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EPIDEMIOLOGY, PATHOGENESIS & ETIOLOGY, COMPLICATIONS, CLASSIFICATION, EVALUATION TECHNIQUES AND THERAPEUTICS OF OBESITY

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Abstract: Obesity is a persistent, complex multifactorial, and morbid disease characterized by excess adiposity, which is excess body fat that has a negative impact on health. Obesity is a global health concern with a significant increase in occurrence over the previous limited years. Obesity has a complex etiology that involves interactions between hormones, the environment, and genetics. The foremost reason for obesity is a persistent energy disproportion between ingested and depleted calories. Excess energy intake triggers lipocytes and fat cell overgrowth, and the creation of organ fat or intra-abdominal fat in non-adipose tissues, resulting in cardiovascular and liver diseases. The complications of obesity are very extensive. There are various problems linked to obesity are hypercholesterolemia, hypertriglyceridemia, atherosclerosis, hypertension, type-2 diabetes mellitus, hyperinsulinemia, cholelithiasis or gallstone, non-alcoholic fatty liver disease, osteoarthritis, respiratory problems, obstructive sleep apnea, hypoventilation or pick-wickian syndrome, stroke, cancer, dementia, depression, gynaecologic problems, polycystic ovarian syndrome, skin problems, social-psychological problems, chronic kidney disease and urologic problems. Based on genetic involvement, obesity can be classified into 3 types that is syndromic obesity, monogenic obesity and polygenic obesity. The anti-obesity agents may be evaluated using the following techniques that are diet-induced obesity, seasonal obesity, exotic models of obesity, non-human primate models of obesity, virus-induced obesity, hypothalamic obesity, genetic obesity models, assays of anti-obesity activities, assays of obesity-regulating peptide hormones and other models of obesity and associated metabolic changes. There are various approaches for the management and treatment of obesity, that is lifestyle modifications, anti-obesity medicines, bariatric surgery and faecal microbiota transplantation. Lifestyle modification is still the backbone of managing obesity. Anti-obesity medicines are used when an individual whose body mass index is superior than 30 kilograms per meter squared, is not able to reduce weight by lifestyle modifications. Bariatric surgical procedure, also acknowledged as weight loss surgery, is used for people with a body mass index of more than 35 or 40 kilograms per meter squared, who have coexisting and are unable to reduce weight with lifestyle modifications and anti-obesity medicines. Transplantation of healthy human faecal microbiota microorganisms into obese patients may have an impact on weight loss and management by faecal microbiota transplantation method.

Index Terms - Obesity, Adiposity, Pick-Wickian Syndrome, Body Mass Index, Bariatric Surgery and Faecal Microbiota Transplantation.

I. INTRODUCTION

Obesity is a persistent, complex multifactorial, and morbid disease characterized by excess adiposity, which is excess body fat that has a negative impact on health. It is regarded as a foremost community health apprehension and is graded as the fifth primary source of death globally, affecting approximately 650 million people (Wharton, S. *et al*., 2020; Busetto, L. *et al*., 2021). Obesity is the presence of extra bodily fat. It is one of the most prevalent nutritional problems in the developed world. Obesity is diagnosed using the waist or belly circumference-to-height ratio, which should be less than half of the height (Ashwell. *et al*., 2012), as well as the body mass index. Body mass index is heaviness in kilograms per height in meters squared; the normal body mass index ranges from 19.8 to 26, the overweight ranges from 26.1 to 29, and the obese ranges from more than 30. Obesity is demarcated as a body mass index above or equal to 30, whereas overweight is demarcated as a body mass index between 26.1 and 29. Obesity and overweight standards vary by population (Consultation, W.H.O.E. 2004). For example, Chinese people have a different standard instead of WHO. The suggested standards for the Chinese public are as follows: underweight (body mass index less than 18.5 to 23.9 kilograms per meter squared), overweight (body mass index 24 to 27.9 kilograms per meter squared), and obese (body mass index more than 28 kilograms per meter squared) (Zeng, Q. *et al*., 2021; Bei-Fan, Z. 2002). Raised body mass index is a menacing aspect of noncommunicable diseases such as diabetes mellitus, cardiovascular disease, and musculoskeletal disorders, subsequent in a significant decrease in life excellence and expectation. Currently, 1.3 billion individuals worldwide are overweight or obese (N.C.D.R.F. 2017). As a result, obesity is the fifth leading source of non-communicable diseases. Obesity rates have risen worldwide. Over the previous 50 years, the worldwide obesity rate has increased significantly. Obesity has become a major issue in recent decades, and failure to control the obesity pandemic is expected to reverse the steady increase in life expectancy. Being obese is associated with extra deaths than being underweight, and it is further widespread worldwide (Al Kibria, G.M. 2019). Being obese increases the menace of a numeral of diseases and ailments that are connected with an advanced death proportion. Numerous epidemiological studies have shown that obesity exhibits a significant part in the development of a number of metabolic complications, such as type-2 non-insulin-dependent diabetes mellitus, metabolic-dysfunction associated steatotic liver disease earlier identified as non-alcoholic fatty liver disease, cardiovascular diseases, metabolic syndrome, chronic kidney disease, hyperlipidemia, hypertension, some types of cancer, and mechanical complications like depression, osteoarthritis, and obstructive sleep apnea. These conditions place a significant load on the general community and healthcare organizations each year (Kinlen, D. *et al*., 2018; Swinburn, B. A. *et al*., 2011). One of the most significant negative effects of obesity is cardiovascular disease. It is regarded as a critical risk factor for heart failure, hypertension, and coronary heart disease. Healthcare systems may face additional burdens in treating such diseases. For instance, research indicates that overweight people have 30 percent greater medical expenses than people with a typical body mass index (WHO Consultation on Obesity, 2000). Treating the impacts of obesity presents a costly problem for patients since related total healthcare expenses increase every ten years (Bray, G.A. *et al*., 2017).

figure-(1): waist measurement of obese women (https://www.istockphoto.com/photo/obesity-unhealthy-weight-nutritionist-inspecting-a-womans-waist-using-a-meter-tape-gm1314797892-402936622?searchscope=image%2cfilm)

II. EPIDEMIOLOGY OF OBESITY

Obesity is nowadays widely acknowledged as a long-lasting, relapsing, and complex disease that impacts practically each organ arrangement with its linked biotransformation disorders or other associated complications, like type-2 non-insulin dependent-diabetes mellitus, cardiovascular disease, cerebrovascular diseases, and tumors. It affects mutual physical and psychological well-being in various ways that are incapable of effortlessly resolving by losing weight. Obesity is determined by heredity, biology, health-care accessibility, psychological health, sociological aspects, social economics, individual lifestyle, and other ecological inducers (Ruze, R. *et al*., 2023). Typically, the body mass index is used to characterize obesity. However, this approach is more appropriate for the general public than for characterizing the complexities of obesity as an illness, which calls for an additional thorough and complete analysis. Inadequate extensive prevention, treatment, and management, coupled with the ineffectiveness of programs aimed at resolving the problem, are contributing to the increased incidence of obesity across numerous prosperous and middle-income nations. The way that obesity is seen differently across cultures is another important factor contributing to this phenomenon. The fundamental reason for the increasing incidence of obesity in most industrialized countries, including parts of Europe and North America, is a strengthened socio-economy. However, the global epidemiology varies among countries and the incidence of obesity is fluctuating at high stages in some areas, like portions of Europe and North America, both male and female obesity is currently increasing worldwide, with none attaining a decay in the widespread across its community. The WHO Americas area has the maximum rates and numbers of obese individuals, although low-and middle-income nations as well as tiny island developing states are currently seeing the fastest rates of obesity population growth. Due to factors like age, menopause, and reproductive status, women are more likely than males to be obese globally. By 2030, over 1 billion people worldwide approximately 14 percent of males and 20 percent of females will be obese. Among grown persons with overweightness (Class 1, 2, and 3, body mass index more than 30 kilograms per meter squared), severe obesity (Class 2 and 3, body mass index more than 35 kilograms per meter squared), and severe obesity (Class 3, body mass index more than 40 kilograms per meter squared), the percentages will be 18 percent, 6 percent, and 2 percent, respectively. The Middle East and Western Pacific areas are expected to suffer an increased proportion of people with juvenile obesity by 2030, with older people actuality more responsible for the change. The Western Pacific area has an extreme incidence and number of children with obesity. The effects and complications of obesity are immeasurable, necessitating immediate and efficient action from all nations. However, the main cause of the differences in the ability of different countries to prevent obesity is their economic inequality. The World Obesity Federation-World Obesity predicts that the countries with higher incomes are better equipped to address the issue of obesity prevalence, while low- and middle-income countries are the least prepared. Even though there have been calls for action to prevent obesity since the 1970s (Kumanyika, S. *et al*., 2020), we haven't done a very good job of addressing one of the most significant risks to community well-being in the twenty-first generation. Our most recent defeat is to meet the 2025 goal to obstruct obesity incidence ahead of 2020 (World Obesity Federation. 2022) is already raising alarms that, if we don't increase our efforts to address obesity globally, the actual number of obese people in 2030 maybe even more unexpected and unbelievable. Notably, nations with greater adult obesity rates but comparatively lower childhood obesity rates may profit more from successful obesity preventive measures.

III. PATHOGENESIS AND ETIOLOGY OF OBESITY

Obesity has a complex etiology that involves interactions between hormones, the environment, and genetics. Even though several candidate genes have been linked to the etiology of obesity, these results are not entirely consistent (Clement, K. *et al.*, 1995; Ristow, M. *et al*., 1998). These genes include the chromosome 10p, melanocortin-4 receptor, peroxisome-proliferator-activated receptor gamma-2, beta-3-adrenergic receptor and other genetic polymorphisms (Clement, K. *et al.*, 1995). The regulation and pathogenesis of obesity are influenced by many hormones, including adipokines, gut-related hormones, and others.

3.1 Causes for obesity

There are various reasons for obesity-hereditary errors, hormone imbalance, and other reasons.

3.2 Hereditary errors

Satiation indication not sent or perceived, incapability to exploit deposited energy and incapability to enhance brown fat thermogenesis to get free of excess consumption energy.

3.3 Hormone imbalance

Increased glucocorticoids, hypothyroidism, hyper-insulinaemia and unfortunate neuropeptide levels.

3.4 Other reasons

Damage to the hypothalamus and socio-cultural nourishing behaviour (Maheshwari, K. K. 2023).

The primary reason for obesity is a chronic energy disproportion between ingested and burned calories (Lin, X. *et al*., 2021). Excess energy intake causes lipocytes and fat cell overgrowth, and the creation of organ fat or intra-abdominal fat in non-adipose tissues, resulting in cardiovascular disease and liver diseases. Fatty tissue can also release adipokines and inflaming cytokines, influencing the local microenvironment, inducing insulin resistance, and hyperglycemia, and activating inflammatory signalling paths. This impairs the growth and development of diseases linked with obesity (Jin X. *et al*., 2023). There are various pathways that contribute to obesity. The traditional belief is that the fundamental explanation is that the body stores substantially more energy than it uses. The overabundance of energy is dumped in adipose cells, subsequent in the classic obesity disease. The pathologic enlargement of adipose cells will interrupt the nutritious indications that cause obesity (Heymsfield, S. B. *et al.*, 2017). Interestingly, new studies have demonstrated that, when it comes to controlling weight and preventing disease, sources of food and nutritional value matter more than the amount in the diet (Sacks, F. M. *et al*., 2009). As a result of the struggle between environment and microenvironment, genetics and epigenetics, nurture and nature, an increasing number of etiologies or defects that lead to obesity are being found. More research is being done to understand how the brains of obese individuals elevate their desire for food, how abdomen hormones, fatty tissue, and microbial communities in the abdomen keep appetite and satiety in the hypothalamus, how abdomen dysbiosis contributes to the progression of obesity, and how impaired glucose and lipid biotransformation leads to secondary issues with health (Singer-Englar, T. *et al*., 2018). Furthermore, hereditary aspects are identified to play important parts in defining a person's susceptibility to weight expansion (Singh, R. K. *et al*., 2017). Current phenotypic research has provided valuable aid for studying the global obesity epidemic (Lopomo, A. *et al*., 2016). All of the energy human beings require for basic biotransformation processes, and thermogenesis comes from the diets and beverages they consume. This energy is then stored as extremely energetic molecules. The body's energy intakes and outputs are balanced in a constant state. 60 to 80 percent of the surplus energy is retained as fat when the consumption of energy exceeds energy utilization (Boron, W. F. *et al*., 2017). The remainder is retained as glycogen, utilized in protein production, or lost, such as during thermogenesis (Boron, W. F. *et al.*, 2017).

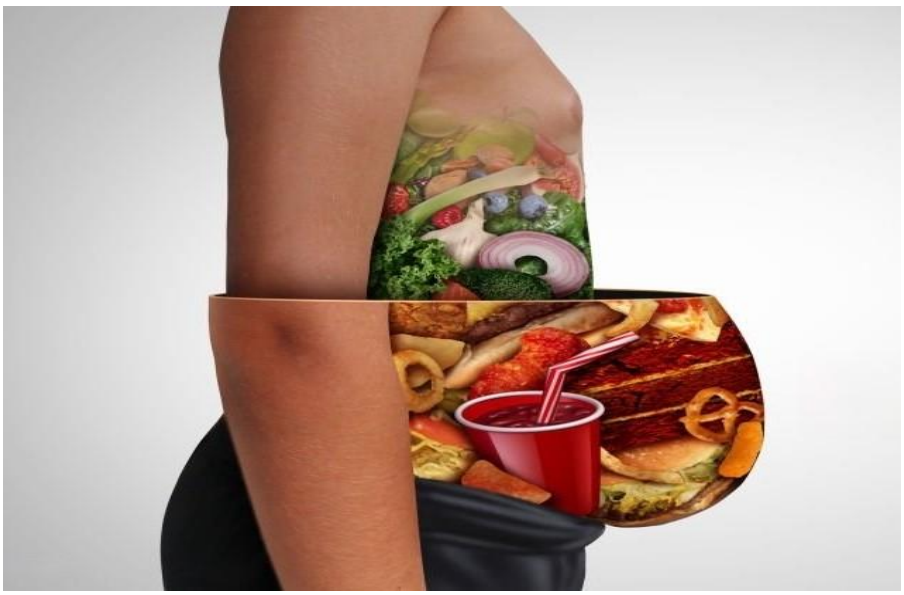

figure-(2): effect of normal and high-fat diet (https://www.istockphoto.com/photo/losing-weight-and-nutrition-gm1358869003-432373863?searchscope=image%2cfilm)

The Western diet, which is heavy in body fat and sweet, has been related to an enhanced menace of obesity. Obesity has recently been related to the stomach's microbial ecology. The Western diet has a deleterious effect on the diversity and alignment of the abdomen microbiota. Western diet eaters have been found to have a less diversified abdomen microbiome, which is marked by a greater number of pathogenic and less helpful microbial species. This changed microbial composition is linked to enhanced food absorption, inflammatory processes, and biotransformation dysfunction all of which may exacerbate obesity and lead to weight gain (Turnbaugh, P. J. *et al.*, 2008). Furthermore, the abdomen microbiota plays a critical part in regulating metabolism, energy homeostasis, and fat storage. It also plays a role in the production of short-chain fatty acids, the abstraction of energy units from diet, and the variation of hormones intricate in appetite regulators. Dysbiosis, or a disproportion in the abdomen flora ecology, can hinder these processes and may also promote weight gain. Research on experimental animal models and human being data indicates that foods rich in fiber, starch, and plant-based polysaccharides provide better abdomen microbial assortment and well-being benefits, while foods more in body fat, sweet, and animal protein support less assortment and a higher menace of obesity and cardiovascular diseases and biotransformation diseases (Wan, Y. I. *et al.*, 2020). A major factor in regulating the diet-related cardiometabolic risk is the synthesis of short-chain fatty acids. The composition of the abdomen flora is positively impacted by meals high in fiber or prebiotic fiber supplements, but diets high in fat, especially saturated fat, have the opposite effect (Afshin, A. *et al.*, 2017).

figure-(3): comparative effect of diets on the human body (https://www.istockphoto.com/photo/losing-weight-with-healthy-eating-gm1431596489-474145331?searchscope=image%2cfilm)

3.5 FLOW CHART FOR THE PATHOGENESIS OF OBESITY

Hyperphagia and extreme obesity are the outcomes of leptin signalling insufficiency caused by alterations in the leptin gene or its associated receptor.

⬇

When leptin levels are insufficient, neuropeptide-Y neurons are triggered and pre-opiomelanocortin neurons are suppressed, which leads to hyperphagia.

⬇

By encouraging the uptake of fatty acids and glucose by adipocytes and the storage of calories as fat, enhanced insulin production plays a role in the pathophysiology of obesity while simultaneously inhibiting lipolysis.

⬇

Agouti-related peptide neurons are stimulated during negative energy balance fasting, with lower insulin and leptin plasma concentrations.

⬇

Two single nucleotide polymorphisms in the receptor, Alanine-204-Glutamic acid and Phenylalanine-279-Leucine, have been associated with obesity and very short height. Uncommon alterations and single nucleotide polymorphisms in the gene expressing the ghrelin receptor are correlated to human-being obesity and short stature.

IV. COMPLICATIONS OF OBESITY

The complications of obesity are very extensive. The number of people who are overweight or obese has increased significantly over the preceding few decades, making the worldwide obesity pandemic currently the most critical health issue. Diabetes mellitus has also become increasingly common along with this rise. In addition to being a major predictor of type-2 diabetes, obesity has been related to gastrointestinal, musculoskeletal, integumentary, respiratory, and reproductive system diseases as well as cardiovascular and some malignancies. It has also been associated with social stigma and the psychological issues that result from it. Overweight and obesity in kids and teenagers are also on the rise, leading to the development of diseases that were formerly exclusive to the elderly. Obesity from childhood typically persists throughout adulthood, making it a chronic issue. When chronic obesity becomes so widespread, it can deplete families' funds and overload systems in terms of economic costs (Moini, J. *et al*., 2020).

4.1 Problems due to obesity

Hypercholesterolemia, hypertriglyceridemia, atherosclerosis, hypertension, type-2 diabetes mellitus, hyperinsulinemia, cholelithiasis or gallstone, osteoarthritis, hypoventilation or pick-wickian syndrome, stroke, cancer (Maheshwari, K.K. 2012).

4.2 Coronavirus disease-19 and obesity

Since the beginning of the COVID-19 severe acute respiratory syndrome coronavirus-2 epidemic, epidemiologists, community well-being administrators, and medicinal professionals have been dedicated to a way to stop and manage this epidemic (Prendergast, H. *et al*., 2022). Those infested with severe acute respiratory syndrome coronavirus-2 were shown to have several risk factors, including diabetes, hypertension, and other cardiovascular illnesses (CDC, A. W. 2020). Subsequently, obesity was recognized as a separate risk factor for Coronavirus disease-19 and added to the high-risk list maintained by the Centres for Disease Control (CDC, Coronavirus Disease-19. 2020). Since then, several systematic reviews and retrospective studies from various nations have been conducted to investigate the occurrence and severity of severe acute respiratory syndrome coronavirus-2 in obese individuals. In many countries (Simonnet, A. *et al*., 2020; Cummings, M. J. *et al*., 2020; Monteiro, A. C. *et al*., 2020; Lighter, J. *et al*., 2020; Asare, S. *et al*., 2020; Sharma, A. *et al*., 2020; Pietrobelli, A. *et al*., 2020), coronavirus disease-19 patients having unfavourable consequences had a significant rate of obesity (21-46 percent) and overweight (48 percent). Nearly half (46 percent) of the critically sick coronavirus disease-19 patients in New York were fat (body mass index more than 30 kilograms per meter squared), according to a study (Cummings, M. J. *et al*., 2020). A survey from Detroit found that 38 percent of African Americans were obese (Asare, S. *et al*., 2020), and a study from France revealed that 67 percent of its critically ill coronavirus disease-19 patients were obese (Pietrobelli, A. *et al*., 2020). Similarly, obese individuals older than 60 years old had a higher risk of serious disease, according to a comprehensive review combining eight retrospective studies (Seidu, S. *et al*., 2020). Conversely, a study conducted in Greece revealed that obesity rates were significantly reduced in the older population, with 34 percent of obese intensive care unit patients being younger than 55 years (Halvatsiotis, P. *et al*., 2020). In grownups person treated with severe acute respiratory syndrome coronavirus-2 infection, obesity is also linked to the development of severe coronavirus disease-19 (Simonnet, A. *et al*., 2020; Lighter, J. *et al*., 2020; Cai, Q. *et al*., 2020; Yudong, P. *et al*., 2020), with obese sufferer experiencing more severe coronavirus disease-19 infection than non-obese sufferer. Likewise, a dose-response relationship was found between testing positive for body mass index and abdomen border in a sizable prospective cohort study of 502,543 middle-aged grownups person in the United Kingdom (Yates, T. *et al*., 2020). Similarly, obesity in men was reported to significantly increase the probability of developing severe coronavirus disease-19 compared to women in case series research conducted in China (Cai, S. H. *et al*., 2020). Obesity's adverse impacts on respiratory function have been connected to the correlation between obesity and coronavirus disease-19 infection. Obese people have changed respiratory physiology, which lowers expiratory reserve volume and functional residual capacity. These anomalies in ventilation-perfusion eventually culminate in hypoxemia (Zammit, C. *et al*.,2010). These frameworks are still not completely understood, yet. However, preventing obesity is still essential to limiting the spread of more severe coronavirus disease-19 strains.

figure-(4): obese patient with coronavirus disease-19 (this image is created by generative a.i. “adobe firefly” https://firefly.adobe.com/)

4.3 Type-2 diabetes mellitus and obesity

over the past three decades, diabetes mellitus, a progressive degeneration metabolic illness, has become epidemically prevalent and is closely associated with the obesity epidemic (Nathan, D. M. 2015; American Diabetes Association. 2016). A body mass index of 23 or more is seen in 90 percent of individuals with type-2 diabetes. In the USA, 28 million people have type-2 diabetes. The fact that over 80 million people are classified as prediabetic is even more concerning (Grundy, S. M. 2016). Significant morbidity and death are caused by the long-term consequences of diabetes, which are directly related to the microvascular damage that is associated with the disease. It has been demonstrated that microvascular disease leads to renal failure, retinopathy, neuropathy, and atherogenesis in addition to hastening the onset of heart failure (Grundy, S. M. 2016). The majority of diabetes's financial impact is ascribed to the condition's complications. More adult experiences with last-stage kidney disease, limb exclusions, and visual loss are caused by diabetes and its complications than by any other disease (Grundy, S. M. 2016). Most obese people have elevated blood glucose, which can be classified as prediabetes or diabetes. A haemoglobin A1C of 5.6-7.4 percent, a 2-hour post-cenal level of 140-199 mg/dl, or abstaining from food that is fasting glucose level in the range of 100-125 mg/dl serve as indicators of prediabetes. A sugar level above 126 mg/dl during abstaining from food that is fasting or 200 mg/dl after meals constitutes categorical diabetes (American Diabetes Association. 2016). Although insulin resistance is the main cause of hyperglycemia in obese patients, hyperglycemia is not the initial sign of metabolic syndrome; rather, it appears far ahead (Grundy, S. M. 2016). Insulin resistance, a key component of type-2 diabetes and a risk factor for atherosclerosis, hypertension, hyperlipidemia, polycystic ovarian disease, and metabolic syndrome, is closely associated with obesity. The pancreas secretes the hormones glucagon and insulin, which are both used by the human body to keep blood glucose levels within a very specific range. Whether a person develops diabetes or hypoglycaemia, such as it is ultimately determined by the synthesis of these endocrine hormones. Although in different ways, both hormones are released in response to blood glucose levels. There are still several unidentified pathways by which body fat leads to systemic insulin resistance. However, medical professionals are now aware of the leptin-related adipocyte hormone and the adipo-insulin axis. It controls the amount of food consumed and the amount of energy used. Peripheral glucose, insulin responsiveness, and the insulin-glucose axis are all regulated by leptin (Moini, J. *et al*., 2020). In the USA, the yearly prevalence of diabetes mellitus may be declining for the first time in 30 years as a result of endeavour to lower the load of cardiovascular disease and microvascular disease (American Diabetes Association. 2016). It is commonly known that controlling weight may prevent type-2 diabetes from developing from prediabetes and show promise in treating the disease. Metformin therapy has been demonstrated to decrease the progression of prediabetes to diabetes mellitus in addition to the preferred treatment, which incorporates mass loss and improved physical action (American Diabetes Association. 2016). Persons with type-2 non-insulin dependent diabetes mellitus with a body mass index of more than 35 who have not responded well to medication and lifestyle changes might be suitable for bariatric surgery.

figure-(5): administration of insulin in type-2 diabetic obese women (this image is created by generative a.i. "adobe firefly" https://firefly.adobe.com/)

4.4 Cardiovascular disease-hypertension and obesity

Numerous epidemiological studies have demonstrated that obesity is an important menace aspect for cardiovascular system diseases. The probability of coronary artery disease, cardiac infarction, stroke, and heart failure is markedly increased by obesity. About 18,000 of the more than 300,000 participants in a meta-analysis of 21 cohort studies experienced coronary artery disease through continuation. Time of life, gender, exercise, and emitted fumes were taken into account while estimating. Obese people had an 81 percent elevated menace of emerging coronary artery disease than subjects of ordinary weight. Additionally, there was a 32 percent rise in hazards for individuals who were considered overweight. Even with the cholesterol levels taken into account, these risks were still clinically important. Thus, it can be said that having a high body mass index or being fat has a negative impact on blood pressure and cholesterol in 45 percent of patients (Moini, J. *et al*., 2020). More than any other risk factor, hypertension in the presence of obesity increases the probability of cardiovascular disease. A sign of subclinical heart disease left ventricular hypertrophy, is seen in 70 percent of obese women with hypertension (Maggs, F. G. 2012). The Asia-Pacific Cohort Cooperation Study showed that there was a 9 percent rise in occurrences due to ischemic heart disease for every unit change in body mass index. Abdominal obesity has a significant correlation with acute myocardial infarction, according to the inter-heart study (Maggs, F. G. 2012). Patients with a body mass index of more than 25 account for 85 percent of cases of hypertension, and those who are obese are five times more likely to have the problem (Maggs, F. G. 2012). Numerous theories have come into existence to explain the link between obesity and hypertension. Enhanced renal absorption of sodium supplementary, increased intravascular volume, stimulation of the thoracolumbar nervous system and renin-angiotensin system, production of angiotensinogen from fatty tissue, and impaired insulin sensitivity are among the contributing components (Grundy, S. M. 2016). Adolescent hypertension cases have significantly increased during the past ten years. The sharp rise in teenage obesity has been connected to the rising trend in teenage hypertension. The strongest relationship between blood pressure and body mass index is observed in teenagers who are overweight or obese (Kelly, R. K. *et al*., 2015). The aspect of this teenage patient that concerns us the most is how it may affect adult cardiovascular risk and mortality, which is projected to be 12.8 percent globally. Low weight at birth, non-white ethnicity, low levels of exercise, irregular sleep patterns, and a family history of hypertension were among the risk variables (both modifiable and non-modifiable) related to an increased chance of developing hypertension (Kelly, R. K. *et al*., 2015). Treating obesity-related hypertension throughout adolescence may help reduce the risk of cardiovascular disease in later life. Resolving adolescent hypertension lowers the risk of coronary heart disease that is not symptomatic. Research indicates that reversing adolescent obesity before reaching adulthood is linked to a decreased risk of hypertension later in life. Additional risk reduction is linked to the resolution of excessive blood pressure before adulthood. According to certain research, adolescence is the best time to avoid irreversible heart disease. There is no doubt that treating hypertension in obese individuals can reduce chronic disease and death from cardiovascular system disease. Generally, studies point to calorie restriction as a critical treatment or adjuvant for managing adult obesity-related hypertension (Grundy, S. M. 2016). People who follow the Dietary Approaches to Stop Hypertension diet and have bariatric surgery have shown successful outcomes in controlling their hypertension. When choosing an antihypertensive drug, it is better to avoid drugs that increase impaired insulin sensitivity or other biotransformation syndrome menace aspects. Angiotensin-converting enzyme inhibitors, also known as angiotensin-2 receptor blockers, unselective beta/alpha-1 receptor halting, and calcium channel halting are drugs that fall into this group (in order of

preference). On the other hand, medications such as beta-1 halting and thiazide diuretic drugs that have been linked to increasing insulin resistance should be avoided by obese people (Grundy, S. M. 2016).

4.5 Dementia and obesity

According to a meta-analysis, overweightness and the chances of impaired thinking, remembering, reasoning, and Alzheimer's dementia disease are moderately correlated (Magalhaes, C. A. *et al*., 2015). Elderly people who suffer from age-related dementia experience a steady deterioration in their cognitive abilities due to a mix of pathogenic and cerebrovascular causes (Ishii, M. *et al*., 2016). Considering a predictable 35.6 million cases universal, this incurable disease is on pace to develop a significant well-being epidemic. There is a growing indication that midlife vascular menace aspects are associated with dementia in later life. Considering a disease frequency of one in nine seniors 65 years of age or older, Alzheimer's dementia disease is the utmost frequent reason of ongoing mental illness in the aged population (Magalhaes, C. A. *et al*., 2015). Research indicates that lifestyle variables are crucial at the beginning of Alzheimer's disease and that obesity may occur before dementia. It has been determined that being overweight or obese in middle age is a significant and independent menace aspect for the progress of Alzheimer's dementia disease far along in life (Magalhaes, C. A. *et al*., 2015). Research on the function of fatty tissue in brain well-being has found a link between adipokines and intelligible deterioration. Adipokines, which translate to "fatty cell in motion," influence functions of the brain, spinal cord, and peripheral nervous systems. The active translocation of leptin through the blood-brain barricade has a significant impact on hippocampus growth and function, particularly on functions related to memory and cognition. Standard anthropometric measures might not be as effective in predicting dementia or moderate cognitive impairment as standard adipokines like leptin, based on various studies. In comparison to women with obesity, one study indicated that there was a stronger correlation between elevated blood leptin levels and a decreased incidence of mental illness in females with an ordinary body mass index (Magalhaes, C. A. *et al*., 2015). Furthermore, obesity restricts leptin's neuroprotective effects on the brain, resulting in leptin resistance (Magalhaes, C. A. *et al*., 2015). The significance of leptin in Alzheimer's disease pathology is still under discussion, despite some recent research confirming that variations in leptin levels may be a menace aspect linked to the onset of the disease. However, further research did not consistently demonstrate the involvement of leptin in Alzheimer's disease pathology. Although opinions on the functions of certain adipokines differ, there seems to be a strong and detailed correlation between midlife obesity and age-related dementia. The human body of research indicates that obesity in middle age increases the risk of dementia while weight decrease in later life indicates the onset of dementia (Ishii, M. *et al*., 2016). Researchers can now look into potential therapeutic targets and new diagnostic methods to combat age-related dementias.

4.6 Hyperlipidemia and obesity

Patients with metabolic syndrome experience an adverse change in lipid biotransformation, as is associated with many disorders brought on by or affected by obesity, most notably visceral fat. Raised triglycerides and free fatty acids are associated with decreased higher-density lipoprotein-C and altered high-density lipoprotein function, while increased low-density lipoprotein is part of the general pattern of the lipid profile (Klop, B. *et al*., 2013). The entire context of future lipid metabolism changes is favourable to the production of these denser, smaller low-density lipoprotein particles in response to high fasting and postprandial triglycerides. These lipid profile alterations, when combined with insulin resistance, constitute an extremely atherogenic context. Enhanced suppression of hormonal responsive to lipase, an essential aspect in the production of lipolysis of intracellular fats, is brought about by higher insulin levels in the postprandial state. While most of the free fatty acids are still in the blood plasma, where it is leap by serum albumin and sent to the hepatic duct, there is an enhancement in free fatty acid uptake in the adipocytes and myocytes. Excessive triglyceride deposits in the liver cause the production of very low-density lipoprotein and directly hamper lipoprotein lipase's ability to metabolize chylomicrons, which increases the number of leftover triglycerides that are transported to the liver. The interactions of cholesterol esters and triglycerides are altered by chronic hypertriglyceridemia, leading to a biased pattern of reduced high-density lipoprotein-C and reduced triglycerides concentration in low-density lipoprotein, which is then processed by hepatic lipase to create enhanced amounts of low-density lipoprotein. The low-density lipoprotein metabolizes slowly leading to a rise in atherogenicity. The focus of managing hyperlipidemia in obese people is a mix of dietary and lifestyle alterations. Consumption of total fat and calories is the most evident goal for managing the imbalance in lipid profile since it is directly related to postprandial lipemia. Low-density lipoprotein is reduced and lipoprotein lipase activity increases when weight loss is the only factor. The kind of fat consumed also influences postprandial lipemia, with diets strong in

monounsaturated fatty acids and low in carbohydrates being preferred. Exercise has been shown to positively impact triglyceride metabolism and lipoprotein lipase activity, which in turn influence the lipid profile (Malnick, S. D. *et al*., 2006). While there is still discussion over the impact on high-density lipoprotein-C levels, decreased triglyceride levels have been adequately confirmed. Pharmacological therapy may be necessary for managing chronic hyperlipidemia in addition to diet and physical activity. For individuals who show improvement in lower-density lipoprotein and non-higher-density lipoprotein-C plasma levels, statins continue to be the first choice for treatment. Nonetheless, it seems that changes in triglyceride metabolism are the main cause of hyperlipidemia, and statins have minimal impact on triglyceride profile. In certain populations with co-occurring conditions such as diabetes or established cardiovascular disease, combination therapy using fibrate or niacin may be taken into consideration.

4.7 Gastrointestinal problems-liver disease and obesity

Numerous gastrointestinal issues have been linked to obesity. When it comes to the pathophysiology of obesity and the facilitation of calorie imbalance, the gastrointestinal tract plays a crucial role. Abdominal obesity and body weight have a direct correlation with fatty liver diseases including non-alcoholic steatohepatitis and gastroesophageal reflux disease. Additionally, gallstones and liver cirrhosis can be brought on by obesity. Because obesity affects the gallbladder's cholesterol versus lecithin and bile acid balance, it can result in gallstones. Being overweight impedes the gallbladder's ability to empty, which allows cholesterol-rich bile to build up and solidify into gallstones. Obesity may interact with other pathways and cause an earlier presentation of the disease or consequences when it is a risk factor for gastrointestinal issues (Moini, J. *et al*., 2020). Triglyceride excess also plays a role in the progression of hepatic steatosis, after explaining the general change in lipid metabolism (Fabbrini, E. *et al*., 2010). Data on prevalence imply a direct correlation between the level of liver steatosis and fatty liver hepatitis and the body mass index. The corresponding rates for non-obese persons with a body mass index of fewer than 30 kilograms per meter squared are 15 percent and 3 percent. In patients with a body mass index between 30 and fewer than 40 kilograms per meter squared, the rates rise to 65 percent and 20 percent, respectively, while in patients with a body mass index larger than 40 kilograms per meter squared, they rise to 85 percent and 40 percent, respectively. Intrahepatic triglyceride accumulation is mostly caused by the biotransformation of non-esterified fatty acids. Intrahepatic triglyceride buildup is mostly caused by the metabolism of non-esterified fatty acids. Non-esterified fatty acids circulate via the portal vein and hepatic artery, entering the liver. Visceral adipose tissue lipolysis adds significantly less to the burden of free fatty acids than subcutaneous fat metabolism (Fabbrini, E. *et al*., 2010). Therefore, when the body mass index increases, so does the quantity of non-esterified fatty acids given to the hepatic duct. The amount that the liver creates its free fatty acids becomes a significant contributing factor for people exhibiting signs of insulin resistance. Insulin-resistant skeletal muscle causes a shift in the metabolism of carbohydrates from the synthesis of intramuscular glycogen stock to the hepatic duct, which leads to an increase in free fatty acids production and the buildup of intrahepatic triglyceride. Sick persons with metabolic-associated steatohepatitis disease exhibit elevated levels of hepatic lipase and hepatic lipoprotein lipase gene expression, which directly enhance hepatic triglyceride metabolism in addition to the elevated circulating free fatty acid load. Other genetic factors probably play a part in addition, since obese people with higher intrahepatic triglyceride with more typical intrahepatic triglyceride also express proteins intricate in the absorption of free fatty acid from blood plasma to tissue. Hepatic steatosis is thought to be caused by an association of factors including elevated intrahepatic triglyceride metabolism, substantial circulating free radicals, and hereditary predispositions. It is unidentified, consequently, how this elevated intrahepatic triglyceride load and insulin resistance are related. It has proven difficult to determine if impaired insulin sensitivity is a consequence of the enhanced intrahepatic free fatty acid buildup or a sign of a different pathway causing both diseases. In any event, the trend toward metabolic-associated steatohepatitis disease increases when these are present. Metabolic-associated steatohepatitis disease encompasses a broad variety of illnesses, including frank cirrhosis, non-alcoholic steatohepatitis, and hepatic steatosis. In the absence of a liver biopsy, identifying people within this spectrum is still difficult but essential to reducing the risk of liver failure. Although abnormal transaminases may be a sign of non-alcoholic steatohepatitis, underdiagnosing non-alcoholic fatty liver disease while you wait for the markers to change could be the outcome. Raised transaminases and imagination demonstrating enhanced fatty permeation could be helpful in the diagnosis of non-alcoholic steatohepatitis syndrome, but not in determining the stage of the illness. When hepatic steatosis progresses to cirrhosis from liver inflammation, the liver sustains irreversible damage. Losing weight is strongly related to managing metabolic-associated steatohepatitis disease. Liver steatosis and fatty liver hepatitis are reduced with as little as a between 5 and

10 percent fall, and biomarkers such as transaminases improve as a result. It is recommended that individuals with similar conditions abstain from consuming alcohol and excessive amounts of acetaminophen (Clark, J. M. *et al*., 2003). Controlling the degree of hepatic steatosis may be helped by co-managing other contributory diseases such as diabetes. Patients with this condition will need to be managed similarly to those with other forms of liver failure after it has developed into cirrhosis.

4.8 Gynaecologic problems and obesity

Obesity substantially increases the risk of gynaecologic issues. These conditions, which include irregular or light periods, excessive bleeding, or no menstruation at all, may be linked to menstruation. A poor response to fertility medications, as well as an elevated risk of infertility and inability to ovulate, could exist. The chance of miscarriage is higher in obese people, both before and after infertility treatments. Additionally, it raises the menace of pregnancy-associated illnesses like gestational diabetes mellitus, high blood pressure brought on by pregnancy, cesarean sections, and anomalies in the developing foetus. Complications during labour and delivery could endanger both the mother and the child. Numerous metabolic and reproductive disorders are linked to polycystic ovarian syndrome, and many of these conditions are made worse by obesity (Moini, J. *et al*., 2020).

4.9 Polycystic ovarian syndrome and obesity

Obesity and variations in reproduction continue to have a complicated relationship. Elevations in adipose tissue impact the amounts of hormones in circulation. The patient's hormonal environment has a direct impact on the circulation of this fatty tissue, with greater testosterone amounts causing an additional androidal circulation of fat accumulation to the superior body. Therefore, it should come as no surprise that the interaction between fat and the hormonal outcome might directly affect fertility. The utmost predominant endocrinal condition impacting females of generative age, polycystic ovary syndrome affects approximately 7 percent of them (Sam, S. 2007). Enhanced androsterone creation along with inappropriate gonadotropin hormonal amounts cause Te-syndrome, which manifests as irregular menstruation, hirsutism, infertility, and chronic anovulation. Patients with polycystic ovarian syndrome sometimes exhibit various metabolic abnormalities, including a predisposition toward impaired insulin sensitivity and type-2 non-insulin dependent diabetes mellitus, in addition to the reproductive effects (Sam, S. 2007). These results are strongly associated with obesity, with 40 to 80 percent of polycystic ovarian syndrome patients being overweight or obese. The findings show an alternative and justify screening obese people for polycystic ovarian syndrome, even though they do not sustenance an underlying link among overweight and polycystic ovarian syndrome. When polycystic ovarian syndrome is present, it may affect the circulation of fatty tissue, causing it to deposit in locations above the waist and increasing the risk of subsequent visceral fat deposition. Losing weight has been demonstrated to help manage polycystic ovarian syndrome, as it does with many other conditions, with special emphasis on treating insulin resistance and persistent anovulation.

4.10 Cancer and obesity

According to the American Institution for Cancer Research and the World Cancer Research Fund, excess body fat accounts for 14 percent to 20 percent of all cancer-related fatalities in the United States and about 100,500 new cases of cancer each year. Based on an analysis of more than 7000 publications, this study calculates the proportion of cancer cases associated with overweight for several cancer types. Over 33,000 post-menopause mammary gland cancers, 20,700 endometrium cancers, 13,900 renal cancers, 13,200 colon cancers, 11,900 gutbread cancers, 5800 oesophageal cancers, and 2000 chole-cyst cancers are thought to be associated with excess body fat annually in the United States. Not every subgroup is impacted in the same way. Fatty men, for instance, are additional likely than women to progress colon cancer. For postmenopausal females, obesity raises the menace of mammary gland cancer; this is not the case for women who are not yet menopausal. This is thought to be because, after menopause, fatty tissue becomes the main basis of estrogen (Moini, J. *et al*., 2020). There is a significant horseshoe-shaped linkage between cancer risk and body weight. Extremely sick patients of the weight range are more likely to develop cancer. On the lower end of the spectrum, a low body mass index is probably caused by the existence of malevolence and menace aspects for malignancy. On the higher end of the spectrum, it is thought that obesity increases the chance of developing a wide range of malignancies, including those of the breast, uterus, colon, kidney, gallbladder, pancreas, and oesophagus (Wolin, K. Y. *et al*., 2010). The elevated body mass index's mortality effect goes beyond raising the chance of developing. The mechanism and causes of the elevated risk have been determined for several malignancies. Women's excess adipose tissue-derived estrogen production is correlated with an enhanced menace of cancer. There is a strong

correlation between the menace of emerging mammary gland cancer and endometrium cancer with weight increase seen after menopause. Increased risk for post-menopausal breast cancer has been linked to elevated circulating estrogen, and the administration of estrogen receptor modulators is believed to enhance the cause-and-effect relationship by reducing incidence. Persistent anovulation is thought to increase the risk of endometrial cancer through a similar mechanism. There is a higher risk of gastrointestinal tract pathology in both men and women. The effects of persistent reflux esophagitis and local inflammation are thought to be the cause of the greater incidence of oesophageal cancer in the obese patient. The incidence of colon cancer is also on the rise, and one mechanism linked to this elevated menace is long-lasting impaired insulin sensitivity and the results of insulin-like growth factors. Changes in insulin production are also thought to be the cause of pancreatic cancer. It is said that persistent excess production and an advanced prevalence of bilestones with persistent local swelling are linked with an enhanced menace of gallbladder malignancy. Finally, there seems to be a connection between the higher frequency of non-alcoholic steatohepatitis, and cirrhosis in the obese and liver cancer. In addition to the direct risk of cancer growth that a patient's body mass index carries, obesity makes it challenging to diagnose and treat such individuals, elsewhere enhanced menace for overweight delays cancer analysis, handling. Certain individuals may have experienced more interactions with the medical system, resulting in more blood tests to control their sickness and imaging investigations to look into other medical concerns, which in some cases may have enhanced the diagnosis of tumours. In other cases, the size of the patient affects how successful screening and detection occur. A higher inflammatory response at the pathological location can be shown on computed tomography imaging of the abdomen when there is an increase in intra-abdominal fat. However, in nuclear imaging tests, the same increased circumference causes more reduction, which reduces the efficiency of positron release tomography or further nuclear studies. Excess body bulk may impair the physical examination itself. The extra body fat might hinder the sufferer and doctor from identifying an issue in its early stages, either directly by preventing tactile acumen or indirectly over physical barriers such as appropriate table dimensions, mass limitations, or instrument dimensions. In addition, obesity presents an abundance of additional difficulties for postdiagnosis management. Chemotherapy and radiation therapy dosage strategies present difficulties for the morbidly obese, frequently leading to under-dosing with inadequate chemotherapeutic treatment and excess medicating to attain infiltration for radiation treatment, enhancing radiation contact and menace of de novo malevolence. Operational difficulties in fatty people present an additional set of issues in the control of cancer in overweight people. When it comes to managing obese patients with cancer, it has been demonstrated that losing weight lowers the risk of various malignancies in people who are at risk for cancer. Studies on bariatric surgery have recently demonstrated a lower incidence of malignancies linked to obesity. Additionally, observational research indicates that losing weight after menopause lowers the risk of breast cancer. The evidence supporting the benefits of weight loss after diagnosis is limited. Research indicates that gaining weight following a diagnosis is unhealthy. However, the severity of the condition and the effects of treatment may exacerbate weight loss after assessment. The idea that mass control and physical exercise should be promoted in overweight cancer patients is supported by abundant research showing that increased activity after diagnosis enhances quality of life.

4.11 Respiratory problems and obesity

Although the impact of obesity on the respiratory system is sometimes underestimated, it undoubtedly alters lung physiology and directly influences morbidity and mortality. Additionally, obesity changes the way of adipose tissue functions, causing systemic inflammation that compromises central respiratory regulation. Asthma, hypoventilation, and obstructive sleep apnea are all associated with obesity. Obese persons are more likely to experience a range of difficulties when under general anaesthesia. Forced expiration volume, forced essential capacity, purposeful residual capacity, and expiration reserve volume all decrease with an elevated body mass index. Remaining volume and whole lung capacity are similarly decreased in morbidly obese individuals. Obesity, diabetes, cardiovascular disease, and pulmonary vascular diseases are known to be interrelated (Moini, J. *et al*., 2020).

4.12 Joint-connective tissue disorder and obesity

The muscular-skeletal arrangement that is, the linkages, skeletons, muscles, sinews, and ligaments is also impacted by long-term obesity. The plantar fascia, Achilles tendon, and patellar tendon are among the load-bearing tendons compromised by obesity. In addition to several damaged ligaments, obesity can induce dislocations of the knee. Chronic plantar heel discomfort may also be associated with obesity. The human body is made up of many kinds of joints. Motion in the form of flexion, extension, rotation, and abduction is possible at the synovial joints. The ball and socket linkages of the hips and shoulders, the

hinge linkages of the knees and elbows, the pivot linkages of the axis and atlas, the condyloid linkages of the radiocarpal, the saddle linkages of the pollex, and the gliding linkages of the fingers are the different types of these joints. Many disorders, such as degenerative joint disease, rheumatism, gouty arthritis, and those affecting the spinal cord, will affect the joints and cause lower back pain. Additionally, declining muscle mass and bone density are associated with obesity, which increases the risk of slips and bone fractures. Adipocytes that are obese emit bioactive peptides that disrupt the structure of connective tissues (Moini, J. *et al*., 2020).

4.13 Urologic problems and obesity

Urologic issues are directly linked to obesity Because of several factors, like hormone disproportions, phospholipid and fatty acid issues, vascular disease, high blood pressure, and biotransformation disease. Sperm counts are frequently lower in obese males than in males of ordinary mass, and sperm purposes are commonly compromised. Both men and women who are obese have higher urine acid loads on their renal tubules. Stress urine incontinence and pelvic prolapse are more common in obese individuals. Being overweight makes several urologic conditions associated with obesity more challenging to cure (Moini, J. *et al*., 2020).

4.14 Skin problems and obesity

Numerous factors can contribute to skin issues associated with being overweight or obese. Hormonal fluctuations may give rise to striae and acanthosis nigricans, or darkened velvety patches. Increased pressure on leg veins can result in varicose veins, ulceration, dermatitis, fluid retention, and the bursting of superficial capillaries. Moisture retention in body folds promotes the growth of bacteria and fungi, which can lead to illnesses including intertrigo, skin rashes, and possible skin disintegration. Increased perspiration and skin secretions, lymphedema, cellulitis, and hirsutism are further obesity-related diseases. Due to the difficulty in reaching body parts that need to be surgically accessible, as well as the increased risk of infections, nerve damage, and even heart attacks, obesity also leads to surgical complications (Moini, J. *et al*., 2020).

4.15 Social-psychological problems and obesity

In addition to being a medical issue, obesity also has social and psychological consequences. The etiology of eating disorders and obesity involves an interaction of biological, genetic, environmental, and psychosocial factors. Anxiety and depression sufferers could find it more difficult to exercise regularly and limit their food intake. Obesity is often associated with an endless cycle of mood swings, overeating, and weight gain. It is possible for a pattern of eating to deal with stress and emotions to be maintained. Obesity is viewed negatively by society, and those who are obese are frequently stigmatized as weak-willed and uninspired to take better care of themselves. They experience discrimination at work as well. However, there are pharmacological, behavioural, cognitive, psychological, and surgical approaches to help overcome obesity and its associated societal and psychological problems (Moini, J. *et al*., 2020).

4.16 Obesity in children

Over the previous 40 years, childhood obesity has become more commonplace worldwide. Complications from being overweight, such as type-2 diabetes, which was once thought to be exceptionally unusual in youngsters, are now frequently treated in older children. A youngster who is obese has a much-increased chance of becoming obese for the rest of their life, along with numerous possible concomitant medical issues. Hesitant parents frequently avoid talking to others about their child's excessive weight. Younger individuals might not know what a "good diet" really entails because they are overwhelmed with advertisements for less-than-ideal food options. For obese children, pharmacologic therapies are not frequently advised. Since obesity is difficult to treat after it has been established, it must be avoided in younger people. The dedication of parents, kids, siblings, teachers, caretakers, health professionals, and society in general must be coordinated to achieve this (Moini, J. *et al*., 2020).

4.17 Obesity in the elderly

As individuals age, the attributes of obesity and its impact on them may vary from their earlier years. As people mature, their muscular mass decreases and is substituted by fat. Although a person's body mass index may not vary, obesity and its associated diseases are more likely to impact those with higher body fat percentages. Because osteoporosis and spinal vertebral abnormalities cause us to all "shrink" with age, a body mass index might also be skewed in the elderly. An aged person who weighs the same as they

did a year ago but is now shorter will have a higher body mass index even though they have not gained any weight because body mass index is determined by both height and weight (Moini, J. *et al*., 2020).

V. CLASSIFICATION OF OBESITY

Based on genetic involvement, obesity can be classified as follows:

5.1 Syndromic obesity

Syndromic obesity is defined as obesity with low frequency, high variability, neurological development delaying, and a Mendel outline of inheritance linked to intellectual disability, dysmorphic characteristics, or disorders affecting several organs and systems (Kalinderi, K. *et al*., 2024; Koves, I. H. *et al*., 2018) and monogenic overweight is usually infrequent, initial beginning, unadorned, and hereditary in a Mendel outline, leading to single gene alterations with huge outcomes. This categorization has been re-evaluated since occurrences of monogenic overweight may have neurocognitive abnormalities or psychological disorders that are often associated with syndromic occurrences. Accordingly, overweight disorders and polygenic obesity can be assessed independently (Sohn, Y. B. 2022). Various types of obesity are classified under syndromic overweight as-prader-labhart-willi syndrome, Laurence-moon-bardet-biedl syndrome, pseudohypoparathyroidism, alstrom disorder, 16p11.2 deletion disorder, WAGR disorder, smith-magenis disorder, cohen syndrome, myelin transcriptional factor-1 variants syndrome, borjeson-forssman-lehmann syndrome, carpenter syndrome, down syndrome and kallmann syndrome.

5.2 Monogenic obesity

Patients with monogenic obesity, which typically exhibits a Mendel outline of inheritance and is accompanied by alterations in a particular gene, generally become extremely obese. Monogenic obesity is largely linked to alterations in genetics intricate in the leptin-melanocortin pathway. Proopiomelanocortin is stimulated in this route by the fatty tissue impetus leptin, which fixes to the hypothalamus leptin receptor. Melanocortin peptides, like alpha and beta melanocyte stimulating impetus, are produced when proprotein convertase subtilisin/kexin type-1 breaks down pre-opiomelanocortin. This accelerates the combining and stimulation of the melanocortin-4 receptor, which decreases diet consumption and increases energy expenditure. In this approach, brain-derived neurotrophic factor also plays a regulatory role (Koves, I. H. *et al*., 2018). Various types of obesity are classified under monogenic obesity as-congenital leptin deficit, congenital leptin receptor deficit, pre-opiomelanocortin deficit, proprotein convertase subtilisin kexin-1 deficiency, melanocortin-4 receptor deficit, src homology-2B1 deficiency, carboxypeptidase-E deficiency and steroid receptor coactivator-1 deficiency.

5.3 Polygenic obesity

Polygenic obesity is a condition that arises from the combination of hereditary and environmental variables. Common polygenic obesity is caused by hundreds of polymorphisms, each of which has a minor impact. The development of genome-wide association studies has contributed to the identification of various genes and loci, including transmembrane protein-18, Fat mass and obesity-associated gene, cell adhesive molecules-1, cell adhesive molecules-2, and neuronal growth regulator-1, that are linked to an elevated risk of common, polygenic obesity (Kalinderi, K. *et al*., 2024).

VI. EVALUATION TECHNIQUES OF OBESITY

The anti-obesity agents may be evaluated using the following techniques (Maheshwari, K. K. 2023).

1. **DIET-INDUCED OBESITY**
   i. Diet-induced obesity in mice
   ii. Diet-induced obesity in rats
2. **SEASONAL OBESITY**
   i. Syrian and Siberian hamsters
3. **EXOTIC MODELS OF OBESITY**
4. **NON-HUMAN PRIMATE MODELS OF OBESITY**
   i. Age-associated obesity in macaques
5. **VIRUS-INDUCED OBESITY**
6. **HYPOTHALAMIC OBESITY**
   i. **Surgical method:** abrasion of the ventromedial hypothalamus and abrasion of the hypothalamic paraventricular nucleus.

ii. **Chemical method:** abrasion of the arcuate nucleus.

7. GENETIC OBESITY MODELS

i. **Monogenic models:** ob/ob mouse, db/db mouse, carboxypeptidase-E mutation (CPE^{fat}/ CPE^{fat}), s/s mouse, yellow obese ($A^{Y}A$) mouse, tubby mice, WDF/TA-FA rat, JCR: LA-corpulent rat and obese spontaneously hypertensive rat.

ii. **Polygenic models:** zucker-fatty rat, new zealand obese mouse and otsuka long evans tokushima fatty rat.

iii. **Transgenic models:** proopiomelanocortin knockout mouse, proopiomelanocortin/agouti-associated peptide knockout mice, melanocortin-4 receptor knockout models, melanocortin-3 receptor knockout mouse, melanocortin-4 receptor/melanocortin-3 receptor knockout mouse, agouti-related peptide overexpression, corticotrophin-releasing feature transgenic/overexpressing animals, glucose transporter subtype-4, melanin-concentrating impetus, beta-3 adrenergic receptor knockout, serotonin 5-HT-2c receptor knockout, neuropeptide-Y-1 receptor knockout mouse, neuropeptide-Y-2 receptor knockout mice, bombesin-3 receptor knockout mice, neuronal insulin receptor knockout mice and 11beta-HSD-1 upregulating (Lutz, T. A. *et al*., 2012; Maheshwari, K. K. 2023).

8. ASSAYS OF ANTI-OBESITY ACTIVITIES

i. **Anorexigenic Activity:** diet ingesting in mice and rats and computer-aided measurement of diet ingesting in mice and rats.

ii. **Biotransformation Activity:** indirect calorimetry, bomb calorimetry, GDP-binding in brown fatty tissue and uncoupling protein and glucose transporter-4 in brown fatty tissue.

9. ASSAYS OF OBESITY ADAPTABLE PEPTIDE IMPETUS

i. **Hormone Regulation of Diet Consumption:** resistin, leptin, neuropeptide-Y, orexin, galanin, adipsin and ghrelin.

10. ADDITIONAL MODELS OF OBESITY AND LINKED METABOLISM VARIATIONS

i. Lipodystrophy

ii. Growth hormone-deficient dwarf rat (Hock, F. J. and Herling, A. W. 2015).

6.1 Diet-induced obesity

Animals exposed to high-fat diets frequently develop overweight however, the exact role of high-fat foods in human being obesity is controversial (Willett, W. C. *et al*., 2002). Particular strains of rats that are susceptible to developing diet-inducing obesity have decreased insulin and leptin responsiveness; however, high-fat foods have comparable outcomes in both thin and diabetic rats. High-fat diets instantly and precisely decrease the central effects of insulin and leptin, which is probably due to a post-receptor outcome (Banks, W. A. *et al*., 2004; Benoit, S. C. *et al*., 2009; Clegg, D. J. *et al*., 2011; Hariri, N. *et al*., 2010; Woods, S. C. 2009). The fatty density of high-fat foods and the resulting greater consumption of whole energy donate to this outcome. This impact appears quickly, usually within a few days of exposure to high-fat. High-fat food appears to straight alter the corresponding intracellular signalling routes in hypothalamic mark nerve cells, which may also have an impact on other brain regions. This is demonstrated by changes in neuropeptide expression (such as lacking an insulin effect on pre-opiomelanocortin expression). Since saturated fat, such as palmitic acid, is more harmful than unsaturated fat, the amount of fat appears to play a significant influence in this effect. Rats can be made obese by feeding meals rich in fat or high in fat combined with high levels of sugar and carbohydrates (cafeteria diets). Rats become obese when fed a variety of tasty foods that resemble the so-called Western diet (cafeteria diet) that humans consume (Perez, C. *et al*., 1999; Rogers, P. J. *et al*., 1984; Rothwell, N. J. *et al*.,1979). Obesity resulting from the cafeteria diet is primarily caused by hyperphagia, which is partially offset by increased energy expenditure, particularly diet-induced thermogenesis, which is brought on by the sympathetic activation of brown fat. Increased average meal sizes and frequency are the causes of excessive consumption in cafeteria diets (Lutz, T. A. *et al*., 2012).

6.2 Seasonal obesity

Various smaller mammals demonstrate that yearly reproductive cycles coincide with changes in body mass and adiposity. Photoperiodic-driven leptin resistance causes a significant rise in adiposity (30-40 percent) in hamsters, voles, and lemmings that are switched from a short-day time (8 hours) photoperiod to a long-day time (16 hours) photoperiod for 12-18 weeks (Maheshwari, K. K. 2023).

6.3 Exotic models of obesity

Bats and seals are prominent instances of wild animals whose patterns of variation in fat mass are natural (Maheshwari, K. K. 2023).

6.4 Non-human primate models of obesity

In particular, non-human primates constitute superior models for researching obesity in human beings. Maintaining a relatively low fat (10 percent) ad-libitum diet prevents age-related obesity in 10 to 15 percent of captive macaques, baboons, and rhesus monkeys (Maheshwari, K. K. 2023).

6.5 Virus-induced obesity

Mice (20-40 gm) exposed to canine distemper virus, avian retrovirus, rous-linked virus-7, avian adenovirus SMAM-I, human virus Ad-36, or borna illness virus experience obesity within 8-10 weeks of infection (Lyons, M. J. *et al*., 1982).

6.6 Hypothalamic obesity

The hypothalamus is thought to be a particularly important organ that governs food intake and energy balance by regulating feelings of satiety and hunger in response to energy stores and nutrient availability. Following hypothalamic lesions, hyperphagia in rats has been demonstrated (Hock, F. J. and Herling, A. W. 2015; Liu, C. M. *et al*., 1974). Hypothalamic obesity is categorized into 2 methods: surgical method and chemical method.

6.6.1 Surgical method

(Bray, G. A. *et al*., 1979) female rats weighing 150-200g are nourished a high-fat food for five to nine days. The incisions are placed 1 mm lateral to the midline, 8.5 to 5.5 mm frontal to the auricle bars, and 3 mm dorsally from the brain's base (Maheshwari, K. K., 2023). Rats that are sham-operated act as controls. At the time of surgery, rats that are kept apart and starved for the entire night are sacrificed to collect data on their initial body composition. The location of blade cuts and abrasions is confirmed histologically in brains embedded in paraffin and preserved in a 10 percent buffered formaldehyde solution. Histological examinations are performed on sequential slices across the brain's hypothalamus region (Hock, F. J. and Herling, A. W. 2015).

6.6.2 Chemical method

(Olney, J. W. 1969; Alarcon-Aguilar, F. J., *et al*., 2007) chemicals like monosodium L-glutamate (2 gm/kg, subcutaneous for 5 days); gold thio-glucose (30-40 mg/kg, intraperitoneal); bipiperidyl mustard (5-50 mg/kg, intraperitoneal); 4-nitroquinoline-l-oxide (intra-cerebroventricular) are administered to mice or rats (2-40 days of age) can stimulate overweight by demolition of hypothalamic parts intricate in diet consumption and energy equilibrium. Information on food consumption, weight increase, locomotor activity, and blood insulin level are compared between the treated and control animals.

6.7 Genetic obesity models

Energy is homeostatically retained in the appearance of fats in adipose tissue, according to an extensive literature of studies in humans and animals. The maintenance of consistent levels of energy stores is achieved through a complex and multifaceted process known as energy homeostasis. This process involves various interrelating homeostasis and behavioural routes, such as glucose equilibrium, lipid equilibrium, hypothalamic-pituitary-adrenal axis, short-term satiation, and additional macronutrient routes. Several disorders, including overweight, anorexia nervosa, malady, and disappointment to succeed, are brought on by abnormalities in genes essential to energy balance. In the past, the animals were found to have five of these mutations: the agouti (Ay), fat (fat), tubby (tubby), obese (ob), and diabetic (db) genes. The identification of leptin, the primary adipocyte impetus expressed by the overweight (ob) gene that informs the brain of the amount of energy warehoused as fat, was made possible by the duplicating and depiction of these altered genes. Following the identification of the leptin receptor, which is expressed by the diabetes mellitus (db) gene, and the realization that obesity is produced by the agouti (Ay) gene product inhibiting the melanocortin-4 receptor, essential brain circuits intricate in energy equilibrium regulation were identified. However, a huge amount of transgenic and knockout animals with overweight, anorexia nervosa, malady, or overweight resistance have been developed following the identification of these initial obesity genes (Robinson, S. W. *et al*. 2000). Genetic obesity models are categorized into 3 models: monogenic models, polygenic models and transgenic models (Maheshwari, K. K., 2023).

6.7.1 Monogenic models

Genetically obese animals, such as ob/ob, db/db, Cpe^{fat}/Cpe^{fat}, $A^{Y}a$, tub mutation mouse and rat fa/fa, WDF/TA-FA, JCR: LA-corpulent, and SHR rats, were identified following spontaneously occurring single gene mutations. These animals are extensively utilized as animal models of obesity. After 6-8 weeks

of life, these animals exhibit hyperphagia, hyperinsulinemia, hyperlipidemia, and become several times more obese than their lean counterparts. These animals have deficiencies in the leptin signalling pathways (Maheshwari, K. K. 2023).

6.7.2 Polygenic models

(Speakman, J. *et al*., 2007): these models recommend that a grouping of multiple genes and ecological aspects causes obesity in humans. These models have become more applicable to human obesity. Polygenic animal model includes mice such as M-16, kuokondo, tsumura Suzuki obese diabetes, and New Zealand obese, and rats such as otsuka-long evans-tokushima-fatty, wistar fatty rat, and zucker fatty rat. After 2 to 3 months of life, the body weight starts to increase and reaches a maximum of 50 to 70 grams in six to nine months. These animals experience moderate hyperglycemia, polyuria, polydipsia, hyperphagia, and hyperinsulinemia (Maheshwari, K. K. 2023).

6.7.3 Transgenic models

(West, D. B. 1996) transgenic animal models of obesity are created using the over-expression or elimination of target genes approach. Transgenic animals provide a novel way to investigate the etiology of obesity and options for treatment. Many transgenic mice with varying levels of body fat have been created due to the possibility of introducing additional genetic material into mammals (Bray, G. *et al*., 1997). Gene knockout mice frequently exhibit reduced body weight (Reed, D. R. *et al*., 2008). It was shown that many genes affect body weight when they are knocked out in investigating for overweight applicant genes in a specific section of the mouse genetic material. The Jackson Laboratory Mouse Genetic Material Database for knock-out mouse lineage and their characteristics was accessed to identify whether this was a common trait of gene knockout or a random manifestation. 31 percent of feasible knockout mouse lineage assessed fewer and 3 percent weighed more than controls, according to data collected from 1977 knockout strains. It is estimated that about 6,000 genes affect a mouse's size, considering the knockout genes that were studied are significant. The usage of corresponding knockout mice in which a certain mark is knocked out contrasted with uninhabited type mice may be useful for characterizing the particularity of a potential compound to a particular mark intricate in body mass management. The compounds should only be dynamic in uninhabited type mice but non-active in the corresponding knockout mouse models (Lutz, T. A. *et al*., 2012). When the neuropeptide-Y gene is delivered directly into the brain, it may encourage eating, leading to obesity and hyperphagia in the animal (Maheshwari, K. K. 2023).

6.8 Assays of anti-obesity activities

There are 2 approaches for the assays of anti-obesity activities, anorexigenic activity and biotransformation activity (Hock, F. J. and Herling, A. W. 2015).

6.8.1 Anorexigenic activity

Mainly 2 anorectic activities are used for the assays of anti-obesity activities, diet ingesting in mice and rats and computer-aided measurement of diet ingesting in mice and rats.

6.8.2 Biotransformation activity

Various metabolic activities are used for the assays of anti-obesity activities, indirect calorimetry, bomb calorimetry, GDP-binding in brown fatty tissue and uncoupling protein and glucose transporter-4 in brown fatty tissue (Hock, F. J. and Herling, A. W. 2015).

6.9 Assays of obesity adaptable peptide impetus

Various peptide hormones are used for the assays of anti-obesity activities, resistin, leptin, neuropeptide-Y, orexin, galanin, adipsin and ghrelin (Hock, F. J. and Herling, A. W. 2015).

6.9.1 Hormone regulation of diet consumption

Peptide neurotransmitters, the common of which are found in the brain, especially in the hypothalamus and the stomach, control food intake and fat deposition (Elmquist, J. K. *et al*., 1999; Kalra, S. P. *et al*., 1999). This comprises anorectic (appetite-inhibiting peptides) and orexigenic (appetite-stimulating peptides). Although alpha-melanocyte-stimulating impetus, corticotropin-releasing impetus, cholecystokinin, cocaine and amphetamine-regulated transcript, neurotensin, glucagon-like peptide-1, calcitonin gene-associated peptide, bombesin, and ciliary neurotropic factor (Xu, B. *et al*., 1998) have appetite-inhibiting actions, neuropeptide-Y, orexins A and B, galanin, melanin-concentrating impetus, and agouti-associated peptide have appetite-stimulating actions (Tritos, N. A. *et al*., 1999). Animal obesity is

caused by mutations that decrease the functional activity of melanocortin-4 receptors, alpha-melanocyte-stimulating hormone, leptin, and the leptin receptor. Because MTII, a melanocyte-stimulating hormone-like antagonist, has no anorectic effect on melanocortin-4 receptor-deficient mice, it is possible that alpha-melanocyte-stimulating hormone largely inhibits feeding via activating melanocortin-4 receptor (Marsh, D. J. *et al*., 1999).

VII. THERAPEUTICS OF OBESITY

There are various approaches for the management and treatment of obesity, lifestyle modifications, anti-obesity medicines, bariatric surgery and faecal microbiota transplantation.

7.1 Lifestyle modifications

Lifestyle alteration is still the backbone of dealing with overweight since there are no specific pharmacological treatments available (WHO. 2000). It is recommended that overweight individuals drop a minimum of 10 percent of their body mass through diet, exercise, and behavioural therapy, also known as lifestyle modification (Guidelines for Managing Overweight and Obesity in Adults. 2014). Ingesting a portion-measured food can affect substantial short-term mass loss (Lee, E. Y. *et al*., 2018). Obesity control over the long term can be achieved with high levels of physical activity and constant patient health care provider contact. Making lifestyle modifications usually results in a noticeable drop in body weight, which substantially decreases the menace of cardiovascular system disease (Nguyen, B. *et al*., 2017). Because individual dietary preferences are largely impacted by their surroundings, governments must improve legislation and the surrounding culture to minimize the availability of undesirable meals and boost the availability of beneficial ones. Policies should be changed to encourage the manufacture of foods with lower sugar, fat, and salt content and to limit the availability of foods that can make youngsters obese (Mozaffarian, D. *et al*., 2011). Food manufacturing companies should be encouraged to create and promote weight-friendly food products, but lawmakers and medical practitioners should also be made aware of the potential impact advertising for food may have on people's behaviour and well-being. Food advertisements should be evaluated with the assistance of nutrition educators (Struben, J. *et al*., 2014). The obesity crisis is likely to be significantly reduced by treatments that aim to enforce actions that decrease the root sources of overweight (e.g., strategy changes, regulations, and commandments) and encourage modifications in behaviour (e.g., well-being advancement, education on nutrition, benefits for healthy existing, sugar-sweet drink tax, and community advertising) (Lal, A. *et al*., 2020).

7.2 Anti-obesity medicines

If an individual's body mass index is greater than 30 (or higher than 27 with concomitant diseases) and they are not able to reduce weight by lifestyle adjustment alone, pharmacotherapy may be required (Telles, S. *et al*., 2016). There are several anti-obesity medicines available and classified into various categories given below.

7.2.1 Classification of anti-obesity medicines

1. **ANOREXIC AGENTS OR HUNGER SUPPRESSANTS**
   a. **centrally acting adrenergic drugs:** Benzphetamine, Diethylpropion, Mazindol, Phendimetrazine, Phentermine, Phenylpropanolamine, Sibutramine.
   b. **5HT drugs:** Dexfenfluramine, Fenfluramine, Fluoxetine.
   c. **5HT/adrenergic drugs:** Sibutramine.
2. **THERMOGENESIS DRUGS**
   a. **adrenergic drugs:** Ephedrine + Caffeine.
   b. **beta-3 agonists:** BRL 26830A, BRL 35135, RO 40-2148, RO-16-8714, CL-316243.
3. **ASSIMILATION SUPPRESSANTS**
   a. **lipase inhibitors:** Olestra, Orlistat.
   b. **fat substitutes:** Caprenin, Guar gum, Microparticulated egg white, Milk protein, Polydextrose, Sugar beet fibre.
4. **HORMONE MODIFIERS:** Leptin analogues, Neuropeptide antagonists.
5. **BULK ANOREXIATS:** Methyl cellulose, Dietary fibre, Guar gum, Karaya gum.
6. **DRUGS FROM PLANTS:** Commiphora Mukul, Cannabinoid receptors antagonists-Rimonabant, Garcinia cambogia, Hydrophilic mucilages, non-carbohydrate sweeteners, Paeonia suffructicose, Senna pods, Preparations from plantago seeds, Teucrium chamaedrys.

7. **OTHER AGENTS:** Amphetamine, d- Amphetamine, Chitosan (Maheshwari, K. K. 2012).
8. **FDA-PERMITTED MEDICINES FOR MONOGENIC SYNDROMES OF OBESITY:** Setmelanotide, Metreleptin.
9. **FDA-PERMITTED MEDICINES FOR NON-SYNDROMIC OBESITY:**

a. **gastric and pancreatic lipase inhibitor:** Orlistat
b. **N.E. agonist/GABA agonist, glutamate antagonist:** Phentermine/ Topiramate.
c. **opioid receptor antagonist/D.A. and N.E. reuptake inhibitor:** Naltrexone/ Bupropion.
d. **GLP-1 analogue:** Liraglutide, Semaglutide.
e. **GIP/GLP-1 dual agonist:** Tirzepatide.

7.2.2 Orlistat

Orlistat is a common anti-obesity medication that is prescribed to obese people. The anti-obesity drug orlistat (tetra-hydro-lipstatin) is permitted by the United States Food and Drug Administration. It is extracted from Streptomyces toxytricini and is a saturated derivative of endogenous lipstatin. Those with obesity and a body mass index of over 30; those with a body mass index of above 27; and those with risk factors such as diabetes, hypertension, and dyslipidaemias are among the groups for which orlistat has been permitted by the United States Food and Drug Administration. Reducing the chance of gaining weight following previous weight loss. When combined with diet and exercise, orlistat produces the most effectiveness. Within two weeks of starting orlistat, the weight begins to decrease (Bansal, A. B. *et al*., 2022). Pancreatic and stomach lipases are reversibly inhibited by orlistat. The breakdown of dietary fat is significantly facilitated by these lipases. By dissolving the triglycerides into monoglycerides and absorbable free fatty acids, they act. Lipases active sites are turned inactive by orlistat's covalent binding to their serine residues. Triglycerides cannot be hydrolysed when lipases are inactivated, which inhibits the absorption of free fatty acids. (Guerciolini, R. 1997). Orlistat's main mechanism of action is the inhibition of local lipase in the stomach. Orlistat does not require systemic absorption for effectiveness. Orlistat inhibits approximately 30 percent of the absorption of dietary fat at the recommended dosage. A slight drop in blood pressure is likewise correlated, according to the American Hospital Association, with the percentage change in weight (Hall, M. E. *et al*., 2021). Orlistat exhibits various adverse effects, Gastrointestinal: steatorrhea, faecal spotting, diarrhoea, abdominal pain, anal fissures, cholelithiasis, pancreatitis, acute cholestatic hepatitis and reverse steatosis; (Wang, H. *et al*., 2018) Hepatotoxicity; Renal: acute kidney injury, nephropathy and renal stones; (Humayun, Y. *et al*., 2016) Musculoskeletal: osteoporosis and Oncology: colorectal cancer (Bansal, A. B. *et al*., 2022).

7.3 Bariatric surgery

Bariatric surgical procedure, often identified as weight loss surgical procedure, is an additional choice for individuals with a body mass index of more than 40 or a body mass index of more than 35 who have coexisting conditions and are incapable of decreasing mass with lifestyle modifications or medication (Telles, S. *et al*., 2016). Individual's metabolism profiles improve to wide-ranging degrees from standard bariatric surgical procedures, like parietal gastrectomy, Roux-en-Y gastric bypass, laparoscopic adjustable gastric banding, and biliopancreatic diversion (Aminian, A. *et al*., 2015). Conferring to research, bariatric surgical procedure has advantages elsewhere in weight loss. According to several studies (Osto, M. *et al*., 2013; Al-Rubaye, H. *et al*., 2019; Kops, N. L. *et al*., 2021), bariatric surgery changes the gut microbiome, biomarkers, and long-term remission for Type 2 Diabetes Mellitus. It also decreases chronic inflammation associated with obesity. For instance, subsequent to a Roux-en-Y gastric bypass method, the complete microbial richness of the gut increased in human participants (Kong, L. C. *et al*., 2013). Subsequent investigation showed that Roux-en-Y gastric bypass increased the appearance of certain genes found in white fatty tissue, upregulated genes essential to the converting growth factor-b signalling routes, and remarkably downregulated genes related to inflammatory responses and metabolism routes (Zhang, H. *et al*., 2009). Usually, after bariatric surgery, serum leptin levels which are linked to a lowered body mass index drop. It's interesting to note that women with greater presurgical baseline leptin levels found it easier to maintain their weight loss following surgery, but women with lower presurgical baseline levels found it simpler to gain the weight back. Although a patient's blood serum leptin amount cannot expect the degree of surgical achievement, there is a relationship between starting point leptin levels and changes in body mass, body mass index, and overall weight loss (Van Leiden, H. A. *et al*., 2002).

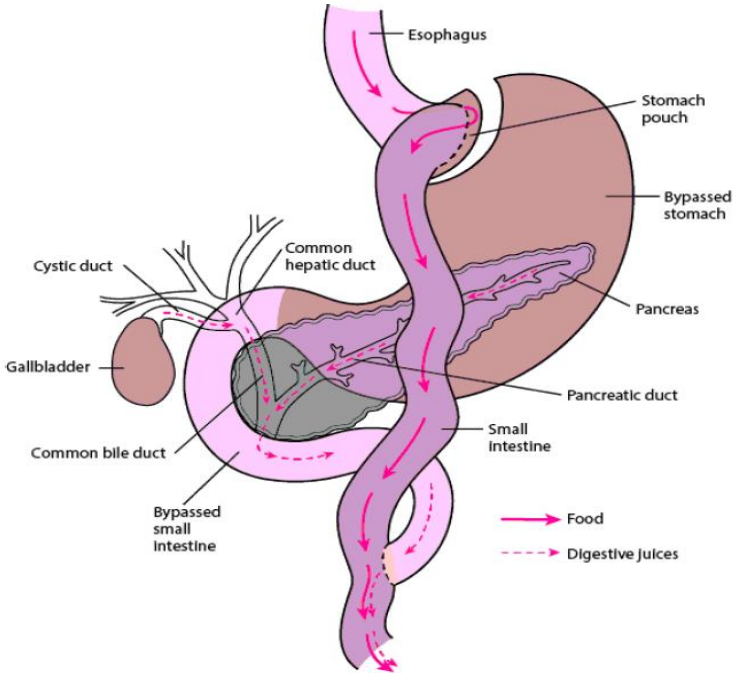

figure-(6): bypassing part of the digestive tract (https://www.msdmanuals.com/en-in/home/disorders-of-nutrition/obesity-and-the-metabolic-syndrome/metabolic-and-bariatric-surgery#types_v769522)

7.4 Faecal microbiota transplantation

Recently, there has been a lot of interest in the treatment of obesity using faecal microbiota transplantation (Yu, E. W. *et al*., 2020). There are encouraging signs that the transplantation of healthy human faecal microbiota microorganisms into obese patients may have an impact on weight loss and management. Ridaura et al. transplanted faecal slurries from human beings double divergent for overweight into hygienic mice in a ground-breaking important study (Ridaura, V. K. *et al*., 2013). Mice with the microbiota of fat persons efficiently established overweight, whereas lean mice with the microbiome of healthy individuals remained thin. According to Ridaura, V. K. *et al*., (2013), the sequencing results of faeces samples taken from mice after surgery demonstrated that the human microbiomes could be effectively infused, indicating the transmission of activities linked to the thin or obese microbiota communities, correspondingly. Studies on people are also showing promise. Vrieze, A. *et al*., found that transplanting taxa from thin donors improved insulin sensitivity and microbial diversity in adult males with diabetes who were obese (Vrieze, A. *et al*., 2012). There was a rise in Bacteroidetes and butyrate-producing bacteria, which suggests that the microbial community is changing toward one that is associated with a slimmer phenotype. Although it's still early, transplanting faecal microbiota may be a possibility to replace microbial populations that cause obesity (Zhang, Z. *et al*., 2019).

VIII. CONCLUSION

Obesity, a complex multifactorial disease, has emerged as a important global wellbeing apprehension. The escalating incidence of obesity across the globe underscores the need for a comprehensive understanding of its epidemiology, pathogenesis, etiology, complications, evaluation techniques, and therapeutics. The epidemiological data highlight the alarming rise in obesity rates, with a higher incidence in developed countries. However, developing nations are not spared, witnessing a surge due to lifestyle transitions. The pathogenesis and etiology of obesity are intricate, involving a complex interplay of genetic, environmental, and behavioural factors. It underscores that obesity is not merely a consequence of overeating or lack of physical activity. The complications associated with obesity are manifold, affecting almost every organ arrangement in the body. It significantly escalates the risk of several diseases. These complications underscore the dire need for effective management strategies for obesity. Various evaluation techniques are used to assess obesity, these techniques help in determining the severity of obesity and the associated health risks, thereby guiding the therapeutic approach. The therapeutics of obesity necessitate a comprehensive approach, encompassing lifestyle modifications, pharmacotherapy, and in severe cases, bariatric surgery. The advent of newer therapeutic agents has revolutionized the treatment background for obesity, offering hope for better management of this condition. In conclusion, obesity is a significant public health issue that requires a comprehensive and multidisciplinary approach to effective management. It necessitates further research to unravel the complex pathophysiology of obesity

and develop more effective therapeutic strategies. The fight against obesity is a long one, but with concerted efforts from researchers, clinicians, policymakers, and individuals, it is a battle that can be won.

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