The Impact of Weight Loss as a Possible Index of the Metabolic Syndrome in Obese People

Assaf Ray

Charles University 3rd Faculty of Medicine, Prague

Department of Preventive Medicine

March 28, 2006

Received 23rd March 2006

Acknowledgements

I would like to thank the following colleagues for their assistance in making this paper possible...

Doc. MUDr. Vladimir Stich

Dr. Bohumer Prochazka

Gil Kovac

Torill Landquist

The Impact of Weight Loss as a Possible Index of the Metabolic Syndrome in Obese People

Abstract

We have studied the impact of weight loss as a possible index for the metabolic syndrome in obese subjects. Glucose disposal rates (use as inverse index for insulin resistance) were measured at one month intervals for 4 months before and after weight reduction, and a weight maintenance diet given to 33 obese females. Weight loss was recorded for all subjects, and glucose disposal rates increased for most of the study group during the study periods. Statistical calculations found that the correlations between these two variables are insignificant. These results therefore indicate that an inverse relationship does exist between weight loss and glucose disposal rates, but that the correlation between these two variables are insignificant and therefore, weight loss as an independent factor is a poor index for the metabolic syndrome.

Introduction

Obesity is a chronic disease that is increasing in prevalence, and that carries a significant risk for the development of diabetes mellitus, hypertension, heart disease, gallbladder disease, as well as certain types of cancer(breast, endometrial, colorectal, prostate). Over half of Americans between the ages of 20-75 years of age are overweight. The WHO has acknowledged that obesity is a worldwide problem which also affects many developing countries. The term obesity implies excess storage of body fat, and results from cumulative ingestion of more calories than the body uses to maintain its energy needs. The WHO defines obesity as a body mass index(BMI) greater than 30kg/m^2 (see below).

Most patients suffer from what is referred to as simple obesity. In other conditions, such as hypothyroidism, Cushing's syndrome, hypothalamic damage(trauma, tumor, surgery), genetic syndrome(ex:Prader-Willi syndrome), and drug induced(ex:corticosteroids), obesity is an associated feature. Simple obesity is that which is not associated with other primary conditions as mentioned above, but is clearly related to the ingestion of excess caloric intake.

Pathogenesis

For some reasons that may be obscure, an individual enters into positive caloric balance. The suggested mechanism by which obesity develops has been studied extensively over the years, and most likely will need much more research in the future.

Genetics and Environmental:
These have always been difficult to separate when studying the pathogenesis of obesity, however refeeding experiments in monozygotic and dizygotic twins suggest that a genetic influence accounts for 70 % of the change in body mass index later in life, and that childhood environment has little or no influence. Genetic factors have

lead to the discovery of a putative gene, firstly in the obese (ob/ob) mouse and now in humans. The ob gene is found on chromosome 17 and produces a 16Kda protein called leptin. The ob gene was shown to be expressed only in both brown and white adipose tissue. In the ob/ob mouse, a mutation the ob gene leads to production of non-functioning protein. Administration of leptin to these obese mice reduces food intake and corrects the obesity. A similar situation has been described in a very rare genetic condition in humans in which leptin is not expressed. Leptin is secreted from fat cells and can act as a feedback mechanism between adipose tissue and the brain, controlling fat storage by regulating hunger, satiety and energy expenditure(see later). In obese subjects, leptin mRNA in subcutaneous adipose tissue is higher that in controls, plasma levels in obese subjects are very high, correlating with BMI. On the other hand, weight loss due to food restriction reduces plasma levels of leptin. This supports the notion that leptin plays an important part in regulation of food intake, however in the obese subjects the structure of the leptin was found to be normal so that the problem may actually be in the leptin receptor. Finally, also supporting the argument for genetic influence is the idea that from an evolutionary perspective it seems that humans have evolved to defend against energy deficit better than against energy excess. Therefore, it is not surprising that obesity is largely restricted to human and domestic animals.

Food Intake:
We may regard food intake as part of environmental influence in obesity. Factors related to home environment such as finances and availability of snacks, sweets and the way that food is presented, can influence food intake. It has been shown that obese patients eat more than they admit, and over the years small daily excess can lead to large accumulations of fat. For example, daily excess of 10.5 kilocalories can lead to a 10kg weight gain over 20 years.

Control of Appetite:
Appetite is the desire to eat and is usually initiates food intake. The control of appetite is a complex of interactions between external stimuli such as company, type of food, the surroundings and the patient's habitual behavior. Satiation occurs following a meal. Satiety depends on the following: gastric and duodenal distension, and the release of substances working centrally and peripherally. Following a meal, cholecystokinin, bombesin, enterostatin and somatostain are released from the small intestine. Glucagon and insulin are released from the pancreas. All of these hormones have been implicated in the control of satiety. Leptin mediates its action by receptors located in the hypothalamic nuclei, particularly ventromedial, dorsomedial, paraventricular and arcuate. Activation of these nuclei produces a complex of responses which can be functionally viewed as the following: a)inhibition of signals that have positive effect on appetite, mediated by neuropeptideY in the arcuate nucleus. b) stimulate signals that have a negative effect on appetite such as pre-opiomelanocortin precursor polypeptide in the arcuate nucleus, and corticotrophin releasing factors in the paraventricular nucleus. This system potentially provides sensitive feedback regulation by which a reduction in adipose tissue will result in decreased release of leptin and will stimulate appetite to restore energy deficit. In contrast, increased adipose tissue results in increased leptin release which is expected to reduce appetite. The complexity of this system lies in the fact that obese people have excess adipose and increased levels of circulating leptin, but appetite is not reduced. As mentioned above, the defect may lie in the leptin receptor or in the

intracellular mechanism. New mediators are being discovered in mammals and their role in appetite regulation remains to be defined.

Energy Expenditure:
The basal metabolic rate in obese subjects is higher than in non-obese individuals. This is associated with increased lean body mass. Also, as obese individuals have larger mass to move, they tend to expend more energy during physical activity, in contrast to the non-obese. However, obese people tend to decrease their amount of physical activity. In addition, physical activity plays a small part in the total energy expenditure, but the increase in body fat takes place over many years so any change in energy balance is important.

Thermogenesis:
About 10% of ingested energy is dissipated as heat. This dietary-induced thermogenesis has been reported to be lower in obese and post-obesity subjects than it is lean subjects. This tends to favor energy accumulation in obesity and those predisposed to obesity. Insulin resistance and its role in the genesis of obesity will be discussed later as part of the section regarding metabolic syndrome.

From the above suggested mechanisms for the development of obesity, we can assume that obesity can be viewed as a consequence of the interaction between environmental, socio-economic, psychological and cultural forces and in the individual's genetic base. In particular, this refers to genes involved in the storage of fat when energy is limited, and create an increased risk for obesity when food is abundant and energy expenditure is decreased.

Morbidity and Mortality
Obese patients are at risk of early death. This is mainly due to diabetes mellitus, coronary artery disease, and cerebrovascular disease. A direct correlation has been shown between the degree of obesity and morbidity and mortality rates. For example, a male who is 10% overweight has a 13% increased risk for death, while the increase in morbidity in those 20% overweight, is 25%(3). Weight reduction decreases this mortality and therefore should be encouraged, especially with greater degrees of obesity.

Clinical Features
Most patients recognize their own problem. Many symptoms are related to a psychological problem or social pressures. Assessment of the degree of obesity can be made by many methods, among which the most common are BMI(comparison with table of ideal weight for height), skin fold thickness and waist/hip ratio. Ranges of BMI can be used to classify the degrees of overweightness and the associative risks of Co-morbidity. The following is the WHO classification:

	BMI(kg/m^2)	Risk of co-morbidities
Overweight	25-30	Mildly increased
Obese	>30	
Class I	30-35	Moderate
Class II	35-40	Severe
Class III	>40	Very severe

Skin fold thickness is measured over the midpoint of the triceps muscle. Normal values are equal or below 20mm in men and 30mm in women. A central type of fat distribution with waist/hip ratio of more than 1.0 in men and 0.9 women is associated with a higher risk of morbidity and mortality than in peripheral type of body fat distribution(waist/hip ratio <0.85 in men, <0.75 in women). The central type of fat distribution, mostly intra-abdominally, is more sensitive to lipolytic stimuli. This results in more severe metabolic abnormalities and the complications associated with obesity. These complications include: psychological problems, osteoarthritis of knees and hip, hiatus hernia, gallstones, back strain, hypertension, ischemic heart disease, stroke, non-insulin dependent diabetes mellitus, hyperlipidemia, menstrual abnormalities and increased morbidity and mortality.

Treatment

Obesity is a chronic disease of which the etiology is usually unknown, making a definitive cure unlikely. Therefore, prevention and palliation are the main therapeutic goals. These objectives require lifelong commitment and are therefore very hard the follow. It requires nutritional, psychological, medical as well as surgical support.

Prevention in obesity must always be the goal. As most obese people have difficulties to maintain any weight loss they have managed to achieve, all health professionals must be aware of the danger related to obesity and should encourage children as well as adults to avoid gaining too much weight. It is important to remember that small amounts of weight gain each year over a long period can produce an obese individual.

Dietary control is largely dependant on reduction of food intake. The most commonly used diets allow daily caloric intake ranging from 1000-1500Kcal for someone with physical work. This requires permanent change in eating habits and prolonged dieting is necessary for large amounts of fat to be lost, as well as to maintain the lowered weight. Long-term success with low-calorie diets among obese patients is poor, with an overall success rate of ten percent. An increase in exercise will increase energy expenditure and if not contraindicated, should be encouraged since maintaining new low weight level is usually not achieved without exercise. Exercise alone will usually produce little long-term benefits. On the other hand, there is evidence showing that in combination with dietary control, exercise can prevent weight from being regained. In addition, regular exercise can improve general health and support motivation. The diet must contain adequate amounts of protein, vitamins, and trace elements. For example, 1000Kcal per day should be made up of more than 50grams of proteins, 100grams of carbohydrates and 40grams of fat. The carbohydrates should be in the form of complex carbohydrates such as fruits, vegetables and fiber-containing grains and oats. Some research suggests that increased dietary fat intake may be associated with increased risk of development of obesity, and also indicates that diet with less than 25% of fat should contribute to prevention and palliation of obesity. Alcohol should be avoided, as it contains large amounts of calories and often reduces willpower. A balanced diet that increases the frequency of food intake, makes meal presentation more attractive, and includes a variety of foods can play an important role in helping one maintain a healthy dietary regime, and make dietary supplements unnecessary.

Most obese people oscillate in weight, regaining any achieved loss in weight and managing to lose this weight again. This cycling in body weight may play a role in the development of coronary artery disease. Another major issue related to palliation involves behavior modification. The principle of behavior modification is to encourage the obese patient to take personal responsibility for changing lifestyle, which will determine dietary habits and physical activity. Family therapy may be useful, especially when obese children are involved.

Drugs should not be used as a sole means of therapy. When used they should be in combination with dietary regime and exercise. They must not be substitute for strict dieting and should be reserved for individuals with BMI >30 or more than 27 with co-morbidity. Drugs acting on neurogenic pathways to suppress appetite, such as phenteramine or drugs working on serotogenic pathways to suppress appetite such as fenfluoramine are associated with the development of valvular heart disease and pulmonary hypertension and are no longer used in some countries. Peripherally acting drugs, such as Orlistat, act by inhibiting pancreatic and gastric lipases, reducing the absorption of dietary fat. The patient may complain of diarrhea during treatment, and to avoid this they take a low-fat diet which results in weight loss. When the drug is stopped, weight regain occurs.

Few surgical procedures are available, and should be reserved for cases of severe morbid obesity(BMI>40 or >35 with Co-morbidity). Gastric banding involves the encirclement of an adjustable band around the proximal stomach, which divides it into a small pouch and large remnant. This gives the patient a feeling of fullness after the consumption of small amounts of food. The results are variable. Gastroplasty involves the creation of a small pouch by stapling the stomach vertically and employs the same principle as for gastric banding. Good results have been reported, but slow weight regain occurs as the patient adopts new eating patterns such as ingesting small, frequent meals, or drinking calorie-containing shakes which do not cause discomfort. Finally, gastric bypass surgery has resulted in good weight reduction over long periods of time, but is associated with many long-term complications.

For most people, obesity refers to someone who cannot control his/her appetite. It is true that excess calories are the central cause of excess body fat accumulation, but the genesis of obesity is much more complex and involves many factors of which many are poorly understood. This discussion of obesity includes some of these factors which are seen as being very important, but does not mention of all them. Established obesity is very difficult to treat, and requires the adoption of new life habits related to diet and exercise if weight loss is to be achieved and maintained. Therefore, prevention must be considered as to avoid entering the stage of obesity and its related health problems.

Metabolic syndrome

The metabolic syndrome is a cluster of abnormalities associated with insulin resistance which play a major in the development of coronary heart diseases. Insulin resistance is suggested to be the root cause of the metabolic syndrome, also know as syndrome x(7).

The normal physiologic response to the defect in insulin mediated glucose uptake by cells is an increase in the plasma concentration of insulin(7). This state of

hyperinsulinaemia leads to varying degrees of glucose intolerance, dyslipidaemia(high plasma concentration of triglycerides(TG)), and low concentrations of high density lipoprotein(HDL) cholesterol, hypertension, hyperuricaemia, abnormalities in the fibrinolytic system, the development of obesity(2) and polycystic ovary syndrome(PCOS)(10).
When the pancreas is no longer able to sustain compensatory hyperinsulinaemia, non-insulin dependent diabetes mellitus (NIDDM) can develop(7).
The following is the WHO, and the American Heart Association criteria for having the metabolic syndrome:

Component	WHO	NCEP/ATP III
Obesity	BMI >30, WHR > 0,85 w, 0,90 m	Waist circumference >88 w, >102 m .
Glucose metabolism	Type 2 diabetes Impaired glucose tolerance	Fasting blood glucose > 110 mg/dl
Dyslipidemia	Plasma triglycerides > 1,7 mmol/l HDL cholesterol < 0,9 mmol/l w < 1,0 mmol/l m	Triglycerides > 150 mg/dl HDL cholesterol < 40 mg/dl w < 50 mg/dl m
Hypertension	Current antihypertensive therapy or BP > 140/90 mm Hg	Current antihypertensive therapy or BP > 130/85 mm Hg
Other	Microalbuminuria . 20 ug/min	
Diagnosis criteria	DM 2 or IGF and 2 criteria or Any 3 criteria	Any 3 criteria

The following discussion will be made on the suggested pathogenesis of the metabolic syndrome and the relation between the metabolic consequences of insulin resistance and/or hyperinsulinaemia , the diseases which are associated with these abnormalities and the possible ways of prevention and treatment of this metabolic state.

The exact cause of the metabolic syndrome is not known. Insulin resistance and compensatory hyperinsulinaemia are believed to be the root causes of these metabolic abnormalities, and the other parameters of this syndrome are secondary to the hyperinsulinaemia. This can be supported by the observations that improving the insulin sensitivity with a corresponding decrease in plasma insulin levels either by diet, exercise, or by drugs, all show to improve all the other parameters of the syndrome(7). There are believed to be many factors contributing to the genesis this syndrome and include our environment and lifestyle, high fat, refined sugar diets which are consumed in many western societies, and lack of movements and exercise. Some people may also have a genetic predisposition to insulin resistance, while others can develop the condition through high stress and unhealthy lifestyles. The belief that diet is a major underlying factor in the genesis of insulin resistance comes from a long (2-year) feeding study where rats were raised on either a very low fat, high complex carbohydrate diet, or high fat, sucrose diet(9). After two years the high fat, sucrose

diet fed rats were obese, hyperinsulinaemic, hypertensive, hypertriglyceridaemic and hypercoagulable.

There are genetic determinants for the development of insulin resistance. For example, the offspring of persons with NIDDM shown to be insulin resistant compared with those with no NIDDM relatives(9). Studies on groups such as the Australian Aburigines, the American Pima Indians and other similar populations were found to have a very high incidence of insulin resistance and some aspect of the metabolic syndrome, since these societies have adopted western types of diets and lifestyles(9).
A relationship between physical fitness and insulin-stimulated glucose uptake in humans has been well established in cross–sectional and exercise training studies(7). Furthermore, a trained athlete who do not exercise for several days shows a deterioration in glucose and insulin responses to oral glucose tolerance testing, in the absence of changes in body weight or the percentage of body fat(7).
Animal studies have shown that exercise training prevents the development of insulin resistance and/or hyperinsulinaemia when normal rats are fed diets enriched with simple sugars(7).
Stress is associated with the rise of hormones, especially glucocorticoids, that antagonize the action of insulin. Glucocorticoids cause an elevated level of free fatty acids and blood sugar level, both of which may lead to insulin resistance and/or hyperinsulinaemia. Obesity as a cause for insulin resistance and/or hyperinsulinaemia is discussed below.

Insulin Resistance and Glucose Metabolism:
Insulin resistance, impaired glucose tolerance(IGT) and non-insulin dependent diabetes mellitus (NIDDM): Patients with IGT and NIDDM have tissue resistance to the action of insulin which results in hyperglycaemia. Some studies have demonstrated a defect in insulin stimulated glucose uptake in subjects with normal blood glucose levels(7) and suggest that in these subjects, like those with IGT, normoglycaemia is maintained by virtue of hyperinsulinaemia(1065). Therefore, the resistance for insulin is widespread within the population, and the increase in plasma insulin levels allow most persons to overcome their defect in the action of insulin(7). However, when the state of hyperinsulinaemia can no longer be sustained, the glucose tolerance will deteriorate with the development of hyperglycaemia(7). A number of studies support the idea that the development of NIDDM may start as insulin resistance with compensatory hyperinsulinaemia, which maintains normal glucose level, followed by IGT and finally as NIDDM(7).

Insulin Resistance and Dyslipidaemia:
Over the past several years, an increasing amount of evidence indicates that insulin resistance and hyperinsulinaemia have an important role in the development of dyslipidaemia, which is characterized by high plasma TG, and low HDL cholesterol concentrations(7). Numerous studies on human insulin resistance show a direct relation between the plasma insulin and TG concentration. Hyperinsulinaemics have increased rates of TG secretion from the liver, and a modulation of the insulin action and/or plasma insulin concentration leads to the expected change in the secretion rate from the liver and the plasma concentration of TG(7). Diets rich in simple sugar(sucrose or fructose (7)) fed to Sprague-Dawly rats resulted in the development of insulin resistance, hyperinsulinaemia and hypertriglyceridaemia. This suggests that

a diet high in carbohydrate can result in the increase of plasma insulin levels, which correlates directly with the increase in the TG concentration (7). Furthermore, when these rats were exercise trained, which prevents the development of insulin resistance, they did not develop hyperinsulinaemia and hypertriglyceridaemia(7). All this data provides us with evidence for a major role for insulin in the regulation of TG synthesis and concentration. Finally, the increase in TG synthesis and its mobilization to the periphery for storage in adipocytes, may lead to weight gain and the development of obesity.
The relation between insulin resistance and insulin concentration to HDL cholesterol has been demonstrated as well. Studies of populations have demonstrated that plasma insulin concentration is inversely correlated with the concentration of HDL cholesterol(7), and that this relationship is independent of factors such as obesity or the level of physical fitness(7). The mechanism to explain the relation of insulin resistance and hyperinsulinaemia to HDL cholesterol level has been incompletely elucidated, but hyperinsulinaemia has been show to correlate with the catabolic rate of apolipoprotein A1 HDL, and with the decrease in plasma HDL cholesterol concentration (7).

Insulin resistance and plasminogen activator inhibitor 1(PAI-1):
PAI-1 forms a complex with tissue plasminogen activator to inhibit its action, and by this mechanism plays an important role in fibrinolytic activity. An increased level of PAI-1 will result in impaired fibrinolysis which may increase the risk for the development of coronary heart disease(7). PAI-1 levels were found to be high in patients with NIDDM, hypertriglyceridaemia, and hypertension(1067). This association of PAI-1 with other metabolic disorders that are known to be related to insulin resistance suggest that PAI-1 in itself may be related to insulin resistance(7). Evidence that insulin resistance and/or insulin concentration may play a role in the regulation of PAI-1 levels comes from studies where intervention that enhances insulin sensitivity and/or concentration also decreased PAI-1 levels(7). The same was true for low caloric diets, and for physical activity(7). When metformine, an anti-hyperglycaemic oral medication was administrated to non- diabetic women, it resulted in decreased plasma levels of insulin, TG, and a fall in the PAI-1 concentration as well(7).

Obesity and Insulin Resistance:
It as already been recognized 50 years ago that obesity can leads to a decrease in insulin mediated glucose uptake by cells, and to hyperinsulinaemia(7). However, the baseline of insulin level is independent of body weight, or on the body fat distribution(9). Obesity is not the only condition where these metabolic disorders can be observed. The fact that insulin resistance is observed mainly in obese individuals suggests that obesity is an important pathological condition by which insulin resistance can develop. The mechanism by which obesity can effect these metabolic changes are poorly defined, but these metabolic defects may be corrected by weight loss(7). Many studies reported that the central type of obesity which is determined by waist-to-hip ratio, and by computed tomography, correlated more strongly with metabolic factors than do the total weight or the BMI(9). It has been shown that woman with predominantly upper body fat distributions appears to have greater resistance to insulin than do women at the same BMI but with lower body fat distributions(7). The linked between obesity and insulin resistance may be related to fat distribution and to the size of the adipocytes. The abdominal fat distributions have

greater rates of lipolysis and FFA mobilization to the liver, and this may decrease the ability of the liver to clear the insulin from the circulation which results in hyperinsulinaemia. FFA may also directly impair the actions of insulin. The increase in basal lipolysis is also associated with increased supply of glycerol which is released from the large adipocytes and can stimulate hepatic gluconeogenesis, contributing to increased blood glucose levels and further stimulate insulin release (1). The cytokine TNF, which is produced by adipocytes, is over expressed in the obese, and is capable of inhibiting the action of insulin.

Insulin Resistance and Diseases:
It has been confirmed by many that plasma insulin concentrations are higher in persons with hypertension compared with those who are normotensive(7). Furthermore, hyperinsulinaemia in persons with hypertention persists despite normalization of blood pressure by antihypertensive medications(7). The mechanism by which insulin resistance and/or hyperinsulinaemia cause hypertension is unclear. One hypothesis suggests that insulin resistance and hyperinsulinaemia enhance sodium reabsorption by the renal tubule, and also increase the sympathetic outflow to promote the increase in peripheral resistance(2). The relation of insulin resistance and/or hyperinsulinaemia to the risk for the development of coronary heart diseases (CHD) can be linked by the metabolic consequences that are associated with insulin resistance, including hypertension, dyslipidaemia, and the changes in the clotting system. All of these factors are known to increase the risk for CHD independent of one another.

Obesity, insulin resistance and polycystic ovarian syndrome(PCOS):

PCOS affects approximately 5-10% of reproductive aged women. The hallmark features of this syndrome are androgen excess and chronic anuvulation(10). Clinically, the most common symptoms associated with this syndrome are hirsutism(90%), menstrual irregularities(90%), infertility(75%), and obesity, found in approximately 50%(10). There is no universal agreement regarding the pathogenesis of PCOS, and recent reviews have suggested a multifactorial etiology(10). There are at least five major systems that may contribute to the development of this syndrome, including: (1)the hypothalamus and pituitary; (2)ovary; (3)skin; (4)adrenal; and (5) pancreas. The characteristic biochemical abnormalities include ovarian hyperandrogenism, adrenal hyperandrogenism, inappropriate gonadotropin secration, peripheral hyperandrogenism, and hyperinsulinaemia. It has been suggested that these hormonal abnormalities represent a vicious cycle of events that perpetuate PCOS. The inappropriate gonadotropin secretion involves an elevated level of lutenizing hormones (LH), and a normal or low level of follicle-stimulating hormone(FSH). These abnormalities in gonadotropin levels may be due to a primary central defect in the hypothalamus and/or pituitary, or to the extraglandular conversion of androstendion to esrone, which result in elevated levels of LH and decreased levels of FSH, resulting in anovulation. The extraglandular formation of estrone predominantly takes place in the adipose tissue, and as obese women have greater a amount of fat tissue, this extraglandular formation of estrone will also be greater. Fifty percent of patients with PCOS have an elevated level of dehydroepiandrosterone sulfate. This hormone is secreted from the adrenal gland and may have a role in the pathogenesis of the

PCOS. The severity of insulin resistance is strongly correlated with the degree of hyperinsulinaemia which in turn is highly correlated with the severity of the hyperandrogenism, and it is not the hyperandrogenosm which causes the insulin resistance. Lowering the ovarian androgen production has no effect on insulin resistance and/or hyperinsulinaemia(10). Insulin resistance and/or hyperinsulinaemia may lead to the development of PCOS by at least two mechanisms. Firstly, an excess of insulin can directly stimulate the ovaries to produce a large amount of the male hormone testosterone, which may lead to the prevention of ovulation, infertility, menstrual irregularities, and hirsutism. Hyperinsulinaemia can also increase the conversion of androgens to estrogens. Upsetting the delicate balance between these hormones can lead to weight gain and the formation of PCOS. Secondly, insulin resistance can cause an excess accumulation of body fat, and is associated with the development of obesity. As mentioned above, the greater the body fat, the higher the extraglandular estrogen formation which in turn can lead to inappropriate gonadotropin secretion.

In the past, the diagnosis of PCOS was based on the anatomical findings of polycystic or sclerocystic ovaries. Today it has become increasingly clear that PCOS is a heterogenous syndrome, and there has been considerable debate regarding its diagnostic criteria. The following is the Lobo's Diagnostic Criteria for PCOS:

Perimenarcheal onset of menstrual irregularity.

Androgen excess.

Chronic anovulation.

Inappropriate gonadotropin secretion(LH:FSH ratio more than 3).

Obesity.

Euprolactinaemia.

(1).

Controlling the metabolic syndrome conservatively:
Realizing that insulin resistance and/or hyperinsulinaemia are the central factors responsible for the metabolic syndrome, it can be inferred that controlling insulin resistance may improve all other aspects of this syndrome. Both diet and exercise are important in preventing and controlling the syndrome. Reports from studies show that when healthy adults were switched from the typical western high-fat, refined sugar diet to a high-complex carbohydrate, high fiber diet, the peripheral insulin sensitivity was significantly increased(6). Supportive data show that a high complex carbohydrate, high fiber diet improved the metabolic control of insulin resistance(6). Exercise has been shown to dramatically increase skeletal muscle glucose transport (5), and therefore plays an important role in preventing and controlling insulin resistance. Although the intensity of the exercise seems to be important in decreasing

the degree of insulin resistance, insulin sensitivity can be modified by brisk walking. The term 'metabolic fitness' describes the importance of physiological changes that result from low levels of exercise(9) which is probably suitable for most people, especially the elderly, obese, and patients with hypertension. Decreasing the level of insulin should also improve other parameters of this syndrome. Several studies reported that when insulin resistance is decreased by exercise, the insulin level is reduced with corresponding reduction in plasma TG and increases in HDL cholesterol levels(9). This data clearly indicates that regular exercise can play an important role in the management of the metabolic syndrome. The combination of regular exercise training and diet low in animal fat and high in complex-carbohydrate and fiber can change all the parameters of the metabolic syndrome as well reduce the BMI.

MATERIALS AND METHODS

Subjects: the study consisted of 30 obese females, divided into two subgroups. Subgroup A consisted of 13 obese, PCOS females, and subgroup B consisted of 17 obese, non PCOS females. Table 1 presents the clinical and metabolic features of these two groups (The table preset in the results section).

After giving informed consent, all subjects were placed on a weight reduction diet for the first two months and on a weight maintenance diet for the third month. All subjects remained active to approximately their pre-study exercise levels. None of the subjects had any evidence of disease state or ingested any agent known to affect carbohydrate or insulin metabolism.

Diet: all subjects were placed on a weight reduction diet. The first month they were put on a very low caloric (800kcal\per day) liquid diet, the second month on a low caloric (1200kcal\per day) diet, and the third month on a weight maintenance (30kcal\kg\per day). Glucose disposal was measured by glucose clamp technique after over night fast.

RESULTS

One subject from group A was excluded from the study following the first month, and three subjects from group A and one subject from group B were excluded from the study following the second month.

Table 1Presents the clinical and metabolic features of the study group. The weight is expressed in kilograms. Weight 1 was recorded at the beginning of the study period and weight 4 three months later at the end of the study period.
'Disp' represents glucose disposal, measured as Glucose/Minute/Kilogram.
Parameters are mean.

TABLE 1.

subjets	Wight 1	Weight 2	Weight 3	weight 4	Disp 1	Disp 2	Disp 3	Disp 4
A	95,4	89,1	86,94	81.7	2.778	3.517	3.683	3.847
B	102.1	94.7	91.5	89.5	2.565	3.203	3.678	4.175
A+B	98.7	91.9	89.3	86.6	2.672	3.360	3.681	4.012

SE CH 7 B1

It can be see that most of the subjects had significant weight loss during the study periods. The mean weight loss for group A was 14.3% the mean weight loss for group B was 12.5% and the mean weight loss for the all group was12.3%. And the overall change in the glucose disposal rate during the study had an inverse relationship to the weight loss, the mean glucose disposal for group A increased by 38%, for group B the mean glucose disposal increased by 63%, and for the all group mean glucose disposal increased by 50%.

STATISTICAL CALCULATIONS

We used the Spearman correlation at significant level of 5% coefficient to find if any correlation exists between weight loss and glucose disposal. The calculation was made for all the groups, and for group A and B individually. The results are presented in tables 2, 3, and 4. It is apparent that the weight loss is consistent with the changes in the glucose disposal rate, although an inverse relationship exists, the correlation between these two variables are insignificant, and therefore, from the results of this study weight loss is shown to be a poor index for the metabolic syndrome.

DISCUSSION

We found in our study that weight loss and glucose disposal rates in obese people have an inverse relationship, however we did not find correlations between these two parameters. Therefore, other factors that we did not study must play role in the change in glucose disposal in these obese people. Olesky et al, and DeFronzo et al, also found in their studies that weight loss can correct the defect in the resistance to insulin-stimulated glucose uptake, but they could not define the mechanism responsible for these changes(8,4). Barnard, J. and Wen, S. conclude in there report on exercise and diet in prevention and control of the metabolic syndrome that regular aerobic exercise, especially when combined with a very low-fat, and high complex-carbohydrate diet, can reverse the metabolic syndrome. They also stress in their report that insulin and lipid changes are greater when accompanied by reduction in abdominal fat(9). We can see from our study and these two reports that weight loss does play some role in the changes of the resistance for insulin, and it is possible that we need to make a larger study taking into consideration these other factors which can influence the results of the changes in insulin resistance and try to study each one separately in order to see the importance of weight loss as an independent factor, and this may help establish any correlations between these two variables that may exist.

Conclusion

The available data suggest that obesity which is a result of a genetic predisposition and the typical sedentary lifestyle, combined with a high fat, high refined sugar diet consumed by many western societies is a common problem in developed countries and is becoming more common in developing countries. The data also indicates that obesity is associated with the increasing prevalence of many disease conditions, which have a direct relation to the degree of obesity. Obesity is an important pathological state for the genesis of the metabolic syndrome, and since this syndrome is made up many factors shown to be important risk factors for coronary heart diseases, it must be playing an important role in the etiology of the number one cause of death in western societies. Since diet and inactivity appears to be major factors contributing to obesity and the metabolic syndrome, it can also reverse these

conditions. We believe that the results of our study, and the results of studies made by others support the importance of diet and/or weight loss in controlling and reversing the degree of insulin resistance and the other parameters of the metabolic syndrome. Fukagawa et al(6). reported that when healthy adults were switched from the typical Western high fat, refined sugar diet to high-complex-carbohydrate, high fiber diet, peripheral insulin sensitivity was significantly increased. Despres at al(5). point out in there study that insulin sensitivity as well as plasma lipids can be modified by exercise. Insulin and lipid changes can also be observed without changes in body composition, but the changes are grater when accompanied by reductions in abdominal fat(5). We observed in our study that there exists an inverse relationship between weight loss and the glucose disposal rate. However, this study does not tell us if the control over the metabolic syndrome is achieved by the weight loss per se, by the diet or the combination of both, as these two factors may influence the metabolic syndrome independently. We can suggest that weight loss can improve the degree of insulin resistance and other metabolic parameters in obese peoples by decreasing the amount of abdominal fat, and by reducing the size of the adipocytes, which may lower the rate of lipolysis, decrease the amount of circulating FFA and the over expression of cytokines(TNF). Furthermore, as adipocytes get smaller in size, their sensitivity to insulin may increase. It will be difficult to test this hypothesis, as weight loss can not be achieved without diet and/or exercise training, as both seem to be independent factors which can improve the sensitivity of insulin and the other metabolic parameters of this syndrome in obese people.

Table 2, present the statistical calculation of the all groups.

Correlations

		Disp1	Disp2	Disp3	Disp 4	dif12	dif23	dif34	dif13	dif14	difr12	difr23	difr34	difr13	difr14
Disp1	Pearson Correlation	1	,507(**)	,456(*)	,561(**)	-,331	-,398(*)	,080	-,424(*)	-,382	-,065	-,276	,089	-,235	-,250
	Sig. (2-tailed)		,004	,013	,003	,074	,033	,704	,022	,060	,734	,147	,673	,219	,228
	N	30	30	29	25	30	29	25	29	25	30	29	25	29	25
Disp2	Pearson Correlation	,507(**)	1	,664(**)	,459(*)	-,213	-,418(*)	-,151	-,391(*)	-,421(*)	-,041	-,329	-,118	-,256	-,343
	Sig. (2-tailed)	,004		,000	,021	,258	,024	,470	,036	,036	,830	,081	,575	,179	,093
	N	30	30	29	25	30	29	25	29	25	30	29	25	29	25
Disp3	Pearson Correlation	,456(*)	,664(**)	1	,627(**)	-,269	-,306	-,181	-,320	-,291	-,096	-,180	-,157	-,164	-,208
	Sig. (2-tailed)	,013	,000		,001	,158	,106	,387	,091	,159	,620	,351	,455	,395	,318
	N	29	29	29	25	29	29	25	29	25	29	29	25	29	25
Disp 4	Pearson Correlation	,561(**)	,459(*)	,627(**)	1	-,218	-,163	,311	-,211	,023	-,001	-,020	,330	-,029	,176
	Sig. (2-tailed)	,003	,021	,001		,295	,437	,131	,312	,913	,997	,924	,107	,892	,400
	N	25	25	25	25	25	25	25	25	25	25	25	25	25	25
dif12	Pearson Correlation	-,331	-,213	-,269	-,218	1	,634(**)	,191	,883(**)	,730(**)	,760(**)	,487(**)	,177	,664(**)	,560(**)
	Sig. (2-tailed)	,074	,258	,158	,295		,000	,361	,000	,000	,000	,007	,398	,000	,004
	N	30	30	29	25	30	29	25	29	25	30	29	25	29	25
dif23	Pearson Correlation	-,398(*)	-,418(*)	-,306	-,163	,634(**)	1	,153	,923(**)	,747(**)	,485(**)	,936(**)	,124	,841(**)	,701(**)
	Sig. (2-tailed)	,033	,024	,106	,437	,000		,466	,000	,000	,008	,000	,554	,000	,000
	N	29	29	29	25	29	29	25	29	25	29	29	25	29	25
dif34	Pearson Correlation	,080	-,151	-,181	,311	,191	,153	1	,191	,704(**)	,136	,106	,993(**)	,130	,694(**)
	Sig. (2-tailed)	,704	,470	,387	,131	,361	,466		,361	,000	,518	,613	,000	,535	,000
	N	25	25	25	25	25	25	25	25	25	25	25	25	25	25
dif13	Pearson Correlation	-,424(*)	-,391(*)	-,320	-,211	,883(**)	,923(**)	,191	1	,832(**)	,658(**)	,811(**)	,166	,841(**)	,718(**)
	Sig. (2-tailed)	,022	,036	,091	,312	,000	,000	,361		,000	,000	,000	,428	,000	,000
	N	29	29	29	25	29	29	25	29	25	29	29	25	29	25
dif14	Pearson Correlation	-,382	-,421(*)	-,291	,023	,730(**)	,747(**)	,704(**)	,832(**)	1	,546(**)	,641(**)	,682(**)	,684(**)	,912(**)
	Sig. (2-tailed)	,060	,036	,159	,913	,000	,000	,000	,000		,005	,001	,000	,000	,000
	N	25	25	25	25	25	25	25	25	25	25	25	25	25	25
difr12	Pearson Correlation	-,065	-,041	-,096	-,001	,760(**)	,485(**)	,136	,658(**)	,546(**)	1	,587(**)	,130	,847(**)	,679(**)
	Sig. (2-tailed)	,734	,830	,620	,997	,000	,008	,518	,000	,005		,001	,535	,000	,000
	N	30	30	29	25	30	29	25	29	25	30	29	25	29	25
difr23	Pearson Correlation	-,276	-,329	-,180	-,020	,487(**)	,936(**)	,106	,811(**)	,641(**)	,587(**)	1	,082	,926(**)	,733(**)
	Sig. (2-tailed)	,147	,081	,351	,924	,007	,000	,613	,000	,001	,001		,696	,000	,000
	N	29	29	29	25	29	29	25	29	25	29	29	25	29	25
difr34	Pearson Correlation	,089	-,118	-,157	,330	,177	,124	,993(**)	,166	,682(**)	,130	,082	1	,111	,683(**)
	Sig. (2-tailed)	,673	,575	,455	,107	,398	,554	,000	,428	,000	,535	,696		,597	,000
	N	25	25	25	25	25	25	25	25	25	25	25	25	25	25
difr13	Pearson Correlation	-,235	-,256	-,164	-,029	,664(**)	,841(**)	,130	,841(**)	,684(**)	,847(**)	,926(**)	,111	1	,802(**)
	Sig. (2-tailed)	,219	,179	,395	,892	,000	,000	,535	,000	,000	,000	,000	,597		,000
	N	29	29	29	25	29	29	25	29	25	29	29	25	29	25
difr14	Pearson Correlation	-,250	-,343	-,208	,176	,560(**)	,701(**)	,694(**)	,718(**)	,912(**)	,679(**)	,733(**)	,683(**)	,802(**)	1
	Sig. (2-tailed)	,228	,093	,318	,400	,004	,000	,000	,000	,000	,000	,000	,000	,000	

N	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

Table 3, present the statistical calculation of group A.

Correlations

		Disp1	Disp2	Disp3	Disp 4	dif12	dif23	dif34	dif13	dif14	difr12	difr23	difr34	difr13	difr14
Disp1	Pearson Correlation	1	,560(*)	,362	,763(*)	-,265	-,454	,564	-,421	-,520	,009	-,340	,593	-,245	-,371
	Sig. (2-tailed)		,047	,248	,017	,382	,139	,113	,173	,152	,976	,279	,093	,444	,325
	N	13	13	12	9	13	12	9	12	9	13	12	9	12	9
Disp2	Pearson Correlation	,560(*)	1	,825(**)	,633	-,219	-,230	,396	-,289	-,302	-,100	-,184	,424	-,194	-,238
	Sig. (2-tailed)	,047		,001	,068	,472	,473	,291	,362	,430	,744	,568	,255	,546	,537
	N	13	13	12	9	13	12	9	12	9	13	12	9	12	9
Disp3	Pearson Correlation	,362	,825(**)	1	,753(*)	-,439	-,196	,215	-,326	-,225	-,356	-,120	,263	-,228	-,095
	Sig. (2-tailed)	,248	,001		,019	,153	,541	,579	,301	,561	,256	,710	,494	,476	,808
	N	12	12	12	9	12	12	9	12	9	12	12	9	12	9
Disp 4	Pearson Correlation	,763(*)	,633	,753(*)	1	-,553	-,274	,452	-,429	-,260	-,333	-,103	,464	-,215	-,021
	Sig. (2-tailed)	,017	,068	,019		,123	,475	,222	,250	,500	,381	,792	,208	,579	,957
	N	9	9	9	9	9	9	9	9	9	9	9	9	9	9
dif12	Pearson Correlation	-,265	-,219	-,439	-,553	1	,737(**)	-,090	,915(**)	,895(**)	,827(**)	,595(*)	-,116	,727(**)	,657
	Sig. (2-tailed)	,382	,472	,153	,123		,006	,819	,000	,001	,000	,041	,766	,007	,055
	N	13	13	12	9	13	12	9	12	9	13	12	9	12	9
dif23	Pearson Correlation	-,454	-,230	-,196	-,274	,737(**)	1	-,380	,947(**)	,818(**)	,715(**)	,961(**)	-,405	,928(**)	,810(**
	Sig. (2-tailed)	,139	,473	,541	,475	,006		,313	,000	,007	,009	,000	,279	,000	,008
	N	12	12	12	9	12	12	9	12	9	12	12	9	12	9
dif34	Pearson Correlation	,564	,396	,215	,452	-,090	-,380	1	-,274	,121	-,096	-,376	,985(**)	-,304	,118
	Sig. (2-tailed)	,113	,291	,579	,222	,819	,313		,476	,756	,807	,319	,000	,426	,763
	N	9	9	9	9	9	9	9	9	9	9	9	9	9	9
dif13	Pearson Correlation	-,421	-,289	-,326	-,429	,915(**)	,947(**)	-,274	1	,922(**)	,805(**)	,856(**)	-,302	,899(**)	,804(**
	Sig. (2-tailed)	,173	,362	,301	,250	,000	,000	,476		,000	,002	,000	,430	,000	,009
	N	12	12	12	9	12	12	9	12	9	12	12	9	12	9
dif14	Pearson Correlation	-,520	-,302	-,225	-,260	,895(**)	,818(**)	,121	,922(**)	1	,769(*)	,709(*)	,086	,787(*)	,877(**
	Sig. (2-tailed)	,152	,430	,561	,500	,001	,007	,756	,000		,015	,033	,825	,012	,002
	N	9	9	9	9	9	9	9	9	9	9	9	9	9	9
difr12	Pearson Correlation	,009	-,100	-,356	-,333	,827(**)	,715(**)	-,096	,805(**)	,769(*)	1	,734(**)	-,164	,898(**)	,860(**
	Sig. (2-tailed)	,976	,744	,256	,381	,000	,009	,807	,002	,015		,007	,674	,000	,003
	N	13	13	12	9	13	12	9	12	9	13	12	9	12	9
difr23	Pearson Correlation	-,340	-,184	-,120	-,103	,595(*)	,961(**)	-,376	,856(**)	,709(*)	,734(**)	1	-,419	,957(**)	,840(**
	Sig. (2-tailed)	,279	,568	,710	,792	,041	,000	,319	,000	,033	,007		,262	,000	,005
	N	12	12	12	9	12	12	9	12	9	12	12	9	12	9
difr34	Pearson Correlation	,593	,424	,263	,464	-,116	-,405	,985(**)	-,302	,086	-,164	-,419	1	-,357	,065
	Sig. (2-tailed)	,093	,255	,494	,208	,766	,279	,000	,430	,825	,674	,262		,345	,867
	N	9	9	9	9	9	9	9	9	9	9	9	9	9	9
difr13	Pearson Correlation	-,245	-,194	-,228	-,215	,727(**)	,928(**)	-,304	,899(**)	,787(*)	,898(**)	,957(**)	-,357	1	,908(**
	Sig. (2-tailed)	,444	,546	,476	,579	,007	,000	,426	,000	,012	,000	,000	,345		,001
	N	12	12	12	9	12	12	9	12	9	12	12	9	12	9
difr14	Pearson Correlation	-,371	-,238	-,095	-,021	,657	,810(**)	,118	,804(**)	,877(**)	,860(**)	,840(**)	,065	,908(**)	1
	Sig. (2-tailed)	,325	,537	,808	,957	,055	,008	,763	,009	,002	,003	,005	,867	,001	
	N	9	9	9	9	9	9	9	9	9	9	9	9	9	9

* Correlation is significant at the 0.05 level (2-tailed).

** Correlation is significant at the 0.01 level (2-tailed).

Table 4, preset the statistical calculation of group B.

Correlations

		Disp1	Disp2	Disp3	Disp 4	dif12	dif23	dif34	dif13	dif14	difr12	difr23	difr34	difr13	difr14
Disp1	Pearson Correlation	1	,392	,597(*)	,329	-,428	-,301	-,129	-,414	-,296	-,164	-,154	-,146	-,200	-,195
	Sig. (2-tailed)		,120	,011	,214	,086	,240	,633	,098	,265	,530	,556	,590	,441	,470
	N	17	17	17	16	17	17	16	17	16	17	17	16	17	16
Disp2	Pearson Correlation	,392	1	,610(**)	,220	-,143	-,707(**)	-,511(*)	-,529(*)	-,586(*)	,125	-,602(*)	-,480	-,360	-,513(*)
	Sig. (2-tailed)	,120		,009	,414	,585	,001	,043	,029	,017	,633	,011	,060	,155	,042
	N	17	17	17	16	17	17	16	17	16	17	17	16	17	16
Disp3	Pearson Correlation	,597(*)	,610(**)	1	,560(*)	-,166	-,413	-,310	-,351	-,328	,111	-,253	-,300	-,124	-,260
	Sig. (2-tailed)	,011	,009		,024	,524	,100	,243	,167	,214	,672	,327	,260	,634	,332
	N	17	17	17	16	17	17	16	17	16	17	17	16	17	16
Disp 4	Pearson Correlation	,329	,220	,560(*)	1	,214	-,006	,299	,110	,246	,409	,130	,317	,294	,364
	Sig. (2-tailed)	,214	,414	,024		,425	,983	,260	,685	,358	,115	,631	,231	,269	,166
	N	16	16	16	16	16	16	16	16	16	16	16	16	16	16
dif12	Pearson Correlation	-,428	-,143	-,166	,214	1	,484(*)	,337	,826(**)	,653(**)	,639(**)	,337	,332	,571(*)	,533(*)
	Sig. (2-tailed)	,086	,585	,524	,425		,049	,202	,000	,006	,006	,185	,210	,017	,034
	N	17	17	17	16	17	17	16	17	16	17	17	16	17	16
dif23	Pearson Correlation	-,301	-,707(**)	-,413	-,006	,484(*)	1	,427	,893(**)	,747(**)	,157	,913(**)	,406	,712(**)	,671(**)
	Sig. (2-tailed)	,240	,001	,100	,983	,049		,099	,000	,001	,547	,000	,118	,001	,004
	N	17	17	17	16	17	17	16	17	16	17	17	16	17	16
dif34	Pearson Correlation	-,129	-,511(*)	-,310	,299	,337	,427	1	,457	,872(**)	,243	,387	,995(**)	,398	,863(**)
	Sig. (2-tailed)	,633	,043	,243	,260	,202	,099		,075	,000	,365	,139	,000	,127	,000
	N	16	16	16	16	16	16	16	16	16	16	16	16	16	16
dif13	Pearson Correlation	-,414	-,529(*)	-,351	,110	,826(**)	,893(**)	,457	1	,834(**)	,430	,762(**)	,441	,752(**)	,720(**)
	Sig. (2-tailed)	,098	,029	,167	,685	,000	,000	,075		,000	,085	,000	,087	,000	,002
	N	17	17	17	16	17	17	16	17	16	17	17	16	17	16
dif14	Pearson Correlation	-,296	-,586(*)	-,328	,246	,653(**)	,747(**)	,872(**)	,834(**)	1	,439	,666(**)	,860(**)	,688(**)	,932(**)
	Sig. (2-tailed)	,265	,017	,214	,358	,006	,001	,000	,000		,089	,005	,000	,003	,000
	N	16	16	16	16	16	16	16	16	16	16	16	16	16	16
difr12	Pearson Correlation	-,164	,125	,111	,409	,639(**)	,157	,243	,430	,439	1	,352	,267	,766(**)	,590(*)
	Sig. (2-tailed)	,530	,633	,672	,115	,006	,547	,365	,085	,089		,166	,318	,000	,016
	N	17	17	17	16	17	17	16	17	16	17	17	16	17	16
difr23	Pearson Correlation	-,154	-,602(*)	-,253	,130	,337	,913(**)	,387	,762(**)	,666(**)	,352	1	,383	,871(**)	,722(**)
	Sig. (2-tailed)	,556	,011	,327	,631	,185	,000	,139	,000	,005	,166		,143	,000	,002
	N	17	17	17	16	17	17	16	17	16	17	17	16	17	16
difr34	Pearson Correlation	-,146	-,480	-,300	,317	,332	,406	,995(**)	,441	,860(**)	,267	,383	1	,407	,871(**)
	Sig. (2-tailed)	,590	,060	,260	,231	,210	,118	,000	,087	,000	,318	,143		,118	,000
	N	16	16	16	16	16	16	16	16	16	16	16	16	16	16
difr13	Pearson Correlation	-,200	-,360	-,124	,294	,571(*)	,712(**)	,398	,752(**)	,688(**)	,766(**)	,871(**)	,407	1	,803(**)
	Sig. (2-tailed)	,441	,155	,634	,269	,017	,001	,127	,000	,003	,000	,000	,118		,000
	N	17	17	17	16	17	17	16	17	16	17	17	16	17	16
difr14	Pearson Correlation	-,195	-,513(*)	-,260	,364	,533(*)	,671(**)	,863(**)	,720(**)	,932(**)	,590(*)	,722(**)	,871(**)	,803(**)	1
	Sig. (2-tailed)	,470	,042	,332	,166	,034	,004	,000	,002	,000	,016	,002	,000	,000	

N	16	16	16	16	16	16	16	16	16	16	16	16	16	16

* Correlation is significant at the 0.05 level (2-tailed).

** Correlation is significant at the 0.01 level (2-tailed).

REFERENCES

1. Angel.A, Hollenberg.C, And Daniel A.K. Roncari. the Adipocyte And Obesity. Ravent Press New York 1993. p.p 1-298.

2 . Harrison Principles Of Internal Medicine 15th Edition. McGraw-Hill New York 2001.p.p 479-486.

3. Clark. M, Kumar.P. Kumar and Clark Clinical Medicine 5th edition. W.B. Saunders london 2002. p.p 241-245.

4. DeFronzo AR Soman V, Shaerwin RS, Hendler R & Felig P (1978) Insulin binding to monocytes and insulin action in human obesity, starvation and refeeding. Journal of Clinical Invastigation 62: 204-213.

5. Despres J-P, Prud' Homme D, Tremblay A, et al. Conribution Of low Intensity Exercise Training To Treatment Of Abdominal Obesity. In: Guy-Grand B. Ricquier D, Lafontan M et al. Importance of 'Metabolic Fitness' In Obesity In Urope 91. London: John Libby, 1992: 177-81.

6. Fukagawa NK, Anderson JW, Hogmeman G, et al. High Carbohydrat Diet, High Fiber Diet Increase Periferal Insulin Sensitivity In Healthy Young And Old Adults. Am J Clin Nutr 1990; 52.524-8.

7. Laws. Ami And M.Revaren Gerald. Bailliere's Clinical Endocrinology And metabolism, Volium. 7.No. 4. October 1993. ISBN 0-7020-1699-3. p.p 1063-1072

8. Oleski JM, Reaven GM & Farquhar JW (1974b) Effect of weight reduction on obesity: studies of carbohydrate and lipid metabolism. Journal of Clinical Investigation 53: 64-76.

9. R.James, Barnard, And Stephan J. Wen. Exercise And Diet In The Prevention And Control Of The Metabolic Syndrome. Sport Med.18 (4) 1994

10. Ryan .K, Berkowitz.R, And Robert L.Barbiari. Kistmer's Gynecology, Principles and Practice 6th Edition. Mosby 1995 new york. p.p 289-290.