



REVIEW ARTICLE

Role of LDL and Triglycerides in Hyperlipidemia in Diabetes Mellitus

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Abstract

Diabetes mellitus (DM) is one of the diseases affecting people worldwide, regardless of region, race, blood type, and many more. So, the management of DM has been a challenging issue all over. Hyperlipidemia or Dyslipidemia is one of the main root causes of DM, leading to severe cardiovascular diseases. Behavioral therapies like diet and exercise can improve diabetic Dyslipidemia; however, most patients require drug therapy to meet treatment objectives. Statins, fibrates, niacin, and thiazolidinediones are a few drug families that can treat the abnormal lipid and lipoprotein levels linked to insulin resistance and type 2 diabetes. Since, Type I DM is an autoimmune disorder with no significant relationship with the levels of lipoproteins. This current paper focuses on patients with elevated levels of lipoproteins in DM-2.

Keywords

LDL, Triglycerides, Hyperlipidemia, Diabetes mellitus, Cholesterol, Hypertension

Introduction

People have changed their usual behavior by changing their food and lifestyle choices as a response to the mounting problems of modernity. As a result, man's lifestyle in the twenty-first century is being negatively impacted by fast food, inactivity, stress, and numerous addictions, to name a few. As a result, a mismatch between the outside world and a person's internal system leads to various diseases, many of which are caused by a malfunctioning metabolism and are thus commonly referred to as lifestyle diseases [1].

Diabetes mellitus

Diabetes mellitus [2] is a metabolic disease characterized by elevated levels of sugar in the blood

caused due to malfunction of insulin secretion or action. It is of two types: DM Type-I [3]- An autoimmune disorder caused due to pancreatic β cell loss and leads to hyperglycemia; DM Type-II [3]- Insulin resistance is the reduced ability to respond to insulin that characterizes T2DM. This condition causes insulin to become inefficient, which is initially countered by increased insulin synthesis to maintain glucose homeostasis. However, over time, insulin production falls, leading to T2DM.

Hyperlipidemia

Increase in the levels of fats and lipids in the blood are called as Hyperlipidemia [4]. This disease does not show signs or symptoms but can be very harmful and affect the cardiovascular system.

Dyslipidemia

Any abnormality in the lipid levels is known as Dyslipidemia.

Low-Density Lipoprotein [5] (LDL) - Most of your body's cholesterol is LDL (low-density lipoprotein), sometimes referred to as "bad" cholesterol. The risk of heart disease and stroke increases with prominent LDL cholesterol levels.

Triglycerides

Blood triglycerides [5] are a form of fat that the human body utilizes as fuel. LDL and triglycerides can collectively cause serious health problems.

Diabetes is a condition of hyperglycemia brought on by insufficient insulin activities. However, insulin also has a significant impact on serum lipids. Therefore,



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despite an insulin deficit or resistance, elevated serum lipid levels are frequently observed in diabetic populations. Without a doubt, low-density lipoprotein and cholesterol are the main contributors to the development of coronary artery disease and other atherosclerotic cardiovascular illnesses (CVD). However, among communities of people with diabetes, severe hypercholesterolemia is less commonly seen than hypertriglyceridemia and low high-density lipoprotein [6].

The World Health Organization (WHO) reports that among people older than or equal to 25 years, high plasma levels of total cholesterol were present in roughly 39% of cases globally in 2008, and elevated plasma LDL levels were responsible for more than one-third of CVD-related death [7]. Recent years have seen a rise in CVD rates in Southeast Asia due to the region's fast urbanization, socioeconomic growth, longer life expectancy, unbalanced food, and lifestyle adjustments. As a result, type 2 diabetes is becoming more common everywhere, and this growth is exponential. Almost 90% of all cases of diabetes are of type 2, which is also the most prevalent kind. Adults with diabetes accounted for almost 463 million people in 2019; by 2045, this figure is projected to rise to 700 million [7]. According to the most recent World Bank data, 8.8% of people in the 20- to 79-year-old age group worldwide have either type 1 or type 2 diabetes. According to the World Diabetes Federation's most recent figures, 8.9% of Indian people have diabetes. Between 1990 and 2016, there were 26.0 million and 65.0 million diabetes patients in India, respectively, and the disease prevalence among persons under 20 climbed from 5.5% to 7.7%. Elevated cholesterol is thought to cause 56% of ischemic heart disease and 18% of cerebrovascular illnesses worldwide. 40.4 million adjusted for disability years, and these disorders cause 4.4 million deaths (7.9% of the total) [8,9].

Over the last few decades, we can see a tremendous and continuous increase in the prevalence of DM. There is evidence that the prevalence of Dyslipidemia among diabetes patients is more significant in Asian countries. According to some research, body mass index, age, the length of time a person has had diabetes, Hypertension, diabetic nephropathy, and renal insufficiency are all linked to Dyslipidemia in people with diabetes mellitus. Coronary artery disease is the leading cause of mortality among people with diabetes. Diabetes is frequently linked to lipid problems, especially in type 2 diabetics [10]. Hypertriglyceridemia and decreased levels of HDL-C are the most prevalent lipid abnormalities in these individuals. While lipid abnormalities typically improve with improved glycemic management, normalization does not always occur since there is a significant correlation between type 2 diabetes, hyperlipidemia, and all kinds of vascular disease. These lipid abnormalities must be looked for and treated [10,11].

The incidence of type 2 diabetes in young people is rising, and it seems to strike them more quickly than it does adults, necessitating insulin therapy early, leading to greater complications from the disease and increased mortality. With type 2 diabetes, cardiovascular disease is one of the leading causes of morbidity and death in adults, and Dyslipidemia is a recognized modifiable factor for cardiovascular risk in adults [11]. Cardiovascular disease has precursors that are already present in youth. Unfortunately, there is a serious lack of longitudinal studies, and published data are constrained by limited sample sizes, retrospective nature of studies, shorter duration of follow-up, and inclusion of people taking lipid-lowering medication [12,13]. Although uncommon, Dyslipidemia has been documented in young people with type 2 diabetes.

A group of large organic molecules, including proteins and carbohydrates, are the lipids that constitute the structural components of our cells. Fats are not the sole component of lipids, but they also consist of some water-soluble substances necessary for the body's metabolism and physiology, such as triglycerides [14]. Among other things, lipids are crucial for signal storage, conversion, and cell-to-cell communication. Lipids are carried inside larger molecular complexes called lipoproteins because they are somewhat insoluble in water and do not circulate freely in the blood. As a result, adipose cells are continually breaking down and resynthesizing to provide energy, where triglycerides are stored [15,16].

Triglycerides are either created by the body or taken in from food. They are made up of three fatty acids bonded to glycerol [17]. Triglycerides rank second in importance to glucose as an energy source in human physiology. Increased synthesis or reduced breakdown of triglyceride-rich lipoproteins can cause hypertriglyceridemia, which increases the amount of atherogenic residual particles in blood [8]. The metabolic factors most linked to hypertriglyceridemia include obesity and uncontrolled or poorly managed diabetes. In addition, triglyceride levels can be raised by drinking alcohol, which raises plasma VLDL levels [15]. Hypertriglyceridemia is also linked to the VLDL-raising conditions of nephrotic syndrome and uremia. Type 2 diabetes, insulin resistance, metabolic syndrome, Cushing's syndrome, HIV infection, hypothyroidism, hypopituitarism, acromegaly, and some autoimmune diseases, including systemic lupus erythematosus are other ailments linked to increased triglyceride levels [15].

Hyperlipidemia

One of the most common lifestyle problems is hyperlipidemia. Its significance in the manifestation of major illnesses such as ischemic heart disease, diabetes, stroke has been recognized. It has been recognized as a possible risk factor for several illnesses, including cardiovascular conditions, metabolic syndrome, and

hypertension [1]. A high amount of lipids in the blood, such as cholesterol and triglycerides, is a sign of hyperlipidemia. Inconsistencies in the control of lipid metabolism constitute the primary pathophysiology of hyperlipidemia. The capacity of hyperlipidemia to contribute to the pathophysiology of atherosclerotic illnesses like coronary heart disease (CHD), a major source of morbidity and mortality globally, has sparked research on a global scale. In addition to coming from food sources, cholesterol is also created by the liver [15].

Dyslipidemia is a significant contributor to the risk of cardiovascular disease in people with diabetes mellitus. High plasma triglyceride levels, low HDL cholesterol levels, and an increase in the number of tiny, dense LDL cholesterol particles characterize diabetes-related Dyslipidemia. In developed regions, hyperlipidemia, or an increase in lipids in the blood, makes up the majority of dyslipidemias [18]. Diet and lifestyle are frequently to blame for this. High insulin levels can also bring on Dyslipidemia over time. The high-density lipoprotein (HDL) transports cholesterol away from the arteries and back to the liver, where it is processed and removed. It was discovered in some studies that the most critical factors causing dyslipidemia illness can also be creatinine, salt, and gender. LDL cholesterol, on the other hand, is referred to as "bad" cholesterol because it aids in the development of atherosclerosis, a condition marked by the buildup of plaque in the arteries [10].

The liver may overproduce cholesterol in hyperlipidemia, or the liver and intestines may be unable to eliminate LDL cholesterol from circulation properly. Additionally, a diet rich in trans and saturated fats can raise total and LDL cholesterol levels. An increase in the risk of heart attack, stroke, and peripheral artery disease can result from the buildup of plaque in the arteries, as can reduced blood flow, elevated blood pressure, and these conditions [19].

Dyslipidemia plays a significant role in the metabolic (vascular) syndrome, a key risk factor for cardiovascular illnesses, as a controlled risk factor for diabetes and cardiovascular disease. In type 2 diabetes mellitus, incorrect control of plasma glucose can aggravate Dyslipidemia and increase insulin resistance, which increases the risk of developing cardiovascular diseases. Also, it has been discovered that treating Dyslipidemia lowers diabetes odds of developing atherosclerotic heart disease. Remarkably, some studies show that the management of Dyslipidemia is not given the same priority as the management of hyperglycemia in patients with diabetic Dyslipidemia. Although hyperglycemia and Dyslipidemia are co-morbid conditions in diabetics, hyperglycemia in these patients is frequently handled without doctors requesting a lipid profile to track and control their blood lipid levels. There are several different lipid patterns observed in Type 2 diabetic

patients. This illustrates how many variables affect the plasma lipid profile [17,20].

The lipid patterns seen in diabetes individuals may change because of genetic variables, concurrent conditions, lifestyle choices, medication use, and other factors all impacting lipid levels. While total cholesterol may be normal or increased, many Type 2 diabetic patients have characteristically mixed Dyslipidemia, which includes hypertriglyceridemia, low HDL-C, and a predominance of tiny dense LDL. LDL-C content is not the primary anomaly and is frequently just modestly increased [13].

The most prevalent blood lipid abnormality in populations of diabetics is hypertriglyceridemia [21]. In addition to being raised in proportion to the degree of hyperglycemia, serum TG levels are also tightly associated with caused by insulin resistance. In addition to aberrant fasting lipid levels, individuals have abnormal postprandial lipoprotein metabolism. This is especially true and clear for postprandial triglyceride levels. In the postprandial stage, triglyceride-rich lipoproteins are frequently present in higher concentrations and for longer in diabetic individuals. However, in addition to aberrant concentration, diabetic Dyslipidemia is also characterized by a changed lipoprotein composition. However, triglyceride-rich lipoproteins may also exhibit aberrant composition. In particular, the composition of HDL and LDL may be changed. Throughout the globe, type 2 diabetes mellitus (T2 DM) is still the most significant cause of mortality, accounting for fewer than 5% of all fatalities [13].

Generally, patients with DM-2 have a high risk of developing life-threatening coronary diseases [22]. Diabetes is related to an increased risk of cardiovascular diseases, so managing diabetes with hyperlipidemia is crucial in preventing cardiovascular diseases in patients with DM-2. The alarming rise in Dyslipidemia around the globe has been attributed to accelerating socioeconomic change and a shift in lifestyle. Research has indicated that almost 50% of the population's risk of developing cardiovascular disease is linked to anomalies in lipoprotein metabolism. The most prevalent lipoprotein pattern associated with diabetes sometimes referred to as diabetic Dyslipidemia or atherogenic Dyslipidemia, is characterized by a moderate triglyceride increase, low HDL, and small dense LDL [22]. The lipoprotein pattern is associated with insulin resistance before the onset of diabetes, so levels of these lipoproteins play an essential role in DM-2. A study found that, in Nigeria, at least one lipid abnormality is found in 70% of persons with type 2 diabetes mellitus. As a result, effective interventional strategies are required to treat Dyslipidemia in T2DM patients [23].

Although there have been advances in treatment methods, there has been a slight improvement in the long-term prevention and management of

cardiovascular disease, particularly in diabetes mellitus, and the morbidity and death rates are still relatively high. Epidemiology studies have shown that diabetes mellitus is a standalone risk factor for cardiovascular disease and exacerbates the effects of other well-known risk factors such as Hypertension, smoking, and high cholesterol. Compared to non-diabetics, the mortality associated with a coronary episode is considerably higher in patients with diabetes mellitus. Cardiovascular disease, particularly coronary heart disease (CHD) and stroke are by far the leading cause of mortality among people with type 2 diabetes and is associated with a significant risk of atherosclerosis [11]. The risk of major vascular events is decreased by statins by around one-fifth of each millimole per liter decrease in LDL cholesterol, with proportionally equal reductions in major coronary events, stroke, and the requirement for coronary revascularization. However, the residual risk is still substantial [24,25].

The exact cause of vascular damage is unknown, even though diabetes people have a higher-than-average risk of developing atherosclerosis, and Dyslipidemia appears to be a significant relationship. It appears essential to have more apoB-containing lipoproteins (either in the form of remnants, small dense LDL, or VLDL). The scavenger receptor and tiny dense LDL interact more favorably, promoting the development of foam cells and atherogenesis [17].

LDL cholesterol and Lp(a) concentrations had a clear correlation. Diabetic individuals are inversely linked with lipid levels. Consequently, managing diabetic Dyslipidemia may indirectly impact Lp(a) concentrations. Both in the general population and in diabetic patients, lipoprotein(a) [Lp(a)] is a significant risk factor for atherosclerosis. A disulfide linked to apolipoprotein B (apo B) attaches apolipoprotein(a) [apo(a)] to an LDL-like particle called Lp(a). Genetic variation at the LPA gene is the primary genetic factor influencing Lp(a) serum levels; however, nongenetic variables may also have an impact. Undoubtedly, several types of research have demonstrated the impact of nutrition, the use of various medicines, and hormones on Lp(a) levels. Diabetic nephropathy appears to be the factor most correlated with the factors that might affect Lp(a) concentrations in diabetic individuals [26,27].

The therapy of high triglyceride (TG) and low HDL cholesterol levels is still unclear, despite current guidelines calling for an aggressive therapeutic approach to lower LDL cholesterol, blood pressure, and glucose levels in diabetic patients. The American Diabetes Association [22] has given standard levels for lipoproteins as follows-

- LDL- < 100 mg/dl,
- HDL- < 40 mg/dl in men and > 50 mg/dl in women
- Triglycerides- < 150 mg/dl

Increased triglyceride levels and decreased levels of HDL is the most common type of manifestation of Dyslipidemia seen in type-II DM patients. People with type 2 diabetes do not substantially vary from those without the disease in terms of the mean LDL cholesterol content. LDL cholesterol, however, may have undergone some qualitative alterations. Patients with diabetes tend to have larger proportions of smaller, denser LDL particles, which are more prone to oxidation and may raise the risk of cardiovascular events. Renal disease, hypothyroidism, and some genetic disorders are some of the factors which cause Dyslipidemia in patients without diabetes mellitus. Overuse of alcohol and estrogen may also cause hypertriglyceridemia [19].

The condition of elevated levels of triglycerides in the blood is called hypertriglyceridemia. Insulin resistance and high blood sugar are two major contributors to hypertriglyceridemia. In addition, the liver overproduces lipoproteins, their clearance is slowed down, and in certain circumstances, the metabolism of postprandial lipoproteins is changed because of these processes. Hypertriglyceridemia is directly related to the causes of low HDL-C and the preponderance of small dense LDL. While it seems likely that each of these abnormalities is connected to atherosclerosis [28], it is unknown if any one of them-and if so, which-is the leading risk factor or whether the aggregate of lipid blood triglyceride levels have been demonstrated to be an independent risk factor for coronary heart disease after adjusting for LDL and HDL cholesterol [28,29].

If a lipid-lowering medication is necessary, statin treatment should generally be the first option, given the efficacy of these drugs in diabetic participants, as shown by outcome data. Fibrates may be utilized in individuals with severe isolated hypertriglyceridemia. Combination treatment to further reduce LDL-C or address LDL-C, HDL-C, and triglycerides should be considered in individuals at very high risk [21,30].

Some genetic disorders, such as Familial hypercholesterolemia, also cause an increase in the levels of LDL. Familial hypercholesterolemia is a dominantly inherited condition marked by high plasma levels of low-density lipoprotein (LDL) cholesterol and poor hepatic cholesterol absorption. Although many problems are largely due to insulin resistance (and not hyperglycemia), Dyslipidemia can worsen with high blood sugar levels. It is especially true for hypertriglyceridemia, which hyperglycemia can make worse. It's significant from a therapeutic perspective. Decreasing high glucose readings improves dyslipidemia [31].

Early in pregnancy, lipidemia is somewhat elevated; by the second and third trimesters, it is more evident. Nowadays, it is challenging to determine whether a lipid rise is pathogenic or normal at a certain level. There is disagreement over the diagnostic standards for

hyperlipidemia during pregnancy. During pregnancy, the body's various organs must work much harder, which may raise the risk of developing metabolic illnesses. Up to 22% of pregnancies may have gestational diabetes mellitus (GDM), a metabolic condition prevalent in pregnant women. Women with GDM during pregnancy are more likely to experience maternal and newborn problems, such as cesarean delivery, postpartum hemorrhage, preterm birth, macrosomia, and small for gestational age. Being a known contributor to metabolic disorders, Dyslipidemia is a risk factor. Compared to women without GDM, patients with GDM had a higher lipid profile, according to earlier research. Also, evidence supports the notion that hypertriglyceridemia is one of the most typical changes in GDM-complicated pregnancies. The use of lipid profiles in predicting GDM is contentious in any case. Maternal Dyslipidemia and pregnancy problems also bring on adverse perinatal outcomes. During 15-27 weeks of gestation, a study reported that high levels of triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and total cholesterol (TC) were associated with a higher risk of spontaneous preterm birth. Recent research has shown a link between gestational Dyslipidemia and low birth weight outcomes. Pregnancy-induced hyperlipidemia has also shown a solid connection between cesarean section and postpartum hemorrhage. Even though moderately elevated lipidemia plays a crucial role throughout pregnancy, disagreements exist regarding the connection between maternal lipid abnormalities and perinatal outcomes [30,32-34].

A recent study shows Type 2 diabetes is becoming more common in kids of all racial and ethnic backgrounds at a rate that has outpaced predictions and is already concerning. Nowadays, type 2 diabetes diagnoses among Mexican American children are viewed as an epidemic. Although obesity and abnormal lipid levels are established risk factors for developing major diabetic complications in adulthood (American Diabetes Association [ADA] 2003), the current care guideline for type 2 diabetes in children does not require evaluating lipid profiles. It is unclear in that study if type 2 diabetes in MA children predisposes them to major diabetic problems at a young age by causing aberrant lipid levels. The study reveals Significant correlations between obesity as evaluated by BMI and aberrant TC, HDL, and triglyceride values seen in Mexican American children with type 2 diabetes. Only good eating and regular exercise are currently recognized therapeutic options for Dyslipidemia in children. Children have not been approved for medications used in the adult population that have significantly reduced lipid levels [35,36].

In a study, research documenting the changes in lipid concentrations and lipid status over an average of seven years in a large multiethnic cohort of adolescents and young adults with youth-onset type 2 diabetes who were

not receiving lipid-lowering treatment was examined. This finding indicates that adolescents and young adults with type 2 diabetes who first had the disease during childhood risk developing permanent abnormal lipids without using a lipid-lowering medication and that control may be linked to this Dyslipidemia. The study also concluded that most young people with type 2 diabetes had abnormal LDL and triglycerides that progressed over time or remained constant. Moreover, glycemic management may, over time, be linked to the development of unstable abnormal LDL and triglycerides. The study's findings highlighted the significance of lipid screening in adolescents and young adults with type 2 diabetes of early onset and the potential role of glycemic management in enhancing long-term cardiovascular health and decreasing the impact of chronic illness [37,38].

Prevention

Screening and identification of Dyslipidemia and related risk factors are crucial first measures to stop the progression and occurrence of cardiovascular illnesses in every country. Nevertheless, most underdeveloped nations lack accurate data on the prevalence of Dyslipidemia and the factors that influence it. Before beginning or stepping up treatment, it is crucial to identify secondary causes of Dyslipidemia. The requirement for treatment may be drastically reduced if the underlying problem is treated and Dyslipidemia is improved. The co-morbidity may change subsequent therapy choices if it is recognized. Certain dyslipidemias may appear resistant to therapy in an unidentified secondary etiology [35,39].

To rule out patients who could be treated or cured using methods other than triglyceride- or cholesterol-lowering medicines, secondary causes of Dyslipidemia should be identified once the condition has been recognized. A thorough medical, familial, and nutritional history must be taken before a physical examination to identify other risk factors. Glucose, TSH, plasma creatinine, protein electrophoresis, alkaline phosphatase, and transaminases are typical laboratory tests that help rule out a secondary cause of Dyslipidemia. Urinalysis is another standardized test. Also, should include all the prescriptions, over-the-counter medicines, and nutritional supplements. After determining the secondary cause of Dyslipidemia, it is necessary to continue monitoring lipid levels since some illnesses raise the chance of developing ASCVD and call for more aggressive lipid-lowering treatment [8].

Cardiovascular risk scores are regarded as valuable tools in the management of diabetes, especially when they are developed in the same population. Well-categorized risk scores are excellent for identifying high-risk individuals so that therapy may be focused on them. On the other hand, the process of precisely

computing absolute risk to provide prognostic information is helped better by risk scores. Framingham models -the 10-year risk of CHD events, ASSIGN (CV risk estimation model from the Scottish Intercollegiate Guidelines Network) -the 10-year risk of first CVD event, QRISK3 - the 10-year risk of CVD event, Prospective Cardiovascular Munster Study (PROCAM) Two separate scores calculate 10-year risk of major coronary events and cerebral ischemic events, Reynolds Risk Score- the 10-year risk of incident myocardial infarction, stroke, coronary revascularization, or CV death, CUORE- the 10-year risk of first CVD event, Pooled Cohort equations- the 10-year risk of CVD event, Globorisk- the 10-year risk of CVD mortality are some of the known risk score calculating methods [8,40].

In addition to glycemic control, type 2 diabetes requires effective treatment of lipid parameters and Hypertension to avoid chronic issues, notably harmful macrovascular outcomes. Conditions will be better controlled, and the risk of cardiovascular disease will be reduced with early detection and optimal care. Despite the right therapy being started for this illness, studies demonstrate that poor adherence to the prescribed course of action prevents patients from reaching their control goals [28]. Regular exercise is presently one of the lifestyle changes advised for those with diabetes since it has been shown to break down fat molecules through beta-oxidation in healthy people. It postpones poor glucose metabolism and insulin receptor desensitization [13]. Diabetic lipid abnormalities must be managed with diet, exercise, and weight loss in overweight people [22].

The NCEP and the ADA recommend cutting back on saturated and trans-fats to reduce LDL cholesterol levels. The NCEP ATP III advises keeping cholesterol consumption to 200 mg daily and keeping saturated fat intake to 7% of daily calories. Adding 2g of plant stanols or sterols to the diet daily, increasing the quantity of soluble dietary fiber in the diet to 10-25 grams, and including soy protein are other dietary alternatives to decrease LDL cholesterol. A 5-15% decrease in LDL cholesterol readings has been linked to these therapies. For people with high triglycerides and low HDL cholesterol, ATP III advises keeping carbohydrate consumption under 60% of total calories. The ADA also suggests switching out saturated fat with monounsaturated or carbohydrate fat. Because of the rising prevalence of associated disorders, including obesity, insulin resistance, and type 2 diabetes, controlling patients' triglyceride levels is particularly crucial [41,42].

Some studies state that those at high risk require treatment on a scale with secondary CVD prevention. The most crucial stage in setting treatment objectives for diabetic individuals with Dyslipidemia is a thorough evaluation of their cardiovascular risk, with LDL-C as the primary aim and non-HDL-C, HDL-C, and apo B as

additional targets [35]. Managing Dyslipidemia requires a comprehensive approach to control cholesterol levels, address the associated metabolic abnormalities, and address modifiable risk factors. Essential factors to consider to lower the risk of CVD and enhance glycemic control and lipid profile are to obtain a healthy weight and amount of aerobic activity [8]. Adopt a diet that is well-balanced and limited in energy. Alcohol use should be avoided or kept to a minimum, and smoking (or other tobacco) should be stopped. Every person with diabetes must actively participate in self-management, education, and treatment planning with their health professionals, as well as the combined formulation of a customized dietary plan. Medical nutrition therapy is a crucial component of diabetes management. A greater risk of vascular events is thought to exist in those with type 2 diabetes. Therefore, they should be evaluated for Dyslipidemia independent of any risk factors found through a physical examination or history (such as smoking, Hypertension, obesity, or polycystic ovarian syndrome in women). Screening for Dyslipidemia in people with type 1 diabetes should start at twelve years old. Screening should start at age two when there is a known family history of hypercholesterolemia or early CVD or if there is no known family history. If test results fall within acceptable ranges, screening should be performed every five years until maturity and once a year after that [8].

Non-Pharmacological Therapy

Improving glycemic control and decreasing weight should be the first steps in treating hyperlipidemia. Exercise should be included in a weight reduction program since research shows it can help with weight loss and maintenance. Triglyceride levels will drop, and HDL levels will rise due to losing weight. Concomitant medical disorders that might enhance the hazards of exercise should be considered before recommending an exercise program, such as proliferative retinopathy, neuropathy, and foot difficulties, among others. It is prudent to recommend an exercise tolerance test to rule out silent myocardial ischemia, particularly in patients older than thirty-five. Lipid profile examination must be done regularly to check and be up to date regarding the levels of lipids, which may be concerning at times [43,44].

Patients with better diets and more exercise report fewer cardiovascular events. The ADA has offered medical nutrition treatment (MNT) and exercise advice. Reduced triglyceride, elevated HDL cholesterol levels, and a little reduction in LDL cholesterol will result in weight loss and increased physical activity. Therefore, MNT and increased physical activity should be prescribed to diabetic patients who are overweight. In addition, the meal plan should have less saturated fat overall. To compensate for the decrease in saturated fat, the ADA advises increasing either carbohydrate

or monounsaturated fat. According to some research, a high-monounsaturated fat diet may have better metabolic benefits than a high-carbohydrate diet, while other experts have argued that this dietary change may make it harder for obese individuals with diabetes to lose weight [22,45].

Addressing abdominal fat and insulin resistance is more crucial. The main objective is to maintain a healthy lifestyle and average weight. Losing weight lowers triglycerides and raises HDL-C levels. Simultaneously, the distribution of LDL subtypes changes from primarily small-dense LDL to less-dense LDL. The lipid profile improvement can be furthered by exercise [17].

In addition to these basic guidelines, it is essential to emphasize that individuals with raised triglycerides should avoid consuming alcohol and glucose because they may specifically exacerbate hypertriglyceridemia. The mainstay of therapy is a lifestyle change. Taking an interdisciplinary strategy that involves talking to a licensed dietitian¹⁶ could be advantageous. The goal for overweight individuals is to lose weight by eating fewer calories and exercising more often daily; cutting back on carbohydrates can also help patients lose weight and lower their triglycerides. Physical exercises have been demonstrated to lower triglycerides by up to 20% in people with levels more than or equal to 150 mg/dL. Excessive alcohol use is known to enhance the production of VLDLs and cause hypertriglyceridemia, even if the evidence shows that low-to-moderate alcohol consumption may reduce triglyceride levels. Because the kind of alcohol consumed and other factors, such as a high-fat diet, might worsen hypertriglyceridemia, doctors should advise patients with high triglyceride levels to cut back on or stop drinking alcohol. Also, doctors should advise patients to eat fresh produce, whole grains, and fish with omega-3 fatty acids, as well as plants and plant-based foods with omega-3 fatty acids, like flaxseed, walnuts, and soybeans. Diets with moderate amounts of plant-based proteins and unsaturated fats may also reduce triglyceride levels [19,46].

According to the American Heart Association's recommendations for CVD patients, the maximum MNT often lowers LDL cholesterol by 15-25 mg/dl (0.4-0.65 mmol/l). Lifestyle intervention may be monitored regularly while considering pharmaceutical therapy after three to six months [47]. Test for lipid abnormalities in adult patients at least once a year and more frequently if necessary to meet objectives. Repeat lipid tests every two years in people with low-risk cholesterol levels (LDL 100 mg/dl, HDL 50 mg/dl, and triglycerides 150 mg/dl). Patients with clinical CVD, low HDL, and near-normal levels of LDL have a lower risk of cardiovascular events when their triglyceride levels are lowered, and their HDL cholesterol is increased [8].

The primary treatment strategy was to lower the

LDL to < 100 mg/dl, and recommended level to start the drug therapy is > 100 mg/dl for LDL with coronary heart disease and > 130 mg/dl in patients without coronary heart disease. Some studies state that statin therapy achieves an LDL cholesterol lowering of up to 30% irrespective of actual LDL cholesterol levels, which is appropriate [22]. The NCEP report sets an optional objective of 70 mg/dl in the latter category of patients, and the guidelines make it possible to start statins almost independently of LDL cholesterol in patients regarded to be at high or extremely high risk. The main factors influencing the statin selection should be the LDL reduction required to reach the objective (100 mg/dl [2.60 mmol/l]) and the doctor's assessment [22].

Pharmacological Therapy

Among other metabolic risk factors, lowering cholesterol levels can considerably lower the likelihood of developing CVD. Patients with type 2 diabetes mellitus (T2DM) have also shown a substantial reduction in CVD occurrences when treated with statin treatments. In addition, statins are, by nature, safe to use. Cardiovascular advantages with statin treatment are shown in the DM population for primary and secondary prevention. For everyone mmol/L decrease in LDL, the incidence of significant cardiovascular disease (CVD) events over five years decrease by 23%. As a result, major society recommendations support statin medication as a first-line treatment for primary and secondary prevention of CVD. When combined with statin medication, the non-statin therapy ezetimibe has been shown to drop further LDL-C levels and considerably lower the primary efficacy of Cardiovascular outcomes [8]. Another study found that Statin alone was generally the most popular lipid-lowering treatment among the group, followed by combined statin and fibrate medication and fibrate monotherapy. Simvastatin was the statin that was most frequently given, followed by atorvastatin [30].

Cardiovascular events are highly likely to occur in diabetic patients with combined Dyslipidemia, particularly those with coronary heart disease or other types of atherosclerosis. If the patient's lipid goals are not met with monotherapy, combination therapy should be considered. Numerous combinations are available in this scenario. The choice of combination therapy is made based on the lipid profile seen during monotherapy. However, despite taking statins, many diabetic individuals still have LDL, triglycerides, and/or HDL levels over the target range. Therefore, in this instance, niacin and statins may be mixed [48-62].

Conclusion

Despite various guidelines given for diet and exercise, and drug management therapy, the seriousness of diabetes evolving is not being decreased in the real world due to the lifestyle people have these days. Moreover, abnormalities in lipoproteins continue to

persist and create health problems. Therefore, LDL and triglycerides have a significant role in patients with diabetes associated with hyperlipidemia. Nevertheless, proper diet, exercise, non-smoking habits, and regular health checkups can help prevent serious health diseases. In short, a healthy lifestyle can only decrease the incidence of these metabolic diseases.

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