Utilization and Adherence to Guidelines Recommended for Use of Statins in the Management of Hypercholesterolemia and Their Cost Utility Analysis

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Authors’ contributions

This work was carried out in collaboration among all authors. Author MDA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors NB and AY managed the analyses of the study. Author MP managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Objective: The study was aimed to evaluate utilization and adherence to guidelines recommended in the use of statins for management of cholesterol and their cost utility analysis in a clinical setting in Saudi Arabia.

Materials: A cross-sectional retrospective study was conducted in a private hospital in Saudi Arabia. World Health Organization (WHO) Defined Daily Dose (DDD) was used to compute the Daily price of each statins.

Results: The utilization of statins is higher in males, Saudis and people with the age group 40-59 as compared to females or non-Saudis or other age groups. Over all, Atorvastatin was the most preferred statin therapy followed by Rosuvastatin, Simvastatin and Fluvastatin. The average cost unit wise was found to be highest for Atorvastatin SR 5.58 (USD 1.49) being lowest for Rosuvastatin SR 4.02 (USD1.07).

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Conclusion: The study aimed to evaluate the use of statins for management of cholesterol is found to be consistent with international guidelines given by ACC/AHS. Our study suggests having further research to fully understand the barriers to guideline adherence to have improved utilization and considerably neutral cost effects of statins for all.

Keywords: Statins; cholesterol; drug utilization pattern; defined daily dose.

1. INTRODUCTION

Statin is used to reduce the level of cholesterol in the blood, and it does so by suppressing some of the activities of the liver that leads to increasing cholesterol [1]. This cannot be interpreted that cholesterol has no benefit, as it plays an important role in the level of cellular activity, but increasing it causes blockages in the arteries and impeding blood flow. This blockage can be fatal, as it leads to the vessels being unable to transport oxygen to the heart and brain, causing heart attacks or strokes [2]. There is a prevalence of cholesterol-related disorders in Saudi Arabia which mostly results from lifestyle changes [3,4]. To help prevent this risk and reduce cholesterol, one can decrease saturated fat intake, a healthy diet, and regular exercise. However, this system may not be beneficial to everyone [5].

“Statin” is usually prescribed for those who complain of atherosclerosis, because of the drug's ability to decrease the deterioration of the condition [6]. And for those who have diabetes and arterial related diseases and fear complications in the situation that affects blood flow. And for those who are under a family-history of heart attacks, and as a kind of prevention of atherosclerotic cardiovascular disease (ASCVD) for the elderly [7]. A huge international study finds statins to be highly effective for Heart illness prevention [8].

Medical reports also indicate that the drug is effective in preventing high cholesterol among those who have a high risk of it, even if it has not already been raised. Physical activity while taking the drug increases its effectiveness in achieving the goal of preventing complications from increasing cholesterol by lowering the level of cholesterol in the blood, the risk of feeling chest pain and the threat of a heart attack is reduced. As per guidelines issued by American College of Cardiology/American Heart Association, High, Moderate or low Intensity Statin therapy is recommended for patients as per the need of their health conditions with different statins such as Atorvastatin (C10AA05) Fluvastatin (C10AA04) Rosuvastatin (C10AA07) or Simvastatin (C10AA01) [6,9].

Even though statins have been used since a long time, they are not that affordable. There are several brand and generic selections, and the price variance between them can differ greatly. A common generic like simvastatin might cost cheaper than $50 monthly, but a branded statin which may not have a universal alternative, can cost more than $350 [10]. Using generic simvastatin as first line could save £2bn over five years in England [11]. The current pharma industry market in Saudi Arabia is flooded with various brands of statin tablet imported from Asia, Europe and Western countries [12].

In our study we aim to explore the utilization and guidelines adherence for use of statins for management of cholesterol and their cost utility analysis for a clinical setting in Saudi Arabia.

2. MATERIALS AND METHODS

The study was designed as a single centered, cross-sectional retrospective pharmacy database study of utilization of statin therapy and their cost analysis. Data for the period from 1st January 2019 to 31st December 2019 were retrieved from the inpatients and outpatient electronic pharmacy records along with the unit dose prices of statins in Al-Mana General Hospital- Al-Khobar, Saudi Arabia. The daily price of each drug was computed based on the World Health Organization (WHO) Defined Daily Dose (DDD) and American College of Cardiology/American Heart Association (ACC/AHA). Patients who were not prescribed and dispensed any medications for statin therapy were excluded from the study.

The cost analysis of each studied drug was calculated in terms of the average price of each unit dose of each prescription. Lastly, the prescribing pattern was evaluated based on the adherence of guidelines and protocols of the American College of Cardiology/American Heart Association (ACC/AHA).
2.1 Data Analysis

Demographic characteristics were demonstrated as frequencies and percentages (with Wilson 95% confidence intervals for proportions). The Chi-square (for p-value calculation) was used as appropriate to compare the utilization rates of statins for the treatment of various diseases. All statistical analyses were conducted using SPSS® version 26 (SPSS Institute Inc., Cary, NC, USA) and Microsoft Excel 2013. P-value ≤ 0.05 considered as statistically significant.

3. RESULTS

Baseline demographic characteristics of the studied total 11,611 patient’s shows that the utilization of statins is higher in males, Saudis and people with the age group 40-59 as compared to females or non-Saudis or other age groups (Table 1).

As Table 2 shows, the prescription of Atorvastatin and Rosuvastatin is found to be more significant with p=0.00, in comparison to Simvastatin and Fluvastatin which also have significant relation to prescription with p value of ≤0.05. Over all, Atorvastatin was the most preferred statin therapy followed by Rosuvastatin, Simvastatin and Fluvastatin. In almost all age groups 20-39 Years (22.41%), 40-59 Years (21.25%) and 60-79 Years (27.26%) Simvastatin was the first choice of prescription, last being Atorvastatin or Rosuvastatin. For elderly age group of 80-99 Years Fluvastatin (24.64%) was the first preference and Atorvastatin (15.92%) being the last.

### Table 1. Baseline demographic characteristics of the studied patient’s

| Characteristics | Total 11,611 (95% CI) (N) |
|----------------|--------------------------|
| **Gender**     |                          |
| Male           | 65.80% (64.94-66.67) (7641) |
| Female         | 33.20% (33.33-35.06) (3970) |
| **Age (Years)**|                          |
| 20-39          | 6.64% (6.21-7.12) (772)   |
| 40-59          | 52.62% (51.71-53.53) (6110) |
| 60-79          | 36.62% (35.75-37.50) (4252) |
| 80-99          | 4.10% (3.76-4.49) (477)   |
| **Nationality**|                          |
| Saudi          | 51.77% (50.87-52.69) (6012) |
| Non-Saudi      | 48.23% (47.31-49.13) (5599) |

### Table 2. Adherence of prescribing pattern of Statins drug as per American College of Cardiology/American Heart Association (ACC/AHA) among different age group of hypercholesterolemia patients

| Statins (ATC) | 20-39 Years | 40-59 Years | 60-79 Years | 80-99 Years | P-Value |
|---------------|-------------|-------------|-------------|-------------|---------|
| Atorvastatin  | 11.5% (2.31-2.88) | 10.20% (25.47-20.26) | 19.79% (18.54-19.25) | 15.92% (2.08-2.34) | 0       |
| Total 5856, % (95% CI) (N) | 300 | 3049 | 2235 | 272 | |
| Fluvastatin  | 19.58% (0.01-0.08) | 19.58% (16.84-22.65) | 15.98% (0.47-0.75) | 24.64% (0.01-0.08) | ≤0.05   |
| (C10AA04), 12 5, % (95% CI) (N) | 3 | 68 | 50 | 4 | |
| Rosuvastatin | 17.97% (2.63-3.24) | 16.08% (17.77-19.19) | 10.48% (11.25-12.42) | 17.74% (0.8-1.15) | 0       |
| (C10AA07), 3968, % (95% CI) (N) | 339 | 2145 | 1373 | 111 | |
| Simvastatin  | 22.41% (0.94-1.33) | 21.25% (6.84-7.79) | 27.26% (4.73-5.54) | 22.10% (0.64-0.96) | ≤0.05   |
| (C10AA01), 1662, % (95% CI) (N) | 130 | 848 | 594 | 90 | |

P-Value calculated by using Chi-Square test. P-Value ≤0.05 consider as statistically significant
Table 3. Cost analysis of statins used among studied patients

| Drug category (ATC code) | DDD (mg) | Dose Oral | Average therapy of duration in days | Average Cost Unit wise in SR (USD) |
|--------------------------|----------|-----------|------------------------------------|-----------------------------------|
| Atorvastatin (C10AA05)   | 20       | 10 to 80 mg OD | 74.81                              | 5.58(1.49)                        |
| Fluvastatin (C10AA04)    | 60       | 40-80 mg OD/BD | 67.55                              | 4.24(1.13)                        |
| Rosuvastatin (C10AA07)   | 10       | 10-20 mg OD/BD | 76.69                              | 4.02(1.07)                        |
| Simvastatin (C10AA01)    | 30       | 10 to 80 mg OD | 74.36                              | 5.28(1.41)                        |

ATC, anatomical therapeutic chemical; DDD, defined daily dose. SFDA, Saudi Food and Drug Authority. SR= Saudi Riyal, USD= United State Dollar. 1 USD = 3.76 SR

As per Table 3, the DDD for Fluvastatin was found to be highest (60mg) with lowest average therapy duration of 67.55 days whereas, for Rosuvastatin DDD was found to be lowest 10 mg with highest average therapy duration of 76.69 days. The average cost unit wise was found to be highest for Atorvastatin SR 5.58 (USD1.49) being lowest for Rosuvastatin SR 4.02 (USD1.07).

4. DISCUSSION

Our study recorded that the statin therapy was prescribed and utilized more for males compared to the females which are in consistent with the study made on Sex Differences in the Statins use in Community Practice in 2019 by Nanna et al [13]. Even though the statin therapy has similar benefits for both the genders, lesser women receive it, since recent studies have demonstrated that women either stop or switch their statin because of various side-effects including worsening muscle symptoms [14]. Our data also confirmed that the younger adults and older people have fewer probabilities to be on statins, which is the same as the report recently published [15].

Significant p-values for both Atorvastatin and Rosuvastatin are similar to the earlier findings, where both the statins are equally harmless and effective in minimising cholesterol and feasibly backing plaque accumulation with high intensity treatment [16]. Atorvastatin is more efficient in comparison to simvastatin in patients with hyperlipidemia [17]. The Fluvastatin is a low-intensity statin as it lowers LDL cholesterol by less than 30%, so it is prescribed less [18]. Our study also confirms that the prescription of statins is in adherence to the guidelines given to start with low to moderate-intensity of statins and increase to high-intensity with risk enhancers [19]. Though atorvastatin made accessible as a generic alternative in 2012, it is relatively more expensive compared to the other generic statins, our study confirms the same [20].

5. CONCLUSION

Statins have become a noteworthy influence in the management of cholesterol, prevention of ASCVD and death related to it, as showed in numerous proven trials. The well-known generic convenience of statins has made these agents progressively more accessible. Basic accessibility of statins permits patients to satisfy the expense of treatment. However, price might be always a matter if an aggressive statin, like atorvastatin, is prescribed.

Enhanced communication between the doctors and the patient about the usefulness, importance and danger of statin therapy will increase adherence, cholesterol management, and results in those patients undergoing statin therapy.

The study aimed to evaluate the usage of statins for management of cholesterol is found to be consistent with the international guidelines given by ACC/AHS, however further research is needed to fully understand the barriers to guideline adherence to have improved utilization and considerably neutral cost effects of statins for all.

CONSENT

As per international standard or university standard, patients’ written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).
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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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