

Isolated Hypertriglyceridemia – A Missed Out Mystery Killer In Need Of Imminent Indispensable Investigations !!!

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ABSTRACT

Isolated Hypertriglyceridemia can be inherent right from the childhood days but goes undetected as they are silent and symptom-less among the majority. This becomes quite alarming as it starts manifesting the glimpses of its drastic complications at a later age. The Terminology Hypertriglyceridemia is coined to high triglycerides (fats) in blood beyond the normal range. Normal triglyceride level in adults is up to 150 milligrams per deciliter (mg/dL). and when the level is enormously increased it raises the risk of Atherosclerosis, Heart ailments and Pancreatic diseases. Majority with hypertriglyceridemia are symptomless and clueless. Individuals with severe hypertriglyceridemia may have xanthomas, that are skin bumps formed when lipids accumulated under your skin. The common causes of Hypertriglyceridemia include Dietary and Lifestyle factors and Genetic lipid disorders. Dietary and Lifestyle factors have powerful influence on the triglyceride level resulting in the conversion of extra calories into triglycerides. A genetic disorder with dietary and lifestyle factors usually combine to cause hypertriglyceridemia. The increased Serum triglyceride levels also leads to increased risk of cardiovascular disease in joining hands with other risk factors such as Obesity, Metabolic syndrome, and type 2 Diabetes mellitus. The increased risk of acute pancreatitis is another complication when serum triglyceride level is very high. A 10 -12 hours fasting serum lipid panel diagnoses hypertriglyceridemia. Certain causes like aging and some medical ailments can never be altered. Still a lot to be practiced in daily life to prevent hypertriglyceridemia. The suggested dietary and lifestyle are Eating regularly a heart-healthy diet and adopting an active Lifestyle involving planned regular exercise.

Introduction:

A silent and a mysterious abnormality that is on the rise among the adolescent and adult individuals is Isolated Hypertriglyceridemia. serum triglycerides are commonly higher in men than in women, especially upto 70 years of age. The levels increase with age in both genders. The prevalence of hypertriglyceridemia is increasing among youth and adolescents due to increasing rates of obesity and Diabetes mellitus. The prevalence of hypertriglyceridemia was about 42% in people aged 60 years or older. This terminology can be inherent right from the childhood but goes undetected as they are silent and symptomless among the majority. This becomes quite alarming as it starts manifesting the glimpses of its drastic complications at a later age. Subjecting the individuals to the investigative procedures when they throw few non specific vague symptoms detects the enormous increase in this serum triglycerides and this abnormal increase leads to various serious systemic complications involving the Heart, Liver, Pancreas etc. Prompt Diagnosis of the same and early institution of therapy to reduce the enormous increase of Serum Triglycerides can avert the major debacles of complicated ailments thereby leading onto a normal healthy life expectancy. Consistent periodic screening Of this particular lipid parameter initiated earlier through the clues from the detailed family and Genetic

History will be a major eye opener in the preventive mode of life threatening ailments attacking the Homo sapiens.[1]

The Term Hypertriglyceridemia refers to high triglycerides (fats) in blood beyond the normal range. Normal triglyceride level in adults is up to 150 milligrams per deciliter (mg/dL). A triglyceride level below 100 mg/dL is ideal and when the level is enormously increased it raises the risk of atherosclerosis, heart and pancreatic diseases. Lifestyle changes are the need of the hour to tackle this condition. Triglycerides are lipids that provide energy to the body. Sources of triglycerides from foods we eat are butter and oils. Importantly when we consume Increased calories than the normal requirement, the body converts the calories into triglycerides. [1,2,3]

Hypertriglyceridemia is a commonly encountered lipid abnormality with other lipid and metabolic derangements. A fasting lipid panel in adults over the age of 20 will enable the early diagnosis. The discovery of hypertriglyceridemia must always be evaluated for secondary causes such as excessive alcohol intake, history of medications and medical conditions such as diabetes mellitus, hypothyroidism. patients should also be checked for other components of the Metabolic syndrome like abdominal obesity, insulin resistance, low High-density lipoprotein (HDL) and hypertension.[1,2,3] Hypertriglyceridemia is designated as primary hypertriglyceridemia when the cause of the same is not due to any secondary causes. Primary hypertriglyceridemia is due to multiple genetic defects leading to abnormal triglyceride metabolism. It is vital to treat hypertriglyceridemia at the earliest to prevent pancreatitis complication. Furthermore, decreasing the serum triglycerides level while treating for dyslipidemias and components of the Metabolic syndrome will minimize the coronary events. Dietary and lifestyle changes are the ultimate line of treatment for hypertriglyceridemia. These changes advocated are a low saturated fat, carbohydrate-controlled diet, alcohol reduction, quitting smoking and regular exercises. Increased intake of omega-3 fatty acids from fish and fish oil supplements will lower serum triglyceride levels significantly. When patients do not reach their goals by dietary and lifestyle changes, drug therapy should be initiated. In cases of isolated hypertriglyceridemia, fibrates are the first line therapy. [1,4]

Majority with hypertriglyceridemia are symptomless. Individuals with severe hypertriglyceridemia may have xanthomas, that are skin bumps formed when lipids accumulated under your skin. The common sites of xanthomas are around the eyelids. They do appear on the knees, elbows or palms of the hands.[1]

The common causes of Hypertriglyceridemia include Dietary and lifestyle factors, Medications, Genetic lipid disorders. Dietary and Lifestyle factors have powerful influence on the Serum Triglyceride level resulting in the conversion of extra calories into more serum triglycerides. Increased consumption of sugars or too many refined carbohydrates, saturated fats or drinking too much of alcohol and sedentary lifestyle can lead onto the abnormal level of serum triglycerides. [5,6]

Genetic Lipid disorders may affect triglycerides and or cholesterol. In Familial combined hyperlipidemia High serum triglycerides and LDL cholesterol are seen. In familial hypertriglyceridemia (type IV familial dyslipidemia) high serum triglycerides are observed. Familial dysbetalipoproteinemia (type III hyperlipoproteinemia) results in high serum triglycerides and Total cholesterol. Familial chylomicronemia syndrome (FCS) results in serum triglyceride levels higher. A genetic disorder along with lifestyle factors usually combine to cause hypertriglyceridemia.[1,6,7]

Many undetected medical conditions like insulin resistance, liver diseases, Diabetes mellitus, Hypothyroidism, Metabolic syndrome, obesity can raise the triglycerides although they come under a separate category as Secondary Hypertriglyceridemia. Certain medications such as Antipsychotic drugs, Antiretroviral protease inhibitors, non selective Beta-blockers, Corticosteroids, Tamoxifen, Cyclophosphamide can cause raised serum triglycerides.[1,6,7]

The increased Serum triglyceride levels also leads to increased risk of cardiovascular disease by keeping bad company with risk factors such as obesity, metabolic syndrome, and type 2 diabetes mellitus. The increased risk of acute pancreatitis is another complication when serum triglyceride level is very high. The two main sources of serum triglycerides are exogenous (i.e., from dietary fat) carried in chylomicrons, and endogenous (from the liver) carried in very-low-density lipoprotein (VLDL) particles. In fat and muscle tissue, these VLDL and chylomicrons are hydrolysed by

lipoprotein lipase into free fatty acids. Post meal, 90% of the circulating triglycerides originate in the intestine and are secreted in chylomicrons and during fasting, endogenous triglycerides secreted by the liver as VLDL predominate. These increase in serum of triglyceride-rich lipoproteins are due to the increased production from the liver and intestine (upregulation of synthetic and secretory pathways) or through diminished peripheral catabolism (reduced lipoprotein lipase activity). The most important differentiating features of familial chylomicronemia and primary mixed hyperlipidemia are early manifestation during childhood for the former and in adulthood for the latter; Deficiency of lipoprotein lipase, apo CII activity or homozygous gene mutations in the former, and moderate functional deficiency and infrequent detection of gene mutations in the latter.[8-11]

Familial hypertriglyceridemia (hyperlipoproteinemia type IV) is defined by an isolated elevation of VLDL. Its molecular basis is likely to be polygenic, requiring a secondary factor for expression. Typically, patients with this disorder have moderately elevated serum triglycerides with low levels of high-density lipoprotein-cholesterol (HDL-C). Familial hypertriglyceridemia is commonly associated with increased risk of cardiovascular disease, obesity, insulin resistance, diabetes, Hypertension. The familial combined hyperlipoproteinemia (type IIB) is of an autosomal dominant type of inheritance. The lipoprotein abnormalities are increased VLDL and low-density lipoprotein (LDL) with decreased HDL. Also these people can have obligate heterozygosity for *LPL* or *APOC3* gene mutations. A recently defined gene that may be causative for this disorder is *USF1*, although several other genes (including *APOA5* and *APOC3*) have been variably claimed as causative.[2] Familial dysbetalipoproteinemia (hyperlipoproteinemia type III) is associated with an increase in intermediate-density lipoproteins or β -VLDL, which produce an equimolar elevation of serum total cholesterol and triglyceride levels. They are homozygotic for the binding-defective *APOE* E2 isoform, by a substitution of cysteine for the normal arginine at residue 158 in the receptor-binding domain. Plasma levels of LDL are decreased because of interrupted processing of VLDL. An increased VLDL-C: triglyceride ratio and E2/E2 homozygosity are diagnostic. Affected individuals have xanthomata on the extensor surfaces of their extremities, palmar-crease xanthomata and increased risk of cardiovascular disease.[1,2]

The hypertriglyceridemia is almost certainly an independent risk factor for cardiovascular disease. The Complex mechanisms underlying the association of triglycerides and atherosclerosis obscure the detection of any direct causal relation. Proatherogenic metabolic or biochemical abnormalities (e.g., obesity, type 2 diabetes, decreased levels of HDL-C, increased LDL, increased free fatty acids, increased plasma viscosity, increased inflammatory molecules, impaired fibrinolysis, prothrombosis) are often associated with elevated levels of triglycerides. Furthermore, triglyceride-rich lipoproteins and their remnants may directly play a role in the formation of arterial-wall foam cells. In comparison to Chylomicrons, the chylomicron remnants, VLDL and intermediate-density lipoproteins are more atherogenic. A novel concept is that postprandial lipemia is an independent predictor of cardiovascular disease, although sample collection and assay conditions are nonroutine.[9-12]

Hypertriglyceridemia increases the risk of acute pancreatitis. Although a few patients can develop pancreatitis when their fasting serum triglyceride level is 5–10 mmol/L, its risk becomes clinically significant when fasting measurements exceed 10 mmol/L. A value beyond 1000 mg/dL (about 11.3 mmol/L) is often cited for the pancreatic involvement.[12-15] Some patients with triglyceride-related pancreatitis may have pre-existing abnormalities in their lipoprotein metabolism. Pancreatitis risk is increased by any factor that can increase plasma triglycerides past 10 mmol/L. A 10 -12 hours fasting serum lipid panel diagnoses hypertriglyceridemia Treatment of Hypertriglyceridemia includes Dietary and Lifestyle changes, Medications and Managing the underlying causes of high serum triglycerides. In general, treatment gets initiated with Dietary and lifestyle changes to lower the serum triglycerides like avoiding alcohol and refined carbohydrates and sugars; Eating more seafood, especially fishes containing omega-3 fatty acids, regular exercise, restricting calorie intake to help lose excess weight, replacing saturated fat and trans fats with healthier fats.[1,10]

High Serum triglyceride concentration is a common biochemical finding, but the evidence for the benefit of treating this lipid disturbance is less robust than that for treating elevated low-density lipoprotein-cholesterol. The difficulty in the provision of specific recommendations of therapy has

been the frequent coexistence of elevated triglycerides with conditions that affect cardiovascular disease risk, such as decreased high-density lipoprotein–cholesterol, obesity, metabolic syndrome, proinflammatory and prothrombotic biomarkers, and diabetes mellitus.[1,10,12,13]

The Drug therapy especially important for people with severe hypertriglyceridemia are fibrates eg fenofibrate, prescription of omega-3 fatty acids, statins .The onset of full-blown acute pancreatitis can be prevented by restricting dietary fat and /or the usage of fibrates drugs. Treatment of emergency cases includes hemodynamic stabilization, NIL oral intake, placement of a nasogastric tube and continuous monitoring and control of metabolic disturbances. Restricted energy intake is associated with a rapid decrease in plasma triglyceride levels. Plasmapheresis with transient benefit.[1,10,12,13] The goal is to make adjustments that will aid in the raised triglycerides return to a normal level by managing the underlying causes along with newer medications needed to tackle the medical condition. Certain causes cannot be changed (aging or certain medical conditions). Still a lot to be implemented in daily life to prevent hypertriglyceridemia. The suggested dietary and lifestyle are eating regularly a heart healthy diet, adopting an active Lifestyle involving planned regular exercise and moving around more during the daily routine, Maintaining a healthy weight, Limiting or Avoiding alcohol, reducing sugar, refined carbohydrates, saturated fats and Trans fats.

The peculiarity is that the hyperglyceridemia apart from being the risk factors for the aforementioned diseases it can also result due to these diseases and the nomenclature Secondary hypertriglyceridemia is coined. Even certain medications can result in secondary hypertriglyceridemia. Otherwise Isolated Hypertriglyceridemia is predominantly due to the risky dietary and lifestyle behavioral pattern and also due to the Genetic lipid disorders.[1,10,12,13]These two predominant causes of isolated Hypertriglyceridemia must be tackled effectively by early detection and intervention in order to avert the serious systemic diseases with long array of complications and thereby enabling the individuals to lead a healthy life with normal life expectancy.

Conclusion:

The silent killer Isolated Hypertriglyceridemia deserves prompt attention and remedial action through regular screening of the same. Since it is silent and symptomless usually, if left undetected and untreated at the earliest , this may result in grave complications like Metabolic Syndrome, Diabetes, Hypothyroidism, Obesity, liver Disorders, atherosclerosis, Coronary artery disease , Pancreatitis etc. Scientific based healthy Dietary and Lifestyle changes with or without proper medications will keep the deleterious effects of Isolated hypertriglyceridemia at bay in the long run. As far as this risk factor is concerned Prevention is the Primary need of the hour rather than advocating treatment for the diseases and complications arising out of Isolated hypertriglyceridemia.

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