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Lipid Profile and the Risk of Stroke: A Study from North of Iran

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ABSTRACT

Stroke is the second cause of mortality in the world and third in Iran and lipid abnormalities are the main cause of stroke. The relation of dyslipidemia and the risk of stroke is mater of controversy. The aim of this paper is to determine the relationship of dyslipidemia and the risk of stroke in Sayad Shirazi hospital, Gorgan, Northeastern Iran. Retrospectively, we investigated all medical records with a diagnosis of stroke based on International Classification of Diseases, Revision 10, from August 2015 to August 2016 in Sayyad Shirazi hospital. We include those records with laboratory reports on serum lipid profile. The National Cholesterol Education Program Adult Treatment Panel III guideline was used to classifying lipid profile. The Data management and analysis was performed using SPSS 20. Out of 415 identified records, 9.6% had an unspecified diagnosis of stroke subtype. Only, in 160 records the lipid parameters were measured. The majority of cases with dyslipidemia was men (56.6%) and age older than 60 years (71%). There was a significant difference between ethnic groups and dyslipidemia (p=0.04) and between discharge outcome and lipid profile in women (p=0.05). Furthermore, the relation between dyslipidemia and another comorbid risk factor for stroke including diabetes (p=0.004), ischemic heart disease (0.035), and prior stroke (0.002) was significant. This study has shown that dyslipidemia coexisting with diabetes, ischemic heart diseases, and prior stroke increases the risk of stroke especially in older age. In general, therefore, it seems that lipid-lowering therapy must be one of the priorities in this population.

Key words: Diabetes, Dyslipidemia, High low-density lipoprotein, Hypercholesterolemia, Hypertriglyceridemia, Low high-density lipoprotein, Prior stroke, Stroke

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INTRODUCTION

Stroke after ischemic heart diseases is the second leading cause of death and the third cause of disability worldwide [1, 2]. Pathologically, stroke comprises ischemic and hemorrhagic subtypes, which occurs in about 87 and 13 percent of all stroke respectively [3]. The most common cause of ischemic and hemorrhagic stroke is embolism and hypertension, respectively [4]. Stroke has different modifiable risk factors, among which hypertension, hyperlipidemia, atrial fibrillation, diabetes and sedentary lifestyle are the major causal risk factors [4-7].

Dyslipidemia in the form of increased level of triglyceride (TG), low-density lipoprotein (LDL) and cholesterol level and decreased high-density lipoprotein (HDL) level is a risk factor for atherosclerosis and the main predictor of cardiovascular diseases including stroke [8]. Abnormality of serum lipid parameters is the major risk factor for ischemic stroke [9]. Elevated serum cholesterol level is another risk factor for

stroke, especially in the case of atherosclerosis and increased blood pressure [10].

The correlation between cholesterol level and the risk of stroke and its mortality is well documented [11-12]. HDL-C exerts beneficial effects on atherosclerosis but it is the main ischemic stroke risk factor [12]. Also, the anti-inflammatory and anti-oxidant properties of HDL may reduce the risk of thrombosis by inhibition of LDL oxidation, expression of adhesion molecules, platelet activation and aggregation [13]. Increased TG level is associated with ischemic stroke [12]. Evidence indicates that increased TG level, particularly with low HDL and high LDL level increases the risk of cardiovascular events, including stroke [14]. It was shown that carotid plaque formation or the carotid intima-media thickness (CIMT) positively associated with increased LDL-C level [12, 15-16]. LDL-C lowering therapy reduces CIMT and consequently reduces the risk of ischemic stroke [17], so that 10% reduction in LDL-C leads to a 15.6% risk reduction of all strokes [18].

In Iran, stroke is the third leading cause of mortality [19]. According to many hospital-based studies from Iran, dyslipidemia is one of the major risk factors for cardiovascular disease [20-21]. In a study by Sarrafzadegan *et al*., (2012) high level of LDL-C was a strong risk factor for stroke among Iranians [22]. Higher levels of TG and LDL-C are strong predictors of the cerebrovascular event in women's of Iranian population [23]. The third national Surveillance of Risk Factors of Non-Communicable Disease (SuRFNCD-2007) in Iran, reported that the prevalence of high TG>=150 mg/dl was 36.4 (34.1-38.9) and the national estimate of TG was 148.83±2.45 mg/dl. In the case of cholesterol, the national estimate of high cholesterol was 195.63±1.10 mg/dl and the prevalence of high cholesterol >=200 and >=240 mg/dl was 42.9 (40.4-45.4) and 14.1 (12.6-15.9), respectively. According to this report, dyslipidemia was more common in the urban area and older age groups. The high cholesterol and high TG level were more common in women and men, respectively [24].

The present study was carried out to indicate the association of serum lipid profile in patients with a stroke in Gorgan.

MATERIALS AND METHODS

This was a retrospective hospital-based study, conducted in Sayad Shirazi hospital affiliated to Golestan University of Medical Sciences (GoUMS), Gorgan, Northeastern Iran. The Sayyad Shirazi hospital is the main referral hospital of the stroke cases in this area. All patients admitted during August 2015 and August 2016, screened for final confirmed diagnosis codes in the categories of I60-I64, based on International Classification of Disease, 10 revision (ICD).

The diagnosis was assigned by attending physicians. Magnetic Resonance Imaging (MRI) or Computed Tomography (CT scan) reports were used for confirming final diagnosis. The first laboratory blood test reports were used to capture the lipid parameter measures. National Cholesterol Education Program Adult Treatment Panel III guideline [25] was used for dyslipidemia as low HDL-C <40 mg/dl, high LDL-C >=160 mg/dl, high cholesterol >=240, and high triglyceride >=200 mg/dl.

For the purpose of data capturing from medical records, we used a reliable and validated data gathering form. Chi-square test was used to analyze the categorical data. Statistical significant was P-value<0.05. All statistical analyses were performed by SPSS software, version 20 (IBM SPSS Statistics).

RESULTS

Out of 415 identified records, 40 (9.6%) records had an unspecified diagnosis of stroke subtype, 63.9% reported ischemic stroke and 26.5% diagnosed with the hemorrhagic stroke. Of all cases with a diagnosis of hemorrhagic and ischemic stroke, in 160 records the lipid parameters were measured which include triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and total cholesterol. Of 160 records, 47.5% reported dyslipidemia. The mean TG, HDL, LDL, and cholesterol level was 136.6±80.1, 45.1±10.2, 113.6±57.6, and 181.3±48.9 mg/dl, respectively.

Analysis of demographic parameter indicated that the majority of the population with dyslipidemia was male gender (56.6%) and 71% had an age of higher than 60 years old. There was a significant association between ethnicity and lipid profile (p-value=0.040). The relationship between lipid

profile and age group (p-value=0.598) and gender (p-value=0.703) was not significant (Table 1).

Table 1: Distribution of age and ethnicity and their association with lipid profile

	Normal lipid profile	Dyslipidemia	Total	p value
Age group (N., %)				
<40	3 (3.6)	2 (2.6)	5 (3.1)	0.598
40-49	7 (8.3)	8 (10.5)	15 (9.4)	
50-59	17 (20.2)	12 (15.8)	29 (18.1)	
60-69	20 (23.8)	26 (34.2)	46 (28.8)	
>=70	37 (44)	28 (36.8)	65 (40.6)	
Total	84 (100)	76 (100)	160 (100)	
Mean ±SD	65.71±14.2	65.24±13.7	-	0.829
Ethnicity (N., %)				
Fars	62 (73.8)	68 (89.5)	130 (81.2)	0.040
Turkmen	19 (22.6)	7 (9.2)	26 (16.2)	
Baluch/ Sistani	3 (3.6)	1 (1.3)	4 (2.5)	
Total	84 (100)	76 (100)	160 (100)	

The relation of discharge outcome and lipid profile was varied by gender. In women, there was a significant relation between discharge outcome and lipid profile (p-value=0.05) but in men, there was no significant association. There was no significant relation between residence status and dyslipidemia (Table 2).

The chi-square test showed that there was no significant difference between stroke subtypes and lipid parameter (Table 3).

Statistical analysis of some comorbid stroke risk factor and lipid profile in a stroke patient with chi-square test indicated that there was a significant difference between lipid profile and diabetes (p-value=0.004), ischemic heart disease (p-value=0.035), and previous stroke (p-value=0.002). There was no significant association between hypertension and lipid profile (p-value=0.986) (Table 4).

Table 2: Distribution of gender and discharge outcome by sex and their association with lipid profile

	Normal lipid profile	Dyslipidemia	Odd`s ratio	95% Confidence Interval		P value
				Lower	Upper	
discharge outcome						
	Male					
Death	3 (9.4)	2 (5.7)	1.707	0.266	10.937	0.57
Live	29 (90.6)	33 (94.3)				
Total	32 (100)	35 (100)				
	Female					
Death	1 (3.1)	5 (17.9)	0.148	0.016	1.358	0.05
Live	31 (96.9)	23 (82.1)				
Total	32 (100)	28 (100)				
	Total					
Death	4 (6.2)	7 (11.1)	0.533	0.148	1.921	0.33
Live	60 (93.8)	56 (88.9)				
Total	64 (100)	63 (100)				
Residence						
	Male					
Urban	25 (55.6)	30 (69.8)	0.542	0.225	1.302	0.169
Rural	20 (44.4)	13 (30.2)				
Total	45 (100)	43 (100)				
	Female					
Urban	25 (64.1)	19 (57.6)	1.316	0.508	3.406	0.571
Rural	14 (35.9)	14 (42.4)				
Total	39 (100)	33 (100)				
	Total					
Urban	50 (59.2)	49 (64.5)	0.810	0.427	1.538	0.520
Rural	34 (40.8)	27 (35.5)				
Total	84 (100)	76 (100)				

Table 3: Distribution of lipid profile (TG, HDL-C, LDL-C, and cholesterol) as well as their association with stroke subtypes

	Hemorrhagic N (%)	Ischemic N (%)	Odd`s ratio	95% Confidence Interval		P value
				Lower	Upper	
Hypertriglyceridemia						
Have	5 (26.3)	22 (17.9)	0.610	0.199	1.870	0.383
Don't have	14 (73.7)	101 (82.1)				
Low HDL-C						
Have	3 (16.7)	35 (29.9)	2.134	0.581	7.840	0.245
Don't have	15 (83.3)	82 (70.1)				
High LDL-C						
Have	0 (0)	16 (13.4)	-	-	-	0.108
Don't have	17 (100)	103 (86.6)				
Hypercholesterolemia						
Have	3 (16.7)	13 (10.7)	0.596	0.152	2.339	0.454
Don't have	15 (83.3)	109 (89.3)				

TG: triglyceride, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol

Table 4: Distribution of main comorbid risk factor of stroke and their association with lipid profile in stroke patient

	Normal lipid profile	Dyslipidemia	Odd`s ratio	95% Confidence Interval		P value
				Lower	Upper	
Hypertension						
Have	62 (73.8)	56 (73.7)	0.994	0.491	2.011	0.986
Don't have	22 (26.2)	20 (26.3)				
Diabetes						
Have	34 (40.5)	48 (63.2)	2.521	1.332	4.771	0.004
Don't have	50 (59.5)	28 (36.8)				
Ischemic heart disease						
Have	11 (13.1)	20 (26.3)	5.349	1.050	5.349	0.035
Don't have	73 (86.9)	56 (73.7)				
History of cerebrovascular accident						
Have	14 (16.7)	29 (38.2)	3.085	1.476	6.448	0.002
Don't have	70 (83.3)	47 (61.8)				

DISCUSSION

In the current study, we investigated the serum lipid parameters include TG, HDL-C, LDL-C, and cholesterol and its relation to risk of stroke. None of them had a significant relation to stroke and its subtypes. But, comorbid stroke risk factor including diabetes, ischemic heart disease and history of the cerebrovascular accident was significantly related to lipid profile in a stroke patient.

A meta-analysis of 29 articles in Iran indicated that the prevalence of hypercholesterolemia >=200 mg/dl, hypertriglyceridemia >=150 mg/dl, high LDL-C >= 130 mg/dl, and low HDL-c <40 in men and <50 in women was 41.6% (36.1-47.0), 46.0% (43.3-48.7), 35.5% (24.0-47.1), and 43.9% (33.4-54.4), respectively. In women, hypercholesterolemia, high LDL-Cm, and low HDL-C were more common whereas hypertriglyceridemia was common in men. All lipid parameters were more common in the urban area. A population-based study of 4737 people aged 45-69 years in Shahroud, Iran, reported that the prevalence of dyslipidemia was 63.4% (CI 95%: 62.0-64.9%) [26]. According to this cohort study, the prevalence of high TG, low HDL-C, high LDL-C, and high cholesterol level was 28.8%, 42.3%, 13.4%, and 13.4%, respectively. In the SuRFNCD-2007 study [24], the prevalence of hypertriglyceridemia >=150 mg/dl and hypercholesterolemia >=240 mg/dl was 36.4 (34.1-38.9) and 14.1 (12.6-15.9), respectively. In our data set, the prevalence of dyslipidemia was 47.5%. Furthermore, the prevalence of high TG, low HDL-C, high LDL-C, and high cholesterol was 20.3%, 28.5%, 12.5%, and 12.1%, respectively. Compared to Shahroud and SuRFNCD-2007 study, the prevalence of dyslipidemia and lipid component in our population was lower.

In the present study, there was a significant relationship between ethnic groups and dyslipidemia (p=0.04). Reports about the role of ethnicity and the risk of dyslipidemia in stroke patients are rare. Although the ethnicity was not significant in relation to cardiovascular risk factor [27], more investigation about the role of ethnicity and stroke risk factor such as dyslipidemia is needed.

In our population, dyslipidemia was more common in urban and age older than 60 years. These findings are in line with SuRFNCD-2007[24] and Shahroud [26] study. Unhealthy lifestyle including diet and physical activity [28-29] is likely related to increasing dyslipidemia and its parameter in urban residents. These findings indicate that urbanization and increasing age increased the risk of dyslipidemia.

Another important finding was that dyslipidemia had a significant relation with stroke mortality in women (p=0.05). The present findings seem to be consistent with other research which found that some lipid parameters had relation to cardiovascular mortality. In the study of Ghasemzadeh and colleagues [30], there was no association between hypercholesterolemia and low HDL level with all-cause mortality. But hypertriglyceridemia inversely associated with all-cause mortality. In Tehran Lipid and Glucose Study [31], demonstrated that total cholesterol >=6.21 mmol/L had a positive association (p=0.027) with cardiovascular mortality. Also, it was shown that HDL-C level had no significant relation to cardiovascular event and mortality. Although, increasing TG level increases the cardiovascular event, there was no significant relation with cardiovascular mortality. Consistent with our finding, a recent study showed that hypertriglyceridemia increases the risk of cardiovascular disease mortality [32]. These results, therefore, need to be interpreted with caution. Future studies on the current topic are therefore recommended.

In many studies from Iran, dyslipidemia is the main risk factor for stroke and clinically used as a stroke predictor [20, 22-23]. Despite similar studies in Iran, there was no significant association of dyslipidemia and stroke subtype in the current study. But, analysis of main comorbid risk factors of stroke showed that there was a significant relationship between dyslipidemia and diabetes, ischemic heart disease (IHD), and previous stroke. In a diabetic patient, dyslipidemia is a potential risk factor for stroke [12] as it increases the atherosclerotic plaque and CIMT thickness [33]. Hypertriglyceridemia and low HDL-C is a predictor of stroke in type II diabetes mellitus [9] which doubles the risk of stroke [34]. As a result, the coexistence of dyslipidemia and diabetes increase the risk of stroke. Lipid abnormality, especially hypertriglyceridemia had a positive association with IHD and diabetes [14]. Hence, it can be concluded that dyslipidemia and IHD can also be a predictor of stroke. Furthermore, lipid-lowering therapy can reduce the risk of stroke in cases with diabetes [35], IHD [16] and prior stroke [36].

CONCLUSION

The present study was designed to determine the relation of dyslipidemia and the risk of stroke in Gorgan, Northeastern Iran. Dyslipidemia is a risk factor for stroke especially in ischemic type, but its effect on stroke is varied by serum parameters. This study has shown that dyslipidemia is more common in men, urban resident, and older age. It was also shown that coexisting of dyslipidemia with another risk factor, increases the risk of stroke, especially with diabetes, IHD, prior stroke, and increasing age. The results of this research support the idea that lipid-lowering therapy must be considered as a first priority to reduce the risk of stroke.

The current study was limited by the completeness aspect of the medical records quality. So we had to reduce the sample size. Considerably more work has to be done to determine the prevalence of dyslipidemia and its parameters in this area. More broadly, research is also needed to determine the relationship between stroke subtypes and lipid parameters.

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