

# Effects of Statins Lipid Lowering Drugs on Lipid Profile

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## Abstract:

**Background:** Hyperlipidemia has become one of the most common problems in day-to-day life. Lipid-lowering drugs, especially 3-hydroxy-3-methylglutaryl Coenzyme A HMGCoA reductase inhibitors, are widely used in the treatment and prevention of cardiovascular disease. Blood cholesterol levels are a strong predictor of mortality and morbidity associated with CVD.

**Patients and methods:** Serum samples were collected from thirty patients (age range was 45-70 years old), taking antilipids drugs. Then lipid profile (Total cholesterol, HDL, LDL, vLDL) were detected by specific kits.

**Results:** Results showed the presence of normal HDL and LDL in the patients taking lipid lowering drugs in compare with the control group. While TGs and vLDL levels were still high in these patients in compare with the control group.

**Discussion:** The results reflect partial effectiveness of statins and it may need a combination with other lipid lowering drug like ezetimibe and nicotinic acid which form effective combination

**Conclusion :** Statins affected (HDL and LDL), but it may need a combination with other lipid lowering drug to decrease TGs and vLDL.

## INTRODUCTION:

Plasma lipids consist of triacylglycerols (16%), phospholipids (30%), cholesterol (14%) and cholesteryl esters (36%) and a much smaller fraction of unesterified long-chain fatty acids (4%). This latter fraction, the free fatty acids (FFA), is metabolically the most active of the plasma lipids.<sup>1</sup>

Plasma lipids are transported in complexes called lipoproteins. Metabolic disorders that involve elevations in any lipoprotein species are termed hyperlipoproteinemias or hyperlipidemias. Hyperlipidemia denotes increased levels of triglycerides.<sup>2</sup>

Hyperlipidemia has become one of the most common problems in day-to-day life. The sedentary life today has particularly enhanced its risk. It has become a house-to-house disorder, especially in higher middle class and higher societies. Intake of fat and high carbohydrate rich diet style of India has also added to its increasing intensity. Some of them include refined low polyunsaturated fatty acid (PUFA), increased use of egg and meat, 'refined' low fiber containing carbohydrate tuffs.<sup>3</sup> Hyperlipoproteinemias or hyperlipidemias are included under metabolic disorders; vascular or cyclic vomiting syndrome (CVS) disorders are secondary to them.<sup>4</sup>

Lipid-lowering drugs, especially 3-hydroxy-3-methylglutaryl Coenzyme A HMGCoA reductase inhibitors, are widely used in the treatment and prevention of cardiovascular disease. Blood cholesterol levels are a strong predictor of mortality and morbidity associated with CVD.<sup>5,6</sup>

## Comparison among lipid-lowering agents

### Statins:

atorvastatin (Lipitor and generic); lovastatin (Altoprev, Mevacor, and generic); pravastatin (Pravachol and generic); Fluvastatin (Lescol, Lescol XL), Pravastatin (Pravachol), and simvastatin (Zocor and generic)<sup>7</sup>

### -Mechanism of action

Statins' primary mechanism of action is through the competitive, reversible inhibition of HMG-CoA reductase, the rate-limiting step in cholesterol biosynthesis. HMG-CoA reductase catalyses the conversion of HMG-CoA to L-mevalonate and coenzyme A via a four-electron reductive deacetylation. The pharmacophore of all statins bears resemblance to the endogenous HMG-CoA moiety. It competitively binds to the catalytic domain of HMG-CoA reductase, causing steric hindrance and preventing HMG-CoA from accessing the active site.<sup>8</sup>

Irreversible liver damage leading to death or liver transplantation appears to be extremely uncommon with statins. Asymptomatic

elevation of aminotransferases under statins has been found in trials but does not necessarily indicate hepatic damage. Decompensated cirrhosis, acute liver failure and significant cholestasis are contraindications for statin therapy, but not compensated chronic liver disease such as non-alcoholic fatty liver disease. Possible interactions (mainly with CYP3A4 inhibitors) deserve particular attention, and when statin therapy is needed the lowest effective dose should be prescribed in adults at risk for liver problems.<sup>9,10</sup>

The rate of acute liver failure associated with lovastatin is one per 1- 1.1 million patient-treatment years, which is the same as the background rate of idiopathic acute liver failure.<sup>11</sup>

### Niacin;

Nicotinic acid is used primarily to increase HDL. Acute hepatic failure has been reported but is very rare.<sup>12</sup>

### mechanism

Decreases catabolism of apo A1 reduces VLDL secretion from liver.<sup>13</sup> The typical pattern of injury involves elevation of aminotransferase levels although a mixed pattern of hepatocellular and cholestatic injury can be seen. This potential hepatotoxicity is common with sustained-release formulations (SR) but rare with immediate-release or extended-release (ER). The increase in liver toxicity with SR niacin chiefly occurred with doses >1500 mg/day.<sup>14</sup>

### Fibrates

Mechanism: peroxisome proliferator activated receptor- $\alpha$  (PPAR- $\alpha$ ) agonists.<sup>15</sup>

Some case reports have found that gemfibrozil results in cholestatic hepatitis and other rare reported cases of hepatocellular injury.<sup>15</sup>

Fenofibrate was reported to be potentially involved in a case of hepatitis and fibrosis that was possibly increased due to use in combination with statins.<sup>16</sup>

As a general rule, high doses of statin should be avoided in patients

who are taking a fibrate. The risk of fibrate toxicity is higher in patients with impaired renal function, because these drugs are largely excreted by the kidney.

### Ezetimibe

Mechanism: Blocks sterol transporter NPC1L1 in intestine brush border.<sup>13</sup>

This drug inhibits intestinal absorption of cholesterol, but it enters the circulation and some authors found that it may in rare cases cause hepatotoxicity in the form of severe cholestatic hepatitis and acute autoimmune hepatitis.<sup>17</sup>

In some case reports it was noted that the frequency of increased transaminases was potentially higher in patients receiving ezetimibe when associated with statins<sup>18</sup>

HDL, LDL, and vLDL) by using specific kits and depending on the protocol supplied with the kits.

**PATIENT AND METHODS:**

Research included collection of blood samples in Tabarak lab for pathologic analysis, and the patient's number was (30) realistically (male, female), ages ranged (45-70), for the period from (20\7- 25\10 ; 2017). Blood samples were collected, then blood was up process centrifugal separation (3000 RPM ) for 5 minute , after that it was measured the levels of lipid profile (TGs,

**RESULTS:**

Results showed the presence of normal HDL and LDL in the patients taking lipid lowering drugs in compare with the control group, as represented in the figures (2 and 3) respectively. While TGs and vLDL levels were still high in these patients in compare with the control group as showed in the figures (1 and 4) respectively.

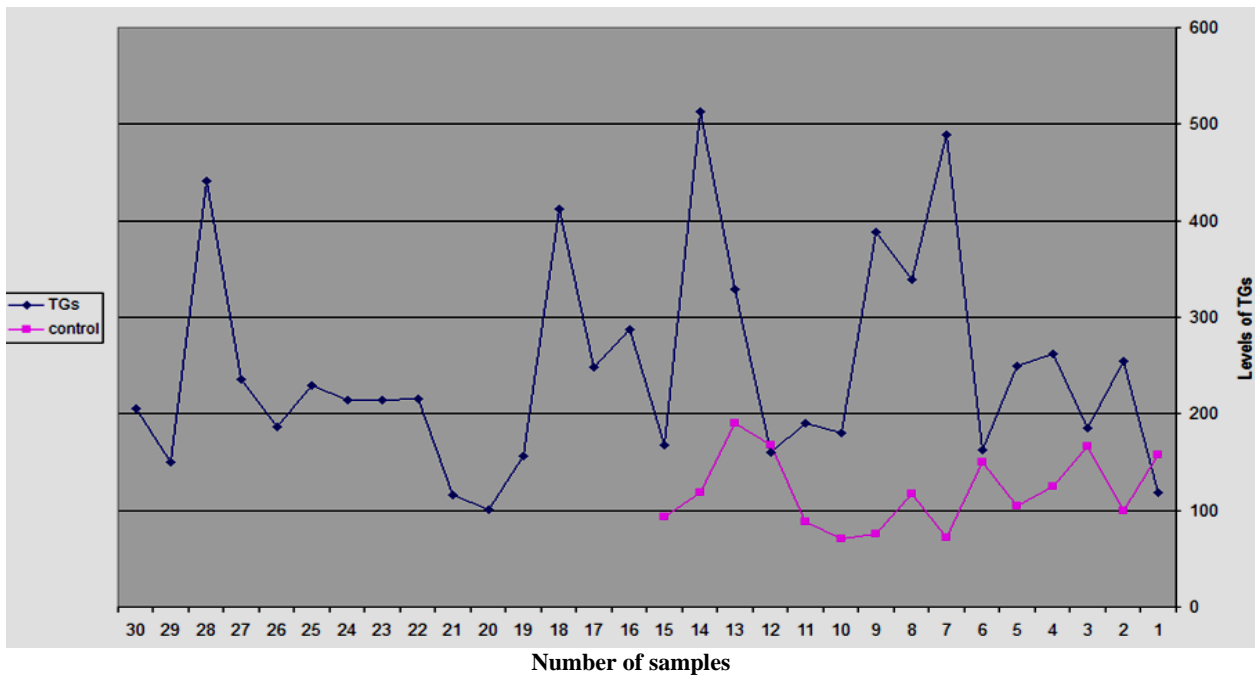


Figure 1 : The levels of TGs in patients taking lipid lowering drugs in compare with the control group.

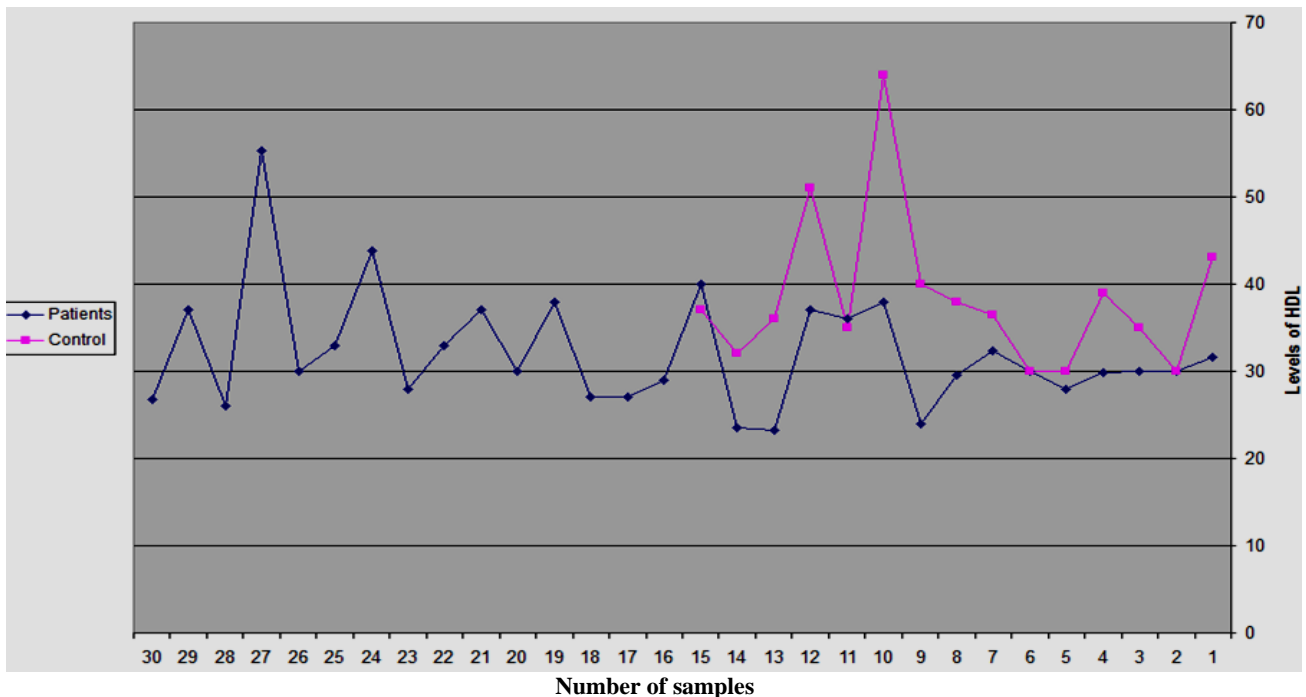


Figure 2 : The levels of HDL in patients taking lipid lowering drugs in compare with the control group.

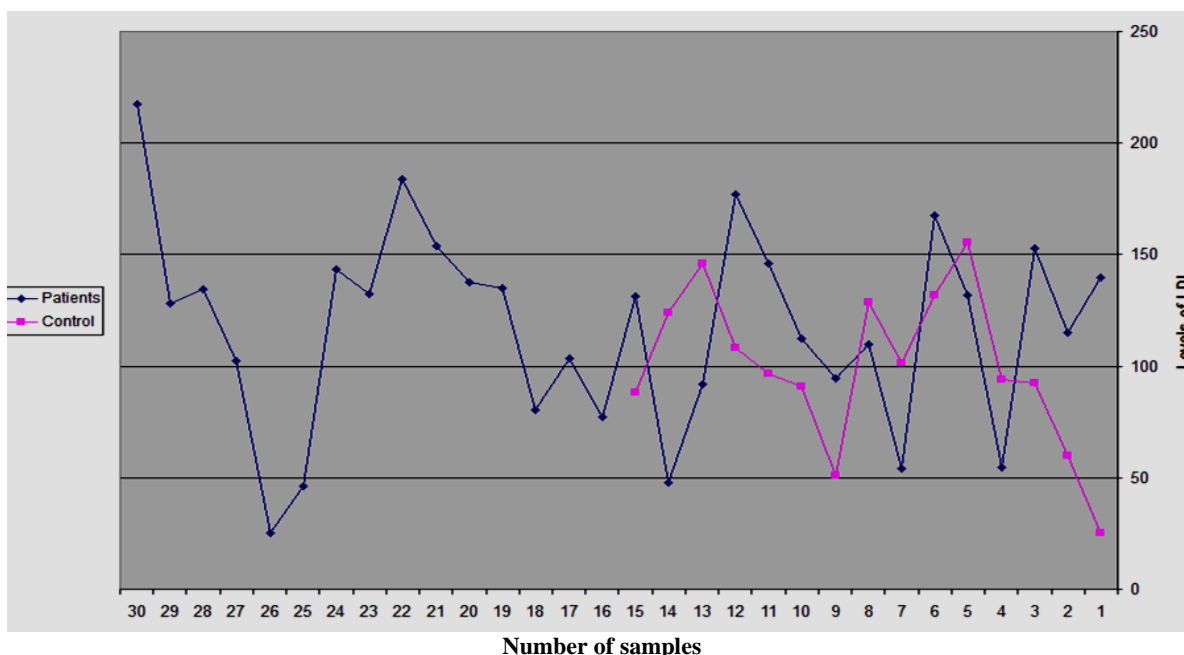


Figure 3 : The levels of LDL in patients taking lipid lowering drugs in compare with the control group.

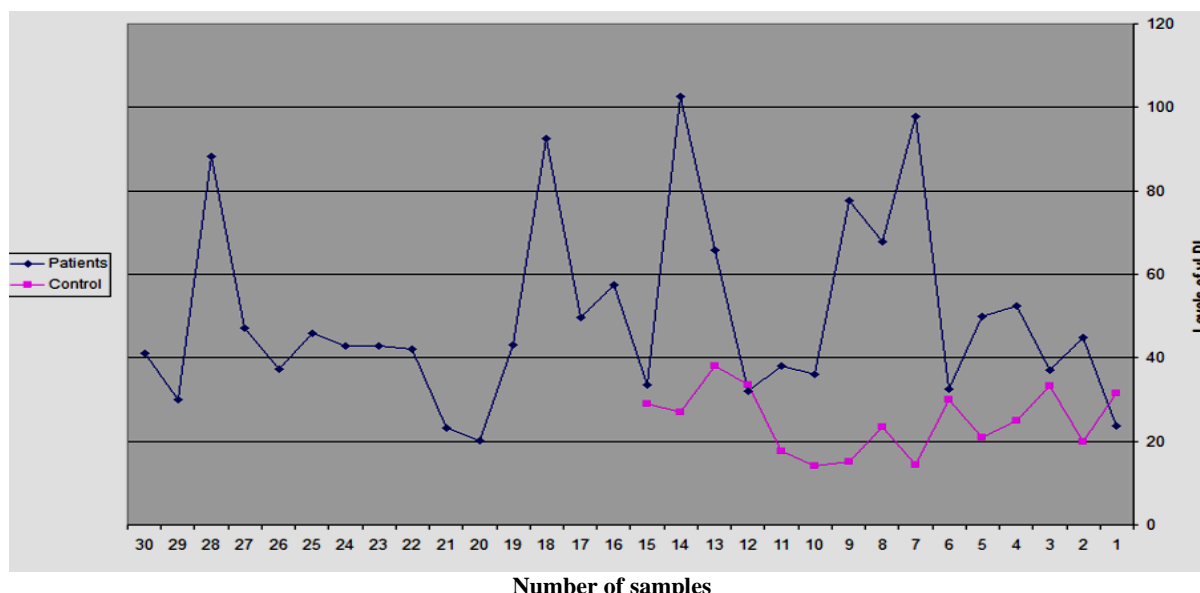


Figure 4 : The levels of vLDL in patients taking lipid lowering drugs in compare with the control group.

**DISCUSSION:**

The results showed significant effects of lipid lowering drugs to decrease the elevated levels of LDL, and this result reflects part of the efficiency of these drugs which accompanied with the other previous results, that showed that large-scale, prospective, randomized trials have demonstrated that intensive statin therapy significantly reduces lipid levels and the incidence of coronary events in individuals with low or average cholesterol levels. Also its showed that most effective agents for reducing LDL levels are the HMG-CoA reductase inhibitors (“statins”), because they block cholesterol synthesis at its rate limiting step [ 6, 8, 19, 20 ]. For the vLDL and TGs, levels stilled elevated, and this may be related to the doses used, as a previous study showed that high-dose simvastatin therapy significantly decreases TRL-TG in obese diabetic subjects and indicates that this reduction appears to be attributable to increased TRL-TG clearance rather than to

decreased production. The most likely cause is an increase in intravascular lipolytic activity [19].

Or it may explained as the statins may need combination with other lipid lowering drug like ezetimibe and nicotinic acid which form effective combination, significantly increases HDL while decreasing LDL, TGs and total cholesterol) but its adverse side effects can limit its usefulness because of decreased patient compliance [21 ], or it may be related to the patients themselves and the irregular use of statins, or to the use of low effectiveness value drugs mark.

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