A Dissertation On

"EFFECT OF MOXIBUSTION ON C-REACTIVE PROTEIN(CRP) AND LIPID PROFILE IN OBESE INDIVIDUALS"

Submitted by

Dr. S. Sonia., B.N.Y.S (Reg. No.461813004)

Under the Guidance of

Prof. Dr. N. MANGAIARKARASI, B.N.Y.S, M.Sc. (Psych), PGDHAN.

Submitted to

The Tamil Nadu Dr. M. G. R. Medical University, Chennai.

In partial fulfilment of the requirements for the award of degree of

DOCTOR OF MEDICINE

IN BRANCH–III: ACUPUNCTURE & ENERGY MEDICINE

GOVERNMENT YOGA AND NATUROPATHY MEDICAL COLLEGE AND HOSPITAL, ARUMBAKKAM, CHENNAI – 600106.

OCTOBER 2021

GOVERNMENT YOGA AND NATUROPATHY MEDICAL COLLEGE AND HOSPITAL, ARUMBAKKAM. CHENNAI.106

CERTIFICATE BY THE GUIDE

I certify that the dissertation entitled **"EFFECT OF MOXIBUSTION ON C-REACTIVE PROTEIN(CRP) AND LIPID PROFILE IN OBESE INDIVIDUALS"** is the record of original research work carried out by **Dr. S. Sonia., B.N.Y.S** in the Department of Acupuncture & Energy Medicine, Government Yoga & Naturopathy Medical College & Hospital, Chennai – 600106 submitted for the degree of **DOCTOR OF MEDICINE M.D. (ACUPUNCTURE & ENERGY MEDICINE) Branch - III** under my guidance and supervision, in partial fulfilment of regulations of **The Tamilnadu Dr.M.G.R Medical University, Chennai** during the academic period from 2018 to 2021.

Date: **SIGNATURE OF THE GUIDE**

Place:

Dr.N.MANGAIARKARASI,

B.N.Y.S,M.Sc(Psych),PGDHAN

Head of Acupuncture &Energy Medicine Department

Government Yoga & Naturopathy Medical College

& Hospital, Arumbakkam, Chennai -600106

GOVERNMENT YOGA AND NATUROPATHY MEDICAL COLLEGE AND HOSPITAL, ARUMBAKKAM.CHENNAI-106

ENDORSEMENT BY THE PRINCIPAL

I certify that the dissertation entitled **"EFFECT OF MOXIBUSTION ON C-REACTIVE PROTEIN(CRP) AND LIPID PROFILE IN OBESE INDIVIDUALS"** is the record of original research work carried out by **Dr. S. Sonia., B.N.Y.S** in the Department of Acupuncture & Energy Medicine, Government Yoga & Naturopathy Medical College & Hospital, Chennai – 600106 submitted for the degree of **DOCTOR OF MEDICINE (M.D) IN ACUPUNCTURE & ENERGY MEDICINE** under my guidance and supervision, and that this work has not formed the basis for the award of any degree, associateship, fellowship or other titles in this University or any other University or Institution of higher learning.

SIGNATURE OF THE PRINCIPAL

Dr.N.MANAVALAN

N.D(OSM),M.A(G.T),M.Sc(Y&N),M.Phil,P.G.D.Y,P.G.D.H.M,P.G.D.H,

Government Yoga & Naturopathy Medical College & HospitaL,

Arumbakkam, Chennai - 600106.

GOVERNMENT YOGA AND NATUROPATHY MEDICAL COLLEGE & HOSPITAL, ARUMBAKKAM.CHENNAI-106.

DECLARATION BY THE CANDIDATE

I, **Dr. S. Sonia., B.N.Y.S** solemnly declare that dissertation titled **"EFFECT OF MOXIBUSTION ON C-REACTIVE PROTEIN(CRP) AND LIPID PROFILE IN OBESE INDIVIDUALS"** is a bonafide and genuine research work carried out by me at Government Yoga & Naturopathy Medical College & Hospital, Chennai from May 2019 - May 2020 under the guidance and supervision of **Dr.N.MANGAIARKARASI,** Head of the Department, Department of Acupuncture and Energy Medicine, Govt. Yoga & Naturopathy Medical College & Hospital, Chennai. This dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards partial fulfilment of requirement for the award of M.D. Degree (Branch – III) in Acupuncture & Energy Medicine.

Date: Signature of the candidate

Place :

(Dr. S. Sonia., B.N.Y.S)

INSTITUTIONAL ETHICAL COMMITTEE

GOVERNMENT YOGA AND NATUROPATHY MEDICAL COLLEGE

AND HOSPITAL, CHENNAI-600 106.

CERTIFICATE OF APPROVAL

The Institution Ethical Committee of Government Yoga & Naturopathy Medical College Hospital, Chennai reviewed and discussed the application for approval of **"EFFICACY EFFECT OF MOXIBUSTION ON C-REACTIVE PROTEIN(CRP) AND LIPID PROFILE IN OBESE INDIVIDUALS"** for project work submitted by **Dr. S. Sonia., B.N.Y.S,** 2nd Year M.D. Acupuncture & Energy Medicine, Post Graduate, Government Yoga & Naturopathy Medical College & Hospital, Chennai – 600 106.

The proposal is APPROVED

The Institutional Ethical Committee expects to be informed about the progress of the study and adverse drug reaction during the course of the study and any change in the protocol and patient information / informed consent and asks to be provided a copy of the final report.

COPY RIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the Tamilnadu Dr. M. G. R. Medical University, Chennai, Tamilnadu shall have the rights to preserve, use and disseminate this Dissertation / Thesis in print or electronic format for academic / research purpose.

DATE: **SIGNATURE OF THE CANDIDATE**

PLACE: CHENNAI

ACKNOWLEDGEMENT

Foremost, I express my sincere gratitude to **Dr. N. Manavalan,** Principal, Govt. Yoga & Naturopathy Medical College, Chennai, for giving me this opportunity to pursue my Post Graduation degree in M.D. Acupuncture & Energy Medicine from this prestigious institute.

It is a great pleasure to express my deep sense of thanks and gratitude to my mentor, philosopher and guide (late) **Dr. R.S. Himeshwari**, H.O.D, Dept. of Acupuncture and Energy Medicine, GYNMC, Chennai, for her constant guidance and tireless motivation all the way.

I express my heartfelt gratitude to **Dr. S.T.Venkateswaran**, H.O.D., Department of Yoga for his support and guidance

I thank **Dr.N.Mangaiarkarasi** H.O.D. Dept. of Acupuncture and Energy Medicine, GYNMC, Chennai, for her constant support and motivation all the way.

I also thank **Dr. P.Prabu, M.D (yoga),** Dept of Acupuncture and Energy Medicine, GYNMC, Chennai, for his constant guidance and support all the way.

I express my heartfelt gratitude to **Dr. A. Moovendhan, M.D(Naturopathy)** for helping me throughout the statistical analysis and its interpretations needed for the study.

I thank my parents **Mr.I.Samiyadian & Mrs.S.Mariyammal** for their encouragement for this Dissertation.

I express my thanks to my family members for always being there and helping me with their moral support completing this Dissertation.

I thank to my beloved juniors for helping me in this Dissertation.

I thank my colleagues of all departments for their support and encouragement and I also thank all the teaching & non-teaching staffs of GYNMCH for their support.

My sincere thanks to all my Post-Graduate and Undergraduate friends who have been there at all phases of this study including the preparation of this Dissertation. I also thank the support of all the subjects who participated in this study.

Date: Signature of the Candidate

Place:

(Dr. S. Sonia., B.N.Y.S)

LIST OF ABBREVATIONS

BMI	Body Mass Index
CCK	Cholecystokinin
CRP	C-Reactive Protein
HDL	High Density Lipoprotein
IL-1	Interleukin 1
LDL	Low Density Lipoprotein
NASH	Non-Alcoholic Steato Hepatitis
PAI	Plasminogen Activator Inhibitor
PDE-3B	3B Phosphodiesterase
PKB	Protein Kinase B
TC	Total Cholestrol
TG	Triglycerides
TNF	Tumor Necrosis Factor
WHR	Waist Hip Ratio

ABSTRACT

Background: Obesity, the most prevalent non-communicable diseases and a major concern for public health worldwide, mainly due to lifestyle modification and its alterations leads to, such as insulin resistance and diabetes, atherosclerosis, hypertension, or some types of cancer, among others. Obesity presents inflammatory component. Indeed, it is now widely agreed that obesity is also a state of low-grade chronic inflammation. However, to the best of our knowledge there are no studies evaluated the effects of moxibustion on C-reactive Protein (CRP) and Lipid profile in obese individuals. Thus, the present study was conducted to evaluate the effect of moxibustion on C-reactive Protein (CRP) and lipid profile levels in patients with obesity.

Methods: A total of 60 subject with obesity were included in the study. Due to Covid-19 pandemic n=20subjects where dropout only 40 subjects were taken into the study. Baseline and post-test assessments of CRP and lipid profile levels were measured before and after intervention with moxibustion. Anthropometric measurement was taking before and after the intervention. Statistical analysis was performed using statistical package for the social sciences, version 16. P value

Results: There is a significant reduction in CRP levels and lipid profile. There is no significant reduction in Waist Hip Ratio(WHR)

Conclusion: The present study demonstrated that 4 weeks of moxibustion is effective in reducing CRP and lipid profile in obesity.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Obesity, the most prevalent non-communicable diseases and a matter of life and death for public health worldwide, mainly due to its well-established relationship with adjustments, such as insulin resistance and diabetes, atherosclerosis, hypertension, or some types of cancer, between others. Obesity, like individual's chronic diseases mentioned earlier, present an inflammatory component. Indeed, it is now widely fixed that obesity is also a state of low-grade chronic inflammation. [1,2]

According to WHO "Obesity is well-defined as the abnormal or excessive fat accumulation that may impair health" Obesity is determined over the anthropometric measurements which is considered by body mass index [BMI]., measured by height in m^2 and weight in kg. [3]

Recent studies have stated that globally, more than 1.9 billion adults are overweight and 650 million are obese. Nearly 2.8 million deaths are reported as a result of being overweight or obese. Due to the feasting of energy dense food (i.e., unhealthy food habits), inactive life style, lack of health care services and financial support, the developing countries are facing high risk of obesity and their adversative consequences (i.e., diabetes, ischemic heart disease, etc). [4]

In India, more than 135 million entities were affected by obesity. The prevalence of obesity in India varies due to age, gender, topographical environment, socio-economic status, etc. In India, abdominal obesity is one of the major hazards for cardiovascular disease (CVDs). [5]

In Tamilnadu the total prevalence rate of overweight/obese among adult was 52.4%, more over females overweight/obese was 22.8% -34.8% and in males' overweight/obese was 23.4-22%. Changes in dietary and physical activity patterns are often the result of environmental and societal changes associated with development and lack of supportive policies in sectors such as health, agriculture, transport, urban planning, environment, food processing, distribution, marketing, and education. [6]

Elevated BMI is a major risk factor for noncommunicable diseases such as: cardiovascular diseases [heart disease and stroke]., which were the leading cause of death in 2012; diabetes, musculoskeletal disorders [especially osteoarthritis – a highly disabling degenerative disease of the joints]; some cancers [including endometrial, breast, ovarian, prostate, liver, gallbladder, kidney, and colon]. The risk for these noncommunicable diseases increases, with increased in BMI.

Obesity is a chronic and multi-factorial disease and one among of the most important causes of morbidity and early mortality worldwide. Non-surgical and non-pharmacotherapeutical treatment options contain diet, exercise, behavior change and psychological support. The effect size has been reported with a single digit weight loss in kilograms which can be sustained.[7]

The Centers for Disease Control and Prevention (CDC), the National Health and Nutrition Examination Survey (NHANES) and the National Health Interview Survey (NHIS) report that 6.3% of males and 8% of females 20 years of age and older have BMI values of 40 or higher and classify as extremely obese. [8 ,9]

Serum C-reactive protein (CRP) is a feature of systemic inflammation and is positively linked with measures of adiposity such as body mass index (BMI) and waist circumferences (WCs) as recognized by 2 large cross-sectional studies. While obesity is connected to higher levels of CRP, following weight loss reduction in CRP levels has been also reported. [10,11,12] Being one among the most active modalities in Complementary and Alternative Medicine, Acupuncture harmonizes energy balance inside the human body which leads to optimum physiological functions through its positive influence over the HPA axis by restoring the balance between Sympathetic and Parasympathetic Nervous system [13,14,15]. It would be needed to control obesity by safe and effective treatment modalities, and among the various methods of acupuncture is one of the most popular complementary treatments. Acupuncture is accomplished by stimulating particular points on the body called acupoints. Acupoints stimulation is done by needling, its stimulation can either be manual or electrical (electroacupuncture). Needle therapy has been used in the treatment of several diseases including obesity. [16,17]

Two popular alternative medicine treatments, acupuncture and moxibustion, ascended from traditional Chinese medicine. However, moxibustion uses moxa (dry herbal leaves) to warm body regions and acupoints by stimulating circulation and by inducing a normal flow of blood and qi. [18]

Moxibustion can be applied to patients directly (burn cones up to 1 cm in size are placed directly onto the skin) or indirectly (a medium is placed in between the burning moxa and the skin). Moxibustion may be a good alternative for patients who want to avoid skin penetration during acupuncture. Moxibustion treats the inflammatory condition has obesity is considered

as the inflammatory disease, Moxa helps to reduce inflammation by stimulating certain points of acupuncture through Moxibustion.[19]

There are many studies in chronic diseases with acupuncture such as asthma, hypertension, diabetes, and chronic obstructive pulmonary disease, where the effective role of moxibustion in chronic disease is explained. Many trials have shown that acupuncture & moxa can promote weight loss, abdominal obesity & inflammatory markers & quality of life. Studies have also confirmed the reduction in anthropometric, lipid profile levels were observed in both cases and controls, but the changes were only statistically significant in the group treated with authentic acupuncture. However, to the best of our knowledge there are no studies to evaluate the effects of Moxibustion on CRP and Lipid Profile in Obese individuals

2.0 REVIEW OF LITERATURE

Obesity is a chronic disease that is growing in prevalence since 1980 in the United States and other parts of Western World. It comprises a serious risk factor for the development of diabetes mellitus along with insulin resistance, cardiovascular disease, non-alcoholic fatty liver disease, endocrine problems, and certain other forms of cancer, that leads to the risk of overall mortality. Obesity differs by age and sex, and by race-ethnic group. WHO reports that in 2016, more than 1.9 billion grownups aged 18 years and older were overweight? Of these 650 million adults were obese. In 2016, 39% of adults aged 18 years and over (39% of men and 40% of women) were overweight. [20]

2.1: Definition:

Obesity is defined as abnormal or excessive fat accumulation that may impair health. Body mass index (BMI) is a simple index of weight-for-height that is commonly used to classify overweight and obesity in adults. The most widely used formula for relating the height and weight of an individual is Body Mass Index (BMI). BMI is defined as a ratio of weight (kilograms) and height^2 (squaremeters) (BMI; kg/m2).[21]

Subsequently, in 1998, the cutoff point midst normal and overweight was reduced to a BMI of 25 to fetch it into line with the 4 categories in the WHO guidelines. Incidentally, this instantaneously converted millions of Americans from being “normal weight” to “overweight.” In 1997, the International Obesity Task Force expanded the number of BMI categories to take in different degrees of obesity and reformed the terminology modestly.[22] A BMI of 25 to 29.9 is stated as “preobesity,” a BMI of 30 to 34.9 is class I obesity, 34.9 to 39.9

is class II obesity, and a BMI of 40 or greater is class III obesity.[23]

FIGURE 1: Body Mass Index (BMI) Chart

Obesity				
	Desirable	Grade I	Grade II	Grade III
BMI	(Up to 25)	(25–29.9)	(30–40)	(≥40)
Percentage				
Women	67.6	24	8	0.4
Men	58.2	34	6	0.2
Abbreviation: BMI, body mass index				

Source: Report of a WHO consultation on obesity

Obesity relays to the molecular regulation of appetite that affects energy homeostasis, mainly as positive energy balance upsets lipid and glucose metabolism. [24-25] Obesity appears to play a vital role in the dysregulation of cellular metabolism that access for insulin resistance in diabetes mellitus type 2. Excess adipocytes secrete abundant cytokines that contribute to vascular dysfunction in hypertension and dyslipidemia, as exposed by hypercholesterolemia and triglyceridemia. These conditions sooner or later contribute to significant atherosclerosis, and when related with obesity and/or diabetes and insulin resistance, it constitutes the metabolic syndrome. [26-27]

New knowledge related to fatty liver and its association with inflammation, as well as visceral adiposity's outcome on gastroesophageal reflux, gallstone disease, and cancer of the bowel, also affect the liver and gut vulnerable to comorbidities of obesity. [28,29]

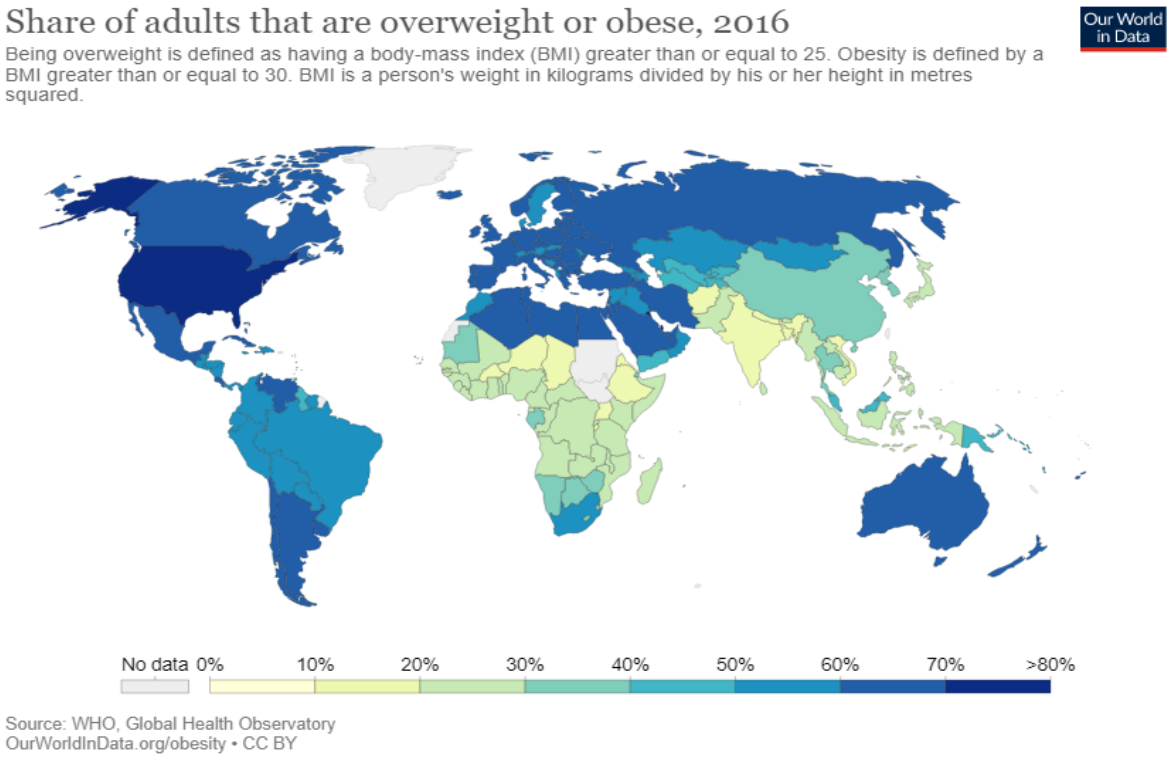
Table 1: The International Classification of Adult Underweight, Overweight and Obesity According to BMI

Classification	**BMI (kg/m^2)**	
	Principal cut-off points	**Additional cut-off points**
Underweight	**<18.50**	**<18.50**
Severe thinness	<16.00	<16.00
Moderate thinness	16.00 - 16.99	16.00 - 16.99
Mild thinness	17.00 - 18.49	17.00 - 18.49
Normal range	**18.50 - 24.99**	**18.50 - 22.99**
		23.00 - 24.99
Overweight	**≥25.00**	**≥25.00**
Pre-obese	25.00 - 29.99	25.00 - 27.49
		27.50 - 29.99
Obese	**≥30.00**	**≥30.00**
Obese class I	30.00 - 34.99	30.00 - 32.49
		32.50 - 34.99
Obese class II	35.00 - 39.99	35.00 - 37.49
		37.50 - 39.99
Obese class III	≥40.00	≥40.00

2.2:Prevalence:

Obesity is found in every population in the world and in all regions, including rural parts of low- and middle-income countries. The number of people with Obese is steadily rising, some recent WHO global estimates follow.

FIGURE 2: Demographic & Geographic Outline



Source: WHO, Global Health Observatory Our WorldInData.org/obesity

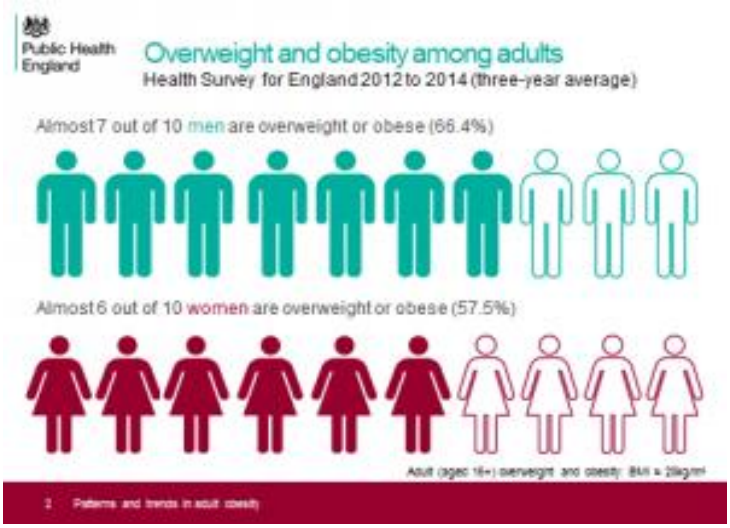
• In 2016, more than 1.9 billion adults aged 18 years and older were overweight. Of these over 650 million adults were obese.

• In 2016, 39% of adults aged 18 years and over (39% of men and 40% of women) were overweight.

• Overall, about 13% of the world's adult population (11% of men and 15% of women) were obese in 2016.

• The worldwide prevalence of obesity nearly tripled between 1975 and 2016.[30]

FIGURE 3: Ration of Obesity



SOURCE: Public Health survey for England

2.3:Factors causing Obesity:

The etiology of obesity is multifactorial, involving complex connections among the genetic background, hormones and different social and ecological factors, such as sedentary lifestyle and unhealthy dietary behaviors.[31] Table .1 lists the key factors that might promote or protect against weight gain and obesity as suggested by the WHO. [32]

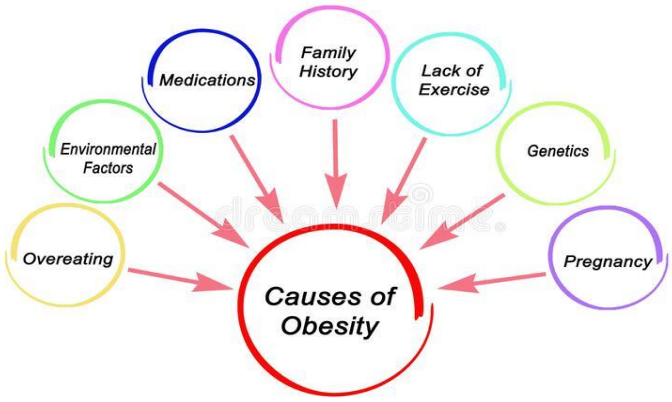
TABLE.2: Key factors that might promote or protect against weight gain and Obesity as suggested by the WHO

Summary of strength of evidence on factors that might promote or protect against weight gain and obesity. Strength of evidence	Decreased risk	Increased risk
Convincing	Regular physical activity	Sedentary lifestyle
High dietary intake of fiber	High intake of energy-dense foods	
Probable	Home and school environments that support healthy food choices for children Breastfeeding	Adverse socioeconomic conditions in developed countries
Possible	Low glycemic index foods	Large portion sizes
High proportion Of Food prepared Outside The home (Developed countries)		

Rigid restraint/periodic disinhibition eating patterns		
Insufficient	Increased eating frequency	Alcohol

2.4: Factors driving obesity up:

FIGURE 4: Factors of Obesity



SOURCE: Obesity Diagram Illustrations

2.4.1: Genetics and Obesity

Genetic can either play a major role in the pathogenesis of obesity or enhance susceptibility to its progress. The dysmorphic forms of obesity in which genetics play a major part include the Prader-Willi syndrome, Ahlstrom's syndrome, the Laurence-Moon-Biedl syndrome, Cohen's syndrome and Carpenter's syndrome. [33] Reportedly, 244 genes, when it is mutated in the mouse, result in an obese phenotype. An increasing number of studies indicate relations

between DNA sequence variation in specific genes and the occurrence of obesity.

Interestingly, the involvement of 22 such genes was reported in at least five separate studies. The obesity gene map shows putative loci on all chromosomes except Y. [34] In the *ob/ob* mice both copies of the leptin gene are defective resulting in shortened protein. In contrast to humans, treatment of obese mice with leptin diminishes both food intake and body fat. Splicing defects on the leptin receptor are responsible for the obesity in the *db/db* mouse, which is phenotypically alike to the *ob/ob* mouse. The gene defect called *tub* results in a defective phosphatase and causes retinitis pigmentosa and obesity in mice, making it similar to the Laurence-Moon-Biedl syndrome in humans. Linkage of human obesity to other factors related to energy balance has been reported. For example, the Trp/64/Arg mutation of the human β3 adrenergic receptor (β3AR) gene is associated with a prior age of onset of NIDDM and characteristics of insulin resistance as well as weight gaining in patients with morbid obesity. However, such findings have not same in different ethnic populations [35]. It has been reported that plasma IL-8 levels are raised in obese subjects. IL-8 is associated with fat mass and Tumor necrosis factor system. Elevated circulating IL-8 could be one among the factors that lead obesity to greater cardiovascular risks [36]. Most of genomic studies in humans, demonstrated substantial genetic heterogeneity influencing BMI regulation [37].

2.4.2: Environmental Factors and Obesity

Environmental factors interrelate with genetic susceptibility in the pathogenesis of obesity. For example, hypothalamic injury due to trauma or surgery and destructive lesions in the

region of the ventromedial or the paraventricular nuclei can cause obesity. The two major influences in hypothalamic obesity are hyperphagia and a disturbance in the ANS activity. An explanation for this is altered secretion of NPY, which is secreted in arcuate nucleus and stimulates eating.[38] Other probable explanations are impairment in reproductive function, decline in sympathetic and increase in parasympathetic activity– key features of hypothalamic obesity. [39] Endocrine disorders such as Cushing's disease, polycystic ovary syndrome and administration of few drugs (phenothiazines; such as chlorpromazine, antidepressants; amitriptyline, antiepileptics; valproate, steroids; glucocorticoids, antihypertensive agents; terazosin) may be in relation with obesity. [40,41]

2.4.3: Food intake and Obesity

A typical obese subject will put on 20 kg over 10 years. This means that there is daily excess of energy input over output of 30-40 kcal initially, increasing gradually the body weight. The type of food taken can play a role in disturbing the energy balance. Fat has more added calories per gram when compared to carbohydrates or proteins. i.e., 9 calories per gram of dietary fat, whereas caloric value of carbohydrates and proteins is only 4 calories. It is possible that the mechanisms of regulating appetite reacts more slowly to fat than to protein and carbohydrate, so satiety system come into the picture too late. Increase in density of foods, portion size, better tastiness of food, increase in availability and low cost promote obesity.[42]

Obese people try to diet to lose weight. But when a subject cuts calorie intake, there is a shift into negative energy balance. An individual loses weight but, in parallel, the latent

metabolic rate decreases, and there is a concomitant drop in energy expenditure. Probably, the system is trying to reshape the body weight to the “set- point A”, which implies maintenance of energy balance is dependent on numerous metabolic reaction loops that are tuned by an individual’s susceptibility genes. Thus, an individual who were previously obese and is now of normal weight, generally needs fewer calories for maintaining the same weight than an individual who has never been obese.The decrease in energy expenditure appears to be large, due to an alteration in the conversion efficiency of chemical energy to mechanical work in skeletal muscle. This adaptation to the caloric restriction pays to the difficulty of maintaining weight loss by diet. [43]

2.4.4: Mental Factors

In patients with obesity, attention to mental factors should be paid. Numerous studies showed that depression is linked to obesity, in a bidirectional manner. This is not surprising, as changes in food intake are considered symptoms of depression. The associations are stronger for patients with a symptom profile that is often labeled as “atypical.” Also, anxiety disorders are cross-sectionally associated with obesity

Binge-eating disorder is characterized by recurrent binge-eating episodes where more food is consumed than is normal for most people and where feelings of lack of control and distress play a role. Importantly, binge-eating can also be a sign of hyperphagia and may thus be a diagnostic clue for either genetic or hypothalamic obesity, as demonstrated in Clinical Case B.

Evidence is mounting that stress leads to more appetite (in comfort food), induces abdominal obesity, and may counteract the effects of a healthy diet. Additionally, the weight stigma that

individuals with obesity often suffer from may also lead to extra weight gain. It is therefore conceivable that a non-stigmatizing attitude, as well as stress reduction, is beneficial when treating obesity. Furthermore, events during early life have been identified as risk factors for obesity. Adolescents with a history of childhood sexual abuse have a higher risk of obesity (in men) or disordered eating (in women).

2.4.5: Physical activity and Obesity

Physical activity can be broadly classified into exercise and non-exercise activities. Non-exercise activities include employment related work and the activity of day-to-day living. It is difficult to measure the energy exhausted in non- exercise activity. In general, an increase in sedentary behavior and reduction in activity of daily living and employment physical activity promotes obesity.[44] It is now recognized that increased energy expenditure by physical activity has a more constructive role in reducing stored fat and adjusting energy balance in obese, especially when it is combined with modification of the diet.

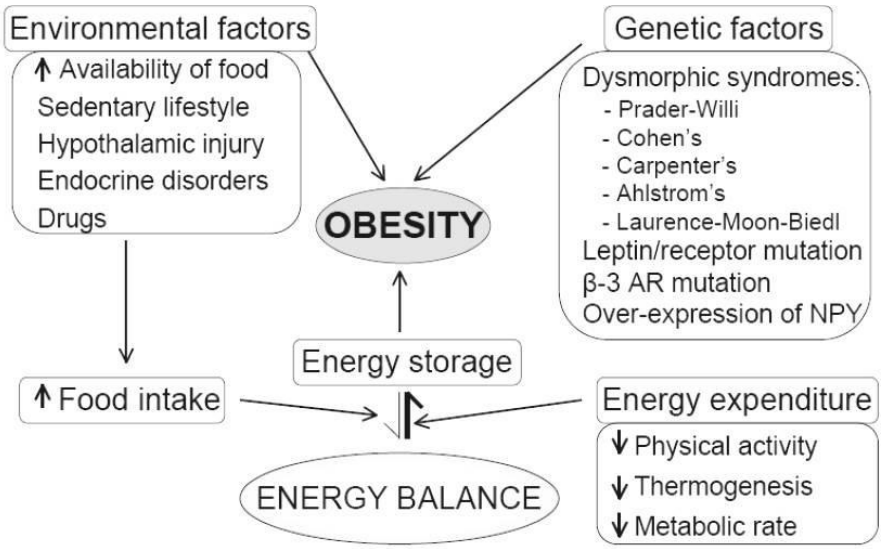
Native population study gives an example. Many years ago, a tribe of Pima Indians was separated into two groups: one of them was settled in Mexico and continued with simple life, eating economically and spending most of time in hard physical work. They are typically lean and have low incidence of NIDDM. Another group moved to USA – an environment with easy access to calorie rich food and less necessity for hard physical work.They are on average 57 pounds heavier than the Mexican group and have a higher prevalence of early onset NIDDM. [45,46]

2.4.6: Energy balance in the body

Fat accounts between 21-37 % of the body weight of middle-aged men and women. In case ofobese individual, more calories are consumed than used and appetite does not subsequently reduce to compensate for the increase in energy stores (Fig. 5). The amount of the adipose tissue is strongly regulated through neural and humoral signals transmitted to the brain. Incase failure of fat cells to send adequate signals or if the brain doesn't respond to appropriate signals causes obesity.[47] An effective way for the regulation of energy balance requires sensors of energy stores in adipose tissue, mechanisms of, relay of information to central control sites (hypothalamus) for consequent integration, which in turn will determine food intake and energy expenditure.[48]

Food intake is regulated by four processes: olfactory and gustatory factors, gastrointestinal distension, release of gastrointestinal hormones such as insulin, cholecystokinin (CCK) and gastrin-releasing peptide and activation of thermogenic components of the efferent sympathetic nervous system (SNS). [49,50]

FIGURE 5: Energy balance and etiology of Obesity



SOURCE**:** Current Medicinal Chemistry, 2009, 16, 506-521 1

Energy balance is determined by the food intake, energy expenditure and energy storage. Obesity is a multifactorial disorder resulting from grouping of several environmental and genetic factors. Reduced physical activity, metabolic rate and thermogenesis eventually decreases energy expenditure leading to increased energy storage and obesity. Availability of appetizing food as well as hypothalamic injury and different drugs stimulate food intake. A growing tilt of genetic factors including dysmorphic syndromes, leptin/receptor mutation, β3AR mutation and overexpression of NPY contribute to progress of obesity. Energy expenditure is estimated by physical activity, metabolic rate and thermogenesis. The metabolic side of energy expenditure contains cardio-respiratory work, the maintenance of ion gradients and various enzymatic activities. Physical activity increases energy expenditure by work of the skeletal muscle in addition to above-mentioned factors. The SNS affects not only

skeletal muscle and cardiovascular system but also thermogenesis. [51] Brown fat is specialized in adaptive thermogenesis. Its thermogenic capacity is expressed through the uncoupling protein-1 (UCP-1), which uncouples oxidative phosphorylation from electron transport through mitochondrial respiratory chain.[52] Brown fat cells are more in mitochondria, and produce increased heat and less ATP than white fat cells. UCP-2 occurs in both brown and white fat and is upregulated if mice are fed a high-fat diet. In human beings, fat cells express the product of a gene similar to the mouse gene for UCP-2. Infants and children have much more brown fat than adults, it has extensive sympathetic innervations. Therefore, heat is produced through the action of noradrenalin on β3AR in brown fat. Activation of β3AR increase lipolysis and fatty acid oxidation. In genetically obese mice the expression of β3AR s is decreased. [51]

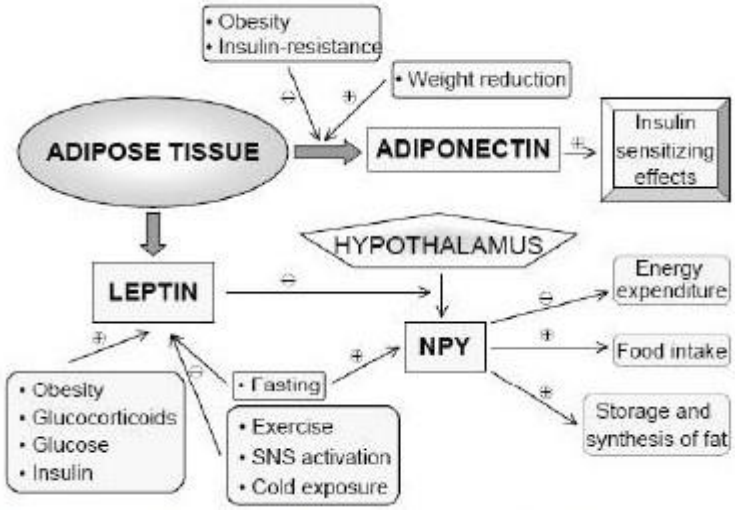
2.5: ADIPOSE TISSUE - ITS PHYSIOLOGY

2.5.1: Physiological features of white adipose tissue innervations

The regulation of whole-body fat stores explains the complex nature of adipose tissue integrative physiology. Glycogen stores are small in relation to adipose tissue triacylglycerol (TG) is therefore the long-term source for excess energy. The amount of TG stored within adipocytes must be a correct reflection of the imbalance between energy intake and energy expenditure. The TG store of adipocytes in turn reflects the net balance between fat deposition and fat mobilisation.[53] The pathways of fat storage and mobilisation in adipocytes are therefore regulated in accordance with whole-body energy balance. The fat cell is under multiple influences, including autonomous nervous system (Fig. 6), local blood flow changes and various hormones and factors delivered from plasma. Adipose tissue secretes leptin in

conditions of food deprivation, SNS stimulation, exercise and cold exposure. Leptin secretion from adipose tissue is inhibited by obesity, glucocorticoids,glucose and insulin. Leptin in turn reaches hypothalamus, to inhibit the secretion of NPY that naturally reduces energy expenditure, improves appetite and stimulates synthesis and storage of fat. Adiponectin normally sensitizes tissues for insulin effects. Obesity and insulin resistance negatively regulate adiponectin secretion from adipose tissue, whereas weight reduction enhances its secretion.

Figure (6). Physiologic regulation and metabolic effects of leptin and adiponectin



SOURCE: Current Medicinal Chemistry, 2009, 16, 506-521 1

Following SNS stimulation, noradrenaline and NPY are released from sympathetic nerve terminals, whereas adrenal medulla secretes adrenaline. The major pathways regulating lipolysis is adrenergic. In human fat cells, both β1& β2 AR adrenergic receptors (ARs)

activate lipolytic cascade by stimulation of cyclic adenosine monophosphate (cAMP) production.

This activation of cAMP-dependent protein kinase A (PKA) leading to phosphorylation of perilipin and hormone-sensitive lipase (HSL), and promotion of lipolysis *in vitro.* [54] Human fat cells exhibit large number of 2 adrenergic receptors, their stimulus inhibits cAMP production and lipolysis. Rodents possess β3AR in the white fat cells, whereas in human fat cells the role of the β3AR s is uncertain.

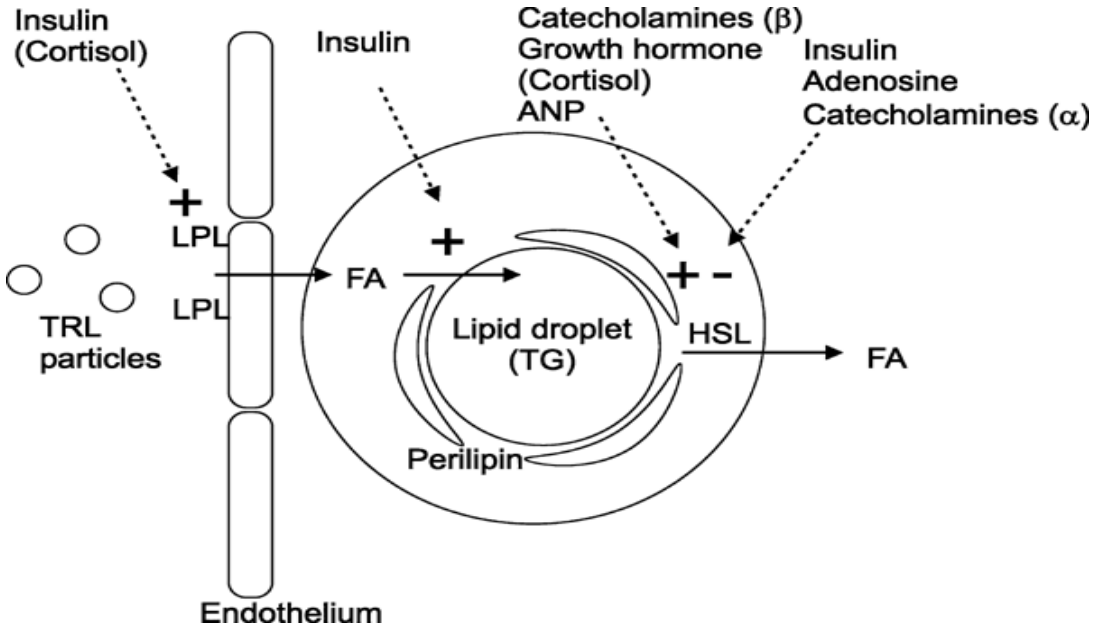
Differences in the adrenergic regulation of lipolysis in adipose tissues from different sites in normal-weight subjects and in obese subjects. The lipolytic response ofisolated fat cells to the catecholamines in subcutaneous is weaker (abdominal/femoral) than in visceral adipose tissue.[55] Lipolysis increases steadily, *β*-adrenergic stimulation appears not to be involved; progressive removal of insulin inhibition may be more important. Overnight secretion of Growth Hormone (GH) [56] and the morning rise in Cortisol play extra modulatory roles. Atrial natriuretic peptide has been suggested as an activator of HSL, but its physiological importance remains uncertain.

These pathways have been further explained recently using data from human genetics and from genetic modulations in animals. Clearly, fat deposition can still occur in the absence of Lipoprotein Lipase(LPL) , because it has been known that patients with LPL deficiency has relatively normal adipocytes.[57,58] Mice lacking LPL specifically in adipose tissue has normal fat mass, but this is attained by upregulation of *de novo* fatty acid synthesis.[59] Whatever the source of the fatty acids Diacylglcyerol acyltransferase (DGAT) is the terminal enzyme in TG

deposition .These are in two isoforms of DGAT, DGAT1 and DGAT2, both expressed in white adipose tissue. Adipose tissue fat storage is reduced but deficient in DGAT1.[60] Energy balance in these mice is attained, despite an increase in energy intake, or by an increase in energy expenditure.[61] Murine adipocytes lacking HSL are enlarged. It displays a normal basal lipolytic activity, suggesting that other lipases may play a role, then catecholamine stimulation of lipolysis is severely reduced. [62,63] Mice deficient in perilipin are lean, but their adipocytes show elevated basal lipolysis and impaired catecholamine stimulation.[64] These findings consensus with the view that phosphorylation of both HSL and perilipin is significant for catecholamine stimulated lipolysis.

The aim of this brief explanation of the pathways of fat deposition and mobilisation, summarised is not to be comprehensive, but to show that a variety of hormonal and neural influences may be involved. The adipocyte regulates the fat it stores, partly through its own gene products. Adipose tissue capillaries have LPL itself a product of adipocyte gene expression, generates an excess of fatty acids, and the adipocyte takes up and esterifies a proportion of these: the remainder mix with Non-Esterified Fatty Acid NEFAs released from adipocyte lipolysis.[65] Production of ASP (an adipocyte-derived stimulator of fat storage) represents which the adipocyte may regulate how much fat it takes up. In order to regulate how much fat to be stored and mobilize, the adipocyte must respond to the signaling mechanisms. If fat storage is decreased, for instance in the situation of DGAT deficiency, then other pathways take role to maintain energy balance (in that case, increased energy expenditure including an increase in physical activity). The integrative nature of adipose tissue physiology is apparent.

FIGURE 7: Pathways of Fat Deposition and Mobilization.



SOURCE: Endocrine Reviews 23(2):201–229

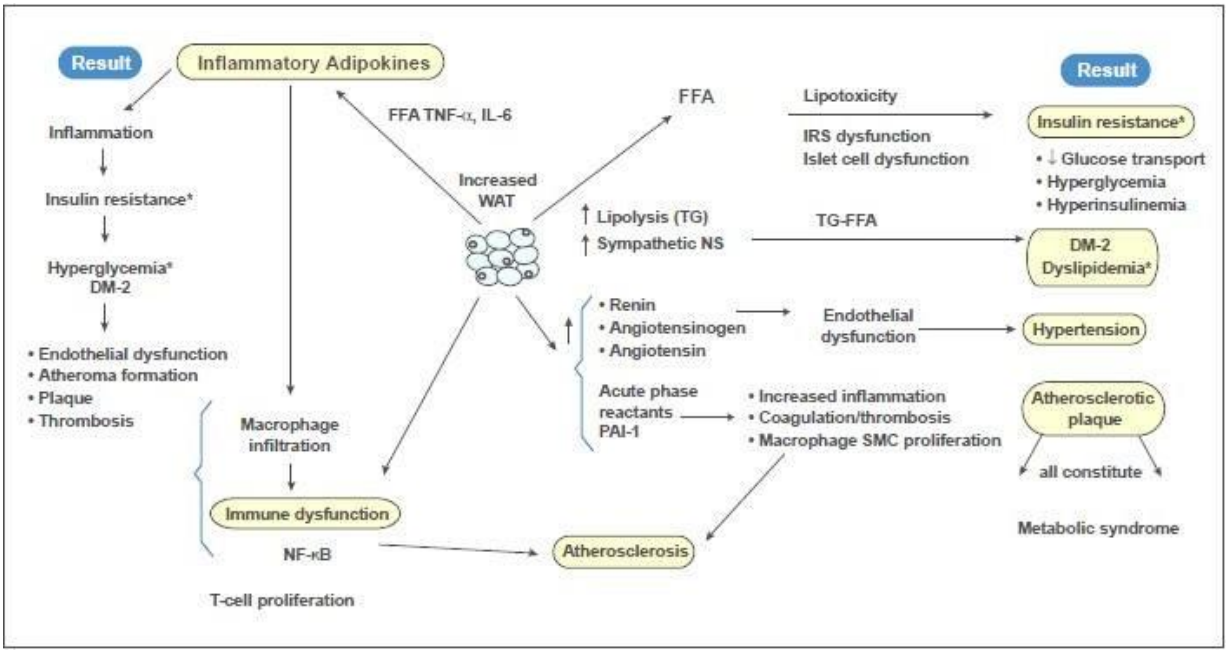
2.5.2: Insulin signaling in the Adipocytes:

Insulin plays a major role in the control of adipose tissue development and function. Insulin not only regulates lipogenesis but also the rate of lipolysis and NEFA efflux. Insulin controls glucose uptake and causes fatty acid transport protein translocation and enhanced fatty acid uptake in adipocytes. Insulin inhibits basal and catecholamine stimulated lipolysis through phosphorylation via the Ser/Thr protein kinase B (PKB) dependent action and activation of type 3B phosphodiesterase (PDE- 3B), leading to a decreased cAMP level, that prevents HSL activation. Insulin-induced antilipolysis and activation of NEFA re-esterification are blunted in omental compared to subcutaneous fat cells. Various functional differences have been identified at the receptor level and the post-receptor level of insulin signaling cascade.[66] Other substances possibly playing a role in lipolytic pathways are atrial natriuretic peptide

(ANP), growth hormone (GH), and miscellaneous agents such as nitric oxide (NO). Although GH treatments in adults reduce visceral obesity and affect insulin sensitivity, the physiological contribution of GH to the control of human adipose tissue lipid mobilization remains elusive.

2.5.3: Dysregulation of Lipid and Glucose Metabolism: Lipotoxicity and Insulin Resistance in Obesity

FIGURE.8. Role of Lipotoxicity and Inflammation on Obesity.



Source:https://www.researchgate.net/publication/329129023DietaryandLifestyle_Risk_Factors_and_Metabolic_Syndrome_Literature_Review_httpwwwfoodandnutritionjournalorgp7511

White adipose tissue (WAT) releases pre–fatty acids and adipokines, which are lipotoxic and inflammatory and result in diverse effects, outlined in the left-hand columns. Their correlation to the metabolic syndrome is shown on the right-hand column, whereas all the effects

culminate in atherosclerosis on the bottom of the figure. *Perturbed glucose and lipid metabolism. DM-2=diabetes mellitus-2; FFA=free fatty acids; IL=interleukin; IRS=insulin receptor substrate; NF- KB=nuclear factor kappa beta; NS=nervous system; PAI-1=plasminogen activator inhibitor-1; SMC=smooth muscle cell; TG=triglyceride; TNF=tumor necrosis factor.

The amount of stored fat is required for survival during nutritionally destitute states such as starvation. In prolonged abundance of food, however results in the excessive storage of fat, eventually resulting in obesity. [67-69] It has been hypothesized that the storage of fatty acid as triacylglycerol within adipocytes fight against fatty acid toxicity; otherwise, free fatty acids will circulate freely in the circulation and produce oxidative stress by disseminating throughout the body. However, the excessive storage creates obesity ultimately leads to the release of excessive fatty acids from enhanced lipolysis, which is stimulated by the enhanced sympathetic activity existing in obesity. The release of these excessive free fatty acids thenin cites lipotoxicity, as lipids and their metabolites produce oxidant stress to the endoplasmic reticulum and mitochondria. This affects adipose as well as non-adipose tissue, results for its pathophysiology in many organs, such as the liver and pancreas, and in the metabolic syndrome.[70,71] The free fatty acids released from stored deposited triacylglycerol also inhibit lipogenesis, that leads to preventing adequate clearance of serum triacylglycerol levels that contribute to hypertriglyceridemia.

Release of free fatty acids from increased serum triglycerides by endothelial lipoprotein lipase within elevated β lipoproteins causes lipotoxicity that results in insulin- receptor dysfunction. The subsequent insulin-resistant state creates with hyperglycemia compensated hepatic

gluconeogenesis. Atlast increases hepatic glucose production, further accentuating the hyperglycemia caused by insulin resistance. Free fatty acids also decrease utilization of insulin-stimulated muscle glucose, contributing further to hyperglycemia. [72,73] Lipotoxicity from excessive free fatty acids also decreases secretion of pancreatic β-cell insulin, which eventually results in β-cell exhaustion. [74]

2.5.4: Sites and Function of Adipokines

Adipocytes, comprising of over one billion cells, not only to store triacylglycerol in fat depots in various body sites to provide energy reserves, but also aggregate constitute the largest endocrine tissue that constantly connects with other tissues by adipocyte- released secretagogues, such as the proteohormones lectin, adiponectin, and vastatin. Along with insulin, these proteohormones helps to regulate body-fat mass.[75] Other groups that contribute to adipocyte adipokines include cytokines, growth factors, and complement proteins. [76] These include the inflammatory adipokines tumor necrosis factor (TNF)-α, interleukin (IL)-1, and IL-6 that cause local steatonecrosis, also distributed by the vascular system and cause inflammation elsewhere.[77] The enhanced fat content in muscle develops so significant in severe obesity that whole-body magnetic resonance imaging reveals cumulative fat depots in muscle site, similar in size to that of total visceral adipose tissue. [78] Buttock fat largely appears to be inert with respect to endocrine function, as this fat is stored for long-term energy reserves.[79] Visceral fat depots release inflammatory adipokines, leads to pathophysiologic basis for comorbid conditions associated with obesity such as insulin resistance and diabetes mellitus type 2. [80] Visceral adipokines are transported by the portal circulation to the liver,

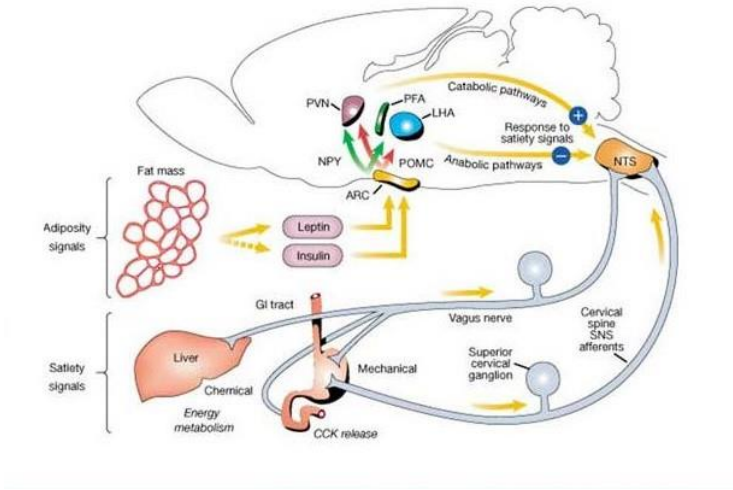
enhancing nonalcoholic steatohepatitis (NASH), and also by the systemic circulation to other diverse sites. Along with fatty- acid lipotoxicity, visceral adipokines also contribute to the pancreatic β-cell dysfunction, which, in turn, decreases insulinsynthesis and secretion.

2.6: THE PHYSIOLOGY OF OBESITY

The amount of fat in the body (adiposity) is not, as a passive result of bad habits or over-indulgence. Rather, it is precisely regulated as part of the process of energy homeostasis, a process by energy intake (food intake) is coordinated to energy expenditure (metabolism and exercise) and the extent of the body's energy stores (the fat mass).

Brain is the major organ regulating in this system, although multiple systems take part in the process gastrointestinal system to control all aspects of energy homeostasis. Adiposity signals are connected through centres of central autonomic pathways that process satiety signals. [81]

Figure .9: Pathways by which signals signals received from the fat mass are integrated with signals from the gastrointestinal system (satiety signals) to control energy homeostasis.



Source: Neuroendocrine regulation of food intake: physiology and pathophysiology

Adiposity signals enter the brain at hypothalamus. Neural signals from the gastrointestinal system and the liver deliver the information about the food that is being eaten, for example, the taste of the food, how much the stomach is inflated, and the chemical content of the food. These satiety signals are sent to the hindbrain and the brain react to the hormone signals via integrated neuropeptide pathways, directly related to energy homeostasis. These consist of: neuroendocrine activation from the pituitary gland; motor behaviour (eating, exercise, etc); autonomic activity. In recent years it has become apparent that the autonomic nervous system had a much more impact than it was once thought upon various fundamental processes of metabolism, including lipolysis, the secretion of insulin and glucagon from the pancreas, and glucose synthesis and secretion from the liver. It is significant to note that, while energy expenditure tends to decrease with ageing, mainly due to the absence of occupational activity and extreme physical exertion, energy intake doesn't tend to decrease to the same extent, for a number of reasons, including lifetime behaviors. Thus, there is a tendency over period of time for the body to increase weight.

2.6.1: What Are Lipids?

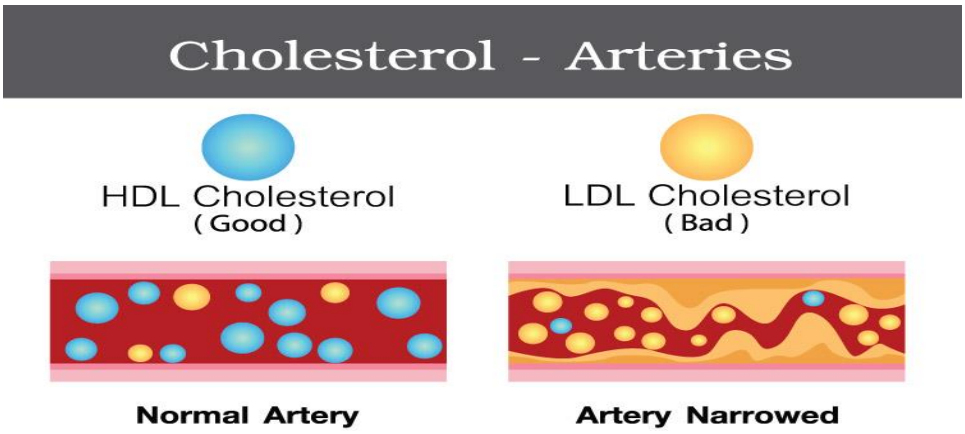
Lipid is a fat or fat-like substance which is essential for the proper functioning of our body. It is source of energy for body, normally stored in both blood Vessels and tissues. However, too much lipid leads to diseases like Obesity and are even life-threatening, for instance, coronary artery disease, stroke or heart attack. Both triglycerides and cholesterol are lipids. [82]

A lipid profile usually gives results for four different types:

- Total cholesterol

- LDL (low-density lipoprotein), the "bad cholesterol"
- HDL (high-density lipoprotein), the "good cholesterol"
- Triglycerides, the most common type of fat in body

- **FIGURE 10: Good & Bad Cholestrol in Arteries**



Source: avitahealth.org/health-library/cholesterol-good-vs-bad/

LDL Cholesterol

LDL cholesterol is known as bad cholesterol. Therefore, lower levels of LDL are essential for healthy condition of heart. LDL cholesterol can accumulate in the artery walls with time, which leads to many heart diseases. If LDL level is exceedingly more than 190, then it's regarded as very high. Therefore, a medicine that considerably reduces the level of LDL.

HDL Cholesterol:

For men- lower than 40mg/dL indicates high risk.

For women- lower than 50mg/dL indicates high risk.

HDL cholesterol is referred to as good cholesterol. It is considered as low risk if the HDL level is higher. This is because HDL protects from heart diseases by preventing the accumulation of bad cholesterol in your artery walls.

Triglycerides

Triglycerides are the form in which most fat exists in food and the body. A high triglyceride level has been linked to higher risk of coronary artery disease. When there is a high triglyceride levels, theirs is low levels of HDL "good" cholesterol and high levels of LDL "bad" cholesterol. This combination raises the chance that will lead to stroke. Other reasons for elevated levels of triglycerides include genetic disorders and underlying diseases. People with diabetes or heart disease also have higher levels of triglycerides. [83]

Total Cholesterol:

Total cholesterol is a measure of LDL cholesterol, HDL cholesterol, and other lipid components.

For total cholesterol:

- 200 milligrams per deciliter (mg/dL) or less is normal.
- 201 to 240 mg/dL is borderline.
- More than 240 mg/dL is high.

For HDL ("good cholesterol"), more is better:

- 60 mg/dL or higher is good -- it protects against heart disease.
- 40 to 59 mg/dL is OK.
- Less than 40 mg/dL is low, raising your chance of heart disease.

For LDL ("bad cholesterol"), lower is better:

- Less than 100 mg/dL is ideal.
- 100 to 129 mg/dL can be good, depending on your health.
- 130 to 159 mg/dL is borderline high.
- 160 to 189 mg/dL is high.
- 190 mg/dL or more is very high.

For triglycerides, lower is better:

- 150 mg/dL or less may be the goal, though the American Heart Association recently suggested that a lower level is best for health.
- 151 to 200 mg/dL means you’re on the way to a higher risk for heart disease.
- More than 200 mg/dL means have a higher risk of heart disease.

For instance, someone's total cholesterol may be high, but this may be due to very high HDL ("good cholesterol") cholesterol levels, which can actually help to prevent cardiac disease (the test is mainly concerned with high LDL, or "bad cholesterol" levels). So, while a raised total cholesterol level may help give an indication that there is a problem with cholesterol levels, the components that make up total cholesterol should also be measured.[84]

Traditional clinical biochemistry uses measurements of cholesterol (TC), triglyceride (TG),

low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) levels as tools to identify the health status and disease risk.[85] However, neither all obese individuals present with dyslipidaemia and nor all patients with dyslipidaemia are obese.

After the application of lipidomics, researchers have observed the complexity of the plasma lipidome and performed in-depth analyses of the relationship between the lipid profile and obesity .[86] Lipidomics is the systematic indication of the lipid species present in a cell, tissue, biofluid, or whole organism, which is known as a frontier of omics research and provides possibilities to identify next-generation biomarkers for complex diseases .[87]

The lipidome characterizes the intermediate product and end product of lipid metabolism that reflects physiological dysfunction and earlier stages of changes in metabolism. Therefore, lipidomic studies might be able to detect the obesity-related metabolic alarm at an early stage, which would help to identify new biomarkers.

TABLE.3: LIPID PROFILE

	Unit	Optimal	Intermediate	High
Total Cholesterol	mg / dL	< 200	200 – 239	> 239
	mmol / dL	< 5.2	5.2 – 6.2	> 6.2
LDL Cholesterol (calculated)	mg / dL	< 130	130 – 159	> 159
	mmol / dL	< 3.36	3.36 – 4.11	> 4.11
HDL Cholesterol	mg / dL	> 60	60 – 40	< 40
	mmol / dL	> 1.55	1.55 – 1.03	< 1.03
Triglycerides	mg / dL	< 150	150 – 199	> 199
	mmol / dL	< 1.69	1.69 – 2,25	> 2,25
Non-HDL-C (calculated)	mg / dL	< 130	130 – 159	> 159
	mmol / dL	< 3.3	3.3 – 4.1	> 4.1
TG to HDL ratio (calculated)	mg / dL	< 3	3 – 3.8	> 3.8
	mmol / dL	< 1.33	1.33 – 1.68	> 1.68

2.6.2: C-REACTIVE PROTEIN(CRP):

Adipose tissue produces proinflammatory cytokines such as tumor necrosis factor-a and interleukin-6, and is considered a vital source of basal production of interleukin-6, the principal stimulator of the production of CRP in the liver. [88]

C-reactive protein (CRP), the major acute-phase protein, is an exquisitely sensitive and objective indicator of bacterial infection, physical tissue damage, and other inflammatory conditions.[89] CRP is regulated by the proinflammatory cytokines including interleukin-1 (IL-1), tumor necrosis factor-a (TNF-a), and specifically interleukin-6 (IL-6), and is exclusively produced by hepatocytes (Liver cells).[90]

As a common rule, 1.00 mg/dl has been used as the cutoff point to signify the clinically significant levels. Recently, however, some studies 5–13 have reported that elevated levels of CRP with a new high-sensitive CRP assay, although still it is part in the healthy range, were associated with increased risk of upcoming cardiovascular events. CRP is of being identified

as an independent, prospective risk factor of cardiovascular disease.

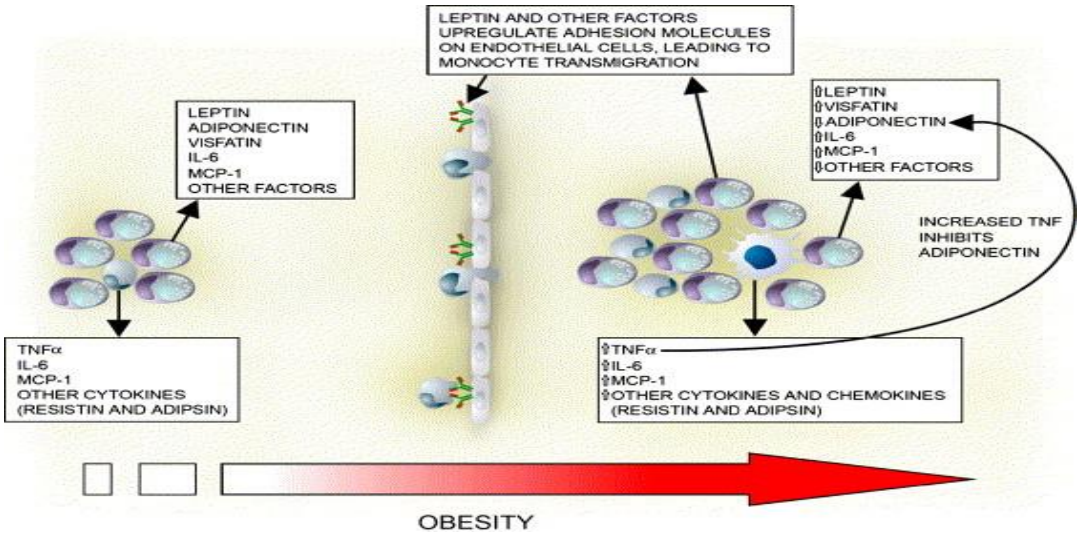
Adipose tissue previously considered as a passive storage place for fat but is now known to be play an active role in metabolism.[91] Among the recently discovered compounds that are expressed in human adipose tissue is the proinflammatory cytokine interleukin 6 (IL-6).[92] Moreover, IL-6 produced in the adipose tissue of healthy humans' beings is released into the blood circulation.[93]

Adipose tissue is assessed to produce about 25% of the systemic IL-6 in vivo. Because of the inflammatory properties of IL-6, as well as the stimulation of acute- phase protein production in the liver,[94,95] the release of IL-6 from adipose tissue may induce low-grade systemic inflammation in persons with excess body fat.

Obesity, hypertriglyceridemia, hypo-HDL-cholesterolemia, hyper-LDL-cholesterolemia, diabetes, hyperinsulinemia, hyperuricemia, and hypertension were significantly associated with moderately elevated CRP. Obesity still showed the strongest association with mildly and moderately elevated CRP.[96]A sensitive marker for systemic inflammation is the acute-phase C-reactive protein (CRP). In a meta-analysis of pro- spective studies, elevated serum CRP concentration was exposed to predict future risk of coronary heart disease. C-reactive protein levels well under the conventional clinical upper limit of normal of 1 mg/dL have been associated with a 2- to 3-fold rise in risk of myocardial infarction, ischemic stroke, peripheral arterial dis ease, and coronary heart disease mortality in healthy men and women.

This study tested whether overweight and obesity are associated with low-grade systemic inflammation as measured by serum CRP concentration.[97-99]

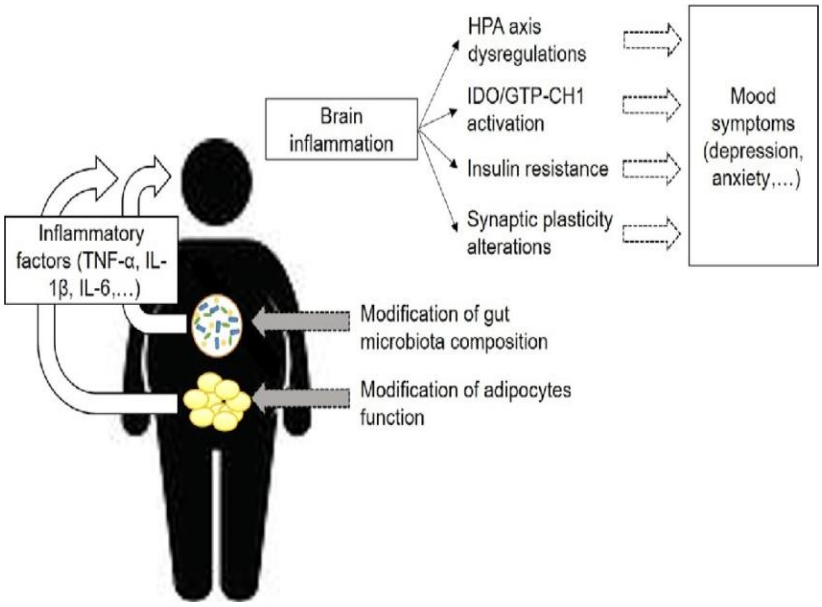
FIGURE 11: Modulatores of CRP (IL-1,6) raised in Obesity Individuals



Source: The Inflammatory Profile Associated with abdominal Obesity

The mechanisms for the apparent association between CRP and obesity are unclear, but still several explanations are possible.[100] The chief modulators of CRP are IL-1, IL-6, and TNF-a. TNF-a messenger RNA has been regarded to be overproduced by adipocytes in obese humans,[101] and a circulating concentration of TNF-alpha increases in such people.[102,103]Since TNF-alpha is a strong inducer of IL-6 in various cells, serum levels of IL-6, which encourages the production of CRP,[104]is raised in obese individuals. This fact may explain the strong association between CRP and obesity. CRP may indirectly reflect the association between other factors such as TNF-a, IL-6, and obesity.[105] Obesity is the most important factor associated with elevated CRP in individuals with the metabolic syndrome. CRP levels in the range signifying a source of infection or inflammation (>10 mg/l) are more common among obese subjects than in nonobese subjects.[106]

FIGURE12: Role of IL-1,IL-6 in Brain inflammation



SOURCE: Role of inflammation in Neuropsychiatric Comorbidity of Obesity: Experimental and Clinical Evidence

2.6.3: Control of meal size

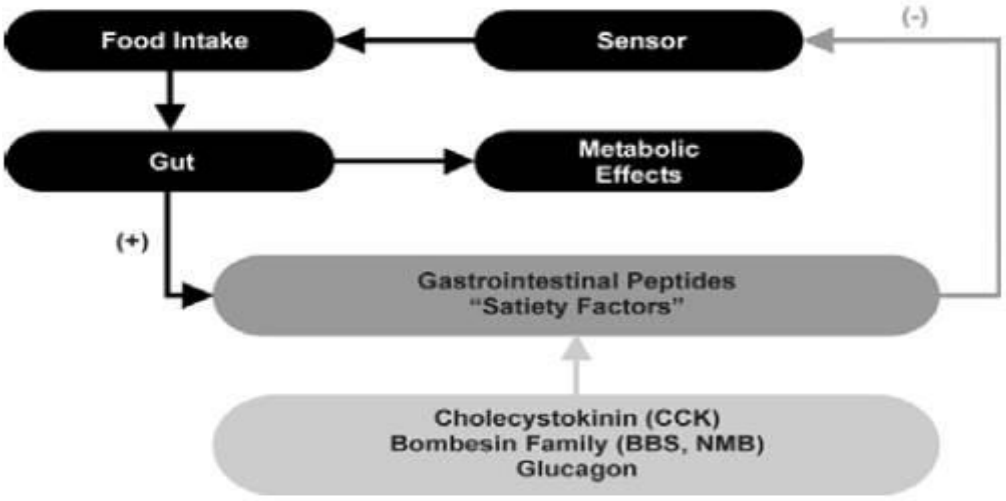
There is slight physiological evidence that appetite and meal initiation are controlled by metabolic or hormonal signals, such as low blood glucose. Relatively, the available evidence proposes that, under normal circumstances, meal initiation is based on learned associations, for example, habit and the social atmosphere. Regulation therefore has to involve is how much to be eaten and there is compelling evidence that meal cessation (that is, meal size) is controlled and enhanced by pre-absorptive gut signals.

In recent years a mechanism for this regulation has been explained. As illustrated in previous, gastrointestinal peptides provide a signal to tell the brain how much has been eaten,

how many calories have accumulated and help to create the feeling of satiety.[107] The best known of satiety factors is cholecystokinin (CCK). A number of experiments have done in humans in which CCK was given intravenously prior to a test meal and, in every occasion, there was a significant reduction of meal size. An important aspect is that CCK is most effective in reducing meal size when the subject has been given a preload, that is, when the stomach is slightly distended, then when no preload is given. [108] Therefore giving CCK can reduce food intake, but does endogenous CCK also contribute to satiety? A recent paper by Beg linger and colleagues illustrates that administration of CCK antagonist loxiglumide to humans before to a test meal was associated with a significant increase in the amount of food intaken. This shows that endogenous CCK normally acts to limit meal size, that has been shown in several animal species.

Although the size of each meal to individual can therefore be manipulated, therapies are intended to be mimic satiety mechanisms are not in themselves likely to be efficient for weight loss. There are no studies have proven that in which CCK has been given on a chronic basis to humans, but animal studies suggest that this would possibly not lead to loss of body weight.

Figure 13: How satiety factors, such as cholecystokinin, control meal size.

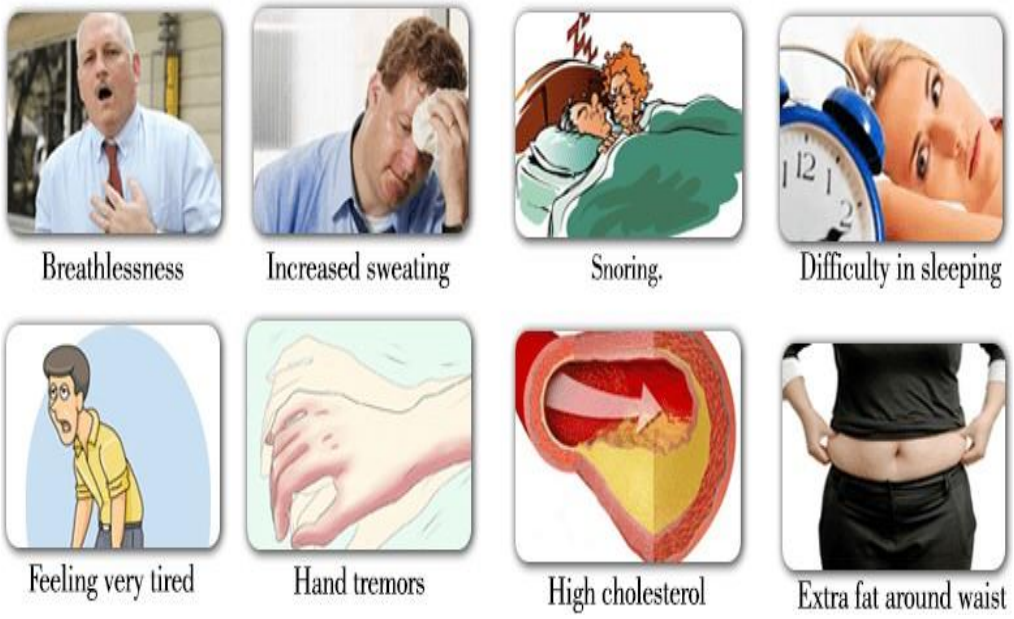


2.6.4: Control of body fat

There is strong evidence that key hormonal regulatory signals—the adiposity hormones control both how much food is eaten and how much energy is exhausted. These hormones circulate in the blood in direct proportion to body fat content. These signals enter the brain and act on receptors in areas of the hypothalamus recognized to regulate food intake and energy expenditure. If weight is decreased, the hormone levels fall, food intake goes up and energy expenditure is reduced. The opposite reaction occurs when an individual has gained excess weight. Thus, body weight tends to be sustained relatively constantly over time.

2.7: Symptoms:

FIGURE 14: SYMPTOMS OF OBESITY



Source: article 1000.com/obesity-symptoms

- Breathlessness
- Insomnia
- Snoring
- Increased cholesterol level
- Profuse sweating
- Palpitations
- Increased appetite

Some studies conducted in western countries stated that obesity was associated with increased depression prevalence. [109-111] There is also some systematic review indicating that obesity increase the risks of depression.[112,113] In further, other studies defined a U-shaped association between obesity and depression (both underweight and obesity were associated with high levels of depression). [114-116] However, several studies conducted in China shown a negative correlation between obesity and the risk of depression. These inconsistencies may be due to dissimilar study populations, different perceptions regarding obesity, different body weight and depression criteria, and other factors.

2.8: Complications (risk factors):

Numerous epidemiological studies have been explored to show the relationship between excess weight, abdominal fatness and risk of a wide range of illnesses .[117,118] Table.2. summarizes the approximate relative risk of physical health problems associated with obesity. [119]

TABLE.4. APPROXIMATE RELATIVE RISK OF PHYSICAL HEALTH PROBLEMS ASSOCIATED WITH OBESITY.

Relative risk >3	Relative risk 2−3	Relative risk 1−2
Type II diabetes	Coronary heart disease	Cancer
Gallbladder disease	Hypertension	Reproductive hormone Abnormalities
Dyslipidemia	Osteoarthritis	Polycystic ovary syndrome
Insulin resistance	Hyperuricemia and gout	Impaired fertility
Breathlessness		Low back pain
Sleep apnea		Increased risk of anesthesia Complications
		Fetal defects (associated with maternal obesity)

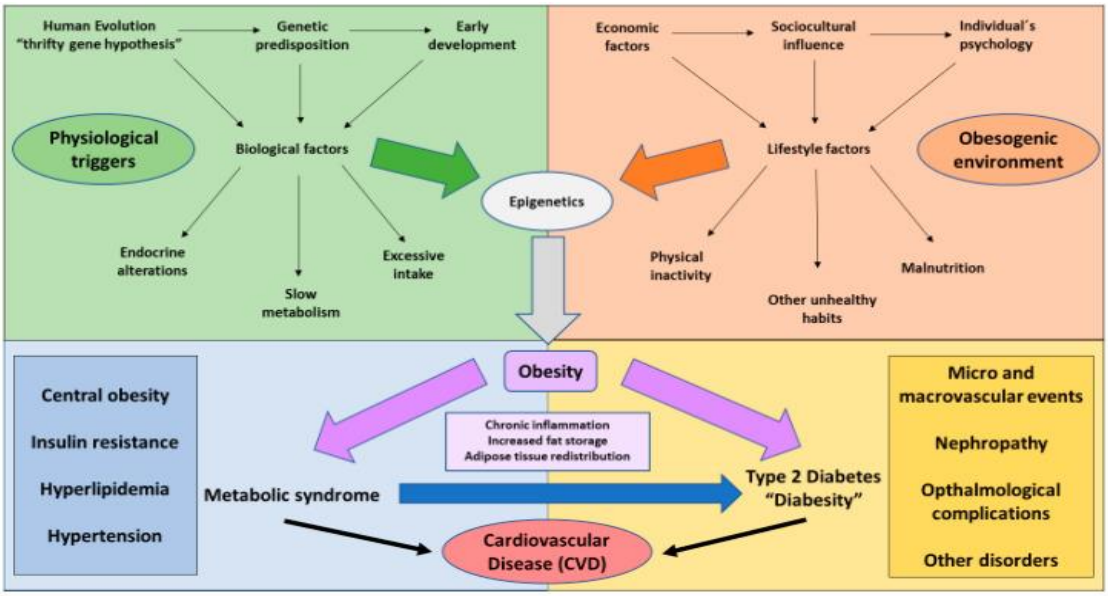
2.8.1: TYPE II DIABETES MELLITUS

Excessive adipose tissue and fat redistribution in obese patients, which is directly implicated with hyperglycemia, hyperlipidemia, insulin resistance, endothelial dysfunction, and chronic inflammation. [120] T2DM, also known as non-insulin dependent diabetes, is a condition

commonly found in obese patients, and some authors consider them as a unique entity termed as “diabesity”. [121] In fact it is known that up to an 85.2% of people with T2DM have been affected with overweight or obese [122] and by 2025, more than 300 million of people will have T2DM accompanying with obesity [123]so, in the majority of cases it is not possible to understand this pathophysiology separately.

Three hypotheses have been proposed to explain the relationship between these conditions: (1) chronic inflammation associated with obesity and their proinflammatory cytokines released by macrophages in adipose tissue affects insulin dependent tissues and beta cells, (2) Lipotoxicity produced by the increased lipid stores in obese people induce and promote the damage and cytotoxicity in peripheral tissues and (3) adipokines stressed adipocytes release a set of autocrine and paracrine products that finally conduct to the loss of insulin sensitivity and to the capacity of beta cells in the pancreas. [124] Moreover, other mechanisms have described these conditions by connecting, such as the role of leptin. Leptin is a hormone responsible for governing food intake to its anorexigenic effect on the hypothalamus, having been observed how, in obese people, the levels of this hormone are increased, leading to a state of leptin resistance.[125] On the other hand, it has been stated that, consumption of hypercaloric foods and high fat diets is associated with a mitochondrial dysfunction and endoplasmic reticulum stress in the hypothalamus, thus promoting not only leptin but also insulin resistance and T2DM. [126]

Figure 15: Obesity and Diabetes



2.8.2: Abnormal Cholesterol Levels

Cholesterol is a kind of fat produced by the liver and found in the blood. There are two kinds of cholesterol: Low Density Lipoprotein (LDL) and High-Density Lipoprotein (HDL). LDL can build up and clog the blood vessels. High levels of LDL cholesterol raise the risk of developing heart disease. Another type of blood fat, triglycerides, also can raise the risk of heart disease.[127]

2.8.3: Cardio Vascular Disease

Obesity is a pro-inflammatory state connected with an increased risk of cardiovascular disorders.[128] Inflammation caused by obesity predisposes to a low-grade inflammatory state, resulting in numerous metabolic deregulations, such as increased insulin resistance and endothelial dysfunction, condensation CVD. Mahabadi A.A. et al. (2009) conveyed that visceral adipose tissue and pericardial fat were associated with coronary heart disease (CHD)

and myocardial infarction.[129] This is because adipokines that are produced by adipose tissue, which is also epicardial and a visceral location, contributing to adversative cardiometabolic complications.

A study found that obese patients with highest BMI quartile (BMI: 40.3–61.2 kg/m^2) had significantly higher CRP levels (4.83 μg/mL vs. 3.03 μg/mL; $p = 0.033$) and high leptin levels (44.97 ng/mL vs. 24.64 ng/mL; $p = 0.042$) than patients in the lower quartile of BMI (BMI, 28.6–32.4) with heart failure, type 2 diabetes mellitus.[130] Thus, obesity-related inflammation occurs mainly in adipose tissue due to modifications in metabolic homeostasis, which leads to increased secretion of pro-inflammatory cytokines and process of making inflammatory signaling pathways in the body. Moreover, the increased CPR levels in obese patients with Metabolic Syndrome and the reduced correlation with weight loss are symptomatic link between CPR and obesity-related risk for cardiovascular diseases.[131] Therefore, CPR level increases with side-by-side BMI increases, a low-grade marker of inflammation. J. Lopez-Sandoval S. et al. (2018) reported that high level of inflammatory markers and reduce plasma adiponectin levels in obese adolescents can be at high risk for the development of CHD and T2DM. A study reported that obesity was a low-grade chronic inflammatory condition characterized by increase in levels of pro-inflammatory cytokines and acute-phase proteins in the blood circulation.[132] Thus, in obese individuals the increased secretion of proinflammatory cytokines contributes to inflammation-related Metabolic Syndrome, such as insulin resistance and other CVD risk factors in obesity.

2.8.4: Obesity and Cancer

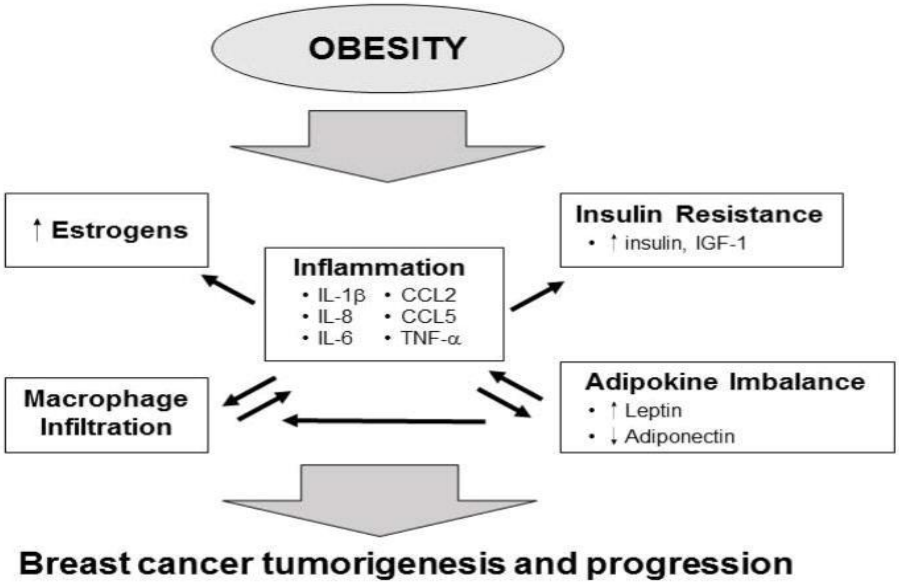
Obesity is associated with increased risk of a variety of different types of cancer almost 13% of incident cases worldwide, and approximately 20% of incident cases in Europe and North America, are regarded to obesity.[133]

Obesity and breast cancer:

The association between obesity and breast cancer risk is multifaceted, varying by menopausal status and by breast cancer subtype. Obesity is reduced in breast cancer incidence to premenopausal women, but increased breast cancer incidence in postmenopausal women.[134] While the association between obesity and breast cancer risk varies by menopausal status, obesity is increased in risk of breast cancer recurrence and mortality in both pre and postmenopausal women. [135]

The recognition of breast cancer as a heterogeneous disease in mouse models which reflect human breast cancer subtypes. One particular change in models of breast cancer is that estrogen receptor (ER) is weakly expressed in mouse mammary tumors, particularly in genetically-engineered mice. [136] However, diet-induced obesity has been verified to drive tumor growth in a variety of mouse models with both luminal and basal-like tumor characteristics lending support to epidemiologic observations.[137] Finally, a study showed that diet-induced obesity improved the growth of luminal-like tumors in ovariectomized mice, but not in mice with intact ovaries,[138] signifying that the connection between obesity and postmenopausal luminal breast cancer should be tested in ovariectomized mice in order to model the human postmenopausal environment.

FIGURE 16: Obesity and breast cancer



Source: Obesity and adverse breast cancer risk and outcome

Murine models of human malignancies afford important systems to study the impact of energy balance, including diet, obesity, and exercise on tumor initiation and progression. Overall, these studies have revealed that high-fat diets (HFDs) and diet-induced obesity (DIO) assist as tumor promoters resulting in earlier appearance, greater frequency, enhanced growth, larger tumor size, and, in some cases, more frequent metastasis of genetically initiated tumors. These genetic modifications may develop spontaneously and/or be developed hereditarily, they may be induced by DNA-damaging agents or they may be created by genetic manipulation. [139]

How Obesity is diagnosed among Indians?

Three parameters which are used to measure obesity are Body Mass Index, Waist circumference WC and Waist-hip-Circumference ratio (WHR). The most accepted method to

define thinness and fatness is BMI, a ratio of weight in kilograms divided by height in meters squared (kg/m^2)

2.9: ACUPUNCTURE:

A thousand of years in the Far East, Acupuncture has been a foremost therapeutic method. According to Traditional Chinese Medicine (TCM), acupuncture is based on the concept of vital energy (qi) flows through the body by means of numerous meridians.[140] When there is a disturbance in this energy flow, it causes disease. Stimulation of points on meridians is said to restore Yin-Yang balance and to have a therapeutic effect. The efficient use of acupuncture increased popularity in the early 1970s. A meeting held on 1979, the WHO issued a list of diseases that can be treated and managed with acupuncture.[141] Most significantly, FDA approved acupuncture needles as a medical instrument in 1996.[142] The NIH published a report concluding that "there is adequate evidence of acupuncture's value to increase its use into conventional medicine".[143]

Acupuncture is defined as inserting very fine needles into the particular points on the surface of the body. Its name comes from the Latin words *acus* means "needle" and *pungue* means "pricking".[144] The acupuncture points are stimulated either by manual needling, electrical stimulation (electroacupuncture), heat (moxibustion), pressure (acupressure) or laser energy in order to manipulate the body's "vital energies"

2.9.1 History of Acupuncture

In early ancient period the people were unknown about the metals, so they were used sharp stones, woods, and blunt objects as a needle. Sho Wen Jie Zi of the second century used the

word *„bian"* as a sharp stone to prick at the body surface of acupuncture points for treating the ailments. These *bian* stones were replaced by needles made up of bone or bamboo. During Shang Dynasty about 16-11 century B.C. uses of bronze needles came into existence. In the course of progression, needles were replaced by iron, silver and gold. In an archaeological site of an ancient tomb in 1968 in Maohing established golden and silver historic needles. Conferring to the ancient text, acupuncture and herbal therapy was established by two ancient deities known as Huang Di and Shen Nung. (3737-2697 BC)[144]

Later in 2697 B.C. Neijing conveyed the typical Chinese medicine, principles of anatomy, health and well-being in a book called "Huang Di Nei jing Su Wen, Yellow emperor's classic of internal medicine". The first part of the book contains the ideologies of medicine and the philosophy of the universe as it narrates the human health. Second part of the book explains about the acupuncture, deals with the prevention and cure of illness or aliments.[145] In the theory of ancient chinese philosophy, the five elements and the concept of yin and yang have developed during the period of spring and autumn. (770-467 B.C.) The theory of meridians, Luo connecting and flow of *„Qi"* are core of the acupuncture philosophy. [146]

Acupuncture points were first systemically termed during Tsin Dynasty (A.D. 250-420) and clarified about 657 acupuncture points including 354 basic acupuncture points. In the Tang Dynasty (A.D. 618 – 907) a distinctive acupuncture department was established at the Imperial medical college of China. During A.D. 960 – 1297 acupuncture was further systematized and officially standard by forming official manual.

In Han Dynasty spreading of Taoism in China leads to standardization of acupuncture and herbal medicine. During this period, they have presented theories of yin and yang and were promoted as the source of life. Huang Fu-Mi (215 – 282 A.D.) wrote a book named *"chia ching on moxibustion and acupuncture"*. Wang Shu wrote book entitled *"Ne-Jing"* he described about pulse diagnosis, at the end of Han era.[147] During Ming Dynasty (1368 – 1644) China had started using combined understanding of western medicine and acupuncture. During the both ching Dynasty (1644 – 1911) and the nationalist China (1911 – 1949) acupuncture lost the support of the rulers. After the beginning of People's Republic of China in 1949, development of traditional acupuncture raised again. Most new methods are needling of hands, nose, ears, face and scalp, needling with long fine needles, hot needles and injection of distilled water in certain points, an instrument for identifying the points and a glass figure marked with acupuncture points. These advances were done in 1958. Scientific medical science, researchers were revealed some light on acupuncture and mechanism of acupuncture through neurophysiology, relation with the hypnosis, and Darwin theory of evolution. The outstanding offerings of Ronald Melzack and Anton Jayasuriya are motor gate control theory of late motor recovery for get rid of the pain. Advance development of Kirilian photography revealed a new dimension on acupuncture.

2.9.2 Philosophy of TCM

Traditional Chinese Medicine (TCM) highlight on philosophic understanding of Yin –Yang (the bi- polarity) and the theory of Five Element, conferring to which the whole universe depends and function. As said "Microcosm is the manifestation of macrocosm" The above specified theories also explain the cause of health and ailment in humans. The Other key

concepts deal with TCM consist of the (Zang-Fu Visceral organ), Qi (energy), Blood, Body Fluid and meridian theories.[148]

2.9.3. Theories of Acupuncture

Ancient philosophical theories are significant to understand the fundamentals of acupuncture. The theory of acupuncture is grounded on meridians and acupuncture points. Meridians are designated ways through *„Qi"* or *„Chi"*.

Concept of Qi

„Qi" is a vital energy flow in the body. This vital energy neither been recognized nor measured, it can be only experienced and valued. In Indian philosophy it is well-known as *Prana.* Yogis well-defined it as a *prana vayu*. The principle of *prana* and *prana vayu* is quite associated with the traditional Chinese concept of *„Qi"* or energy of life. *„Qi"* is universal and it present all over as well as in altered forms. In body *qi* infuses all living cells and tissues. It is indistinguishable force responsible for circulation, respiration, digestion, reproduction and elimination. [149]

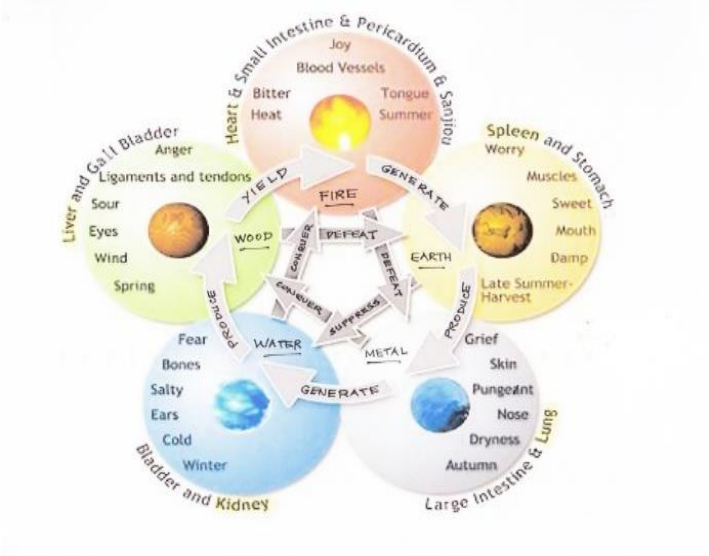
Principles of Yin and Yang

Yin and Yang are the two characteristics of the *Qi* energy. Yellow emperors have described the principle of yin and yang is the origin for whole universe. State of good health can be conserved by balancing the yin and yang and their conflicts may results in a disease. They function as two opposite poles, negative and positive and balancing to each other. Yang denotes for male and yin denotes female.

Concept of five elements

According to the traditional Chinese theory the whole universe is divided into five elements. In the living body it represents as the internal organs and their cycles explain the phenomenon of nature. Theory of five elements with constructive and destructive principles is described in the figure 17

FIGURE 17: Five elemental theory



Traditional law of energy flow

„Qi" flows through certain rules or laws in respect of the direction, time and side of the body. The facts of the energy flow are essential for selecting the meridian and acupuncture points for specific disease.

Mother and son law:

"Qi" always runs from mother to son. For the proper flow of energy mother should be well promoted herself to provide and the child should be strong adequate to receive the energy. In

the flow of energy, the son becomes the mother of the consequent meridian after receiving the energy and in turn the recipient organ becomes the mother of the next following organ. Thus, the mother of heart is liver, then the mother of spleen is heart and so on.

Husband and wife law:

Husband rules the wife, *yang* dominates *yin* and left wrist pulse dominates right wrist pulse. Organs associated to the husband are small intestine, heart, gall bladder, liver, urinary bladder and kidney. Wife connected organs are large intestine, lung, stomach, spleen, triple warmer and pericardium. In the normal balanced, left wrist pulse should be slightly dominate than the right wrist pulse.

The mid-day mid-night law and organ clock:

It defines the relationship between the organs receiving maximum flow of energy. The organ clock shows the circulation of vital energy through various organs and meridian in relation to time. Having knowledge of this law is helpful in selecting the time to treat disease in order to achieve maximum benefit.

2.9.4. Modern Theories

Neurophysiological mechanism

Nervous system and nerve impulses, conductions are the main factor to understand acupuncture in a scientific way. Previous trials assessed that pre-anaesthetised acupuncture points were not showed any effect. This specifies that acupuncture mechanism may involve through the nerves system. Autonomic nervous system (ANS) also plays an important role in the mechanism of acupuncture.[150] Ling and Clive *et al* have verified the involvement of ANS

by applying electrical stimulation at acupuncture point Liver 8 to cat.[151] They have perceived those potential variations in the hypothalamus control the centres of ANS in brain. Another research has done on rat by lee, he has applied electrical stimulation to ST 36 in rat. He observed significant reduction in blood velocity after 10 min of stimulation of sympathetic nerve controlling vasoconstriction.[152]

Sensation and functions of internal organs are controlled through the sensory nerve impulses, coding pattern and frequency of ANS. If the pattern or frequency alterations before reaching the destination, it may reflect changes in the sensation. This physical mechanism involved in the nerve impulse can be altered by external stimulation. Acupuncture is one of the main external stimulation for changing neural coding by electrical and thermal intervention.[153]

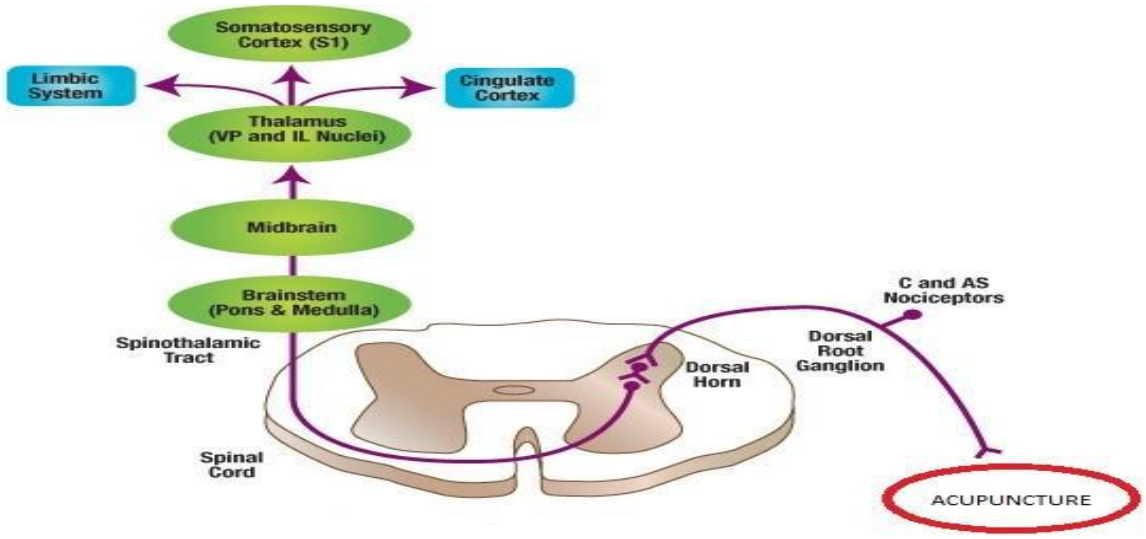
Gate control theory

This theory describes about the physiology of pain. Pain impulses are first controlled and modified in the substantia gelatinosa of the spinal cord known as first functional gate, then impulses permits up through opposite spinothalamic tracts called second functional gate.[154] When it influences cerebral cortex, patients may feel pain. Wald has recommended existence of some other functional gates, namely paraventricular, contralateral nuclei of the thalamus and the medial reticular formation of the mid-brain. Stimulation of acupuncture points produces over-crowding of the impulses at the functional gates and blocks the nerve impulses then give increases pain threshold and analgesia.

Gate theory highlights stimulation of large, highly myelinated (afferent A-beta fibers) block the transmission of pain signals by comparatively small, nociceptive fibers with no myelination (A-delta and C fibers) at the level of the spinal cord. Small, unmyelinated C

fibers are liable for chronic and throbbing pain. However, larger A-delta fibers with minimal myelination are responsible for fast transmission, acute and strong pain. It is hypothesized that electrical stimulation reduces the perception of pain by increasing the activation of A-beta fibers. Hence, Over-crowding of pain signal pathway may close the gate of transmission in the spinal cord.[155] These target cells are situated in the substantia gelatinosa of the dorsal horn.

Figure 18: Mechanism of gate control theory



Source: the gate control theory Dr. Melzack and Wall,1965

Motor gate theory

The phenomenon of motor gate theory was described by jayasuriya and Fernando in 1977. According to theory of motor gate, functional motor gates are obstructed in the pathological conditions. Mechanism of motor gate theory includes of efferent pathway which arises from axons of anterior horn cells to the motor end plates. Secondly, Renshaw cells located in the ventro-lateral part of the ventral horn of grey matter and cajal cells are in the intermediate nucleus of cajal are in synaptic connection with anterior horn cells. Efferents give synaptic

stimuli to renshaw cells, which are excitatory in type. Renshaw cells in turn to have axons which effect synaptic influences back to anterior horn cells.[156]

Hyperactivity of the cells leads to a rise in the inhibitory effect exerted on anterior horn cells through renshaw and cajal cells comprising return to neutral activity. Normally gates are located between anterior horn, renshaw cells and cajal cells are open. When an acupuncture needle inserted in a definite point afferent pathway is potentially capable of acting on the anterior horn cells through the intermediate cells of cajal.

2.10: Causes of Obesity from a Traditional Chinese Medicine Perspective

Obesity is a comparatively untouched subject, and there is only a few mentioning in the Inner Classic of the Yellow Emperor, [157] depending upon their bodily proportions of fat and muscles it divides overweight patients into two types. It mentions that both types are result from overeating heavy, rich, and sweet foods and that continuous consumption will lead to idiopathic thirst, urination, and eventually sudden loss of consciousness, currently postulated as symptoms of diabetes and stroke. However, there is only less much explanation on treatment. Therefore, current day primary obesity has to be approached by applying basic Team principles of maintaining harmony and balance of the five vital organs [158] and taking into account the consequent problems that may arise when such system goes awry.

In Team, the five vital organs that maintain our everyday health are the Liver,[159] Heart, Spleen, Lung, and Kidney. These five vital organs work in cooperation to maintain homeostasis by either supporting or hindering each other's functions. In obesity, the Spleen plays a significant role, and to understand this mechanism, we have to first peer into the digestive system.

Once the food enters the body, the Spleen starts it functions like the “energy/qi transformer,” or the “dynamo” in a machine—to transform and accumulate worthy energy and essential materials from it. However, it needs help from another organ to do so and right it is, the Stomach, is the “burner” which supports to heat up and combust the food for the Spleen. Thus, the food that has been combusted from the Stomach is separated into either essential substances that is then collected by the Spleen and transported to the organs and extremities as wastes—which are sent to the Small or Large Intestines for excretion. Next to the Spleen and Stomach, the Liver acts as a “booster” help to spread the clean energy, up and outward absorbed by the Spleen, while the Kidney resides below the whole combustion site to fuel all organs fundamentally.

Yet, this is a very idealistic case, assuming that all organs are operating in optimal condition. When a person starts to gain weight in a pathological manner, the root of most causes arises with the deficiency of qi/energy in the Spleen. Deficiency of Spleen qi may be induced either congenitally or by actual unsparing, harmful use of the Spleen such as frequent binges and fasting. When our body’s “energy transformer” is weakened, it not only becomes difficult to store enough energy sources for our body but it also becomes difficult to spread it around. Hence, the body gets congested with slow flowing traffic, and just like today’s traffic congestion, all the essential substances get overcrowded failing to reach the place of its destination on time. The body will feel heavy and react like there is not enough energy, which is why most overweight people tend to feel more and more lethargic, with lower level of tolerance for hunger, and crave for snacks or junk food that provides fast energy. Truthfully, it is not that the person actually lacks theessential nutrients; it is that they lack the sufficient and

efficient flow of open traffic to get the materials to their places.

When the deficiency of qi in Spleen becomes chronic, and the transportation function decreases, this leads the Spleen to fail to move and transform water fluids efficiently as well, leading humid to gather and collect and to accumulate into symptoms of dampness and to even congeal into phlegm. When phlegm [4,98] is produced, a myriad of other problems arises with it, and at this stage, the patient feels fatigued, experiences lower immunity, frequently develops edema and chest oppression, and develops a lot of sputum in the Lungs. Since the patient is lethargic, it leads to less exercise, starting a vicious cycle of accumulation of more phlegm and eventually of fat. Therefore, the basic treatment principle for all the aforementioned problems is to balance and strengthen the Spleen, which will eventually help the body to stop craving food and also effectively get rid of humidity and phlegm from the body. With Spleen qi deficiency in the background, there are multiple factors that aggravate the situation. One is excessive heat in the Stomach. Too much heat combusts foods too fast, produces hunger, and leads the person to develop a tendency to overindulge. A person can naturally have a lot of innate heat compared to others, but it can also be kindled up by eating a lot of heat-producing foods such as hot, spicy, greasy, and oily foods.

In Traditional Chinese Medicine (TCM), good health contains the body's systems acting in harmony according to the individual's constitution. TCM takes a holistic approach to obesity by focusing on the fundamental changes in the body. According to TCM principles, development of obesity is due to the following pathological changes (Integrated Chinese Medicine Holdings LTD. [ICMHL], Shen- Nong Info. a)

2.10.1: The pathological changes in obesity:

- ✓ Dyspepsia causes stomach heat and deprived spleen function; the spare metabolic products turn into turbid fluid and phlegm.
- ✓ When dampness and turbid fat arrives the water passages, they are further distributed by the lungs, allowing diffusion into all the organs internally.
- ✓ The liver can fail to regulate qi (vital energy) flow that in turn disturbs digestion and blood flow. The resulting sluggish qi (vital energy) and blood flow have a tendency to block the meridians.
- ✓ Kidney essence exhaustion causes disharmony; the vaporization processes are reduced causing more fluid accumulation.[160]

2.10.2: Types of Obesity according to TCM Perspective

Syndrome identification is the principle and foundation of TCM treatment. Currently there is no standardized obesity patterns, ranging from 3 to 12 patterns by clinical reports. Most often, simple obesity was categorized into deficiency syndrome and excess syndrome by syndrome differentiation of TCM, which again classified into four types (ICMHL, Shen-Nong Info.b).[161]

Excessive internal Phlegm and Dampness due to Spleen Deficiency

Phlegm is a vital concept in TCM. TCM holds that fat or adipose tissue is generally due to phlegm and dampness evils. The spleen is considered to be at the root of all phlegm

production. When the spleen becomes damaged, such as eating too much sweet foods and perform too little exercise, it will fail in its duty to move and transform waste fluids and foods. Instead, these metabolic wastes will come together, collect and transform into evil dampness. If dampness evils tolerate over time it will convert into phlegm, and become fat tissue. The excessive internal phlegm reveals itself as excess weight, accompanied by tiredness, body heaviness, chest and/or stomach distension, and in some cases decrease appetite. The tongue has a slimy covering of fur, meanwhile there is a rolling, taut pulse. This type of obesity is primarly due to an eating disorder, or secondarily by some other illness. Treatment involves sweeping away phlegm and removing stagnation. Once the phlegm is swept away, the qi can be move smoothly and easily. This promotes the movement of phlegm and reduction of fat with the subsequent result of decreasing obesity.

Stagnation of Qi and Blood

Patients displaying this condition may suffer from irritability or low inspiration chest breast fullness, sleep deprivation, a dreamy state, menstrual disorder or amenorrhea (absence of menstruation), and infertility. A few patients may complain of headaches. There may be unsteadiness and numbness of the four extremities, and the tongue is dark red with a white thin fur or a thin and greasy fur. The pulse is thready and rolling. This is because the movement of blood is not smooth or effectively flowing. Stasis blocks the vessels and restrain the qi mechanism. Therefore, fat and dampness collect and accumulate inside the vessels, making the blood more viscous. If this lasts over time, obesity and arteriosclerosis (thickening and hardening of the arteries) will result. The major treatment is to speed up the blood flow and remove stagnation.

Yang Deficiency of Spleen and Kidney

On account of yang deficiency of spleen and kidney, there is not enough qi to transform or dissolve the mucus. People in this category often feel exhausted or weary. They may encounter lower back and knee weakness, shortness of breath, impotence, or low libido. The pulse is deep and fine, the tongue is whitish and without any fur covering. Genetic factors can impact in this condition. It may also be the result of other illnesses, stress, or an undesirable way of life. Treatment involves stimulating the spleen and rectifying the kidney deficiency.

Liver Stagnation

Liver stagnation caused by prolonged period of strong emotions or depression leads to disharmony between the spleen and the liver and leads to fluid retention. Due to this liver disturbance, the gall bladder is also depressed and depleted; the ebb and flow of these organs become unstable, and the qi mechanism does not flow freely. Hence fat turbidity is hard to be transformed and over time it leads to obesity.[162]

2.11: MOXIBUSTION:

Moxibustion is a traditional Chinese medicine technique that involves the burning of

mugwort, a small, spongy herb, to promote healing with acupuncture. The purpose of moxibustion, as with most forms of traditional Chinese medicine, is to strengthen the blood, stimulate the flow of qi, and maintain general health.

Moxibustion is used on people who have a cold or stagnant condition. The practice expels cold and warms the meridians, which leads to smoother flow of blood and qi. In Western medicine, moxibustion has been used to turn breech babies into a normal head-down position prior to childbirth.

FIGURE 19: Methods of Moxa application

Source: uniqueholistic.com

How Does Moxibustion in Acupuncture Work?

There are two types of moxibustion: direct and indirect. In direct moxibustion, a small, cone-shaped amount of moxa is placed on top of an acupuncture point and burned. Broken down further, direct moxibustion can be scarring or non-scarring. In scarring moxibustion the moxa burns on the acupuncture point until it does out completely. In non-scarring moxibustion, the

moxa is placed on the point and lit, but is extinguished or removed before it burns the skin. Patients feel a pleasant heating sensation that penetrates deep into the skin, but should not experience any pain, blistering or scarring unless the moxa is left in place for too long. The more popular form of moxibustion is the indirect type because it comes with a lower risk for pain or burning. In indirect moxibustion, an acupuncture practitioner lights one end of a moxa stick and holds it close to the treatment area for a few minutes until the area turns red. Another form of indirect moxibustion uses both acupuncture needles and moxa. A needle is inserted into an acupoint and retained. The tip of the needle is then wrapped in moxa and ignited, which creates heat in the point and the surrounding area. Once the person experiences relief, the moxa is extinguished and the needle is taken out. [163]

2.11.2: Mechanism of Moxibustion:

TCM usually takes “needling” and “moxibustion” collectively, for both of them are similar therapeutics based on the same theory of meridian and acupoint. In other words, the moxibustion therapeutic effect is partly dependant on the body's nonspecific system of meridians.

Moxibustion is closely related to meridians, cutaneous regions, and acupoints. Meridian system consists of channels and collaterals; they are pathways of communicating internal and external, contacting organs, running qi-blood, and regulating the whole body. Ling Shu, Hai Lun says that there are twelve regular channels, the inner ones belong to viscera and the outer ones connect with limbs. TCM believes that a person is as a whole. The organs and limbs communicate and interact through the meridian system, which plays a very important role in

physiological functions and pathological processes. The cutaneous regions are the surface part of the twelve regular channels, which are nourished by channel-qi. The cutaneous regions can show the status of qi-blood from meridians and organs, also it can receive treatment stimulation and then make effects. Acupoints are the sites on the body surface, in which the qi of organs and meridians assembled, that act as target points and response points of treatment.

In the moxibustion treatment process, the cutaneous regions and acupoints are the terminals of the meridian system, as the receivers, by which moxibustion stimulations can be transmitted into the body. Through the meridian system, moxibustion can reinforce insufficiency and reduce excessiveness and directly correct the disease state of the human body or activate the meridian system self-healing function and play a therapeutic role. For example, the different acupoints can cure different diseases in moxibustion, and the same acupoints can get similar results regardless of acupuncture or moxibustion; all of these proved that the body meridian and acupoint system play an important role in the treatment of moxibustion. [164]

2.11.3: Obesity and Moxibustion:

Moxibustion, arose from TCM, has been widely practiced in clinical. A number of studies have demonstrated that moxibustion is effective in improving the immune system, and changing neurotransmitter levels of central nervous system through repeated acupoint stimulation. Studies have shown that moxibustion stimulates a smoother flow of qi and blood in the human body by warming acupoints and body regions, accelerates the blood circulation overall, thereby attaining the effects of disease prevention and health care. Moxibustion can be applied to patients indirectly (placing a medium between the skin and the burning moxa) or

directly (placing burn cones directly onto the skin). Studies have shown that moxibustion improves positive effects on anthropometry measures can be achieved by moxibustion intervention in combination with a weight loss education program. Especially waist circumference and waist-to-hip ratio had more clinically significant and more noticeable for health reasons. Test results suggest that moxibustion may offer an effective and inexpensive treatment for excess weight that can be used in addition to more conventional treatments such as exercise, diet control, medicine and surgery. [165]

Moxibustion intervention may help to improve some bodily and psychological variables of adolescent with overweight, including the WHR as well as the BMI. This simple and safe therapeutic method is worthy of promotion by public health authorities.[166]

3.0 AIM & OBJECTIVE

3.1 Aim:

- To evaluate the effect of Moxibustion on C-reactive protein (CRP) and lipid profile in obese individuals

3.2 Objective of the Study:

Primary Objective: To evaluate the effect of moxibustion on C-Reactive Protein (CRP) and Lipid profile in obese persons.

Secondary Objective: To assess the effect of Moxibustion on Anthropometry measures in obese patients.

4.0: HYPOTHESIS

4.1: Null hypothesis: Moxibustion at specific acupuncture points may not produce changes in CRP, Lipid profile, weight, BMI, WHR.

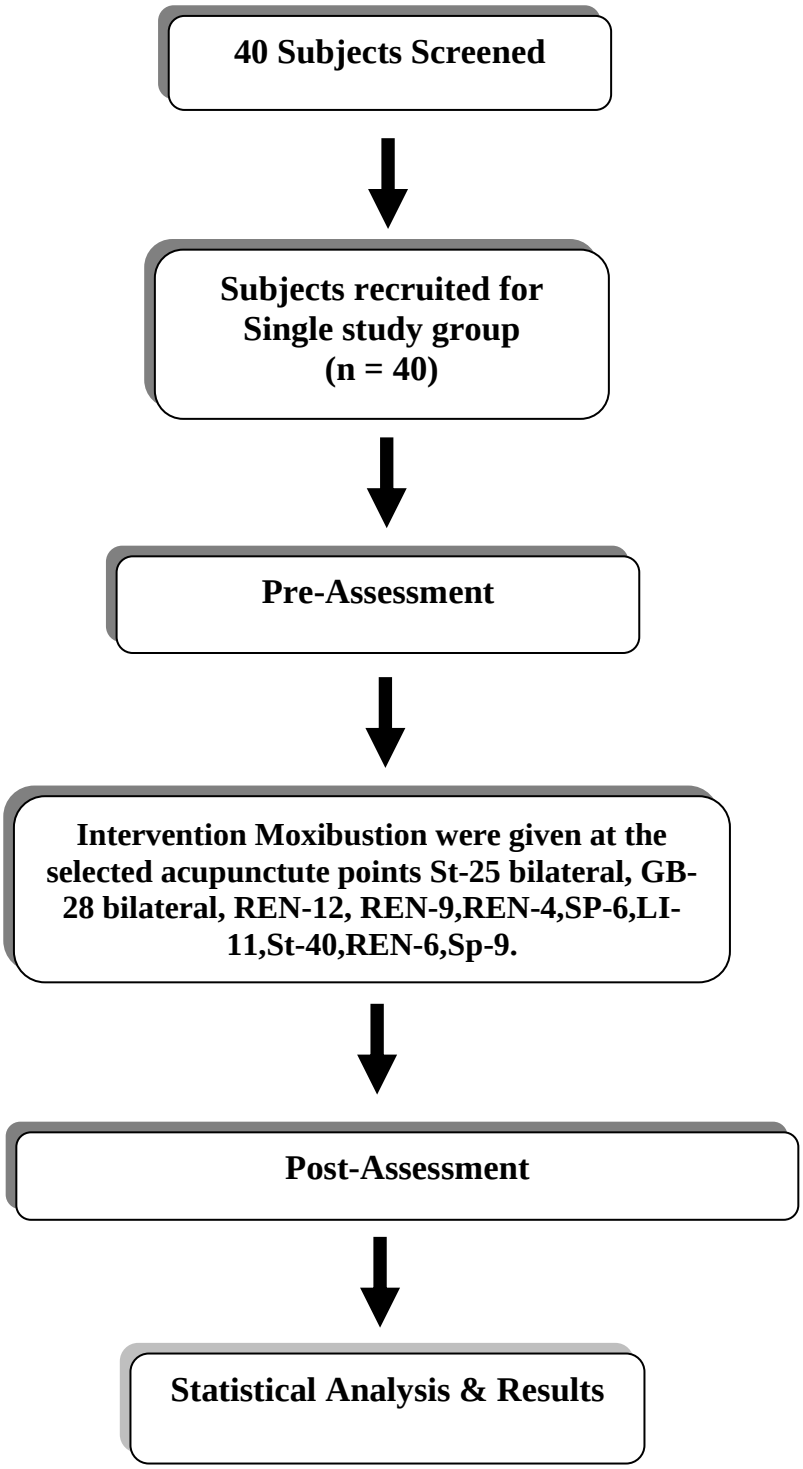
4.2: Alternative Hypothesis: Moxibustion at specific acupuncture points may produce changes in CRP, Lipid profile, weight, BMI, WHR.

5.0: MATERIALS AND METHODS

5.1: Study Design

Pre – Post Experimental Study. The study group was given Moxibustion (TCM herb therapy) on acupuncture point ST-25 (B/L), GB-28 (B/L), REN-12, REN-9, REN-4, SP-6, LI-11, ST-40, REN-6, SP-9 along the skin for the duration of 20minutes (6days/week), for 4weeks.

5.2: Trial Profile



5.3: Selection of study population

Total sample size N = 60

Subjects are recruited from Government Yoga and Naturopathy Medical College and Hospital, Arignar Anna Hospital of Indian Medicine & Homeopathy, Chennai – 106.

Subjects who satisfied the following inclusion & exclusion criteria were recruited for the study.

5.5.1 Inclusion criteria

- Body Mass Index (BMI) above 25(kg/m^2)
- All genders
- Age is between 17yrs – 35yrs
- Person Willingness and ability to accept moxibustion intervention and to comply with the requirements of the study protocol.
- Person are willing and able to attend all the session of the hospital-based program

5.5.2 Exclusion criteria

- currently participating in any other clinical trial in the same hospital or other site
- Hypertension, myocardial infarction, Chronic bronchitis, Rheumatoid arthritis
- Degenerative disorders, nervous diseases, psychiatry illness
- Under medication for chronic illness
- Women during pregnancy and lactation
- Smoker& Estrogen users
- Subjects undergone surgery in the past 6 months

5.5 ETHICAL CONSIDERATION

5.5.1 Ethical Clearance

Ethical clearance was sought from the Institutional Ethics Committee prior to the start of the study and the approval for the same was granted.

5.5.2 Written Informed Consent

Subjects who fulfilled inclusion criteria were apprised about the purpose of the study and their rights as research subjects. Informed consent form was administered in English. As few subjects did not understood English, translating the signed informed consent form into native language i.e., Tamil was done. Adequate time was given to each patient to go through the information sheet and their queries were answered. Their right to withdraw anytime from the study and the need for willingness to participate voluntarily in the study was explained. All the subjects expressed their willingness to participate in the study by giving a signed informed consent. A sample information sheet and consent form were enclosed as Annexure.

5.5.3 Withdrawal criteria

All subjects are free to withdraw from participation in the study at any time for any reason specified or unspecified. Subjects who are withdrawn from the study were not be replaced.

5.6 Assessment

Primary Outcome Variables:

C-Reactive Protein(CRP) and Lipid Profile (LDL, HDL, TG):

C-reactive Protein and Lipid profile (Triglycerides, Low Density Lipoprotein, High Density Lipoprotein) was assessed by hematological test done by laboratory diagnosis before and after giving intervention were estimated under automatic analyzer .

Secondary Outcome Variables:

BMI:Body Mass Index (BMI)[kg/m^2]

Weight in kilograms:

Weight (in kilograms) will be measured with an electronic weighing scale (SECA Model 807, Seca Gmbh Co, Hamburg, Germany) that was kept on a firm horizontal flat surface. Subjects were asked to wear light clothing, and weight was recorded to the nearest kg.

Height in meters^2 Standing Height

Standing height is an assessment of maximum vertical size. Standing height ismeasured with a fixed vertical backboard and an adjustable head piece.Direct the subject to the platform. Ask him or her to remove any hair ornaments, jewellery, buns, or braids from the top of the head. Exhibit the correct position for the measurement of standing height. First, have the subject stand up straight against the backboard with the body weight evenly distributed and both feet flat on the platform. Instruct the subject to stand with the heels together and toes apart. The toes should point slightly outward at approximately a 60ºangle. Check that the back of the head, shoulder blades, buttocks, and heels make contact with thebackboard. Body mass index (BMI) was calculated using the formula weight (kg)/height (m) 2. [168]

Waist Hip Ratio (WHR)

Waist circumference

Remove clothing from the waist line. Stand with feet shoulder width apart (25 to 30 centimeters or 10 to 12 inches) andback straight. Locate the top of the hip bone. This is the part of the hip bone at the side of the waistnot at the front of the body. Use the area between the thumb and index finger to feel forthe hip bone at the side of the waist. Align the bottom

edge of the measuring tape with the top of the hip bone. Wrap the tape measure all the way around the waist. Ensure that the tape measure is parallel to the floor and not twisted. Take two normal breaths and on the exhale of the second breath tighten the tape measure so it is snug but not digging into the skin.

Hip circumference:

At a level parallel to the floor, at the largest circumference of the buttock**.** Make both measurements with a stretch-resistant tape that is wrapped snugly aroundthe subject, but not to the point that the tape is constricting. Keep the tape level and parallel to the floor at the point of measurement. Finally, Waist hip ratio is calculated by dividing the waist measurement with hip measurement as measured by the non- stretchable tape (centimeters)[169]

Subjects will be Screened (n=40)

Pre-Assessment anthropometric measurements Such as weight, BMI, waist circumference, waist -hipratio, CRP and Lipid profile ((Triglycerides, LDL, HDL).

After screening the subjects will be given moxibustion with a set classical acupuncture points for six days in a week for 4 weeks. Post Assessment-anthropometric measurements such as weight, BMI, waist circumference, waist -hip ratio, to assess the changes took place in the subjects.

4.7 Intervention

The Moxibustion at acupuncture point Bilateral TIANSHU (ST25), Bilateral WEIDAO (GB 28), GUANYUAN (CV4), QIHAI (CV6), ZHONGWAN (REN 12), SHUIFEN (REN 9), SANYINJIAO (SP 6), FENGLONG (40), QUCHI (LI 11), YINLINGQUAN (SP 9) was given to the subject for 20minutes (6days/week) for 4weeks. Subjects were asked to come for

6 days in a week for four weeks. After the fourth week, the subjects were assessed for Post line data by hematological assessment (CRP and Lipid Profile), Post assessment anthropometric measures such as Weight, Height, Body Mass Index (BMI), Waist Hip Ratio (WHR).

ACUPUNCTURE POINTS:

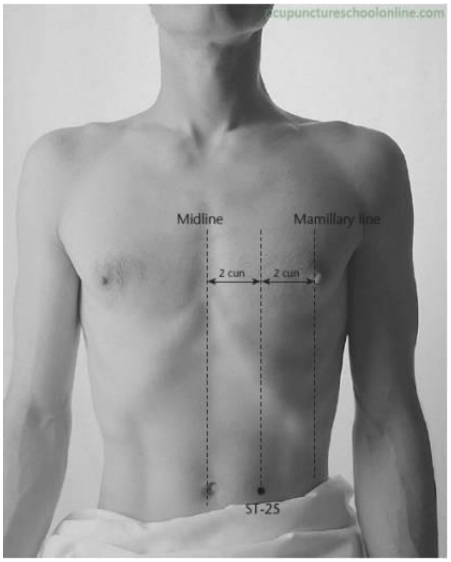
TIANSHU: HEAVEN'S PIVOT

ST-25: FOOT YANGMING STOMACH 25

LOCATION:

On the abdomen, 2 cun lateral to the umbilicus.

FIGURE:20.1



Source: atlas of acupuncture

Moxibustion given:

Indirect Moxibustion is given by moxa stick at the acupuncture point

Duration: 2minutes for a point

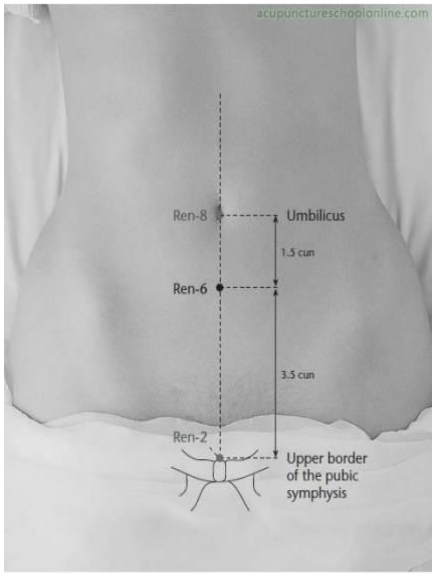
QIHAI: SEA OF QI

REN-6: EXTRAORDINARY CONCEPTION VESSEL 6

LOCATION:

On the midline of the lower abdomen, 1.5 cun inferior to the umbilicus and 3.5 cun superior to the pubic symphysis.

FIGURE:20.2



Source: Atlas of Acupuncture

Moxibustion given:

Indirect Moxibustion is given by moxa stick at the acupuncture point

Duration: 2minutes for a point

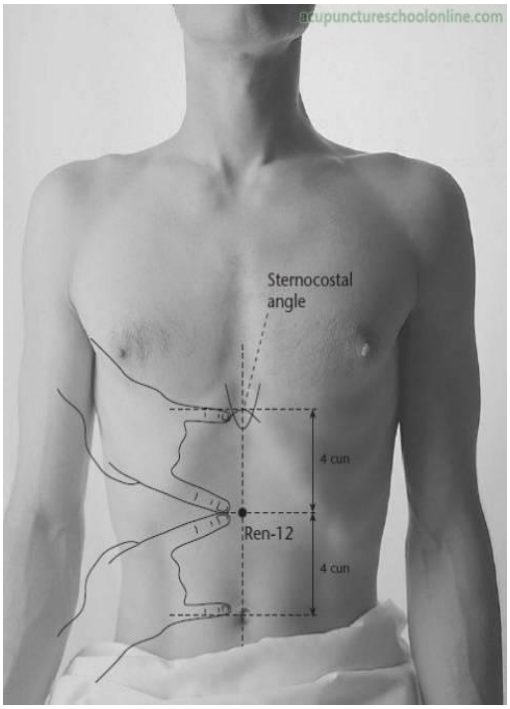
ZHONGWAN: MIDDLE CAVITY

REN-12: EXTRAORDINARY CONCEPTION VESSEL 12

LOCATION:

On the midline of the abdomen, 4 cun above the umbilicus and midway between theumbilicus and the sternocostal angle.

FIGURE:20.3



Source: Atlas of Acupuncture

Moxibustion given:

Indirect Moxibustion is given by moxa stick at the acupuncture point

Duration: 2minutes for a point

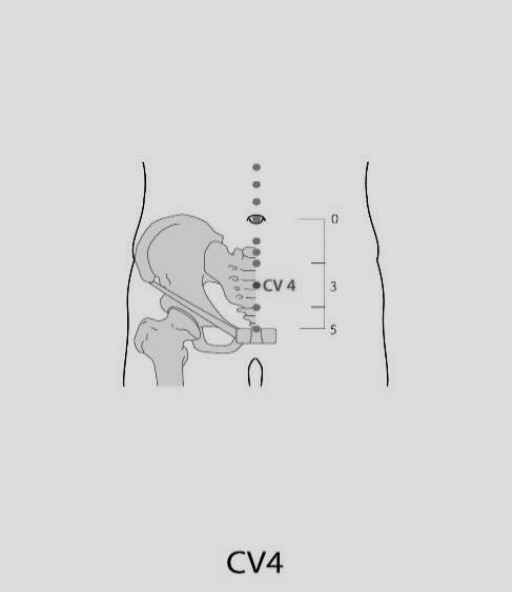
GUANYUAN Gate of the Source

REN-4: EXTRAORDINARY CONCEPTION VESSEL 4

Location:

On the anterior midline, 2 cun superior to the upper border of the pubic symphysis or 3 cun inferior to the umbilicus.

FIGURE:20.4



Source: Atlas of Acupuncture

Moxibustion given:

Indirect Moxibustion is given by moxa stick at the acupuncture point

Duration: 2minutes for a point

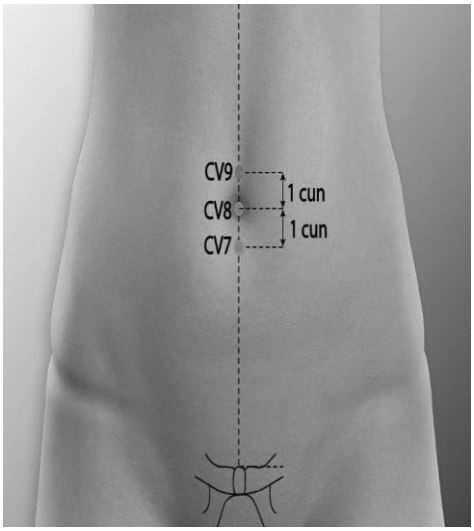
SHUIFEN Water Separation

REN-9: EXTRAORDINARY CONCEPTION VESSEL 9

Location:

On the anterior midline, 1 cun superior to the umbilicus

FIGURE:20.5



Source: Acupuncture index

Moxibustion given:

Indirect Moxibustion is given by moxa stick at the acupuncture point

Duration: 2minutes for a point

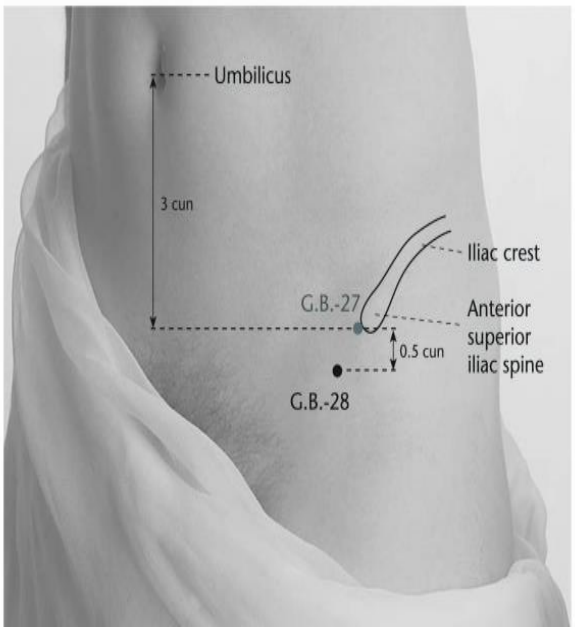
Linking Path WEIDAO

GB-28: Gall Bladder 28

Location:

On the lateral aspect of the abdomen, anterior and inferior to the anterior superior iliac spine (ASIS), approximately 0.5 cun anterior and inferior to ➞ G.B.-27

FIGURE:20.6



Source: Atlas of Acupuncture

Moxibustion given:

Indirect Moxibustion is given by moxa stick at the acupuncture point

Duration: 2minutes for a point

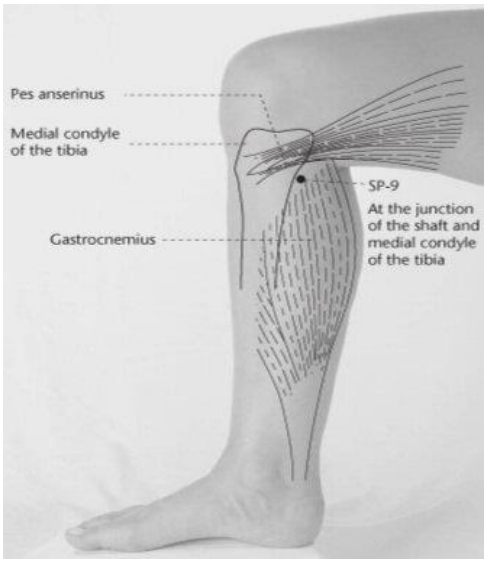
YINLINGQUAN -Yin Mound Spring

SP-9: Spleen 9

Location:

With the knee flexed, this point is located in a depression distal to the medial condyle of the tibia, at the junction of the shaft and the medial condyle.

FIGURE:20.7



Source: Atlas of Acupuncture

Moxibustion given:

Indirect Moxibustion is given by moxa stick at the acupuncture point

Duration: 2minutes for a point

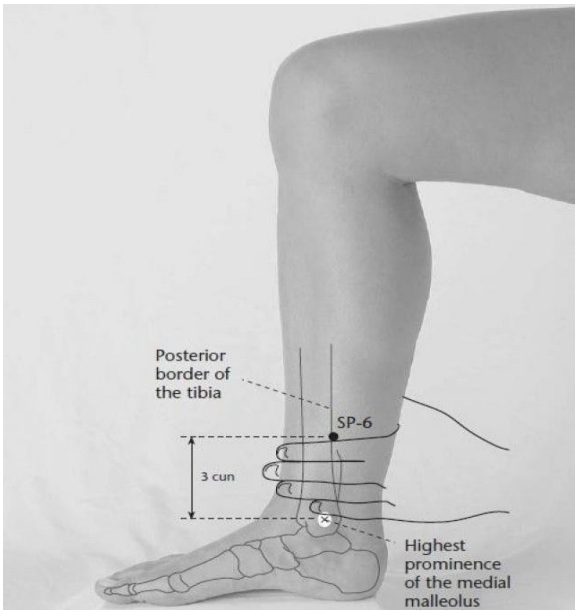
SANYINJIAO -Three Yin Intersection

SP-6: Spleen 6

Location:

3 cun proximal to the highest prominence of the medial malleolus, on the posterior border of the medial crest of the tibia.

FIGURE:20.8



Source: Atlas of Acupuncture

Moxibustion given:

Indirect Moxibustion is given by moxa stick at the acupuncture point

Duration: 2minutes for a point

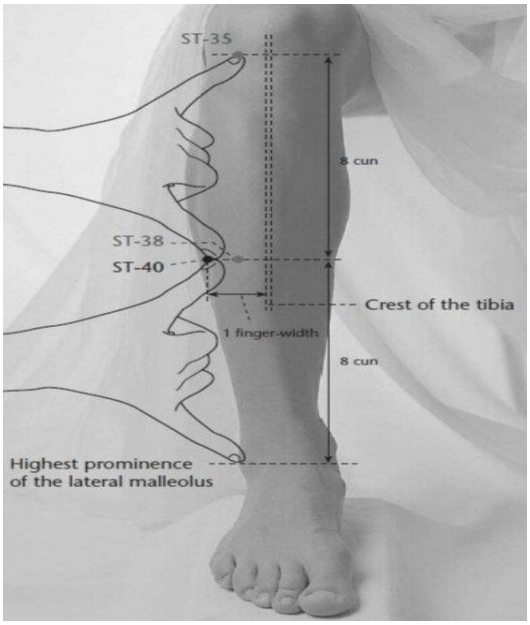
FENGLONG -Abundant Bulge

ST-40:Stomach 40

Location:

At the midpoint of the line joining ➞ ST-35 and ➞ ST-41 and 2 fingerbreadths lateral to the anterior crest of the tibia or 1 finger breadth lateral to ➞ ST-38, between the extensor digitorum longus and peroneus brevis muscles. [167]

FIGURE:20.9



Source: Atlas of Acupuncture

Moxibustion given:

Indirect Moxibustion is given by moxa stick at the acupuncture point

Duration: 2minutes for a point

Moxibustion Methods:

Fully expose the acupoints with mild moxibustion method, that is, ignite the moxa sticks, and then apply to the acupuncture points.). The ignited moxa sticks should be maintaining about 2–3 cm away from the skin to allow the patient to feel warm, but not burning (local skin should not appear red). The patient should be lying down, and the acupoints including Bilateral Tianshu (St25), Bilateral Weidao (Gb 28), Guanyuan (Cv4), Qihai (Cv6), Zhongwan (Ren 12), Shuifen (Ren 9), Sanyinjiao (Sp 6), Fenglong (40), Quchi (Li 11), Yinlingquan (Sp 9) should simultaneously apply moxibustion. Each moxibustion lasts for 20 min. Gently massage the acupoints after moxibustion. The moxibustion should be performed once daily.[170] After the period of 4 weeks same assessment will be done to assess the effectiveness of the intervention.

Data analysis:

Data analysis was done using paired samples t-test with the use of statistical package for the social sciences, version 16

6.0 RESULT

The present study was conducted to study the effect of moxibustion in obese individual with primary variables viz., CRP and Lipid profile (LDL, HDL, TG). compared results of before and after Moxibustion intervention was taken, wherein data was extracted at the baseline and post- intervention after 4 weeks. Paired sample t-test was conducted for this study. When the Before and after data were collected, it was analyzed through Paired sample "t-test" and it showed that statically significant reduction (P value < 0.001) in Results of this study showed a significant reduction in CRP, Lipid profile, Weight and BMI. while there is no significant reduction in waist Hip Ratio

TABLE 1: Demographical variable of the study participants

Variable	STUDY GROUP (Mean standard deviation)
Age(yrs)	28.38±5.85
Gender	females n=33, males n=7
Height(m)	1.61±0.09
Marital status	Unmarried n=18, Married n=22
Occupation	Student n=11, homemaker n=12,selfwork n=8, teacher n =2, IT profession n=5, Doctor n=2
SBP (mmHg)	123.15±10.63
DBP (mmHg)	81.88±6.78
PR (bpm)	86.08±5.65

Note: Values are presented as Mean ±Standard Deviation.

TABLE 2:

Table 2: **Comparison of variables of study group before and after the intervention**

Variable	**Pre_test**	**Post_test**	**Mean standard deviation**	**P value**
Weight(kg)	85.03	80.28	16.78±16.44	<0.001
BMI (kg/m^2)	33.13	31.19	6.68±6.54	<0.001
WHR	0.90	0.90	0.08±0.07	0.078
CRP (mg/dL)	7.92	6.60	0.91±0.86	<0.001
LDL (mg/dL)	140.37	117.93	32.76±24.76	<0.001
HDL (mg/dL)	57.34	54.26	8.30±5.87	<0.001
TG (mg/dL)	165.58	140.88	25.84±21.58	<0.001

Note: 1. BMI: body mass index, 2.WHR: Waist Hip Ratio, 3.CRP: C-Reactive Protein, 4.LDL: Low Density Lipoprotein, 5.HDL: High Density Lipoprotein, 6.TG: Triglycerides

Hint: Values are presented as Mean standard deviation and p value is obtained from t-test.

7.0 DISCUSSION

The present study shows significant reduction in the C-Reactive Protein (CRP), Lipid Profile, weight and Body Mass Index (BMI) for the experiment group. On analysis marked changes in CRP, Lipid profile, weight and BMI was observed in the experimental group where the acupuncture points are stimulated with moxibustion

There are many studies which have been proven that, the effect of acupuncture on Obese individuals has significant improvement. We designed this study to examine the safety and efficacy of moxibustion in obesity. As one of the most chief traditional medical techniques in China, moxibustion has certain advantages in treating metabolic disorders.[171]

In accordance with the previous studies findings on acupuncture and its effects on lipid profile and anthropometric measures, our study results are also significantly matched with the previous studies by making marked changes in weight loss and CRP, lipid profile with moxibustion. A number of studies presented that moxibustion had some positive effects on the obesity-related parameter in abdominal obesity patients; however, inadequate evidence on moxibustion treatment duration made results troublesome to interpret.[172]

Li et al conducted a randomized controlled trial in 2018, which engaged 60 obesity patients with phlegm dampness stagnation syndrome and stated that warming needle moxibustion had positive effects on controlling clinical symptoms in those patients. Another randomized control trial in 2012 used a combination treatment of acupuncture and moxibustion in obesity patients at a frequency of 3 times per week for 12 weeks and found that there was significant variance in results between the control group and the treatment group.[173] Although some studies confirmed such beneficial effects of moxibustion or lifestyle changes in improving abdominal obesity symptoms, the combined effects of moxibustion, and characteristic

lifestyle intervention of TCM which includes lifestyle changes on abdominal obesity still remains unclear.

The age of moxa sticks also play a role in bringing the desired effects in the treatment. Study on finding the effect of old moxa with that of the less old moxa roll resulted in the high significant changes in CRP, LDL, HDL, TG by the usage of age-old moxa in comparison with less old one. Also, moxibustion have many other advantages, including low-cost, stable efficacy, and low risks of complications.

The acupuncture points given for moxibustion used in our study was corresponding to other studies where to reduce lipid profile and anthropometric measures significantly noted. In this study protocol, we will use moxibustion at acupoints Bilateral Tianshu (St25), Bilateral Weidao (Gb 28), Guanyuan (Cv4), Qihai (Cv6), Zhongwan (Ren 12), Shuifen (Ren 9), Sanyinjiao (Sp 6), Fenglong (40), Quchi (Li 11), Yinlingquan (Sp 9) for the treatment frequency of 6 times per week for 4weeks intervention of TCM. The outcome assessments will include analyses of obesity-related anthropometric measurement indicators, serum biochemical indexes.

There are evidences that validate the fact that elevated CRP levels are closely associated to obesity. It has been also suggested that adipose tissue releases the proinflammatory cytokines, so it is logical that weight loss is associated with decrease in CRP levels. Other studies reduction in CRP levels following weight loss have been found the same result as ours. Finally, future studies should focus on explaining the mechanisms by which moxibustion treatment affects body composition. Although there are no studies assessing the role of moxibustion on CRP and lipid profile changes during weight loss.

Hence, in the view of to evaluate the effect of moxibustion on obese individuals there is a

significant reduction in CRP and Lipid Profile. However, the changes in Waist hip ratio [WHR] in anthropometric measurement were not significantly different.

7.1 Limitation:

- The current study measures only a month effect.
- The study has only limited dependent variables.
- The current study was done with a minimum number of subjects and further follow up was not done in the study.

7.2 Recommendations for Future Study:

• The same study can be conducted on a larger population and longer duration with suitable study design and some objective kind of outcome variables could be included to validate the current results.

• A large number of Single point study reveals the efficacy of certain point and feasibility to treat the diseases.

8.0 CONCLUSION

The present study demonstrated that 4 weeks of moxibustion is effective in reducing CRP, lipid profile, weight, BMI(Body Mass Index) in obesity.

9.0 REFERENCES:

1. Hotamisligil GS. Inflammation and metabolic disorders. Nature. 2006 Dec13;444(7121):860
2. Bastard JP, Maachi M, Lagathu C, Kim MJ, Caron M, Vidal H, Capeau J, Feve B.
3. http://www.who.int/mediacentre/factsheets/fs311/en/
4. Pradeepa R, Anjana RM, Joshi SR, Bhansali A, Deepa M, Joshi PP, et al. ICMR-INDIAB Collaborative Study Group.Indian J Med Res. 2015;142(2):139-50. doi: 10.4103/0971-5916.164234.
5. Ahirwar R, Mondal PR. Prevalence of obesity in India: A systematic review. Diabetes MetabSyndr.2019 Jan-Feb;13(1):318-321. Doi:10.1016/j.dsx.2018.08.032
6. Murugan, Rajalakshmi. (2016). Prevalence And Associated Factors of Obesity Among Adults in Tamil Nadu State, South India. International Journal of Current Research. 8. pp.38193-38200.
7. Wirtz, Veronika J. "Background Paper 6.18 Obesity." Priority Medicines for Europe and the World “A Public Health Approach to Innovation (2004).
8. Fegal KM, Carroll MD, Kit BK, Ogden CL. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999–2010. J Am Med Assoc. 2012;307:491–7.
9. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity and trends in body mass index among US children and adolescents, 1999–2010. J Am Med Assoc. 2012;307:483–90 Centers for Disease Control and Prevention. Summary health statistics for U.S. adults: National Health Interview Survey; 2010.
10. Atar, O. Gulmez, A. Atar et al., “The effects of prior beta-blocker therapy on serum C-reactive protein levels after percutaneous coronary intervention,” Clinical Cardiology, vol. 28, no. 5, pp. 243–246, 2005: S. Mora, I. M. Lee, J. E. Buring, and P. M. Ridker, “Association of physical activity and body mass index with novel and traditional

cardiovascular biomarkers in women," Journal of the American Medical Association, vol. 295, no. 12, pp. 1412– 1419, 2006

11. M. Visser, L. M. Bouter, G. M. McQuillan, M. H. Wener, and T. B. Harris, "Elevated C-reactive protein levels in overweight and obese adults," Journal of the American Medical Association,vol. 282, no. 22, pp. 2131–2135, 1999.
12. J. W. Anderson, E. C. Konz, and D. J. A. Jenkins, "Health advantages and disadvantages of weight-reducing diets: a computer analysis and critical review," Journal of the American College of Nutrition, vol. 19, no. 5, pp. 578–590, 2000. A. E. Hak, C. D. A. Stehouwer, M. L. Bots et al., "Associations of C-reactive protein with measures of obesity, insulin resistance, and subclinical atherosclerosis in healthy, middle-aged women," Arteriosclerosis, Thrombosis, and Vascular Biology, vol. 19, no. 8, pp. 1986–1991, 1999.
13. http://medcraveonline.com/IJCAM/IJCAM-01-00007.php
14. http://www.journalinformationalmedicine.org/hbf.htm
15. Shu, Q. J. Review Study of The Impact of Globalisation on Motivation's Health Personnel of TCM And Western Medicine on The Quality of Care In Developing And Low Countries.
16. J. M. Lacey, A. M. Tershakovec, and G. D. Foster, "Acupuncture for the treatment of obesity: a review of the evidence," International Journal of Obesity, vol. 27, no. 4, pp. 419–427, 2003.M. S. Lee, J. Hwan Kim, H. J. Lim, and B. C. Shin, "Effects of abdominal electroacupuncture on parameters related to obesity in obese women: a pilot study," Complementary Therapies in Clinical Practice, vol. 12, no. 2, pp. 97–100, 2006.
17. C. H. Hsu, K. C. Hwang, C. L. Chao, J. G. Lin, S. T. Kao, and P. Chou, "Effects of electroacupuncture in reducing weight and waist circumference in obese women: a randomized crossover trial," International Journal of Obesity, vol. 29, no. 11, pp. 1379–1384, 2005

18. Oleson T. Auriculotherapy manual: Chinese and western systems of ear acupuncture. 2nd ed. Los Angeles: Health Care Altern; 1996.
19. Vickers A, Zollman CC. ABC of complementary medicine: acupuncture. BMJ. 1999;319:973–6. & Lien CY, Liao LL, Chou P, Hsu CH. Efects of auricular stimulation on obese women: a randomized, controlled clinical trial. Eur J Integr Med. 2012;4:e45–53
20. World Health Organization. Obesity and Overweight, Fact Sheet, October 2017, http://www.who.int/mediacentre/factsheets/fs311/en/ World Health Organization. Report of a joint WHO/FAO Expert. Consultation. Diet, nutrition and the prevention of chronic diseases. WHO technical report series No.916,http://whqlibdoc.who.in/trs/who TRS 916.pdf (PubMed)
21. Pagsisihan, D., Sandoval, M. A., Paz-Pacheco, E., & Jimeno, C. (2016). Low indices of overweight and obesity are associated with cardiometabolic diseases among adult Filipinos in a rural community. Journal of the ASEAN Federation of Endocrine Societies, 31(2), 97-97.
22. World Health Organization. (1998). Obesity: preventing and managing the global epidemic: report of a WHO consultation on obesity, Geneva, 3-5 June 1997 (No. WHO/NUT/NCD/98.1). World Health Organization.
23. WHO? Obesity: Preventing and Managing the Global Epidemic. Geneva, Switzerland: WHO; 2000. [Google Scholar]
24. Schoonjans K, Staels B, Auwerx J. Role of the peroxisome proliferator-activated receptor (PPAR) in mediating the effects of fibrates and fatty acids on gene expression.J Lipid Res. 1996;37:907-925.
25. Vergès B. Clinical interest of PPARs ligands. Diabetes Metab. 2004 Feb;30(1):7-12. doi: 10.1016/s1262-3636(07)70083-6.
26. Shirai K. Obesity as the core of the metabolic syndrome and the management of coronary

heart disease. Current medical research and opinion. 2004 Mar 1;20(3):295-304.

27. Rajala MW, Scherer PE. Minireview: The adipocyte—at the crossroads of energy homeostasis, inflammation, and atherosclerosis. Endocrinology. doi: 10.1210/en.2003-0580.
28. Berg AH, Scherer PE. Adipose tissue, inflammation, and cardiovascular disease.Circ Res. 2005;96:939-949.
29. Lau DC, Dhillon B, Yan H, Szmitko PE, Verma S. Adipokines: molecular links between obesity and atheroslcerosis. Am J Physiol Heart Circ Physiol. 2005 May;288(5):H2031-41. doi: 10.1152/ajpheart.01058.2004. Epub 2005 Jan 14.
30. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
31. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000;894:i-xii, 1-253.
32. Diet, nutrition and the prevention of chronic diseases. World Health Organ Tech Rep Ser. 2003;916:i-viii, 1-149, backcover.
33. O'Rahilly, S.; Farooqi, I.S. Genetics of obesity. Philos. Trans. R. Soc. Lond. B. Biol. Sci., 2006, 361, 1095-1105.
34. Rankinen, T.; Zuberi, A.; Chagnon, Y.C.; Weisnagel, S.J.; Argyropoulos, G.; Walts, B.; Perusse, L.; Bouchard, C. The human obesity gene map: the 2005 update. Obesity (Silver Spring), 2006, 14, 529-44.
35. Azuma, N.; Yoshimasa, Y.; Nishimura, H.; Yamamoto, Y.; Masuzaki, H.; Suga, et al. The significance of the Trp 64 Arg mutation of the beta3-adrenergic receptor gene in impaired glucose tolerance, non- insulin-dependent diabetes mellitus, and insulin resistance in Japanese subjects. Metabolism, 1998, 47, 456-60.
36. Straczkowski, M.; Dzienis-Straczkowska, S.; Stepien, A.; Kowalska, I.; Szelachowska, M.; Kinalska, I. Plasma interleukin-8 concentrations are increased in obese subjects and related to fat mass and tumor necrosis factor-alpha system. J. Clin.Endocrinol. Metab.,2002, 87,

4602-6.

37. Specchia, C.; Barlera, S.; Chiodini, B.D.; Nicolis, E.B.; Farrall, M.; Peden, et al. Quantitative trait genetic linkage analysis of body mass index in familial coronary artery disease. Hum. Hered., 2008, 66,19-24.
38. Jhanwar-Uniyal, M.; Beck, B.; Jhanwar, Y.S.; Burlet, C.; Leibowitz, S.F. Neuropeptide Y projection from arcuate nucleus to parvocellular division of paraventricular nucleus: specific relation to the ingestion of carbohydrate. Brain Res.,1993, 631, 97-106.
39. Lee M, Korner J. Review of physiology, clinical manifestations, and management of hypothalamic obesity in humans. Pituitary. 2009;12(2):87-95. doi: 10.1007/s11102-008-0096-4.
40. Weaver, J.U. Classical endocrine diseases causing obesity. Front. Horm. Res., 2008, 36, 212-28. doi: 10.1159/000115367
41. Ness-Abramof, R.; Apovian, C.M. Drug-induced weight gain. Timely. Top. Med.cardiovasc.Dis.,2005,E31.
42. Mattes, R.D. Food palatability, rheology, and meal patterning. JPEN. J. Parenter. Enteral. Nutr., 2008, 32, 572-4.
43. Blundell, J.E.; Gillett, A. Control of food intake in the obese. Obes. Res., 2001, 9.Suppl. 4, 263S-70S.
44. Hill, J.O.; Wyatt, H.R. Role of physical activity in preventing and treating obesity. J.Appl. Physiol., 2005, 99, 765-70.
45. Ravussin, E.; Valencia, M.E.; Esparza, J.; Bennett, P.H.; Schulz, L.O. Effects of a traditional lifestyle on obesity in Pima Indians. Diabetes Care, 1994, 17, 1067-74.
46. Schulz, L.O.; Bennett, P.H.; Ravussin, E.; Kidd, J.R.; Kidd, K.K.; Esparza, J.;Valencia, M.E. Effects of traditional and western environments on prevalence of type 2 diabetes in Pima Indians in Mexico and the U.S. Diabetes Care, 2006, 29, 1866-71.

47. Berthoud, H.R. Multiple neural systems controlling food intake and body weight Neurosci. Biobehav. Rev., 2002, 26, 393-428.

48. Berthoud, H.R.; Morrison, C. The brain, appetite, and obesity.Annu. Rev. Psychol., 2008, 59, 55-92.

49. Sakurai, T.; Amemiya, A.; Ishii, M.; Matsuzaki, I.; Chemelli, R.M.; Tanaka, H.et al. a family of hypothalamic neuropeptides and Gprotein-coupled receptors that regulate feeding behavior. Cell, 1998, 92, 573-85.

50. Dulloo, A.G.; Seydoux, J.; Jacquet, J. Adaptive thermogenesis and uncoupling proteins: a reappraisal of their roles in fat metabolism and energy balance. Physiol. Behav., 2004, 83, 587-602.

51. Bachman, E.S.; Dhillon, H.; Zhang, C.Y.; Cinti, S.; Bianco, A.C.; Kobilka,et al. betaAR signaling required for dietinducedthermogenesis and obesity resistance. Science, 2002, 297,843-5.

52. Rousset, S.; Alves-Guerra, M.C.; Mozo, J.; Miroux, B.; Cassard- Doulcier, A.M.; Bouillaud, F.et al. The biology of mitochondrial uncoupling proteins. Diabetes, 2004, 53. Suppl. 1, S130- 35.

53. Coleman RA, Lewin TM, Muoio D . Physiological and nutritional regulation of enzymes of triacylglycerol synthesis. Ann Rev Nutr 2000; **20**: 77–103.

54. Robidoux, J.; Martin, T.L.; Collins, S. Beta-adrenergic receptors and regulation of energy expenditure: a family affair. Annu. Rev. Pharmacol. Toxicol., 2004, 44, 297-323. 30]

55. Robidoux, J.; Martin, T.L.; Collins, S. Beta-adrenergic receptors and regulation of energy expenditure: a family affair. Annu. Rev.Pharmacol. Toxicol., 2004, 44, 297- 323.

56. Samra JS, Clark ML, Humphreys SM, Macdonald IA, Bannister PA, Matthews DR, et al. Suppression of the nocturnal rise in growth hormone reduces subsequent lipolysis in subcutaneous adipose tissue. Eur J Clin Invest 1999; **29**: 1045–1052.

57. Julien P, Despres J-P, Angel A . Scanning electron microscopy of very small fat cells and

mature fat cells in human obesity. J Lipid Res 1989; **30**: 293–299.

58. Peeva E, Brun DL, Ven Murthy MR, Després J-P, Normand T, Gagné C, Lupien P-J, Julien P . Adipose cell size and distribution in familial lipoprotein lipase deficiency. Int J Obes Relat Metab Disord 1992; **16**: 737–744.

59. Weinstock PH, Levak Frank S, Hudgins LC, Radner H, Friedman JM, Zechner R,et al. Lipoprotein lipase controls fatty acid entry into adipose tissue, but fat mass is preserved by endogenous synthesis in mice deficient in adipose tissue lipoprotein lipase. Proc Natl Acad Sci USA 1997; **94**: 10261–10266.

60. Smith SJ, Cases S, Jensen DR, Chen HC, Sande E, Tow B, et al. Obesity resistance and multiple mechanisms of triglyceride synthesis in mice lacking Dgat. Nat Genet 2000; **25**: 87–90.

61. Chen HC, Ladha Z, Smith SJ, Farese Jr RV . Analysis of energy expenditure at different ambient temperatures in mice lacking DGAT1. Am J Physiol Endocrinol Metab 2003; **284**: E213–E218.

62. Osuga J, Ishibashi S, Oka T, Yagyu H, Tozawa R, Fujimoto A, et al. Targeted disruption of hormone-sensitive lipase results in male sterility and adipocyte hypertrophy, but not in obesity. Proc Natl Acad Sci USA 2000; **97**: 787–792.

63. Wang SP, Laurin N, Himms-Hagen J, Rudnicki MA, Levy E, Robert M-F, et al . The adipose tissue phenotype of hormone-sensitive lipase deficiency in mice. Obes Res 2001; **9**: 119–128.

64. Tansey JT, Sztalryd C, Gruia-Gray J, Roush DL, Zee JV, Gavrilova O, et al. Perilipin ablation results in a lean mouse with aberrant adipocyte lipolysis, enhanced leptin production, and resistance to diet-induced obesity. Proc Natl Acad Sci USA 2001; **98**: 6494–6499.

65. Frayn KN, Coppack SW, Fielding BA, Humphreys SM . Coordinated regulation of hormone-sensitive lipase and lipoprotein lipase in human adipose tissue in vivo: implications for the control of fat storage and fat mobilization. Adv Enzyme Regul 1995; **35**: 163–178.

66. Zierath, J.R.; Livingston, J.N.; Thorne, A.; Bolinder, J.; Reynisdottir, S.; Lonnqvist, F.; et al. Regional difference in insulin inhibition of non-esterified fatty acid release from human adipocytes: relation to insulin receptor phosphorylation and intracellularsignalling through the insulin receptor substrate-1 pathway. Diabetologia, 1998, 41, 1343-54. Spiegelman BM, Flier JS. Obesity and the regulation of energy balance. Cell.2001;104:531-543.

67. Ravussin E, Bogardus C. Relationship of genetics, age, and physical fitness to dailyenergy expenditure and fuel utilization. Am J Clin Nutr. 1989;49(5 suppl):968-975.

68. Seeley RJ, Woods SC. Monitoring of stored and available fuel by the CNS: Implications for obesity. Nat Rev Neurosci. 2003;4:901-909.

69. Evans RM, Barish GD, Wang YX. PPARs and the complex journey to obesity. NatMed. 2004;10:355-361.

70. Hutley L, Prins JB. Fat as an endocrine organ: relationship to the metabolicsyndrome. Am J Med Sci. 2005;330:280-289.

71. Pan DA, Lillioja S, Kriketos AD, Milner MR, Baur LA, et al. Skeletal muscle triglyceride levels are inversely related to insulin action. Diabetes. 1997;46:983-988.

72. Boden G, Chen X, Ruiz J, White JV, Rossetti L. Mechanisms of fatty acid-induced inhibition of glucose uptake. J Clin Invest. 1994;93:2438-2446.

73. Unger RH. Lipotoxicity in the pathogenesis of obesity-dependent NIDDM: Genetic and clinical implications. Diabetes. 1995;44:863-870.

74. Niswender KD, Baskin DG, Schwartz MW. Insulin and its evolving partnershipwith leptin in the hypothalamic control of energy homeostasis. Trends Endocrinol Metabolic.

2004;15:362-369.

75. Matsuzawa Y, Funahashi T, Kihara S, Shimomura I. Adiponectin and metabolicsyndrome. Arterioscler Thromb Vasc Biol. 2004;24:29-33.
76. Lafontan M. Fat cells: afferent and efferent messages define new approaches to treat obesity. Annu Rev Pharmacol Toxicol. 2005;45:119-146.
77. Gallagher D, Kuznia P, Heshka S, Albu J, Heymsfield SB, et al. Adipose tissue inmuscle: a novel depot similar in size to visceral adipose tissue. Am J Clin Nutr. 2005;81:903-910.
78. Tan GD, Goossens GH, Humphreys SM, Vidal H, Karpe F. Upper and lower body adipose tissue function: a direct comparison of fat mobilization in humans. Obes Res. 2004;12:114-118.
79. McKeigue PM, Shah B, Marmot MG. Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians. Lancet. 1991;337:382-386.
80. Schwartz MW, Woods SC, Porte D Jn, Seeley RJ, Baskin DG. Central nervous system control of food intake. Nature 2000; 404: 661 – 671.
81. M. Ghayour-Mobarhan, A. Sahebkar, S. M. R. Parizadeh et al., “Antibody titres to heat shock protein 27 are elevated in patients with acute coronary syndrome,” International Journal of Experimental Pathology, vol. 89, no. 3, pp. 209–215, 2008
82. M. Ghayour-Mobarhan, S. A. New, D. J. Lamb et al., “Dietary antioxidants and fat are associated with plasma antibody titers to heat shock proteins 60, 65, and 70 in subjects with dyslipidemia,” The American Journal of Clinical Nutrition, vol. 81, no. 5, pp. 998–1004, 2005.
83. Klop B., Elte J., Cabezas M. Dyslipidemia in obesity: mechanisms and potential targets. Nutrients. 2013;5(4):1218–1240. doi: 10.3390/nu5041218.American Heart Association: "How to Get Your Cholesterol Tested," "Triglycerides," "Triglycerides:

84. Han J. C., Lawlor D. A., Kimm S. Y. Childhood obesity. The Lancet. 2010;375(9727):1737–1748. doi: 10.1016/s0140-6736(10)60171-7. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

85. Friedewald WT, Levy RI, Fredrickson DS (1972). "Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge". Clin.Chem. **18** (6):499502. doi:10.1093/clinchem/18.6.499. PMID 43373 82. (Cited in: Clin. Chem. 1990; 36:15-19).

86. Rai S., Bhatnagar S. Novel lipidomic biomarkers in hyperlipidemia and cardiovascular diseases: an integrative biology analysis. OMICS: A Journal of Integrative Biology. 2017;21(3):132–142. doi: 10.1089/omi.2016.0178. [PubMed] [CrossRef] [Google Scholar]

87. Aronson, D., Bartha, P., Zinder, O., Kerner, A., Markiewicz, W., Avizohar, O., … Levy, Y. (2004). Obesity is the major determinant of elevated C-reactive protein in subjects with the metabolic syndrome. International Journal of Obesity, 28(5), 674–679. doi:10.1038/sj.ijo.0802609

88. Pepys MB. C-reactive protein fifty years on. Lancet. 1981 Mar 21;1(8221):653-7. doi: 10.1016/s0140-6736(81)91565-8.

89. Gauldie J, Richards C, Northemann W, Fey G, Baumann H. IFN beta 2/BSF2/IL-6 is the monocyte-derived HSF that regulates receptor-specific acute phase gene regulation in hepatocytes. Ann NY Acad Sci 1989; 557: 46–58.

90. Hotamisligil GS, Shargill NS, Spiegelman BM. Adipose expression of tumor necrosis factor-alpha: direct role in obesity-linked insulin resistance. Science 1993; 259: 87–91.

91. Purohit A, Ghilchik MW, Duncan L, et al. Aro- matase activity and interleukin-6 production by nor-mal and malignant breast tissues. J Clin Endocrinol Metab. 1995;80:3052-3058.

92. Mohamed-Ali V, Goodrick S, Rawesh A, et al. Sub-cutaneous adipose tissue releases interleukin-6, but nottumor necrosis factor-α, in vivo. J Clin EndocrinolMetab. 1997;82:4196-4200.

93. Fried SK, Bunkin DA, Greenberg AS. Omental and subcutaneous adipose tissues of obese subject's re- lease interleukin-6. J Clin Endocrinol Metab. 1998; 83:847-850.
94. Banks RE, Forbes MA, Storr M, et al. The acute phase response in patients receiving subcutaneous IL-6. Clin Exp Immunol. 1995;102:217-223. Papanicolaou DA, Wilder RL, Manolagas SC, Chrou- sos GP. The pathophysiologic roles of interleukin-6 in human disease. Ann Intern Med. 1998;128: 127-137.
95. Heinrich PC, Castell JV, Andus T. Interleukin-6 and the acute phase response. Biochem J. 1990 Feb 1;265(3):621-36. doi: 10.1042/bj2650621.
96. Kuller LH, Tracy RP, Shaten J, Meilahn EN. Relation of C-reactive protein and coronary heart disease in the MRFIT nested case-control study. Multiple Risk Factor Intervention Trial. Am J Epidemiol. 1996 Sep 15;144(6):537-47. doi: 10.1093/oxfordjournals.aje.a008963.
97. Koenig W, Sund M, Frohlich M, et al. C-reactive protein, a sensitive marker of inflammation, predicts future risk of coronary heart disease in initially healthy middle-aged men. Circulation. 1999;99:237-242.
98. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Plasma concentration of C-reactive protein and risk of developing peripheral vascular dis- ease. Circulation. 1998;97:425-428.
99. Mohamed-Ali V, Goodrick S, Rawesh A, Katz DR, Miles JM, Yudkin JS, Klein S, Coppack SW. Subcutaneous adipose tissue releases interleukin-6, but not tumor necrosis factor-alpha, in vivo. J Clin Endocrinol Metab 1997; 82: 4196–4200.
100. Fernandez-Real JM, Vayreda M, Richart C, Gutierrez C, Broch M, Vendrell J, Ricart W. Circulating interleukin 6 levels, blood pressure, and insulin sensitivity in apparently healthy men and women. J Clin Endocrinol Metab 2001; 86: 1154–1159.
101. Hotamisligil GS, Arner P, Caro JF, Atkinson RL, Spiegelman BM. Increased adipose tissue expression of tumor necrosis factoralpha in human obesity and insulin resistance. J

Clin Invest 1995; 95: 2409–241589.

102. Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW. C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? Arterioscler Thromb Vasc Biol 1999; 19: 972–978.

103. Kern PA, Saghizadeh M, Ong JM, Bosch RJ, Deem R, Simsolo RB. The expression of tumor necrosis factor in human adipose tissue. Regulation by obesity, weight loss, and relationship to lipoprotein lipase. J Clin Invest. 1995 May;95(5):2111-9. doi: 10.1172/JCI117899.

104. Baumann H, Gauldie J. Regulation of hepatic acute phase plasma protein genes by hepatocyte stimulating factors and other mediators of inflammation. Mol Biol Med 1990; 7: 147–159. 30 Vgontzas AN

105. Atar, O. Gulmez, A. Atar et al., "The effects of prior beta-blocker therapy on serum C-reactive protein levels after percutaneous coronary intervention," Clinical Cardiology, vol. 28, no. 5, pp. 243–246, 2005.

106. Muurahainen NE, Kissileff HR, Lachaussee J, Pi-Sunyer FX. Effect of a soup preload on reduction of food intake by cholecystokinin in humans. Am J Physiol 1991;260: R672 – 680.

107. Role of Inflammation in Neuropsychiatric Comorbidity of Obesity: Experimental and Clinical EvidenceDO - 10.1016/B978-0-12-811073-7.00020-9

108. Tyrrell J, Mulugeta A, Wood AR, et al. Using genetics to understand the causal influence of higher BMI on depression. Int J Epidemiol. 2019;**48**(3):834–848. doi: 10.1093/ije/dyy223.

109. Koksal UI, Erturk Z, Koksal AR, Ozsenel EB, Kaptanogullari OH. What is the importance of body composition in obesity-related depression? Eurasian J

Med. 2017;**49**(2):102–106. doi: 10.5152/eurasianjmed.2017.16129.

110. Dolatian A, Arzaghi SM, Qorbani M, Pishva H. The relationship between body mass index (BMI) and depression according to the rs16139NPY gene. Iran J Psychiatry. 2017;**12**(3):201–205.

111. Atlantis E, Baker M. Obesity effects on depression: systematic review of epidemiological studies. Int J Obes. 2008;**32**(6):881–891. doi: 10.1038/ijo.2008.54

112. Luppino FS, de Wit LM, Bouvy PF, et al. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. Arch Gen Psychiatry. 2010;**67**(3):220–229. doi: 10.1001/archgenpsychiatry.2010.2.

113. Lee JH, Park SK, Ryoo JH, et al. U-shaped relationship between depression and body mass index in the Korean adults. Eur Psychiatry. 2017;**45**:72–80. doi: 10.1016/j.eurpsy. 2017.05.025

114. Martin-Rodriguez E, Guillen-Grima F, Aubá E, Martí A, Brugos-Larumbe A. Relationship between body mass index and depression in women: a 7-year prospective cohort study. The APNA study Eur Psychiatry. 2016;**32**:55–60. doi: 10.1016/j.eurpsy.2015.11.003.

115. Carey M, Small H, Yoong SL, Boyes A, Bisquera A, Sanson-Fisher R. Prevalence of comorbid depression and obesity in general practice: a cross-sectional survey. Br J Gen Pract. 2014;**64**(620):e122–e127. doi: 10.3399/bjgp14x677482.

116. Guo HJ, Zhang C. [a study on the relationship between obesity and depression in the elderly of China]. Journal of Sichuan University. Med Sci Edition. 2019;**50**(5):725–730.

117. Schelbert KB. Comorbidities of obesity. Prim Care. 2009 Jun;36(2):271-85. doi: 10.1016/j.pop.2009.01.009.

118. World Cancer Research Fund and American Institute for Cancer Research. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective; American Institute for Cancer Research: Washington, DC, USA, 2007.

119. Barcones-Molero M.F., Sánchez-Villegas A., Martínez-Gonzalez M.A., Bes-Rastrollo M., Martínez-Urbistondo M., Santabárbara J, et al. The influence of obesity and weight gain on quality of life according to the SF-36 for individuals of the dynamic follow-up cohort of the University of Navarra. Rev. Clín. Esp. 2018;218:408–416. doi: 10.1016/j.rce.2018.05.005.

120. Karastergiou K., Mohamed-Ali V. The autocrine and paracrine roles of adipokines. Mol.Cell.Endocrinol. 2010;318:69–78. doi: 10.1016/j.mce.2009.11.011.

121. Zimmet P., Alberti K.G.M.M., Shaw J. Global and societal implications of the diabetes epidemic. Nature. 2001;414:782–787. doi: 10.1038/414782a.

122. Bhupathiraju S.N., Hu F.B. Epidemiology of Obesity and Diabetes and Their CardiovascularComplications. Circ.Res. 2016;118:17231735.doi. 10.1161/CIRCRESAHA. 115.306825

123. Dyson P. The therapeutics of lifestyle management on obesity. Diabet. Obes. Metab. 2010;12:941–946.doi:10.1111/j.1463-1326.2010.01256..

124. Chadt A., Scherneck S., Joost H.G., Al-Hasani H. et al., Molecular links between Obesity and Diabetes: "Diabesity" editors. Endotext [Internet] MDText.com, Inc.; SouthDartmouth,MA,USA:2000.[(accessedon25May2020)].Availableonline: https://www. ncbi.nlm.nih.gov/books/NBK279051/ [Google Scholar]

125. Myers M.G., Jr., Leibel R.L., Seeley R.J., Schwartz M.W. Obesity and leptin resistance: Distinguishing cause from effect. Trends Endocrinol. Metab. 2010;21:643–651. doi: 10.1016/j.tem.2010.08.002.

126. Garvey W.T., Van Gaal L., Leiter L.A., Vijapurkar U., List J., Cuddihy R., et al. Effects of canagliflozin versus glimepiride on adipokines and inflammatory biomarkers in type 2 diabetes. Metabolism. 2018;85:32–37. doi: 10.1016/j.metabol.2018.02.002.

127. Mahabadi A.A., Massaro J.M., Rosito G.A., Levy D., Murabito J.M., Wolf P.A ,et al. Association of pericardial fat, intrathoracic fat, and visceral abdominal fat with cardiovascular disease burden: The Framingham Heart Study. Eur. Heart J. 2008;30:850–856. doi: 10.1093/eurheartj/ehn573.

128. Motie M., Evangelista L.S., Horwich T., Lombardo D., Zaldivar F., Hamilton M,et al. Association between inflammatory biomarkers and adiposity in obese patients with heart failure and metabolic syndrome. Exp. Ther. Med. 2014;8:181–186. doi: 10.3892/etm.2014.1673.

129. Esposito K., Pontillo A., Di Palo C., Giugliano G., Masella M., Marfella R, et al. Effect of Weight Loss and Lifestyle Changes on Vascular Inflammatory Markers in ObeseWomen. JAMA. 2003;289:1799–1804. doi: 10.1001/jama.289.14.1799

130. Protein R.C. Energy Restriction and Weight Loss on Very-Low-Fat Diets Healthy Women. Arterioscler. Thromb. Vasc. Biol. 2001;21:968–971.

131. Lopez-Sandoval J. Cardiovascular Risk Factors in Adolescents: Role of Insulin Resistance and Obesity. Acta Endocrinol. (Bucharest) 2018;14:330–337. doi: 10.4183/aeb.2018.330.

132. World Cancer Research Fund / American Institute for Cancer Research. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington DC: AICR; 2007.

133. World Cancer Research Fund / American Institute for Cancer Research. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington DC: AICR; 2007.
134. Niraula S, Ocana A, Ennis M, Goodwin PJ. Body size and breast cancer prognosis in relation to hormone receptor and menopausal status: a meta-analysis. Breast Cancer Res Treat. 2012;134:769–781.
135. Herschkowitz JI, Simin K, Weigman VJ, Mikaelian I, Usary J, Hu Z, Rasmussen KE, Jones LP, Assefnia S, Chandrasekharan S, et al. Identification of conserved gene expression features between murine mammary carcinoma models and human breast tumors. Genome Biol. 2007;8:R76.
136. Pape-Ansorge KA, Grande JP, Christensen TA, Maihle NJ, Cleary MP. Effect of moderate caloric restriction and/or weight cycling on mammary tumor incidence and latency in MMTV-Neu female mice. Nutr Cancer. 2002;44:162–168.
137. Nunez NP, Perkins SN, Smith NC, Berrigan D, Berendes DM, Varticovski L, Barrett JC, Hursting SD. Obesity accelerates mouse mammary tumor growth in the absence of ovarian hormones. Nutr Cancer. 2008;60:534–541.
138. https://www.niddk.nih.gov/healthinformation/diabetes/overview/preventing-problems/heart-disease-stroke
139. World Health Organization. (2002). Acupuncture: review and analysis of reports on controlled clinical trials.
140. Eskinazi DP, Jobst KA. Editorial. J Altern Complement Med. 1996 Feb 1;2(1):3–6.
141. NIH Consensus Conference. Acupuncture. JAMA. 1998 Nov 4;280(17):1518–24.
142. Beal M. Acupuncture and Oriental Body Work: Traditional and Biomedical Concepts in Holistic Care: History and Basic Concepts. Holist Nurs Pract. 2000 Apr;14(3):69–78.
143. Hicks A, Hicks J, Mole P. Five Element Constitutional Acupuncture E-Book. Elsevier

Health Sciences; 2010. 448 p.

144. Science and Civilisation in China | History of science and technology [Internet]. Cambridge University Press. [cited 2020 Jun 17]. Available from: https://www.cambridge.org/in/academic/subjects/history/history-science-and-technology/science-and-civilisation-china-volume-2,

145. Jagirdar PC. The theory of five elements in acupuncture. Am J Chin Med. 1989;17(3–4):135–8.

146. Dorfer L, Moser M, Bahr F, Spindler K, Egarter-Vigl E, Giullén S, et al. A medical report from the stone age? Lancet Lond Engl. 1999 Sep 18;354(9183):1023–5.

147. Treatment of Diabetes Using Traditional Chinese Medicine: Past, Present and Future | The American Journal of Chinese Medicine [Internet]. [cited 2020 Jun 17]. Availablefrom:https://www.worldscientific.com/doi/abs/10.1142/S0192415X12500656

148. Kong J, Gollub R, Huang T, Polich G, Napadow V, Hui K, et al. Acupuncture de qi, from qualitative history to quantitative measurement. J Altern Complement Med N Y N. 2007 Dec;13(10):1059–70.

149. Acupuncture Effect and Central Autonomic Regulation [Internet]. [cited 2020 Jun 17]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3677642/

150. Dipole theory of interactions of nerve signals | SpringerLink [Internet]. [cited 2020 Jun 17]. Available from: https://link.springer.com/article/10.1007/BF02462367

151. The status and future of acupuncture mechanism research. - Abstract - Europe PMC [Internet]. [cited 2020 Jun 17]. Available from: https://europepmc.org/article/pmc/pmc3155097

152. Melzack R, Wall PD. Pain mechanisms: a new theory. Science. 1965;150(3699):971–979.

153. Kandel ER, Schwartz JH, Jessell TM, Biochemistry D of, Jessell MBT, Siegelbaum S, et al. Principles of neural science. Vol. 4. McGraw-hill New York; 2000.

154. Anton Jayasuriya A. Clinical Acupuncture. B. Jain Publishers; 2002. 1072 p.

155. Gunn CC, Ditchburn FG, King MH, Renwick GJ. Acupuncture Loci: A Proposal for Their Classification According to Their Relationship to Know Neural Structures. Am J Chin Med. 1976 Jan;04(02):183–95.

156. Schnyer RN, Conboy LA, Jacobson E, McKnight P, Goddard T, Moscatelli F, Legedza AT, Kerr C, Kaptchuk TJ, Wayne PM. Development of a Chinese medicine assessment measure: an interdisciplinary approach using the delphi method. J Altern Complement Med. 2005;11(6):1005–13.

157. O'Brien KA, Birch S. A review of the reliability of traditional East Asian medicine diagnoses. J Altern Complement Med. 2009;15(4):353–66.

158. Sharpe P, Blanck H, Williams J, Ainsworth B, Conway J. Use of complementary and alternative medicine for weight control in the United States. J Altern Complement Med. 2007;13(2):217–22.

159. http://www.shen-nong.com/eng/lifestyles/tcmrole_obesityweight_cause.html

160. https://www.linkedin.com/pulse/fight-obesity-needles-4-duanyang-zhang

161. Moxibustion in Acupuncture: What You Should Know. American Institute of AlternativeMedicine.Retrivedfromhttps://www.aiam.edu/acupuncture/moxibustion/.

162. Deng H, Shen X. The mechanism of moxibustion: ancient theory and modern research. Evidence-Based Complementary and Alternative Medicine. 2013 Aug;2013.

163. Wang LH, Huang W, Zhou W, et al. Moxibustion combined with characteristic lifestyle intervention of Traditional Chinese Medicine in the treatment of abdominal obesity: A study protocol for a randomized controlled trial. Medicine (Baltimore). 2020;99(43):e22855.

164. Yeh, Yuan-Chieh et al. “The Beneficial Effects of Moxibustion on Overweight Adolescent Girls.” Evidence-based complementary and alternative medicine : eCAM vol. 2021 1943181. 10 May. 2021, doi:10.1155/2021/1943181

165. https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm

166. Tantawy SA, Kamel DM, Alsayed N, Rajab E, Abdelbasset WK. Correlation between body mass index, neck circumference, and waist-hip ratio as indicators of obesity among a cohort of adolescent in Bahrain: A preliminary cross-sectional study. Medicine (Baltimore). 2020;99(17)

167. Text of acupuncture (Atlas of acupuncture, Claudia flocks)

168. Ji, Y., Li, S., Zhang, X. et al. The prophylactic and therapeutic effects of moxibustion combined with traditional Chinese medicine decoction for treating chemotherapy-induced myelosuppression in early-stage breast cancer: study protocol for a randomized controlled trial. Trials **21,** 844 (2020).

169. Wang LH, Huang W, Zhou W, Zhou L, Zhou XL, Zhou P,. Moxibustion combined with characteristic lifestyle intervention of Traditional Chinese Medicine in the treatment of abdominal obesity: A study protocol for a randomized controlled trial. Medicine (Baltimore). 2020 Oct 23;99(43):e22855. doi: 10.1097/MD.0000000000022855.

170. Morell-Azanza L, Ojeda-Rodríguez A, Ochotorena-Elicegui A, et al. Changes in objectively measured physical activity after a multidisciplinary lifestyle intervention in children with abdominal obesity: a randomized control trial. BMC Pediatr 2019;19:90.

171. Li WQ, Jiang W, Liu J. Treatment of simple obesity patients with phlegm dampness stagnation syndrome with warming needle moxibustion. Zhen Ci Yan Jiu 2018;43:522–5. [35] Ren BB, Liu ZC, Xu B. Observation on the efficacy of female obesity complicated with climacteric syndrome treated by acupuncture and moxibustion. Zhongguo Zhen Jiu 2012;32:871–6

172. Abdi H, Zhao B, Darbandi M, Ghayour-Mobarhan M, Tavallaie S, Rahsepar AA, Parizadeh SM, Safariyan M, Nemati M, Mohammadi M, Abbasi-Parizad P, Darbandi S, Akhlaghi S, Ferns GA. The effects of body acupuncture on obesity: anthropometric parameters, lipid profile, and inflammatory and immunologic markers. ScientificWorldJournal. 2012;2012:603539. doi: 10.1100/2012/603539. Epub 2012 Apr 29.

173. Berman BM, Lao L, Langenberg P, Lee WL, Gilpin AM, Hochberg MC. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. Annals of internal medicine. 2004 Dec 21;141(12):901-10.

10.0 ANNEXURE-I

INFORMED CONSENT FORM

Government Yoga and Naturopathy Medical College, Arumbakkam, Chennai-600106

Title of the study: Effect of moxibustion on c-reactive protein (CRP) and lipid profile in obese individuals – a pre- post design

Principal Investigator (PI): Dr.S.Sonia

Participant's Name:

Name of the Institution: Government Yoga & Naturopathy Medical College & Hospital, Chennai – 600 106

I have been invited to participate in the research study titled "Effect of Moxibustion On C-Reactive Protein(CRP) And Lipid Profile in Obese Individuals – A Pre- Post Design". I understand that it will involve Moxibustion (a mode of heat treatment), which may be useful for my well-being.

I am aware that there may be no benefit to me personally and that I will not be compensated whatsoever.

I had given the opportunity to ask questions about the study and the questions what I asked have been answered to my satisfaction.

I understand that I have the right to withdraw from the research at any time without affecting my medical care or legal rights.

Hereby, I confirm that I have understood the above study. I myself consciously give consent to participant in this study.

Date: **Patient's Signature:**

I have accurately read or witnessed the accurate reading of the consent form to the potential participant, and the individual has given opportunity to ask questions. I confirm that theindividual has given consentconsciously.

Date: **PI's Signature:**

ANNEXURE-II

PROFORMA

Government Yoga and Naturopathy Medical College, Arumbakkam, Chennai-600106

Title of the study: Effect of moxibustion on C - reactive protein (CRP) and lipid profile in obese individuals – a pre- post design

Demographic Details:

Subject Code: Name:

Gender: Age (years): Marital status:

Education: Occupation:

Address (PIN): Residing at: Urban/Rural

Outcome measures:

Parameter		**Pre-test**	**Post-test**
Anthropometry Measurement	Height (meter)		
	Weight (kg)		
	Body Mass Index (kg/m^2)		
	Waist hip ratio		
C-Reactive Protein (mg/dL)			
Lipid Profile	LDL-C (mg/dL)		

	HDL-C (mg/dL)		
	Triglycerides(mg/dL)		

Note: LDL-C = Low Density Lipoprotein Cholesterol; HDL-C = High Density Lipoprotein Cholesterol.

ANNEXURE-III

SCREENING FORM

Government Yoga and Naturopathy Medical College, Arumbakkam, Chennai-600106

Title of the study: Effect of moxibustion on C-reactive protein(CRP) and Lipid profile in obese individuals – a pre- post design

Demographic Details:

Screening ID No.: Date:

Name of the participant: Contact No:

Gender: Age (years): Address:

Eligibility criteria:

Inclusion criteria:

Are you willing to give written informed consent?	Yes	No
Are you aged between 17yrs – 35yrs?	Yes	No
Is your BMI >25(kg/m^2)	Yes	No
Are you Willingandaccept moxibustion intervention and to comply with the requirements of the study protocol.	Yes	No
Are you willing and able to attend all the session of the hospital based program?	Yes	No

Exclusion criteria:

Are you currently participating in any other clinical trial in the same hospital or other site?	Yes	No
Do you have any of the following conditions or other conditions that would prevent the participant completing the trial follow up duration?		
• Hypertension, myocardial infarction, Chronic bronchitis, Rheumatoid arthritis	Yes	No
• Degenerative disorders, nervous diseases, psychiatry illness	Yes	No
• Under medication for chronic illness	Yes	No
• Women during pregnancy and lactation	Yes	No
• Smoking & Estrogen use	Yes	No
• Undergone any surgery for the past 6 months	Yes	No

*The subject is **Eligible/Not eligible** to participate in the study based on the eligibility criteria

Principle investigator's signature: Date: