Assessment of Serum Total Cholesterol, Low Density Lipoprotein and High Density Lipoprotein among Obese Hypertensive Patients With Diabetes Mellitus Type2, ELHassahiesa Hospital Gezira State, Sudan (2017)

By

ELSIDDIG AHMED ALI ABDALLA

A Dissertation
Submitted to the University of Gezira in Partial Fulfillment of the Requirements for the Award of the Degree of Master of Sciences in Medical Laboratory Sciences

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Department of Clinical Chemistry
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Assessment of Serum Total Cholesterol, Low Density Lipoprotein and High Density Lipoprotein among Obese Hypertensive Patients With Diabetes Mellitus Type2, El Hassahiesa Hospital Gezira State, Sudan (2017)

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Supervision Committee:

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<tr>
<td>Dr. Shams Eldein Mohammed Ahmed</td>
<td>Main supervisor</td>
<td>.... ........</td>
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<tr>
<td>Dr. Fath Elrahman Eriebi</td>
<td>Co – supervisor</td>
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Date
April 2018
Assessment of Serum Total Cholesterol, Low Density Lipoprotein and High Density Lipoprotein among Obese Hypertensive Patients With Diabetes Mellitus Type2, El Hassahiesa Hospital Gezira State, Sudan (2017)

Elsiddig Ahmed Ali Abdalla

Examination Committee:

Name Position Signature

Dr. Shams Eldein Mohamed Ahmed Chairperson

Dr. Suhair awad Mahmoud External Examiner

Dr. Albadawi Abdalbage Talha

Internal Examiner

Date
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Firstly, I thank Allah for blessing my life, helped me to start this work, and supported my strength to complete this humanity Work. I would like to give my great sincere thanks to my supervisor Dr. SHAMS- ALDEIN MOHAMMED AHMED for his constructive guidance, help, and support in each step to establish valuable and useful work. I would like to extend special thanks to my lovely mother and gorgeous father for their kind supporting and motivating me to do my best and they never complain from my needs. I am very thankful for the staff of Al -Gezera University for offering me an ideal environment to perform my research project. I would like to extend thanks to my brothers and sisters, my teachers, friends and all people support me and believe me.
Declaration

I authorized that my dissertation Assessment of Assessment of Serum Total Cholesterol, Low Density Lipoprotein and High Density Lipoprotein among Obese Hypertensive Patients with Diabetes Mellitus Type2, At Alhasahisa hospital- Gezira State, Sudan (2017)

”, submitted by me, under the supervision Dr. Shams Eldein
Mohammed Ahmed for the partial fulfillment for the award of Master degree in Medical Laboratory Sciences in Clinical Chemistry. University of Gezira Faculty of Medical Laboratory Sciences Department of Clinical Chemistry; Wad- Madani, Sudan and this is original and it was not submitted in part or in full, in any printed or electronic means, and is not being considered elsewhere for publication.

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Dedication

To my Father who gave me confidence
To my mother who taught me the meaning live and gave me love
To my brothers and sisters
To my teachers
To my friends
Dedication

To my Father who gave me confidence
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Assessment of Serum Total Cholesterol, Low Density Lipoprotein and High Density Lipoprotein among Obese Hypertensive Patients With Diabetes Mellitus Type 2, El Hassahiesa Hospital Gezira State, Sudan (2017)

ABSTRACT

Lipids and lipoproteins are risk factors for CHD. It has been demonstrated that high levels of serum total cholesterol (TC), triglycerides (TG), LDL cholesterol, very-low-density lipoprotein (VLDL), low concentration of HDL cholesterol, and increased body mass index (BMI) are significantly associated with CHD. Dyslipidemia is one of the top five major risk factors leading to cardiovascular disorders. This study was conducted to assess the levels of total cholesterol high-density lipoprotein (HDL) low-density lipoprotein (LDL) for Sudanese patients who were above normal weight, and they had type II diabetes and hypertensive. The study was conducted in Sudan -gezira state, between May to December 2017. The number of patients participating for this study was 90 patients divided into three groups. Group 1 diabetic patients group 2 hypertensive patients’ group 3 diabetic hypertensive patients. Blood samples were taken from the participants taking into consideration the quality control in the collection and preservation of samples. The samples were analyzed by enzymatic reaction solutions and the concentration levels were measured by the spectrophotometer analyzer. The statistical analysis of the results was then analyzed by the statistical packages for social sciences version 17. The present study demonstrates that the mean of cholesterol group 1(diabetic patients) was 206.5 (±52.7) and in group 2(hypertensive patients) was 177.1(±78.1), and group 3(diabetic hypertensive patients) was 220.(±34.6) the difference was statistically significant (P= 0.016). the mean of HDL in group 1(diabetic patients) was 40.6(±5.4) and in group 2(hypertensive patients) was 55.5±17.9, and group 3 (diabetic hypertensive patients) was 43.9(±7.2) the difference was statistically significant (P= 0.000). Finally, the mean of LDL in group1 (diabetic patients) was 114.3(±35.1) and in group2(hypertensive patients) was 102.4(68.6), group3(diabetic hypertensive patients) was 120.2(±22.2) and the difference was statistically insignificant (P= 0.31). Lipid profile should be monitored routinely for diabetic and hypertensive patients.
تقييم مستوي الكولسترول الكلي في الدم، البروتين الدهني منخفض الكثافة والبروتين الدهني عالي الكثافة بين مرضى ارتفاع ضغط الدم الذين يعانون من السمنة المفرطة مع داء السكري النوع الثاني، في مستشفى الحصاحيصا ولاية الجزيرة، السودان (2017)

الصديق أحمد على عبدالله

ملخص الدراسة

الدهون والبروتينات الدهنية هي مؤشرات خطر امراض الجهاز القلبي الوعائي. وثبت أن ارتفاع مستويات الكولسترول الكلي في الدم، والدهون الثلاثية والبروتين الدهني منخفض الكثافة وانخفاض تركيز البروتين الدهني عالي الكثافة وزيادة مؤشر كثافة الجسم ترتبط بشكل كبير مع اضطراب القلب والأوعية الدموية. أجريت هذه الدراسة لتقييم معدل الكولسترول الكلي والكولسترول عالي الكثافة ومنخفض الكثافة كما تم تحليل مستوي التروبونين للمرضى السودانيين الزائدين أوزانهم عن المعدل الطبيعي كما انهو مصابون بالسكري النوع الثاني وارتفاع ضغط الدم. هدفت هذه الدراسة لإكتشاف تأثير مستوي الدهون لهؤلاء المرضى على الجهاز القلبي الوعائي. أجريت هذه الدراسة في السودان في ولاية الجزيرة في الفترة مابين أغسطس إلى ديسمبر 2017. تم اختيار المرضى بعد ان تم التأكد من اصابتهم بمرض السكري وضغط الدم كما حسب نسبة السمنة باستخدام المعايير الدولية لتحديد مستوي السمنة لديهم. عدد المرضى المشاركون في هذه الدراسة تسعون مريضا قسمو الى ثلاثة مجموعات. المجموعة الأولى مرضى السكري، المجموعة الثانية مرضى الضغط، المجموعة الثالثة مرضى السكري والضغط معا. اخذت عينات الدم من المشاركين في هذه الدراسة لقياس مستوي الكوليسترول الكلي والكوليسترول عالي الكثافة ومنخفض الكثافة. تحليل عينات الدم اجري بعد فصل الدم، ويتم قياس معدلات الانتانج بواسطة جهاز مسح الطيف الضوئي. مجموعات النتائج أوضحت ان متوسط معدل الكولسترول للمجموعة الأولى (مرضى السكري) كان 206.5 (±52.7) وفي المجموعة (2) (مرضى ارتفاع ضغط الدم) كان 220.2 (±34.6) ومتوسط معدل الكولسترول في المجموعة الثانية (مرضى الضغط) كان 55.5 (±17.9) بالمجموعة الثالثة (مرضى السكري والضغط) كان 43.9 (±7.2) وان الفرق المعنوي (0.016). متوسط الكولسترول عالي الكثافة للمجموعة الأولى (مرضى السكري) كان 40.6 (±5.4) للملسية (0.00) ومتوسط معدل الكولسترول منخفض الكثافة للمجموعة (1) (مرضى السكري) كان 114.3 (±35.1) وعكم (0.00) ومتوسط معدل الكولسترول عالي الكثافة والمتوسطة أفضل (0.319). خلصت هذه الدراسة إلى أنه يوجد ارتفاع في مستوي الكولسترول الكلي والكولسترول عالي الكثافة ولا يوجد ارتفاع في مستوي الكولسترول منخفض الكثافة. يجب قياس مستوي الدهون روتينيا لدى مرضى داء السكري وضغط الدم.

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<td>15</td>
<td>Mg/dl</td>
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CHAPTER ONE

1. Introduction

1.1 Introduction

Obesity, defined as a body mass index (BMI) ≥ 30 kg/m², presently affects an estimated 72.5 million US adults, with an overall prevalence of 26.7%. Despite efforts to address this epidemic, prevalence continues to increase; for example, the number of states with a prevalence of ≥ 30% increased from zero in 2000 to 9 in 2009 (Sherry et al., 2010). The annual cost of managing obesity in the United States alone amounts to approximately $190.2 billion per year, or 20.6% of national health expenditures, according to a study (Cawley et al., 2012). Compared with a non-obese person, an obese person incurs $2741 more in medical costs (in 2005 dollars) annually. In addition, the annual cost of lost productivity due to obesity is approximately $73.1 billion (Finkelstein et al., 2010), and almost $121 billion spent annually on weight-loss products and services (Franz et al., 2007).

Nowadays, DM is one of the most challenging health problems of the 21st century. Prevalence of diabetes worldwide was 8.3% in 2014 and is estimated to rise to 10.1%. Diabetes incidence is increasing due to population growth, aging, urbanization and the increasing prevalence of obesity and physical inactivity the world health organization (WHO) deems the prevention, diagnosis, and treatment of type ii DM a priority (WHO, 2008). The international diabetes federation has recently release estimates of the numbers of people with diabetes for 2014 and forecasts for 2035 with 378.3 million and 583.7 million, respectively (International Diabetes Federation, 2014).

Lipids and lipoproteins are risk factors for CHD. It has been demonstrated that high levels of serum total cholesterol (TC), triglycerides (TG), LDL cholesterol, very-low-density lipoprotein (VLDL), low concentration of HDL cholesterol, and increased body mass index (BMI) are significantly associated with CHD (George and Ludvik, 2000). Dyslipidemia is one of the top five major risk factors leading to cardiovascular disorders. It is characterized by elevated LDL cholesterol and TG and decreased HDL cholesterol. Although there are differences in defining dyslipidemia, however, European guideline on
CVD prevention in clinical practice recommends TC below 190 mg/dL (5.0 mmol/L) and an LDL cholesterol below 115 mg/dL (3.0 mmol/L) for the general population. The goals are even lower: i.e., <175 mg/dL (4.5 mmol/L) for TC and <100 mg/dL (2.6 mmol/L) for LDL cholesterol in the case of multiple disorders like CHD, other diseases of CVD, or DM (De Backer et al. 2003). Lipid abnormalities significantly contribute to the increased risk of cardiovascular disease and other morbidity in diabetics. VLDL and chylomicrons (CM) are major sources of fatty acid supply to the heart, but little is known about their metabolism in diabetic myocardium. Males and females appear to be equally susceptible to the effects of risk factors such as hypertension, increased plasma LDL cholesterol, and low levels of plasma HDL cholesterol. Estrogens have a favorable effect on lipid profile. It has been observed that they lower LDL cholesterol and elevate HDL cholesterol. Estrogens are thought to increase HDL cholesterol by reducing hepatic triglycerides’ lipase activity that catabolizes HDL cholesterol. Global studies of either gender have demonstrated that the risk of atherosclerosis is inversely related to blood levels of HDL cholesterol: the higher the level of HDL cholesterol, the lower will be the risk. It is indicated that for every 1 mg/dL rise in HDL cholesterol, the risk for developing cardiovascular disease decreases by 2–3 % (Toth 2005). HDL cholesterol helps to extract excess cholesterol deposited in blood vessel walls and deliver it back to the liver for elimination through the gastrointestinal tract. HDL cholesterol helps to keep blood vessels dilated, thereby promoting better blood flow. It also reduces blood vessel injury through its antioxidant and anti-inflammatory functions, among other effects. HDL cholesterol carries “old” cholesterol that has been discarded by cells back to the liver for recycling or excretion. The main function of LDL cholesterol is to transport cholesterol from the liver to the tissues that incorporate it into the cell membranes. The oxidation of LDL cholesterol is believed to have a central role in atherogenesis. Oxidized LDL cholesterol may be involved in atherogenesis by inducing smooth muscle cell proliferation. Acute MI is the most important consequence of coronary artery disease. Some studies have defined TG also as an independent risk factor for MI (Haffner et al. 1998). High TG value could result from the elevation of several lipoproteins such as chylomicrons, different subclasses of VLDL, or intermediate-density lipoproteins (IDL cholesterol). The risk of MI in patients with DM without a history of myocardial
infarction is as high as that in patients without MI who have had a myocardial infarction. Mortality after first MI is higher in both males and females with DM. Lipid abnormalities significantly contribute to the increased risk of CVD in diabetes mellitus. Diabetes affects virtually all lipids and lipoproteins. Persons with DM typically have increased plasma concentrations of TG, low plasma concentrations of HDL cholesterol, and slightly raised plasma concentrations of LDL cholesterol. DM is also considered as an independent risk factor for cardiovascular disease (up to fivefold), and as many as 80 % of patients with type II diabetes die from cardiovascular complications (Johnson et al. 2004). Persons with high blood cholesterol levels have a higher prevalence of hypertension, and those with high blood pressure have a higher prevalence of hypercholesterolemia (O’Brien et al. 2003). Abnormalities in plasma lipoprotein metabolism play a central role in the pathogenesis of atherosclerosis, and arterial hypertension with elevated systolic or diastolic blood pressure is positively and independently associated with CHD. The risk of developing CVD associated with the presence of both hypertension and Dyslipidemia has been shown to be greater as compared to hypertension or Dyslipidemia alone (Johnson et al. 2004). Moreover, patients with these two conditions found to have three to four times higher prevalence of MI (Wald and Law 2003). Dyslipidemia causes endothelial damage and consequent loss of physiological vasomotor activity, which may be manifested as increased blood pressure. Asians experience the largest proportion of the worldwide burden of CVD. Further, Asians include several distinct ethnic subpopulations (South Asians, Chinese, etc.), who may differ in their lipid profiles. These differences may be the result of both genetic and environmental factors such as high-cholesterol carbohydrate diets, reduced physical activity, and obesity (Radhika et al. 2009). In a study it has been estimated that LDL-cholesterol, HDL-cholesterol, and TG levels are lower among Asians compared with non-Asians. Also the associations of elevated LDL cholesterol and lower levels of HDL cholesterol for the risk of AMI were found to be broadly similar among Asians and non-Asians.
2.1 Justification:
1- Obesity represents an important and common cardiovascular risk factor whilst the prevalence of obesity is still rising (across all ages) and affecting both the developed and developing world.
2- Assuming that diabetes is a micro vascular disease and therefore contributes to chronic myocite injury
3- Lipids and lipoproteins are risk factors for CHD. It has been demonstrated that high levels of serum total cholesterol (TC), triglycerides (TG), LDL cholesterol, very-low-density lipoprotein (VLDL), low concentration of HDL cholesterol, and increased body mass index (BMI) are significantly associated with CHD

3. Objectives:

3.1 General objective:
To assess plasma lipids on adult obese hypertensive and diabetics Sudanese patient

3.2 Specific objectives:
1- To measure total cholesterol level
2- To measure serum LDL level
3- To measure serum HDL level
CHAPTER TWO

2.1 Literature Review

Diabetes is among the many serious health conditions associated with obesity. It has recently been projected that, by 2020, the overall prevalence of pre diabetes and diabetes in the United States will be approximately 50% (UCFHR et al., 2010). We know that certain individual factors are predictive of increased risk for the development of diabetes. Early identification is of paramount importance, as early intervention may improve long-term health outcomes. Targeted screening for populations with increased diabetes risk can help to inform prevention or management strategies at all points of the progression from overweight to obesity (Garber et al., 2008).

In a 2016 position statement, the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) proposed a new name for obesity, adiposity-based chronic disease (ABCD). The AACE/ACE did not introduce the name as an actual replacement for the term obesity but instead as a means of helping the medical community focus on the pathophysiologic impact of excess weight. (Wang et al., 2008)

2.1 Measurements of obesity

Obesity represents a state of excess storage of body fat. Although similar, the term overweight is parasitically defined as an excess of body weight for height. Normal, healthy men have a body fat percentage of 15-20%, while normal, healthy women have a percentage of approximately 25-30%. (Gallagher et al., 2000) However, because differences in weight among individuals are only partly the result of variations in body fat, body weight is a limited, although easily obtained, index of obesity.

The body mass index (BMI), also known as the Quenelle index, is used far more commonly than body fat percentage to define obesity. In general, BMI correlates closely with the degree of body fat in most settings; however, this correlation is weaker at low BMIs. An individual’s BMI is calculated as weight/height², with
weight being in kilograms and height being in meters (otherwise, the equation is weight in pounds \( \times 0.703/\text{height in inches}^2 \)).

A person’s body fat percentage can be indirectly estimated by using the Deurenberg equation, as follows:

\[
\text{Body fat percentage} = 1.2(\text{BMI}) + 0.23(\text{age}) - 10.8(\text{sex}) - 5.4
\]

With age being in years and sex being designated as 1 for males and 0 for females. This equation has a standard error of 4% and accounts for approximately 80% of the variation in body fat. (Finkelstein et al., 2010)

Although the BMI typically correlates closely with percentage body fat in a curvilinear fashion, some important caveats apply to its interpretation. In mesomorphic (muscular) persons, BMIs that usually indicate overweight or mild obesity may be spurious, whereas, in some persons with sarcopenia (e.g. elderly individuals and persons of Asian descent, particularly from South Asia), a typically normal BMI may conceal underlying excess adiposity characterized by an increased percentage of fat mass and reduced muscle mass.

In view of these limitations, some authorities advocate a definition of obesity based on a percentage of body fat. For men, a percentage of body fat greater than 25% defines obesity, with 21-25% being borderline. For women, over 33% defines obesity, with 31-33% being borderline.

Other indices used to estimate the degree and distribution of obesity include the 4 standard skin thicknesses (i.e. subscapular, triceps, biceps, supra-iliac) and various anthropometric measures, of which waist and hip circumferences are the most important. Skinfold measurements are the least accurate means by which to assess obesity. (Gallagher et al., 2000)

Dual-energy radiographic absorptiometry (DXA) scanning is used primarily by researchers to accurately measure body composition, particularly fat mass and fat-free mass. It has the additional advantage of measuring regional fat distribution. However, DXA scans can't be used to distinguish between subcutaneous and visceral abdominal fat deposits.

The current standard techniques for measuring visceral fat volume are abdominal computed tomography (CT) scanning (at L4-L5) and magnetic resonance imaging
(MRI) techniques. A simpler technique, using bioelectrical impedance, was recently introduced (Ward et al., 2012). However, these methods are limited to clinical research.

### 2.2 Classification of obesity

Although several classifications and definitions for degrees of obesity are accepted, the most widely accepted classifications are those from the World Health Organization (WHO), based on BMI. The WHO designations include the following:

- **Grade 1 overweight (commonly and simply called overweight)** - BMI of 25-29.9 kg/m²
- **Grade 2 overweight (commonly called obesity)** - BMI of 30-39.9 kg/m²
- **Grade 3 overweight (commonly called severe or morbid obesity)** - BMI greater than or equal to 40 kg/m²

The cut-off for each grade varies according to an individual’s ethnic background. Other BMI cutoffs identified as potential public health action points in the populations are 32.5 and 37.5 kg/m² (Shiwaku et al., 2004).

The surgical literature often uses a different classification to recognize particularly severe obesity. The categories are as follows:

- **Severe obesity** - BMI greater than 40 kg/m²
- **Morbid obesity** - BMI of 40-50 kg/m²
- **Super obese** - BMI greater than 50 kg/m²

In children, a BMI above the 85th percentile (for age-matched and sex-matched control subjects) is commonly used to define overweight, and a BMI above the 95th percentile is commonly used to define obesity.

Earlier in this decade, the Diabetes Prevention Program (DPP) demonstrated successful loss of 5 – 10% of body weight with an intensive lifestyle intervention, revealing the potential of regular, supervised diet and exercise in delaying or preventing the progression from prediabetes to T2DM (Knowler et al., 2003). Since the DPP, a number of pilot projects have successfully replicated its results. However, the intensive DPP intervention included a 16-class curriculum taught one-on-one by case managers; this type of program would require large-scale
implementation, combined with payer-based reimbursement or coverage strategies (Knowler et al., 2003).

2.3 The Progression to Obesity, and from Obesity to Diabetes:

Obesity results from a combination of individual and societal factors. Although obesity is often attributed to dietary choices, such as overeating large portions of calorically dense foods, genetics can also play a strong role in patient predisposition (Gade et al., 2010). For example, certain humans have evolved with a 'thrifty' metabolism; many of us retain excess calories, stored as fat, to aid survival during food scarcity and famine. Once necessary to prevent starvation, a thrifty metabolism makes it difficult to sustain weight loss (Garber et al., 2012, Wells et al., 2009). Not surprisingly, the increased incidence of T2DM has paralleled the obesity epidemic. Half of the individuals with T2DM are obese, and nearly 90% are overweight. However, research shows that even moderate weight loss of 5 to 10% of body weight can prevent or delay the progression to T2DM development in high-risk adults (Runge et al., 2007, Yu et al., 2007).

The factors contributing to obesity can be complex and polygenic. Additionally, certain monogenic factors, such as deficiencies of leptin, leptin receptors, or genes controlling hypothalamic feedback, can result in decreased appetite suppression and early-onset obesity. Patients with hypothyroidism experience a reduced basal metabolic rate (BMR) (Gade et al., 2010, Garber et al., 2012 & Zimmet et al., 2011). Because decreased caloric intake leads to lowered BMR and extra production of ghrelin (sometimes called the 'hunger hormone') dieting can lead to decreased metabolism paired with increased appetite (Gade et al., 2010). Each of these physical and genetic factors can contribute to obesity and thwart weight-loss efforts, creating a condition that is likely to worsen over time. Considering that diabetes is also a progressive disease, it is not surprising that prevalence increases with advancing age; adults ≥ 65 years have a 27% prevalence of diabetes, the highest of any age group (Wells et al., 2009).

The T2DM pathophysiology involves both insulin resistance and progressive β-cell dysfunction; the eventual inability of β-cells to adequately increase insulin secretion in response to reduce insulin uptake leads to the development of
hyperglycemia (Bays et al., 2004). Obesity is a pro-inflammatory state, and the role of inflammation may present a partial etiologic explanation. Increased levels of adipocytes and cytokines such as interleukin-1 (IL-1), IL-6, and tumor necrosis factor α (TNF α) trigger a network of signal in g pathways (Barbarroja et al., 2010). The resulting inflammatory activation of adipose tissue can cause insulin resistance and may also be the underlying cause of obesity-related hypertension (Purkayastha et al., 2011). Additionally, post-meal levels of incretions’ such as glucagon-like peptide-1 (GLP-1), largely responsible for postprandial insulin secretion and the key to the regulation of blood glucose levels, are lower than average in patients with T2DM (Holst et al., 2009 & Ross et al., 2010). In other wise healthy obese adults, increased systemic inflammation is associated with the development of prediabetes and prehypertension (Antuna-Puente et al., 2008 & Vandanmagsar et al., 2011). In a study of 24 morbidly obese patients, those who were insulin resistant had significantly higher levels of mRNA expression of IL-1 β, and IL-6 as compared to morbidly obese non-insulin resistant patients; these patients also had significantly higher mRNA expression of TNF α as compared to non-obese controls (Barbarroja et al., 2010).

Although obesity is a major determinant of insulin resistance, 10 to 25% of obese adults remain metabolically healthy and insulin-sensitive, and not all insulin-resistant persons are obese (Blüher et al., 2010). These findings support the emerging belief that not all excess body weight carries equal risk. Abdominal obesity, in particular, is likely to contribute heavily to risk, and adipose tissue inflammation appears to be a factor in the development of insulin resistance and subsequent T2DM, along with certain kinds of fat (e.g. ectopic fat in the liver and skeletal muscle) (Gregor et al., 2011 & Yki-Järvinen et al., 2002).

2.4 Early Identification of At-Risk Patients:

Diabetes is a progressive disease, and late treatment failure highlights the importance of the early identification of patients likely to have prediabetes. To accomplish this, we need to find better ways to identify individuals with increased risk at an earlier stage (Finkelstein et al., 2010). For example, we know that patients with metabolic syndrome progress to diabetes at 5 times the rate of patients without.
Furthermore, patients with both metabolic syndrome and IFG progress to diabetes at roughly 20 times the rate of patients without either condition (Lorenzo et al., 2007). Ideally, intervention early in the diabetes continuum can help to preserve β-cell function and lead to improved long-term outcomes (Wajchenberg et al., 2007). Early identification and treatment of prediabetes may also reduce or delay progression to CVD and/or micro vascular disease. Lacking intervention, however, existing research indicates that approximately one-third of patients with pre diabetes are likely to convert to T2DM, one-third will remain in a prediabetic state and one-third will revert to normo-glycaemia. Further, nearly two-thirds of patients with pre diabetes who have both IGT and IFG are likely to progress to diabetes (de Vegt et al., 2001). Screening based on obesity alone will not capture all at-risk patients: many overweight/obese individuals remain insulin-sensitive, and not all individuals with insulin resistance are obese. For some individuals, genetic β-cell dysfunction may be the first demonstrable defect in the development of T2DM (Wajchenberg et al., 2007). For example, data from the Insulin Resistance Atherosclerosis Study (IRAS) found that insulin resistance and β-cell dysfunction were predictors of diabetes risk independent of obesity and glucose tolerance. The study measured insulin sensitivity and secretion in subjects with IGT or normal glucose tolerance, using a frequently sampled glucose tolerance test, and first-phase insulin response was determined by assessing insulin concentrations following glucose injections. At 5-year follow-up, insulin sensitivity and acute insulin, response predicted the risk of progression to diabetes in non-Hispanic White, African-American and Hispanic individuals. With both variables stratified by tertiles, the likelihood of progression to diabetes decreased as insulin sensitivity and β-cell function increased the association between insulin sensitivity and β-cell function to diabetes risk was not mediated by BMI (Lorenzo et al., 2010).

Additionally, parental history of diabetes is a consistent predictor of T2DM, and may also predict early β-cell dysfunction (Wilson et al., 2007 & Wilson et al., 2011). A study completed in Mexico evaluating 48 non-obese subjects found that β-cell function, as measured by the HOMA-β % test, was significantly impaired in patients with a family history of diabetes. The mean HOMA-β % for patients with a
family history of diabetes was 186.1, compared with 252.7 for patients with no family history (p = 0.01) (Guerrero-Romero et al., 2005). Therefore, it is important to ask patients about their family history of diabetes, even if other risk factors are not present.

2.5 Therapeutic options for the prevention or management of obesity:

Interventions for obesity can help alleviate both the severity of negative health outcomes and the costs associated with treatment. For example, an economic evaluation of the impact of body weight reduction, conducted by a Massachusetts health maintenance organization, found that every 1% of body weight lost corresponded with a 3.1% ($213) reduction in total annual health care costs in patients with T2DM who were treated with ant diabetic medications (Kreider et al., 2011).

A variety of programs have been investigated to aid overweight and obese individuals with weight-loss efforts. These include reduced calorie diets, meal replacement plans, varying macronutrient diets, increased fiber diets and increased physical activity and energy expenditure programs. These programs are often accompanied by behavioral interventions including social support, monitoring, education and/or counseling (Heikes et al., 2008). A recent study randomized 90 sedentary women to receive either a meal replacement program (MRP) accompanied by encouragement to increase their exercise level or a structured diet and supervised exercise (SDE) plan. After completion of the 10-week program, the participants who had followed the SDE plan lost more weight (p = 0.03), more fat (p = 0.02) and more abdominal fat (p = 0.05) than participants who followed the MRP. SDE patients also experienced greater increases in strength and aerobic activity. Furthermore, these effects persisted through the 24-week follow-up period (Gudmundsson et al., 2005). These results indicate the need for structure, support and close monitoring in weight-loss programs with IFG and IGT were provided.
Figure 1. American diabetes association diabetes risk calculator to determine the probability of an individual developing type 2 diabetes (DM) or prediabetes (PDM, %) (Gelber et al., 2008).

With a lifestyle intervention involving diet and exercise, they experienced a 58% reduction in progression to diabetes, alongside a mean loss of 4 kg of body weight. Patients who were given metformin experienced a 31% decrease in T2DM development and a body weight loss of approximately 2 kg (Bays et al., 2004 & Holstein et al., 2009). Since the DPP, a number of pilot projects have successfully replicated its results (Barbarroja et al., 2010). In addition, a meta-analysis of four studies evaluating obesity reduction/diabetes prevention programs for patients with IGT found that interventions that combined exercise and diet had the potential to decrease progression to T2DM by nearly 50% (Santaguida et al., 2005). In 2007, an ADA Consensus Panel published recommendations that all individuals with IGT and/or IFG be counseled on lifestyle changes and provided with exercise and dietary goals similar to those of DPP. Additionally, metformin has been recommended as a preemptive medication for patients who have both IFG and IGT, along with ≥ 1
risk factor for diabetes, such as hypertension, elevated triglycerides or morbid obesity (BMI ≥ 35 kg/m²) (Apple et al., 2012, Poolsup et al., 2008 & Rhee et al., 2010).
CHAPTER 3

Materials and Methods

3. Material and Methods:

3.1 Study design:
This was descriptive cross-sectional study.

3.2 Study area and duration:
The study was conducted at Alhasahisa, Gezeira state during August to December 2017.

3.3 Study population and sample size:
Total numbers of volunteers were 90 obese Sudanese patients distributed in three groups
- Group 1 are obese diabetics patients
- Group 2 are obese hypertensive patients
- Group 3 are obese hypertensive diabetic patients

3.4. Inclusion criteria:
- obese diabetics patients
- obese hypertensive patients
- obese hypertensive diabetic patients

3.5 Exclusion criteria:
Patients with any disease that affects lipid profile.

3.6 Ethical consideration:
Ethical approval obtained from the ethical committee of University of Al Gazeira, and informed consent taken from all the participants prior to their inclusion in the study.

3.7 Data collection:
Patient data collected by scientific questionnaire (appendices1)

3.8 Sample collection:
A blood sample was collected from vein of each subject in lithium heparin container centrifuged for 15 minutes at 3500 rpm, and plasma was separated and used for the
estimation of Lipid profile using Bio-system analyzer the sample was processed and analyzed according to manufacturer instruction.

**3.9 principles of measurements:**

**Principle of method**

**3.9.1 cholesterol:** (appendices 2)

Enzymatic assay procedure (Bio-system based device assay)

**3.9.2 LDL:** (appendices 3)

Enzymatic assay procedure (Bio-system based device assay)

**3.9.3 HDL:** (appendices 4)

Enzymatic assay procedure (Bio-system based device assay)

**3.10 Statistical analysis:**

All data performed using the Statistical Package for the Social Sciences software package (SPSS).v17

**3.11 interpretation of result:**

1- serum total cholesterol normal range (150 to 200 mg/dl)
2- serum LDL normal range (65 to 170 mg/dl)
3- serum HDL normal range (35 to 160 mg/dl)
CHAPTER 4

RESULTS and Discussion

4.1 Result:

A total of 90 individuals participated in this study, 30 were clinically diagnosed obese with Diabetic (group one), 30 were obese with hypertension (group two) and 30 were obese with diabetic and hypertension.

The present study demonstrates that the mean of cholesterol group 1 was 206.5 (±52.7) and in group 2 was 177.1 (±78.1), and group 3 was 220(±34.6) the difference was statistically significant (P= 0.016). the mean of HDL in group 1 was 40.6 (±5.4) and in group 2 was 55.5 (±17.9),and group 3 was 43.9 (±7.2) the difference was statistically significant (P= 0.000). Finally, the mean of LDL in group1 was 114.3 (±35.1) and in group 2 was 102.4 (±68.6), group 3 was 120.2(±22.2) and the difference was statistically insignificant (P= 0.31)
Table 1: Comparison of serum total cholesterol in the three Groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Means</th>
<th>Std. Deviation</th>
<th>P.Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group1 (diabetic patients)</td>
<td>206.5</td>
<td>52.7</td>
<td></td>
</tr>
<tr>
<td>Group2 (hypertensive patients)</td>
<td>177.1</td>
<td>78.1</td>
<td>.016</td>
</tr>
<tr>
<td>Group3 (diabetic hypertensive)</td>
<td>220.2</td>
<td>34.6</td>
<td></td>
</tr>
</tbody>
</table>
Table 3: Distribution of serum HDL in the three groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Means</th>
<th>Std. Deviation</th>
<th>P.Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (diabetic)</td>
<td>40.6</td>
<td>5.5</td>
<td>.000</td>
</tr>
<tr>
<td>Group 2 (hypertensive patients)</td>
<td>55.5</td>
<td>17.9</td>
<td></td>
</tr>
<tr>
<td>Group 3 (diabetic hypertensive)</td>
<td>43.9</td>
<td>7.2</td>
<td></td>
</tr>
</tbody>
</table>
Table 2: Comparison of serum LDL in the three groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Means</th>
<th>Std. Deviation</th>
<th>P.Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group1 (diabetic patients)</td>
<td>114.3</td>
<td>35.1</td>
<td></td>
</tr>
<tr>
<td>Group2 (hypertensive patients)</td>
<td>102.4</td>
<td>68.6</td>
<td></td>
</tr>
<tr>
<td>Group3 (diabetic hypertensive)</td>
<td>120.2</td>
<td>22.2</td>
<td>.319</td>
</tr>
</tbody>
</table>
4.2 Discussion:

Type 2 diabetes mellitus and dyslipidemia are important risk factors for cardiovascular disease. Elevated serum levels of LDL-C and TG and low levels of HDL-C are strongly associated with increased risk for macrovascular events (e.g., myocardial infarction, ischemic stroke, and coronary mortality) among patients with T2DM. Small dense LDL particles are more atherogenic because these particles, especially when glycated, are more easily oxidized and ‘picked up’ by the scavenger receptor on the macrophage which has a much greater affinity for oxidized LDL than for non-oxidized LDL. Macrophages therefore facilitate the transportation of these particles through the intima to the subintimal space and media of the artery where the process of atherogenesis is initiated and accelerated by these highly atherogenic particles.

This study confirm that diabetes and hypertension have strong effect on cholesterol level both are causes of cholesterol elevation the mean level for diabetic patients (206.5 mg/dl, hypertensive patients 177.1 mg/dl and diabetic hypertensive patients 220.2 mg/dl, P value (0.016) significant

This study agreed with study done by Lemia Mohameed Yahia which is done in 2003 (Sudan University of Science and Technology) her study conclude to that there was a significant difference in cholesterol level in diabetic patients (p value 0.012)

HDL, LDL levels:

The mean level of LDL among the study groups is 114 mg/dl for diabetic patients, 102.4 mg/dl for hypertensive patients and 120.2 mg/dl for diabetic hypertensive patients, while the mean level for HDL is 40.6 mg/dl for diabetic patients, 55.5 mg/dl for hypertensive patients and 43.9 mg/dl for diabetic hypertensive patients.

The difference in LDL is not significant (P value 0.32) this illogical result may be due the small sample size also may be due that samples was taken from well medicated patient as our questionnaire prove that (all patients have good follow up by physician) a good control is the main reason for this difference.

There was significant difference in HDL (P value 0.00). The alteration in blood lipids and lipoproteins in patients with type 2 diabetes mellitus (represented by significantly higher TC, TG, LDL-C, VLDL-C and Lower HDL) can be as a consequence to defects in both insulin action and hyperglycemia.
Our findings agree with the study done by Sara Osman Yousif her study was done in 2010 at Jaber Abu Alezz center in Khartoum state, Sudan. The mean of the plasma levels of high density lipoproteins was significantly raised (p=0.000).
Chapter Five

Conclusions and Recommendations

5.1 Conclusions:

Serum total cholesterol level and HDL were elevated in diabetic hypertensive patients.

5.2 Recommendations:

- Lipid profile should be regularly monitored for both diabetic’s and hypertensive patient
- Increase sample size and further studies needed to study the assessment of lipid profile.
Chapter six

6. References

6.1 References


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of coronary atherosclerosis is associated with increasing circulating levels of high sensitive cardiac troponin T. Arteriosclerosis, thrombosis, and vascular biology, 30(6), pp.1269-1275.


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Appendices

1-Questionnaire:

Sex: Male ( ) Female ( )

Age: .............................................................

Occupational: ...................................................

Duration of disease: .................................

Weight: ..........................................................

Length: ..........................................................

Diabetics yes ( ) no ( )

Smoking: yes ( ) no ( )

Physical activity yes ( ) no ( )

Hypertensive yes ( ) no ( )

Diet yes ( ) no ( )

Results:

FBS.................................

LDL:.................................

HDL.................................

T-CHOL..............................

Troponin............................
2- Cholesterol:

Free and esterified cholesterol in the Sample originates by means of the coupled reaction described below, a colored complex that can be measured by spectrophotometry.

\[
\text{Cholesterol ester} + \text{H}_2\text{O} \rightarrow \text{cholesterol} + \text{fatty acid}.
\]

\[
\text{Cholesterol} + \frac{1}{2} \text{O}_2 + \text{H}_2\text{O} \rightarrow \text{cholestenone} + \text{H}_2\text{O}_2.
\]

\[
2 \text{H}_2\text{O}_2 + 4 \text{-Aminoantipyrine} + \text{phenol} \rightarrow \text{Quinoneimine} + 4 \text{H}_2\text{O}.
\]

3-LDL:

low-density lipoprotein (LDL) in the sample precipitate with polyvinyl sulfate. Their concentration is calculated from the between serum total cholesterol and cholesterol supernatant after centrifugation.

4-HDL:

The assay is a homogeneous method for directly measuring HDL –cholesterol concentration is serum or plasma, without any off-line pretreatments or centrifugation steps. Accelerator selective detergent methodology.

During the first phase LDL, VLDL particles and chylomicrons generate free non –HDL cholesterol, which through an enzymatic reaction, produce hydrogen peroxide, the generated peroxide is consumed by a peroxidase reaction with DSBmT yielding colorless products.

During the second phase, specific detergent solubility HDL –cholesterol. In conjunction with cholesterol oxidase CO and cholesterol esterase CE action, peroxidase and 4-AAP develop a colored reaction which is proportional to HDL –cholesterol concentration.