

Republic of Iraq

Ministry of Higher Education and Scientific Research

University of Babylon

College of Pharmacy



Studying the Relationship between Obesity and Drug and Their Effect on Overweight

A project Submitted to the College of Pharmacy/ University of Babylon In partial fulfillment of the requirement for the degree of Bachelor in Pharmacy

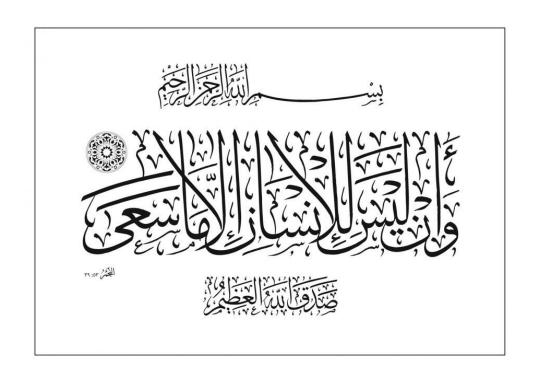
By Students:

Adyan Haider Abd Al-Rahman Amna Lewaa Ali Shahad Jawad Abdul-Kadhim

Supervisor:

Dr. Ruqaya Munther Jalil

2024



Dedication

"Everything we are Or ever will be, we owe it to our mothers ".

Our success is because of them. To my dear mother's, this is just the beginning

To our biggest supporters, Who keeps saying, "We are proud of you to my father's.

To our great teachers, will be always appreciated to you for your efforts and all hard worked you did to us

Thanks to All

Acknowledgments

At the outset, we thank God Almighty for enabling us to complete this research, to Him be praise and thanks, then I would like to thank my supervisor (Dr. Ruqaya Munther Jalil), whose experience was invaluable in formulating the most important topics and methodology of the research,

I offer you the most beautiful expressions of thanks and gratitude from a loving heart full of love and affection, and all respect and appreciation to you for your tireless efforts with us

We would like to give special thanks to the staff of Babylon University/College of Pharmacy

List of contents

Ν	Content	Page				
-	Abstract	III				
	CHAPTER ONE: INTRODUCTION					
1.	Introduction	1-2				
1.1	Aim of study	3				
	CHAPTER TWO: REVIEW OF LITERATURE	C				
2.1	Obesity	5				
2.1.1	Causes of obesity	5-6				
2.2	Body mass index (BMI)	6-7				
2.3	Obesity and Medication	8				
2.3.1	Corticosteroids Medications and Obesity	8-9				
2.3.2	Antihistamines Medications and Obesity	9				
2.3.3	Antidepressants Medications and Obesity	10				
2.3.4	Diabetes Medications and Obesity	11				
2.3.5	Anticonvulsant Medications and Obesity	11-12				
2.3.6	Contraceptives, Hormones and Steroids and Obesity	12				
2.3.7	Beta Blockers and Obesity	12-13				
2.3.8	Calcium channel blockers and Obesity	13				
2.3.9	NSAID and Obesity	14				
3.	CHAPTER THREE: PATIENT AND METHODS	16				
4.	CHAPTER FOUR: RESULTS	18-20				
5.	CHAPTER FIVE: DISCUSSION	22-24				
6.	CHAPTER SIX: CONCLUSION	26				
-	References	28-34				

List of figure

Ν	Content	Page
Figure 1	Body mass index (BMI)	7

List of Tables

Ν	Content	Page
Table 4.1	Main features of the study population with obesity diseases	18
Table 4.2	Clinical characteristics of the study population.	19
Table 4.3	Prevalence of blood parameters among male and females in the study groups	20

Abstract

Obesity is the excessive or abnormal accumulation of fat or adipose tissue in the body that impairs health via its association with risk of development of diabetes mellitus, cardiovascular disease, hypertension, and hyperlipidemia. The study was face- to- face model structured interview using questionnaire paper to collect information from 68 patients and Al-Sadig Hospital in Babylon province was the focal setting of this study. This hospital serves a population of different in Babylon province. Obesity classes of samples are 26.4% Class I, 25.0% Class II, 14.7 % Class III and 33.9% Over weight, Class of drug most samples used Corticosteroid 14.8%, Antihistamine 19.2%, and NSAID 11.8%. The most Treatment used are Slim up Cap 31(45.6%), Vit D3 17(25.0%), and Metformin 11(16.1%). There are other Treatment that are used less frequently, such as (Lifestyle Modification, Thyroxine, Iron supplement). A nutritional-balanced diet especially important for obese individuals, to maintain health and support pharmacotherapies and other lifestyle modification strategies. Vitamin supplementation that takes into consideration all of following criteria may

lead to a better treatment outcome.

Chapter One Introduction

Chapter One

1. Introduction

Obesity is the excessive or abnormal accumulation of fat or adipose tissue in the body that impairs health via its association with the risk of development of diabetes mellitus, cardiovascular disease, hypertension, and hyperlipidemia. It is a significant public health epidemic which has progressively worsened over the past 50 years. Obesity is a complex disease and has a multifactorial etiology. It is the second most common cause of preventable death after smoking. Obesity needs multiprong treatment strategies and may require lifelong treatment. A 5% to 10% weight loss can significantly improve health, quality of life, and economic burden of an individual and a country as a whole. **[1-3]**

There has been a significant global increase in obesity rate during the last 50 years. Obesity is defined as when a person has a body mass index (BMI) (kg/m2), dividing a person's weight by the square of their height] greater than or equal to 30, overweight is defined as a BMI of 25.0-29.9. Being overweight or obesity is linked with more deaths than being underweight and is a more common global occurrence than being underweight. [4]

There are several possible mechanisms leading to obesity. Actually, the traditional view is usually that the main cause is the significantly more excess energy stored than the energy the body used. The excess energy is stored in fat cells, thereby developing the characteristic obesity pathology. The pathologic enlargement of fat cells will alter the nutrient signals responsible for obesity. However, the latest research showed



that the food sources and quality of nutrients matter more than their quantities in the diet for weight control, and also for disease prevention. [5,6]

Some medicines can cause certain people to put on weight. This can be a good thing if are underweight to start with. If are at a normal weight, then gaining a few pounds also might not be a big deal. But, if are already overweight, weight gain might be more of a problem. Weight gain depends on a number of factors. These include specific medicine, age, sleep patterns, and other medical conditions have. might only gain a few pounds over a year. But some people gain more weight, like 10 or 20 pounds in a few months. If need to take the medicine for months or years, might gain a lot of weight. **[7]**

Medicine-related obesity gain is not uncommon, especially with certain types of medicines. For example, many steroids can cause weight gain. So can medicines that treat mental health problems, such as depression and schizophrenia. Men and women of all ages can have medicine-related weight gain. Medicine-related obesity gain can have many causes. Some medicines might stimulate appetite. This causes to eat more and gain extra weight. Some medicines might affect metabolism. This causes body to burn calories at a slower rate. Some medicines might cause to retain water. This makes weigh more even if don't put on extra fat. Other medicines might affect how body stores and absorbs sugars and other nutrients. might notice that have gained a few pounds since starting medicine. In some cases, this happens quickly. But in other cases, it happens more slowly. might not notice that gained weight until healthcare provider points it out to at a medical visit. [8]

1.1 Aim of study

To studying the relationship between obesity and drugs and their effect on overweight.



Chapter Two literature Review



Chapter Two

2. Literature Review

2.1 Obesity

The worldwide prevalence of overweight and obesity has doubled since 1980 to an extent that nearly a third of the world population is now classified as overweight or obese. Obesity adversely affects nearly all physiological functions of the body and comprises a significant public health threat.**[9]** It increases the risk for developing multiple disease conditions, such as diabetes mellitus, cardiovascular disease, several types of cancers, an array of musculoskeletal disorders, and poor mental health, all of which have negative effects on the quality of life, work productivity, and healthcare costs. In the US, it has been estimated that the health costs incurred by a single obese individual was US\$1901 per annum in 2014, extrapolating to US\$149.4 billion at the national level. In Europe, the total direct and indirect cost attributable to overweight and obesity was equivalent to 0.47–0.61%. **[10]**

2.1.1 Causes of obesity

Several factors can play a role in gaining and retaining excess weight. These include: **[11,12]**

• Food and Activity: People gain weight when they eat more calories than they burn through activity. This imbalance is the greatest contributor to weight gain.



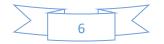
- Environment: The world around us influences our ability to maintain a healthy Not having area parks, sidewalks, and affordable gyms makes it hard for people to be physically active.
- Genetics: Research shows that genetics plays a role in obesity. Genes can directly cause obesity in such disorders as Prader-Willi syndrome.
- Medications: Certain medicines also may cause weight gain, including some corticosteroids, antidepressants, and seizure medicines.
- Stress, Emotional Factors, and Poor Sleep: ome people eat more than usual when they are bored, angry, upset, or stressed.

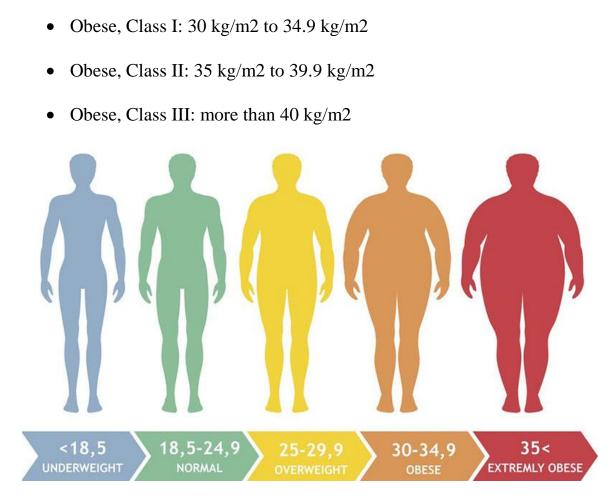
2.2 Body mass index (BMI)

Body mass index (BMI) is one of the ways to measure obesity in the population. Other ways to measure obesity include the waist-to-hip ratio, the percentage of the body or visceral fat, and waist circumference. Body mass index (BMI) can be calculated via mathematical operations where height and weight values are used to estimate the health status of a person. **[13]**

BMI as a measurement is typically used to gauge the risk of developing chronic conditions such as diabetes, hypertension, depression, and cancer. The BMI calculation will fall within a numerical range, which places an individual into one of four categories. This data is used by researchers and physicians to educate patients and the public of potential health risks detected within a specified category. **[14,15]**

A standard screening tool for obesity is the measurement of body mass index (BMI). BMI is calculated using weight in kilograms divided by the square of height in meters. Obesity can be classified according to BMI: [16]





Underweight: less than 18.5 kg/m2

Normal range: 18.5 kg/m2 to 24.9 kg/m2

Overweight: 25 kg/m2 to 29.9 kg/m2

Fig.1 Body mass index (BMI)

The BMI has been useful in population-based studies by virtue of its wide acceptance in defining specific categories of body mass as a health issue. However, it is increasingly clear that BMI is a rather poor indicator of percent of body fat. Importantly, the BMI also does not capture information on the mass of fat in different body sites. The latter is related not only to untoward health issues but to social issues as well. Lastly, current evidence



indicates there is a wide range of BMIs over which mortality risk is modest, and this is age related. For children, a BMI that is less than the fifth percentile is underweight and above the 95th percentile is considered obese. [17]

2.3 Obesity and Medication

Sometimes the adverse effects of the medication cause weight gain rather than the drug itself. Certain medicines increase your appetite, which makes eat more. Others might have an impact on how body takes in and stores glucose, which could result in fat accumulation in middle. Some alter body's metabolism, causing calories to be burned more slowly. Others make it harder for people to exercise because they make them tired and short of breath. may retain water as a result of using other medicines, which can increase weight but not necessarily fat. **[18]**

The amount of weight acquired varies depending on the medicine and the individual. While some people may put on a few pounds over the course of a year, others may put on ten, twenty, or even more pounds in a matter of months. may take these drugs for years at a time, and since many of them are used to treat chronic diseases, using them might cause noticeable weight gain over time. **[18]**

2.3.1 Corticosteroids Medications and Obesity

Corticosteroids including cortisone and other gluco corticosteroids can be used for the treatment of conditions such as asthma, dermatological or inflammatory disorders and rheumatic or autoimmune diseases. Corticosteroids significantly alter the body's metabolic functions when they



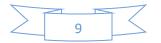
are introduced. They boost the desire to eat by arousing the appetite. This frequently leads to weight gain when combined with a sluggish metabolism. In addition to causing the body to retain more water and salt than usual, steroids can promote bloating and fluid retention. They also have an impact on how fat is distributed throughout the body, which makes the abdomen, face, and back of the neck more densely concentrated in fat. **[19,20]**

The short-term use of corticosteroids has not been shown to be associated with significant changes in body weight. Conversely, literature on the long-term usage (\geq 3 months) of corticosteroids suggests the opposite, with prednisone, prednisolone and cortisone being associated with significant weight gains. [21]

2.3.2 Antihistamines Medications and Obesity

Antihistamines are a pharmaceutical class of drugs that act to treat histamine-mediated conditions. There are two main classes of histamine receptors: H-1 receptors and H-2 receptors. Antihistamine drugs that bind to H-1 receptors are generally used to treat allergies and allergic rhinitis. Drugs that bind to H-2 receptors treat upper gastrointestinal conditions that are caused by excessive stomach acid. **[22]**

The exact reason why antihistamines could make gain weight is appetite. But because of how it affects appetite, histamine is assumed to be involved. Histamine release in the body typically causes you to eat less. This is due to the fact that it reduces hunger. Histamine is blocked by antihistamines. Additionally, research on animals has demonstrated that histamine blocking may cause an individual to overeat. Antihistamines can also make you sleepy, which might reduce level of activity. Histamine may



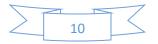
have a role in appetite control and metabolism as well. There are many animal studies that demonstrate a reduction of food intake in response to histamine release. This suggests that it could make us feel more full or be a signal to stop eating. [23]

2.3.3 Antidepressants Medications and Obesity

Antidepressants are a type of medicine used to treat clinical depression. They can also be used to treat a number of other conditions, including: obsessive compulsive disorder (OCD) generalised anxiety disorder. posttraumatic stress disorder (PTSD). **[24]**

Weight gain and antidepressants are common side effects during psychopharmacological treatment with specific antipsychotics and antidepressants. The antipsychotics clozapine and olanzapine, and antidepressants tricyclics and mirtazapine have a high risk of inducing weight gain. Recently discovered pathophysiological mechanisms include antihistaminergic effects. activation of hypothalamic adenosine monophosphate-activated protein kinase (AMPK), modulation of hormonal signaling of ghrelin and leptin, changes in the production of cytokines such as tumor necrosis factor-alpha (TNF)-alpha and adipokines such as adiponektin, and the impact of genes, in particular the melanocortin 4 receptor (MC4R), serotonin 2C receptor (HTR2C), leptin, neuropeptide Y (NPY) and cannabinoid receptor 1 (CNR1) genes. [25]

Antidepressants associated with weight gain include disturbances of glucose and lipid metabolism. Clozapine and olanzapine may, in addition to mechanisms resulting from weight gain, impair glucose metabolism by



blockade of the muscarinic M3 receptor (M3R). Antidepressants associated with weight gain appear to have fewer unfavourable effects on glucose and lipid metabolism than the second-generation antipsychotics clozapine and olanzapine. To assess the risk of weight gain and its consequences for the patient's, assessing body weight changes and metabolic monitoring in the first week of treatment as well as in long-term treatment is recommended. **[25]**

2.3.4 Diabetes Medications and Obesity

Diabetes mellitus (DM), also known simply as diabetes is a complex metabolic disorder characterized by hyperglycemia, a physiologically abnormal condition represented by continued elevated blood glucose levels. Major therapeutic classes of medications used for Type 2 diabetes, such as thiazolidinediones. [26]

Thiazolidinediones improve insulin sensitivity via several mechanisms, including altered free fatty acid supply to the skeletal muscles. They act as a central regulator of adipose differentiation, promoting the production of small, more insulin-sensitive fat cells. They also act via other factors, such as increasing adiponectin and decreasing free fatty acids and tumor necrosis factor- α . Weight gain has been identified as a class effect with the use of thiazolidinediones. The magnitude of weight gain correlates in part with improved metabolic control (ie, better responders are more prone to increases in body weight). **[27,28]**

2.3.5 Anticonvulsant Medications and Obesity

Anticonvulsants, or antiepileptics, are an ever-growing class of medications that act through multiple different mechanisms to control

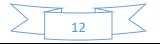


seizures, known to cause weight gain include valproic acid, carbamazepine and gabapentin. Anticonvulsants enhancing effect of gamma-aminobutyric acid-mediated neurotransmission may increase appetite for carbohydrates and reduce energy expenditure. An antidiuretic hormone-like effect or effects norepinephrine (noradrenaline) or serotonin-mediated on neurotransmission are more rarely considered. Many studies on anticonvulsant-associated bodyweight gain illustrate how we could better define the risk factors for the development of anticonvulsant-induced bodyweight gain and uncover the mechanisms behind it. [29]

2.3.6 Contraceptives, Hormones and Steroids and Obesity

Some women who use oral, injectable, and transdermal contraceptives complain of weight gain, which might lead to treatment termination. More specifically, weight gain has been linked to the usage of the progestins megestrol acetate and depo-medroxyprogesterone acetate. Megestrol acetate is administered to patients with wasting diseases like cancer and acquired immunodeficiency syndrome (AIDS) in order to cause them to gain weight. According to studies, women who took depo-medroxyprogesterone consistently for a year or two gained more weight on average than those who did not. [30]

Drug-induced weight gain may be a factor in menopausal women on hormone replacement therapy (HRT), increasing their risk of cardiovascular disease and resulting in poor patient compliance. Because menopause itself is linked to changes in energy metabolism, physical activity, and body composition, it is challenging to pinpoint the precise effect of HRT on body weight and fat distribution. As a side effect of hormone replacement therapy,



weight increase has not been consistently reported; instead, results vary widely in terms of changes in both weight and fat distribution. [31]

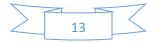
2.3.7 Beta Blockers and Obesity

Beta blockers have been used for the treatment of hypertension for decades and have been shown to decrease cardiovascular morbidity and mortality rates in patients with essential hypertension.[**32**] The effects on obesity can be in large part explained by changes in energy metabolism. Several investigators have shown that total energy expenditure may be reduced 4% to 9% with β -blocker treatment. In a recent study, we showed that β -blockade reduces the basal metabolic rate by 12% in obese hypertensive patients, compared with obese hypertensive patients receiving other antihypertensive agents. [**33**]

Apart from their direct metabolic effects, β -blockers may also have a negative impact on total energy expenditure by increasing feelings of tiredness and decreasing anxiety. Such effects reduce so-called purposeless movement, or "fidgeting." This non–exercise-associated thermogenesis (NEAT) was recently shown to play a major role in the metabolic response to overeating. A low NEAT has been associated with remarkable weight gains in normal individuals. β -Blockers also have negative effects on maximal and submaximal exercise capacity, which should be considered when prescribing β -blockers to physically active hypertensive patients. **[34]**

2.3.8 Calcium channel blockers and Obesity

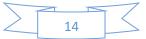
Calcium channel blockers are medicines used to lower blood pressure. They stop calcium from entering the cells of the heart and arteries. alcium channel blockers like verapamil can cause fluid to build up in body to the



point where might feel or notice changes in weight, The reason because Calcium channel antagonists block the inward movement of calcium by binding to the L-type "long-acting" voltage-gated calcium channels in the heart, vascular smooth muscle, and pancreas. Numerous variables can impact obesity, such as the dosage of calcium-channel blockers, their formulation, their combination with other heart-pumping drugs like betablockers, the age of the patient, and any coexisting medical conditions. [35,36]

2.3.9 NSAID and Obesity

Nonsteroidal anti-inflammatory drugs (NSAIDs) are a drug class FDAapproved for use as antipyretic, anti-inflammatory, and analgesic agents. NSAIDs cause water retention and edema in some people. may notice ankles look puffy or weight rapidly increases within a few hours of taking ibuprofen. Having all that extra water on board can exacerbate pre-existing conditions such as high blood pressure or heart failure. because COX-1 and COX-2 facilitate the production of prostaglandins that play a role in renal hemodynamics. Clinicians should be aware that patient-reported weight gain and increases in blood pressure can occur with all NSAIDs, and may be particularly increased with rofecoxib. **[37,38]**



Chapter Three Patient and Methods



Chapter Three

3. Patient and Methods

This study was face- to- face model structured interview using questionnaire paper to collect information from 68 patients and Al-Sadiq Hospital in Babylon province was the focal setting of this study. This hospital serves a population of different in Babylon province. For a period of (25/12/2023–25/3/2024), the following information was obtained which consisted of three part, part one: age, gender, Obesity classes, Medical history, class of drugs, Treatment, part two: Clinical characteristics of the study population, part three: Prevalence of blood parameters among male and females in the study groups.



Chapter Four Results



Chapter Four

4. Results

This chapter presents the findings of the data analysis systematically in tables in correspond with the objectives of the study as follows: The mean age of the sample was 45.00 ± 10.21 years, with 34 of participants being females and a total of 34 belonging to male groups with mean age 48.50 ± 7.04 , The description of the remaining variables in the study can be seen in Table 1.

Variations	NO%					
	Gender					
Male	34 (50.0%)					
Female	34 (50.0%)					
Total	100%					
Age groups						
14-44	35(51.4%)					
45-64	15(22%)					
More than 65	18(26.6%)					
Total	100%					
Obe	sity classes					
Class I	18(26.4%)					
Class II	17(25%)					
Class III	10(14.7%)					
Over weight	23(33.9%)					
Total	100%					
Med	ical history					
None	16(23.5%)					
Arthritis	8(11.7%)					
Allergic Bronchitis	8(11.7%)					
Hypertension	8(11.7%)					
D.M	6(8.8%)					
Thyroid Cancer	8(11.7%)					
Polycystic Ovary Syndrome	4(5.8%)					
Hypothyroidsim	4(5.8%)					
heart failure	6(8.8%)					
Total	100%					
Clas	s of Drugs					
Corticosteroid	10 (14.8%)					

Table (1): Main	features of the study	population wit	h obesity diseases
		r · r · · · · · · · · · · · · · · · · ·	

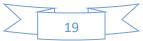


Antihistamine	13 (19.2%)
NSAID	8 (11.8%)
	· · · · ·
Biguanide / Sulfonylurea	2 (3.0%)
Beta Blocker	4 (5.8%)
ARB / CCB	3 (4.4%)
Thyroid Agent	3 (4.4%)
Contraceptive Steroid Hormones	8 (11.7%)
Calcium Channel Blocker	2 (3.0%)
Anticonvulsant	5 (7.3%)
Antihistamine With Serotonin-Antagonist Activity	4 (5.8%)
Central Acting Alpha 2 Agonist	3 (4.4%)
Estrogen Receptor Modulator	3 (4.4%)
Total	100%
Treatment	
Slim Up Cap	31 (45.6%)
Vit D3	17 (25.0%)
Metformin	11 (16.1%)
Lifestyle Modification	2 (3.0%)
Thyroxine	5 (7.3%)
IRON	2 (3.0%)
Total	100%

Table (2): Clinical characteristics of the study population.

Descriptive Statistics							
	N	Range	Minimum	Maximum	Sum	Mean	Std. Deviation
age	68	64.00	12.00	76.00	2650.00	38.9706	16.09762
weight	68	93.00	73.00	166.00	7277.00	1.0701E2	27.13124
height	68	30.00	150.00	180.00	1.12E4	1.6424E2	8.24642
BMI	68	25.60	28.00	53.60	2634.80	38.7471	6.19211
Valid N (listwise)	68						

Descriptive Statistics



Parameters	Male Mean±S.err	Female Mean±S.err	T test	P= value
S.calicum mmol/L	2.31 ± 0.05	2.26 ± 0.05	0.55	0.05
RBC 10^12/1	4.96 ± 0.08	4.64 ± 0.10	2.27	0.025*
HGB g/dl	14.40 ± 0.19	12.52 ± 0.11	8.57	0.000*
HCT %	41.92 ± 0.75	40.80 ± 0.48	1.30	0.19
R.B.S. mmo/L	5.42 ± 0.15	4.93 ± 0.09	2.84	0.006*
T.S.H μ IU /ml	1.91 ± 0.12	1.61 ± 0.06	2.21	0.03*
S. Vit D3 ng /ml	22.55 ± 1.18	29.26 ± 1.99	2.62	0.01*

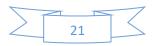
 Table (3): Prevalence of blood parameters among male and females in

 the study groups

Comparison of hematological indices shows that value was significantly higher in male with obesity than in female obese people while there was no significant difference in values of HCT among male with obesity than in female obese people as shown in table 3.



Chapter Five Discussion



Chapter Five

5. Discussion

The World Health Organization defines obesity as individuals having body mass index (BMI) equals to or greater than 30 kg/m2. Obesity is associated with adipose tissue (AT) dysfunction, which is contributed mainly by adipocyte hypertrophy [**39**]. The adipocyte remodeling induces macrophages infiltration, inflammatory cytokine production and synthesis of collagens that limits adipogenesis, and reduces AT's storage capacity [**40**], leading to triglyceride accumulation in liver, heart and around blood vessels [**41**]. Weight loss improves AT dysfunction and adipogenic effects [**42**].

There was significant difference in hematological parameters of male obese and female obese people and no difference in values of HCT among male with obesity than in female obese people, this implies that weight gains has no effect on hematopoietic processes and iron metabolism, this result is in agreement with an earlier report that overweight and obese subjects does not have lower hemoglobin and red blood cell count and obesity occur when excess energy intake exceeds energy usage, which does not considerably affect iron metabolism to cause anemia in adult obese subjects [43].

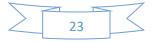
The higher blood pressure observed in obese subjects may be attributed to the positive energy balance which eventually leads to adipose tissue hypertrophy to a complex adaptive changes in the adipocytes and overtime these changes altered functionality of cell signaling proteins known as adipocytes and increased production of inflammatory markers. Excessive weight gains lead to increased cardiac heart beats and blood output flow, which increases the arterial walls pressure coupled with stiffness of vascular



walls due to inflammation eventually cumulate in hypertension overtime [44,45]. Anthropometric variables such as weight (Wt), height (Ht), and body mass index (BMI), were higher in people with obesity than in no obese subject this result in conformity with an earlier report by Sarry et al. and the higher values anthropometric variable in obese people is due to excessive body fat accumulation which results to negative alterations in body build configuration that characterizes obesity. [46]

Obesity is commonly linked to a lack of VD3–Calicum, which are nutrients that regulate body fat. The prevalence of obesity may be decreased by a dose of VD or CAL. Evidence suggests that VD–CAL intake can decline body fat. The higher the concentration of 25(OH)D, the lower the body fat mass [47]. Similar to VD, a low CAL intake can negatively impact the levels of various lipid metabolic markers (glucose, triglyceride, and insulin) and increase body fat [48]. BMI and body fat levels strongly correlate with 25(OH)D concentration and CAL-phosphorus product [49].

VD–CAL have been gaining increasing interest in obesity management. These nutrients have been tested in combination and also formulated in food products. A VD-enriched Lentinula edodes preparation reduced total body fat accumulation and hepatic fat content in obese C57BL/6 mice [50]. Similarly, a study showed that consumption of VD-fortified yoghurt drink (containing 170 mg CAL and 12.5 g VD3/250 mL) for twelve weeks led to a decrease in waist circumference, body fat mass, and truncal fat in people with type-2 diabetes aged 30–60 years old [51]. In addition, supplementation of CAL and VD3 caused a significant reduction in weight, BMI, waist circumference, and body fat percentage in obese women aged 18–48 years old [52]. In another study on overweight or obese males aged 18–25 years

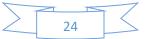


old, a 12-week supplementation of CAL and VD3 (600 mg of CAL and 125 IU of VD3) resulted in body fat loss and visceral fat loss [53].

Based on the literature review, it can be concluded that the role of CAL and VD in metabolic disorders and obesity is well understood. However, the results on the impact of the deficit or the supplementation used on body weight, fat content, or biochemical parameters obtained especially in human studies are often ambiguous. It seems that many factors, including population diversity, may lead to the inconsistency of results of VD–CAL in the obese. The cited studies were conducted on a variety of populations, geographies, and races. For instance, low VD status affects the occurrence of a VD deficiency in Western European residents during the wintertime periods, South Africa, Oceania, and Asian countries (Middle East, China, Mongolia, and India) [54].

In the same vein as the global VD status, many countries have low average dietary CAL ranges between 175 and 1233 mg across half the world's nations, such as Asia, Africa, and Latin America, and only a handful of European countries [55].

The study shows that common drugs like antihistamines, NSAIDs, corticosteroids, and contraceptive steroids are associated with weight gain. Patients on these medications were more likely to be obese compared to those not taking them, suggesting a potential role of these drugs in contributing to weight gain .



Chapter six Conclusions



Chapter Six

6. Conclusions

A nutritional-balanced diet is especially important for obese individuals, to maintain health and support pharmacotherapies and other lifestyle modification strategies. Vitamin supplementation that takes into consideration all of the following criteria may lead to a better treatment outcome.



References



References

- 1. Saalbach A, Anderegg U. Thy-1: more than a marker for mesenchymal stromal cells. FASEB J. 2019 Jun;33(6):6689-6696.
- Kozlov AI. [Carbohydrate-related nutritional and genetic risks of obesity for indigenous northerners]. Vopr Pitan. 2019;88(1):5-16.
- Gowd V, Xie L, Zheng X, Chen W. Dietary fibers as emerging nutritional factors against diabetes: focus on the involvement of gut microbiota. Crit Rev Biotechnol. 2019 Jun;39(4):524-540.
- 4. Al Kibria GM. Prevalence and Factors Affecting Underweight, Overweight and Obesity Using Asian and World Health Organization Cutoffs Among Adults in Nepal: Analysis of the Demographic and Health Survey 2016. Obes Res Clin Pract (2019) 13(2):129–36.
- Lee SJ, Shin SW. Mechanisms, Pathophysiology, and Management of Obesity. N Engl J Med (2017) 376(15):1491–2.
- Sacks FM, Bray GA, Carey VJ, Smith SR, Ryan DH, Anton SD, et al.. Comparison of Weight-Loss Diets With Different Compositions of Fat, Protein, and Carbohydrates. N Engl J Med (2009) 360(9):859–73.
- Wu Y, Duan H, Tian X, Xu C, Wang W, Jiang W, et al.. Genetics of Obesity Traits: A Bivariate Genome-Wide Association Analysis. Front Genet (2018) 9:179.
- Kasuga M. [Genetic Factor for Diabetes and Obesity]. Nihon Rinsho (2010) 68(Suppl 8):359–63.
- Lauby-Secretan B, Scoccianti C, Loomis D, et al. Body Fatness and Cancer--Viewpoint of the IARC Working Group. N Engl J Med 2016; 375(8): 794-798.



- 10.Anandacoomarasamy A, Caterson I, Sambrook P, et al. The impact of obesity on the musculoskeletal system. Int J Obes (Lond) 2008; 32(2): 211-222.
- 11.Rosin, Odelia. "The economic causes of obesity: a survey." Journal of Economic Surveys 22.4 (2008): 617-647.
- 12.Wright, Suzanne M., and Louis J. Aronne. "Causes of obesity." Abdominal Radiology 37 (2012): 730-732.
- 13.Association between sex and body mass index as mediated by temperament in a nonclinical adult sample. Oniszczenko W, Stanisławiak E. Eat Weight Disord. 2019;24:291–298.
- 14. The risk of chronic diseases in individuals responding to a measure for the initial screening of depression and reported feelings of being down, depressed, or hopeless. Khatib M, Badillo N, Kahar P, Khanna D. Cureus. 2021;13:0.
- 15.Distribution and association of chronic disease and mobility difficulty across four body mass index categories of African-American women. Clark DO, Mungai SM. Am J Epidemiol. 1997;145:865–875.
- 16.Shiozawa B, Madsen C, Banaag A, Patel A, Koehlmoos T. Body Mass Index Effect on Health Service Utilization Among Active Duty Male United States Army Soldiers. Mil Med. 2019 Oct 01;184(9-10):447-453.
- 17.Frank Q. Nuttall, Body Mass Index, Nutr Today. 2015 May; 50(3): 117– 128.
- 18.Bray, George A. "Medications for obesity: mechanisms and applications." Clinics in chest medicine 30.3 (2009): 525-538.
- 19.Berthon, Bronwyn S., Lesley K. MacDonald-Wicks, and Lisa G. Wood. "A systematic review of the effect of oral glucocorticoids on energy



intake, appetite, and body weight in humans." Nutrition Research 34.3 (2014): 179-190.

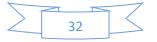
- 20.Berthon, B. S., et al. "Effects of short-term oral corticosteroid intake on dietary intake, body weight and body composition in adults with asthma– a randomized controlled trial." Clinical & Experimental Allergy 45.5 (2015): 908-919.
- 21.Wung, Peter K., et al. "Effects of glucocorticoids on weight change during the treatment of Wegener's granulomatosis." Arthritis Care & Research: Official Journal of the American College of Rheumatology 59.5 (2008): 746-753.
- 22.Monczor F, Fernandez N. Current Knowledge and Perspectives on Histamine H1 and H2 Receptor Pharmacology: Functional Selectivity, Receptor Crosstalk, and Repositioning of Classic Histaminergic Ligands. Mol Pharmacol. 2016 Nov;90(5):640-648.
- 23.Saad, Michelle, et al. "Antihistamines increase body mass index percentiles and Z-scores in Hispanic children." Children 7.12 (2020): 305.
- 24.Gutiérrez-Rojas L, Porras-Segovia A, Dunne H, Andrade-González N, Cervilla JA. Prevalence and correlates of major depressive disorder: a systematic review. Braz J Psychiatry. 2020 Nov-Dec;42(6):657-672.
- 25.Himmerich, Hubertus; Minkwitz, Juliane; C. Kirkby, Kenneth, Weight Gain and Metabolic Changes During Treatment with Antipsychotics and Antidepressants, Bentham Science Publishers, Volume 15, Number 4, 2015, pp. 252-260.
- 26.American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2014;37:S81–90.



- 27.Arner P: The adipocyte in insulin resistance: key molecules and the impact of the thiazolidinediones. Trends Endocrinol Metab 2003, 14:137–145.
- 28.Wilding J: Thiazolidinediones, insulin resistance and obesity: fi nding a balance. Int J Clin Pract 2006, 60:1272–1280.
- 29.P Jallon, F Picard, Bodyweight gain and anticonvulsants: a comparative review, Drug Saf. 2001;24(13):969-78.
- 30.Gallo MF, Lopez LM, Grimes DA, Schulz KF, Helmerhorst FM. Combination contraceptives: effects on weight. Cochrane Database Syst Rev 2014; (1): CD003987. [PubMed]
- 31.Lopez LM, Ramesh S, Chen M, Edelman A, Otterness C, Trussell J et al. Progestin-only contraceptives: effects on weight. Cochrane Database Syst Rev 2016; (8): CD008815.
- 32.The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med.1997; 157:2413–2446.
- 33.Kunz I, Schorr U, Klaus S, Sharma AM. Resting metabolic rate and substrate use in obesity hypertension. Hypertension.2000; 36:26–32.
- 34.van Baak MA. Beta-adrenoceptor blockade and exercise: an update. Sports Med.1988; 5:209–225.
- 35.Lin Y, Ma L. Blood pressure lowering effect of calcium channel blockers on perioperative hypertension: A systematic review and meta-analysis. Medicine (Baltimore). 2018 Nov;97(48):e13152.
- 36.Pavasini R, Camici PG, Crea F, Danchin N, Fox K, Manolis AJ, Marzilli M, Rosano GMC, Lopez-Sendon JL, Pinto F, Balla C, Ferrari R. Anti-anginal drugs: Systematic review and clinical implications. Int J Cardiol. 2019 May 15;283:55-63.



- 37.Phillips WJ, Currier BL. Analgesic pharmacology: II. Specific analgesics. J Am Acad Orthop Surg. 2004 Jul-Aug;12(4):221-33.
- 38.Whelton A. Nephrotoxicity of nonsteroidal anti-inflammatory drugs: physiologic foundations and clinical implications. Am J Med. 1999 May 31;106(5B):13S-24S.
- 39.Laforest, S, Labrecque, J, Michaud, A, et al. (2015) Adipocyte size as a determinant of metabolic disease and adipose tissue dysfunction. Crit Rev Clin Lab Sci 52, 301–303.
- 40.Sun, K, Tordjman, J, Cle'ment, K, et al. (2013) Fibrosis and adipose tissue dysfunction. Cell Metab 18, 470–477.
- 41.Heilbronn, L, Smith, SR & Ravussin, E (2004) Failure of fat cell proliferation, mitochondrial function and fat oxidation results in ectopic fat storage, insulin resistance and type II diabetes mellitus. Int J Obes Relat Metab Disord 28, S12–S21.
- 42.Rossmeislová, L, Mališ ová, L, Kračmerová, J, et al. (2013) Weight loss improves the adipogenic capacity of human preadipocytes and modulates their secretory profile. Diabetes 62, 1990–1995.
- 43.Revelo XS, Luck H, Winer S Winer DA (2014). Morphological and inflammatory changes in visceral adipose tissue during obesity. Endocrine Pathology 25(1):93-101.
- 44.Harwood HJ (2012). The adipocyte as an endocrine organ in the regulation of metabolic homeostasis. Neuropharmacology 63(1):57-75.
- 45.Mathieu P, Poirier P, Pibarot P, Lemieux I Despres JP (2009). Visceral obesity: the link among inflammation, hypertension, and cardiovascular disease. Hypertension 53(4):577-584.
- 46.Sarry El, Din AM, Zaki ME, Kandeel WA, Mohammed SK Wakeel KH (2014). Cut off values of Anthropometric Indices for the Prediction of



Hypertension in a sample of Egyptian Adults. Macedonian Journal Medical Sciences 2(1):89-94.

- 47.Salehpour, A.; Hosseinpanah, F.; Shidfar, F.; Vafa, M.; Razaghi, M.; Dehghani, S.; Hoshiarrad, A.; Gohari, M. A 12-week doubleblind randomized clinical trial of vitamin D3 supplementation on body fat mass in healthy overweight and obese women. Nutr. J. 2012, 11, 78.
- 48.Wamberg, L.; Kampmann, U.; Stødkilde-Jørgensen, H.; Rejnmark, L.; Pedersen, S.B.; Richelsen, B. Effects of vitamin D supplementation on body fat accumulation, inflammation, and metabolic risk factors in obese adults with low vitamin D levels—Results from a randomized trial. Eur. J. Intern. Med. 2013, 24, 644–649.
- 49.Agbaht, K.; Mercan, Y.; Kutlu, S.; Alpdemir, M.F.; Sezgin, T. Obesity with and without metabolic syndrome: Do vitamin D and thyroid autoimmunity have a role? Diabetes Res. Clin. Pract. 2014, 106, 27–34.
- 50.Villa, C.R.; Chen, J.;Wen, B.; Sacco, S.M.; Taibi, A.;Ward,W.E.; Comelli, E.M. Maternal Vitamin D beneficially programs metabolic, gut and bone health of mouse male offspring in an obesogenic environment. Int. J. Obes. 2016, 40, 1875–1883.
- 51. Cha, K.S.; Park, C.Y.; Lee, S.E.; Kim, T.Y.; Han, S.N. The effects of 1,25-dihydroxyvitamin D3 on markers related to the differentiation and maturation of bone marrow-derived dendritic cells from control and obese mice. J. Nutr. Biochem. 2020, 85, 108464.
- 52.Wang, Y.; Buckendahl, P.; Sharma, K.; Miller, J.W.; Shapses, S.A.
 Expression of vitamin D hydroxylases and bone quality in obese mice consuming saturated or monounsaturated enriched high-fat diets.
 Nutr. Res. 2018, 60, 106–115. [CrossRef]
 66. Kim, S.J.; Cho, D.H.; Lee, G.Y.; An, J.H.; Han, S.N. The effects of



dietary vitamin D supplementation and in vitro 1, 25 dihydroxyvitamin D3 treatment on autophagy in bone marrowderived dendritic cells from high-fat diet-induced obese mice. J. Nutr. Biochem. 2021, 100, 108880.

- 53.Luger, M.; Kruschitz, R.;Winzer, E.; Schindler, K.; Grabovac, I.; Kainberger, F.; Krebs, M.; Hoppichler, F.; Langer, F.; Prager, G.; et al. Changes in Bone Mineral Density FollowingWeight Loss Induced by One-Anastomosis Gastric Bypass in Patients with Vitamin D Supplementation. Obes. Surg. 2018, 28, 3454–3465.
- 54.van Schoor, N.; Lips, P.Worldwide Vitamin D Status. Vitam. D Fourth Ed. 2017, 2, 15–40.
- 55.Balk, E.M.; Adam, G.P.; Langberg, V.N.; Earley, A.; Clark, P.; Ebeling, P.R.; Mithal, A.; Rizzoli, R.; Zerbini, C.A.F.; Pierroz, D.D.; et al. Global dietary calcium intake among adults: A systematic review. Osteoporos. Int. 2017, 28, 3315–3324.

