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Review Article

### ADVANCES IN THE MANAGEMENT OF DYSLIPIDEMIA

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**Abstract:**

**Introduction:** Dyslipidemia mainly refers to a disbalance of any form of lipid in the body. Any disbalance of lipid in the body puts the body at a higher risk of coronary and peripheral artery diseases. With the discovery of statins, there has been a huge revolution in the treatment of dyslipidemias. They have shown evidence of reduced levels of LDL with statin leading to a reduction in evidence of CVD.

**Aim of work:** This review aims at discussing the various therapies and new management strategies developed for managing dyslipidemias associated with CVD or Chronic kidney diseases.

**Methodology:** The review is a comprehensive research of PUBMED, Google Scholar, and WHO official page from the year 2010 to 2021

**Conclusion:** Dyslipidemias tend to increase the patients' risk for major cardiovascular events, which can lead to a higher mortality rate in patients with existing cardiac or kidney disorders. There has been an increased interest in the treatment of dyslipidemias, and various genetic therapies and novel medication, including plant-based proteins, have shown a major breakthrough in the management of dyslipidemias. These novel therapies have proven to be a good adjunct to conventional treatment strategies and hence should be tested more thoroughly.

**Keywords:** Dyslipidemias, Cardiovascular disease, Apolipoproteins, Chronic kidney disease.

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**INTRODUCTION:**

Dyslipidemia mainly refers to a disbalance of any form of lipid in the body. Any disbalance of lipid in the body puts the body at a higher risk of coronary and peripheral artery diseases. A lot of epidemiological studies have shown that a disbalance in the lipid content of the body causes increased chances of developing any ischemic heart disease. Increased incidence of insulin resistance also increases the level of low-density lipids and decreases high-density lipid, which in turn increases the chances of arterial diseases.<sup>[1]</sup>

Dyslipidemia can be divided into two groups, primary and secondary. When Dyslipidemia is not associated with any underlying disease and is independently present in the patient, that's the primary form; if the cause of Dyslipidemia is another underlying disease, it falls under the secondary dyslipidemia category. Dyslipidemia also shows a genetic pattern of presentation and is generally seen in the offspring if both the parents suffer from it.<sup>[1]</sup>

**Clinical Sequelae of Dyslipidemia**

Dyslipidemia seen in patients with renal disorders increases the chances of atherogenic and cardiovascular diseases. Apart from this, it also causes increased deposition of lipids, which in turn causes a decline in kidney function. This increased quantity of lipids damages the cellular structure of the kidney, including the mesangial, endothelial, and glomerular cells, by causing inflammation which leads to glomerulosclerosis and reduction in the function of nephrons which in turn causes reduced renal function. Patients who have cardiovascular diseases have a higher rate of mortality when accompanied by increased levels of LDL. Clinicians have concluded that secondary Dyslipidemia generally accompanied by renal impairment increases chances of mortality in cardiovascular diseases and should be treated vigorously like any other metabolic diseases, for, e.g., diabetes mellitus.<sup>[2]</sup>

**Management of Dyslipidemia**

Due to the increased chances of mortality associated with cardiovascular disease and a strong correlation of dyslipidemias with CVD, the management of dyslipidemias has become extremely important. LDL-C has an increased probability of causing atherogenic diseases and hence has been a core topic for researchers. With the discovery of statins, there has been a huge revolution in the treatment of dyslipidemias. They have shown evidence of reduced levels of LDL with statin leading to a reduction in evidence of CVD. In cases where the patient has taken

maximum statin dose and is still not showing any improvements, other enzymes like ezetimibe, Proprotein convertase subtilisin-Kexin type 9, etc., can be used as adjunct therapies with statins. This review further aims at discussing the various therapies and new management strategies developed for managing dyslipidemias associated with CVD or Chronic kidney diseases.<sup>[3]</sup>

**Management of Dyslipidemia associated with Cardiac Diseases****Therapy based on Apolipoproteins**

Apolipoprotein helps in decreasing the chances of cardiovascular disease. In a meta-analysis that comprised eight trials with 38,153 patients who were currently taking statins, the quantity of Apolipoprotein, when increased, showed a decrease in any major cardiovascular events. There are three ways to administer Apolipoproteins which include intravenous administration, Apolipoproteins mimetic peptides, and medicines that could induce Apolipoproteins.<sup>[4]</sup>

A phase II trial, including 798 patients with coronary artery disease, was done with Apolipoprotein releasing medicine Apabetalone. The patients were randomly distributed into two groups, in which one group received the Apabetalone and the other was put on placebo; the group receiving the medication showed a lower incidence of cardiac events. This incidence was found to be higher in patients who also had a history of Diabetes Mellitus.<sup>[5]</sup>

**RNA based therapies**

Genetic modification is another way to tend to dyslipidemias. Antisense Oligonucleotide and small interfering RNA have shown evident success in managing dyslipidemias through genetic modification. They tend to alter, inhibit or split the RNA interference and hence tend to alter the genetic expression of the disease.<sup>[6]</sup>

**Therapies based on Viral Vectors**

Dyslipidemia conditions have shown remarkable improvement after administration of Adeno-associated virus. Significant reduction in the number of triglycerides was seen in patients administered with Alipogene tiparvovec (a gene that forms a copy of the LPL gene) because of the high maintenance cost as compared to the functionality of the medicine was put out of use.<sup>[6]</sup>

**Management of Dyslipidemias in Kidney Disease Chronic Kidney disease**

Statins have shown very promising results in lowering the lipid value and reducing the chances of cardiovascular disease. Patients suffering from uremia when put on statins have shown a reduction in levels of cholesterol and LDL, but the efficacy of statin on patients with kidney dysfunction depends largely on the severity of the existing disease. Statins tend to reduce the inflammatory process in the interstitial cells and hence increases the renal blood flow and decrease the severity of proteinuria from the glomerulus, thereby reducing renal dysfunction. In a study conducted by Mesquita et al., where two groups of patients were included, one receiving 80mg atorvastatin and the other receiving 10mg for a 5year duration. The group with 80mg showed a significantly higher rate of glomerular filtration.<sup>[7]</sup> Fibrates have also shown good results in patients with chronic kidney disease by decreasing the levels of serum triglycerides. The KDIGO guidelines recommend dietary and lifestyle changes for adults with Chronic kidney diseases, which include changing the overall diet of the patient, switching to low fat and low carbohydrate diet, increased physical exercises, reduction in alcohol consumption, etc.; these lifestyle modifications should be done very carefully in patients with existing dietary issues like malnourishment.<sup>[8]</sup>

#### **Nephrotic Syndrome:**

Patients with nephrotic syndromes have an increased rate of protein secretions, and a reduction in the same may decrease levels of dyslipidemia. Medicines like Angiotensin II receptor blockers and ACE inhibitors have shown a reduction in urine protein, thereby improving the kidney dysfunction in patients with nephrotic syndrome.<sup>[8]</sup>

#### **Emerging therapies and management plan for Dyslipidemias.**

**A plant-based diet:** A plant-based diet which includes a vegan or vegetarian diet, Nordic diet pattern have shown to decrease the risk of cardiovascular diseases in patients with dyslipidemias. The main components of a plant-based diet are dietary fibers, fat from the vegetables, and phytonutrients like phytosterols.<sup>[9]</sup>

**Polyphenols:** Polyphenols are antioxidant in nature and are found in plant-based foods; they have shown an increased efficacy in lowering the triglycerides level in the body, although very strong clinical evidence is lacking, which necessitates further study to associate polyphenol treatment in case of dyslipidemias.<sup>[10]</sup>

**Niacin or Nicotinic Acid:** Niacin has been shown to decrease the incidence of major cardiac events and mortality related to it by reducing the low-density lipoprotein levels and increasing the HDL. Niacin also tends to enhance the blood vessels' health and reduce atherogenesis.<sup>[11]</sup>

**Recombinant LCAT:** The enzyme present on the surface of HDL causes the esterification of cholesterol to cholesteryl esters. This, in turn, causes a reversal in the transportation of cholesterol. LCAT showed an increase in the levels of HDL-C by 6 to 42%.<sup>[11]</sup>

**Evinacumab:** Evinacumab is an antibody to Angiopoietin-like protein (ANGPTL3 ) that has been shown to reduce the levels of LDL-C in patients with homozygous (HoFH) familial hypercholesterolemia.<sup>[4]</sup>

#### **CONCLUSION:**

Dyslipidemias tend to increase the patient's risk for major cardiovascular events, which can lead to a higher mortality rate in patients with existing cardiac or kidney disorders. There has been an increased interest in the treatment of dyslipidemias, and various genetic therapies and novel medication, including plant-based proteins, have shown a major breakthrough in the management of dyslipidemias. These novel therapies have proven to be a good adjunct to conventional treatment strategies and hence should be tested more thoroughly.

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