Effects of Statin Drugs on New Onset of Diabetes Mellitus in Post Menopausal Women

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Authors’ contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Statin drugs are using all over the world for the treatment of hypercholesterolemia. There is hypothesis that post menopausal women who used statin drugs long time can develop the onset of type 2 diabetes mellitus because statin drugs inhibit the signal transduction of insulin by inhibiting oxidative phosphorylation resulting in decrease secretion of insulin leads to hyperglycemia. The aim of this study to estimate the effects of statin drugs on blood glucose level and HbA1c% in post menopausal women.

Methodology: This case comparative study was done at LUMHS Jamshoro. The sampling was done by Non Probability method. Total number of 150 subjects were divided in 2 group’s i.e group A (Control group) & group B (Case study group). The fasting glucose level was measured by glucose oxidase method while HbA1c% & serum cholesterol levels were determined by Kit method by using auto analyzer. The statistical analysis was done by SPSS 21 by applying ANOVA test for multiple variants.

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Results: The mean with S.D fasting blood glucose levels in control group was 78± 9.05 mg/dl while in case study group it was 134 ± 12.15mg/dl (p <0.05), HbA1c% levels in control group was 5.3 ± 1.1% while in case study group it was 7.4 ± 1.3% (p<0.05) and serum cholesterol in control group was 157± 9.75 mg/dl while in case study group it was 195 ± 8.78 mg/dl (p<0.05) was significantly (P<0.05). The glycemic index & fasting blood glucose levels significantly observed elevated in post menopausal women who were use statin drugs since last three years.

Conclusion: This study concluded that there was significant relation of statin drugs on increasing of blood glucose levels so they can induce the onset of Type-2 Diabetes Mellitus.

Keywords: Statin drugs; Type-2 Diabetes Mellitus; post menopause; HbA1c%; serum cholesterol.

1. INTRODUCTION

Statin drugs have pleotropic effects in addition to being used to prevent primary and secondary morbidities of cardiovascular Diseases [1,2]. Pleotropic effects have been seen in individuals with hypertension, myocardial infarction, and cardiac arrhythmias [3]. Because statin medications are effective inhibitors of the rate-limiting enzyme of cholesterol production, 3-hydroxy-methylglutaryl coenzyme A (HMG-CoA) reductase, they are also used to treat hypercholesterolemia [4]. When the quantity of cholesterol in the liver falls, the activity of the receptors of low density lipoprotein (LDL) in the liver rises [5]. This aids in the removal of LDL particles from the bloodstream. When statin medicines lower LDL cholesterol levels, they accelerate the degradation of the Apo B100 molecule, resulting in increase in Coenzyme Q10 synthesis through the mevalonate route [6,7]. The pleotropic effects of statin drugs is due to inhibition of isoprenoid synthesis [8].

After the age of 50, the majority of males and females suffer from lipid and cardiovascular diseases, and doctors frequently prescribe statin medicines on a regular basis, sometimes for the rest of their lives. However, other researchers hypothesized that long-term use of statin medicines raised blood glucose levels, resulting in hyperglycemia and eventually diabetes mellitus in people who never had diabetes before [9]. The different researchers postulated that statin drugs inhibit the signal transduction of insulin by inhibiting oxidative phosphorylation, which may cause a decrease in the action of GTPase, so inhibits the proliferation of beta cells in the pancreas and decrease the levels of leptins also, theses all biochemical changes can reduce the rate of secretion of insulin, resulting in hyperglycemia [10, 11].

The aim of this study to evaluate the effects of statin medicines on blood glucose levels and glycemic control in postmenopausal women using statin drugs from along time at least from last three years. So if there is any positive association between statin drugs with development of type-2 diabetes mellitus will observe then need to work up to make preventive measures in post meno pausal women from development of new onset of type-2diabetes mellitus in future.

2. METHODOLOGY

This cross sectional study was done at Liaquat University of Medical & Health Sciences Jamshoro in year of 2020. Total number of 150 postmenopausal women were selected for this study and divided into two groups, each group contained with 75 post meno pausal participants. The women of control group have no any tacking history of statin drugs medications, whereas case study group women having history of taking statin drug at least from last three years. The sampling was done using a non-probability method. Females aged 50 to 70 years old, with a history of at least one year since their last menstrual cycle, and who have been on statin medicines for at least three years. Females over the age of 70, with their last menstrual cycle occurring within the last year, a history of statin drug use of less than three years, known cases of type II diabetes mellitus, renal disease, liver disease, endocrine disorders that cause hyperglycemia, and a history of drugs that cause hyperglycemia were all excluded from this study. The 5 ml of blood sample from each participants were taken early in morning before breakfast with 12 hours night fasting. The fasting blood glucose (FBS) levels was estimated by glucose oxidase method, HbA1c% was measured by microlab while serum cholesterol levels was measured esterase method on cobas auto analyzer . The Statistical analysis was done by SPSS version 21 and statistical mean and SD was measured by applying Independent student t test. The P. value <0.05 consider as significant.
3. RESULTS

This study found a statistically significant increase in the values of fasting blood glucose levels and glycemic index in group B patients who have been taking statin drugs for more than three years. Another important finding was that serum cholesterol levels were near borderline levels in group B patients who were also taking statin drugs, but serum cholesterol levels were statistically ($p < 0.05$) higher in group B than in group A (control group). Table No: 01 and graph no: 01, 02 & 03 presented the graphical presentation of data of this research.

Table 1. Parameters Understudy of Control & Case Study Groups

| Parameters         | Group A       | Group B        | P.Value |
|--------------------|---------------|----------------|---------|
| FBS (mg/dl)        | 78 ± 9.05     | 134 ± 12.15*   | < 0.05  |
| HbA1c%             | 5.3 ± 1.1     | 7.4 ± 1.3*     | <0.05   |
| Cholesterol (mg/dl)| 157 ± 9.75    | 195 ± 8.78*    | <0.05   |

Graph 1. Fasting blood glucose levels

Graph 2. HbA1c% Levels
DISCUSSION

This is a contentious subject since it is still unclear if statin medicines might cause hyperglycemia. On the other hand, diabetologists use statin drugs to avoid diabetic cardiovascular problems. Diabetes type 2 and its complications are the leading cause of morbidity and death worldwide [12]. Dyslipidemia has a negative correlation with diabetes [13]. As a result, statin medicines are used to prevent a variety of vascular problems.

According to the American Diabetic Association (ADA) [14], statin medicines should be started in diabetics with serum cholesterol levels greater than 220 mg/dl and LDL levels greater than 100 mg/dl for the management of dyslipidemia and the avoidance of cardiac problems. On the other hand, a study published in 2012 by the Food and Drug Administration Safety Communication found that while there was a reduction in cardiovascular complications in the statin group compared to the placebo group, there was an increase in the rate of new onset diabetes in the statin drug user group compared to the placebo group [15]. Colver Al et al. [16] conducted a study on over 15000 postmenopausal women and concluded that statin drugs have a statistically significant effect in the induction of diabetes. The same theory was proposed by Mora S et al. [17] but they also concluded that diabetes developed due to statin drugs is due to drug effects because when they stopped taking statin drugs, the diabetes went away within a few months. In general, statin medications cause hyperglycemia through two mechanisms. One is that statin medicines may promote down regulation of glucose transporter 4 (GLUT 4) in adipose tissues because statin drugs limit the formation of isoprenoid molecules, resulting in lower glucose absorption from cells and glucose intolerance [10]. Second, statin medicines inhibit the formation of CoQ10 enzyme, which inhibits the release of insulin from pancreatic beta cells, causing blood glucose levels to rise [18]. This notion is confirmed by Davidson MH et al. [19] who found that high doses of statin medicines increased the risk of diabetes development by 12% in younger onset diabetes. Our study also supported by Yunita EP et al. [20] and Barre D.E et al. [21] that statin drugs can easily develop the new onset of type 2 diabetes mellitus in post menopausal women. As a result of these many types of study, there is debate on whether statin medicines are useful or harmful. This research has some pitfalls that are there is short sample size in future this study can apply on large scale sample size to rule out proper significant relation of statin drugs with induction of diabetes. Second in this study there is no difference between dosages of statin drugs, in future there is need for comparative study between effects of dose dependent statin drugs on blood glucose level.

CONCLUSION

According to the findings, statin medicines have a considerable effect on raising blood glucose levels, which can lead to the formation of type 2 diabetes mellitus.
CONSENT
As per international standard or university standard, Participants’ written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL
It is not applicable.

COMPETING INTERESTS
Authors have declared that no competing interests exist.

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