Majdi Al Qawasmeh\textsuperscript{1}, Ahmed Alhusban\textsuperscript{2,*}, Firas Alfwaress\textsuperscript{3} and Khalid El-Salem\textsuperscript{1}

\textsuperscript{1}Department of Neuroscience, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan; \textsuperscript{2}Clinical Pharmacy Department, Faculty of Pharmacy, Jordan University of Science and Technology, Irbid, Jordan; \textsuperscript{3}Department of Rehabilitation Sciences, Faculty of Applied Medical Sciences, Jordan University of Science and Technology, Irbid, Jordan

Abstract: Background: Stroke is the leading cause of long-term disability worldwide. Stroke recurrence is a major health problem with devastating consequences. Adherence to secondary prevention guidelines reduced stroke recurrence. Data regarding prescriptions adherence to secondary prevention guidelines in the Middle East and North Africa is lacking.

Objectives: The aim of this study is to assess the degree of physician adherence to ASA guidelines and the patient specific factors that affect their prescribing patterns in a major teaching hospital in Jordan.

Methods: Ischemic stroke patients referring to King Abdullah University Hospital were approached and offered a description of the study to obtain their informed consent. After getting the informed consent, their prescription at the time of discharge was evaluated for adherence to secondary prevention guidelines and classified into adherent and non-adherent based on a composite score that included each of the guidelines which indicated therapeutic classes. Odds ratio for adherence and their 95% confidence intervals were calculated and adherence to specific therapeutics classes was evaluated.

Results: Two hundred and seventy-five patients were included in this evaluation. Less than 50% of the patients received guideline’s adherent prescriptions. Patients with hypertension and hyperlipidemia were associated with a lower probability were prescribed a guidelines adherent regimen (OR 0.485, 0.225, respectively). ACEI/ARBs combination with thiazides was prescribed to about 11.52% of the patients.

Conclusion: Adherence to stroke secondary prevention guidelines was suboptimal especially in the antihypertensive prescription component. Further assessments and evaluations are required to improve guidelines adherence.

Keywords: Guidelines adherence, hypertension, prescribers’ attitude, patient factors, secondary prevention, stroke.

1. INTRODUCTION

Stroke is an acute neurologic disease with long-lasting effects on the life and welfare of the patients [1]. It is considered as the fifth leading cause of mortality and the first leading cause of long-term disability [1]. Despite the improvement in acute management of stroke, stroke recurrence is still a major health problem [1-3]. It has been reported that 185,000 patients will experience a stroke recurrence every year [1, 2]. Furthermore, the total direct cost of stroke between 2015 and 2035 is expected to be $94.3 billion [1].

To reduce the risk of stroke recurrence the American stroke association as well as many international associations have released guidelines regarding different aspects of stroke patient’s management [2, 4, 5]. The adoption of these guidelines has been reported to reduce the risk of stroke recurrence dramatically [2-4, 6-12]. Accordingly, assessment of practitioner’s and patient’s adherence to secondary prevention guidelines would shed light on the areas that need further attention and improvement in the management of stroke recurrence. A small number of studies have assessed the level of clinician’s awareness about the guidelines [7, 8, 11]. Asberg \textit{et al.}, reported an association between physician adherence to the guidelines and age of the patient [11]. Prescription of angiotensin converting enzyme inhibitors, statins and anticoagulants was less likely in the elderly [11]. In con-
trast, the elderly were more likely to receive antiplatelet therapy when compared to younger adults [11]. They have also reported a beneficial effect of statins and anticoagulants on mortality. Apart from these reports, data studies assessing physician adherence to guidelines are lacking. Accordingly, this manuscript is an attempt to explore the degree of physician adherence to ASA guidelines and the factors responsible for prescribing patterns in a major teaching hospital in Jordan. The ultimate goal of this work is to raise the awareness and stimulate similar research in the surrounding region and the world in general.

2. METHODS

In this study, patients with stroke or Transient Ischemic Attack (TIA) who referred to King Abdullah University Hospital between January 2016 and March 2017 were approached for inclusion in the study. Following their recruitment, their National Institute of Health Stroke Scale (NIHSS) score was determined. The severity of stroke was classified based on the NIHSS into no symptoms (NIHSS=0), minor stroke (NIHSS=1-4), moderate stroke (NIHSS=5-15), moderate to severe stroke (NIHSS=16-20), and severe stroke (NIHSS=31-42). Additionally, data regarding their basic demographic data and comorbid conditions were gathered using a special form designed by the study investigators. Furthermore, the medications prescribed at the time of discharge were documented and compared with the current American Stroke Association (ASA) secondary prevention guidelines. This comparison was achieved by giving one point for each prescribed therapeutic agent that is in compliance with the ASA guidelines. Regarding hypertension, the ASA recommends a thiazide or a thiazide-based combination that includes an ACEI or an ARB. Accordingly, hypertensive patients were assigned one point if their antihypertensive regimen complies with ASA recommendations. The sum of these points was used to establish a 3 points scale which was further used to categorize the patients into adherent if their score was 3 and non-adherent if the score was less than 3. Additionally, the frequency of prescribing each therapeutic class recommended by the ASA was evaluated.

3. STATISTICAL ANALYSIS

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 24 (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.). Odds ratio and their corresponding 95% confidence interval of the prescriber adherence to secondary prevention guidelines were calculated using the regression analysis model. All estimated were adjusted to the gender, and the established ischemic stroke risk factors are measured as categorical variables. The association between established ischemic stroke risk factors and the prescriber adherence of individual therapeutics classes was assessed using chi square. A p value of less than 0.05 was considered to be statistically significant.

4. RESULTS

4.1. Patients Demographics

Data from two hundred and seventy-five patients was included in this investigation. The median age of participants was 69 years old (59-75). Males constituted more than half of the participants (58%), the majority of participants had hypertension (81.1%) and dyslipidemia (91.6%). About half of the participants had diabetes (49.5%), whereas 35 (12.7%) of the participants had atrial fibrillation at the time of admission, 234 of the participants had either minor or moderate stroke according to the NIHSS (111 and 123, respectively). Table 1 demonstrates the baseline characteristics of the participants.

The distribution of stroke risk factors was similar between both genders, and no significant differences were observed between males and females. Table 2 demonstrates the frequency of stroke risk factors across the gender.

4.2. Adherence to Secondary Prevention Guidelines

Adherence assessment showed that about one hundred and thirty-one patients (47.74%) were prescribed a regimen that was consistent with the secondary prevention guidelines. The antihypertensive element of the regimen was as follows: ACEI/ARBs were prescribed to about 44 of the patients, thiazide diuretics were prescribed to 29 patients, whereas only 25 patients were prescribed a combination of both therapeutic classes (Fig. 1).

Hypertensive (OR 0.458; 0.442-0.710) and patients with hyperlipidemia (OR 0.255; 0.309-0.729) were less likely to be prescribed a regimen consistent with the ASA secondary prevention guidelines (Table 3). The presence of diabetes mellitus (OR 0.033; -0.074-0.139), atrial fibrillation (OR 0.066; -0.056-0.260) or the gender of the patients (OR 0.051; -0.053-0.155) did not alter the probability of being prescribed a regimen consistent with ASA secondary prevention guidelines.

Table 1. Baseline characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
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<tbody>
<tr>
<td>Age, median (IQR)</td>
<td>69 (59-75)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>114 (41.5)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>161 (58.5)</td>
</tr>
<tr>
<td>Medical history, n (%)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>223 (81.1)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>136 (49.5)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>35 (12.7)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>252 (91.6)</td>
</tr>
<tr>
<td>NIHSS, median (IQR)</td>
<td>5 (3-11)</td>
</tr>
<tr>
<td>No symptoms, n (%)</td>
<td>2 (0.75%)</td>
</tr>
<tr>
<td>Minor stroke, n (%)</td>
<td>111 (41.88%)</td>
</tr>
<tr>
<td>Moderate stroke, n (%)</td>
<td>123 (46.41%)</td>
</tr>
<tr>
<td>Moderate to severe stroke, n (%)</td>
<td>22 (8.32%)</td>
</tr>
<tr>
<td>Severe stroke, n (%)</td>
<td>7 (2.64)</td>
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</tbody>
</table>
4.3. Adherence by Therapeutic Category

Among patients who were prescribed a regimen consistent with ASA guidelines, 58% were prescribed an ACEI/ARB and only 28% received a thiazide diuretic (Table 4). Surprisingly, 55.9% of diabetic patients were prescribed an ACE/ARB. Antiplatelets were least prescribed to patients with atrial fibrillation (40%). Similarly, patients with atrial fibrillation were significantly less likely to receive an ACEI/ARB as compared to other risk factors (50%).
The use of thiazide diuretics was consistently lower across the different risk factors. Patients with hypertension and atrial fibrillation were significantly less likely to be prescribed a thiazide diuretic (28 and 37.1%, respectively). The majority of patients were prescribed antiplatelet therapy (86%) (Fig. 2). Aspirin alone was prescribed for 110 patients (58.8%). A combination of aspirin and clopidogrel was prescribed in 48 patients (18%). Anticoagulants were prescribed for 35 patients (12.8%). About 14 patients (5.1%) received the combination of antiplatelet and anticoagulants therapy. Fig. 2 describes the details of antiplatelets prescription patterns.

The prescription of all therapeutic classes was comparable among both males and females with no significant differences (Table 5).

5. DISCUSSION

In our cohort, the majority of stroke patients were treated with statins, antiplatelets, anticoagulants, and an antihypertensive, about half of hypertensive patients were treated with an ACEI/ARB, whereas a minority was prescribed an ACEI/ARB and Thiazide combination. The use of statins and antiplatelets/anticoagulants was remarkably high in this cohort.

Hypertension has been identified as the single most important risk factor for the development of stroke. The American stroke association guidelines have firmly demonstrated the importance of blood pressure management in patients with stroke as a secondary prevention tool [2, 4, 12, 13]. Although their guidelines did not provide clear recommendations regarding the optimum regimen to be used, they have highlighted the use of thiazide and ACEI in this setting [2, 12-16]. In our cohort, most of the stroke patients were hypertensive and all were treated. Notably, about one third of the total number of patients included in this study were prescribed an ACEI/ARB and thiazide combination. A similar trend was reported by Asperg et al., who assessed the adherence to secondary stroke prevention guidelines in a cohort derived from the Swedish stroke registry [11]. Furthermore,
Ma et al., reported that 63.1% of the cohort studied did not receive ACEI/ARBs [7]. This practice is in clear contrast with the findings of the Losartan Intervention For Endpoint reduction in hypertension study (LIFE), that compared the beneficial effect of losartan and metoprolol in patients with high risk of cardiovascular events [14]. In this study, losartan was shown to reduce the incidence of stroke by about 25%. Accordingly, the importance of prescribing an ACEI/ARBs alone or in combination with thiazide diuretics should be stressed and measured to enhance their prescription tendency in this group should be employed.

Our findings have indicated a high rate of statins prescription for stroke patients. This high rate is in conformity with the ASA secondary prevention guidelines regarding the management of stroke [2, 16-18]. Additionally, it reflects an understanding of the beneficial effects of reducing LDL levels using statins therapy.

Antiplatelets use has been recommended by the ASA secondary prevention guidelines as an essential tool to reduce the risk of stroke recurrence. This effect has been consistently reported in the prevention of myocardial infarction and stroke. Most of the evidence supporting the importance of antiplatelets was derived from studies evaluating aspirin for secondary prevention [2, 4, 5, 10, 19-23]. About 60% of the patients reported in this report has been using aspirin for secondary prevention. The use of dual antiplatelet therapy in the form of aspirin and antiplatelets was observed in about 18% of the patients. Recently, it has become more evident that a short-term course of aspirin and clopidogrel is more effective that aspirin alone in preventing stroke recurrence [4, 21]. On the other hand, about 40% of patients receiving single agent-antiplatelet therapy were treated with clopidogrel. Despite the reports of higher potency of clopidogrel, its role in secondary prevention after stroke is unclear [20]. Most of the evidence supporting its role in secondary prevention against atherosclerotic diseases was restricted to peripheral vascular disease [20].

CONCLUSION

In conclusion, the application of ASA secondary prevention guidelines in this cohort varied. The use of aspirin and statin was very high, but the use of antihypertensive agents requires major modifications. This can be achieved by developing prescriber’s directed educational interventions that focus on the importance of guidelines recommended agents in the secondary prevention after stroke. Furthermore, the factors that might have affected the prescriber’s decision needs to be thoroughly evaluated. Additionally, measures to ensure that stroke patients are receiving guidelines-based treatment should be developed and employed.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was approved by the institutional review board at the King Abdullah University Hospital (Approval no. 31/96/2016).

HUMAN AND ANIMAL RIGHTS

No Animals were used for studies that are basis of this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2008 (http://www.wma.net/en/20activities/10ethics/10helsinki/).

CONSENT FOR PUBLICATION

Informed consent was provided by each individual.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

FUNDING

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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