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Original article

Frequency and pattern of deranged lipid profile in patients with ischemic stroke: a retrospective study

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Abstract *Background and aim:* Ischemic Stroke has been recognized as the principal cause of disability and the third leading cause of mortality worldwide. The aim of this study was to determine the frequency and pattern of dyslipidemia in patients presenting with ischemic stroke at a tertiary care hospital in Karachi, Pakistan and to evaluate the effect of demographic and clinical factors on the frequency and pattern of dyslipidemia in ischemic stroke subjects. *Methods:* A cross-sectional study carried on a sample size of 235 patients presenting to the out-patient clinic with paralysis, difficulty in speech, and/or loss of consciousness lasting for one hour or more. Blood samples were analyzed for total cholesterol (TC), triglycerides (TG), low-density lipoproteins (LDL), very low-density lipoproteins (VLDL) and high-density lipoproteins (HDL) by the enzymatic colorimetric methodology. These values were recorded on the pre-defined proforma by the investigators. All analysis was performed using SPSS version 23.0. *Results:* The average age of the patients was 50.84±11.51 years and 62.1% of them were males. The frequency of dyslipidemia was observed in more than half (n=134/235, 57.02%) of ischemic stroke patients. Regarding the dyslipidemia pattern, TC, VLDL-C and TG levels were deranged in more than 50% of the cases. The most commonly deranged values were of TC and VLDL-C, followed by TG levels. It was observed that patients with a previous history of DM (73.9%, p=0.002) and HTN (81.3%, p=0.001) had significantly higher rates of deranged lipid profiles. Lipid values were found to be more deranged in patients aged 41-50 years (p=0.002) however, no statistically significant differences were observed with respect to BMI (p=0.192) and symptoms duration (p=0.334). *Conclusions*: Dyslipidemia is an important risk factor for ischemic stroke, and elevated LDL-C is usually the lipid fraction implicated in the pathologic mechanism of stroke. (www.actabiomedica.it)

Key words: Cerebrovascular accident, CVA, stroke, dyslipidemia, triglyceride, TG, LDL

Introduction

Cerebrovascular accidents (CVAs), also termed strokes, have been recognized as the second leading cause of death and the third most common cause of disability globally (**1**). According to the World Stroke Organization (WSO), over 13.7 million new strokes occur each year, with nearly 5.5million people dying of stroke annually worldwide (**2**). A CVA is defined as a rapidly developing sequence of clinical events leading to a focal or global loss of cerebral function lasting for a minimum of 24 hours or leading to death, with no apparent cause other than that of vascular origin. Stroke patients have a higher mortality risk in the first

weeks following the event; nearly 20%-50% lose their lives within the first month depending on the severity and type of CVA, comorbidities, and effectiveness of complications' treatment (**3**). Globally, 70% of strokes and 87% of both stroke-related deaths and disability-adjusted life years occur in low and middle-income countries (LMICs) (**1**). In Pakistan, stroke has a prevalence rate of 4.8% with similar incidence in both men and women, and nearly 350,000 new cases of stroke reported annually (**4,5**).

Stroke is divided into two subtypes, namely ischemic and hemorrhagic, depending on the disturbances of cerebral blood circulation. Ischemic stroke occurs as a result of occlusion of any cerebral artery by a thrombus (thrombotic cerebral infarction) or embolus (embolic cerebral infarction), with ischemia in part or all of the territory supplied by the occluded artery (**3**). Ischemic stroke is the primary cause of hospital admissions due to disability and the third principal cause of death, consuming more than 2.7 million lives each year. In 2016, over 9.5 million cases of ischemic stroke were reported globally (2). However, acute ischemic stroke carries a higher chance of rapid recovery and has a good outcome. Populations with high hypertension (HTN) prevalence, such as Asians, have a higher incidence of ischemic stroke. Furthermore, ischemic strokes affect a wide age group, particularly the seventh, eighth and ninth decades of life (6).

Dyslipidemia, also termed deranged lipid profile, refers to the presence of abnormal lipid levels or lipoproteins in the blood, including elevated low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), total cholesterol (TC) and reduced levels of high-density lipoprotein cholesterol (HDL-C) (7). Although vascular disease is a prime contributor to pathogenesis in stroke, dyslipidemia has not been undoubtedly established as a risk factor for stroke in the same way that it has for coronary artery disease (8-9). Published literature has reported dyslipidemia to be responsible for 32.7% of stroke cases (10). Additionally, serum TG levels confer a significant risk of stroke. Among the distribution of different components of lipid profile in stroke patients' serum, cholesterol, triglyceride, LDL-C and HDL-C are usually deranged in 42%, 4%, 7% and 31% patients respectively (**7**). On the other hand, other studies of serum cholesterol in stroke patients have reported results varying from insignificant changes to a moderate elevation (11). There are several studies that have not found any relationship between lipid profile and ischemic stroke incidence (12,13).

To the best of our knowledge, no such study evaluating the association between deranged lipid profile and incidence of ischemic stroke has been previously conducted in Pakistan. Hence, the primary objective of our study was to determine the frequency and pattern of dyslipidemia in patients with ischemic stroke in our part of the world. A secondary aim was to determine the impact of demographic and clinical factors on the frequency and pattern of dyslipidemia in ischemic stroke subjects.

Material and methods

Study design and duration: This was a prospective cross-sectional study conducted for a duration of 6 months between August 2019 and February 2020, at the medicine out-patient clinics of a tertiary care hospital in Karachi, Pakistan.

Sample size, inclusion, and exclusion criteria: A sample size of 235 ischemic stroke patients was calculated using Openepi (Open Source Epidemiologic Statistics for Public Health) at an anticipating frequency of 32.7% (10) and a 95% confidence interval. The sample population included both female and male patients aged 18-80 years, presenting with paralysis, difficulty in speech, and/or loss of consciousness, for the duration of one or more hours. We excluded all patients taking lipid-lowering medications, diagnosed with hepatic disease, hypothyroidism, or renal disease (nephrotic syndrome).

Sampling technique and data collection: A non-probability convenience-based sampling technique was used to collect data. The principal investigator explained the purpose and the methodology of the study to all participants. They were given the right to decide if they wished to participate and the free will to withdraw at any time during the course of the study. Both verbal and written informed consent was taken from the participants while ensuring their confidentiality and anonymity. Blood samples were obtained from the patients after 14 hours of fasting. The blood samples

were incubated for twenty minutes and centrifuged at 4°C for fifteen minutes for extraction of serum. The serum was analyzed for TC, TG, LDL-C, VLDL-C and HDL-C levels by enzymatic colorimetric methodology, which used the auto analyzer machine. These values were recorded on the proforma by the investigators. Additional demographic and clinical factors including age, gender, height, weight, body mass index (BMI), history of HTN and diabetes mellitus (DM), and duration of symptoms were also noted. The cut-off values for BMI classification were as follows: BMI 18.5-24.9 kg/m2 as normal weight, BMI ≥25.0 kg/m2 as overweight, and BMI ≥30.0 kg/m2 as obese. The cut-off values utilized to label lipid parameters as deranged levels were as follows: total cholesterol levels of >200 mg/dL, LDL-C of ≥100 mg/dL, HDL-C of ≤45 mg/dL, VLDL-C of >40 mg/dL and TG levels ≥150 mg/dL.

Statistical analysis: All statistical analysis was conducted using Statistical Package for Social Sciences (SPSS) version 23.0. Quantitative variables such as age, weight, height, BMI, duration of symptoms, TC, VLDL-C, LDL-C, HDL-C and TG were computed as mean and standard deviation. Qualitative variables such as gender, presence of deranged lipid profile, DM and HTN were computed as frequency and percentages. Chi-square test was applied to determine the effect of modifiers such as gender, age, BMI, DM, HTN and duration of symptoms on the presence and pattern of deranged lipid profile in ischemic stroke subjects. A p-value of ≤0.05 was taken as statistically significant.

Results

Socio-demographic and clinical characteristics of ischemic stroke subjects: Out of a total of 235 ischemic stroke subjects, nearly three-fifths (n=146/235, 62.1%) were males. The mean age of the patients was 50.84±11.51 years. The mean weight, height, BMI, duration of symptoms and lipid levels are reported in Table 1. A large proportion (n=154/235, 65.5%) of our participants suffered from DM while nearly three-quarters (n=171/235, 72.8%) had HTN.

Presence of dyslipidemia and pattern of deranged lipid profile in ischemic stroke subjects: Lipid profiles were deranged in greater than half (n=134/235, 57.0%) of ischemic stroke subjects. Analysis of lipid profile revealed that the most commonly deranged values were TC and VLDL-C levels (n=132/235, 56.2%) for both respectively. The second most commonly deranged value was TG level (n=124/235, 52.8%) followed by HDL-C (n=99/235, 42.1%) and LDL-C levels (n=87/235, 37.0%), as demonstrated in Figure 1.

Association of demographic and clinical factors with dyslipidemia among ischemic stroke subjects: Dyslipidemia was significantly higher in patients above 40 years of age (p=0.002). There were no significant differences in the presence of dyslipidemia with respect to gender (p=0.308), BMI (p=0.192) and duration of symptoms (p=0.334). Most of the patients (n=109/134, 81.3%) with deranged lipid values were hypertensive (p=0.001). Similarly, a large proportion of patients (n=99/134, 73.9%) who had dyslipidemia were positive for a history of DM (p=0.002), as demonstrated in Table 2.

Table 1. Clinical characteristics of the participants

Variables	Mean	Std. Deviation
Age (Years)	50.84	11.51
Weight (kg)	71.88	13.25
Height (cm)	161.66	8.65
BMI (kg/m^2)	27.413	4.25
Duration of symptoms (minutes)	147.91	44.26
TC levels (mg/dL)	202.6	30.31
VLDL-C levels (mg/dL)	47.56	12.33
LDL-C levels (mg/dL)	117.17	45.80
HDL-C levels (mg/dL)	49.82	13.98
TG levels (mg/dL)	180.12	62.85

Note: BMI: body mass index; TC: cholesterol; VLDL-C: very low-density lipoprotein cholesterol;
LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TG: triglyceride.

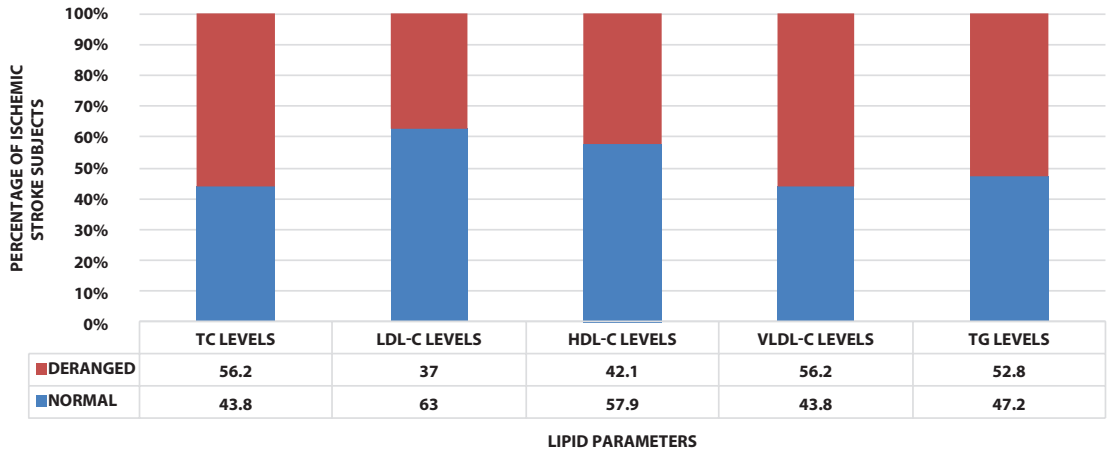


Figure 1. Distribution of ischemic stroke subjects based on pattern of deranged lipid profile
Note: TC: total cholesterol; VLDL-C: very low-density lipoprotein cholesterol; LDL-C: low density lipoproteins cholesterol; HDL-C: high density lipoprotein cholesterol; TG: triglyceride.

Table 2. Association of demographic and clinical factors with dyslipidemia

Variables	Presence of dyslipidemia		P-value
	Yes (n=134; 57.0%)	No (n=101; 42.9%)	
Gender			0.308
Male	87 (64.9)	59 (58.4)	
Female	47 (35.1)	42 (41.6)	
Age (years)			0.002*
≤30	4 (3.0)	11 (10.9)	
31-40	18 (13.4)	16 (15.8)	
41-50	49 (36.6)	17 (16.8)	
51-60	44 (32.8)	47 (46.5)	
>60	19 (14.2)	10 (9.9)	
BMI			0.192
Normal	32 (23.9)	35 (34.7)	
Overweight	60 (44.8)	38 (37.6)	
Obese	42 (31.3)	28 (27.7)	
Duration of symptoms (minutes)			0.334
≤120	44 (32.8)	39 (38.6)	
121-180	79 (58.9)	58 (57.4)	
>180	11 (8.2)	4 (4.0)	
HTN			0.001*
Yes	109 (81.3)	62 (61.4)	
No	25 (18.7)	39 (38.6)	
DM			0.002*
Yes	99 (73.9)	55 (54.5)	
No	35 (26.1)	46 (45.5)	

*p value significant at 5% interval
Note: BMI: body mass index; HTN: hypertension; DM: diabetes mellitus.

Association of demographic and clinical factors with pattern of deranged lipid profile:

Distribution of subjects according to gender based on lipid profile: The most common deranged lipid value among males was an increased TC level (n=87/146, 59.6%) and the second most common deranged lipid profile value was an increased VLDL-C level (n=85/146, 58.2%). With regards to females, the most common deranged lipid value was increased VLDL-C levels (n=47/89, 52.8%) followed by an equal number (n=45/89, 50.6%) of females having both increased TC and TG levels. Subgroup analysis based on lipid profile (Table 3**)** revealed that lipid values were observed to be more deranged in males as compared to females; however, the difference noted was not statistically significant.

Distribution of subjects according to age based on lipid profile: Analysis of ischemic stroke subjects based on lipid profile across different age groups revealed statistically significant differences, with lipid values being more deranged in patients aged 41-50 years compared to other age groups. For instance, more of the patients (n=33/87, 37.9%) with deranged LDL-C values were aged 41-50 years while a small proportion (n=14/87, 16.1%) belonged to the 31-40 years group (p=0.008). HDL-C values were also observed to be more deranged in patients aged 41-50 years (n=39/99, 39.4%) in comparison to other age groups, and this difference was highly statistically significant (p=0.0005). Among the age group with the most deranged lipid profile, that is 41-50 years, the most common lipid value deranged

Table 3. Association of demographic and clinical factors with pattern of deranged lipid profile

Variables	Total N (%)	TC >200 mg/dL N (%)		p-value	LDL≥100 mg/dL N (%)		p-value	HDL≤45 mg/dL N (%)		p-value	VLDL>40 mg/dL N (%)		p-value	TG≥150 mg/dL N (%)		p-value
		Yes (N=132)	No (N=103)		Yes (N=87)	No (N= 148)		Yes (N=99)	No (N=136)		Yes (N=132)	No (N=103)		Yes (N=124)	No (N=111)	
Gender																
Male	146 (62.1)	87 (65.9)	59 (57.3)	0.176	55 (63.2)	91 (61.5)	0.792	64 (64.6)	82 (60.3)	0.497	85 (64.4)	61 (59.2)	0.417	79 (63.7)	67 (60.4)	0.597
Female	89 (37.9)	45 (34.1)	44 (42.7)		32 (36.8)	57 (38.5)		35 (35.4)	54 (39.7)		47 (35.6)	42 (40.8)		45 (36.3)	44 (39.6)	
Age (years)																
≤30	15 (6.4)	4 (3.0)	11 (10.7)	0.005	3 (3.4)	12 (8.1)	0.008	4 (4.0)	11 (8.1)	0.0005	4 (3.0)	11 (10.7)	0.001	4 (3.2)	11 (9.9)	0.002
31-40	34 (14.5)	18 (13.6)	16 (15.5)		14 (16.1)	20 (13.5)		16 (16.2)	18 (13.2)		18 (13.6)	16 (15.5)		18 (14.5)	16 (14.4)	
41-50	66 (28.1)	47 (35.6)	19 (18.4)		33 (37.9)	33 (22.3)		39 (39.4)	27 (19.9)		49 (37.1)	17 (16.5)		45 (36.3)	21 (18.9)	
51-60	91 (38.7)	44 (33.3)	47 (45.6)		23 (26.4)	68 (45.9		24 (24.2)	67 (49.3)		42 (31.8)	49 (47.6)		38 (30.6)	53 (47.7)	
>60	29 (12.3)	19 (14.4)	10 (9.7)		14 (16.1)	15 (10.1)		16 (16.2)	13 (9.6)		19 (14.4)	10 (9.7)		19 (15.3)	10 (9.0)	
BMI																
Normal	67 (28.5)	32 (24.2)	35 (34.0)	0.227	22 (25.3)	45 (30.4)	0.703	22 (22.2)	45 (33.1)	0.182	32 (24.2)	35 (34.0)	0.259	29 (23.4)	38 (34.2)	0.138
Overweight	98 (41.7)	60 (45.5)	38 (36.9)		38 (43.7)	60 (40.5)		44 (44.4)	54 (39.7)		58 (43.9)	40 (38.8)		53 (42.7)	45 (40.5)	
Obese	70 (29.8)	40 (30.3)	30 (29.1)		27 (31.0)	43 (29.1)		33 (33.3)	37 (27.2)		42 (31.8)	28 (27.2)		42 (33.9)	28 (25.2)	

(*Continued*)

Table 3. Association of demographic and clinical factors with pattern of deranged lipid profile (*Continued*)

Variables	Total N (%)	TC >200 mg/dL N (%)		p-value	LDL≥100 mg/dL N (%)		p-value	HDL≤45 mg/dL N (%)		p-value	VLDL>40 mg/dL N (%)		p-value	TG≥150 mg/dL N (%)		p-value
		Yes (N=132)	No (N=103)		Yes (N=87)	No (N= 148)		Yes (N=99)	No (N=136)		Yes (N=132)	No (N=103)		Yes (N=124)	No (N=111)	
Duration of symptoms (minutes)																
≤120	83 (35.3)	44 (33.3)	39 (37.9)	0.345	27 (31.0)	56 (37.8)	0.041	31 (31.3)	52 (38.2)	0.106	42 (31.8)	41 (39.8)	0.227	40 (32.3)	43 (38.7)	0.196
121-180	137 (58.3)	77 (58.3)	60 (58.3)		50 (57.5)	87 (58.7)		58 (58.6)	79 (58.1)		78 (59.1)	59 (57.3)		73 (58.9)	64 (57.7)	
>180	15 (6.4)	11 (8.3)	4 (3.9)		10 (11.5)	5 (3.4)		10 (10.1)	5 (3.7)		11 (8.3)	4 (3.9)		11 (8.9)	4 (3.6)	
HTN																
Yes	171 (72.8)	107 (81.1)	64 (62.1)	0.001	66 (75.9	105 (70.9)	0.414	79 (79.8)	92 (67.6)	0.039	107 (81.1)	64 (62.1)	0.001	100 (80.6)	71 (64.0)	0.004
No	64 (27.2)	25 (18.9)	39 (37.9)		21 (24.1)	43 (29.1)		20 (20.2)	44 (32.4)		25 (18.9)	39 (37.9)		24 (19.4)	40 (36.0)	
DM																
Yes	154 (65.5)	99 (75.0)	55 (53.4)	0.001	69 (79.3)	85 (57.4)	0.001	78 (78.8)	76 (55.9)	0.0005	97 (73.5)	57 (55.3)	0.004	95 (76.6)	59 (53.2)	0.0005
No	81 (34.5)	33 (25.0)	48 (46.6)		10 (11.5)	71 (48.0)		21 (21.2)	60 (44.1)		35 (26.5)	46 (44.7)		29 (23.4)	52 (46.8)	

Note: TC: total cholesterol; VLDL-C: very low-density lipoprotein cholesterol; LDL-C: low density lipoproteins cholesterol; HDL-C: high density lipoprotein cholesterol; TG: triglyceride; BMI: body mass index; HTN: hypertension; DM: diabetes mellitus.

was the increased VLDL-C level (n=49/66, 74.2%), followed by increased TC levels (n=47/66, 71.2%) and TG levels (n=45/66, 68.2%).

Distribution of subjects according to BMI based on lipid profile: Analysis of lipid profile values based on anthropometric measurement, that is BMI, revealed that lipid values were observed to be more deranged in overweight patients compared to normal and obese subjects, but there was no statistically significant correlation. Among the BMI group with the most deranged lipid profile, that is the overweight group, the most common lipid profile value deranged was the increased TC level (n=60/98, 61.2%), followed by increased VLDL-C levels (n=58/98, 59.2%) and increased TG levels (n=53/98, 54.1%).

Distribution of subjects according to symptoms duration based on lipid profile: Analysis of lipid profile based on symptoms duration revealed patients with duration of symptoms between 121-180 minutes to have more deranged lipid profile values; however the difference observed was statistically significant only for LDL-C levels (p=0.041). Among the patients group (121-180 minutes) with the most deranged lipid profile, the most common lipid profile value deranged was VLDL-C levels (n=78/137, 57.7%), the second most common deranged lipid value was TC levels (n=77/137, 56.2%) followed by TG levels (n=73/137, 53.3%).

Distribution of subjects (diabetic and non-diabetics) based on lipid profile: Analysis of lipid profile based on history of DM revealed statistically significant differences between diabetic and non-diabetic groups for all lipid profile values, which were observed to be more deranged in the diabetic group (as illustrated in Table 3 and Figure 2). Among the diabetic group (that has a more deranged lipid profile), the most common deranged lipid profile value was the increased TC level (n=99/154, 64.3%), followed by increased VLDL-C levels (n=97/154, 63%) and increased TG levels (n=95/154, 61.7%). Among the non-diabetic group, the most common deranged lipid profile value was the increased VLDL-C level (n=35/81, 43.2%), followed by increased TC levels (n=33/81, 40.7%).

Distribution of subjects (hypertensive and non-hypertensive) based on lipid profile: Analysis of the lipid profile based on HTN revealed statistically significant differences for all lipid profile values except for LDL-C levels (p=0.414) between hypertensive and non-hypertensive groups (as illustrated in Table 3 and Figure 3). Among the hypertensive group (that had the more deranged lipid profile), the most common deranged

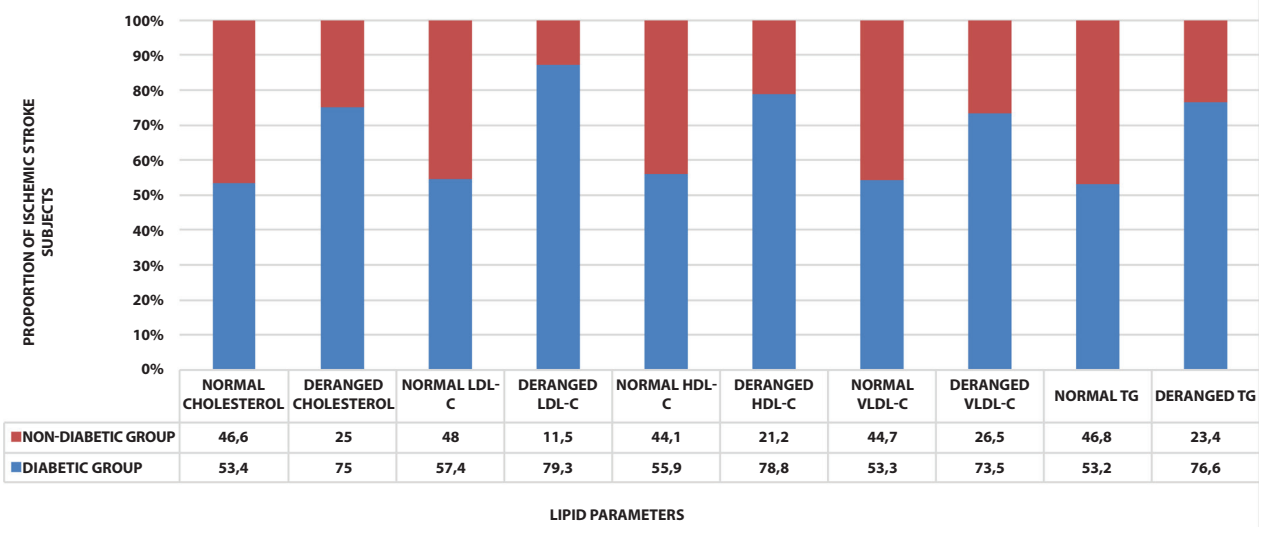
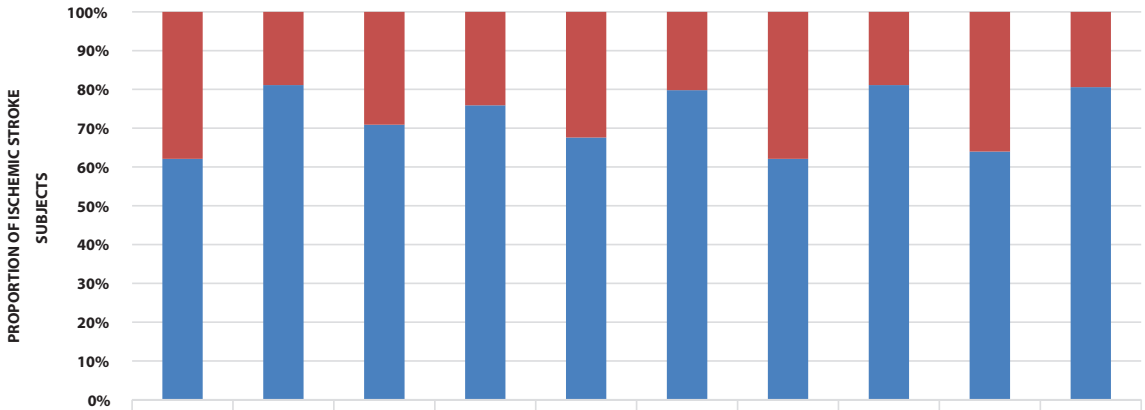


Figure 2. Distribution of subjects (diabetics and non-diabetics) based on lipid profile
Note: TC: total cholesterol; VLDL-C: very low-density lipoprotein cholesterol; LDL-C: low density lipoproteins cholesterol; HDL-C: high density lipoprotein cholesterol; TG: triglyceride.



	NORMAL TC	DERANGED TC	NORMAL LDL-C	DERANGED LDL-C	NORMAL HDL-C	DERANGED HDL-C	NORMAL VLDL-C	DERANGED VLDL-C	NORMAL TG	DERANGED TG
NON-HYPERTENSIVE GROUP	37.9	18.9	29.1	24.1	32.4	20.2	37.9	18.9	36	19.4
HYPERTENSIVE GROUP	62.1	81.1	70.9	75.9	67.6	79.8	62.1	81.1	64	80.6

Figure 3. Distribution of subjects (hypertensive and non-hypertensive) based on lipid profile
Note: TC: total cholesterol; VLDL-C: very low-density lipoprotein cholesterol; LDL-C: low density lipoproteins cholesterol; HDL-C: high density lipoprotein cholesterol; TG: triglyceride.

lipid value was the increased TC (n=107/171, 62.6%) and increased VLDL-C level (n=107/171, 62.6%), followed by increased TG levels (n=100/171, 58.5%). Among the non-hypertensive group, the most common deranged lipid profile value was the increased TC (n=25/64, 39.1%) and increased VLDL-C level (n=25/64, 39.1%), followed by TG levels (n=24/64, 37.5%).

Discussion

Dyslipidemia is considered to be one of the important risk factors for ischemic stroke and the findings of our study established a relationship between the two; more than half (57.02%) of ischemic stroke patients had deranged lipid profiles. A much higher prevalence was reported in a previous multicenter-study conducted in Pakistan, which elucidated that dyslipidemia was the most common risk factor present in 83% of stroke patients (14). Similarly, a cross-sectional survey of 1568 patients in China revealed that the serum levels of TC, LDL-C, and HDL-C were significantly related to the outcome in patients with acute ischemic stroke (15). Another Japanese study identified high-serum TC as a risk factor for ischemic stroke (16).

Our study identified a higher frequency of male patients (n=146/235, 62.1%) than female patients (n=89/235, 37.9%) presenting with ischemic strokes. According to another study (17), the incidence of stroke is higher in males than females until menopause, which is when females lose the anti-thrombotic benefits of endogenous estrogen. The mean age of our study population was 50.84±11.51 years; this could explain why our study revealed more males than females having CVAs, as the mean age of menopause in Pakistan is 49 ±3.6 years (18).

According to the findings of our study (n=235), a significant correlation has been established between dyslipidemia and age groups in patients of ischemic stroke (p=0.002), with the highest (n=49/134, 36.6%) prevalence of dyslipidemia among CVA patients between 41-50 years of age. In contrast, another study with a smaller sample size (n=52) has not recognized a significant association between hyperlipidemia and age among ischemic CVA patients (19). Other studies investigating deranged lipid profiles alone (20,21) indicate that the highest prevalence of dyslipidemia is seen among patients between 50-59 years of age. This disparity could also be attributed to the difference in sample size between our study and those

with larger (n=1995, n= 136945) sample populations (20, 21). With increasing age the levels of plasma TC rise, for which the pathogenesis is poorly understood; one theory tested on animal models suggests that aging is associated with a decrease in growth hormone levels, which would otherwise contribute to a positive impact on cholesterol metabolism (22). Moreover, as the liver is the primary organ for cholesterol clearance from the body (23), aging may be associated with slowing down of processes within the liver, and hence lead to plasma accumulation of lipid. Hence, dyslipidemia is known to be a cerebrovascular disease risk factor and is more likely to have a greater effect on older individuals because of increased vulnerability to lipid accumulation and plaque deposition. Furthermore, the incidence of stroke was observed to be low amongst patients aged >60 years in our study. The usage of public healthcare services amongst the elderly depends upon a range of cultural, socio-demographic, financial factors, and the availability of regional resources. The utilization of the government healthcare services in comparison with the private hospitals has been reported to be low amongst the elderly group (aged >60 years) ($p<0.001$). Since our study was conducted at a public tertiary-care hospital, the low incidence of stroke could be attributed to fewer individuals aged >60 years presenting to the hospital, and being hospitalized with ischemic stroke (24).

A statistically significant difference was observed for TC ($p=0.001$), LDL-C ($p=0.001$), VLDL-C ($p=0.004$), HDL-C ($p=0.0005$) and TG ($p=0.0005$) levels between diabetic and non-diabetic patients with ischemic CVA in our study, with more deranged lipid profile values among the diabetic group. DM causes endothelial cell damage, inflammation and premature arterial stiffness, which contribute to plaque deposition; hence, DM has been recognized as a modifiable risk factor for CVA (25). Another study describes a higher risk (OR=2.928) and prevalence ($p<0.01$) of DM type II in patients with hyperlipidemia than in the control population (26). The pathophysiology of elevated plasma lipids predisposing to DM type II can be attributed to free fatty acids inducing programmed cell death within β cells of the pancreatic islets and inhibiting hepatic gluconeogenesis; therefore, pancreatic insulin secretion is reduced and plasma glucose levels are consistently high.

Our study also revealed a statistically significant difference between TC ($p=0.001$), VLDL-C ($p=0.001$), HDL-C ($p=0.039$) and TG ($p=0.004$) levels between hypertensive and non-hypertensive patients with ischemic stroke, with more deranged lipid profile values among the hypertensive group. Hyperlipidemia is commonly detected among hypertensive patients, possibly because elevated plasma lipids cause vascular endothelial cell destruction, which may ultimately disrupt production of nitric oxide leading to increased vascular tone and elevated blood pressure. Higher blood pressures further increase the stress on vascular endothelium and cause atherosclerosis (27). Unsurprisingly, HTN has been identified as the single most predominant risk factor for stroke (28), and has been included in the Framingham Stroke Risk Score (29,30), along with DM and other stroke risk factors, to calculate the chance of developing a stroke within the following 10 years. A study from the UK analyzed the electronic records of 1.25 million people during 1997 and 2010 and reported that people aged 30 years or older with HTN have a lifetime risk for strokes compared to those with normal blood pressure (31). Another Japanese study observed that high TC, LDL-C, and non-HDL-C levels were generally associated with an increased risk of HTN in subjects of age less than 40 years and those with systolic BP ≥120 mm Hg (32). This could be explained by the fact that dyslipidemia may predispose individuals to development of HTN by reducing sensitivity to the baroreflex (32).

The country has a high proportion of its population suffering either from DM, HTN, or both; this could partly be attributed to rapid urbanization, unhealthy dietary habits and sedentary lifestyles, which contribute to a relatively overweight population. Results from a large community-based epidemiological survey, "National Diabetes Survey of Pakistan (NDSP) 2016–2017" showed that overall, age-adjusted weighted prevalence of HTN was 46.2% (33). Several epidemiologic studies have indicated an independent association between DM and ischemic stroke with a two-fold to six-fold increased risk; it is estimated that nearly 40% of all ischemic strokes can be attributed

to the effects of DM alone, or in combination with HTN (34).

There is a pressing need to launch community-based screening programs for the detection of comorbidities like HTN and DM, which markedly alter the chance of developing an ischemic stroke. Appropriate health-education efforts must be made to reduce the burden of stroke in Pakistan, where patients are equipped with strategies that manage modifiable risk factors for CVAs, such as DM, HTN and dyslipidemia. Lastly, the findings of this study could facilitate health-practitioners to effectively investigate and develop lipid-lowering therapies to therapeutically manage the risk of ischemic stroke.

Our study, like other studies, had certain limitations. This was a hospital-based study conducted in only one tertiary-care hospital in an urban area of Pakistan, and is therefore not representative of the whole population. Secondly, the lipid profiles during the follow-up period may have influenced prognosis, which were not analyzed.

Conclusion

The results of our study conclude that dyslipidemia is an important risk factor for causing ischemic stroke especially in high-risk patients of age 40 and above, those with comorbidities like DM and HTN. It can also be deduced that TC and VLDL-C levels have an important role to play in the disease mechanism and emphasis must be placed on monitoring and regulating their levels especially in high-risk groups to prevent the occurrence of stroke. The findings are important in understanding the role of individual lipid values and their association with various demographic and clinical factors, which can potentially assist in formulating targeted statin therapy and help in better control of the disease.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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