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Comparative Efficacy of Rosuvastatin (Low Vs High Dose) in Lowering Low Density Lipoprotein Cholesterol in Intermediate Risk Cardiovascular Patients

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ABSTRACT

Background: The enzyme 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibition therapy exists as a prevalent method to control blood lipid levels. Higher statin doses demonstrate better efficacy at decreasing cardiovascular events when compared to lower dosage amounts according to the research findings. International guidelines support the use of high dose rosuvastatin yet adverse effect concerns might inhibit its actual prescription. The study evaluated how low dose rosuvastatin treatment performed against high dose rosuvastatin therapy in patients at intermediate cardiovascular risk. **Methodology:** The research took place within Medical OPD Lahore General Hospital stretching from July 2024 until January 2025. Researchers distributed 96 patients between Group A which received 10 mg Rosuvastatin and Group B which received 20 mg Rosuvastatin for a duration of three months. Blood tests checked serum creatine phosphokinase (CPK) and low density lipoprotein cholesterol (LDL-C) at both the study start and three months into the trial. The study evaluated effectiveness through LDL-C reductions. **Results and Discussion:** Group A included 37.5% male participants along with 62.5% female participants whereas Group B comprised 60.4% male participants with 39.6% female participants and their ages showed Group A averaged 49.31±10.96 years while Group B averaged 51.60±11.13 years. Group B participants demonstrated significantly lower mean LDL-C values at 172.94 ± 32.02 mg/dl when compared to Group A at 248.94 ± 53.66 mg/dl ($p < 0.05$). Group B reached statin efficacy at 85.4% whereas Group A achieved it only at 39.6% ($p<0.05$). The mean CPK levels in Groups A and B measured at 85.67 ± 19.30 and 74.65 ± 20.89 µg L− but showed statistically significant differences between these values ($p < 0.05$). High dose rosuvastatin provided more effective LDL-C lowering outcomes than low dose therapy for patients with intermediate cardiovascular risk.

INTRODUCTION

Heart diseases known as CVDs present as the main reasons for global morbidity and worldwide mortality. Data indicated that CVDs generated 17.9 million deaths during 2019 making up 32 percent of total deaths. Superior to eighty percent of these fatalities originated from heart attacks and strokes. The World Health Organization projects that cardiovascular diseases produce 18 million annual deaths as well as 18 million yearly nonfatal cardiovascular events. The diagnosis of hyperlipidemia functions as a primary CVD risk factor because it occurs when you demonstrate elevated triglycerides coupled with reduced HDL cholesterol and elevated total cholesterol together with low HDL cholesterol levels. Medical practitioners employ statins as preventive therapy against heart disease onset as well as therapeutic intervention for existing cardiovascular conditions since these medications offer substantial protection against major heart complications.

Use of statins in people at relatively low to intermediate risk without documented cardiovascular disease (primary prevention) results in important public health consequences.2

Statins competitively inhibit the enzyme 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase and thereby reduce the blood lipid levels. Statins are known to stabilize atherosclerotic plaques, decrease the risk of thromboembolism and retard the progression of atherosclerosis. There are other statins but atorvastatin and rosuvastatin are the best statins for lowering the low-density lipoprotein cholesterol (LDL-C) levels. While there are other statins available, atorvastatin and

rosuvastatin are best at lowering the level of low-density lipoprotein cholesterol (LDL-C).3, 4

The majority of the research involving different statins and their effective dosage that have been conducted on the western population suggests that higher doses of statins are more successful than lower doses at lowering LDL-C levels and at decreasing all cause cardiovascular deaths. The current American College of Cardiology prescription, though, is to have moderate to high intensity statins starting at age 175 if one has clinical risk factors for atherosclerotic cardiovascular disease. There is, however, contradictory evidence for the Asian population.5 Statins are the cornerstone of the lipid lowering regimen. But not all statins have wreaked the same success at reducing LDL-C; it has been found that atorvastatin and rosuvastatin have demonstrated the highest level of success in this category.6 Cholesterol production is controlled by the rate limiting step performed by the liver enzyme reductase. It is very effective in improving lipid profiles compared to other compounds of the same class. Its anti-inflammatory, antioxidant, its antithrombotic qualities are all extremely important for disease prevention, both in primary and secondary cardiovascular disease .7, 8

First, we sought to elucidate whether lower doses of rosuvastatin would decrease LDL-C efficiently in people without known atherosclerosis as compared to Asians and Western subjects, as findings within the Asian and Western populations differed. There are no local guidelines and review guidelines from the international recommend high dose statins so local physicians are compelled to prescribe high intensity statins to the patients and they can still be worried about side effects of higher doses. Hence this research will help doctors to recommend the appropriate doses of rosuvastatin to its patients in such a way that they get the same kind of results with lesser doses than they get negative effects with higher doses of the drug. It will also reduce the financial burden of the therapy for lipid. This study aims to evaluate the low dose (10 mg) and high dose (20 mg) rosuvastatin efficacy to achieve reduction in LDL-C <130 mg/dl or 30% in the patients with intermediate cardiovascular risk. This study aims to provide evidence for optimizing statin therapy to minimize adverse effects and also financial burden specifically for populations where local guidelines are absent and where doubts about the high dose statin side effects remain.

MATERIAL AND METHODS

This was carried out as a randomized control trial, conducted at the Outdoor Patient department (OPD) of Medicine, Lahore General Hospital, Lahore in the period July 2024 to January 2025 over a six-month period. Based on the estimated sample size, 96 patients and 48 patients in each group (Group A and Group B) were sampled. A 95% confidence interval and 90% power of the test were assumed based on a 45% efficacy for the low dose rosuvastatin group and 77% efficacy for the high dose rosuvastatin group at intervention.

The selection criteria were met; therefore, patients were enrolled into a non-probability consecutive sampling technique. This research included patients between 30 and 70 years old from both genders with coronary artery disease intermediate risk determined using the Framingham Risk Score. People falling between a 10% to 20% risk rate for coronary heart disease (CHD) during a 10-year period were considered intermediate risk patients. Test participants needed to have LDL-C levels greater than or equal to 3.5 mmol/l (135 mg/dl). Our research incorporated patients who had LDL-C lower than 3.5 mmol/L (135 mg/dl) as well as non-HDL-C greater than 4.3 mmol/L (193 mg/dl). Graduate patients who exceeded age 50 for men and reached age 60 for women participated in the analysis provided they had at least one risk factor between low HDL-C and hyperglycemia, hypertriglyceridemia, abdominal obesity, tobacco use, and hypertension.

Those who were already on statins or other lipid-lowering drugs, had diabetes or had familial hyperlipidemia syndromes, as well as pregnant females and those with chronic kidney disease were excluded.

Data Collection Procedure: After obtaining informed consent, total 96 patients who meet inclusion and exclusion criteria were included after obtaining the permission from the hospital ethical committee. To be able to meet exclusion and inclusion criteria, a detailed history and physical examination was done. Patients were divided into two groups by the lottery method after its informed consent. Rosuvastatin was given at low dose (10mg) to group A patients and at high dose (20mg) to the group B patients for 03 months. Patient information recorded included all basic demographic information of each patient (name, sex, contact, address, height, weight and waist circumference), presence of smoking, hypertension and diabetes. All patients were also asked to follow dietary precautions as well as exercise. Baseline investigations which includes renal and liver function tests, serum electrolytes, serum CPK and Fasting lipid profile including LDL-C will be performed at the start of study CBC, and LDL-C and CPK will be done at 03 months after start of rosuvastatin. LDL-C level after 03 months of treatment was taken as an end point. The efficacy of statin was determined using achieving LDL-G levels of <130mg/dL or an LDL-C ≥ 30% from baseline decrease observed after 3 months. Statins induced myositis was followed with CPK level. Information was provided by Proforma (Annexed).

Data Analysis: The data analysis occurred through the use of statistical software SPSS version 25. The Chi square test analyzed the effectiveness between both

treatment groups. P-value ≤0.05 was considered significant.

RESULTS

The present study utilized 96 patients who received random assignment into low dose rosuvastatin patients (group A) and high dose rosuvastatin patients (group B). The average patient age within group A measured 49.31±10.96 years. The mean age for patients in group B amounted to 51.60±11.13 years. The patients in group A consisted of 37.5% males who were joined by 62.5% females. The patients selected for Group B included 48 men (40%) along with 71 women (60%) with 29 men (60.4%) and 19 women (39.6%). Each patient in Group A demonstrated 1.64±0.09 meters of height while maintaining 86.79±9.50 kg of weight and 32.53±4.14 kg/m2 BMI. Patients in group B had statistically significant (p<0.01) mean height (1.69±0.10 meters), weight (85.94±10.15 kg), and BMI (30.56±5.30 kg/m2). There were 45 (93.8%), divorced 1 (2.1%) and widow or widowed 2 (4.2%) patients in group A. There were 2.1 percent (1) of single patients in group B, 81.3 percent (39) were married, 10.4 percent (5) were divorced and 6.3 percent (3) were widow / widowed. In group A, with history of hypertension, 21 (43.8%) patients, family history of CVD, 21 (43.8%) and 26 (54.2%) patients were smokers. About 25 (52.1%) patients in group B had history of hypertension, 26 (54.2%) had family history of cardiovascular disease and 25 (52.1%) were smoker. Table 1

Research analysis determined no statistically significant contrasts existed between both research groups (p>0.05) when assessing initial LDL measurements from 340.44 ± 66.59 mg/dl in group A and 313.77 ±75.18 mg/dl in group B. The 3-month LDL mean level for Group A patients was 248.94±53.66 mg/dl yet Group B patients maintained 172.94±32.02 mg/dl. Results demonstrated statistically relevant differences (p<0.05) between the group A and B participants. The LDL cholesterol reduction percentages reached 26.78±7.43% in group A patients and 43.18±10.61% in group B patients. The reduction rate recorded in Group B surpassed the reduction rate of Group A at a statistical level of p<0.05. A total number of 19 patients or 39.6% achieved efficacy in treatment in Group A and 85.4% of patients reached efficacy in Group B. The outcome measurements demonstrated greater effectiveness in Group B compared to Group A at a p value below 0.05. The total determinations of CPK levels in group A reached 57.67±25.17 µg /L while tests in group B measured 54.96±23.77 µg /L (P=0.000). The CPK measurements did not show a statistically relevant difference between the investigated groups at p>0.05. The researchers measured 85.67±19.30 µg/L as the average CPK value in treatment group A following therapy for three months yet found 74.65±20.89 µg/L as the average CPK value in group B at the same time point. A statistical distinction emerged between the treatment groups at p < 0.05 level. Participants in group A experienced a greater rise in CPK level measuring 28.00±13.95 µg/L than participants in group B who had a 19.69±10.43 µg/L increase. This difference was significant (p<0.05). Table II

Mean LDL level at baseline in group A was 340.44±66.59 mg/dl that decreased to 248.94±53.66 after 3 months of treatment. The mean baseline LDL level for group B was 313.77±75.18 mg/dl and was reduced to 172.94±32.02 after 3 months of the 3-month treatment. Both groups had a significant mean fall in LDL level (p<0.05). Efficacy was achieved in 60 (62.5%) of 96 cases (fig I). Fig II

Table I

Basic demographics of patients enrolled in both groups (n = 96)

	Group	
	Low dose	**High dose**
n	48	48
Age (years)	49.31±10.96	51.60±11.13
Gender		
Male	18 (37.5%)	29 (60.4%)
Female	30 (62.5%)	19 (39.6%)
Height (m)	1.64±0.09	1.69±0.10
Weight (kg)	86.79±9.50	85.94±10.15
BMI (kg/m^2)	32.53±4.14	30.56±5.30
Marital status		
Single	0 (0%)	1 (2.1%)
Married	45 (93.8%)	39 (81.3%)
Divorced	1 (2.1%)	5 (10.4%)
Widow	2 (4.2%)	3 (6.3%)
Hypertension	21 (43.8%)	25 (52.1%)
Family history	21 (43.8%)	26 (54.2%)
Smoking	26 (54.2%)	25 (52.1%)

Figure 1

Basic demographics of patients enrolled in both groups (n = 96)

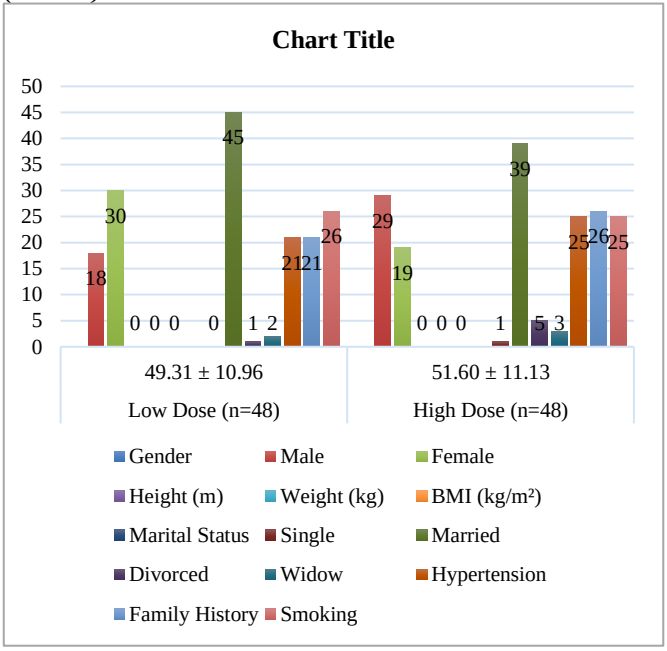
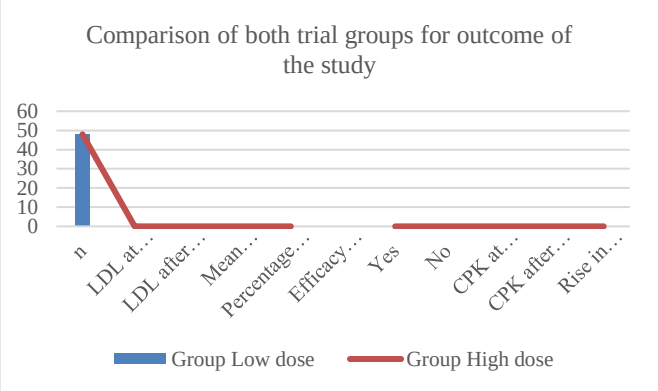


Table II

Comparison of both trial groups for outcome of the study.

	Group		P-value
	Low dose	High dose	
n	48	48	
LDL at baseline	340.44±66.59	313.77±75.18	0.069
LDL after 3 months	248.94±53.66	172.94±32.02	0.000
Mean reduction	0.27±0.07	0.43±0.11	0.000
Percentage reduction in LDL level	26.78±7.43	43.18±10.61	0.000
Efficacy achieved			
Yes	19 (39.6%)	41 (85.4%)	0.000
No	29 (60.4%)	7 (14.6%)	
CPK at baseline (µg/L)	57.67±25.17	54.96±23.77	0.589
CPK after 3 months (µg/L)	85.67±19.30	74.65±20.89	0.009
Rise in CPK level (µg/L)	28.00±13.95	19.69±10.43	0.001

Figure 2



DISCUSSION

In order to avoid and cure cardiovascular illnesses, it is important to estimate cardiovascular risk. The most widely used scoring method worldwide is the Framingham Risk Score, despite the fact that there are several risk estimating techniques. Six criteria are included in this system: systolic blood pressure, smoking behaviours, total cholesterol, I-IDL-C, age, and gender. According to Framingham Risk Score, patients with intermediate cardiovascular risk include those whose 10-year heart diseases risk is between to 10% to 20%.[1]

Hypercholesterolemia is the main cause of atherosclerosis and a cardiovascular risk factor. Therefore, cholesterol (LDL-C) must be lowered to levels recommended by clinical practice guidelines in order to lower the risk of vascular issues. There is presently minimal control over LDL-C, even in those who are high and extremely high risk. This is mostly because the lipid-lowering medication has not been sufficiently intensified.[11]

In our trial, we observed that the reduction in mean LDL level was observed as from 340.44±66.59 mg/dl to 248.94±53.66 mg/dl with low dose, while from 313.77±75.18 mg/dl to 172.94±32.02 mg/dl with high dose. The mean fall in LDL level was significant for both groups ($p<0.05$). Thus, the efficacy was achieved in 19 (39.6%) patients with low dose rosuvastatin and in 41 (85.4%) patients with high dose rosuvastatin. There was significantly better efficacy achieved with low dose rosuvastatin ($p<0.05$) as compared to high dose rosuvastatin.

In a study conducted in Mayo hospital Lahore on 140 patients, Atique M. et al, reported that Low dose Atorvastatin was efficacious in 49 (70%) patients in reducing serum LDL-G to <100 mg/dl, while High dose Atorvastatin was effective in 54(77%) patients, of Intermediate cardiovascular risk patients. Both doses were highly effective with lower dose group having fewer side effects.[10]

The findings of Kim H S et al (2010-2012) at Seoul St Mary's Hospital demonstrated that LDL-G reductions reached 45% with atorvastatin (20 mg) and rosuvastatin (10 mg) therapy but atorvastatin (10 mg), Pitavastatin (2 mg), pravastatin (40 mg) and simvastatin (80 mg) resulted in 35–37% downellation. The prescribed medium-intensity statins included one million dosage amounts which stayed beneath the recommended dosing limits per statin type.9

Dulay et al. carried out research with findings that daily medicine administration produced a 48.5% LDL-C reduction while alternate day regimen resulted in a 40.9% reduction in cholesterol levels. Daily administration of the intervention resulted in a complementary 7.6% absolute reduction (95% CI 1.8 to 13.4%, P=0.012) of absolute cholesterol (LDL-C). Improvements in high-density lipoprotein cholesterol and triglycerides were similar for both dosage schedules.12 An extra 7.6% decrease in cholesterol (LDL-C) lowering was achieved by the daily dosing schedule; this is equivalent to the decrease anticipated from doubling daily dosage of rosuvastatin from 10 mg to 20 mg daily.13 A previous study was able to get similar cholesterol (LDL-C) reductions with alternate-day dosage and daily dosing regimens by using a titration approach, in which atorvastatin was titrated as required to achieve goal cholesterol (LDL-C) reductions. Still this assumption needs further investigation to prove a daily dose of 10 mg rosuvastatin would produce similar or lower cholesterol outcomes than an alternate day use of 40 mg rosuvastatin.

Karlson et al conducted a study and compared four doses i.e. 5, 10, 20 and 40 mg of rosuvastatin. The research experiment established that 5 mg of rosuvastatin produced non-HDL-C reduction by 35% and LDL-C reduction at 39%. The reduction of LDL-C required 39 mg simvastatin but 15 mg atorvastatin for equivalent results. When comparing non-HDL-C reduction levels rosuvastatin at 10 mg was equivalent to taking simvastatin 42 mg or atorvastatin 14 mg. This

same level of LDL-C reduction could be achieved through either simvastatin 72 mg or atorvastatin 29 mg. Simvastatin 77 mg produced a 45% reduction in non-HDL-C which matched the results of arosuvastatin 27 mg. Also, rosuvastatin 20 mg achieved a 45% decrease in non-HDL-C and a 50% reduction in cholesterol (LDL-C). Simvastatin doses up to 80 mg demonstrated less pronounced effects in lowering both cholesterol (LDL-C) and non-HDL – C compared to atorvastatin 70 mg and atorvastatin 62 mg and rosuvastatin 40 mg. Likewise, neither simvastatin (80 mg) nor atorvastatin (80 mg) decreased to similar levels.15

Li YF et al showed in a Met analysis, that Asian patients require less intense LDL G lowering therapy or lower statin dose to achieve the regression of coronary atherosclerosis than Western patients. At follow up, atorvastatin (Mean 18.9 mg daily) and rosuvastatin (mman 14.1 mg daily) reduced volumes of coronary atherosclerotic plaque (Mean 18.9 mg daily) and cholesterol (LDLc) to < 100 mgrdl.16

CONCLUSION

This study compared the efficacy of low-dose (10 mg) versus high-dose (20 mg) rosuvastatin in reducing LDL-C levels among patients with intermediate cardiovascular risk. High-dose rosuvastatin treatment showed increased LDL-C reduction effectiveness than the low-dose group results revealed. The high-dose group achieved significantly more LDL-C reduction at 43.18% following three months but the low-dose group demonstrated 26.78% reduction ($p<0.05$). The high-dose rosuvastatin group reached the LDL-C efficacy target of <130 mg/dL among 85.4% of patients ($p<0.05$) but the low-dose group showed lower attainment at 39.6% ($p<0.05$). While both groups experienced a rise in CPK levels, the increase was more pronounced in the low-dose group, suggesting a potentially lower risk of statin-induced myositis with higher doses.

These findings support the use of high-dose rosuvastatin for superior LDL-C reduction and cardiovascular risk management. However, local guidelines should be developed to optimize statin prescription, balancing efficacy with side effect profiles and economic burden. Further research is recommended to explore long-term safety and adherence in diverse populations.

REFERENCES

1. Collaborators, GRF. (2016). Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet (London, England)*, *388*(10053), 1659.
2. Bansal, S. K. (2015). Conventional and advanced lipid parameters in premature coronary artery disease patients in India. *JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH*. https://doi.org/10.7860/jcdr/2015/14818.6844
3. Ma, G., & Bi, S. (2018). Effect of rosuvastatin on vascular endothelial functions and inflammatory factors of patients with type 2 diabetes mellitus and coronary heart disease. *Experimental and Therapeutic Medicine*. https://doi.org/10.3892/etm.2018.6923
4. Ma, Q., Zhou, Y., Zhai, G., Gao, F., Zhang, L., Wang, J., Yang, Q., & Cheng, W. (2015). Meta-analysis comparing Rosuvastatin and Atorvastatin in reducing concentration of C-reactive protein in patients with hyperlipidemia. *Angiology*, *67*(6), 526-535. https://doi.org/10.1177/0003319715599863
5. Grundy, S. M., Stone, N. J., Bailey, A. L., Beam, C., Birtcher, K. K., Blumenthal, R. S., ... & Yeboah, J. (2019). 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Journal of the American College of Cardiology*, *73*(24), e285-e350. https://www.jacc.org/doi/abs/10.1016/j.jacc.2018.11.003
6. Mach, F., Baigent, C., Catapano, A. L., Koskinas, K. C., Casula, M., Badimon, L., ... & Wiklund, O. (2020). 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society

(EAS). *European heart journal*, *41*(1), 111-188. https://academic.oup.com/eurheartj/article/41/1/111/5556353

7. Cortese, F., Gesualdo, M., Cortese, A., Carbonara, S., Devito, F., Zito, A., Ricci, G., Scicchitano, P., & Ciccone, M. M. (2016). Rosuvastatin: Beyond the cholesterol-lowering effect. *Pharmacological Research*, *107*, 1-18. https://doi.org/10.1016/j.phrs.2016.02.012
8. Lee, Y., Hong, S., Kang, W. C., Hong, B., Lee, J., Lee, J., Cho, H., Yoon, J., Lee, S., Ahn, C., Kim, J., Kim, B., Ko, Y., Choi, D., Jang, Y., & Hong, M. (2023). Rosuvastatin versus atorvastatin treatment in adults with coronary artery disease: Secondary analysis of the randomised lodestar trial. *BMJ*, e075837. https://doi.org/10.1136/bmj-2023-075837
9. Kim, H., Lee, H., Park, B., Park, S., Kim, H., Lee, S., Cho, J. H., Yoon, K., Cha, B., Kim, J. H., & Choi, I. Y. (2016). Comparative analysis of the efficacy of low- and moderate-intensity statins in Korea. *Int. Journal of Clinical Pharmacology and Therapeutics*, *54*(11), 864-871. https://doi.org/10.5414/cp202332
10. Atique, M., Shehzad, N., Khan, D. M., Randhawa, F. A., Tanveer, S., Sulehria, S. B., & Athar, C. A. A. (2020). Comparative effectiveness of atorvastatin (low vs high dose) in lowering low-density lipoprotein cholesterol in intermediate risk cardiovascular patients. *Pakistan Journal of Medical and Health Sciences*, *14*(2), 312-315.
11. Mostaza, J. M., & Escobar, C. (2024). Rosuvastatin-based lipid-lowering therapy for the control of LDL cholesterol in patients at high vascular risk. *Journal of Clinical Medicine*, *13*(7), 1894. https://doi.org/10.3390/jcm13071894
12. Dulay, D., LaHaye, S. A., Lahey, K. A., & Day, A. G. (2009). Efficacy of alternate day versus daily dosing of rosuvastatin. *Canadian Journal of Cardiology*, *25*(2), e28-e31. https://doi.org/10.1016/s0828-282x(09)70480-5
13. Olsson, A. G., McTaggart, F., & Raza, A. (2002). Rosuvastatin: A highly effective new HMG-CoA reductase inhibitor. *Cardiovascular Drug Reviews*, *20*(4), 303-328. https://doi.org/10.1111/j.1527-3466.2002.tb00099.x
14. Matalka, M. S., Ravnan, M. C., & Deedwania, P. C. (2002). Is alternate daily dose of atorvastatin effective in treating patients with hyperlipidemia? The alternate day versus daily dosing of Atorvastatin study (ADDAS). *American Heart Journal*, *144*(4), 674-677. https://doi.org/10.1067/mhj.2002.124399
15. Karlson, B. W., Palmer, M. K., Nicholls, S. J., Lundman, P., & Barter, P. J. (2015). Doses of rosuvastatin, atorvastatin and simvastatin that induce equal reductions in LDL-C and non-HDL-C: Results from the voyager meta-analysis. *European Journal of Preventive Cardiology*, *23*(7), 744-747. https://doi.org/10.1177/2047487315598710
16. Li, Y., Feng, Q., Gao, W., Zhang, X., Huang, Y., & Chen, Y. (2015). The difference between Asian and western in the effect of LDL-C lowering therapy on coronary atherosclerotic plaque: A meta-analysis report. *BMC Cardiovascular Disorders*, *15*(1). https://doi.org/10.1186/1471-2261-15-6