

Secondary stroke prevention among stroke survivors in Riyadh city, Saudi Arabia

Risk Knowledge, adherence to stroke discharge medications and preventive strategies

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ABSTRACT

الأهداف: تقييم معرفة مرضى السكتة الدماغية بوسائل الوقاية من الإصابة بسكتة دماغية أخرى ومدى التزامهم بهذه الوسائل، وكذلك دراسة الأسباب المرتبطة بعدم الالتزام.

المنهجية: شملت هذه الدراسة المقطعية 82 مريضاً ممن أصيبوا بسكتة دماغية وتم معالجتهم في مستشفى الأمير محمد بن عبدالعزيز بالرياض، في المملكة العربية السعودية، خلال الفترة من يوليو 2015م إلى أغسطس 2018م. تم تقييم مستوى الالتزام بالأدوية باستخدام سلم استبياني تم تطويره من قبل فريق بحثي بقيادة سيدور كيفيش (2016).

النتائج: من بين 82 مجموع المشاركين، 63.4% كانوا على دراية بارتفاع نسبة حدوث السكتة الدماغية الثانية و 70.7% بأن نتيجهتها أسوأ بالمقارنة بالإصابة الأولى. من بين قائمة 7 وسائل وقائية، كان أعلى نسب إجابات صحيحة تخص علاج عوامل الخطر كمرض السكري وارتفاع ضغط الدم (80.5%)، المحافظة على نظام غذائي صحي (65.9%)، والتدخين الرياضي المنتظم (63.4%). أما بالنسبة لأكثر أسباب عدم الالتزام شيوعاً بين المرضى فقد لوحظ أن النسيان كان الأكثر بمعدل (51.2%)، يليه تعدد الأدوية ب (18.3%) ثم الشعور بالتحسن بنسبة (17.1%). على مستوى المرضى، بلغت نسبة الالتزام المقبول 46.8% من المجموع، والتي كانت أعلى بين الإناث (60.0% مقابل 35.7%، دلالة إحصائية $p=0.033$) والمتزوجين (52.2% مقابل 0.0%، $p=0.006$) وأدنى بين المدخنين (22.2% مقابل 54.2%، $p=0.029$)، بالمقارنة مع أقرانهم. أبرز الانحدار اللوجستي التدخين كعامل هام، إذ قاربت نتيجهته الدلالة الإحصائية بنسبة احتمالات $4.28 [0.99, 18.41]$ ، $p=0.051$ للتنبؤ بعدم الالتزام.

الخلاصة: رغم أن الغالبية من مرضى السكتة الدماغية في الدراسة كانوا على دراية جيدة بأساليب ووسائل الوقاية من السكتة الدماغية الثانية، إلا أن التزامهم بها كان دون المستوى الأمثل، مما يجعلهم عرضة لسكتة دماغية ثانية. يتعين على مقدمي الرعاية تشخيص العوائق التي تحول بين المريض والتزامه بالأدوية، وتنفيذ الاستراتيجيات الفعالة لتخطي تلك العوائق لأجل تحسين مستوى التزام المرضى الذي يمثل خطوة أساسية في نجاح الخطة العلاجية والوقائية من السكتة الدماغية على حد سواء.

Objectives: To assess knowledge about secondary stroke and adherence to stroke discharge medication and prevention strategies among stroke survivors, and to identify possible causes of poor adherence.

Methods: A cross-sectional study that involved 82 stroke survivors who were treated at Prince Mohammed Bin Abdulaziz Hospital (PMAH) in Riyadh, Saudi Arabia, from July 2015 to August

2018. Patient adherence level (PAL) was assessed using a tool developed by Sidorkiewicz et al (2016).

Results: Of the 82 participants, 63.4% believed that the risk of secondary stroke is higher and 70.7% believed it would result in worse outcome, compared to primary stroke. Out of a list of 7 preventive strategies, treating risk factors (80.5%), keeping a healthy diet (65.9%) and regular exercise (63.4%) were the most frequently identified. Forgetfulness (51.2%), polypharmacy (18.3%) and patient-perceived improvement (17.1%) were the most frequently reported causes for nonadherence. At the patients' level, PAL was adequate among 46.8%, and was higher among females (60.0% versus 35.7%, $p=0.033$) and married (52.2% versus 0.0%, $p=0.006$) ones, and lower among smokers (22.2% versus 54.2%, $p=0.029$), compared to their counterparts. No correlation of adherence level with knowledge was observed. Regression showed approximation to statistical significance for smoking (OR=4.28 [0.99, 18.41], $p=0.051$) as a predictor for inadequate adherence.

Conclusion: Stroke survivors have suboptimal adherence to discharge prescriptions and preventive strategies, despite a relatively sound knowledge, which exposes them to high risk of secondary stroke. It is part of the healthcare providers' role to identify eventual barriers to adherence and to implement efficacious strategies to alleviate such barriers and improve patients' adherence.

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Stroke is an acute neurological deficit that involves a specific area of the central nervous system due to an impairment of the cerebral perfusion or vasculature. This causes ischemia of the affected area, depolarization of cells, and a series of oxidative changes that finally lead to apoptosis and excitotoxicity.¹ In majority cases (85%), stroke is due to a thrombotic or embolic event that reduces the blood flow to the brain (ischemic stroke [IS]), whereas the second more frequent entity, hemorrhagic stroke (HS) is due to intracerebral hemorrhage by rupture of the small cerebral arteries.²

Stroke ranks second among the leading causes of mortality worldwide and its epidemiological picture of stroke emphasizes its significant burden on the health. In 2016, about 5.5 million deaths were attributable to stroke, with an approximate equal gender distribution (52.7% in males).³ Stroke is also the second leading cause of disability-adjusted life years (DALYs).⁴ The disease is still prevalent among more than 80 million survivors globally and the absolute numbers of incident cases and deaths are increasing. In Saudi Arabia, several risk factors of stroke, such as hypertension, smoking, and obesity, are still not adequately managed.⁵ Furthermore, stroke care is still suboptimal as compared to developed countries,⁶ and there is a lack of robust organizational processes of care and inadequate allocation of resources.^{6,7} This would in turn cause significant consequences in the affected patients.

Stroke survivors are generally at an increased risk for significant morbidity. Of note, after the onset of stroke, patients with hypertension, atrial fibrillation, diabetes, and coronary heart disease are prone to stroke recurrence.⁸ About 11% of patients might have a recurrent event within one year, 26% within the next 5 years, and 40% within 10 years.⁹ Therefore, in addition to the specific medical and rehabilitative interventions, preventing stroke recurrence is an essential element of post-stroke patient care.¹⁰ Secondary stroke prevention comprises of several approaches, including nutritional interventions, anti-hypertensive measures, anticoagulation, antiplatelet therapy, lipid-lowering therapy, and management of intracranial stenosis.¹¹ The key to select the best management approach is to identify the cause of the event. It has been previously estimated that approximately 80% of secondary events could be prevented via medical

and lifestyle interventions.¹² However, it is imperative to ensure patients' adherence, particularly with the pharmacological therapy. Additionally, barriers to adherence, which may be patient-related or -unrelated, should be explored and alleviated for better efficacy of the preventive strategy.

In essence, compliance to treatment is one of the major challenges to preventing stroke recurrence. Non-adherence, defined as a lack of correspondence with the agreed recommendations by a health professional,¹³ can cause increased morbidity, poor health outcomes, and increased costs to healthcare systems.¹⁴ Additionally, compliance might be compounded by the factors related to caregivers as important providers of care. However, these factors are primarily dependent on scarce studies. In the Saudi context, only 5% of patients receive care at specific units for stroke;⁶ the impact of the specific knowledge of patients and caregivers on the outcomes of stroke prevention may be more prominent. Understanding the determinants of poor compliance would help in improving post-stroke care and preventing secondary stroke in Saudi Arabia. In this context, the present study aimed to explore the knowledge of stroke patients and or their caregivers regarding the risk of and preventive strategies against secondary stroke events, and to assess their level of adherence to the prescribed medications and to general preventive rules. Further, the association of adherence with knowledge was analyzed and factors and predictors of nonadherence were explored.

Methods. Design & Setting. A cross-sectional study was conducted among stroke survivors, who were treated at Prince Mohammed Bin Abdulaziz Hospital (PMAH), Riyadh City, Saudi Arabia, during the past 3-year period.

Riyadh is the capital and most populous city of Saudi Arabia, with an estimated population of 6,506,700 and an area of 380,000 square kilometers. Prince Mohammed Bin Abdulaziz Hospital (PMAH) is a 500-bed hospital that provides secondary and tertiary healthcare services. The range of services PMAH provides makes it one of the largest referral hospitals in the country for diagnosis and treatment of various acute and chronic medical and surgical conditions.

Population and sampling. The total number of patients who were admitted to PMAH, for stroke, during the period from July 2015 to August 2018 was estimated at 156 patients, approximately. A convenience sampling was used to include all survivors among these patients, who accepted to participate either personally or via their caregiver. Participants who were not reachable by telephone and those who were not able to

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understand and or complete the questionnaire were not included.

Data collection. A semi-structured questionnaire was used to collect study data, which originated from 2 sources including patients' medical records and structured telephone interviews of the patients or their respective caregivers. The questionnaire was developed based on literature reviews¹⁵⁻¹⁷ and comprised 4 sections. The first section consisted of general demographic and clinical data including age, gender, social history, presence of major stroke risk factors (hypertension, diabetes, smoking, etc.), time since stroke, stroke type (ischemic, hemorrhagic, or transient ischemic attack) and number of medications taken per day. The second section assessed participants' knowledge regarding secondary stroke among stroke survivors, including risk level (lower, similar or higher) and outcome severity (worse, similar and better), by reference to primary stroke among general population. Additionally, participants' knowledge about a panel of 7 prevention strategies (treatment of risk factors, healthy diet, regular exercise, etc.) was assessed, along with their eventual sources of knowledge. The third section evaluated patients' adherence to secondary stroke prevention including drugs that were prescribed at primary stroke discharge, among 6 prelisted types including antiplatelet, anticoagulant, antihypertensive, oral hypoglycemic medication, insulin, and lipid lowering agents. Adherence level was measured for each drug individually, by using the self-reported adherence questionnaire developed by Sidorkiewicz et al, 2016.¹⁷ The questionnaire describes the different medication-taking behaviors, which enables classifying drug adherence into 6 levels: level 1 "high", level 2 "good", level 3 "moderate", level 4 "poor", level 5 "very poor" and level 6 "drug discontinuation".¹⁶ Besides, adherence to lifestyle recommendations (healthy diet, smoking cessation, weight control, and regular exercise) was assessed using binary questions (yes or no). The fourth section explored eventual reasons for nonadherence using a panel of 12 most probable reasons such as forgetfulness, concerns about side effects, lack of support, etc., completed by an open item for further non-listed items.

Outcome definition. The primary outcome consisted of the patient adherence level (PAL), which was computed using 2 different methods:

In the first method, PAL was defined as the adherence level for the drug for which the patient was the most non-adherent, i.e. the drug that had the highest score. We obtained a discrete variable ranging from 1 to 6, with higher values indicating poorer adherence.

In the second method, PAL was calculated as the

Table 1 - Socio demographic and clinical characteristics of patients. (N=82)

Parameter Category	n	(%)
<i>Demographic data</i>		
<i>Age group (years)</i>		
31-50	19	(23.2)
51-50	17	(20.7)
>60 years old	46	(56.1)
<i>Gender</i>		
Male	47	(57.3)
Female	35	(42.7)
<i>Marital status</i>		
Single	5	(6.1)
Married	70	(85.4)
Divorced or widowed	7	(8.5)
<i>Level of education</i>		
Non-educated	25	(30.5)
Primary	19	(23.2)
Elementary	7	(8.5)
High school	12	(14.6)
University and above	14	(17.1)
Not answered	5	(6.1)
<i>Clinical data</i>		
<i>Type of stroke</i>		
Ischemic stroke	55	(67.1)
Hemorrhagic stroke	4	(4.9)
Transient ischemic attack	5	(6.1)
Do not know	18	(22.0)
<i>Time since stroke</i>		
≤1 year	52	(63.4)
>1 year	30	(36.6)
<i>Risk factors</i>		
No risk factor	6	(7.3)
One risk factor	14	(17.1)
2+ risk factors	62	(75.6)
<i>Type(s) of risk factor†</i>		
Hypertension	64	(78.0)
Diabetes Mellitus	48	(58.5)
Hypercholesterolemia	47	(57.3)
Smoking	18	(22.0)
Alcohol abuse	0	(0.0)
<i>No. medications per day</i>		
<5	52	(63.4)
≥5	30	(36.6)
<i>Tobacco use before stroke</i>		
Yes	18	(22.0)
No	64	(78.0)
<i>Lifestyle after stroke</i>		
<i>Quite smoking[‡]</i>		
Yes	5	(27.8)
No	13	(72.2)
<i>Regular exercise</i>		
Yes	26	(31.7)
No	56	(68.3)
<i>Healthy diet</i>		
Yes	58	(70.7)
No	24	(29.3)
<i>Weight control</i>		
Yes	56	(68.3)
No	26	(31.7)

Table 2 - Knowledge of patients toward secondary stroke.

Item / answering option	N (%)
<i>Compared to the general population, patients with previous strokes have a _____ risk of stroke recurrence</i>	
Lower	4 (04.9)
Similar	26 (31.7)
*Higher	52 (63.4)
<i>Compared to previous stroke, the outcome of the second stroke will be _____</i>	
*Worse	58 (70.7%)
Same	15 (18.3%)
Better	9 (11.0%)
<i>†Strategies that help prevent a secondary stroke</i>	
Risk factors treatment (Diabetes, Hypertension, etc.)	66 (80.5%)
Healthy diet that is low in fat and salt	54 (65.9%)
Regular exercise	52 (63.4%)
Usage of antiplatelet therapy and anticoagulants	47 (57.3%)
Quit smoking	41 (50.0%)
Weight control	40 (48.8%)
Reduction and avoidance of alcohol	20 (24.4%)
<i>Sources of information †</i>	
Doctors and hospital teams	51 (62.2%)
Family and friends	29 (35.4%)
Social media and internet	18 (22.0%)
Mass media	5 (6.1%)
Other	9 (11.0)

†Variable with multiple responses. *The correct answers (questions 1&2).

mean drug adherence level using the following formula: $PAL = (\sum \text{drug adherence levels}) / (\text{number of drugs prescribed at stroke discharge})$

We obtained a continuous variable ranging from 1 to 6, with higher values indicating poorer adherence.

Statistical methods. Data was entered and analyzed using the Statistical Package for Social Sciences version 21.0 for Windows (SPSS Inc., Chicago, IL, USA). Descriptive statistics were carried out to present sociodemographic and clinical data, patterns of answers to the different questionnaire sections, and the drug and patient adherence levels. Findings were summarized as numbers and percentages for categorical variables and mean (SD) values for continuous variables. The discrete PAL variable was transformed into a binary variable, by dichotomizing adherence level into adequate (high or good [score=1, 2]) versus inadequate (moderate or poorer [score≥3]) adherence. The percentage of patients with adequate adherence was compared across the different factor categories using chi square or Fisher's exact test, as appropriate. Further, the continuous PAL variable was compared between the factors' categories using nonparametric tests, including Mann-Whitney U and Kruskal-Wallis tests for factors with binomial and

multinomial variables, respectively. Multivariate binary regression was carried out to analyze the independent factors of nonadherence, including factors that showed significance in either 2 previous analyses; results were presented as odd ratio (OR) with 95% confidence interval (95% CI). For all the test, statistical significance was assumed for a p -value<0.05.

Ethical considerations. Informed consent was obtained verbally from all participants, who were invited

Table 3 - Drug and patient adherence levels (N=77).

Outcome	N	Adherence level, N (%)	
		Adequate (1 – 2)	Inadequate (3 – 6)
<i>Drug adherence level</i>			
Antiplatelet	61	41 (67.2)	20 (32.8)
Anticoagulant	40	21 (52.5)	19 (47.5)
Anti-hypersensitive	62	52 (83.9)	10 (16.1)
Oral hypoglycemic	36	24 (66.7)	12 (33.3)
Insulin	23	23 (100.0)	0 (0.0)
Lipid-lowering agent	46	37 (80.4)	9 (19.6)
Patient adherence level	77	36 (46.8)	41 (53.2)

Table 4 - Factors association with patient adherence level.

Factors Category	Adequate n (%)	P-value ¹	Mean Patient adherence level	P-value ²
<i>Demographic factors</i>				
<i>Age group (years)</i>				
31-50	9 (50.0)		2.16	
51-50	7 (43.8)	.935	2.44	.941
>60	20 (46.5)		2.11	
<i>Gender</i>				
Male	15 (35.7)	.033*	2.62	.003*
Female	21 (60.0)		1.67	
<i>Marital status</i>				
Single or separated	0 (0.0)	.006*	3.04	.025*
Married	36 (52.2)		2.09	
<i>Level of education</i>				
Low (up to elementary)	27 (54.0)	.072	1.91	.014*
High (high school+)	8 (32.0)		2.80	
<i>Clinical data</i>				
<i>Type of stroke</i>				
Ischemic	21 (42.0)	.255	2.33	.291
Other	15 (55.6)		1.94	
<i>Time since stroke</i>				
≤ 1 year	26 (53.1)	.142	2.04	.166
>1 year	10 (35.7)		2.45	
<i>No. medications per day</i>				
<5	24 (51.1)	.343	2.28	.788
≥5	12 (40.0)		2.06	
<i>Tobacco use</i>				
Yes	4 (22.2)	.029*	2.82	.011*
No	32 (54.2)		2.00	
<i>Lifestyle</i>				
<i>Regular exercise</i>				
Yes	15 (60.0)	.106	1.93	.151
No	21 (40.4)		2.23	
<i>Healthy diet</i>				
Yes	27 (48.2)	.675	2.07	.285
No	9 (42.9)		2.53	
<i>Weight control</i>				
Yes	27 (50.0)	.382	2.07	.337
No	9 (39.1)		2.48	
<i>Knowledge level</i>				
<i>Risk of recurrence</i>				
Incorrect	15 (50.0)	.648	1.95	.312
Correct	21 (44.7)		2.35	
<i>Severity of second stroke</i>				
Incorrect	11 (45.8)	.913	2.02	.755
Correct	25 (47.2)		2.27	
<i>Prevention strategies identified</i>				
<3	8 (38.1)	.351	2.26	.614
3+	28 (50.0)		2.17	
<i>Source of knowledge</i>				
<i>Doctor</i>				
No	11 (40.7)	.437	2.42	.413
Yes	25 (50.0)		2.07	
<i>Family & Friends</i>				
No	22 (45.8)	.835	2.16	.925
Yes	14 (48.3)		2.25	
<i>Social media</i>				
No	25 (42.4)	.163	2.23	.294
Yes	11 (61.1)		2.06	

*statistically significant result; test used; ¹Chi square or Fisher's exact test, as appropriate; ²nonparametric tests (Mann-Whitney U or Kruskal-Wallis test, as appropriate)

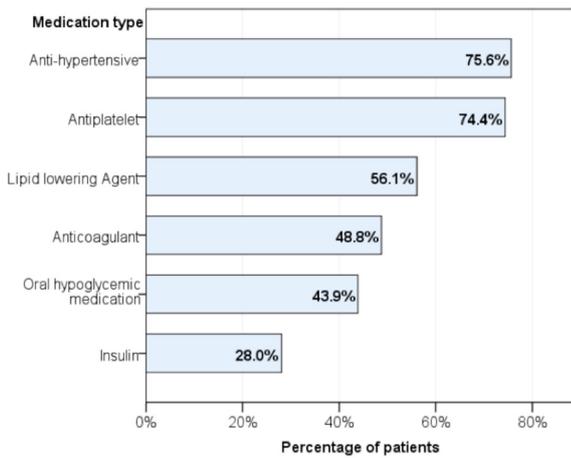


Figure 1 - Discharge prescribing pattern by medication type

to participate with their complete volunteering and without any suggestive emotional or mental pressure to participate. Respect and dignity were maintained during the interview, along with utmost confidentiality throughout and the entire research process. The study protocol was reviewed and approved by the ethical committee of PMAH.

Results. Socio demographic characteristics of patients. Of 156 patients who fulfilled eligibility criteria, 82 patients completed the question-naire (response rate=52.6%), while the remainders included those who refused to participate (13, 8.3%), were unresponsive (55, 35.3%) or deceased (6, 3.8%). Of the 82 participants, majority were elderly (56.1%), males (57.3%) and married (85.4%). Type and time of stroke showed majority of ischemic stroke (67.1%) that occurred recently (63.4%). Hypertension was the most prevalent risk factor (78.0%), followed by diabetes (58.5%) and hypercholesterolemia (57.3%), and 36.6% declared having 5 or more medications per day (Table 1). According to participants, discharge prescriptions included antihypertensive treatment (75.6%), antiplatelet (74.4%), and lipid lowering agents (56.1%), while anticoagulants were prescribed for only 48.8% of the patients (Figure 1). Subsequent to stroke episode, lifestyle was marked by low percentage of regular exercise (31.7%), whereas majority declared complying with a healthy diet (70.7%) and controlling their weight (68.3%). Further, 72.2% of smokers continued smoking after their stroke episode (Table 1).

Knowledge of patients regarding secondary strokes. Majority of the patients believed that history of stroke

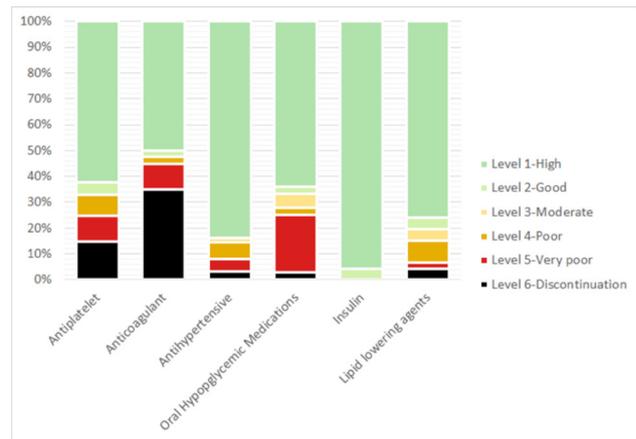


Figure 2 - Drug adherence level by different medication classes. Bar correspond to medication classes, and colored segments correspond to the percentage of patients with the respective drug adherence level, within the given medication class.

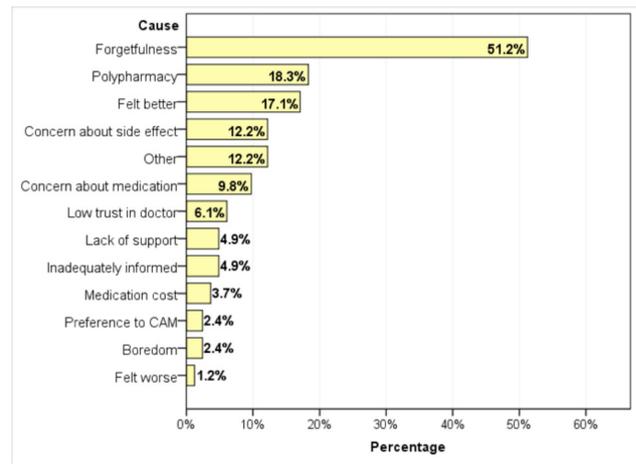


Figure 3 - Causes of non-adherence to post-stroke medications. Bars represent the percentage of patients who reported the given cause as a plausible motivation for nonadherence. CAM - Complementary and alternative medicine

exposes to higher risk of having a secondary episode (63.4%), while others believed the risk of recurrence was either similar to (35.4%) or lower (4.9%) than primary stroke among general population. Majority correctly stated that an eventual secondary stroke would results in worse outcome than the primary one (70.7%), while the remainders believed the outcomes would be similar (18.3%) or better (11.0%). Treating risk factors such as diabetes, hypertension, etc. (80.5%), keeping a healthy diet (65.9%) and regular exercise (63.4%) were the 3 most frequently identified strategies to prevent secondary stroke. On the other hand, majority failed to identify weight control and reduction

of avoidance of alcohol as preventive strategies. Doctors and hospital teams were the most common sources of survivors' information (62.2%) regarding secondary strokes, followed by family and friends (35.4%); while only 22% of the patients referred to social media and internet sources and 6.1% to mass media (Table 2).

Causes of non-adherence. The most frequently reported cause for non-adherence was forgetfulness (51.2%), followed by polypharmacy (18.3%) and patient-perceived improvement (17.1%) (Figure 3).

Level of adherence. Of the 82 participants, 5 had none of the 6 explored medications. Consequently, the following analysis will concern the remaining 77 ones. At the medication level, all 23 patients on insulin had adequate (high or good) drug adherence level (100%). Other medications showed relatively high drug adherence level for antihypertensive (83.9%), followed by LLD (80.4%); whereas adherence to antiplatelet and anticoagulants was 67.2% and 52.5%, respectively; and the 2 medications had the highest percentage of discontinuation (Table 3, Figure 2). At the patient level, adherence was high (35, 45.5%), good (1, 1.3%), moderate (2, 2.6%), poor (7, 8.5%), and very poor (11, 13.4%); while discontinuation was observed among 21 (25.6%) of the 77 patients (results not presented). Consequently, PAL was adequate among 46.8% of the patients (Table 3).

Factors associated with adherence. Adherence was higher among females, who had higher percentage of adequacy (60.0% versus 35.7%, $p=0.033$) and more favorable mean adherence score (1.67 versus 2.62, $p=0.003$) compared to males. Likewise, adherence rate was higher among married participants (52.2% versus 0.0%, $p=0.006$) with more favorable mean adherence score (2.09 versus 3.04, $p=0.025$), compared to their counterparts. Paradoxically, lower educational level (up to elementary school) was associated with better adherence including adequacy rate (54.0% versus 32.0%) and mean adherence score (1.91 versus 2.80), compared to counterparts, respectively; however, the difference was only significant for mean adherence ($p=0.014$). It is worth noting that participants with recent stroke (≤ 1 year) had higher adequacy rate (53.1%) compared to their counter-parts (35.7%), however, the result was not statistically significant ($p=0.142$). On the other hand, tobacco users had lower adherence both using adequacy rate (22.2% versus 54.2%, $p=0.029$) and mean adherence score (2.00 versus 2.82, $p=0.011$), compared to nonsmokers, respectively. No significant association was found between adherence level and knowledge level, source of knowledge or lifestyle factors (Table 4).

Predictors of inadequate adherence. A multivariate binary regression model was carried out to analyze gender, education level and smoking status as independent factors of inadequate adherence, the dependent variable. Results showed

higher risk of non-adherence among active smokers (OR=4.28 [95% CI=0.99, 18.41]) with nearly significant level ($p=0.051$); while male (OR=1.74 [95% CI=0.60, 5.03], $p=0.309$) and high educational level (2.14 [0.72, 6.31], $p=0.170$) were out of range of statistical significance (Results are not presented).

Discussion. Summary of findings. The present study focused on the post stroke phase of 82 stroke survivors, by exploring their level of knowledge and awareness about secondary stroke prevention as well as their level of adherence to post stroke medication and preventive strategies. It also investigated barriers to adherence and analyzed sociodemographic and clinical factors and predictors of nonadherence, in addition to the association of knowledge with adherence level. Findings showed relatively low knowledge regarding the risk and severity of secondary stroke, with inconsistent awareness about the different preventive strategies; along with inadequate adherence to prescribed medications among more than half of the concerned patients. Specific adherence varied by type of medication, and overall adherence was better among females, married and nonsmokers, while it was not associated with knowledge level not predicted by any of the explored factors. Forgetfulness, polypharmacy and perceived improvement: the 3 major barriers to adherence.

Knowledge and awareness about secondary stroke and preventive strategies. Intuitively, awareness and knowledge of stroke patients has a strong implication in reducing the risk of recurrent events. A considerable proportion of patients in the present study correctly perceived the increased risk of having a recurrent stroke after an index event (63.4%), and that such event would have worse outcomes than the primary one (70.7%). Previous studies indicated the importance of considering secondary preventive approaches in older adults with a history of stroke, particularly IS, since experiencing an initial event would be a strong predictor of further events.¹⁸⁻²¹ Besides, recurrent stroke can cause significant morbidity, as indicated by stroke-related hospitalization or admission to complex continuing care, disability, cognitive decline, and dementia and increases the risk of mortality up to 5 years after stroke.^{21,22}

However, the perceived risks of subsequent events as well as the worse outcomes of secondary stroke were rarely investigated previously among stroke survivors. Only 23% and 40% of stroke patients identified the

increased likelihood of having a secondary event in Scotland²³ and Namibia,¹⁵ respectively. Instead, most of the conducted cross-sectional studies were concerned with the assessment of knowledge regarding risk factors of stroke in general. A systematic review of 18 studies (8147 patients) showed limited knowledge and low awareness levels about stroke risk factors, and about 22-33% only were able to describe at least three risk factors.²⁴ Simultaneously, stroke survivors could not recognize stroke symptoms despite their previous experience, and had low awareness about their risk for a secondary stroke. Such unawareness may decrease patients' engagement in the preventive measures against secondary stroke. Contrasting with our findings, studies employing surveys with open-ended questions indicated low rates of knowledge.^{24,25} Nonetheless, the use of closed-ended questions in the present study might have overestimated the real knowledge levels in some domains.

Doctors and other healthcare providers were the major source of information about stroke and its preventive strategies (in 62.2% of patients), in the present study. Healthcare professional have also been the main sources of knowledge in more than 75% of patients in a study conducted in Thailand.²⁵ However, knowledge about stroke did not reach satisfactory levels in our study and other studies. This may indicate that information or the method of providing information may be inadequate to raise knowledge to the adequate levels. The methods of communication and/or barriers of perception may account for these observations. In Saudi Arabia, there is a significant cultural diversity of healthcare providers, which could be a major determinant of communication. Hence, the process of sharing useful information and promoting behavioral and lifestyle changes among stroke patients may be impaired, which would be reflected in low compliance to such changes and inadequate adherence levels to medication-based preventive strategies.

Adherence to post stroke medications and other preventive strategies. In the present analysis, several factors were associated with adherence. Females were significantly more adherent to treatment than males, and this was also evident in other studies.^{26,27} This might emerge from their higher knowledge levels regarding the risk factors of stroke and cardiovascular diseases in general, which have been shown in earlier local and international investigations.²⁸⁻³⁰ Females, who usually hold the caring role, seem to be more knowledgeable about treatment, and they have an increased interest in gaining knowledge from different sources, a matter which supports their compliance with preventive strategies. Additionally, being married was another

factor significantly associated with compliance. Other studies reported the significant impact of the marital status on adherence to oral anticoagulant medications to reduce the risk of recurrent stroke.^{31,32} Caregiver support is an important element in such circumstances, where the patient may be regularly reminded by his/her partner. Conversely, living alone and the lack of family support have been associated with lower compliance in several investigations.^{26,33}

Surprisingly, lower educational level was associated with improved adherence among in the present study. Other studies showed contrasting outcomes, such as in Nigeria, where stroke survivors with a tertiary educational level were 48 time more likely to be knowledgeable about stroke and more compliant to treatment than those with lower education.³⁴ This was in agreement with other large cohort-sized surveys relying on open-ended questions in Norway and China.^{35,36} However, Saengsuwan et al.²⁵ failed to reveal a significant impact of education on stroke knowledge and adherence to post-stroke therapies, possibly due to the small sample size (140 patients). The association between higher adherence and low educational levels in our study may be related to the increased trust in doctors' advice by low-educated patients, which has been consistently reported in patients with hypercholesterolemia.^{37,38}

Other factors associated with improved adherence were repeatedly reported in the literature; however, these factors were not significant in our study. For example, there is an evidence indicating that elderly patients are generally more compliant, while younger stroke patients often forget some doses.^{27,39} Furthermore, several studies showed an inverse relationship between time since stroke and compliance, and this was supported by providing a severe medical care to manage chronic stroke patients.^{26,27,40} Although results from our study suggest higher adherence rates (53.1% versus 35.7%) among patients with a recent episode (≤ 1 year) as compared to those with a former one (> 1 year), respectively, this difference did not reach statistical significance. It is worth noting that failure to demonstrate the significant association of adherence with these factors, in our study, is probably due to the small sample size inducing significant type II error.

Barriers to adherence. On the other hand, we evidenced a number of barriers to adherence. Non-adherence is classified into intentional (patients' decision to stop treatment or take it in a different way than prescribed) or unintentional (due to forgetting or physical disability).¹⁴ Forgetfulness was the most frequent barrier in the present study. Jamison et al.⁴¹ and Chambers et al.⁴² have also emphasized such a problem,

which may be attributed to cognitive impairments implied in stroke patients. Increased number of co-prescribed medications (polypharmacy) and perceived improvements were other significant factors of reduced adherence.⁴³ Specific medication management strategies can help overcome these barriers. These include the use of ergonomic storage devices, such as medication wallets and pillboxes. Moreover, it is possible to create distinct daily activities or routines, which could be linked to taking medications or placing the medication in a cue location that make it easier to routinely receive the medication.⁴¹ Besides, caregivers could be targeted by suitable educational programs to remind patients and to ensure their adherence.

Smoking: a potentially strong predictor of nonadherence. Finally, smoking was a notable factor of adherence and could represent the major predictor of nonadherence in our analysis, by setting the statistical significance to a higher level (e.g. $p < 0.06$). Comparably, cigarette smokers were less persistent to their therapies at one year after stroke in European studies.^{44,45} Therefore, smokers should receive more intensified educational interventions regarding the risks of nonadherence and its relation with secondary stroke.

Education and life after stroke. Based on the aforementioned findings, structured and systematic education appears to be imperative among stroke survivors to enhance their protective behaviors and reduce the risk of recurrence. It should be emphasized that education does not stop at providing the useful information to improve knowledge, but should involve further interventions with broader aims. Inefficacy of knowledge alone may be supported by the lack of association between levels of adherence and knowledge about secondary stroke and preventive strategies in our study. Therefore, education should involve effective and practical actions that improve patient's and or caregiver's proficiency in the management of post stroke care issues including comorbidities, other risk factors, and lifestyle changes. Ovbiagele et al.⁴⁶ have implemented a specialized in-hospital program comprising of 8 measures to ensure adherence, including 4 medication-related (initiating a statin, an antithrombotic, a thiazide diuretic, and an angiotensin-converting enzyme inhibitor) and 4 behavioral-targeting measures (improving stroke awareness diet and exercise counselling and smoking cessation interventions). Ultimately, this led to a significant improvement in the adherence rate and enhanced knowledge about stroke symptomatology and risk factors. Besides, a sustained engagement is warranted on both patient's and care

providers' sides, along with a proactive relationship to ensure the most favorable outcomes and the best quality of life after stroke.

Limitations. The major limitation for this study is the small sample size, probably inducing significant type II error, which hindered the significance of inferential analysis notably the predictors of nonadherence and limits the generalizability of the results. The other significant limitation is the use of a subjective tool to evaluate patients' adherence, which is subject to both recall bias and response bias, which may result in inaccurate and or obliging answers thereby overestimating adherence. Further, the study failed to probe into the level of patient's autonomy and eventual caregiver's factor, which may have impacted adherence. Other factors were not explored, such as the effects of patients' beliefs about medication and treatment and the psychological determinants of adherence (depression, anxiety, etc.). In addition, causes of treatment discontinuation were not explored, as this may be related to physician's recommendation. Finally, the exclusive dependence on close-ended questions may have overestimated the levels of knowledge and consequently its association with adherence.

Conclusion. Knowledge about the risk and severity of recurrent stroke was relatively adequate among stroke survivors in the present study; this was predominantly acquired from healthcare professionals. Concurrently, patients had low awareness about the adequate preventive lifestyle and medication-based strategies, and more than half of them showed inadequate adherence to the prescribed medications. On the other hand, adherence to discharge prescriptions was low, indicating a gap between knowledge and adherence that should be explored and tackled. The facilitators of adherence included the female gender, being married, and a low educational level, whereas the smoking constituted a major factor of nonadherence.

Stroke survivors and their caregivers should be educated not only about knowledge of the risk factors of recurrence, but also the effective self-management of all the health and care issues. The use of reminders and assistive devices should be encouraged to tackle forgetfulness, the major cause of nonadherence. Targeted programs should include healthcare professionals, patients, and caregivers. Doctor orienting programs could be tailored to enhance their capacity to educate patients, considering the cultural diversity of doctors in Saudi Arabia, since they are the major sources of information to patients. The education and

management strategies of stroke survivors should enable raising the patients' and care providers' expectations and promoting a paradigm shift from "life after stroke" to "quality of life after stroke".

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References

- Radak D, Katsiki N, Resanovic I, Jovanovic A, Sudar-Milovanovic E, Zafirovic S, et al. Apoptosis and Acute Brain Ischemia in Ischemic Stroke. *Curr Vasc Pharmacol* 2017; 15: 115-122.
- Writing Group Members, Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, et al. Heart Disease and Stroke Statistics-2016 Update: A Report From the American Heart Association. *Circulation* 2016; 133: e38-e360.
- GBD Stroke Collaborators. Global, regional, and national burden of stroke, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2019; 18: 439-458.
- Gorelick PB. The global burden of stroke: persistent and disabling. *Lancet Neurol* 2019; 18: 417-418.
- Almekhlafi MA. Trends in one-year mortality for stroke in a tertiary academic center in Saudi Arabia: a 5-year retrospective analysis. *Ann Saudi Med* 2016; 36: 197-202.
- Alanazy MH, Barakeh RB, Asiri A, Edrees MF, Abuzinadah AR, Aljafen BN, et al. Practice Patterns and Barriers for Intravenous Thrombolysis: A Survey of Neurologists in Saudi Arabia. *Neurol Res Int* 2018; 2018: 1695014-.
- Al-Senani F, Al-Johani M, Salawati M, ElSheikh S, AlQahtani M, Muthana J, et al. A national economic and clinical model for ischemic stroke care development in Saudi Arabia: A call for change. *Int J Stroke* 2019; 14: 835-842.
- Zheng S, Yao B. Impact of risk factors for recurrence after the first ischemic stroke in adults: A systematic review and meta-analysis. *J Clin Neurosci* 2019; 60: 24-30.
- Mohan KM, Wolfe CDA, Rudd AG, Heuschmann PU, Kolominsky-Rabas PL, Grieve AP. Risk and cumulative risk of stroke recurrence: a systematic review and meta-analysis. *Stroke* 2011; 42: 1489-1494.
- Krishnan S, Pappadis MR, Weller SC, Stearnes M, Kumar A, Ottenbacher KJ, et al. Needs of Stroke Survivors as Perceived by Their Caregivers: A Scoping Review. *Am J Phys Med Rehabil* 2017; 96: 487-505.
- Spence JD. Recent advances in preventing stroke recurrence. *F1000Res* 2017; 6: 1017.
- Hackam DG, Spence JD. Combining multiple approaches for the secondary prevention of vascular events after stroke: a quantitative modeling study. *Stroke* 2007; 38: 1881-1885.
- Lehane E, McCarthy G. Medication non-adherence--exploring the conceptual mire. *Int J Nurs Pract* 2009; 15: 25-31.
- Chapman B, Bogle V. Adherence to medication and self-management in stroke patients. *Br J Nurs* 2014; 23: 158-166.
- Peter J, Justus AH. Knowledge and Practices of Stroke Survivors Regarding Secondary Stroke Prevention, Khomas Region, Namibia. *Journal of Medical Biomedical and Applied Sciences* 2016; 3.
- Sappok T, Faulstich A, Stuckert E, Kruck H, Marx P, Koennecke HC. Compliance with secondary prevention of ischemic stroke: a prospective evaluation. *Stroke* 2001; 32: 1884-1889.
- Sidorkiewicz S, Tran VT, Cousyn C, Perrodeau E, Ravaud P. Development and validation of an instrument to assess treatment adherence for each individual drug taken by a patient. *BMJ Open* 2016; 6: e010510.
- Coull AJ, Lovett JK, Rothwell PM, Oxford Vascular S. Population based study of early risk of stroke after transient ischaemic attack or minor stroke: implications for public education and organisation of services. *BMJ* 2004; 328: 326.
- Clark TG, Murphy MFG, Rothwell PM. Long term risks of stroke, myocardial infarction, and vascular death in "low risk" patients with a non-recent transient ischaemic attack. *J Neurol Neurosurg Psychiatry* 2003; 74: 577-580.
- van Wijk I, Kappelle LJ, van Gijn J, Koudstaal PJ, Franke CL, Vermeulen M, et al. Long-term survival and vascular event risk after transient ischaemic attack or minor ischaemic stroke: a cohort study. *Lancet* 2005; 365: 2098-2104.
- Edwards JD, Kapral MK, Fang J, Swartz RH. Long-term morbidity and mortality in patients without early complications after stroke or transient ischemic attack. *CMAJ* 2017; 189: E954-E61.
- Hardie K, Hankey GJ, Jamrozik K, Broadhurst RJ, Anderson C. Ten-year risk of first recurrent stroke and disability after first-ever stroke in the Perth Community Stroke Study. *Stroke* 2004; 35: 731-735.
- Wellwood I, Dennis MS, Warlow CP. Perceptions and knowledge of stroke among surviving patients with stroke and their carers. *Age Ageing* 1994; 23: 293-298.
- Ellis C, Barley J, Grubaugh A. Poststroke knowledge and symptom awareness: a global issue for secondary stroke prevention. *Cerebrovasc Dis* 2013; 35: 572-581.
- Saengsuwan J, Suangpho P, Tiamkao S. Knowledge of Stroke Risk Factors and Warning Signs in Patients with Recurrent Stroke or Recurrent Transient Ischaemic Attack in Thailand. *Neurol Res Int* 2017; 2017: 8215726.
- Sjölönder M, Eriksson M, Glader EL. The association between patients' beliefs about medicines and adherence to drug treatment after stroke: a cross-sectional questionnaire survey. *BMJ Open* 2013; 3: e003551.
- Cheiloudaki E, Alexopoulos EC. Adherence to Treatment in Stroke Patients. *Int J Environ Res Public Health* 2019; 16: 196.
- Kaddumukasa M, Kayima J, Kaddumukasa MN, Ddumba E, Mugenyi L, Pun-dik S, et al. Knowledge, attitudes and perceptions of stroke: a cross-sectional survey in rural and urban Uganda. *BMC Res Notes* 2015; 8: 819.
- Basfar W, Al-Sebyani A, Aljawi G, Milyani H, Jan M. Public Knowledge of Stroke Amongst a Saudi Population. *World Journal of Research and Review* 2016; 3: 10-12.
- Aljefree N, Ahmed F. Prevalence of cardiovascular disease and associated risk factors among adult population in the Gulf region: a systematic review. *Advances in Public Health* 2015; 2015.
- Luger S, Hohmann C, Niemann D, Kraft P, Gunreben I, Neumann-Haefelin T, et al. Adherence to oral anticoagulant therapy in secondary stroke prevention - impact of the novel oral anticoagulants. *Patient Prefer Adherence* 2015; 9: 1695-705.

32. Tulek Z, Dünya C, Çiftçiöğlü R, Dereci H. Determination of Factors that Impact Adherence to Warfarin in Patients with Stroke. *Turkish Journal Of Neurology* 2019; 25: 146-152.
33. Zhang H, Qian HZ, Meng SQ, Shu M, Gao YZ, Xu Y, et al. Psychological distress, social support and medication adherence in patients with ischemic stroke in the mainland of China. *J Huazhong Univ Sci Technol Med Sci* 2015; 35: 405-410.
34. Vincent-Onabajo G, Moses T. Knowledge of Stroke Risk Factors among Stroke Survivors in Nigeria. *Stroke Res Treat* 2016; 2016: 1902151.
35. Sundseth A, Faiz KW, Rønning OM, Thommessen B. Factors related to knowledge of stroke symptoms and risk factors in a norwegian stroke population. *J Stroke Cerebrovasc Dis* 2014; 23: 1849-1855.
36. Zeng Y, He GP, Yi GH, Huang YJ, Zhang QH, He LL. Knowledge of stroke warning signs and risk factors among patients with previous stroke or TIA in China. *J Clin Nurs* 2012; 21: 2886-2895.
37. Senior V, Marteau TM, Weinman J. Genetic Risk Assessment for FHTSG. Self-reported adherence to cholesterol-lowering medication in patients with familial hypercholesterolaemia: the role of illness perceptions. *Cardiovasc Drugs Ther* 2004; 18: 475-481.
38. Jin J, Sklar GE, Min Sen Oh V, Chuen Li S. Factors affecting therapeutic compliance: A review from the patient's perspective. *Ther Clin Risk Manag* 2008; 4: 269-286.
39. O'Carroll R, Whittaker J, Hamilton B, Johnston M, Sudlow C, Dennis M. Predictors of adherence to secondary preventive medication in stroke patients. *Ann Behav Med* 2011; 41: 383-390.
40. Glader EL, Sjölander M, Eriksson M, Lundberg M. Persistent use of second-ary preventive drugs declines rapidly during the first 2 years after stroke. *Stroke* 2010; 41: 397-401.
41. Jamison J, Sutton S, Mant J, De Simoni A. Barriers and facilitators to adherence to secondary stroke prevention medications after stroke: analysis of survivors and caregivers views from an online stroke forum. *BMJ Open* 2017; 7: e016814-e.
42. Chambers JA, O'Carroll RE, Hamilton B, Whittaker J, Johnston M, Sudlow C, et al. Adherence to medication in stroke survivors: a qualitative comparison of low and high adherers. *Br J Health Psychol* 2011; 16: 592-609.
43. Al AlShaikh S, Quinn T, Dunn W, Walters M, Dawson J. Predictive factors of non-adherence to secondary preventative medication after stroke or transient ischaemic attack: A systematic review and meta-analyses. *Eur Stroke J* 2016; 1: 65-75.
44. Lummis HL, Sketris IS, Gubitz GJ, Joffres MR, Flowerdew GJ. Medication persistence rates and factors associated with persistence in patients following stroke: a cohort study. *BMC Neurol* 2008; 8: 25.
45. Østergaard K, Madsen C, Liu ML, Bak S, Hallas J, Gaist D. Long-term use of antiplatelet drugs by patients with transient ischaemic attack. *Eur J Clin Pharmacol* 2014; 70: 241-248.
46. Ovbiagele B, Saver JL, Fredieu A, Suzuki S, Selco S, Rajajee V, et al. In-hospital initiation of secondary stroke prevention therapies yields high rates of adherence at follow-up. *Stroke* 2004; 35: 2879-83.

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