

Pattern of Dyslipidemias and their Association with Ischemic and Hemorrhagic Stroke

Muhammad Saeed Aslam¹, Khalid Mahmood Nasir², Hajra Hussain³, Muhammad Saeed⁴, Muhammad Salman Walayt⁵, Waqas Ahmad⁶, Muhammad Usman Shabbir⁷

^{1,5} Registrar, Medicine Unit 1, Jinnah Hospital Lahore

² Assistant Professor of medicine, Medicine unit 1, Jinnah hospital Lahore

³ House officer king Edward medical university & Mayo hospital Lahore

⁴ Medical Lab Technologist, Head Pathology Lab, Health Care Dep Govt of Punjab, DHQ Hospital Mb-Din

⁶ Ph.D Scholar (Biochemistry; Molecular biology), University of Gujrat

⁷ Head Blood Bank, Primary & Secondary Health Care Department Govt of Punjab, DHQ Hospital Mb-Din

ABSTRACT

Objective: To find out the association between dyslipidemias and ischemic and hemorrhagic stroke.

Patients and Methods: This cross-sectional study was conducted in Medical Unit I, Jinnah Hospital Lahore (JHL) from 1st January 2015 to 30th Jun 2015. A total of 420 cases of stroke were included via Nonprobability consecutive sampling technique. The sample size was calculated with 95% confidence level, 2% margin of error. At the time of admission, every patient underwent CT scan in the radiology department of JHL, fasting blood samples were taken, on next day of admission. Every sample was processed for lipid profile in pathology department of Allama Iqbal Medical College, (AIMC) Lahore. Based on CT scan findings, patients were labelled as ischemic or hemorrhagic stroke. Demographic details, BMI, blood pressure and Diabetic status were also recorded.

Results: Out of 420 study participants, 47.6% (n=200) were male and 52.4% (n=220) were females, the mean age was 39.29 + 11.82 years, mean BMI was 39.29 + 11.82 kg/m². History of hypertension (HTN) was most frequent risk factor seen in 82.6% (n=347) followed by Diabetes mellitus (DM) 49.8% (n=209) and smoking found in 32.1% (n=135) cases. Frequency of Hypercholesterolemia (>200 mg/dl) was observed in 26.2% (n=110) and Hypertriglyceridemia (>150 mg/dl) in 7.9% (n=33) patients. High LDL (>130 mg/dl) levels were observed in 5.7% (n=24), high VLDL (>35 mg/dl) in 6.9% (n=29) patients, while low HDL (<35 mg/dl) was noticed in 17.1% (n=72) patients. There was significant association between type of stroke & hypercholesterolemia as well as low HDL levels (p-value<0.05). While insignificant association was found between type of stroke & hypertriglyceridemia and high VLDL (p-value>0.05). Effect modifiers i.e.; age, BMI, gender, history of smoking, HTN and DM were not significantly associated with type of stroke (p-value >0.05).

Conclusion: Hypercholesterolemia & HDL levels are significantly associated with type of stroke, whereas serum hypertriglyceridemia, high LDL and high VLDL were not significantly associated with type of stroke.

Key words: Dyslipidemia, Hemorrhagic stroke, Ischemic stroke, Stroke.

Author's Contribution

¹ Conception, synthesis, planning of research and manuscript writing

² Interpretation and discussion

³ Data analysis, interpretation and manuscript writing, ^{4,5} Active participation in data collection

Address of Correspondence

Muhammad Saeed Aslam

Email: m.saeed.aslam@gmail.com

Article info.

Received: Feb 23, 2017

Accepted: August 9, 2017

Cite this article. Aslam MS, Nasir KM, Hussain H, Saeed M, Walayt MS, Ahmad W, Shabbir MU. Pattern of Dyslipidemias and their Association with Ischemic and Hemorrhagic Stroke. *JIMDC*. 2017;6(3):134-139

Funding Source: Nil

Conflict of Interest: Nil

Introduction

Stroke is the commonest neurological cause of morbidity and mortality all over the world and the third leading cause of death. Evaluation of various risk factors for a population is not only helpful for identification of risk factors but this will be a great help for health care providers for management of these patients. Cerebrovascular accident is global health problem. A recent international survey has estimated about 15 million people worldwide suffer from nonfatal stroke annually and 33% being permanently disabled.¹ About 80% of all stroke deaths are registered in lower and middle-income countries.² An estimated annual incidence of stroke in Pakistan is 250/100,000 with an estimate of 350,000 new cases every year.^{3,4} Stroke is a multifactorial disease; some of them are called primary, while the cause for others are uncertain and secondary. Among the latter, hyperlipidemia plays a significant role. As the acute stroke management is expensive and stroke itself is associated with significant morbidity and mortality, the saying that "prevention is better than cure" holds a special meaning here. It is apparent from different studies that stroke can be significantly reduced by taking measures for control of modifiable risk factors. The modifiable risk factors of stroke are similar to western population and comprise of hypertension, cardiac disease, diabetes mellitus and dyslipidemia. Hyperlipidemia causes hardening of the arteries with plaque formation and increases the risk of atherosclerosis.⁵ Lipids and other components of blood are the sources of plaque formation. Plaque formation is a cause of narrowing and hardness of blood vessels. As result, there is reduced blood flow, increasing the risk of stroke. Unfortunately, there are no symptoms for hyperlipidemia, and lipid profile in fasting is the only method to reveal lipid levels. The desired lipid levels include; total cholesterol levels < 200 mg/dl, low-density lipoprotein (LDL) also known as "bad cholesterol" should be < 130mg/dl, high-density lipoprotein (HDL) also called "good cholesterol" should be >40mg/dl and 50mg/dl for males and females respectively. Triglycerides levels should be <200 mg/dl.² Once the person is diagnosed with hyperlipidemia, the next step is to consult a physician who may prescribe treatment or discuss lifestyle and diet plan depending upon the results.⁶

As cholesterol levels increases, the risk of hemorrhagic stroke decreases and the risk of ischemic stroke increases. Stroke mortality is lowest at cholesterol levels between 180mg/dl and 200mg/dl. Mortality increases substantially above 240mg/dl. Mortality is highest from 160mg/dl to 300mg/dl and above. Diet high in polyunsaturated fat and low in antioxidants can make LDL-cholesterol within the blood vulnerable to oxidation. Oxidized LDL can play a role in the development of stroke.⁷ Stroke, also known as cerebral vascular accident (CVA), is a second leading cause of death and disabilities around the globe.⁸ Alarming symptoms include numbness, weakness (often on one side), confusion, visual problems, slurred speech, trouble walking, dizziness, loss of balance loss of coordination and severe headache.⁹ There are two categories of stroke, ischemic & hemorrhagic, both are entirely conflicting to each other. Ischemic stroke is a most common entity, with numerous pathophysiologic mechanisms, results from blockage of a blood vessel supplying the brain, while the more damaging hemorrhagic stroke results from rupture of such a vessel.¹⁰

Hypertension is another significant contributor to stroke, hypercholesterolemia may be an important factor leading to hypertension.¹¹ Polyunsaturated fat and carbohydrates are associated with a higher risk of stroke. Exercise, stress management, proper control of oral or systemic infections, and adequate nutrition can lower the risk of stroke.¹² Important protective nutrients include magnesium, potassium, antioxidants and adequate proteins. Modified lifestyle and timely medical management can treat hyperlipidemia, a major risk factor for stroke. Statins have been shown to decrease lipids and exert a pleiotropic effect on the intracranial vasculature and inflammatory modulators, leading to neuroprotection. Lower low-density lipoprotein and higher high-density lipoprotein levels are associated with decreased risk of stroke. Despite screening guidelines and evidence of the efficacy of statins, there are numerous barriers to maintaining adequate control of lipids.¹³ Therefore evaluation of Dyslipidemia is significantly important. The present study was planned to evaluate spectrum and association of hyperlipidemia

among patients presenting with ischemic & hemorrhagic stroke.

Patients and Methods

This cross-sectional study was conducted at Medical Unit, Jinnah Hospital Lahore. During the period of six months from January 1 to June 30, 2015. All patients presenting with the acute first episode of stroke within one week of onset of symptoms were included while all of the following were excluded, i.e. (1) history of known secondary dyslipidemia, (2) Patients on lipid lowering therapy, (3) Patients with recurrent stroke or cerebrovascular accident (On history). A total of 420 stroke cases were included via non-probability consecutive sampling technique. At the time of admission, every patient was processed for CT scan in the radiology department of Jinnah hospital Lahore (JHL). Blood samples were taken by using aseptic measures and standard procedure after an 8 hour of overnight fasting on next day of admission. Every sample was processed for lipid profile in pathology department (chemical pathology section) of Allama Iqbal Medical College, (AIMC) Lahore. Lipid abnormalities were labelled as Hypercholesterolemia (>200 mg/dl), Hypertriglyceridemia (>150 mg/dl), Increased Low-density lipoproteins (LDL) (>130 mg/dl), Increased very low-density lipoproteins (VLDL) level (>35 mg/dl), decreased HDL (<35 mg/dl). Based on CT scan findings, patients were labelled as ischemic or hemorrhagic stroke as followed.

Ischemic stroke: A stroke was labelled as the ischemic stroke if there was the presence of a hypodense area reported as ischemia on CT scan.

Hemorrhagic stroke: A stroke was labelled as hemorrhagic stroke in case of presence of a hyperdense area reported as hemorrhage on CT scan.

Data Analysis: Numerical variables were analyzed as mean and SD. Frequency and percentage was calculated for categorical variables. Cross tabulation was done between abnormal lipid profile level and type of stroke. Data were stratified by age, gender, BMI, type of stroke, smoking, HTN and DM. Post-stratification Chi-square test was applied. A p-value < 0.05 was considered as statistically significant.

Results

Out of 420 study participants, 47.6% (n=200) were male and 52.4% (n=220) were females. The mean age of the patients was 39.29 ± 11.82 years, mean BMI was 24.5 ± 3.5 kg/m², mean cholesterol level was 171.45 ± 32.7 mg/dl, mean triglycerides level was 133.01 ± 15.39 mg/dl, mean LDL level was 116.87 ± 12.78 mg/dl, mean VLDL level was 21.88 ± 10.93 mg/dl, mean HDL level was 43.41 ± 15.13 mg/dl. Patients suffering from ischemic and hemorrhagic stroke were 42% and 58% respectively (Figure1).

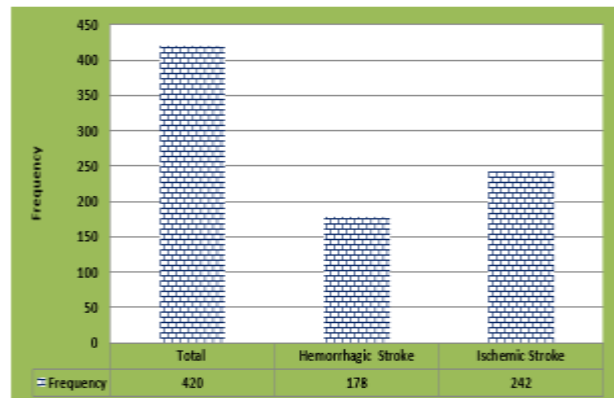


Figure 1: Frequency distribution of strokes (n=420)

Figure 2 represents frequency of different risk factors for stroke. As shown in the figure, history of hypertension was the most frequent risk factor seen in 82.6% (n=347) cases followed by diabetes mellitus in 49.8% (n=209) cases and smoking in 32.1% (n=135) cases.

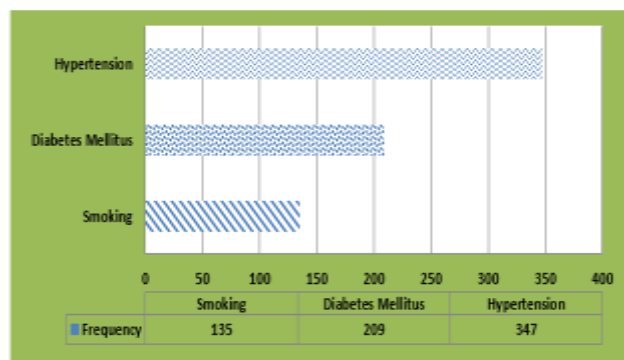


Figure 2: Frequency distribution of risk factor associated with stroke (n=420)

Frequency of hypercholesterolemia was observed in 26.2% (n=110) cases and hypertriglyceridemia was seen in 7.9% (n=33) cases. High LDL levels were observed in

5.7% (n=24), high VLDL in 6.9% (n=29) patients, while low HDL was noticed in 17.1% (n=72) patients (Figure 3).

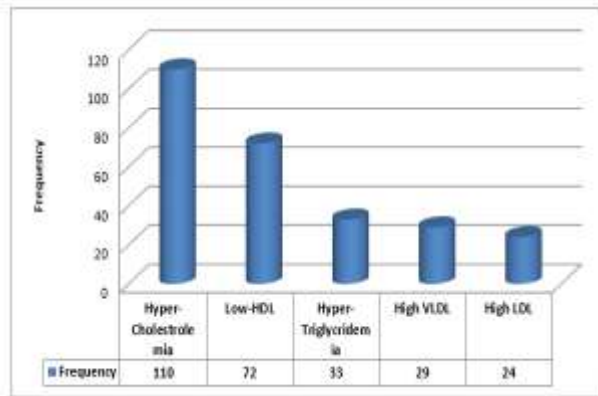


Figure 3: Frequency distribution of study participants with abnormal lipid profile (n=420)

As shown in table 1, there was a significant association between type of stroke & hypercholesterolemia as well as low HDL levels (p-value<0.05). Other factors like age, BMI, gender, history of smoking, HTN and DM were not significantly associated with type of stroke (Table 2).

Discussion

Stroke is a major public health problem that ranks in the top four causes of death in most countries. Dyslipidemias including high-density lipoproteins are the major risk factor for coronary heart disease, cerebrovascular disease, atherosclerosis, thrombosis, and stroke. The present study reported that females were more vulnerable to stroke as compared to males with earlier mean age of presentation (39.29 ± 11.82 years) & mean BMI 39.29 ± 11.82 kg/m. However, majority of studies showed a male predominance in their studies with presentation at a later age. Bain LK et al, in their study reported that male suffered more than female with M:F ratio of 1.73:1 in ischemic group and 1.42:1 in Hemorrhagic group.¹¹ According to present study, hypercholesterolemia was observed in 26.2%, hypertriglyceridemia was noticed in 7.9% (n=33) cases, high LDL levels were observed in 5.7% (n=24), high VLDL in 6.9% (n=29) patients, while low HDL was noticed in 17.1% (n=72) patients. Our results are slightly different, but supported by the previous study

Variable	Results	Hemorrhagic Stroke n=178	Ischemic Stroke n=242	p-value
Hyper-cholesterolemia (n)	Yes	26	84	0.000
	No	152	158	
Hyper-Triglyceridemia (n)	Yes	9	24	0.097
	No	169	218	
High-LDL (n)	Yes	9	15	0.676
	No	169	227	
High-VLDL (n)	Yes	11	18	0.699
	No	167	224	
Low-HDL (n)	Yes	10	62	0.000
	No	168	180	

		Hemorrhagic Stroke n=178	Ischemic Stroke n=242	p-value
Gender	Male	79	121	0.255
	Female	99	121	
Age-Groups (Year)	< 40	83	126	0.271
	≥ 40	95	116	
BMI (kg/m ²)	< 29	93	111	0.196
	≥ 29	85	131	
History of Smoking (n)	Yes	48	87	0.051
	No	130	155	
History of hypertension (n)	Yes	142	205	0.187
	No	36	37	
History of Diabetes mellitus (n)	Yes	89	120	0.933
	No	89	122	

conducted on 100 patients of ischemic stroke patients. According to this study, the mean age of patients with stroke at presentation was 64.2 ± 12 years with a male to female ratio of 3.6:1. They also reported that hypercholesterolemia was seen in 42.0%, hypertriglyceridemia in 4.0%, high LDL-cholesterol in 5.0%, and VLDL-cholesterol in 7.0% patients.

Low Serum HDL-cholesterol was observed in 31.0% cases of ischemic stroke. On the other hand, serum total cholesterol and triglycerides was raised in 05 patients each, LDL-cholesterol in 09 and VLDL-cholesterol in 03 patients of hemorrhagic stroke. Serum HDL-cholesterol was below normal in 04 patients of hemorrhagic stroke. They also reported that there was a significantly greater number of patients with raised serum cholesterol and low HDL-cholesterol in ischemic stroke than hemorrhagic stroke ($p < 0.05$), the finding similar to our results.¹⁴ A greater number of patients in the recent study presented with ischemic stroke (58 %) while Hemorrhagic stroke was observed in (42.4%) cases. In one study among 540 study participants (49.4% females) 19.1% ($n=104$) were observed to have a prior stroke while TIA was found in 9.7% ($n=53$). History of smoking hypertension and diabetes mellitus were 32.1%, 82.6%, 49.8% respectively.¹³ Aquil mentioned that out of the 100 patients with acute ischemic stroke, mean age at presentation was 63.5 years.¹⁵

Risk factor distribution included hypertension 85.0%, diabetes mellitus 49.0%, ischemic heart disease 30.0%, dyslipidemia 22.0%, smoking 9.0%, atrial fibrillation 5.0%, and previous history of stroke in 29.0% cases. According to them, various subtypes of acute ischemic stroke were lacunar infarct seen in 43%, large artery atherosclerosis in 31.0%, cardio embolic type in 8.0%, and stroke of undetermined etiology in 18.0% cases.¹⁵ Chaudhury reported that `fasting serum lipid profile analysis of 50 ischemic stroke patients revealed raised serum total cholesterol in 42.0% patients with the mean serum cholesterol of 190 ± 35 mg/dl whereas only 5 patients among Hemorrhagic CVA showing raised serum cholesterol with the overall mean of 151 ± 29 mg/dl. Serum HDL was found to be low in 16 (32.0%) patients of Ischemic stroke with a mean value of 42.4 ± 6 mg/dl whereas only 6.0% of Hemorrhagic stroke patients showed low serum HDL with a mean value of

45.4 ± 5 mg/dl. Abnormal serum triglyceride level was found to be distributed similarly in Ischemic & Hemorrhagic stroke with the mean value of 137 ± 30 mg/dl & 125 ± 30 mg/dl respectively. High serum LDL was found in 6.0% & 4.0% of ischemic & Hemorrhagic stroke with mean value of 102 ± 21 mg/dl & 93 ± 17 mg/dl respectively. Hypercholesterolemia and low HDL-cholesterol was seen significantly more in ischemic CVA group as compared to those with hemorrhagic disease.¹⁶ Mahmood et al from Pakistan also reported that there were significantly greater number of patients with raised serum cholesterol and low HDL-cholesterol in ischemic stroke than Hemorrhagic stroke ($p < 0.05$). No statistical significance was found on comparing serum values of ischemic and Hemorrhagic stroke for triglycerides, LDL-cholesterol and VLDL-cholesterol. Ischemic stroke patients had high serum total cholesterol and lower HDL-cholesterol levels as compared to hemorrhagic stroke.¹⁴ According to Zhang et al, factors which are significantly associated with ischemic stroke as opposed to hemorrhagic stroke were family history of stroke, obesity, atherosclerotic plaque of the common carotid artery, atrial fibrillation, hyperfibrinogenemia, transient ischemic attack (TIA), atherosclerotic plaque of the internal carotid artery, coronary heart, lower high-density lipoproteins (lower HDL), increasing age, diabetes mellitus, and male gender. Hypertension and family history of hypertension were the significant factors associated with hemorrhagic stroke versus ischemic stroke. Smoking, alcohol intake, kidney diseases and lower HDL-C were the significant factors contributing to ischemic stroke in man. Obesity, family history of hypertension, family history of stroke, hypercholesterolemia and myocardial ischemia were the significant factors for females with ischemic stroke.¹⁷ Osama A et al in their study, conducted on patterns of dyslipidemias in patients of ischemic stroke reported that high LDL and lipoprotein A were more frequent finding in ischemic stroke than other patterns of dyslipidemia.¹⁸ In their study, they observed that hypertension was the most frequent risk factor (74.3%) followed by hyperglycemia(64%) then dyslipidemia (57.1%) then smoking (53.3%), and these results are almost comparable with our results. However, they also reported that prevalence of dyslipidemia in males was 68.4%, which was significantly higher than in females (43.8%), and according to them prevalence of dyslipidemia was

more in the age group >65 years (63.2%) than in the age group ≤ 65 years (53.7%), the findings are not comparable with our results. One of the local study conducted by Khan et al reported, that of 55 patients of ischemic stroke studied, 78% were males and 22% were females, the finding not comparable with our results. They also reported that hypertension (65%), dyslipidemia (32.7%), diabetes mellitus (36.3%) and smoking was found in 32% cases of ischemic stroke patients. (18) Meta-analysis of some studies shows that higher the level of total cholesterol (TC), greater the risk of CVA and higher the high-density lipoprotein cholesterol (HDL), lower the risk and each being an independent risk factor. Moreover, TC to HDL ratio is better predictor of ischemic CVA and is considered a useful clinical tool. The contribution of various risk factors for stroke may be different in different ethnicities.¹⁹

Conclusion

Ischemic stroke was more frequent as compared to hemorrhagic stroke. Serum total cholesterol level and serum HDL level were significantly associated with a type of stroke whereas serum triglyceride level, serum LDL, and serum VLDL did not have significant association with type of stroke.

References

- Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, et al. American Heart Association. Stroke statistics subcommittee 2014 update: A report from the American Heart Association. *Circulation*. 2014; 21;129(3):e28.
- Hoffman A, Dervish Murad, Van Duijgin CM, France O H et al. The Rotterdam study 2014 objectives and design update. *Eur.J. Epidemio*.2013; 28(11):889-926.
- Khatri IA, Wasay M. Can we stop the stroke epidemic in Pakistan? *JCPSP*.2011; 21(4):195-6
- Taj F, Zahid R, Murtaza M, Ahmed S, Kamal AK. Risk factors of stroke in Pakistan: a dedicated stroke clinic experience. *Canadian Journal of Neurological Sciences*. 2010; 37(2):252-7.
- Gusev V, Lvova O, Votty M. 15. Risk Factors for Stroke/prognosis Dyslipidemia as the possible risk factor for arterial ischemic stroke in young. *International Journal of Stroke*. 2015;10:246.
- Barkas F, Milionis H, Mozaffarian D, Benjamin E, Go A, Tell G, et al., editors. *Treating Dyslipidemia for the Primary and Secondary Prevention of Stroke*. Seminars in Neurology-Thieme Medical Publishers. 2017; 37(3):286-293.
- Bain LK, Myint PK, Jennings A, Lentjes MA, Luben RN, Khaw K-T, et al. The relationship between dietary magnesium intake, stroke and its major risk factors, blood pressure and cholesterol, in the EPIC-Norfolk cohort. *International journal of cardiology*. 2015;196:108-14.
- Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. *The Lancet*. 2014; 383(9913):245-55.
- Everson-Rose SA, Roetker NS, Lutsey PL, Kershaw KN, Longstreth W, Sacco RL, et al. Chronic stress, depressive symptoms, anger, hostility, and risk of stroke and transient ischemic attack in the multi-ethnic study of atherosclerosis. *Stroke*. 2014;STROKEAHA. 114.004815.
- Thigpen JL, Dillon C, Forster KB, Henault L, Quinn EK, Tripodis Y, et al. Validity of international classification of disease codes to identify ischemic stroke and intracranial hemorrhage among individuals with associated diagnosis of atrial fibrillation. *Circulation: Cardiovascular Quality and Outcomes*. 2015;8(1):8-14.
- Canoy D, Cairns BJ, Balkwill A, Wright FL, Khalil A, Beral V, et al. Hypertension in pregnancy and risk of coronary heart disease and stroke: A prospective study in a large UK cohort. *International journal of cardiology*. 2016;222:1012-8.
- American Diabetes Association. Standards of Medical Care in Diabetes.2014;37(3):887.
- Al-Rubeaan K, Al-Hussain F, Youssef AM, Subhani SN, Al-Sharqawi AH, Ibrahim HM. Ischemic stroke and its risk factors in a registry-based large cross-sectional diabetic cohort in a country facing a diabetes epidemic. *Journal of diabetes research*. 2016. Article ID 4132589, 9 pages <http://dx.doi.org/10.1155/2016/4132589>
- Mahmood A, Sharif MA, Khan MN, Ali UZ. Comparison of serum lipid profile in ischaemic and haemorrhagic stroke. *J Coll Physicians Surg Pak*. 2010;20(5):317-20.
- Aquil N, Begum I, Ahmed A, Vohra EA, Soomro BA. Risk factors in various subtypes of ischemic stroke according to TOAST criteria. *J Coll Physicians Surg Pak*. 2011;21(5):280-3.
- Chaudhury SR, Ghosh S, Kar D. Comparative lipid profile study between ischemic and hemorrhagic stroke. *J Chem Pharm Res*. 2014;6(11):20-7.
- Zhang J, Wang Y, Wang G, Sun H, Sun T, Shi J, et al. Clinical factors in patients with ischemic versus hemorrhagic stroke in East China. *World journal of emergency medicine*. 2011;2(1):18-23.
- Osama A. Khalil, Fayrouz O. Selim, Hazem M. El-A. Prevalence and Pattern of Dyslipidemia in Acute Cerebral Infarction in Medical Intensive Care in Egypt. *British Journal of Science* 2013;10 (1): 51-66.
- Khan NI, Naz L, Mushtaq S, Rukh L, Ali S, Hussain Z. Ischemic stroke: prevalence of modifiable risk factors in male and female patients in Pakistan. *Pakistan journal of pharmaceutical sciences*. 2009; 22(1):62-67.