Analysis of Ischemic stroke risk factors in young Adults

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Abstract

Background and objectives: Keeping in mind stroke is the leading cause of disability globally, with increasing incidence of Ischemic stroke in young age reaching approximately more than 5-10 % according to multiple studies worldwide especially in developing countries.

Methods: This observational cross-sectional study was conducted at the Neurology Department of the Rizgary Hospital, Erbil, Iraq over 12 months from July 2020 until July 2021. We included consecutive patients whom their age was between 18-45 years with first-ever ischemic stroke fulfilling the definition of The American stroke association. All patients underwent thorough history and clinical examination. Each patient underwent routine stroke assessment, including full blood work up and vascular imaging.

Results: Out of 70 patients, 41 (58.8%) were males and 29 (41.4%) were females. There is a male predominance over females, which is comparable with other studies. Our present study showed that the most obvious risk factor for stroke in young people was hypertension, which was present in (38.6%) of cases followed by diabetes mellitus (20 %.), obesity (17.1%), smoking (17%), alcohol consumption (11.4%). Regarding stroke subtypes; small vessel disease, was the commonest, subtype, it was present in 25.7% of cases. A stroke from a cardiac source is the second most common (24.3%). About (17.1%) of cases were in the large vessel category. The cause of the stroke was undetermined in (14.5 %) percent of cases (cryptogenic).

Conclusion: Our study demonstrated that the traditional atherosclerotic risk factors such as hypertension, diabetes, dyslipidemia, and smoking are responsible for most cases in young adults.

Key words: Erbil city; Stroke; Young.

Introduction

Recently American Stroke Association (ASA) has revised the old definition of the ischemic stroke and made it more precise and understandable : "CNS infarction is brain, spinal cord, or retinal cell death attributable to ischemia, based on pathological, imaging, or other objective evidence of cerebral, spinal cord, or retinal focal ischemic injury in a defined vascular distribution; or clinical evidence of cerebral, spinal cord, or retinal focal ischemic injury based on symptoms persisting ≥24 hours or until death, and other etiologies excluded".[1] Ischemic Strokes in young age person is an event that happens between the ages of 18-45 years.[2] In spite of that, studies do not use an invariant cutoff, with lower age limits varying between 15 years and 18 years, and upper age limits of 45 years to 65 years.[3] Keeping in mind stroke is the leading cause of disability globally, with increasing incidence of ischemic stroke in young adults reaching approximately more than 5-10 % according to multiple studies worldwide especially in developing

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countries, [2, 4-12] showing elevated incidence up to 40% worldwide.[3, 6] A reasonable elucidation for this rising incidence includes better stroke identification owing to advanced neuroradiology techniques, [13, 14] elevated level of prevalence of traditional modifiable risk factors, [6, 9, 15, 16] rising level of illicit and recreational drug use.[17] Strokes in young adults are less prevalent than in the elderly, but they nonetheless have a significant influence on their lives and those of their families since they are the most productive members of society, particularly in developing nations. They also have negative psychosocial consequences after the stroke.[18] The main clinical challenge in management of a young adult with acute stroke is the identification of its cause.[14] Despite the ever-increasing number of young stroke patients, the risk factors and causes of stroke remain unknown in about one-third of all patients.[5, 19] This present study is aimed at delineating the most common risk factors and etiologies of stroke in a younger population to do risk stratification in this age group, detect high-risk patients earlier, prevent future events, and better lifestyle modification, because of the long-term and huge impact of the stroke on the quality of life and dysfunction on this group.[2, 6, 20]

Patients and Method

This observational cross-sectional study was conducted at the Neurology Department of the Rizgary Hospital, Erbil, Iraq over 12 months from July 2020 until July 2021. we included consecutive patients whom their age was between 18-45 years with first-ever ischemic stroke fulfilling the definition of The ASA.[1] who had an age-matched and gender-matched control group of 65 consecutive non stroke patients visited our outpatient department for diseases other than cerebrovascular or cardiovascular issues. Patients who have suffered a traumatic head injury, intracerebral hemorrhage, transient ischemic attack, spinal cord or retinal ischemia, or cerebral venous sinus thrombosis were excluded from this study.[5] All patients underwent focused history and clinical examination. The demographic profile of the patients was recorded, which included age, sex, and ethnicity. Detailed information was obtained about the risk factors of stroke in young people which include diabetes mellitus, hypertension, smoking, alcoholism, family history of stroke in first degree relatives, cardiac disease, and dyslipidemia, migraine, cancer, pregnancy, and postpartum etc. Each patient underwent routine stroke assessment, including body mass index (BMI),

Complete blood picture (CBC), blood sugar (BS) level (random and fasting), lipid profile, electrocardiogram (ECG), echocardiogram, and magnetic resonance imaging (MRI). Vascular imaging was performed for a good proportion of patients, including Doppler ultrasound of neck vessels, magnetic resonance imaging (MRA), magnetic resonance venography (MRV), and CT angiography. Holter monitor, trans-esophageal echocardiography, thrombophilia screens such as protein C and S levels, vasculitis screens, and lumbar puncture were done when routine investigations were unremarkable and when needed. The patient is labeled as hypertensive when two or more properly measured blood pressures are either systolic > 140 mmHg and or diastolic > 90.[21] Diabetes defined as random plasma glucose 200 mg with symptoms, fasting plasma glucose 126 mg/dl, or OGTT 2hour glucose in venous plasma 200 mg/dl or HBA1C 6.5% or more.[22] The patients were taken as dyslipidemic when LDL cholesterol > 130 mg/dl, serum cholesterol > 200 mg/dl, and HDL cholesterol levels were 35mg/dl in females and 40mg/dl in males, unless they were already taking lipid-lowering medications.[23] Smoking, heavy drinking, and illicit drug use were labeled as risk

factors as they were mentioned in the medical records. Obesity was defined as having a body mass index of 30 kg/m2. We used the TOAST classification system to classify our patients according to the mechanism of stroke and the etiology into cardio-embolic stroke, large vessel occlusion, small vessel disease, other determined and stroke of unknown etiology.[4, 5, 24] The ethics committee of Kurdistan Higher Council of Medical Specialties approved the study and all patients signed informed consent. Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 25). Chi square test of association was used to compare proportions. Fisher's exact test was used when the expected frequency (value) was less than 5 of more than 20% of the cells of the table. Student's t test of two independent samples (unpaired t test) was used to compare means of two samples. A p value of ≤ 0.05 was considered as statistically significant.

Results

Seventy (70) cases and seventy (70) controls were included in the study. The mean age (SD) of cases was 35.5 (7.2) years, and that of the controls was 35.3 (7.2) but the difference was not significant (p = 0.851) as presented in Table 1 that presents the age distribution and shows that 69.3% of the whole sample were aged ≥ 35 years but the differences were not significant (p = 0.817). The table shows also that 58.6% of the sample were males and the rest (41.4%) were females (p = 1.000) Table (1).

Table (1): Age and gender distribution of cases and controls.

	Case	Control	Total	
	No. (%)	No. (%)	No. (%)	p value
Age				
< 25	7 (10.0)	7 (10.0)	14 (10.0)	
25-34	13 (18.6)	16 (22.9)	29 (20.7)	
≥ 35	50 (71.4)	47 (67.1)	97 (69.3)	0.817*
Mean (SD)	35.5 (7.2)	35.3 (7.2)	35.4 (7.2)	(0.851)†
Gender				
Male	41 (58.6)	41 (58.6)	82 (58.6)	
Female	29 (41.4)	29 (41.4)	58 (41.4)	1.000*
Total	70 (100.0)	70 (100.0)		

*By Chi square test. †By unpaired t test.

Significantly (p < 0.001) higher rate of hypertension was detected among cases than the controls (38.6% vs 8.6%), and the same for diabetes (20% vs 4.3% respectively, p = 0.004). The proportion of CVSD was 10% of cases compared with 0% among the controls (p = 0.013). No significant differences were detected between cases and controls regarding family history of stroke (p = 1.000), cancer (p = 1.000), and migraine with aura (p = 0.496). It is evident in table 2 that 11.4% of the cases were alcoholics while none of the controls were alcoholics (p = 0.006). The rate of smoking among cases (24.3%) was significantly (p = 0.012) higher than the rate among the controls (11.4%). The table shows that 17.1% of the cases were obese, while none of the controls were obese (p < 0.001). No significant association was detected with atrial fibrillation (p = 0.245), and dyslipidemia (p = 0.115). The oral contraceptive pills (OCP) intake among cases was 34.5% compared with 7.7% among the controls (p = 0.016). No significant differences were detected between cases and controls regarding pregnancy and postpartum stroke (p = 1.000) as presented in Table (2).

Table (2): Risk factors of ischemic stroke in young adults:

	Case (n= 70)	Control (n = 70)	Total n = 140	
	No. (%)	No. (%)	No. (%)	p value
Hypertension	27 (38.6)	6 (8.6)	33 (23.6)	< 0.001**
Diabetes	14 (20.0)	3 (4.3)	17 (12.1)	0.004**
CVSD	7 (10.0)	0 (0.0)	7 (5.0)	0.013*
Family history of stroke	1 (1.4)	0 (0.0)	1 (0.7)	1.000*
Cancer	1 (1.4)	0 (0.0)	1 (0.7)	1.000*
Migraine with aura	2 (2.9)	0 (0.0)	2 (1.4)	0.496*
Alcoholism	8 (11.4)	0 (0.0)	8 (5.7)	0.006*
Smoking				
Smoker	17 (24.3)	8 (11.4)	25 (17.9)	
Non-smoker	49 (70.0)	62 (88.6)	111 (79.3)	
Ex-smoker	4 (5.7)	0 (0.0)	4 (2.9)	0.012*
Obesity (BMI $\geq$ 30 kg.m^2)	12 (17.1)	0 (0.0)	12 (8.6%)	< 0.001**
Atrial fibrillation	3 (4.3)	0 (0.0)	3 (2.1)	0.245 **
Dyslipidemia	21 (30.0)	13 (18.6)	34 (24.3)	0.115**
Women risk factors†				
OCP	10 (34.5)	2 (7.7)	12 (21.8)	0.016
Pregnancy	1 (3.4)	0 (0.0)	1 (1.9)	1.000*
Postpartum stroke	1 (3.4)	0 (0.0)	1 (1.9)	1.000*

*By Fisher's exact. **By Chi square test.

The other rare probable risk factors are listed in Table (3).

Table (3): Other determined risk factors among cases.

	No.	% (n = 70)
Leukemia	1	(1.4)
SLE	1	(1.4)
Antiphospholipid Ab syndrome	1	(1.4)
Factor V leiden mutation	0	(0.0)
Moyamoya disease	1	(1.4)
Antithrombin 3 deficiency	1	(1.4)
Protein C deficiency	1	(1.4)
Protein S deficiency	1	(1.4)
Methylene tetrahydrofolate reductase gene mutation (MTHFR)	1	(1.4)
Behcet's disease	2	(2.9)

The anterior circulation was involved in the majority (83%) of cases according to the imaging results, and the posterior circulation was involved in 20% of cases Figure (1).
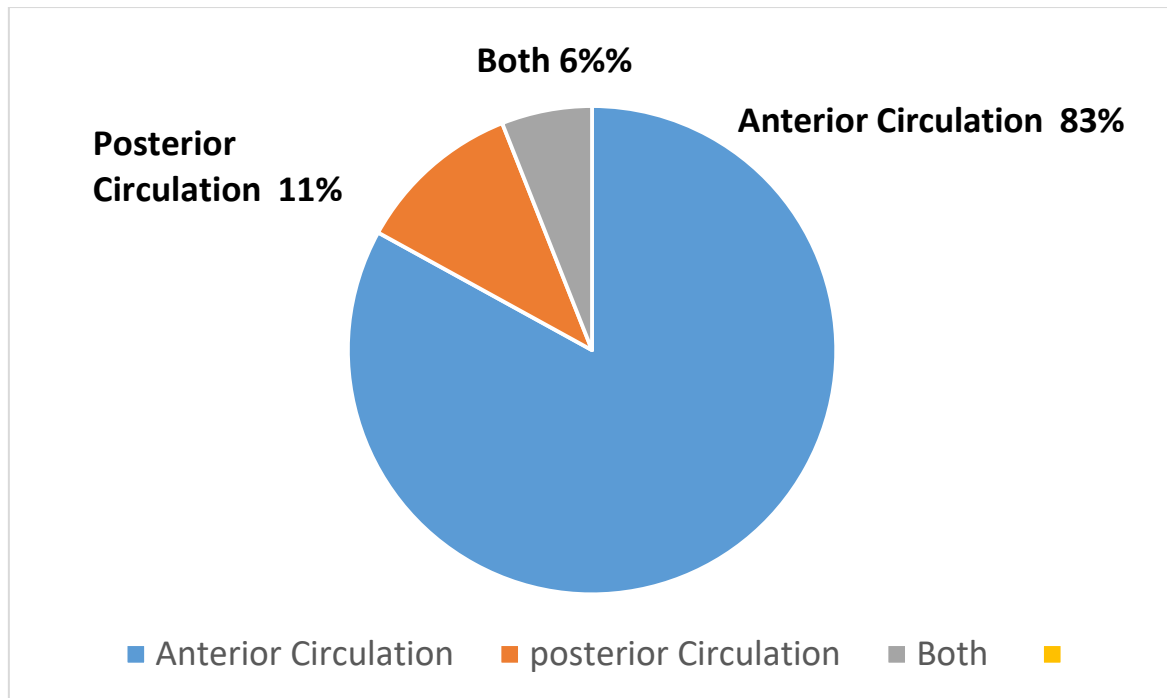
Figure (1): Location of infarction according to imaging.

The main modes of presentations of cases were hemiparesis (48.6%), hemiparesis and speech difficulty (17.1%), and speech difficulty (14.3%) in addition to other rarer findings, and those of the controls were shoulder pain (38.6%), benign positional vertigo (21.4%), paresthesia (21.4%), and neck pain (11.4%). The differences were significant between cases and controls (p < 0.001).

Table (4): Modes of presentations of ischemic stroke in young adults

	Case	Control	Total	
	No. (%)	No. (%)	No. (%)	p value
Speech difficulty	10 (14.3)	0 (0.0)	10 (7.1)	
Hemiparesis	34 (48.6)	0 (0.0)	34 (24.3)	
Hemiparesis + speech difficulty	12 (17.1)	0 (0.0)	12 (8.6)	
Vertigo	4 (5.7)	0 (0.0)	4 (2.9)	
Ataxia	4 (5.7)	0 (0.0)	4 (2.9)	
Seizure	2 (2.9)	0 (0.0)	2 (1.4)	< 0.001*
Loss of consciousness	3 (4.3)	0 (0.0)	3 (2.1)	
Shoulder pain	1 (1.4)	27 (38.6)	28 (20.0)	
Paresthesia	0 (0.0)	15 (21.4)	15 (10.7)	
Upper limb pain	0 (0.0)	5 (7.1)	5 (3.6)	
Neck pain	0 (0.0)	8 (11.4)	8 (5.7)	
Benign positional vertigo	0 (0.0)	15 (21.4)	15 (10.7)	
Total	70 (100.0)	70 (100.0)	140 (100.0)	

*By Fisher's exact test.

The main types of strokes according to TOAST criteria were small vessel disease (25.7%), and cardio-embolic stroke (24.3%), in addition to the other types, listed in Table (5).

Table (5): Types of strokes according TOAST criteria:

Types of strokes	No.	(%)
Cardio-embolic stroke	17	(24.3)
Large vessel occlusion	12	(17.1)
Small vessel disease	18	(25.7)
Other determined causes	13	(18.6)
Unknown cause (cryptogenic)	10	(14.3)
Total	70	(100.0)

Discussion

To our knowledge, this is the first study cared out in our locality about the analysis of risk factors and mechanisms of ischemic stroke in young adults. Out of 70 patients, 41 (58.8%) were males and 29 (41.4%) were females. There is a male predominance over females, which is comparable with other studies.[4, 6, 25] In contrast to the higher proportion of females among old age with ischemic stroke than young adults.[6] We attribute this male dominance to certain behavioral lifestyles that males indulge in more than females, such as smoking and alcohol drinking.[26] Our present study showed that the most obvious risk factor for stroke in young people was hypertension, which was present in 38.6% of cases compared to 8.6% of controls, that is the same as most of the studies.[4, 25, 27] In this present study about 20% of patients had diabetes mellitus as a risk factor for stroke which is nearly the same as Tan et al study,[4] but lower than Kapoor et al.[25] Smoking is a leading cause of ischemic stroke.[4, 28, 29] we found that there statistically significant relationship with smoking as the study of Tan et al.[4] In concordance with our study which showed that alcohol consumption accounted for stroke in 11.4% of cases in alcoholic drinkers. Bevan et al. show the same significant association[30]. As a Finnish study showed that alcohol is a common causative factor in the development of strokes.[31] so it is an important risk factor to take into account. Dyslipidemia is a risk factor for premature atherosclerosis,[32] but it didn't contribute significantly to stroke in our patients, in contrast to a study that was performed by

Kapoor et al. dyslipidemia was present in 37.5% of their cases. It's a well-known fact that obesity contributes to atherosclerosis and stroke.[33] Our study showed that obesity present significantly in cases in comparison to controls (17.1 % vs 8.6 %) p value (< 0.001), as in study by Mitchell et al.[34] Atrial fibrillation, migraine with aura, Family history of stroke, cancer, and were responsible for (4.3%), (2.9%), (1.4%) and (1.4%) respectively, but statistically not significant, this could be contributed to the small sample size. Behcet's disease is one of the rare causes of arterial ischemic stroke[35.] Two of our patients (2.9%) had Behcet's disease. Regarding stroke subtypes small vessel disease, was the commonest it present in 25.7% of cases, partially explained by the fact that a large number of our patients were older than 36 years; they are more liable for small vessel disease than younger ages, while Tan et al. showed that 29.8% had large vessel occlusion (LVO), responsible for the majority of strokes in their reports.[4] A stroke from a cardiac source is the second most common (24.3%), worldwide the incidence of cardio-embolic stroke in young adults ranges from 14% to 47%[36]. In those patients with cardio-embolic source atrial fibrillation was the most common responsible cause the same as the report by done by Schneider et al.[37] About (17.1%) of cases were in the large vessel category nearly the same as some studies (37) (38). Other known causes, such as SLE, antiphospholipid antibody syndrome, Oral contraceptive use, cancer, and moyamoya disease, accounted for 18.6%

of the cases. Combined OCP has been mentioned as a cause of ischemic stroke in young adults (39), In our study, there was a link between cerebral infarction and combined oral contraceptive use, which accounted for 34.5% vs. 21.8% of the controls. but statistically, it has not reached significant value. The cause of the stroke was unknown in (14.5 %) percent of cases (cryptogenic) which is less than that of the report done by Tan et al. (20.7%)(4). It is probably explained by the fact that a good proportion of our patients were aged between 40 to 45 years, as they share the same traditional atherosclerotic risk factors as the elderly population. As the study that conducted by Chraa M et al[40] and Razzaq et al. [41] our study shows that the main clinical presentation was hemiparesis. According to the topographical and radiological distribution of cerebral infarction, anterior circulation represented (83%), posterior circulation (11%), and both anterior and posterior circulation (6%). which was consistent with a study conducted by Dash et al.[42] There were several limitations in our study including the short period of the study, small sample size, single center based nevertheless the strong point was that our data has been collected from the largest stroke center in our city which represented the most of stroke cases in young adults.

Conclusions

Cerebral infarction is regarded as a serious problem in young adults. Our study demonstrated that the traditional atherosclerotic risk factors such as hypertension, diabetes, dyslipidemia, and smoking are responsible for most cases in young adults. Fortunately, most of these factors are modifiable and preventable to some extent. Hence, we need to develop some strategies to know how to early recognize and better manage of the risk factors, to prevent stroke in this age groups as this have great impact on the quality of life and functional disability on them.

Conflicts of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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