

# Drug Utilization Pattern among Stroke Patients – A Cross-sectional Insight

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## Abstract

**Objective:** This study aimed to evaluate drug utilization pattern among stroke patients. **Materials and Methods:** A cross-sectional study was conducted among 96 stroke patients aged from 30 to 92 years in a hospital in Malaysia. A total of 88 patients were available for descriptive analysis and logistic regression analysis. Descriptive and logistic regression analyses were performed. **Results:** On average, patients were aged 67.62 years (standard deviation of 13.14) and had a higher incidence in Malay ethnicity (42.7%). Ischemic stroke accounts for 91.67% of the study, with a slightly higher proportion of female patients (51.04%). Majority of stroke patient complaint generalized body weakness as their major symptom (19.81%). Calcium channel blocker was found to be the most used antihypertensive agent among stroke patients (40.9%) followed by angiotensin-converting enzyme inhibitors (ACEIs) (31.8%). **Conclusion:** Using logistic regression modeling, it was determined that the factors of a subject would affect the choice of prescribing of ACEIs and anticoagulant drugs.

**Key words:** Angiotensin-converting enzyme inhibitors, Drug utilization, Drug utilization Pattern, Hypertension, Ischemic stroke, Pattern, Stroke

## INTRODUCTION

Stroke is a major cause of mortality worldwide and commonly occurs in elderly patients.<sup>[1]</sup> High blood pressure (BP) is the most prominent modifiable risk factor for stroke reduction in BP treatment is one of the most appropriate interventions for both primary and secondary prevention of stroke.<sup>[1,2]</sup> Certain risk factors are rare but usually known for stroke occur among some specific races. The most common and the major risk factors for stroke are hypertension, obesity, diabetes, and smoking.<sup>[1-3]</sup> According to the WHO 2001, 90% of the world stroke mortality has been contributed by the developing countries.<sup>[2]</sup> The WHO data evidenced that around 6 new cases of stroke are being reported per hour in Malaysia. In addition, in Malaysia, among males, stroke is ranked as the 3<sup>rd</sup> leading cause of death and among females as the 2<sup>nd</sup> leading cause of death after ischemic heart disease.<sup>[4,5]</sup>

Angiotensin-converting enzyme inhibitors (ACEIs) have shown promising results in decreasing the incidence and severity of stroke in populations at risk and in improving stroke

outcomes.<sup>[6,7]</sup> Although high BP is the main modifiable vascular risk factor for stroke, evidence from previous studies has shown that ACEIs medications can decrease the risk of stroke by other mechanisms in addition to their antihypertensive effects, including neuroprotective properties and beneficial properties on the endothelium.<sup>[6-9]</sup> Despite having strong evidence that the use of ACEIs aids in preventing secondary stroke, there are cases of underutilization still been reported. The underutilization of ACEIs may be explained by physicians concentrating on the presence of other comorbidities thus showing less attention to the stroke condition.<sup>[9-13]</sup>

Therefore, the objectives of our study were to assess the drug utilization pattern (DUP) among stroke patients/survivors and to evaluate the prevalence of the use of antihypertensive

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**Received:** 08-06-2020

**Revised:** 25-07-2020

**Accepted:** 02-08-2020

drugs. The results of this study might serve as reference data for healthcare providers in determining first-line DUP in the prevention of secondary stroke.

## MATERIALS AND METHODS

### Settings and study design

This was a cross-sectional study conducted among stroke patients, both ischemic and hemorrhagic (history and active cases), admitted to a hospital located in Malaysia. The hospital provides health care and emergency treatment for all illnesses and accidents. Before the initiation of this study, all aspects research approval, including access to and use of patient clinical information, were authorized by the local health authorities and medical research and ethics committee. The study was registered at the clinical research committee of the hospital under research # 30139 and started after the approval from the concerned authorities.

### Participants and data collection

Data were collected for a period of 6 months from May 2016 to October 2016. Patients who had a history or newly diagnosed as ischemic or hemorrhagic stroke were identified. A total 96 stroke patients were conveniently sampled and 88 of them who met the selection criteria were included in this study. Patients with incomplete data and pregnant were excluded from this study.

The information on patients sign and symptoms were collected from the patient medical file for active cases and for the patients with stroke history were collected from computer system. Moreover, the use of ACEIs as the

preventative measurement from getting secondary stroke for both normotensive and hypertensive patients was recorded and further analyzed to study the factors affecting its use. The four classes of medications were reviewed and compared with the recommended medication since both ischemic and hemorrhagic stroke are managed similarly for secondary prevention.<sup>[7]</sup> Hence, the most used medications from each class were identified and recorded.

### Statistical analysis

Data were collected from patients' medical files and analyzed using SPSS statistic version 24 (Statistical Package for the Social Sciences). All recorded information was coded into categorical variables. Categorical data were presented as frequency and percentage while continuous data were reported as mean  $\pm$  standard deviation. Logistic regression analysis was used to describe the DUP of ACEIs and anticoagulants. For the logistic regression analysis,  $P < 0.05$  was considered statistically significant.

## RESULTS

Figure 1 represents the demographic characteristics of the study patients. The average age of these patients was 67.62  $\pm$  13.14 years (range: 30–92). The male-female ratio was 1:1. Malay patients represented 43.20% of the study population followed by Chinese (28.40%) and Indians (28.40%).

Table 1 shows the most common clinical manifestations observed among the studied patients. The majority of them had various signs and symptoms such as 43.20% had general weakness, 20.50% had headache, and 19.30% faced dizziness.

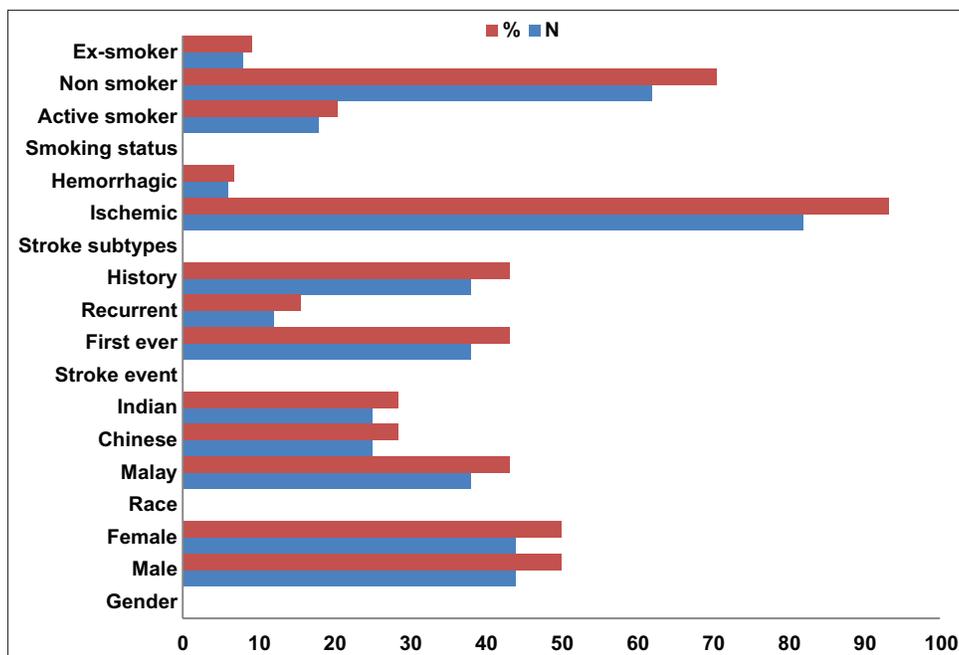


Figure 1: Demographic characteristics of the patients

**Table 1: Clinical manifestations among the patients**

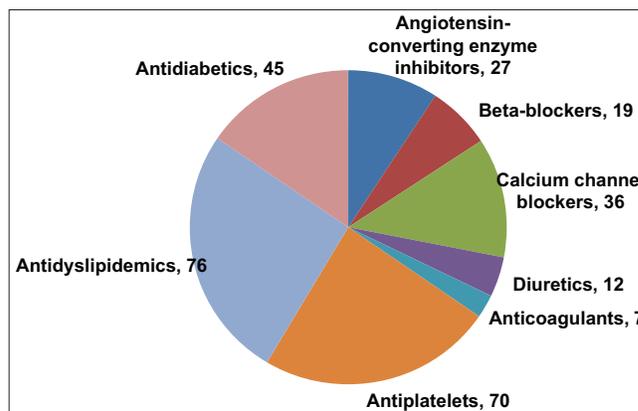
Characteristics	n	%
Headache		
Present	18	20.50
Absent	70	79.50
General weakness		
Present	38	43.20
Absent	50	56.80
Vomiting		
Present	6	6.80
Absent	82	93.20
Nausea		
Present	4	4.50
Absent	84	95.50
Dizziness		
Present	17	19.30
Absent	71	80.70
Convulsions		
Present	3	3.40
Absent	85	96.60
Slurred speech		
Present	24	27.30
Absent	64	72.70
Drooling of saliva		
Present	3	3.40
Absent	85	96.60
Dropping of eyelids		
Present	4	4.50
Absent	84	95.50
Hemianopia		
Present	9	10.20
Absent	79	89.90
General sensory loss		
Present	26	29.50
Absent	62	70.50
Left side hemiparesis		
Present	14	15.90
Absent	74	84.10
Right side hemiparesis		
Present	16	18.20
Absent	72	81.80
Paresis on face		
Present	11	12.50
Absent	77	87.50

Table 2 shows the most common comorbidities found among stroke patients. They were hypertension (84.10%) followed by diabetes mellitus (DM) (60.20%). During the study period,

**Table 2: Comorbidities among the studied patients**

Comorbidities	n	%
Hypertension		
Present	74	84.10
Absent	14	15.90
DM		
Present	53	60.20
Absent	35	39.80
Dyslipidemia		
Present	16	18.20
Absent	72	81.80
Other CVDs		
Present	22	25.10
Absent	66	74.80
Ischemic heart disease		
Present	22	25.00
Absent	66	75.00
Renal impairment		
Present	22	25.00
Absent	66	75.00

CVDs: Cardiovascular diseases



**Figure 2: Drug utilization pattern among patients (%)**

the commonly reported sign and symptoms were general body weakness (43.20%), general sensory loss (29.50%), and slurred speech (27.30%).

Figure 2 demonstrates the DUP among the studied patients. Among all the anti-hyperlipidemia drugs, simvastatin was found to be commonly used. The total percentage of patients that were discharged with antidiabetic drugs was 45% which is 41 out of 88. A total of 60.2% patients were diabetic and only 45% patients were discharged with antidiabetic medication. It was found that metformin accounted for 33% usage among other antidiabetic medications followed by insulin with a total of 25%. It was also found that among 40 patients who received antidiabetic agents at discharge, 16 (40%) were on

monotherapy and 24 (60%) were on polytherapy with 2 or more medications. On the other hand, the study showed that 70% of ischemic stroke patients were discharged with antiplatelet medicines. Among the 70% ischemic stroke patients discharged with antiplatelet, 50% were diagnosed with first stroke attack.

The commonly prescribed antiplatelet medications were aspirin+glycine, clopidogrel, aspirin, and ticlopidine. However, multivariate regression analysis using adjusted odds ratio showed that the usage of these drugs was statistically significant ( $P < 0.05$ ) for ACEIs and aspirin+glycine. The results are presented in Table 3.

## DISCUSSION

This study found that the mean age ( $\pm$  SD) of stroke patients was  $67.62 \pm 13.14$  years. This finding was comparable to a previous study done in Malaysia, where the mean age was found to be  $62.7 \pm 12.5$  years.<sup>[4]</sup> In addition, a study done in another hospital showed 65.3 (SD, 12.28) years as the mean age of stroke.<sup>[14]</sup> The possible factors for increased stroke prevalence among the elderly population were due to the decreased metabolic capacity of neural cells to counteract extreme stressors and/or neurotoxic challenges.<sup>[15-17]</sup> In this study, female and male patients accounted for 50.0% and 50.0%, respectively, giving a female:male ratio of 1:1, where slight higher incidence was seen in female patients 71 years old and older. This result is comparable with another study,<sup>[12]</sup> in which female age 75 or above has 25% higher prevalence of stroke as compared to men, but it was not statistically significant. The possible reasons for the lower incidence rate in females at an early age may be due to the positive effects of estrogen on the cerebral circulation.<sup>[17,18]</sup>

In terms of ethnicity, this study showed that the majority of stroke patients were Malay (43.2%) followed by Indians 28.4% and Chinese 28.4%. Another study conducted in Malaysia about the incidence of stroke among Chinese, Malays, and Indians in multiple states shows, the proportion of Malay was much higher than Chinese followed by Indians.<sup>[4]</sup> The different ratios in ethnicity across all studies reflected the geographical variation in ethnic distribution, rather than the ethnic-specific prevalence in the country.<sup>[16]</sup>

Regarding smoking status, unexpectedly, the study showed that the majority of stroke patients were non-smokers (71.83%). A similar trend was observed in another study,<sup>[8]</sup> where 75.9% of respondents were non-smokers. A meta-analysis<sup>[9]</sup> stated that environmental tobacco smoke exposure could be a suggestive risk factor in those not smoking. Based on the descriptive data, patients admitted with active stroke diagnosis were 58.8% followed by with a history of stroke, accounting for 43.20%. Among the active cases, first stroke attack accounts for 43.20%. A similar trend has been reported by Acute Stroke Registry Malaysia, 2010–2014, where 79.2% of the total study population had experienced their first-ever stroke and 68.2% of them were ischemic.<sup>[4]</sup> In a single-center prospective study, among all stroke patients admitted to another hospital over a 1-year period, 74.8% had a first ischemic stroke.<sup>[9]</sup>

In terms of stroke subtype, these results showed that the majority of them were having an ischemic stroke. This finding was similar to a study done in Malaysia, where an increasing incidence and prevalence trends for ischemic stroke were reported (34.2–96.2/100,000). It was observed that the ischemic stroke cases nearly tripled in the 5 years of study period ranging from 73.3% to 79.9%.<sup>[4]</sup> Increasing prevalence of ischemic stroke in Malaysia was linked with poor control of risk factors such as smoking, diabetes, heart disease, and hypercholesterolemia, with hypertension.<sup>[13]</sup> Regarding the comorbidities, this study found that 84.10% of the study population had hypertension and 60.20% had DM. These findings were comparable to a study conducted on the burden of stroke in Malaysia, in which hypertension was the most common risk factor for stroke (53.2–76.1%) followed by DM (27.4–55.2%).<sup>[13]</sup>

Based on our findings, simvastatin was the commonly used antihyperlipidemic drug for stroke patients among all the other types of antihyperlipidemic medications. This result showed a similar trend to the study done in Taiwan, where the use of statin had significantly increased in recent years due to its neuroprotective effect by regulating cerebral perfusion and improves endothelial function.<sup>[19]</sup> In this study, the most common type of antidiabetic medication prescribed was metformin followed by glielazide and insulin. Based on another study, it was found that metformin has direct antioxidant effects in addition to its glucose-lowering actions, which contributes to improved endothelial cell function and angiogenic effect in the patients with a higher risk of stroke.<sup>[20]</sup> Based on our study, the majority ischemic stroke patients were discharged with antiplatelet therapy. Based on our findings, the use of aspirin+glycine was the highest among all the other types of antiplatelet medications.

The choice of prescribing aspirin+glycine more than the other antiplatelet agents by physicians may be attributed to the glycine's property in the formulation which causes less gastrointestinal complaints than aspirin alone and improves tolerability.<sup>[21-24]</sup> Common drugs to manage/treat stroke

**Table 3: Multivariate analysis of DUP among patients**

DUPs	AOR	P-value
ACEIs	2.13	0.031*
Aspirin+Glycine	0.89	0.048*
Clopidogrel	0.79	0.387
Aspirin	0.93	0.245
Ticlopidine	0.56	0.632

\*Statistically significant. ACEIs: Angiotensin-converting enzyme inhibitors, DUP: Drug utilization pattern, AOR: Adjusted odds ratio

anticoagulants such as warfarin, antiplatelets such as aspirin and clopidogrel, statins or HMG-CoA reductase inhibitors such as atorvastatin and simvastatin, and some BP-lowering drugs such as ACEIs, beta-blockers, or calcium channel blockers. On the other hand, tissue plasminogen activator is a real life-saving drug that actually breaks up a blood clot in a stroke. Mostly, it is used when there is an emergency treatment required in stroke management.<sup>[25,26]</sup>

## CONCLUSION

Our study highlights the review of DUP among stroke patients. In this exploratory study, it was observed that the ACEIs together with other drugs to treat comorbidities were used among the patients for secondary prevention of stroke.

## ACKNOWLEDGMENTS

The authors would like to thank the Deanship of Scientific Research at Prince Sattam Bin Abdulaziz University, Al-Kharj, Saudi Arabia, for the support in the publication of this manuscript. The authors would also like to express their gratitude to everyone who has been involved directly or indirectly in the completion of this study.

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**Source of Support:** Nil. **Conflicts of Interest:** None declared.