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TOAST classification and risk factors of ischemic stroke in Lebanon

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Objectives: Ischemic stroke is a common cause of morbidity and mortality especially in the increasingly older population. The variability in ischemic stroke subtypes and its risk factors across different populations suggest that more effort is needed to describe the stroke characteristics in order to develop a more tailored management for each population. We aim to describe the demographic characteristics, risk factors, and subtype distribution of subjects with ischemic stroke in the Lebanese population.

Materials and methods: We conducted a cross-sectional study based on chart review on patients with ischemic stroke/transient ischemic attack at the American University of Beirut Medical center between 2015 and 2017. Results: A total of 284 cases were included with a mean age of 72 years, and 58% male gender. The most commonly identified risk factors were hypertension (77%), dyslipidemia (62%), and diabetes mellitus (42%), while atrial fibrillation was only found in 27% of cases. The cohort distribution according to TOAST classification was as follows: 15% large artery stroke, 31% cardioembolic stroke, 17% small artery stroke, 10% stroke of other determined causes, and 27% stroke of unknown cause.

Conclusion: This is the first study to address ischemic stroke characteristics in Lebanon.

KEYWORDS
ischemic stroke, stroke in Lebanon, stroke risk, TOAST classification, transient ischemic attack

1 | INTRODUCTION

Stroke is the second most common cause of mortality and the third most common cause of disability globally. Stroke prevalence is increasing among populations mainly in the low/middle-income countries with the ischemic stroke rates being more prevalent than that of hemorrhagic. Specifically, in the Middle East-North Africa region, the prevalence of ischemic stroke was 85% of all stroke types with large-vessel stroke being the most common subtype.[1] In Lebanon as of 2010, the incidence of ischemic stroke was 131.63 (87.60-187.30), with mortality rates of 29.28 (22.42-35.33) per 100 000 person-years.[2,3]

Ischemic stroke can be preventable if the population modifiable risk factors can be addressed appropriately. Studies from different populations showed regional variabilities concerning the distribution of stroke subtypes and prevalence their risk factors.[4-17] Various scores have been developed to help clinicians predict the risk of stroke occurrence in order to promote primary and secondary stroke prevention. CHA^2DS^2-VASc score is used to stratify the risk of developing ischemic stroke in atrial fibrillation.[18] The Framingham stroke score is a validated tool used to predict the 5-year risk of developing a stroke,[19] while the $ABCD^2$ score is validated to predict the risk of stroke after a TIA.[20]

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1.1 | Hypothesis

In the Middle East and specifically in Lebanon, data on the demographics, phenomenology, and the risk factors of ischemic stroke are scarce. The knowledge of the baseline characteristics of patients who were diagnosed with ischemic stroke and a more comprehensive assessment of the potential risk factors may lead to a better understanding and more tailored management of ischemic stroke in this population. Our aim is to explore the characteristics of patients with ischemic stroke in Lebanon.

2 | METHODS

This study is based on patients admitted to the American University of Beirut Medical Center, a large hospital in Beirut, Lebanon between January 1, 2015, and December 31, 2017. This tertiary, university-based private hospital is located in Beirut and considered the main referral center for the greater Beirut area and the country overall. The study was approved by the Institutional Review Board of the American University of Beirut (IRB ID: BIO-2018-0087). As per IRB, subjects were not offered to provide informed consents since the research was based solely on chart review. Patients' characteristics and data were retrieved from chart reviews conducted in 2018-2019. Patients were included in this study if they were aged ≥18 years at the time of admission and received an ischemic stroke or TIA diagnosis during their hospital stay at the American University of Beirut Medical Center between January 1, 2015, and December 31, 2017.

Ischemic stroke was defined as acute onset of neurological deficit of vascular cause with the presence of acute infarction on brain imaging explaining the symptoms. TIA was defined as acute onset of neurological deficit lasting <24 hours of vascular cause with no evidence of an infarct on brain imaging or other causes. Exclusion criteria were minimal and concerned having all criteria for stroke sub-typing. Therefore, patients with no brain imaging (MR or CT) done at the time of onset of symptoms and patients with no echocardiographic imaging within 3-month period from admission were excluded from the study. Each stroke case was categorized according to TOAST (Trial of Org 10172 in Acute Stroke Treatment) stroke subtype classification[21] which defines five groups: large artery stroke (LAS), cardioembolic stroke (CES), small artery stroke (SAS), stroke of other determined cause (SODC), and stroke of undetermined cause (SUC). The latter group included all stroke cases with two or more determined causes and cases with undetermined causes. Data concerning patients' demographics and risk factors (including medical and drug history), in addition to brain imaging, echocardiography, carotid Doppler, and 24 hr-Holter-ECG results, were collected from patients' chart reviews. Risk factors were defined as following: hypertension (HTN)—documented history of high blood pressure (systolic ≥140 and/or diastolic ≥90) on two separate occasions or being treated on anti-hypertensive medication(s); diabetes mellitus (DM)—elevated glycated hemoglobin on one occasion, or being on anti-diabetic medication(s); dyslipidemia (DL)—documented high levels of serum cholesterol of any of its components, or being on a drug for hyperlipidemia; coronary artery disease (CAD)—at least 1 vessel with >50% stenosis by either cardiac catheterization or coronary artery CT, or prior history of myocardial infarction and/or cardiac stent placement or coronary artery bypass graft surgery; heart failure (HF)—echocardiographic documentation of left ventricular ejection fraction <50%; chronic kidney disease (CKD)—documented decreased glomerular filtration rate <60 mL/minute/1.73 m^2 for at least 3 months; and smoking status including both cigarette and hubble-bubble smoking. Risk scores (including CHA_2DS_2VASc, Framingham stroke score, and $ABCD^2$ score) were computed. CHA_2DS_2VASc and $ABCD^2$ scores were categorized to three groups each according (0, 1, >1 and 0-3, 4-5, 6-7, respectively), while Framingham stroke scores were categorized to four groups (0-9, 10-14, 15-20, >20).

TABLE 1 Characteristics of stroke patients admitted to the American University of Beirut Medical Center between 2015 and 2017 (n = 284)

	n (%)
Gender (Male)	166 (58)
Race	
Middle Eastern	282 (99)
Caucasian	2 (1)
Nationality	
Lebanese	254 (89)
Others	30 (11)
Concomitant risk factors	
Hypertension (Yes)	218 (77)
Diabetes mellitus (Yes)	119 (42)
Dyslipidemia (Yes)	177 (62)
Coronary artery disease (Yes)	79 (28)
Heart failure (Yes)	43 (15)
Atrial fibrillation (Yes)	77 (27)
Chronic kidney disease (Yes)	44 (15)
Smoking status (Yes)	85 (30)

TABLE 2 Ischemic stroke characteristics (N = 284)

	n (%)
Ischemic stroke vs TIA	
Ischemic stroke	272 (96)
TIA	12 (4)
Stroke occurrence	
First stroke	226 (80)
Recurrent stroke	58 (20)
TOAST classification	
Large artery stroke	43 (15)
Cardioembolic stroke	88 (31)
Small artery stroke	48 (17)
Stroke of other determined cause	29 (10)
Stroke of undetermined cause	76 (27)

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TABLE 3 Distribution of socio-demographics, concomitant conditions, and risk factors according to TOAST categories

		TOAST classification					
	Total (N = 284)	LAS (n = 43)	CES (n = 88)	SAS (n = 48)	SODC (n = 29)	SUC (n = 76)	
Demographics	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	*P*-value
Gender							
Male	166 (58)	24 (56)	48 (55)	37 (77)	14 (48)	43 (57)	.064
Female	118 (42)	19 (44)	40 (45)	11 (23)	15 (52)	33 (43)	
Nationality							
Lebanese	254 (89)	36 (84)	81 (92)	45 (94)	24 (83)	68 (89)	.350
Others	30 (11)	7 (16)	7 (8)	3 (6)	5 (17)	8 (11)	
Age (mean ± SD)	72 ± 14	72 ± 14	74 ± 13	74 ± 11	61 ± 17	72 ± 14	.000*
Hypertension							
Present	218 (77)	36 (84)	70 (80)	36 (75)	18 (62)	58 (76)	.272
Absent	66 (23)	7 (16)	18 (20)	12 (25)	11 (38)	18 (24)	
Diabetes mellitus							
Yes	119 (42)	18 (42)	37 (42)	22 (46)	9 (31)	33 (43)	.775
No	165 (58)	25 (58)	51 (58)	26 (54)	20 (69)	43 (57)	
Dyslipidemia							
Yes	177 (62)	31 (72)	55 (63)	34 (71)	10 (34)	47 (62)	.012**
No	107 (38)	12 (28)	33 (37)	14 (29)	19 (66)	29 (38)	
Coronary artery disease							
Yes	79 (28)	12 (28)	28 (32)	13 (27)	3 (10)	23 (30)	.253
No	205 (72)	31 (72)	60 (68)	35 (73)	26 (90)	53 (70)	
Heart failure							
Yes	43 (15)	8 (19)	19 (22)	2 (4)	0 (0)	14 (18)	.003*
No	241 (85)	35 (81)	69 (78)	46 (96)	29 (100)	62 (82)	
Chronic kidney disease							
Yes	44 (15)	6 (14)	13 (15)	7 (15)	3 (10)	15 (20)	.777
No	240 (85)	37 (86)	75 (85)	41 (85)	26 (90)	61 (80)	
Atrial fibrillation							
Yes	77 (27)	1 (2)	69 (78)	0 (0)	0 (0)	7 (9)	
No	207 (73)	42 (98)	19 (22)	48 (100)	29 (100)	69 (91)	.000*
Smoking status							
Ever smokers	85 (30)	13 (30)	20 (23)	12 (25)	10 (34)	30 (39)	.176
Non-smokers	199 (70)	30 (70)	68 (77)	36 (75)	19 (66)	46 (61)	

*P-value <.01.

**P-value <.05.

Descriptive statistics including mean, standard deviation, frequency, and percentage were computed for the subjects' socio-demographics, stroke concomitant conditions, and risk factors as well as ischemic stroke characteristics. Chi-square and Fisher's exact tests were used to describe the distribution of categorical subjects' socio-demographics (gender and nationality) and stroke concomitant conditions, risk factors, and risk estimator scores, across the five categories of TOAST classification. In addition, the distribution of the continuous variable "age" across the five categories of TOAST classification was examined using one-way ANOVA test. Statistical significance was considered at a P-value of <.05, and all analyses were conducted using $STATA_{14}$ software. The STROBE cross-sectional reporting guidelines were used to edit this manuscript.[22]

3 | RESULTS

The hospital chart screening revealed 375 cases of subjects discharged with a diagnosis of ischemic stroke over the three-year period. We excluded 91 cases due to the absence of brain imaging/echocardiography,

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TABLE 4 Distribution of stroke risk estimators scores according to TOAST classification (N = 284)

	LAS n (%)	CES n (%)	SAS n (%)	SODC n (%)	SUC n (%)	*P*-value
CHA_2DS_2VASc score						
0	1 (2)	5 (6)	4 (8)	6 (21)	4 (5)	.002*
1	3 (7)	3 (3)	1 (2)	6 (21)	7 (9)	
≥2	39 (91)	80 (91)	43 (90)	17 (58)	65 (86)	
$ABCD^2$ score						
0-3	0 (0)	8 (9)	1 (2)	8 (28)	7 (9)	.002*
4-5	17 (40)	27 (31)	26 (54)	10 (34)	29 (38)	
>5	26 (60)	53 (60)	21 (44)	11 (38)	40 (53)	
Framingham stroke score						
0-9	14 (32)	29 (33)	16 (33)	16 (55)	29 (38)	.503
10-14	15 (35)	32 (36)	21 (44)	6 (21)	24 (32)	
15-20	8 (19)	15 (17)	9 (19)	6 (21)	14 (18)	
>20	6 (14)	12 (14)	2 (4)	1 (3)	9 (12)	
	LAS	**CES**	**SAS**	**SODC**	**SUC**	***P*-value**
CHA_2DS_2VASc score (mean ± SD)	4.00 ± 1.93	4.26 ± 2.07	3.42 ± 1.70	2.34 ± 2.00	3.80 ± 2.03	.000*
$ABCD^2$ score (mean ± SD)	5.72 ± 0.96	5.48 ± 1.35	5.54 ± 1.09	4.72 ± 1.65	5.34 ± 1.44	.027**
Framingham stroke score (mean ± SD)	12.58 ± 6.73	12.80 ± 6.70	11.42 ± 5.57	9.28 ± 6.75	11.93 ± 6.12	.119

*P-value <.01.

**P-value <.05.

pediatric age, different diagnosis, or not being admitted to the center or transfer to another institution from the emergency settings. We therefore had 284 cases with complete data. The mean age of the patients was 72 years with a standard deviation (SD) of 14. Almost all patients (n = 282, 99%) were Middle Eastern, and 89% were Lebanese. Men constituted 58% of the patients (Tables 1, 3).

HTN was the most prevalent risk factor and was documented in 77% of the sample (Table 2), followed by DL, DM, and CAD in 62%, 42%, and 28% respectively. Atrial fibrillation was found in 27% of the cohort, while HF and CKD had an equal prevalence of 15% each. Only 30% of the cohort were ever smokers.

Almost all patients were diagnosed with ischemic stroke (96%) and only 4% had TIA; 20% of patients were admitted for are current ischemic stroke. The distribution of stroke subtypes according to TOAST classification was as follows: 15% LAS, 31% CES, 17% SAS, 10% SODC, and 27% SUC (Table 2).

The gender distribution across stroke subtypes (Table 3) was similar except for the SAS group which had the highest proportion of men: 77% (37/48) (*P*-.064). Mean age was different across subtypes with the SODC having a younger mean age (61 years) and all other subtypes which included older individuals (ranging between 72 and 74 years). Table 3 shows the distribution of concomitant conditions and risk factors according to TOAST categories. Most of the patients with DL and HF were in CES (55/177 and 19/43, respectively) and SUC (47/177 and 14/43, respectively) categories (*P*-.012 and .009, respectively), while almost all patients (69/77) with atrial fibrillation were in CES category (*P*-.00).

Table 4 shows the stroke risk estimator scores according to TOAST classification. A CHA_2DS_2VASc score of ≥2 was found in 244 out of 284 cases (86%) and was the most prevalent in the CES subtypes (80/88) followed by SUC (65/76) categories (*P*-.002; Figure 1). The rest of the cases were equally divided between 0 and 1 scores equally (20 each) with the highest number of cases with a 0 or 1 scores being in SODC category (12/29). A total of 151 cases scored >5 on $ABCD^2$ score, and most of these were in CES category (53/88). A total of 109 cases have an $ABCD^2$ of 4 or 5, and most of these were in SUC category (29/76). Only 24 cases had an $ABCD^2$ score of 3 or less, and most of these were in SODC category (8/29) (Figure 1B). Most cases had a low Framingham stroke score where 104 scored between 0 and 9, 98 scored between 10 and 14, and only 30 scored more than 20. Although there was no statistical significance, most of cases across all score groups were either in CES or SUC categories (Figure 1C).

4 | DISCUSSION

To our knowledge, this is the first study that addresses the baseline characteristics subtypes and risk factors of ischemic stroke in Lebanon. The proportion of males in our cohort (58%) was one of the highest and was comparable to that of Indonesian and Chinese cohorts (59%) in contrast to that of French (45%) and Japanese (48%) cohorts where the proportion of females were more prevalent.[4-7] The mean age in our cohort (72) was comparable to that of German (72.9), Auckland

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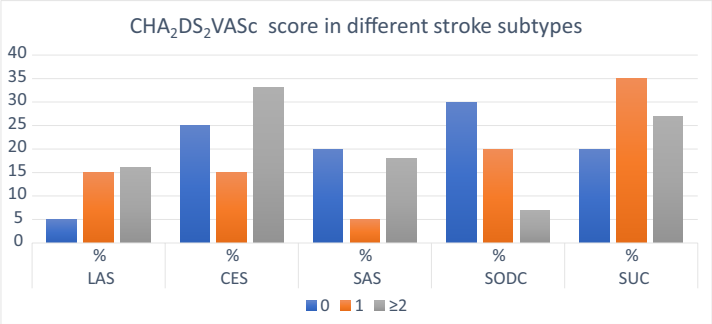
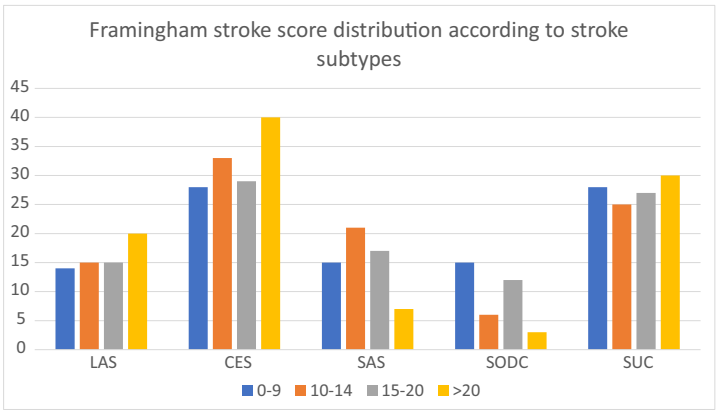
(A)

CHA_2DS_2VASc score	LAS %	CES %	SAS %	SODC %	SUC %
0	5	25	20	30	20
1	15	15	5	20	35
≥2	16	33	18	7	27



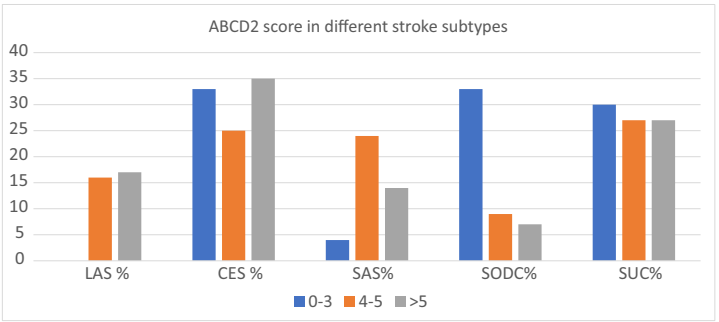
(B)

Framingham stroke score	LAS	CES	SAS	SODC	SUC	
0-9	14	28	15	15	28	0.503
10-14	15	33	21	6	25	
15-20	15	29	17	12	27	
>20	20	40	7	3	30	



(C)

$ABCD^2$ score	LAS %	CES %	SAS%	SODC%	SUC%
0-3	0	33	4	33	30
4-5	16	25	24	9	27
>5	17	35	14	7	27



LAS - Large artery stroke
CES - Cardioembolic stroke
SAS - Small atery stroke
SODC - Stroke of other determined cause
SUC - Stroke of undetermined cause

FIGURE 1 A, B and C CHA_2DS_2VASc, Framingham stroke score, and $ABCD^2$ scores in different stroke subtypes. LAS, Large artery stroke; CES, Cardioembolic stroke; SAS, Small artery stroke; SODC, Stroke of other determined cause; SUC, Stroke of undetermined cause

(71.8), French (74.2), North Dublin (72.2), and South London (71.4) cohorts, and was higher than that of Japanese (56.5), Indonesian (60.9), Iranian (64.1), and Pakistani (65.1) cohorts.[4-13] Concerning the most common risk factors, the prevalence of HTN in our cohort was one of the highest across cohorts (77%) and only being outnumbered by the Indonesian cohort (83%), as compared to other cohorts where it did not cross 66%. Our cohort had high rates of DM (42%) compared to other cohorts and was comparable to that of Pakistani cohort (38.6%).[13] Interestingly, rates of DL (62%) were higher than any of the cohorts where the rates varied between 15% and 51%.[4-17] As for AF, its prevalence was significantly variable across cohorts with that of Dublin cohort being higher (35%) than that of our cohort (27%), while cohorts from Iran (9.7%), China (15.6%), and Indonesia (2.6%) had significantly lower rate.[4,5,9,11] Taken together, the prevalence of the most common vascular risk factors (HTN, DM, DL, smoking) in our cohort was strikingly high compared to other cohorts from other countries.[4-17] Out of 184 subjects (63% of our cohort) with DL, only 122 (66%) were on treatment regimen. In the latter group (cohort with dyslipidemia on treatment), the mean total cholesterol level was 157 mg/dL, low-density lipoprotein level was 96 mg/dL, high-density lipoprotein level was 42 mg/dL, and triglyceride level was 150 mg/dL. The large proportion of subjects with untreated DL calls for more DL screening and vigilant treatment of those with elevated levels, especially that the study population shows an excellent response as evidenced by the mean serum cholesterol levels of treated subjects in this cohort. In patients with AF, only 31 (40%) were on anticoagulation, which suggests that the majority of patients either have undiagnosed or new-onset AF at the time of stroke. The prevalence of TIA in our cohort was 4%. This is lower than that of previous studies reporting the TIA prevalence of 9%[23] and 11%.[24]

The categorization of the stroke subtypes in our cohort differed from any other reported cohort. The proportion of CES subtype was the highest in our cohort (31%) as in Houston (38.7%) and Pakistani (40%) cohorts.[13,14] This can be explained by the relatively high rates

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of AF (27%) found in our cohort. SUC subtype was the second most prevalent in our cohort (27%), same as worldwide prevalence (26%) and that of Pakistani cohort (27%).[13,17] The high rate of SUC stroke subtype found in our cohort is related to the high prevalence of risk factors that cause large artery disease, small vessel disease, and cardioembolism. The relatively short Holter-ECG monitoring time (did not exceed >24 hours in most of the patients) used in our cohort to detect AF and other electrical heart abnormalities as a cause of ischemic stroke leads to higher rates of SUC subtypes. The proportion of SODC subtype was relatively high compared to other cohorts, and this could be due to the relatively high incidence of parental consanguinity leading to higher prevalence of strokes related to inherited conditions.[25]

In conclusion, this is the first study to address ischemic stroke subtypes, demographics, risk factors, and risk score estimators in Lebanon. In our stroke cohort, the mean age was 72 ± 14, with higher male prevalence and high rates of vascular risk factors where the rates of DL in our population surpassed the rates of all other cohorts. Overall, the relatively high rate of all of the risk factors along with AF influenced the stroke subtype distribution according to TOAST in our cohort with CES being the highest (31%) followed by SUC (27%). The study main limitations are its retrospective nature and being conducted in one center in an urban setting. This study and larger future multicenter studies of such kind should promote a more tailored primary and secondary preventive measures specific to this region.

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CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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