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REVIEW ARTICLE

STATIN USE AND TYPE 2 DIABETES INCIDENCE

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1 | INTRODUCTION

The paper was published on April 15th, 2018 is focused on finding out the risk of developing type 2 diabetes on patients who have statin. Statins are drugs used to lower cholesterol levels in the body. It works inhibiting the reductase 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase competitively, limit cholesterol production, anti-inflammatory and plaque stabilization effects. Studies show that it reduces the level of low-density lipoproteins (LDL) by ten percent. The drug also increases the level of High-Density Lipoproteins (HDL) by twenty percent. Examples of statin drugs are Fluvastatin, Lovastatin, Pitavastatin, Pravastatin, Rosuvastatin, and. Simvastatin. The paper focuses on a study conducted to find out if use statin raises the risk of developing type 2 diabetes. My writing will review the various aspects of the paper, the purpose of the article to find if the authors Crandall JP, Mather K, Rajpathak S *et al*. paint a clear and accurate picture of the concepts presented in the paper, strengths and weaknesses, and suggestions on areas that need improvement will be looked at.

ABBREVIATION

TABLE 1:

ADA	American Diabetes Association
ATP	Adult Treatment Panel
BMI	Body Mass Index
	Blood Pressure
CVD	Cardiovascular Disease
DM	Diabetes Disease
DPP	Diabetes Prevention Program
FBG	Fasting Blood Glucose
HDL	High Density Lipoprotein
LDL	Low Density Lipoprotein
OGTT	Oral Glucose Tolerance Test

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2 | AN OVERVIEW OF THE STUDY

This is a mixed rapid and integrative review of the study was conducted on 3234 patients using a longitudinal research method (David, 2019). We summarized and synthesized an existing evidence expediently due to resources limitations and time constrains and comprehensively with clear outlines. Also, we critique, summarize, and evaluate a specific subject area using a precise search to recognize the relevant evidence that answer the clinical research question and the problem.

Participants were followed for ten years. Parameters that were measured include two-hour glucose levels in the blood, insulinogenic index, fasting insulin, LDL cholesterol, HDL cholesterol, triglyceride, different potency of statins, duration of statin exposure, body weight, waist circumference and blood pressure (BP).

The inclusion criteria for the sample of participants were that they had to be obese and overweight. Obesity is one of the risk factors for the development of type 2 diabetes.

Diabetes mellitus (DM) is a lifestyle disease (Fan, 2018). This means that individual lifestyle choices lead to the development of diabetes. There two types of DM. These are type 1 and type 2. Type 1 diabetes is considered juvenile and begins during the early years of life and is insulin-dependent and results when there is insufficient production of insulin from the pancreas in the beta cells. Type 2 diabetes is also called non-insulin dependent diabetes mellitus. It occurs due to body insensitivity to insulin. Factors that lead to insulin insensitivity include obesity and increased body mass index (BMI).

Some of the parameters measured in the study were oral glucose tolerance testing (OGTT), which was conducted annually. Another parameter tested was fasting blood glucose (FBG) semiannually. The incidence of DM type two was confirmed by testing FBG and OGTT. This assessment on the incident of diabetes was done annually over ten years.

The aims to present a thesis as an essential part to complete the master's degree in clinical research. The objectives are successfully discussed findings from a peer-reviewed article, summarize, and evaluate the article, reinforce the evidence-based practice, understand the evidence base of clinical care based upon knowledge gained from literature, can critically appraise evidence-based upon a clinical publication, be familiar with the options of care for patients based upon evidence within literature, critical evaluation/appraisal of the article, which will influence clinical knowledge and practice, identify contradictions, gaps, and inconsistencies in the text, determine if there is enough data or research included to support the author's claims and find any unanswered questions left in the article.

The study was done to find out if there is an association between statin use and the development of type 2 DM. The study did not find out if statin would increase the risk of developing type 2 DM in people with a higher risk of diabetes. The research was focused on reducing the incidence of DM. There has been an increase in diabetes due to shifting to sedentary life and the influence of lifestyle choices (Fan, 2018). According to Fan, 2018 researchers also think some of the drugs used in the clinical area to treat common diseases could contribute to the development of some of the lifestyle diseases. Knowledge about which specific drugs lead to the incidence of DM could lead to better decision making on ways to manage the disease and prevent or delay the development of DM on the high-risk population (Reiffel, 2020). The study provides knowledge that could aid health care providers on ways to monitor patients who are on statin therapy and are at risk of getting diabetes or already have diabetes. The study also enables more exploration of the relationship and association between statin use and diabetes to add to the previously known knowledge.

The new finding of the study includes the knowledge that statin use is one of the contributing factors for the development of diabetes. Other considerations for the increased incidence of DM type two in adults include reduction in physical activity, poor and unhealthy diets: increased use of junk food and sugar, family history of DM in the family, and obesity (Jian, 2018). Once contributing risk factors for disease are known, prevention and treatment become clinically more manageable if patients can follow instructions given to them by their care providers.

3 | THE MAIN BODY/CORE OF THE REVIEW

Significance of the Study to Literature and Knowledge on Type 2 DM.

The core and central focus of the study was on a wide range of variables that affect the incidence of DM. The variables include the various types of statin drugs used for lowering cholesterol levels. The examples of statin drugs include low potency and high potency statins. According to the study, statins have very many functions in the human body apart from lowering the cholesterol levels in the body. Some other benefits of statins in the body include a reduction in systemic inflammation, reduction of oxidative stress.

Clinical trials and meta-Analysis conducted on other studies have seemed to confirm the fact that the use of statins can increase the incidence of diabetes. The increase in the incidence of diabetes provided by these studies shows a small increase of about 10-12%. A couple of post hoc analysis has been done on patients with prediabetes and their use of statin depending on their rise in the glucose readings. The study used this direction to find out the effects of statin therapy on individuals with high risk for development of diabetes. Such individuals are those who are obese and overweight, with no history of diabetes initially. The individuals are then followed over time to find out if they would develop diabetes over ten years with the use of statin.

The measurements on body weight, waist circumference, BP was specific and standard to avoid bias. Bodyweight would be measure half-yearly, and sizes were rounded off to 0.1 kgs to minimize errors of rounding of values to whole numbers. The body weight was used to obtain BMI using height and weight. The waist circumference was measured yearly. According to Fang, 2020 the circumference is obtained by measuring the midpoint between the highest level of the iliac crest and the lowest level of the costal margin at the midaxillary line. The BP levels were obtained by using Mercury specific sphygmomanometers. The BP readings were taken by highly trained staff. The readings were taken when the participants have seated a minimum of two readings to get average BP measurements. Data obtained on race, ethnicity, family history and race were taken based ultimately on self-reporting. Such data was, therefore, difficult to confirm for its accuracy.

Other vital data obtained for the study was on the FBG, glycated hemoglobin known as the HbAIc. HbAIc enables health care providers to test blood sugar levels over the last 2-3 months in the past (Marinella, 2017). HbAIc is therefore used to see trends in individual blood sugar levels. HbAIc is done after 2-6 months (Hiroyuki, 2020).

Insulinogenic index was also measured. Insulinogenic index is gotten by determining fasting insulin; the insulin levels after thirty minutes are also determined. The insulinogenic index is an absolute marker of the beta cells function. Beta cells are the cells in the pancreas that produce insulin (Marinella, 2017). The formula given for insulinogenic to is insulin levels after thirty minutes minus fasting insulin; the value is then divided by glucose levels after thirty minutes minus glucose levels at fasting state.

Important variables on cholesterol levels were also obtained. LDL, HDL, and triglycerides were obtained. BP levels were used to determine the development of hypertension within the period in which the study was conducted. The study also collected information on people with a family and personal history of cardiovascular diseases (CVD). CVDS is a group of diseases that affect the heart and its blood vessels (De Ferrari, 2020). Such conditions include myocardial infarction, angina, Heart attacks, stroke, and rheumatic heart disease.

The diagnosis of diabetes was obtained by measuring FBG done half-yearly. A second test to test fasting blood sugars were done using a standard test recommended by the American Diabetes Association (ADA). Another way to diagnose diabetes was through the testing of the seventy-five oral glucose tolerance test. The seventy-five OGTT is conducted by fasting for 8-14 hours before the test (Anyanwagu, 2015). The participant is then given a drink with seventy-five grams of glucose. Blood sugar levels are then tested before the drink and two times after sixty minutes of taking the drink.

Advanced Knowledge Provided by the Study

The study used data from the Diabetes Prevention Program (DPP). The program has twenty-seven centers where randomized clinical trials are conducted. The program is sponsored by the National Institute of Diabetes and Kidney Diseases (Casula, 2017). The program has followed different participants since the year 2002. The main objective of the institute is to get more information on lifestyle and drug therapy that can delay and or prevent the incidence of diabetes. According to Casula, 2017 the high-risk population for diabetes are individuals with impaired glucose tolerance. People with impaired glucose tolerance have high levels of blood sugar. The levels are borderline and are not as high to warrant the diagnosis of diabetes.

Studies show that statins can increase the rate of incidence of diabetes by approximately 9-12% (Mei, 2015). The figures done in various meta-analysis studies differ from studies to study. The differences in the results from multiple studies could be due to the numerous methods and variables used in the studies (Mei, 2015). Various techniques used could bring about bias and confounders, which either reduce or increase the accuracy of the data and results. Some studies found that statin leads to the diagnosis of diabetes due to the impairment of insulin secretions and sensitivity to insulin of the cells in the body.

Most studies, however, agree that the statins are more essential to use to prevent CVDs, the benefits outweigh the risks such as the risk for diabetes. The study does provide new and advance knowledge that changes how individuals with risk for diabetes or individuals with diabetes will be managed. The study goes beyond the known knowledge of diabetes, and its therapy to include influences of statin treatment, as a predisposing factor to diabetes. A couple of other meta-Analyses and clinical trials have been done similar to the study.

The individuals are then followed over time to find out if they would develop diabetes over ten years with the use of statin wide range of variables that the study used. The wide range of variables provides a broad viewpoint for statin therapy and its risk factors for the development of diabetes. The study was also had several advantages. One of the benefits is that it was able to obtain reliable data from the DPP (Dukyong, 2016). Such accurate information makes the finding from the study more generalizable to the entire population. The study found out that the use of statin therapy before the incidence of diabetes could increase the chances of getting diabetes by an average of 35%.

The study divided participants into three distinctive groups: the placebo group, the metformin group. The third group received great emphasis on lifestyle interventions to prevent diabetes. Metformin is a type of drug that regulates blood sugar by decreasing the amount of glucose produced by the liver and increase cell sensitivity to insulin.

50% of the participants were from minority groups, while 20% were from people aged sixty years and above. All participants were at least 25 years old; their BMI was at least $\geq$24 with a FBG of 95-100 to 125 milligrams. They also had impaired glucose tolerance140-199. Exclusion criteria were the individuals with CVDs, diabetic patients, and those with triglycerides levels of above 600 milligrams per deciliter.

The three groups were then divided into control and case groups for each of the three categories. They received quarterly sessions. Metformin groups received standard metformin medication; the lifestyle group was enrolled in the lifestyle program. All the groups were put on statin therapy. Their lipid levels were assessed and targets for lipid levels confirmed by the Adult Treatment Panel (ATP). Care providers outside the study treated patients on antihypertensive medications.

The ATP reports are used to obtain data used in the management of patients with high levels of blood cholesterol. The reports conduct studies and surveys that provide data to National Cholesterol education programs on how to manage various cholesterol associated disorders (Dukyong, 2016). Some of the details contained in ATP III include management of high levels of triglycerides, focus on risk factors for heart diseases, emphasis on treatment guidelines for people who are at risk for coronary heart disease and instructions on therapeutic lifestyle choice to reduce risk of getting lifestyle diseases.

The study found that incidence of diabetes on statin use for ten years as follows: The placebo group had a

35% chance; the metformin had a 37% chance while the lifestyle group had a 33% chance of developing diabetes while on statin therapy. The study also provided data on the rate of incidence of diabetes, depending on the type of statin use. The low potency statin used includes Fluvastatin, Lovastatin, while the high potency statins were Cerivastatin, Simvastatin, Rosuvastatin, and Atorvastatin.

The findings regarding the statin where simvastatin incidence rate of diabetes was 40%, 37% for Atorvastatin, Lovastatin incidence rate at 90%, and Pravastatin incidence rate was 8%.

The study also found out that the use of statin used was increased after the diagnosis of diabetes. Participants, on statin use, had higher levels of FBG, HbAIc, and had lower levels of the insulinogenic index than the control group participants who were not on statin use. The results from the study also showed that participants on a statin had a more significant history of CVD and hypertension. Social-economic state, which focused on education level and income level and sex, did not affect the results. The findings showed that longer duration of statin therapy resulted in higher risks for diabetes, specifically in the lifestyle, metformin, and in the placebo groups. The results found out no significant effect of statin potency on the incidence of diabetes. The insulinogenic index was shown to decrease with statin therapy. The results also showed no change in fasting insulin.

Clarity and Accuracy of the Authors.

The study was compiled and written by eight authors, all from the DPP. A brief outlook of the report on the study reveals that the authors were quite clear on the findings and discussions that they did from the study. There are, however, a couple of unclear and inaccurate areas in the report that will be discussed below.

Statin therapy increases the incidence of diabetes (Xing, 2020). Other studies on the same have confirmed this data about the increase in the incidence of diabetes with the use of statin. This, therefore, confirms the accuracy of the study and its findings. The authors have presented three distinctive groups that are the placebo, metformin, and lifestyle groups. They have further explained about the participants in the three groups. The explanation on the placebo group is, however, unclear. The readers are left wondering what the participants in the placebo group were given.

Another important issue was on statin therapy. Statin medications are used to lower levels of LDL and increase the levels of HDL (John, 2016). The authors, however, state that the participants who were on the statin use had higher levels of LDL compared to participants who did not use statin hence bring about unclear facts about the benefits of statin.

The issue of the potency of statin uses and the effect on the incidence of diabetes is unclear. The results compiled fail to show a clear relationship on how the potency of the statin increases the incidence of diabetes. The report is also unclear on whether low risk or high-risk populations for diabetes were used for the study. The abstract states that low-risk populations were used in the study, but the study selected participants with high risk for diabetes. Hence the information on which group was used is quite unclear.

The strengths and weaknesses of the study.

The strengths of the study include the fact that the study provides information on which statin therapy is effective for individuals with diabetes. The study can, therefore, be used to develop guidelines and protocols for diabetes mellitus management and statin therapy.

The database from which the study was collected from the DPP database. According, to the ADA the database is reliable and founded by a prominent and transparent organization. This means that most of the data available for the study were accurate. Meaning the findings from the study were quite precise and valid. The study was also able to look at various confounder and tried to reduce bias. These confounders include ethnicity, race, social-economic status, sex, age (Perez, 2020).

The study not only focused on diabetes as a disease. Other diseases that were concentrated on include diabetes and hypertension (Joyce, 2017). The study, hence, can provide more data on statin therapy on other conditions other than diabetes. Protocols and guidelines for statin therapy and use on hypertension

and CVD can also be developed. Eight authors compiled the study report. This increases the accuracy of the study to a certain extent since more experts can brainstorm and generate more accurate information than if only one author were involved.

Some of the weaknesses of the study include the self-reporting aspect of the information in the demographics of the participants. According to Thakker, 2016 self-reporting could reduce the accuracy of information obtained from the participants since they are no ways to confirm the validity of the information provided. Other biases from self-reporting include recall bias and misclassification of participants in the wrong groups. These errors reduce the accuracy of the findings.

Some participants were provided with treatment by health care providers outside the study. These participants include those on antihypertensives. These medications could have modified the results obtained in unknown ways. We recommended for treatment by clinical staff during the period of the study to provide standardized methods of treatment.

Another weakness of the study is the data provided on the benefits of the study. Some of the benefits of the statin listed include the reduction of systemic inflammation and a reduction in oxidative stress. Such benefits are not supported by other websites (Association, America Diabetes, 2020) The significant benefits of statin are their ability to lower bad cholesterol (LDL) in the body and increase good cholesterol (HDL) in the body.

4 | CONCLUSION

Statin therapy is generally considered safe, with a low rate of reversible side effects. The study is such an exciting topic to research. It focuses explicitly on diabetes as lifestyle diseases and seeks to find ways to create effective ways of managing DM in the future. The study also gives data on the number of statins that could be used in the management of diabetes, hypertension, and CVDs. Furthermore, the study could be a pointer and the beginning of more studies on other drugs that may have effects on other diseases. The balance point between the pros and cons of statins in primary prevention is not very clear hence, more research should be conducted to find out drug efficacy and drug interaction with common ailments. The study helps to reduce the incidence of diabetes. According to John, 2016 diabetes is one of the most prevalent lifestyle diseases and comes with a myriad of complications. The reduction of prevalence and incidence of diabetes is still a struggle. The study is a good step towards the reduction of such lifestyle diseases.

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5 | REFERENCES

Anyanwagu.U., I. &. (2015). Drug-Induced Diabetes Mellitus: Evidence for Statins and Other Drugs Affecting Glucose Metabolism.

Association, A. D. (2017). 9. Cardiovascular Disease and Risk Management.

Association, A. D. (2020, 1). 13. Children and Adolescents: Standards of Medical Care in Diabetes−2020.

C., J. B. (2016). The diabetogenic action of statins — mechanisms and clinical implications.

Casula.M, M. E. (2017). Statin use and risk of new-onset diabetes: A meta-analysis of observational studies. Elsevier.

David J. C, B. A. (2019). Statin use, hyperlipidemia, and risk of glioma.

De Ferrari.GM, S. &. (2020, 2). Low-density lipoprotein cholesterol treatment and outcomes in patients with type 2 diabetes and established

cardiovascular disease: Insights from TECOS. 220.

Dukyong. Y, S. S.-S. (2016). Statins and risk for new-onset diabetes mellitus.

Fan.W, P. G. (2018, 7). Prevalence and Predictors of Residual Hypertriglyceridemia According to Statin Use in U.S. Adults with Diabetes.

Hirai.H., H. M. (2020). Dissimilar Effects of Anagliptin and Sitagliptin on Lipoprotein Subclass in Standard or Strong Statin-Treated Patients with Type-2 Diabetes Mellitus: A Subanalysis of the REASON (Randomized Evaluation of Anagliptin versus Sitagliptin on Low-Density Lipopr.

Jian-Yu.E., G. L. (2018). Effect of Metformin and Statin Use on Survival in Pancreatic Cancer Patients: A Systematic Literature Review and Meta-analysis. 25.

Joyce. N. R, Z. E. (2017, 7). Statin Use and the Risk of Type 2 Diabetes Mellitus in Children and Adolescents. 17(5).

Marinella, G. (2017). Statin use and risk of developing diabetes: results from the Diabetes Prevention Program. BMJ Open Diabetes Research & Care (10.1136/bmjdrc-2017-000438).

Mei-Jyh.c., Y.-T.-M.-C.-S.-M.-P. P.-C. (2015). Statins and the risk of pancreatic cancer in Type 2 diabetic patients—A population-based cohort study.

Perez-Calahorra.S, &. C. (2020, 1 8). Behavioural cardiovascular risk factors and prevalence of diabetes in subjects with familial hypercholesterolaemia.

Reiffel.J, G. &. (2020). Statins: Do They Have Beneficial Effects Over and Above Their Actions on Lipids?

Thakker.D, N. &. (2016, 6 9). Statin use and the risk of developing diabetes: a network meta-analysis.

Wang.X., H. W. (2020, 1 10). Lipid-Lowering Therapy and Low-Density Lipoprotein Cholesterol (LDL-C) Goal Achievement in High-Cardiovascular-Risk Patients in Fuzhou, China.

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