

Review Article

Physical Health Impacts of Obesity: Comprehensive Review

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Abstract: Obesity is known as the excess accumulation of body fat which could impair the quality of life. This phenomenon has been witnessed in the drastic elevation of the prevalence of obesity which affected the society in an alarming situation. In line with the rising prevalence, it has depicted the staggering burden of the healthcare system in curbing this health issue and it is also associated with the burden of healthcare costs. Apart from the healthcare aspect, it has also influenced both economic and social development of the country. The rising trend of morbidity not only affected the adults, but also children. Hence, this literature review aimed to summarize the major harmful physical health impacts which are greatly associated with obesity and address the possible types of management to tackle this health issue. The revised evidence on the association of comorbidities with obesity is established. Obesity leads to several comorbidities which include cardiovascular disease, diabetes and disability in which these diseases are also the domain for the increase in mortality rate and potentiating the reduction of human lifespan. Therefore, this review capitalizes this health issue in order to disseminate proper knowledge in public and health practitioners on the severity of obesity with the associated diseases and discuss on the appropriate and effective disease management, either improving the awareness of primary prevention or reducing the severity of illness.

Keywords: obesity; prevalence; morbidity; mortality; physical health impacts; management

1. Introduction

Generally, obesity is classified using Body Mass Index (BMI) which acts as the standard measure for the nutritional status of each individual. In line with the standard index of Body Mass Index, it is suggested that the BMI over 25.0 is considered overweight whereas a BMI higher than 30.0 falls under the obese range. Obesity is further subdivided into three distinct classes, depending on the severity, which consists of Class I (BMI: 30.0–34.9); Class II (BMI: 35.0–39.9), and Class III for the BMI that reaches 40.0 or above^[1]. This health issue has become a threatening global health concern as the rising incidence rate leads to the epidemic of obesity in both developed and developing countries.

Among all the obesity-associated diseases, cardiovascular disease (CVD), diabetes, and other disabilities are found to be the most life-threatening diseases which contribute to the rising burden of obesity, in terms of complications. Preliminary data obtained from a recent study revealed the association between these comorbidities with obesity in which a higher rate of cardiovascular disease and diabetes can be observed as the consequence of the higher prevalence of obesity in Malaysia^[2]. In addition, study has revealed that BMI-related deaths and BMI-related disability-adjusted life-years are caused by CVD among obese individuals. Obese individuals are also prone to a higher prevalence of diabetes, especially Type 2 diabetes mellitus. A recent narrative review has demonstrated the parallel elevation of diabetes along with the rising prevalence of obesity where Indian ethnicity is more prone to diabetes, followed by Malay and Chinese ethnicity^[3].

Owing to the rising prevalence and epidemic of obesity, it is pivotal to emphasize and highlight on the importance of health promotion in disseminating primary and secondary prevention to prevent getting obesity, reduce comorbidities, as well as to reverse the epidemic of obesity. A variety of interventions can be implemented to curb obesity, which includes a proper food intake (balanced diet) and persistent physical activities. Individualized therapy with different methods of management should be developed. Besides, pharmacotherapy which includes the use of medication is also applicable as the second approach to treat obesity.

2. Materials and Methods

2.1 Physical Health Impact

Being overweight or obese can lead to an increase in the incidence of comorbidities such as coronary artery disease, hypertension, stroke, congestive heart failure, pulmonary

embolism, Type II Diabetes Mellitus, asthma, osteoarthritis, chronic back pain, and cancers (breast, endometrial, ovarian, colorectal, oesophageal, kidney, pancreatic, prostate)^[4]. For instance, an increase in the mass of adipocytes may cause osteoarthritis. Next, when the secretion of coagulation and inflammatory molecules from fat tissue increases, diseases like diabetes, hypertension, cerebrovascular disease, liver disease, gallbladder stones, coronary artery disease, and certain types of cancers can be traced^[5].

Three physical health impacts will be discussed, including cardiovascular disease (CVD), diabetes, and other disabilities. First, abnormal fat depots especially at the major coronary artery can affect normal cardiovascular function. Therefore, obesity is related to a broad spectrum of CVD including hypertension, stroke, coronary heart disease, heart failure, sudden cardiac death, ventricular arrhythmias, and atrial fibrillation^[6]. Secondly, obesity is associated with an increased risk of developing Type 2 Diabetes Mellitus (T2DM). Normally, an obese patient will consume a large number of carbohydrates or fat which may increase the amount of glucose and fat produced and stored in the body which will promote T2DM^[7].

Thirdly, obesity might cause disabilities such as physical disability and musculoskeletal illness^[8]. Obesity can cause mobility difficulties which bring many limitations to the patient in doing daily activities. Next, obese patients may experience musculoskeletal pain in the lower limb when standing or walking for long period. A severely obese person may have a reduction of life expectancy at about 5 to 20 years. Besides, obesity may increase the risk of disease and death especially from cardiovascular disease and cancer. The association between obesity and mortality varies over time, populations and causes of death^[5].

2.1.1 Cardiovascular disease

Based on WHO, obesity is measured by body mass index (BMI), which is known as a person's weight measured in kilograms, divided by the square of their height, in meters. Generally, an individual with a BMI of 30 or more is considered obese while an individual with a BMI equal to or more than 25 is considered overweight (Table 1). The Global Burden of Disease Obesity Collaborators (GBD) investigators found an increase in the burden of elevated BMI, with high BMI accounting for 4.0 million deaths in 2015, more than two-thirds of which were caused by CVD. Besides, the study also indicates that a large proportion of both BMI-related deaths (41%) and BMI-related disability-adjusted life-years (34%) were caused by CVD among individuals with obesity^[9]. BMI is very important because the increase of BMI is often an independent risk factor for various cardiovascular risk factors in metabolic syndrome.

Table 1. Classification of Body Mass Index (BMI) by the World Health Organization.

BMI	Category
Below 18.5	Underweight
18.5–24.9	Normal weight
25.0–29.9	Pre-obesity
30.0–34.9	Obesity class

Source: Body Mass Index, World Health Organization (WHO, 2021).

According to a study done among the residents of Community Housing Projects in metropolitan Kuala Lumpur, Malaysia, it has been stated that the highest CVD risk factor is obesity. Obesity is more prevalent among the Chinese community (60%) and the least being the Indian community (49.7%)^[10].

The etiology of obesity can be varied from genetic, environmental, sociocultural, physiological and behavioural. An ectopic or abnormal fat deposition is generally considered a lipid store that's not physiologically put away in adipose tissues such as within the liver, the pancreas, the heart, and skeletal muscle^[11]. This is known as adiposopathy. Adisopathy alludes to the pathogenic extension of adipose cells and tissues that comes about in anatomic and utilitarian anomalies, driving to metabolic disorder and expanded CVD risk. Ectopic fat usually depots in the pericardial and epicardial adipose tissues. According to the Multi-Ethnic Study of Atherosclerosis, pericardial fat was interlinked with a higher risk of CVD. It has also been indicated that all adipose and ectopic fat depots correspond with one another.

Obesity promotes systemic inflammation and it has been stated that inflammation can cause adipogenesis. Epicardial adipose tissue represents visceral fat between the outer wall of the myocardium and the visceral layer of the pericardium^[11]. Adipose tissue originates from embryonic brown adipose tissue and releases cytokines along with chemokines into the vasculature. In contrast, epicardial fat in obese people is more prone to lipolysis, leading to release of fatty acids and reactive inflammation. The deposition of epicardial fat along with chronic inflammation can cause severe coronary artery disease. Generally, the ability of the adipose tissue to expand and produce pro-inflammatory cytokines that can directly impair cardiac systolic and diastolic function as well as the formation of atherosclerotic plaques plays a major role in the consequence of CVD, as well as obesity.

2.1.2 Other disabilities

Obesity can be associated with poor muscular-skeletal condition, which contributes to various physical disabilities across the age spectrum. According to National Health and

Morbidity Survey^[12], physical disability was significantly higher among obese adult populations. Obesity-associated disability significantly correlates with our body mass index (BMI). One of the underlying causes of physical disability is obesity-induced joint pain^[13]. Higher BMI values escalate the prevalence of developing painful joint conditions. It is found that the risk for joint pain increases by 36% for every two-unit rise in BMI^[14]. This condition is recognized as osteoarthritis and the main reason for this condition is the elevated joint pressure caused by excessive body weight.

Apart from that, the excess weight also can be burdening to other spinal structures and causes severe pain such as the back pain. Obesity impacts one's flexibility as well since they might progressively develop fibromyalgia syndromes^[13]. Fibromyalgia syndromes (FMS), is a serious condition characterized by pain, stiffness and tenderness of muscles, tendons, and joints that could disrupt the patients' daily life activities^[15]. These locomotor disorders that correlate with musculoskeletal system which comprised of arthritis, back and neck problems were the most common disabling conditions in obesity^[16]. There is a significant relationship between obesity (measured using BMI) and different disabilities (Table 2). These data shown that the disabling conditions are more prevalent in obese adults compared with their normal-weight counterparts. In line with the finding from Table 2, arthritis resulted in the highest number of claims and obesity odd ratios. This concurrent increase between BMI and disability was also demonstrated in Malaysian populations^[12].

Table 2. The odds of having various disabling conditions in the obese population compared with the ideal weight population for adults.

	N* (of 4781)	Adjusted odds ratio	95% confidence interval
Physical disability	683	2.02	(1.68–2.43)
Musculoskeletal illness	935	1.84	(1.58–2.15)
Back problems	319	1.35	(1.06–1.69)
Rheumatoid arthritis	6	-	-
Osteoarthritis	23	3.69	(1.43–9.52)
Other arthritis and rheumatism	156	4.33	(2.91–6.45)
Locomotive disability	538	2.42	(1.97–2.97)
Sight disability*	95	1.25	NS
Hearing disability*	237	1.57	(1.19–2.07)
Mental disorder*	156	-	-
Communication disability*	48	-	-
Personal care disability*	288	2.47	(1.09–3.22)

** The number of participants in the analysis with the disabling condition.

Muscle/Bone/Joint claims : 213 500.

Back Ailment claims : 229 200.

Arthritis claims	: 522 400.
Blindness*	: 62 400.
Deafness*	: 32 300.

Consequently, obesity leads to functional decline and mobility limitations in obese individuals compared to the non-obese populations. People with obesity are usually experiencing difficulties in their functional mobility due to the musculoskeletal pain, particularly in the lower extremities and their low back. Definition of functional mobility is the ability of people to move from place to place in order to participate in their daily living activities^[17]. For instance, those movements include walking around, standing, climbing and bending. It is strenuous for an obese person to perform those activities especially with ageing. Based on a study, both healthy and unhealthy obese adults showed a higher likelihood of developing the struggles to climb stairs or walking over a 7-years period than healthy normal-weight adult, indicates the worsened physical function in response to obesity^[18]. These situations are linked with joint pain and chronic back pain experienced by the people with obesity. Eventually, it may stimulate fear of movement and activity avoidance in an obese person such as avoidance of doing any weight bearing tasks^[19]. This is known as adaptation behaviour. Example of this behaviour is skipping their household chores that can trigger musculoskeletal pain. Cessation of physical activities may intensify the weight accumulation in an individual and worsen the obesity problem.

Obesity is undeniably affecting the ability of an individual to perform their daily activities. This problem may complicate the everyday life of obese patients to the extent of inability to engage in typical social activities and employment^[20]. Morbidly obese people will lose their functional independence and become more dependent on others' assistance wherever they are. It deteriorated their health-related quality of life. Moreover, obese individuals especially older people suffer a higher mortality rate^[21]. Thus, healthcare providers and policy makers such as the government need to be more aware about this issue, and design the ideal obesity management programmes that are able to ameliorate functional status of older adults and protect them from becoming disabled, with resultant below par of well-being.

2.1.3 Diabetes

Obesity and diabetes, colloquially known as "diabesity," coexist in a modern epidemic. Diabesity has significant diagnostic and therapeutic implications since it is linked to numerous pathophysiological processes centred on insulin resistance and hyperinsulinemia. The two main twin epidemics, the latter fuelled by the former, clearly have no intention of abating. It is also known as a combination of diabetes and obesity, with or

without other risk factors such as related to fat redistribution and excessive fat tissue in obese patients, which also involves hyperglycaemia, dyslipidemia, endothelial dysfunction, insulin sensitivity chronic inflammation and hypertension^[22,23]. Diabesity is thus a subset of metabolic syndrome that mostly occurring in obese persons with a direct relationship between BMI and diabetes^[24,25].

Generally, obesity and diabetes are interconnected due to several hypotheses that are being proposed to justify the relationship between these 3 epidemics. The hypothesis stated that beta cells and insulin-dependent tissue are affected by chronic inflammation combined with obesity and the proinflammatory cytokines produced in adipose tissue via macrophages. Next, lipotoxicity induced by increased ectopic lipids in obese individuals promotes and enhances peripheral tissue damage and cytotoxicity^[23]. Additionally, the adipose hypothesis mentioned that stressed body fat releases several paracrine and autocrine products which eventually lead to a loss of beta-cell function and insulin resistance in the pancreas^[23].

3. Discussions

3.1 Management of Obesity

The advancement of technology and the economy changes the environment which increases the prevalence of obesity epidemic. For instance, lack of physical activity and uncontrolled diet will lead to an imbalance in energy uptake and energy expenditure^[26]. Obesity can bring a lot of adverse effects on physical health, mental health, spiritual health, and social health to obese people^[4]. Apart from that, obesity can increase the healthcare and medication spending for the treatment of obesity and the diseases caused by obesity. Therefore, it is crucial to manage obesity wisely to improve our health and reduce the risk of having obesity related diseases.

There are three ways for obesity management to be discussed, including regular exercise, regular food intake and pharmacotherapy. Firstly, increasing physical activities through exercise can increase energy expenditure which accelerates the breakdown of glycogen and triacylglycerols^[27]. Therefore, it can aid in fat burning and decrease the prevalence of obesity. Secondly, regular food intake is about choosing the right food at the right proportions needed by our body. For a dietary plan, obese patients can consider to reduce their energy intake by 500kcal per day to lose weight^[26]. The obese patient can seek help from dietician or nutritionist in choosing the food that is filling but low in fat and calories. Both obese patients and the practitioners need to put more effort on the prevention and treatment of obesity to reduce the prevalence of obesity^[28].

Majority of the students face a moderate level (64%) followed by severe stress (23%) and mild stress (13%). The higher the mean score of the academic factor, the greater the stress exerted on the students. As shown in Table 2, summary of the response in academic stress,

Item No.8 had the highest mean score (2.8333 ± 0.9129). The second leading academic stress factors were Item No.3, Item No.6, Item No.7 and Item No.10. This indicates, all participating students in this study experienced stress to some extent which might contribute to the poor academic performance being impacted by the pandemic.

3.1.1 Food intakes

A healthy diet and proper food intakes are fundamental in nutrient supply, prevent the risk of chronic diseases and manage obesity effectively. Human body needs optimum energy and nutrients provided by healthy and balanced eating habits in order to maintain a good long-term health condition^[29]. Therefore, there are several considerations suggested by The Malaysian Dietary Guidelines to plan a healthy meal specifically focusing on eating a balanced diet, consuming a wide variety of foods and foods in moderation^[30].

Malaysian food pyramid 2010 is a visual tool to give a proper perspective regarding the right types and amounts of food that can be eaten. As a review of the food pyramid from the top to the bottom levels, each food group size becomes bigger, which portrays more food should be consumed at the pyramid base and at the top pyramid, less of foods should be taken. (Table 3)^[31].

Table 3. Pictorial food guides and related key messages used in FBDCGs.

Malaysia	
Name of pictorial guide	Malaysian Food Pyramid 2010
Format	Pyramid
No. of levels	4
Cereals & products, tubers	Eat adequately 4–8 servings/day
Vegetables	Eat plenty, 3 servings/day
Fruits	Eat plenty, 2 servings/day
Milk & milk products	Eat in moderation, 1–3 servings/day
Fish, poultry, meat, eggs, legumes	Eat in moderation, ½–2 servings of poultry, meat, egg/day; 1 serving of fish/day; ½–1 serving of legumes/day
Fat, oil, sugar, salt	Eat less; no quantitative recommendation

Sources from National Coordinating Committee for Food and Nutrition Malaysia^[30].

Carbohydrate is classified as a macronutrient with a low storage capacity which will undergo oxidation when intakes exceed requirements. Fat contains twice the amount of caloric content compared to protein or carbohydrate. Hence, excess fat will be stored in the body since fats have unlimited capacity^[32]. Studies have been done to prove that a high-carbohydrate diet based on cereals gives an adequate nutritional intake with more than 55% energy supply to humans^[33]. Thus, cereal foods such as whole grain take the largest component in the food pyramid and recommended daily food intake to prevent humans from

overeating to get sufficient energy. The consumption and intake of 20 to 30 grams of dietary fibre per day is highly recommended for nutrient intakes^[34]. By taking vegetables, fruits, whole grain cereals, legumes, and pulses, it can achieve obesity prevention goals. Foods with an adequate amount of fibre is less in energy density which is suitable to cut calorie intakes for a healthy diet. It contributes to effective short-term satiety effect which can avoid obese people from overeating, and manage their weight efficiently^[35].

Fruit and vegetables are recommended to be placed in the second level of Malaysian Food Pyramid. The high intake of low energy dense food was associated with less weight gain and solution against large increases in waist circumference measurements^[36]. Thus, lower energy density food such as vegetables and fruits should be consumed because it contains high-water content, huge amounts of fibres and less fat. Recent research studies show that low-energy dense diet consumption is able to help in hunger control, maintain satiety or fullness feelings and improve satisfaction experience after taking the meals^[36]. The higher consumption of non-starchy vegetables like broccoli, spinach, lettuce and carrots and fruit likes citrus fruits, and melons have been related with a lower weight gain risk and obesity based on the recommendation in Malaysian Food Pyramid with 3 servings per day with perfect calorie reduction^[30].

Humans need to take less amount of fats according to guidelines in Malaysia Food Pyramid. By reducing the fat content in food, it will decrease energy density simultaneously as fats act as the most energy dense food. Clinical trials found that the way can be used in weight management is to reduce energy density in choosing food based on fat^[37]. Lower energy density foods consist lower calories per gram in food which means the obese people will have low calorie satisfying portions of these foods. The desirable range recommended for dietary fats is between 20% to 30% kcal^[30]. Therefore, it is highly recommended to substitute the high dense food with monounsaturated and polyunsaturated fats which includes nuts, avocado, olive oils, peanut oils, and vegetable oils such as sunflower oil^[38].

3.1.2 Exercise

Negative energy balance, i.e., higher energy expenditure than intake, is the main goal to be achieved to acquire an efficient obesity management^[39]. Albeit energy intake limitation through dietary approach is more efficient than exercise in accomplishing significant weight loss, swingeing decline in energy intake could lead to nutritional deficiencies and decreased resting metabolic rate due to loss of lean body mass^[40]. On top of that, weight regain occurs if a dietary intervention is stopped^[41]. A study from Obesity Clinic, Hospital Universiti Sains Malaysia, Kelantan shown that all 28 obese subjects possess significant mean weight change from 89.27 ± 2.78 kg to 83.11 ± 2.42 kg after completed a 12-week weight loss programme consisting of dietary and exercise interventions^[21]. Hence, this has proven that the most effective approach to achieve this energy balance is through a combination of a balanced diet and regular exercise.

Exercise increases energy expenditure through physiological processes and cellular mechanisms that accelerate breakdown of body's major energy stores through glycogen and triacylglycerol. Precisely, exercise speeds up glycogenolysis in muscle and liver; glycolysis, citric acid cycle and oxidative phosphorylation in muscle; lipolysis in adipose tissue and muscle; and fatty acid oxidation in muscle^[27]. Although weight loss is one of the main concerns in the treatment of obesity, visceral adipose tissue reduction may occur regardless of body weight changes and is considered more important than weight loss^[42]. Exercise training in combination with lifestyle modification associated with increased physical activity has been shown to effectively overcome abdominal obesity and tend to decrease visceral fat better than dietary restriction^[42,43]. Beside losing body weight and fat, exercise also helps to maintain optimum body weight and metabolic fitness in obesity^[27].

Before an exercise programme is prescribed for a patient, the attending doctor must provide medical clearance based on the patient's age, symptoms, concomitant risk factors and physical examination. Based on Malaysian Clinical Practice Guidelines on Management of Obesity, an appropriate exercise programme should be chosen according to the FITT criteria; where F stands for frequency, I for intensity, T for time (duration) and the second T is type of exercise. Any exercise programme should be introduced gradually. Patients should be advised on the possible abnormal responses to exercise such as chest pain and excessive breathlessness^[44].

Exercise as simple as walking is an attractive form of physical activity for those who are overweight or obese. A patient can start by walking 10 minutes for 3 days per week, subsequently increasing up to 30 to 45 minutes for more intense walking for at least 3 days per week and increase to the most, every day. The exercise can be done all at once or divided to a few portions throughout the day. A person with extreme obesity may start with simple exercises that can be gradually intensified^[30]. For a formerly obese individual, 60–90 minutes of moderate intensity activity daily or shorter duration of vigorous intensity activity is required to prevent weight regain. In general, there are various options of exercise with different intensities (Table 4)^[44]. Besides, it is encouraged to do flexibility exercises such as stretching to attain full range of joint motion and resistance exercise such as squats to improve muscular fitness^[45].

Table 4. Examples of exercise with various intensities.

Intensity of exercise	Example
Light	Slow walking (15 min/km or 4 km/hour)
	Tai chi
	Golf (without buggy)
Moderate	Brisk walking (10 min/km or 6 km/hour)
	Cycling
	Swimming

Intensity of exercise	Example
High	Badminton
	Jogging (6 min/km or 10 km/hour)
	Basketball
	Climbing
	Football

Sources from Malaysian Clinical Practice Guidelines on Management of Obesity^[44].

It should be emphasized that each level of intensity and duration must be carried on for at least 1 to 2 weeks. Care must be taken to avoid any form of injuries. Expeditious progressing will result in fatigue, decreased motivation, soreness of muscle and increased cardiac risk^[30]. Warm-up and cool-down periods are compulsory to be included before and after each exercise period respectively. Water must be taken in sufficient amounts as well before, during and after exercise to prevent possibilities of dehydration. Furthermore, patients should be encouraged to adopt strategies to increase physical activity in daily life. For instance, walking to the nearby place on foot instead of driving, reducing sluggish behaviours such as watching television by being committed to frequent and less laborious activities^[46].

3.1.3 Pharmacotherapy

In addition to behavioral therapy that centered on lifestyle modification (physical activity and daily dietary intake), pharmacological strategy is the secondary approach for obese patients that have been diagnosed with other concomitant diseases and display a high Body Mass Index (BMI) of more than 27.50 kg/m². On this basis, pharmacotherapy is a therapeutic option for weight control where it is normally used by obese patients who are not responding to lifestyle modification and not qualified for bariatric surgery^[47]. However, pharmacological strategy needs to be monitored closely by certified physicians and only applicable for a long-term obesity management plan. Drug-based regimens need to be carefully evaluated against the risks of possible adverse effects^[48,49].

3.1.4 Orlistat

Orlistat is the only approved pharmaceutical agent that induces weight loss for long term management of obesity. It acts by selectively inhibiting pancreatic lipase which converts dietary fat (lipid) into freely circulating fatty acid, thereby reducing lipid availability in the gastrointestinal system that will be excreted via defecation^[50]. It also binds to fat-soluble vitamins, especially vitamin D, thus patients may experience nutrient deficiencies^[51]. Hence, patients are advised to take a multivitamin supplement separately from current drug regimen, preferably at night^[52]. The standardised dose of Xenical is one capsule containing 120mg of Orlistat thrice daily during main mealtime (breakfast, lunch, dinner). Patients are also advised to take a nutritionally balanced diet over the course of treatment to reduce risk of unfavourable side effects.

The most common adverse effect of orlistat is gastrointestinal system including flatus, incontinence of bowel, leakage of anal cavity and oily stools which may be contributed by a high fat intake as the drug would continuously cause the removal of fat from bowel. However, this side effect can be hindered by advising the patients to consume a low-fat meal when taking the medication. Most drugs related to obesity including orlistat are contraindicated in pregnant women and need to be re-considered in breastfeeding women^[52]. Nevertheless, the use of orlistat is limited to patients who previously showed undesirable dietary therapy outcome and those who were able to demonstrate a weight loss of 2.5 kg in less than a month before they received their first prescription^[51].

A comprehensive randomized clinical trial concerning metabolic effect induced by Orlistat has been conducted with full participation of 39 obese patients who were registered under Obesity Clinic of Universiti Sains Malaysia's (USM) Hospital. For orlistat-treated groups, the patient received a 120 mg hard capsule of orlistat for 9 months. Their baseline level for several parameters such as body weight, body mass index (BMI), body fat composition (BF), waist circumference (WC) and visceral fat (VF) are measured and repeated twice (sixth and ninth months) throughout the treatment.

This clinical trial proves to be highly validated in term of the collected data since it directly tally with the previous studies that highlight the efficacy of orlistat in improving the body weight, BMI, BF, WC and VF after the patients completed the orlistat therapy^[51]. The findings conclude that 58% of the subjects managed to record a 5% loss from initial body weight in the span of nine months which also led to subsequent reduction in subcutaneous and visceral fat^[53]. According to the existing report, a minimum degree of weight loss needs to be at least 5% in order to exert physiological action that can further reduce the visceral fat as well as improve the level of glucose and insulin in the bloodstream^[54].

Other pronounced metabolic effects of orlistat prescription include elevation of adiponectin which shows positive correlation with insulin sensitivity due to direct stimulation of glucose uptake and oxidation of free fatty acid by adiponectin^[55]. The average weight loss of the subjects was approximately 4.6 kg which corroborates with previous meta-analysis that demonstrated a distinct weight loss ranging between 2.5 to 3.2 kg^[56]. This apparent weight loss of the subjects was directly contributed to the reduction in HOMA-IR, insulin resistance level although the value appears less notable. On the other hand, almost all patients display a significant drop in fasting plasma glucose (FPG) toward the end of the clinical trial. The complete results on the core element of anthropometric measurements (height, weight, BMI, WC) and other interconnected parameters including FPG and HOMA-IR are summarized and tabulated clearly (Table 5)^[53].

Table 5. Anthropometrics, body composition, fasting plasma glucose (FPG) and HOMA-IR at baseline, 6 and 9 months.

Parameters	Baseline		6 months		9 months	
	Mean	Standard deviation	Mean	Standard Deviation	Mean	Standard Deviation
Weight (kg)	82.77	14.48	78.63	14.45	78.15	13.73
BMI (kg/m ²)	33.22	3.93	31.55	4.03	31.38	3.79
BF (%)	38.96	3.42	37.75	3.55	37.24	3.78
WC (cm)	96.23	10.80	92.55	10.71	91.69	10.71
VF	16.27	5.73	14.40	5.90	14.02	5.91
FPG (mmol/L)	4.85	0.60	4.65	0.53	4.52	0.55
HOMA-IR	3.28	1.91	2.66	1.72	2.19	2.02

Abbreviations: body mass index, BMI; body fat composition, BF; waist circumference, WC; visceral fat, VF; fasting plasma glucose, FPG; Insulin resistance, HOMA-IR.

Sources from Metabolic and Inflammatory Changes with Orlistat and Sibutramine Treatment in Obese Malaysian Subjects^[53].

4. Conclusion

From the discussion above, it can be concluded that obesity is associated to cardiovascular disease (CVD), diabetes, and other disabilities. Significant research is well developed in proving the correlation. It is evidenced by a statement in which obesity causes and contributes to a complicated disease known as metabolic syndrome, which is closely connected to CVD and Type 2 Diabetes Mellitus (T2DM). Obesity increases the incidence of CVD, which rank top and have been the leading cause of death from 2005 to 2018. Ectopic fat depots in the pericardial and epicardial adipose tissue where both link to CVD.

Other than that, studies have illustrated the interconnection of obesity with T2DM in which both shown a rising trend in Malaysian population. Diabetes (T2DM in obese patients) is mainly associated with a variety of pathophysiological processes contributed by insulin resistance and hyperinsulinemia. There is a hypothesis stated that obesity and diabetes are interconnected due to chronic inflammation, lipotoxicity, and insulin resistance in the pancreas. These three epidemics link between insulin resistance and glucose intolerance in obese patients, thus causing T2DM.

On the other hand, obesity-associated disability significantly correlates with body mass index (BMI). It is concluded that excess weight exerted biomechanical stress towards

the joint of the limb and the spinal structure to induce joint pain, reduced mobility and impact flexibility. Lack of study about the association of obesity with other disabilities have drawn attention to investigate their correlation, future research might be necessary to question this correlation. However, obesity can show a risk of developing disability as observed from a survey of England, arthritis claims the highest ratio among other disabling conditions in obese patient as compared to normal weight population. Obese people suffer functional decline and mobility restrictions as compared to non-obese people. They eventually develop a dread of movement and attempt to avoid exercise. People who are morbidly obese will lose functional independence as well as health-related quality of life.

Obesity has appeared as a consequence of the energy imbalance between energy (calories) intakes and energy (calories) burned. Thus, dealing with this condition entails increasing exercise to burn calories and controlling food intake to regulate the ingested calories. Both diet and lifestyle or more precisely, food intake and exercise have been described other than the secondary approach like pharmacotherapy. Studies have demonstrated how these strategies able to manage a proper weight loss in obesity.

Study has proven that the most effective approach to achieve energy balance is through a combination of a balanced diet and regular exercise. It is because exercise can accelerate the breakdown of the body's energy stores to induce larger elevation in energy expenditure. Malaysian Clinical Guidelines introduce the FITT criteria to be included in an exercise programme to manage obesity. Also, it is recommended to start the exercise with lower intensity to be gradually intensified to avoid any injury as exercise can be categorized into various intensities.

Furthermore, proper healthy diet intake suggested by The Malaysian Dietary Guideline should be taken along with exercise training to manage obesity. Malaysian food pyramid provides a good perspective on the appropriate types and adequate amounts of food that should be consumed. Studies found that low energy density food can be taken in higher amounts as it provides less calories per gram of food, hence, lower weight gain. Meanwhile, fat containing food should be consumed in fewer amounts as it is the most energy dense food.

In term of pharmacotherapy, it is a long-term obesity therapy while obese patient needs to be closely monitored. Orlistat is the weight-loss medication discussed in this context to treat obesity in the long term. It works by blocking pancreatic lipase, which turns dietary fat into circulating fatty acid. Patients are encouraged to take multivitamin supplements and practice a balanced diet as orlistat also binds to fat-soluble vitamins, resulting in certain nutritional deficiencies. A study of nine-month orlistat treatment had proven its efficacy in managing obesity to reduce the weight and other parameters mentioned. However, studies

did not confirm the reason for the improvement of those parameters, whether it is solely due to pharmacotherapy or through modified diet and lifestyle. Hence, further evidence is required to support the findings.

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