addition to measuring waist circumference. Three of five abnormal findings describe the diagnosis of metabesity.

Grade A

Fatty Liver Disease

- Patients with obesity/metabolic syndrome must be routinely screened with liver enzymes and ultrasound.
- Those above 50 years of age or having type 2 diabetes, in addition to metabolic syndrome, must be screened more aggressively for ruling out the risk of chronic liver disease.[25]
- Ultrasound is the first line diagnostic test. In its absence, serum biomarkers or steatosis scores can be used. These do not offer a confirmatory diagnosis to rule out non-alcoholic fatty liver disease but can be used in patients with low risk.
- If fatty liver disease is already diagnosed, the patient must be screened with Enhanced Liver Fibrosis (ELF) every 3 years to rule out the risk of fibrosis.[26]
- Non-alcoholic fatty liver disease score (NFS) and Fibrosis-4 scores are other tests that can be used for detecting advanced fibrosis in patients with high risk. If either of these scores are elevated, patients must be referred for transient elastography.
- Persons at a high risk of fibrosis or those with metabolic syndrome in whom advanced disease is suspected must be considered for liver biopsy using non-invasive techniques.[27]

Recommendations

Ultrasound is the first line diagnostic test for the assessment of chronic liver disease or non-alcoholic fatty liver disease (NAFLD). Those at risk, especially diabetic patients, must be assessed routinely.

Grade A

Practical Recommendations for Screening in Pakistan

Since intensive screening is a major issue in developing countries such as Pakistan, simple tests such as HDL cholesterol or total cholesterol must be used for establishing the diagnosis of metabesity. Simple diagnostic criteria such as the one elaborated below can be successfully applied:[24,28]

Body weight

A simpler method to evaluate risk is waist circumference measuring above 90cm in men and 80cm in women. Further calculating BMI is required as a standard practice to evaluate the risk and identify points for public health action (Table-1).

Lipid panel/Hypertension

Total cholesterol, Triglyceride level: >150 mg/dL.

HDL level: Male: <40 mg/dL; Female: <50 mg/dL.

Hypertension: >135/85mmHg or those receiving antihypertensive medical treatment.

Glucose levels: Impaired glucose tolerance or type 2 diabetes mellitus: fasting plasma glucose: ≥100mg/dL.

Other: Screening for cardiovascular conditions, cancer and other disorders must be performed as recommended after a confirmatory diagnosis of metabesity.

Impact Analysis — Pakistan — Regional Perspective

Table-5: Impact of metabesity on other comorbid conditions (adapted from Mellado-Gil et al[56] and Dhurandhar et al[57]).

Cardiovascular Disease (CVD) Risk:	
Coronary Disease	Increased BMI in metabesity along with other diagnostic factors such as deranged lipid profile and/or hyperglycaemia, all act as independent risk factors for coronary disease. Metabesity also raises the risk of morbidity and mortality among patients with existing disease.
Dyslipidaemia/hypercholesterolaemia	Metabolic complications in obesity worsen the lipid profile of patients which can result in complications such as myocardial infarction (MI) or angina.
Hypertension	Weight gain in metabesity activates the renin-angiotensin-aldosterone system resulting in increased pro-coagulatory activity and endothelial dysfunction. This results in reduced anti-inflammatory and antioxidant mechanisms raising the risk of CVD.
Stroke	Inflammatory and metabolic complications in metabesity increase the risk of repeated episodes of stroke, which may result in muscle weakness, speech disturbances or even severe complications such as hemiplegia due to cell death. All patients with stroke or TIA should be screened for obesity by measuring BMI (ASA/AHA Guidelines for early management of stroke and TIA).[58]
Peripheral Artery Disease	Metabolic complications in metabesity can worsen the lipid profile of the patient as well inflammatory plaques in endothelium, giving rise to complications such as reduced blood flow to lower extremities. This can impact the quality of life and daily functioning of the person due to severe leg cramping, numbness and weakness of the leg. Walking, climbing the stairs and other physical activities are thereby hindered worsening the impacts of metabesity.
Diabetes Mellitus Risk	Insulin resistance in metabesity is an independent risk factor for type 2 diabetes. Metabesity increases the risk of other comorbidities such as CVD in patients with diabetes or can also result in diabetic complications such as nephropathy/neuropathy due to worsening of the condition.
Metabolic Syndrome Risk	Metabesity increases the risk of metabolic syndrome because of similarity in risk factors. This increases the risk of cardiovascular and neurologic complications including cerebrovascular death.
Hepatic Risk	Metabesity increases the risk of non-alcoholic fatty liver disease, which may result in steatohepatitis or have a much serious impact such as cirrhosis/death.
Risk of Cancer	Metabesity increases the risk of prostate and renal cancer because of its effects on sex and endocrine hormones as well as insulin and insulin-like growth factors, which are involved in its pathophysiology. Moreover, it sets a ground of imbalance between pro-inflammatory and anti-inflammatory factors resulting in early cell cycle disruption and apoptosis.
Neurological Risk	Metabolic influences in metabesity, especially in persons with diabetes, result in severe neurodegenerative diseases such as Alzheimer's disease (AD) or Parkinson's disease due to neuronal cell death. This is add-on to the repeated cerebrovascular insults due microvascular disease. Excess fat accumulates in the subcutaneous and visceral adipose tissue compartments and indicators of visceral adiposity, namely, waist circumference (WC), waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR), are better predictors of stroke risk than BMI.
Immunity / Risk of Infections	Inflammatory mechanisms are deranged in metabesity due to negative impacts on neural immune responses, which increases the risk of infections such as influenza or periodontal diseases. Further, there is a greater risk of death due to post-operative complications.
Survival / Life Expectancy	Life expectancy is negatively impacted in patients with metabesity due to the higher risk of cancer, stroke, CVD, diabetic complications, liver cirrhosis, neurologic complications, influenza, Alzheimer's disease and dementia, post-operative infections and cerebrovascular death.
Others: Special Situations	
Women with polycystic ovary syndrome (PCOS) / Fertility issues	Metabesity increases the risk of CVD complications such as dyslipidaemia or glucose intolerance in women with PCOS. It can also worsen the hormonal disturbances in PCOS affecting fertility of women due to the interplay of leptin and insulin resistance.
Fertility issues in men	Metabesity can cause fertility issues in men due to changes in reproductive hormones as well as DNA damage. This can result in reduced sperm count and motility because of reduced serum concentration of testosterone and an increase in serum estradiol.
Children and adolescents	Metabesity in children increases the risk of several chronic and acute conditions which can affect normal bone growth resulting in orthopaedic complications, degenerative conditions, and diabetes, as well as reduction in quality of life due to pain/effects on movement/function. In adolescents, it can disrupt development of secondary sexual characteristics and have an impact on sex hormone production.
Elderly	There is an increased risk of cardiovascular disorders, cerebrovascular complications as well as neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease, which have increased risk of morbidity and mortality and an increased dependence on family members. Other impacts include urinary incontinence, prostate cancer and depression, which affect the quality of life in the elderly.
Psychosocial stress	Chronic stress due to the impact of metabesity and the risk of complications can result in depressive disorders and/or insomnia.
Financial issues	The treatment cost of metabesity has an impact on the whole healthcare as well as individual family systems. Unit cost of physician's fee, medication supply and rehabilitation has an alarming effect on the financial concerns of these people.

ASA/AHA: American Heart Association/American Stroke Association; BMI: Body mass index; CVD: Cardiovascular disease; TIA: Transient ischaemic attack.

Guidelines for Treatment of Metabesity

Lifestyle Changes

Diet-related counselling

Diet-related counselling promotes healthy eating patterns among patients due to an increased control over personal dietary habits with the help of sufficient nutrition-related knowledge.[29] Along with reducing the consumption of undesirable foods, diet-related counselling corrects the patterns of overall eating, dietary intake and lifestyle.[30] Table-6 demonstrates how diet-related counselling can be applied for the control of metabesity.

Table-6: Steps of diet-related counselling.[33]

Step 1	Introduction of the weight control programme to patients as well as assessment of their dietary behaviour
Step 2	Analysis of their dietary intake with the help of 24-hour dietary intake recall methods
Step 3	Caloric/dietary goal-setting on the basis of recall diary
Step 4	Facilitating the use of dietary record diary among the patients
Step 5	Setting target weight based on an understanding of individual caloric requirement and relationship with obesity
Step 6	Prescribing daily meals and recommended food intake levels along with means to facilitate a caloric balance in daily life
Step 7	Describing means to burn daily calories through different types of physical activities as preferred by the individual
Step 8	Enabling healthy dietary behaviours through understanding diverse food labels and nutrition requirements
Step 9	Learning cooking methods for lowering fat consumption such as the use of lean meats and proteins instead of high-fat red meats Lowering the intake of sodium and sugar while making healthy choices while eating out
Step 10	Follow-up with dietary analysis via 24-hour recall method and assessment of weight, body mass index and cardiovascular/inflammatory components with the help of relevant blood tests

Physical Activity

Table-7 outlines the recommended weekly exercise durations for the management of metabesity. In addition to this, there must be:

- An increase in non-exercise leisure time activities to reduce sedentary behaviour in individuals.[31] Examples include walking in the parks or playgrounds, walking to the mosques and using staircase rather than elevators.
- Consideration into physical needs and limitations of the individual so that the exercise plan described is practically implemented keeping in mind their health-related goals as well as the presence of other comorbid conditions.[32]

Ask / Ascertain	Ascertain the patient's height, weight, waist and hip measurement.	
Advise	Advise the patient to lose weight and explain the rationale for the advice.	
Assess	Assess readiness to change according to the stages of change model:	
	Pre-contemplation	Not ready to attempt weight loss
	Contemplation	Interested in weight loss, but not ready for action
	Preparation	Ready to plan for action
	Action	Ready to engage in the effort to lose weight
	Maintenance	Having successfully lost, engage in effort to keep weight off
Assist	Assist with weight loss according to the patient's age.	
Arrange	Arrange follow-up to monitor progress	

Figure-4: 5 'A' approach for providing counselling related to physical activity (Vallis et al[59]).

Table-7: Recommended weekly exercise durations for the management of metabesity.[17]

Type of Physical Activity	Recommended Weekly Duration / Sessions
Moderate – intensity physical exercise	More than 150 minutes
Or Vigorous – intensity physical activities	Greater than 75 minutes
Aerobic activity of moderate intensity	300 minutes
Aerobic activity of vigorous intensity	150 minutes
Muscle – strengthening exercises or Resistance training	2 to 3 weekly sessions

- Exercise programmes can be integrated into the daily routines of the patient with the help of effective counselling sessions such as the 5 'A' method (Figure-4).
- Individual counselling, team-based counselling and group counselling can be provided for the improvement of physical activity in patients.[32]
- Once-a-month counselling facilitated a mean weight loss of 7.4 kg over 2 years in patients with type 2 diabetes.[33]

Recommendations

Moderate-intensity physical exercise for 150 minutes weekly,

or

Vigorous-intensity physical activities for 75 minutes weekly.

Diet-related counselling utilising the 5 'A' approach.

Grade A

Psycho-Social Stress Management

- Relaxation techniques such as meditation along with programmed stress management for a duration of 8 weeks have shown massive weight loss effects.[34]
- A reduction in Beck's Depression Inventory (BDI) score facilitates rational food choices among individuals with metabesity, which is apparent by their choice for picking healthier alternatives compared with previous dietary patterns.[35]
- Maintaining food and intervention diaries for reflecting upon stress management programmes also minimises binge eating sessions by enabling a greater degree of awareness of personal dietary patterns.[34]
- Incorporation of approaches such as cognitive behavioural therapy and management of substance use disorder also helped in managing food dependence in obese individuals.[36]

Recommendations

Cognitive behavioural therapy can be incorporated for psycho-social stress management for reducing food dependence

Meditation techniques are suggested for psycho-social stress management

Grade A

Medical Nutrition Therapy

Medical nutrition therapy (MNT) comprises meal replacements based on the needs of the patient consisting of varied composition of proteins, carbohydrates, and fats. Based on the individual's current diet, total meal replacement or necessary alterations need to be made to achieve a deficit of 500 to 750 kcal per day.[21] Regular weight monitoring (weekly or more) along with high levels of physical activity (200-300 minutes per week) must be combined with MNT in these patients.[30]

Low-fat diet in metabesity

Diets with a fat percentage of 20 to 35% facilitate weight loss and reduce the risk of other comorbidities. A weight loss of 6 to 11kg after 12 months can be expected through the intake of this diet.[37]

High-protein diet in metabesity

Protein intake greater than 25% of the total caloric content is associated with reduction in waist circumference, moderation of the waist-to-hip ratio as well as a reduction in intra-abdominal adipose tissue.[37] It is thus effective in reducing the risk of cardiovascular disorders associated with metabesity. However, it must be avoided in persons with existing cardiovascular diseases or other comorbid conditions because of the risk of adverse events.

Low-carbohydrate diet in metabesity

Low-carbohydrate diet is one of the most standard approaches for MNT in metabesity.[30] Since a high-carbohydrate, low-fat diet has been refuted for the management of comorbid conditions, especially diabetes, the intake of a low-carbohydrate diet forms the mainstay of management.[37] Recent recommendations suggest a low-carbohydrate diet along with low intake of saturated fats.[3]

Specialised diets in metabesity

An ideal mix of macronutrients for all people with metabesity has not been established.[29] Therefore, a suitable combination based on patient's needs must be optimised (Table-8). This may include moderations based on the weight loss needs of the patient.

A recent clinical trial has found evidence in favour of total meal replacement where effective weight loss was induced with the help of this phase. A low energy formula diet consisting of 825-853kcal per day at the inducing phase of 3 months, followed by re-introduction phase, was able to achieve substantial weight loss in patients with diabesity.[23] A weight loss of more than 15kg was achieved in one-fourth of the subjects indicating the strength of a structured MNT. This diet, at the induction phase, consisted of 59% carbohydrate, a major component of the diet. Fats, proteins and fibres were 13%, 26% and 2%,

Table-8: List of foods to be eaten and avoided in the context of Pakistani population. (Adapted from Safdar et al[60] and Iqbal et al[39]).

Foods that must be eaten	Foods that must be restricted
Fresh fruits and vegetables	Saturated and trans-fat contained in fast food products such as fries and red meats such as lamb and beef
Whole grains	Organ meat dishes such as kata kat cooked in high-fat oils/butter
Low-fat dairy products	Biryani, pilaf, nihari, karahi, beef salan, kofta and korma/kebabs comprising of red meats
Protein-based food products except red meats, which also have a high-fat content	High-cholesterol foods such as halwa puri or fried potatoes which are deeply fried
	Sugar and bakery products such as panjiri, Karachi halwa
Eggs and lean meats	Foods containing high amounts of refined carbohydrates such as puri, bhatooras and rooghni naan

respectively. In the phase of food re-introduction, the percentage of carbohydrates was reduced to 50% whereas fats were raised to 35% and proteins at 15%.[23] This was continued for a year along with monthly visits for facilitating long-term maintenance through this diet. Since this dietary approach facilitated an improvement in the metabolic profile of the patient, assisting most in reducing their dependence on anti-diabetic / antihypertensive drugs, customised approaches can be preferred in cases of metabesity.[29]

Recommendations

Low-calorie diet with an intake of 825-853kcal per day for initial 3 months followed by gradual increase in dietary calories

Caloric deficit of 500 to 750kcal for weight reduction

Low-fat, high-protein and low-carbohydrate diet

Grade A

High-carbohydrate, low-protein diet

Grade C

Medical Nutrition Therapy (MNT) in Metabesity (Table-9)

Table-9: Medical nutrition therapy in the presence of comorbid conditions in individuals with metabesity (Adapted from Rochlani et al[42] and Nisak et al[29]).

Type 2 diabetes	Proteins are distributed to meet 15 to 20% of the total energy whereas fats meet 25 to 30% and 50 to 60% must come from carbohydrate sources. The intake of cholesterol is kept to lesser than 200mg per day for reducing the risk of cardiovascular disease. Fibre intake is between 25 to 30grams per day through the intake of whole grain products such as oats or whole wheat/multi-grain bread along with legumes and fresh fruits and vegetables.
Cardiovascular risks	Regular intake of fish - salmon, mackerel or trout - is recommended in patients with metabesity for the prevention of cardiovascular diseases. Two weekly servings are recommended.

Recommendations

Increase the intake of fresh fruits, vegetables, low fat dairy products and whole grains

Avoid the intake of high calorie and fried foods

Avoid red meats and organ meats

For persons with diabetes:

Fibre intake of 25 to 30grams

Grade A

Proteins must comprise 15 to 20% of the total energy needs whereas fats must meet 25 to 30% and carbohydrates must form 50 to 60%

Regular intake of salmon for individuals with cardiovascular disease

Grade B

Pharmacotherapy for Individual Risk Factors

Treatment of Obesity

Pharmacotherapy (Table-10) is indicated in individuals with:

- BMI greater than 25kg/m^2 or those with a BMI greater than 23kg/m^2 who have metabolic complications such as hypertension, type 2 diabetes or dyslipidaemia.[38]
- Metabolic complications in whom the dietary approach and lifestyle modifications have been ineffective for weight loss over 3 to 6 months.[38]

Table-10: Pharmacological agents and their applications in metabesity.

Pharmacological agent	Mechanism of Action	Applications
Orlistat	Facilitates the hydrolysis of dietary fats into fatty acids and monoacylglycerol	Management of patient with obesity and overweight with comorbid condition
Liraglutide	Glucagon-like peptide-1 receptor agonists, also known as GLP-1 receptor agonists or incretin mimetics, are agonists of the GLP-1 receptor.	Management of obesity in patients with or without impaired oral glucose tolerance or the presence of cardiovascular risk factors
Naltrexone / bupropion	Bupropion: a weak dopamine and norepinephrine reuptake inhibitor, enhances POMC cell production and release of alpha-MSH and beta-endorphin in vitro. Naltrexone: An opioid antagonist, blocks the MOP-R, therefore disrupting beta-endorphin inhibitory feedback on POMC cells.	Combination is indicated as an adjunct to increased physical activity and a reduced-calorie diet for chronic weight management in obese adults or in overweight adults with at least one weight-related comorbid condition, such as hypertension, type 2 diabetes, or dyslipidaemia.
Phentermine and topiramate	Phentermine: Also called Alpha-methylamphetamine.	The FDA has approved extended-release phentermine
extended-release	Used as an appetite suppressant Topiramate: blocks voltage-dependent sodium and calcium channels. It also inhibits the excitatory glutamate pathway while enhancing the inhibitory effect of GABA. Moreover, it inhibits carbonic anhydrase activity.	plus topiramate as an addition to a reduced-calorie diet and exercise for chronic weight management in overweight or obese adults. Facilitates 15-30 mg daily weight loss along with 3.6kg additional weight loss at 6 months

Alpha-MSH: Melanocyte-stimulating hormone; MOP-R: mu opioid receptor; POMC: Pro-opiomelanocortin.

Recommendations

Orlistat or liraglutide: For individuals with BMI above 27kg/m^2 with history of cardiovascular/metabolic risk factors or individuals with a BMI above 30kg/m^2.

Orlistat must be preferred for long-term use in patients with metabesity.

Phentermine, topiramate, naltrexone/bupropion: Should only be started after assessing patient profile and risk factors.

Grade A

Treatment Based on Risk Factors

1. Coronary Disease

Coronary disease is consistent with very high risk category according to AACE. Treatment goals for these patients must include reduction of LDL cholesterol under 70mg/dl, which can be managed with the help of dietary and exercise interventions along with pharmacotherapy of the cardiovascular condition.[17]

Treatment of Coronary Disease

A sedentary lifestyle is the primary cause of coronary disease in Pakistan, with 72% of the total cases being attributed to the cause. Family history (42%), dyslipidaemia (31%), obesity (24%), hypertension (19%) and diabetes mellitus (16%) are other top causes of coronary disease identified in the Pakistani population.[39,40] Treatment of coronary disease must involve management of these underlying causes along with the management of metabesity through diet, exercise and/or pharmacotherapy.[41]

2. Dyslipidaemia or Hypercholesterolaemia

A weight loss goal of 5 to 10% must be defined for obese patients with dyslipidaemia or Hypercholesterolaemia with the help of calorie-controlled meal plans and exercise therapies.[17]

Exercise Therapy

- Thirty minutes of moderate-intensity physical activity 4 to 6 times per week must be recommended
- This approach burns 4 to 7kcal per minute and an expenditure of at least 200kcal per day is recommended
- Suggested activities include exercise activities such as brisk walking, water aerobics, stationary bikes or outdoor biking or non-exercise tasks such as playing preferred sports, and performing household activities such as scrubbing, cleaning or mowing the lawn.[17]

Pharmacological Treatment

- Statin therapy is the first-line treatment for achieving the goals of LDL reduction. It is continued even after achieving these targets to further reduce the risks of cardiovascular disease.[42]
- Fibrates and omega-3 fish oil (2 to 4 grams daily) can be prescribed in patients with triglyceride levels above 500mg/dl.[42]

3. Hypertension

- Angiotensin-converting enzyme inhibitors or angiotensin receptor blocker must be the first-line drug therapy for the management of blood pressure.[39]
- Calcium channel blockers can be used as second-line treatment in patients, but may contribute to weight gain.[41] Beta-blockers are not preferred in patients with metabesity and hypertension.

Recommendations

For patients with cardiovascular diseases, the treatment goal must be to facilitate the reduction of LDL cholesterol under 70 mg/dl and blood pressure below disease-specific range.

Recommendations for achieving this goal include caloric reduction along with regular moderate-intensity physical activity for 150 minutes weekly and treatment of existing coronary conditions in collaboration with a cardiovascular team.

Grade A

4. Stroke

For the prevention of subsequent stroke episodes in patients with metabesity:

- Initial weight reduction goal must be set at 5 to 10% for managing the cardiovascular risks. Further weight loss must be facilitated if the cardiovascular risk factors remain abnormal. Regular investigations must be performed to determine these risk factors.[43]
- BMI levels of these individuals must be maintained within the range of 22 to 25 kg/m^2 to reduce the risk of mortality due to stroke. This can be possible with the help of repeated diet-related counselling of the patients along with pharmacological treatment with orlistat 60-120 mg, three times a day, so that weight loss is sustained.[44]

Recommendations

For preventing future stroke episodes, weight loss goal of 5 to 10% must be made to ensure that BMI falls within the range of 22 to 25kg/m^2.

Grade A

5. Diabetes Mellitus

- Patients must engage in 150 minutes of weekly activity such as brisk walking for 15 to 20 minutes along with flexibility and strength training exercises.[17]
- Pharmacological treatment for type 2 diabetes involving the use of oral antihyperglycaemic agents or insulin must be provided alongside the management of metabesity through diet and exercise interventions.[45]
- Preferred first-line medications are the ones with benefits of weight loss, including metformin, sodium-glucose co-transporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP-1) agonist.

6. Liver Disease

- Lifestyle changes are recommended to achieve a target weight loss of 7 to 10 % of the body weight.[46]
- Pharmacotherapy is considered in patients with non-alcoholic fatty liver disease or in those who are at a risk of advancement of the condition.[27]
- Vitamin E can be started in patients without type 2 diabetes, but must be discontinued if enzyme levels do not normalise after 6 months of therapy.[25]
- Pioglitazone/SGLT 2 inhibitors can be considered in

patient with underlying diabetes along with liver disease. Frequent assessment of liver function test should be considered.

7. Neurological or Psychological Risk

- Safety of weight-loss medications must be efficiently tested before prescribing to the patient. In patients with psychological disorders and diabetes, metformin can be administered along with anti-psychotic drugs to facilitate weight loss and reduce metabolic complications.[31]
- Orlistat and phentermine can be used in patients with obesity and depression.

Recommendations

Physical activity, dietary and lifestyle changes are recommended for patients with liver disease and diabetes along with the management of their respective condition.

In diabetic patients, metformin, SGLT2 inhibitor, or GLP 1 agonist can be prescribed alongside orlistat for weight loss.

For patients with existing neurological or psychological conditions, orlistat 120mg must be preferred based on their safety profile. Weight loss medication with neuropsychiatric side effects should not be prescribed to patients with psychiatric disorders.

Grade A

Surgical Approaches

Bariatric Surgery

Bariatric surgery can be combined with other procedures such as lifestyle modifications or pharmacotherapy to enhance patient outcomes. Better treatment outcomes are associated with procedures such as sleeve gastrectomy and gastric bypass surgery.[47]

Indications

- BMI between 30 to 34.9, or above in patients with comorbid condition.[47]
- Comorbid conditions include type 2 diabetes, hypertension, hyperlipidaemia, obstructive sleep apnoea, non-alcoholic fatty liver disease, gastro-oesophageal reflux disease, asthma, venous stasis disease, severe urinary incontinence, debilitating arthritis or patients with an impaired quality of life due to obesity.[48]

Selection of patients

Must be considered in:

- Adults with a BMI above 35kg/m^2, especially in presence of diabetes or presence of other comorbid conditions. Bariatric surgery facilitates normalisation of blood glucose levels in patients with early type 2 diabetes.[47]
- Patients who are not managed with prolonged lifestyle and pharmacological therapy and are in need of lifelong support and repeated screening or monitoring of comorbid conditions.[47]

Recommendations:

Recommendations for bariatric surgery include patients with a BMI above 35kg/m^2 or patients with the presence of comorbid conditions whose lifestyle is affected due to metabesity.

Grade A

New Interventions

Embolisation Approaches

- Embolisation of left gastric artery facilitates a reduction in both waist circumference and waist-to-height ratio in patients after 9 months of treatment.[49]
- However, it must be performed carefully in patients with metabolic disorders due to the risk of serious complications such as mucosal ulcers or severe pancreatitis.[50]
- These procedures require expertise and should be performed in high-volume centres only. Therefore, they need careful planning and referral procedures to be involved from the beginning.

Intragastric Balloon Treatment

- Intragastric balloon treatments with ReShape, ORBERA™, and Obalon are also available. But like all treatment modalities, these treatments carry risk of side effects, especially in patients with metabesity who present with comorbid conditions.[51]
- These risks include post-operative nausea, abdominal pain and vomiting, which are noted in as high as 86.9% of the participants making this approach non-preferable.[52]

Alternative / Herbal Supplements

There are a number of herbal supplements used for the purpose of weight loss. These include but not limited to Amaranthus, papaya seeds, cinnamon, black pepper, Hibiscus tea leaves, green tea, dandelion, coriander leaves, citrus extracts, and peppermint. Figure-5 outlines the possible pathways behind herbal treatment of metabesity.

There is not enough scientific data to support or recommend any of these.

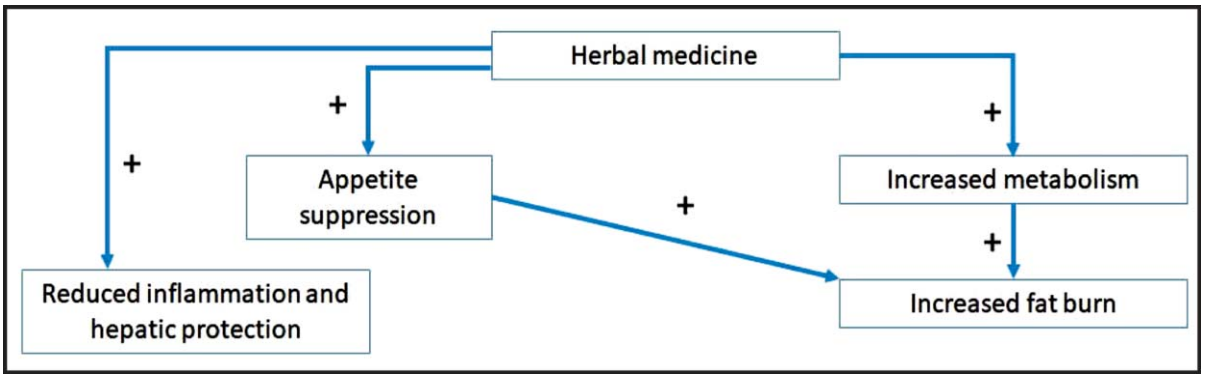

Figure-5: Pathways behind herbal treatment of metabesity.[61]

Recommendations

Newer alternatives such as intragastric balloon placement and embolisation approaches must only be considered in select patients and with the proficiency of doctor performing the procedure.

Grade A

Patient-Centred Treatment

Patient-centred care approach can be utilised in the management of obesity by ensuring involvement of the patient in the process of decision-making and planning, such as in the development of their dietary changes and exercise routines.[53] This can also involve patient education and information on the disease while keeping in mind their needs. This implies that, for patients with an increased risk of cardiovascular disease, education of these risk factors and the need for regular screening must form a part of these sessions.[54]

Similarly, in patients with a family history of cancer or Alzheimer's disease, education plan must be suitably adjusted.[55] Through these approaches, an increased compliance with the management protocol can be obtained and the issue of unawareness of the condition and its risks can be managed. Further, in persons with complex needs such as individuals with an increased psychological stress or patients at a risk of suicide, suitable care coordination and integration must be planned in addition to physical and emotional support, which must be extended to all patients.[31]

Recommendations for Implementation in Pakistan

This clinical practice protocol can be implemented for managing metabesity, after rigorous changes in the existing health care systems for regular screening and diagnosis of metabesity and its related comorbidities. Since Pakistanis are at a greater risk of metabolic complications, it is also essential that health education forms an integral part of implementation so that greater rates of patient compliance can be achieved.[15] During health education, patient's needs, values and preferences must be respected and culturally-sensitive educational strategies such as linking of health education principles with the learning of Islam must be used when deemed appropriate.

Due to close interactions with the community and an increased emotional bond with family members, it is also instrumental to include patient's friends and family members in the process of decision-making, especially in more serious matters such as surgical interventions or matters involving prolonged care.[53] Other recommendations include a proposal for increased access to healthcare services in Pakistan so that metabesity and its risks and complications such as coronary artery disease, which is currently on the rise in

the country, can be effectively managed.[40] Role of primary care physicians in early diagnosis by measuring BMI and other risk factors cannot be overemphasized. General physicians usually interact with these individuals at much earlier stage as compared to specialists and consultants.

Recommendations

Patient-centred approaches for the management of metabesity along with culturally-sensitive educational practices must be adopted by practitioners in Pakistan. Family, caregiver and social and/or religious leader's involvement is pivotal in these programmes.

Grade A

Acknowledgement

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work, and have given final approval for the version to be published.

The authors thank Dr. Punit Srivastava for providing medical writing support and Syed Ikram Raza for research collection in the preparation of this manuscript.

Conflicts of Interests: No competing financial interests.

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