



SEVERITY, TYPES, FACTORS AFFECTING AND STRATEGY TO OVERCOME OBESITY

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Abstract

Obesity is a major health issue that spread rapidly all over the world due to overeating, intake of fast food, and through heredity. India suffered from obesity and gains 3rd position after the USA and China. Nowadays, children are more suffered from obesity in comparison to elders. Obesity leads to mortality due to high cholesterol, high blood sugar, heart disease, and breathing problems. Neuro-tension, oxidative stress, inflammation, lipid profile, genetic, adipokines, and epigenetic are obesity biomarkers that are used to determine the severity of obesity. Several herbs are used for the treatment of obesity viz. *Emblica officinalis*, *Terminalia chebula*, *Triphala*, *Terminalia bellirica*, *Limonia acidissima* Groff, *Cassia siamea* Lam., *Swertia chirayita*, *Oroxylum indicum*. Herbs have no side effects, whereas enhancing health naturally. Therefore, the herbal treatment of obesity is the best option.

Key words: Obesity; Overweight; Biomarkers; Herbs; BMI

Introduction

Obesity is a genuine metabolic problem affecting billions of individuals of all age groups; however, it is ignored by people enormously (Popkin *et al.*, 1998). It is a non-communicable disease (Pervanidou *et al.*, 2013). Obesity as “medadhatu”, an illness as per Ayurveda due to excess intake of calories. Additionally, in the 21st-century obesity has achieved scourge extents in India which is straightforwardly influencing the viability and effectiveness of individuals (Asija *et al.*, 2014). Obesity has expanded in the Indian population because of terrible sustenance tendencies and intake of animal origin foods such as meat, ghee, and fast food. Thusly, obesity should be cured for the wellbeing and change of effectiveness of individuals (Moehlecke *et al.*, 2016). Obesity itself is not lethal, however, it initiates several associated diseases that lead to lethality.

Punjab followed by Kerala, Goa, Tamil Nadu, and Andhra Pradesh are more influenced states by obesity (Asija *et al.*, 2014). World widely obesity influenced 600 million individuals because of interminable sicknesses

(Yach *et al.*, 2006). National Family Health Survey reported that obesity in Indian ladies has increased from 11 to 15% which prompted serious life-threatening diseases (Kalra *et al.*, 2012). The percentage of obese adults showed an increasing trend from 2010-2016 as presented in fig 1 (Hannah *et al.*, 2017).

In India from 2010 – 2016 the obesity was increased in women with a faster rate as compared to men as shown in fig 2 (Hannah *et al.*, 2017).

All age group individuals suffered from obesity and it causes numerous life undermining sicknesses like metabolic disorder; stroke, growth, coronary heart ailments, diabetes sort 2 Mellitus, cardiovascular maladies, handicap, gallbladder illness, hypertension, and osteoarthritis (Colagiuri *et al.*, 2010). Overweight is the initiation stage of obesity. Worldwide 2300 million adults and more than 700 million corpulent suffered from obesity. Sincere steps are needed against this serious disease to reduce the economic burden of the earth (Nock *et al.*, 2010).

The USA gains the first position in obesity followed

by China and India. In India, 44 million people are obese as shown in Fig. 3 (OECD 2017). This indicates the alarming state for the developing country like India. In the 21st century, adolescence obesity is considered a significant wellbeing concern (Scheen *et al.*, 2008; Qi *et al.*, 2008). In India, 10-30% of teenagers were endured by overweight (Kotsis *et al.*, 2005). It reported that overweight and obesity expanded 11-29% in young people in Punjab, Maharashtra, Delhi, and South India. In Ludhiana, 11.6% of youngsters' were obese (Mahan *et al.*, 2012). For T2DM CVD, and stomach weight is the principal factor in Asian Indians (Misra *et al.*, 2011). With the increasing obesity problem in youngsters, the mortality hazard expanded (Kotsis *et al.*, 2005). Females experience more side effects of overweight in India due to intrinsic hormonal distinction, special life events like pregnancy, parturition, lactation, and menopause (Gupta *et al.*, 2009). Fundamentally higher weight problem arises more in an urban region in comparison to rural (Kalra *et al.*, 2012). Obesity brought about by the admission of extensive measure of sugar-based calories which won't be used by the body and put away in fat tissue (Asija *et al.*, 2014).

Obesity is induced by several ways of lifestyle, resting, liquor consumption, limited physical movement. Weight increase is influenced mainly due to physical activeness and heredity (Scheen and A.J, 2008). It's a long-lasting sickness and called constant infections (Yun and J.W, 2010). In Dutch young ladies overweight diminished from 12.6 to 10.9% yet this issue expanded in youngsters from 14.6 to 21.4% from the year 1999 through 2007.

Leptin is an indicator enzyme for elevated body weight. Adipocytes are responsible for the secretion of leptin and it is transferred to the brain through blood, and in CNS it acts on leptin receptors that regulated food intake (Glenn *et al.*, 2011; Kotian *et al.*, 2010).

Numerous pharmaceuticals are prescribed for the reduction of weight, for example, orlistat and sibutramine (Mathew *et al.*, 2008), rimonabant, phentermine, fluoxetine or bupropion, diethylpropion, and mazindol (Kakkar *et al.*, 2015). However, these anti-obesity drugs have several side effects *i.e.* cardiovascular, hepatic, and renal problems. There are several herbs having anti-obesity potential *viz.* *Emblica officinalis*, *Terminalia chebula*, *Triphala*, *Oroxylum indicum* L. Kurz, *Terminalia bellirica*, *Limonia acidissima* Groff, *Swertia chirayita*, *Buch- Ham.*, *Cassia siamea* Lam., *Capparis decidua*, *Carissa carandas* Linn. The obesity is mainly controlled by

bioactive compounds present in the herbs. Either a specific plant part or whole plant is utilized for obesity treatment (García *et al.*, 2014). Herbs have a high potential of reducing obesity even then, a few herbal medicines are developed for the treatment of obesity. *Commiphora mukul*, *Tamarindus indica*, and *Myristica fragrans* reduced cholestrogenesis and weight gain (Nagrani *et al.*, 2016).

The main factors for the uncontrolled increase in weight are sedentary lifestyle like late sleeping and rising, lack of any type of physical work, intake of food rich in calories and limited in fibers, and over-eating (Kumar and S.M, 2017). These habits lead to the expansion of obesity to younger ones and it is the most alarming issue all around the world. It was reported that the overweight issue was striking 42 million children (5 years old) and it is going to expand (Scheen and A.J, 2008). It reported that different biomarkers are omics-based biomarkers, Retinol-binding protein 4 (RBP4), Apolipoprotein A-IV (APOA4) and Alpha-2-HS-glycoprotein (AHSG) (Huang *et al.*, 2015) used for metabolically Health Obesity (MHO), metabolically unhealthy obese (MUO) statuses. Obesity also leads to several diseases like fatty liver disease (non-alcoholic) metabolic disorder (Bhowmik *et al.*, 2012). Obesity also plays a role in the initiation of cardiovascular disease, 2 Diabetes Mellitus (T2DM) and it will impact the metabolic status (Won *et al.*, 2014). Five different types of fat deposits are subcutaneous fat, visceral fat, white subcutaneous fat, beige fat, and brown fat. Overabundance fat deposition, particularly in the stomach region, is responsible for the imbalance of energy. This energy imbalance issue comes due to co-operation of a few factors, for example, increased intake of vitality rich nourishment, a diet deficient in bioactive compounds and micronutrients, diminished physical activity. Factors such as nourishing and hormonal status in early life, hereditary, economic elements, ecological and social also affect obesity (Mathew *et al.*, 2008).

Types of obesity

Obesity is classified into 4 types *viz.* Type 1, 2, 3 and 4.

Type 1: Excess fat deposits in the body without any concentration.

Type 2: A large amount of fat deposited at the trunk and abdominal area. This type of fat also called a male type deposit fat.

Type 3: Deposition of excess fat around the abdominal area is known as abdominal visceral obesity.

Type 4: Gluteofemoral and Gynoid obesity were

mainly observed in females in a large amount and stored in the gluteal and femoral area (Bouchard, 1991).

Types of Fat

Visceral and subcutaneous are types of fat. The fat stored over visceral organs *viz.* abdomen, liver, heart, pancreas, kidney, and intestines are known as visceral fat or active fat. The fat stored under the skin is known as subcutaneous fat and it is feeling under our arms and legs.

Different types of body shapes in obesity

Due to fat accumulation, the body gains some specific shapes:

- a. Apple shape
- b. Pear Shape

Apple Shape is mainly due to the deposition of visceral fat. In an apple shape, fat deposit on upper the waist and fat stored on above waist and abdomen. This shape leads to tremendous health problems and leads to heart attack and type 2 diabetes (Pollex *et al.*, 2006).

Pear Shape

In a pear, shape fat accumulates on thighs and buttocks and contains less amount of visceral fat. This shape contains a lower risk of weight-related health problems.

Body Mass Index (BMI)

BMI is the Gold standard method for the determination of fattiness using body weight and height (in kilogram and meter, respectively) (Yun and J.W, 2010). According to the WHO, the international standard for all ethnic groups for obesity would have a BMI greater than 30.0Kg/m² (BMI). An obesity index for the Asian and Caucasian population was 25 to 30Kg/m² BMI (Kim *et al.*, 2001). BMI is divided into several ranges

Range BMI (Kg/m²)

Healthy: 20.0-25.0

Mildly overweight: 25.1-27.0

Moderately overweight/obese: 27.1-30.0

Overweight/obese: 30.1-40.0

Morbidly obese: >40.0

The risk associated with obesity increased with an increase in the BMI value (Won *et al.*, 2014).

Role of adipocytes in obesity

Leptin and Adiponectin are secreted by adipocytes. Both in animals and human models adiponectin participate and help in the modulation of lipid and glucose metabolism in insulin-sensitive tissues (Deepak *et al.*, 2007).

Peroxisome proliferator-activated receptor gammas (PPAR-gamma) are responsible for the stimulation of adiponectin, whereas, Tumor Necrosis Factor-alpha (TNF-alpha) and catecholamines have an inhibitory effect (Damiani *et al.*, 2010). Leptin is a fat-derived hormone and inhibits hunger by balancing the energy in the body (Manya *et al.*, 2016).

The energy balancing is affected by the activator of transcription which induced several target genes and it's worked with the signal transduction (Mohamed *et al.*, 2014).

Factors affecting Obesity

Psychological factors

It reported that obesity not a single encounter to health, however, a complex interaction within and also between both physical and mental factors. Some factors which were related to depression, externality, social pressure, and other emotional issues (Wiklund *et al.*, 2016; Gaal *et al.*, 2006).

Endocrine and Metabolic factors

There is an intricate relationship between the endocrine and metabolic factors which would be observed to contribute to obesity (Wiklund *et al.*, 2016). Hormones are released when the fat cell increases which lead to imbalance and hence cause various metabolic effects. Several metabolic factors affect obesity such as dehydroepiandrosterone sulfate (DHEA-S), leptin and androstenedione, impaired glucose tolerance, culminating in b-cell failure, insulin resistance, dyslipidemia, hypertension, premature heart diseases and type-2 diabetes (Joon *et al.*, 2011). In the metabolic problem of obesity, some other problem also occurs such as ectopic lipid accumulation, hepatic steatosis, abdominal obesity and sleep apnea (Havel, 2004).

Endocrine also associated with obesity and there should be changes in the hypothalamic-pituitary hormones axes (Skorzewska *et al.*, 1989). Pediatric obesity occurs by the endocrine which causes Cushing's diseases, growth hormone deficiency, hypothyroidism (Pollex *et al.*, 2006). It helps in storing the energy and also shows many factors such as releasing of adipocytes and hormones synthesis. Adipocytes are responsible for the secretion of the proteins such as adipin, visfatin, leptin, adiponectin, and resistin which regulate the tissue insulin sensitivity, inflammation, vascular tone, and food intake (Trevaskis *et al.*, 2005).

Epidemiology of obesity

The obesity problem increased with year by year and crossing the epidemic level (Qi *et al.*, 2008; Nagarani

et al., 2011). The epidemic of obesity and overweight is a serious problem around the world and the major challenge is to prevent the associated chronic diseases and other problems like Type 2 diabetes, intra-uterine and infantile growth (Joon *et al.*, 2011).

Several surveys carried out on obesity at different age groups

A survey on 12-14-year-old school students from the 5 topographical zones of South India. They concluded that obesity depended on their physical condition, for example, stomach and body shape. The stomach was reported as a fundamental part of obesity where the most amount of fat was stored. It was caused due to overeating and junk foods (WHO, 2015). Lack of nutrition and improper exercise is responsible for obesity. Due to this person was suffered from serious diseases like chronic kidney diseases, T2D, atherosclerosis, etc. and in the severe case leads to mortality.

It reported a higher risk of breast cancer in the Asian population (National Family Health survey-4, 2015-2016). There are several reasons behind this increase like higher BMI (Riffel *et al.*, 2002) adiposity and insulin resistance. Breast cancer risk was increased at the age of 10 to 20 years because at this age body size increased due to the adiposity and insulin resistance. According to the OECD analysis of the national health survey, (2015) the obesity problem increased world widely and it expected that up to 2030 this major issue increased as shown in Fig. 4. The Fig. 5, shows that the survey held up on rural and urban area women and men in 2015-2016, was reported that by National Family Health Survey-4. In this survey, BMI below the normal BMI < 18Kg/m² and overweight or obese BMI ≥ 25.0Kg/m² factors would be taken. In the survey, it women are more affected by this major issue as compared to men from rural and urban areas.

Genetic Factors

Genes both directly and indirectly responsible for weight gain, fat accumulation, and distribution but few genes from them are closely related to obesity. Genetic factors associated with obesity are divided into two groups non-syndromic and syndromes. Non-syndromic factors have several human obesity gene maps which are monogenic obesity leptin (LEP), leptin receptor (LEPR), Proopiomelanocortin (POMC), Melanocortin 4 receptor (MC4R), PC1, Neuropeptide Y (NPY), Single-minded 1 (SIM1) and Polygenic obesity (Beta-1 adrenergic receptor (ADRB1), Beta-2 adrenergic receptor (ADRB2), Beta-3 adrenergic receptor (ADRB3), Uncoupling protein 1 (UCP1), Uncoupling protein 2 (UCP2), Uncoupling protein 3 (UCP3). Syndromes factor

includes Pleiotropic syndromes and Chromosomal rearrangement (Sidhu *et al.*, 2017). Leptin works separately and due to mutations in leptin gene monogenic obesity would be caused. The transformation was happening in the leptin quality and its receptors. FTO gene is also known as the obesity gene which is in contact with proteins. These encoded genes interact with food. It is included in the melanocortin pathway. This protein was helped in the reduction of obesity by covering the leptin level in adolescence (Shepherd *et al.*, 1999). It reported that 20 obesity loci which help in maintaining the food intake through action in the central nervous system and also in adipocyte function (Herrera *et al.*, 2010).

Vitality/Energy Balance

Vitality has a critical role in living beings. Energy takes in and takes out was important for the body (Vaidya *et al.*, 2003). When the energy of the body would not be equally distributed in a given period after the intake of food, it leads to instability in the body weight. Energy takes by humans in the form of protein, carbohydrate, fat, and alcohol. Through resting metabolic rate (RMR) humans expend the energy (E OUT). Resting metabolic rate was proportional to body mass (Popkin *et al.*, 1998; Hill *et al.*, 2012).

Associated diseases

Cancer

Obesity in males, related to the higher mortality from cancer, such as colon, esophagus, rectum, pancreas, liver, and prostate (Gallagher *et al.*, 2013). In females, it's was also observed that obesity was associated with the higher molarity from cancer like gallbladder, bile ducts, breasts, endometrium, cervix, and ovaries (Thörne *et al.*, 2002). The conversion rate of androstenedione to estrone in adipose tissue was increased in obese individuals in whom some of them are responsible for cancer (Palmer *et al.*, 2012). Several mechanisms were responsible to induce cancer through the obesity when the estrogen level would be increased and factors which affect the metabolism, adipocytokine levels would be changed *i.e.* adiponectin, leptin and visfatin, which affects the energy balance, growth-promoting cytokines and immune modulation affected by the low-grade inflammation and oxidative stress, changes in microbiomes mainly those composing the intestinal flora, which would increase in insulin and IGF-1 (Insulin-like growth factor) level and bioavailability of growth factors (Hursting *et al.*, 2010; Hursting and S. D., 2014).

Bone, Joint and Cutaneous Disease

Osteoarthritis and joint malignment risk were increased due to obesity. In the obese person, increased

venous stasis was observed (Balaban, G. and A.P.S. Giselia, 2004). Acanthosis nigricans, skin *manifestations* and thickening of the skin fold on the necks, elbows and dorsal interphalangeal spaces. Skin problems also associated with obesity (Hall *et al.*, 2015). It is mainly due to excess weight continuously forces the body joints (Sun *et al.*, 2012).

Cardiovascular disease

In men and women, obesity leads to coronary disease, stroke, and congestive heart failure. The low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C) and triglycerides were increased and the level of vascular protective adipokine adiponectin and HDL-C also decreased (Xu *et al.*, 2013). The higher pervasiveness of cardiovascular infection in fat people related to the expanded rate of recurrence of different understood hazard factors like hypertension, diabetes, and dyslipidemia (Cambridge *et al.*, 2006). In any case, abdominal obesity with the lifted production of pro-inflammatory adipocytokines and dysfunction of adipose tissue are key processes of connecting weight to cardiovascular diseases (García *et al.*, 2014). Consequently, abdominal obesity is considered as the most serious new hazard factor for metabolic and cardiovascular complications. Numerous investigations have shown that isolated obesity in human subjects is related to abnormal diastolic function, through impairment of systolic function, isn't reliably watched (Pednekar *et al.*, 2008). In people, it seems that obesity-related cardiomyopathy problem left heart rebuilding and abnormalities in left ventricular contractile and relaxation functions.

Stress

Stress is psychological and physical stress in nature (Alghasham *et al.*, 2014). Stress is responsible for the activation of adaptive response, if it continues for a long time, then there would be a change in the regulatory neural network (Rasheed and Naila., 2016), which result in weaken the stress-related adaptive process and health problem issue would be increased (Renehan *et al.*, 2008). The stress-induced mechanism is responsible for the affected food intake and induced obesity (Trayhurn *et al.*, 2004; Adam *et al.*, 2007). The hypothalamic-pituitary-adrenal axis (HPA axis) released the glucocorticoids in a huge amount under the stressful conditions which would make changes in the Mesolimbic Dopaminergic system which increases the feeling of hypo-palatable food and help in inducing the obesity. Glucocorticoids also stimulate the insulin, leptin, ghrelin, neuropeptide Y level and reduction in lipolysis process, lipolytic growth hormone

and sex steroids that helps in the accumulation of fat and responsible for obesity (Trayhurn *et al.*, 2004; Adam *et al.*, 2007; Rasheed *et al.*, 2012; Hruby and F.B., 2015).

Hypothalamic disorders

Hypothalamic tumors and lesions were caused due to excessive weight gain. This type of obesity caused due to craniopharyngioma (Stabouli *et al.*, 2005). This obesity also responsible for increasing the hypothalamic dysfunction, inflammation, genetic syndromes, suprasellar tumor, hyperphagia, Type 2 diabetes mellitus, hypertension, sleep apnea, NAFLD, cardiovascular and glucose tolerance (Sahoo *et al.*, 2015; Srinivasan *et al.*, 2004; Deepak *et al.*, 2007; Daousi *et al.*, 2005).

Hypertension

A relationship between weight and hypertension is well-established (Kotsis *et al.*, 2010; Stel and Legler, 2015). Various components have been recommended, including activation of the nervous system, sodium level maintenance, expanded secretion of leptin and different neuropeptides, and also insulin protection and inflammation (Lamb *et al.*, 2008). Damage and dysfunction of the vascular endothelium is a basic factor in the pathogenesis of hypertension. Various other organically dynamic atoms are additionally gotten from obese adipose tissue for example, receptive oxygen species (ROS), vascular endothelial development factor, plasminogen activator inhibitor-1, thromboxane A2 and intense stage response proteins (serum amyloid A proteins, C-responsive protein) (Kim *et al.*, 2001; Kim *et al.*, 2006). These mixes may impede nitric oxide (NO) generation and lead to hypertension. Decreased adiponectin levels in response to obesity create insulin protection in vascular endothelial cells, which at last brings down NO generation, while that of endothelin 1 is marginally expanded. Expanded adipocytes emit pro inflammatory cytokines, plasminogen activator inhibitor 1 (PAI 1) and thromboxane A2 (T × A2) and free unsaturated fats (FFA), which all add to endothelial brokenness and hypertension (Lamb *et al.*, 2008).

Synthetic drugs

Weight loss was also carried out with the consumption of synthetic anti-obesity drugs. At present, 8 synthetic anti-obesity drugs were permitted by the Food and Drug Administration (FDA) *viz.* Diethylpropion, Phentermine, Orlistat, Phendimetrazine, Pramlintide, Amylin, Lorcaserin and Exenatide. These chemical drugs work through three approaches to accomplish weight reduction:

- Drugs, for example, phentermine, diethylpropion, phendimetrazine, and Qsymia TM reduces calorie intake by repressing the desire for food.

- Orlistat restraint of pancreatic lipase which limits the digestion of dietary fats (Parati *et al.*, 2007; Pascual *et al.*, 2003).
- Lorcaserin stimulates the central nervous system (neurotransmitters receptors) which enhances the production of serotonin and norepinephrine helping in checking hunger (Chopra *et al.*, 2014).

Management of Obesity

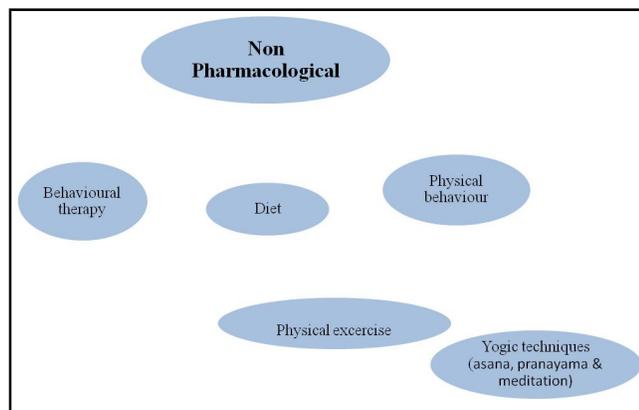
Three main components for the management of obesity are:

- Non-pharmacological treatment
- Pharmacotherapy
- Clinical strategies

Each of these is having its particular advantages and drawbacks.

Non Pharmacological approach:

In this approach main emphasis occur on:



Flow chart 1. Several Non Pharmacological approach

Lifestyle Modifications

The essential approach for accomplishing weight reduction, in most by far of cases, is a way of life adjustment, also decreasing the vitality intake and expansion in physical action (114). Early to bed and early to rise, proper sleep, and time-bound food consumption and cleanliness of the stomach and intestine and quantity of water consumption also affect the chances of obesity.

Diet

The obesity is controlled by reducing the overall consumption of calories by reducing the intake of fat and carbohydrates, incorporation of fiber-rich vegetables and fruits in a diet for a long time. Low-calorie foods could be incorporated in the diet which helps in controlling the hunger, reducing body weight and caloric intake (Rasheed *et al.*, 2010). In Ayurveda, “Nidana Parivarjana” is the main principle to reduce weight and help to fight against

various diseases (Joshi *et al.*, 2009). The Sthaulya Rogi can reduce the main factors (*i.e.* lack of sleep, physical exercise, intake of fast food which not digest easily) and also reduce the intake of high dense food (red meat, cheese, egg yolks, potato chips, pretzels).

To maintain the body fat men should intake 1500-1800 Kcal/day and for women, it is 1200-1500 Kcal/day (Blair *et al.*, 2004). If calorie intake is increased, it reduces by 200-800 Kcal/day as per human body requirement by intake of a very low-energy diet and very low-calorie diet (Avula *et al.*, 2007).

Exercise

Exercise and yoga show a crucial role in physical and psychological health. Several yoga postures help in reducing the fat such as forward bending asanas (mandukasana & paschimottanasana) and backward bending asanas (Katichakrasana and twisting). Ardhamatsyndrasana and Triyakatrikonasana asanas used to reduce the fat near the hips, abdomen and other areas (mostly fat accumulated) (Joshi *et al.*, 2009). Exercise (walking, jogging, swimming, cycling, gyming) also an important part of life (Mellendijk *et al.*, 2015), to reduce the weight and make a healthy. Several other benefits are reducing depression, improving heart, lung functions, and muscle tone, increasing metabolic rate, concentration, burning off calories, reducing stress, prevent from diabetes and high cholesterol (Yach *et al.*, 2006).

Behavioral therapy

It reported that a shift to healthy eating habits plays an important role in reducing weight (Real *et al.*, 1998). This therapy helps in controlling the hunger with the help of mind, social support (family, friends and colleagues) and containing a low cost for this therapy to fight against life-threatening diseases such as obesity. This therapy shows a better result as compared to other therapy such as surgical therapy (Dansinger *et al.*, 2007).

Pharmacological measures of obesity:

Pharmacotherapy is used more nowadays as compared to a non-pharmacological approach due to a busy lifestyle (Despres *et al.*, 2006). FDA (Food and Drug Administration) approved anti-obesity drug therapy to a patient with 30kg/m² or higher BMI and overweight patients (27 to 29.9 kg/m² BMI) (42).

However, this therapy show many side effects due to the intake of anti-obesity drugs (*i.e.* orlistat, sibutramine and rimonabant as shown in table 2) and applying anorectic medications, thermogenic medications or medications that influence lipid activation and usage.

Surgical Approach:

Surgery is the last option for those patients who have

an extreme case of obesity and have already tried all those techniques which helps in reducing fat. This technique is used only for those patients whose BMI $e \geq 40$ kg/m² and with BMI 35 to 40 kg/m² (Fujioka, 2002). Vertical banded gastroplasty (Cornelius *et al.*, 2001) and gastric bypass are two different surgical procedures that remove excess fat from the patient (Brolin and R.E., 2001). Omental fat decrease regarding customizable gastric banding brings about a sensational change in insulin protection and related glucose unsettling influences (Han *et al.*, 2011; Balandrin *et al.*, 1985; How *et al.*, 2007).

Herbs for the treatment of obesity

Herbs are used for the treatment of obesity and its related issues from time immemorial (Sharma *et al.*, 2016a and Sharma *et al.*, 2016b, Chawla *et al.*, 2019). *Rutaceae*, *Apiaceae*, *Aloaceae*, *Cannabaceae*, *Menispermaceae*, *Lamiaceae*, *Sapotaceae* *Phytolaccaceae* are the different families which fight against obesity by creating compounds in our body (Nagrani *et al.*, 2016). Herbs like *Commiphora Mukul*, *Cissus Quadrangularis*, *Melia Azedarach*, *Galega Officinalis* are utilized as a part of Ayurvedic treatment of obesity and helps in the reduction of cholesterogenesis. Inhibition of digestion and ingestion of dietary lipids through an inhibitory activity on pancreatic lipase can be focused on the advancement of anti-obesity agents (Boqué *et al.*, 2013). *Bunium persicum* is an Iranian plant that is generally utilized as anti-obesity, antispasmodic, carminative and lactogage. The oil and methanolic concentrate of *Bunium persicum* strongly inhibited the oxidation of linoleic acid (93.5%) (Bhatt *et al.*, 2003).

Brassica oleraces and Panax Ginseng

The *Brassica oleraces* is utilized as a home-made treatment of obesity (Nagrani *et al.*, 2016). Panax ginseng herb reduces the heaviness of the body in three weeks because of the rough saponin (CS). It is used in Russia, Germany, Korea, Japan and China locale (Wen *et al.*, 2014). Protopanaxadiol (PD) and Protopanaxatriol (PT) of the saponin part are additionally in charge of the reduction of body weight which is seemed by inducing a high-fat diet in rats (Kim *et al.*, 2009). In Diabetic patients, the Panax ginseng plant decreases body weight, blood glucose and furthermore in charge of enhancing the psychophysical execution (Balandrin *et al.*, 1985).

Nicotiana tobacum and Schotia latifolia

Fiber consumption additionally helps in diminishing the weight. By eating of *Nicotiana tobacum* leaves, the nutrient absorption was reduced (Paranjpe *et al.*, 1990;

Hruby *et al.*, 2015). Tobacco leaves would contain nicotine and it would be detached which helps in expanding digestion, fat oxidation, and consumption. It leads to a lesser intake of food and hence reduces body weight (Scheen, 2008). *Schotia latifolia* helped in the treatment of obesity as well as help in tanning, acid reflux, and an after-effect (Shai *et al.*, 2009). For the treatment of these issues, the bark of the *Schotia latifolia* was utilized (Afolayan *et al.*, 2010).

Aframomum Melegutta and Spilanthes Acmella

Aframomum melegutta and *Spilanthes acmella* are the plants that are cultivated in the African continent and these plants contain anti-obesity compounds that inhibit the pancreatic lipase. In *Aframomum melegutta* and *Spilanthes acmella* plant, the lipase inhibitory was reported as 90 and 40%, respectively (Ekanem *et al.*, 2007) and (Yanovski and Yanovski, 2014).

Almond, Apple, Cinnamon, Orange Bloom, Hamamelis, Lime Bloom, Grape Vine and Brich

It reported that the polyphenolic concentrate of almond, apple, cinnamon, orange bloom, hamamelis, lime bloom, grapevine, and brich if fed for 54–64 days, reducing the body weight in rats (Teter *et al.*, 2002; Van *et al.*, 2013). The apple and cinnamon contain a large number of anti-obesity compounds. It helps to lower down the fat of the body. Plant extracts contain some common substance which was conflicted with the counter obesity. In this review, it demonstrates that the restraint of pancreatic lipase (LP) helps in anticipation of obesity. Through the phenolic compound and plant extract Epigallocatechin-3-gallate, Kaemperol, and Quercetin were discovered which helps in the inhibition of pancreatic lipase (PL) (Taira *et al.*, 2017).

Garcinia indica and Cyperus rotundus

It contains a phytochemical compound (Hydroxycitric corrosive (HCA) that helps in reducing the obesity problem caused by 1 factors (Rabkin *et al.*, 2005). *Garcinia indica* contains 7% of HCA. *Cyperus rotundus* is utilized as a conventional Indian medication plant for the treatment of obesity. This plant helps in curing fever, looseness of the bowels, thirst, irritation, blandness, helminthiasis, acid reflux (Ng *et al.*, 2014; Kolaczynski *et al.*, 1996). Extract of *C. rotundus* rhizomes reduces the weight by 10%, due to the activation of the β 3-AR (adrenoreceptor) (Torres *et al.*, 2007).

Azadirachta indica

Azadirachta indica contains phytochemicals that have strong anti-obesogenic, anti-cancer and anti-inflammatory properties (Berg and Philipp, 2005; Foster,

2003). Liposuction or liposculpture suction lipectomy, a corrective surgical technique for fat expulsion from various parts of the body, however, has turned out to be very well known nowadays, causes a few complexities and symptoms. The mechanisms of activity of anti-obesity drugs incorporate hunger concealment, expanded rate of digestion, decreasing the limit of the body to absorb certain sustenance supplements like lipids, setting off the procedure of thermogenesis and improving lysis of lipids (Chopra *et al.*, 2014).

It is well known that dopamine, histamine, serotonin, and their related receptor exercises corresponded with the control of obesity (Amadou *et al.*, 2013). The hypothalamus arcuate core (ARC) is viewed as the most critical area of the mind which assumes a key part in the hunger direction. The hunger can be controlled by neural and endocrine motioning from the gastrointestinal tract, while the data about adiposity level and acute nutritional status, from peripheral hormones, can be gotten and deciphered by the ARC and brainstem neurons (Gaal, *et al.*, 2006; Wilde *et al.*, 2014).

***Exomis microphylla* (Thunb) Aellen**

Sugar beet is *chemopdiace* family plants that have the ability to efficiently decrease body fat. Leaves of these plants can fight against the obesity causing compounds due to the presence of bio-active compounds (Afolayan *et al.*, 2010).

Cissaempelos caenenis*, *Curtisisa dentat*, *Schotia latifolia

It reported that the formulation of *Cissaempelos caenenis*, *Curtisisa dentat*, *Schotia latifolia* effectively reduces body weight (Janiszewski *et al.*, 2007; Hafstad *et al.*, 2013). These plants were used traditionally for anti-obesity remedies. Such a bioactive compound from the plant source helps in the inhibition of the dietary fat absorbed in the body and helps in the treatment of obesity (Yanovski and Yanovski, 2002).

Hogweed

Punarnava is a traditional name of hogweed and its biological name is *Boerhavia diffusa* and it is exceptionally viable in treating obesity. The leaves, roots, and seeds of punarnava are used for the treatment of obesity. This drug contains the alkaloids such as sitosterol, esters of sitosterol, punarnavine, boerhaavia corrosive, boeravinone, palmitic corrosive (Bhowmik *et al.*, 2012). Punarnava additionally keeps maintaining kidney and urinary capacities with its diuretic, purgative, stomachic, diaphoretic, anthelmintic antispasmodic and anti-inflammatory action. As per Ayurveda, Punarnava is unpleasant, cooling, astringent to bowels, helpful in

biliousness, blood pollutions, leucorrhoea, iron deficiency, aggravations, heart ailments, asthma (Chaput *et al.*, 2010). The leaves are valuable in dyspepsia, tumors, spleen expansion, and stomach torments. Seeds are a tonic expectorant, carminative, helpful in lumbago, scabies. The seeds are considered as promising blood purifiers (Bhowmik *et al.*, 2012).

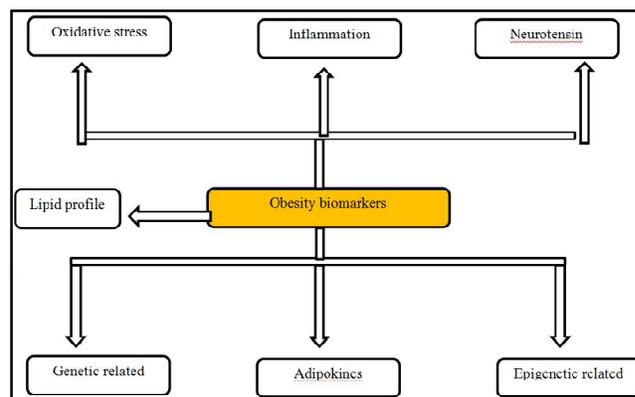
Tabebuia avellanedae

Tabebuia avellanedae is cultivated throughout Brazil and North Argentina, in South America (Shimofuruya *et al.*, 2002). *T. avellanedae* has been generally utilized for antiulcero-genic, antineoplastic, antifungal, antiviral, antimicrobial, antiparasitic, and calming definitions in South and North America (Riffel *et al.*, 2002). Recently, numerous investigations have been led to the natural and pharmacological impacts of *T. avellanedae* and its concentrates and mixes disengaged (Park *et al.*, 2003; Jeong *et al.*, 2015). The intake of *T. avellanedae* reduces body weight and fat

Accumulation in male C57BL/6 mice with high-fat-diet-induced obesity (Won *et al.*, 2014). Bioassay-guided decontamination of the n-butanol extract based on the TG levels in 3T3-L1 cells led to the isolation of compound 2 (1-dehydroxy-3,4-dihydroaucubigenin) which showed the anti-obesity effect of *T. avellanedae* extract because of its ability in keeping the aggregation of adipocyte. *T. avellanedae* extract may be a promising functional food resource capable of ensuring against OVX-instigated obesity (Iwamoto *et al.*, 2016).

Clerodendrum phlomidis

Clerodendrum phlomidis belongs to family *Verbenaceae*. It contains the phytochemical compound shaving anti-obesity effect such as flavonoids, saponines, sitosterols, and tannins (Yun, 2010). *Clerodendrum phlomidis* help in the inhibition of pancreatic lipase activity which delays the intestinal absorption of dietary fat. Methanolic extract of *Clerodendrum phlomidis*



Flow chart 2. Several types of obesity biomarkers

contains β -sitosterol in abundant amount (Taboli, 2013, Nagarani *et al.*, 2011).

Biomarkers for obesity

Neurotensin

It reported that NT contains 13-amino acid peptide that is present in the gastrointestinal tract and the brain. Neurotensin markers are also known as biological markers (Meza *et al.*, 2016). Lack of the NT in the body helps in reducing the intestinal fat absorption and helps in the prevention of obesity, insulin resistance and fatty liver diseases (Adler *et al.*, 2010).

Genetic Biomarker

It plays the most important role between genetic factors and environments. Due to the heritable conditions, there is a 40% variation in obesity (Pollex *et al.*, 2006). It reported that changes occur in fat or a body mass due to the variation in adipocyte, growth, differentiation and apoptosis (Qi *et al.*, 2004). Adipocyte hypertrophy or hyperplasia to closed a greater fat mass (101). Melanocortin-4-receptor (MC4R) is the fat mass obesity (FMO) genes which play an important role in causing the obesity problem and with GWA scans, it would be identified (Trevaskis *et al.*, 2005) PCSK, (PPARG) Peroxisoma Proliferadores – activados receptor gamma, Disociacionde (UCP1, UCP2, UCP3), receptor beta-adrenergico (ADRB2, perilipina (ADRB3, P21N) are the genetically related biomarkers (Abranches *et al.*, 2011; Creemers *et al.*, 2012; Garcia *et al.*, 2014). It seems that the SNPs (Single-Nucleotide Polymorphisms) would be acted on the gene which produces the fat mass and obesity risk (Paracchini *et al.*, 2005).

Epigenetic-related biomarkers

With the different DNA sequences, the epigenetic heritable changed and linked with gene showed the variants of obesity. Several mechanisms are used to regulate gene expressions such as the DNA- methylation of guanine, cytokines, hypermethylation, modifications of histones and RNA non-coding. According to the genome-wide association, it seems that SS genetic coci identified may link with BMI and obesity. Physiological changes interlinked with obesity and insulin resistance (Wen *et al.*, 2014).

DNA methylation is associated with the BMI and due to the increased level of methylation in HIF3A leads to obesity (Huang *et al.*, 2015). Several genes are identified through the bioinformatics analysis in CpG, such as PPARGC1 (Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1), NBOB2 (Small Heterodimer Parture), NR3C1 (Glucocorticoid receptor),

PPARG (Peroxisome Proliferator-activated receptor gamma), FGF2(Basic fibroblast growth factor), PTEN (Phosphatase and tensin homolog), CDKN1A (Cyclin-dependent kinase inhibitor 1A) and ESRI (Estrogen receptor) which are associated with the adipogenesis (Davé *et al.*, 2015). Reported epigenetic potential markers are the first epigenomics which helps in detecting the obesity at birth (Stel and Legler, 2015).

Inflammatory Biomarkers

It reported that a complex reaction, where pathogenesis of insulin resistance and metabolic syndrome, is the component which is responsible to induce a chronic inflammation through obesity (Pinheiro *et al.*, 2015). In adipose tissue of skeletal muscle and liver, it seems that insulin resistance occurs due to the pro-inflammatory cytokines, which are responsible to inhibit the insulin signal transduction (Iantorno *et al.*, 2014). The risk of obesity and CVDs can be reduced if the insulin resistance and glucose control in the insulin patient would be reduced. It seems to be an obesity mechanism where morbi-mortality increasing in and releasing of adipose tissue cytokines which is the main protein phase (Lamb *et al.*, 2008). The adipocytes are responsible for the secretion of leptin, resistin, adiponectin adipokines and are capable to affect the inflammation and insulin resistance (Audrain *et al.*, 1995). Plasminogen activator inhibitor-1 (PAI-1), Interleukin-6 (IL-6), C-reactive Protein (CRP), Tumor necrosis factor-alpha (TNF-alpha), NFK-beta (Nuclear factor Kappa-light-chain- enhancer of activated B cells) are the several factors that work as inflammation markers and help in reducing the risk of CVD and obesity (Carmena *et al.*, 1984; Catalan *et al.*, 2012; Buchanan *et al.*, 2005).

Oxidative stress biomarkers

Oxidative stress was one of the major components of obesity and CVDs problem (Jeong *et al.*, 2015). Detoxification of the reactive intermediate or repairs occurs due to an imbalance between the ROS Production and biological system. Their impacts occur on protein, lipids, DNA. The metabolic signalling pathway was also affected due to the hypertrophied adipocytes which would occur due to the higher level of ROS (Caroll *et al.*, 2006). ROS produced would reduce the insulin-resistant state. Hepatic steatosis and hyperlipidaemia are linked with body fat, visceral fat and also work as antioxidant defence markers (Amy *et al.*, 2013).

Lipid profile

Level of free fatty acids from insulin resistance could be increased due to a change in metabolism which are responsible for the overproduction of LDL (low-density

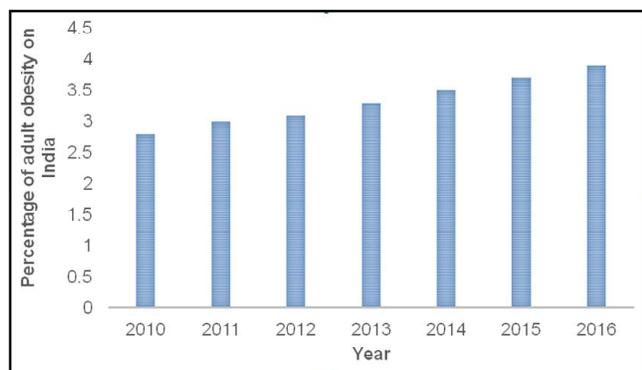


Fig. 1: Total percentage of adult obesity in India 2010-2016.

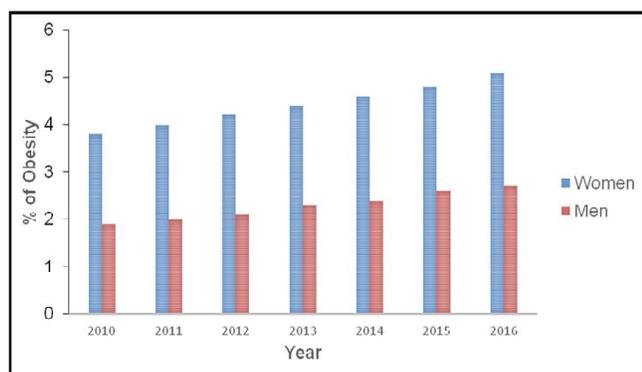


Fig. 2: Men and women suffer from obesity in India 2010-2016.

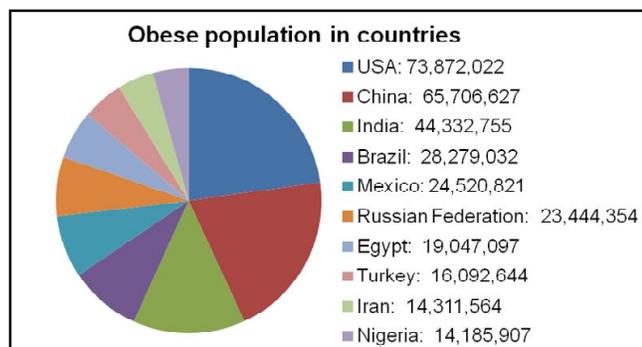


Fig. 3: Total number of populace of top 10 countries which suffered from obesity world widely (OECD 2017).

lipoprotein) -cholesterol, VLDL (very low-density lipoprotein) and triglycerides and decreases in HDL (high-density lipoprotein)-cholesterol (Kalra and Unnikrishnan, 2012). It reported that the production of VLDL is directly related to insulin levels and body fat percent (Anjana *et al.*, 2014). Extra fat deposited to central and intra-abdominal areas responsible for cardiovascular diseases and diabetes (Yach *et al.*, 2006; Palmer *et al.*, 2012). Atherogenic dyslipidemia could be responsible to increase the cardio- metabolic risk in obesity by increasing VLDL, LDL, plasma triglycerides and low concentration of HDL (Palmer *et al.*, 2012). In reported (Yach *et al.*, 2006)

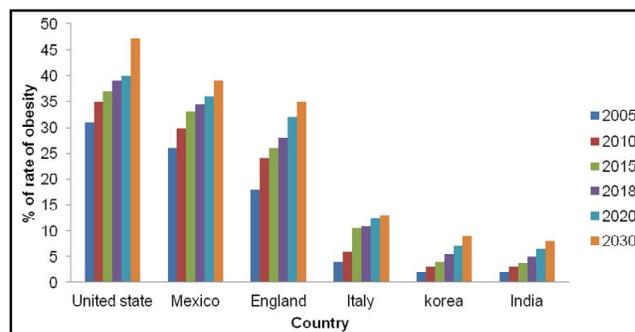


Fig. 4: Obesity rate are expected up to 2030 (OECD, 2015).

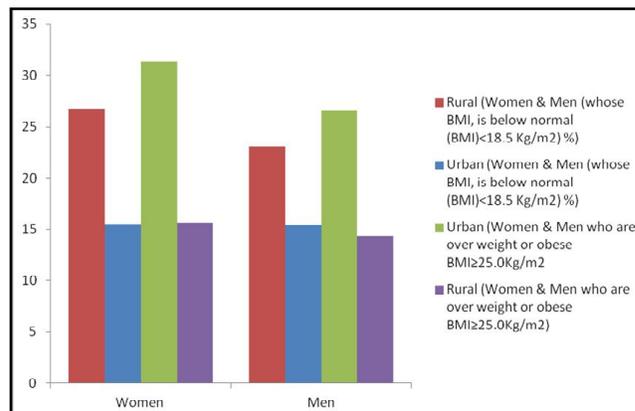


Fig. 5: National Family Health survey-4 (2015-2016), where BMI is below the normal BMI < 18Kg/m² and overweight or obese BMI ≥ 25.0Kg/m².

Table 1: Several mechanism of action anti-obesity drugs such as: (Trevaskis and Butler, 2005).

S.No.	Mechanism	Function	Example	Reference
1.	Appetite suppression	Decreased the hunger through the suppression mechanism <i>i.e.</i> in hypothalamus (norepinephrine stimulates β -adrenergic receptor)	Phentermine, benzphetamine, phendimetrazine, diethylpropion	(Sun <i>et al.</i> , 20120)
2.	Nutrient absorption	Inhibition of gastric and pancreatic lipase through Orlistat which have ability to reduce the absorption of dietary fat <i>i.e.</i> triglyceride not be metabolized unto free fatty acid (absorbable) and monoglycerols.	Orlistat	(Havel, 2004)
3.	Energy used	Weight loss due to the ephedrine, which stimulates thermogenesis in living being. (Intake 150mg/day)	Ephedrine	(Scheen and Lefebvre, 1999)

Table 2: Several synthetic drugs are available and they contain major side-effects such as.

S.No.	Obesity drug	Major side-effects
1.	Orlistat	Steatorrhoea
2.	Sibutramine	Hypertension, serotonin syndrome
3.	Melformin	Lactic acidosis, Gastro-intestinal upset
4.	Rimonabant	Severe depression and predisposes to neurodegenerative diseases e.g. Alzheimers disease

peroxidation, imbalanced fatty acid composition responsible for changes in the function of individual lipids.

12. Conclusion

Several natural remedies are present for the treatment of obesity as compare to artificial remedies which contain several side effects. Herbal treatment of obesity has associated benefits also like anti-oxidant, antineoplastic, antifungal, antiviral, antimicrobial and antiparasitic.

Declaration of interest statement

There is no conflict of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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