Journal of Physical Chemistry and Functional Materials

Home Page of Journal: https://dergipark.org.tr/jphcfum

Investigation of thyroid function tests and lipid levels in cerebrovascular patients

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ABSTRACT

Worldwide, cerebrovascular diseases rank third as the cause of death after heart diseases and cancer, and ranks first as the cause of handicap and disability. It is a disease that needs to be well known and recognized, especially due to the high risk of mortality in the acute period and the severe loss of function in the majority of surviving patients, requiring long-term care and assistance. In this study, it is aimed to contribute to the literature and to examine the relationship between thyroid dysfunction and cerebrovascular diseases in patients with hyperlipidemia. When the patient and control groups were evaluated in terms of blood lipid levels, HDL levels were found to be significantly lower in the patient group compared to the control group. VLDL, TG and cholesterol levels were found to be significantly higher in the patient group compared to the control group. The T3 value was found to be statistically significantly lower in the patient group. In some cases, such as hyperthyroidism, hypothyroidism and hyperlipidemia, it may not show serious clinical symptoms, which increases the importance of these investigations. We believe that the detected thyroid dysfunction and dyslipidemia treatments will decrease the acute stroke prevalence and improve the prognosis.

ARTICLE INFO

Keywords:
Cerebrovascular
Cholesterol
Lipid
Thyroid
Triglyceride

Received: 2024-03-28
Accepted: 2024-04-16
ISSN: 2651-3080
DOI: 10.54565/jphcfum.1459969

1. Introduction

Cerebrovascular disease (CVD) is defined as the temporary or permanent involvement of a certain region of the brain as a result of bleeding or ischemia and / or the primary pathological damage of one or more blood vessels involving the brain. A large number of unrelated risk factors that facilitate the formation process of the disease have been identified. Heart disease (HD), hypertension (HT), diabetes mellitus (DM), atrial fibrillation (AF), and hyperlipidemia are some of the definite risk factors. According to the criteria of the World Health Organization (WHO), stroke is a focal or generalized neurological deficit that occurs suddenly, lasts more than 24 hours or ends with death in this time, for which no other cause is presented from a vascular cause, and that is focal or generalized. According to the population, cerebrovascular diseases are the second leading cause of death in the world, after coronary heart diseases over the age of sixty. It is seen as the primary cause of loss of work force and disability [1-4].

Unclear links between cerebrovascular diseases and thyroid dysfunctions have begun to be presented. Cardioembolic stroke is directly associated with thyrotoxic AF in marked hyperthyroidism, and the incidence of AF is increasing in subclinical hyperthyroidism. There is insufficient evidence to suggest that overt hypothyroidism is associated with risks of atherosclerosis, particularly HT, hyperhomocysteinemia and hyperlipidemia. In subclinical hypothyroidism, the certainty of this relationship is rather insufficient [5-8].

In this study, it is aimed to examine the connection between thyroid dysfunction and cerebrovascular diseases in patients with hyperlipidemia and to contribute to the literature.

2. Materials and Methods

The study was conducted between the dates of 02.06.2019 and 31.12.2019, with a retrospective examination of 379 people, 250 of whom were patient group and 129 as control group, who applied to Istanbul Erenköy Mental and Neurology Training and Research Hospital Neurology Polyclinic with a diagnosis of cerebrovascular disease.

This research was based on Helsinki Principle's Declarations. The study protocol was approved by the Institutional Ethics Committee for Research on Human Subjects of Firat University (number and date 05/30, 28.03.2019, respectively) and all participants signed an informed written consent form prior to the study. All the information was kept confidential.

TSH, Total T3, Total T4 were routinely examined among the thyroid function tests of the patients included in the study. For lipid parameters, total cholesterol and high density lipoprotein (HDL), low density lipoprotein (LDL) levels, very low density lipoprotein (VLDL) and triglyceride levels were routinely measured. The samples were taken in mm of blood at the blood serum level and combined in cuvettes with their own test kits and they were routinely examined photometrically in the Abboot Brand Ci4100 Autoanalyzer. The anamnesis of the patients, who were preferred to be included in the study, were scanned and the file information of the patients was examined. Whether the patient had coronary heart disease, HT, arrhythmia, hyperlipidemia, MI, DM, thyroid dysfunction and whether he/she was treated for these diseases were recorded in their history. Neurological and systemic examination epicrises on admission were evaluated. Electrocardiography results were recorded in terms of blood glucose and blood pressure values measured at the time of admission to the hospital and rhythm irregularity. Lipid parameter values and thyroid function tests data were recorded during the patient's hospitalization.

Thyroid function tests and lipid parameters were routinely examined photometrically by taking mm of blood at the blood serum level in the Abboot Brand Ci4100 Autoanalyzer Device, combined with its own test kits in cuvettes.

2.1. Statistical Evaluation

Statistical evaluations in the study were carried out in the SPSS 22.0 program. In addition to descriptive statistical methods (standard deviation, mean) for the analysis of the data, one-way analysis of variance was used for the comparison of the data, and the Chi-square test for the comparison of qualitative findings. The significance level of the results was evaluated at $p<0.05$.

3. Results

In this study, 379 subjects aged between 15 and 100 years were analyzed retrospectively. Thyroid function tests and lipid parameters were evaluated as 145 male, 105 female, 250 of these subjects as the patient group, 56 male, and 73 female (totally 129) as control group. The patient group was determined from those who were admitted or hospitalized with a diagnosis of CVD, and the control group was determined from those who did not have CVD who applied to the neurology outpatient clinic. HDL, Triglyceride (TG), LDL, Cholesterol, TSH, T3, T4 and VLDL values of the patient and control group included in the study were taken and compared statistically.

The mean age of the treatment group was 69.4±13.2, and the control group was 55.7±18.5. There were 145 males and 105 females in the treatment group while there were 56 male and 73 female cases in the control group (Table 1).

Table 1. Demographic characteristics of patient and control groups

	Patient	Control
Age	69.4±13.2	55.7±18.5
Gender	145M+105F	56M+73F

When the treatment and control groups were evaluated in terms of blood lipid levels, HDL levels were found to be significantly lower in the treatment group compared to the control group *($p<0.001$). VLDL and TG levels were found to be significantly higher in the treatment group compared to the control group. *($p=0.006$, $p=0.006$, respectively). No statistically significant difference was found between the treatment and control groups in terms of LDL levels. Cholesterol levels in the treatment group were found to be significantly higher than the control group *($p<0.001$) (Table 2).

Table 2. Blood lipid levels in the treatment and control groups

	HDL	LDL	VLDL	Triglyceride	Cholesterol
Patient	37.1± 9.68	134±65.4	32.2±23.9*	161±119*	221±48.1*
Control	49.1±10.6*	128±40.6	26.8±15.8	134±79.1	176±40.7

When the treatment and control groups were compared, the T3 value was found to be statistically significantly lower in the treatment group compared to the control group. No statistically significant difference was found between the treatment and control groups in terms of T4 and TSH values. ($p=0.942$, $p=0.095$, respectively) (Table 3).

Table 3. Evaluation of average T3, T4 and TSH in treatment and control groups

	T3	T4	TSH
Patient	2.34±0.407*	1.04±0.158	1.68±1.93
Control	2.77±1.16	1.05±0.264	1.83±1.91

4. Discussion

Stroke is a very serious health problem due to the fact that it takes the third place among the causes of mortality in all countries of the world and because of the long-term disability in morbidity [9]. Many risk factors for cerebrovascular diseases have been identified with epidemiological data. While race, gender, age, and pedigree are among the risk factors that cannot be changed, DM, HT, HD, obesity, hyperlipidemia, eating habits and hemostatic factors are among the risk factors that can be changed [10-13].

Cerebrovascular diseases are basically diseases whose incidence increases as age increases [14]. In our study, the risk of developing stroke increased as the age increased. Thyroid diseases also increase with age. In a study conducted on 344 healthy individuals over the age of 60, they found that the rate of TSH (TSH) was significantly higher in 22 individuals (5.9%). Free T4 (ST4) and serum thyroxine (T4) levels were found to be low in 10 of these 22 individuals [15]. In another study they conducted, TFB was transmitted more in female individuals (5.9%) than male individuals (2.3%) [16]. As a result of their studies, Cappola et al. [17] found that subclinical thyroid dysfunction is more common in women than in men. Thyroid dysfunction was more common in women in our retrospective study. In another study, it was concluded that hypothyroidism has positive results on both prognosis and clinical presentation in acute stroke. The reason for this has been shown the decrease of sensitivity in patients with hypothyroidism against adrenergic stimulus, which increases during acute stress [18]. Thyroid hormones have various effects on the cardiovascular system [19]. Hyperthyroidism has various effects on the cardiovascular system, such as systolic hypertension, sinus tachycardia, diastolic function and ventricular systolic changes, changes in peripheral vascular resistance and rhythm disturbances, especially increased tendency to atrial fibrillation, and many clinical symptoms of hyperthyroidism develop due to the effects of thyroid hormones on the cardiovascular system [20]. Thyroid hormone directly increases myocardial inotropy and heart rate. T3 decreases peripheral vascular resistance (PVR) and increases cardiac output by dilating the resistant arterioles of the peripheral circulation. In hyperthyroid patients, there is more than 50% reduction in PVR [21]. In the study conducted by Walsh et al. [22] when the subclinical hypothyroid group of 105 people was compared with the euthyroid group of 1859, it was concluded that hypothyroidism was not associated with hypertension. In the same study, blood pressure was found to be higher in 35 subclinical hyperthyroid patients compared to the euthyroid group [22]. Since our study is a retrospective study, patients do not have any recorded information about blood pressure. In a study of 20 patients with iatrogenic subclinical hyperthyroidism, Biondi et al. [23] found that atrial premature beats were higher and mean heart rate increased by 20% compared to the control group. They found left ventricular hypertrophy in 6 of 20 patients on echocardiography [23]. In the study conducted by Cappola et al. [17] on 3233 individuals over 65 years of age, no difference was found between the subclinical hyperthyroidism, hypothyroidism and subclinical hypothyroid group and the euthyroid group between coronary artery disease, cerebrovascular disease, cardiovascular diseases and mortality [17]. In our retrospective study, no significant difference was found between patients with cerebrovascular disease and thyroid except for T3 levels.

As a result, the treatment of thyroid dysfunction, which is determined as the thyroid function tests should be controlled in cerebrovascular patients, has an important role in preventing the progression of cerebrovascular disease and improving the prognosis.

It has been observed in more than one study that there is a continuous and strong relationship between serum cholesterol level and atherosclerotic vascular disease. Atherosclerosis plays a primary role in the most common thromboembolic form of stroke [24]. Atherosclerotic plaques are rich in cholesterol and cholesterol esters made up of lipoproteins in the blood. Atherosclerosis can be caused by a diet rich in cholesterol in experimental animals. LDL is the richest lipoprotein of cholesterol. The risk is also increased in hyperlipidemia rich in VLDL. The relationship with HDL is inversely proportional. HDL cholesterol below 35 mg/dL is an independent risk factor for the development of atherosclerosis. Hyperthyroidism decreases the total LDL level by increasing the LDL turnover, the HDL level does not change or decrease. Formation and transport of lipoproteins are severely impaired in patients with hypothyroidism. Hypothyroidism is characterized by hypercholesterolemia and increases in LDL and apoprotein B levels. Fractional LDL clearance decrease due to the decreasing of LDL receptors in the liver of these patients. HDL levels are normal or may be elevated in severe hypothyroidism. In these patients, hepatic lipase and cholesterol ester transfer protein activity, which are enzymes that regulate thyroid hormone, decreased. Subclinical hypothyroidism is characterized by normal or moderately elevated total cholesterol levels, an increase in LDL level and a decrease in HDL level [25]. In the study of Kanaya et al. [26], it was found that the cholesterol level was increased in patients with high TSH levels, and the cholesterol level was decreased in patients with low TSH levels. When compared with the control group, it was observed that the total and LDL cholesterol levels were significantly higher and the carotid artery intima-media thickness (IMT) increased. After L-thyroxine replacement therapy total and LDL cholesterol 63 levels and IMT were decreased [27]. Treatment of stroke is difficult and still ineffective. Therefore, the main goal is

protection from stroke. Prevention of stroke has been proven by correcting modifiable risk factors [28].

For many years, lipid abnormalities have been suspected to cause atherosclerosis, and numerous epidemiological and cohort studies found a strong relationship between the incidence of diseases on the basis of atherosclerosis, such as ischemic heart disease, stroke and peripheral vascular disease, and total cholesterol (TC), low density lipoprotein (LDL), and high-density lipoprotein (HDL). Recent studies show that, apart from these traditional serum lipid markers, TC / HDL, LDL / HDL, Triglyceride (TG) / HDL ratios may be better predictors of vascular risk [29,30].

Most epidemiological studies have found an association between high cholesterol levels and increased risk of ischemic stroke. Overall, epidemiological studies indicate that higher total cholesterol levels may be associated with an increased risk of ischemic stroke. In addition, a relationship has been found between cholesterol levels and carotid artery atherosclerosis [31]. Hyperlipidemia was present in 16% of stroke patients, and in the Khan et al. [32] and Tanveer's study [33], hyperlipidemia was the third most common risk factor in stroke. In the study of Mahmood et al. [34], it was determined as a risk factor in 21% of 200 stroke patients. Among many cardiovascular risk factors, increased cholesterol level is one of the important factors that play a role in the development of atherosclerosis despite the absence of other known risk factors [35].

Similarly, in the study of Nirmala et al. [36], TC, TG, LDL, VLDL, TK / HDL, LDL / HDL ratios were found to be significantly higher in young stroke patients compared to controls, and a positive correlation was found with the risk of stroke. In our study, in support of this research, cholesterol triglyceride levels in stroke patients were found to be significantly higher than controls.

Triglyceride / HDL ratio is an indicator of harmful low density LDL particles. High LDL, together with high TG and HDL levels, causes a greater risk of developing coronary artery disease compared to LDL elevation alone [37,38].

In the study of Park et al. [39] the risk of major vascular events and recurrent stroke was found to be significantly higher in the 2-year follow-up of patients with high TG / HDL ratio, so it was stated that it may have prognostic value in detecting patients with high risk for recurrent stroke.

Low molecular weight cholesterol is considered as enatherogenic lipoprotein and constitutes the majority of cholesterol in plasma. In the study of Nirmala et al. [36], serum levels were found to be significantly higher in stroke patients. Lipoprotein metabolism shows some changes with age. The most important factor affecting the cholesterol level is changes in body weight. Cholesterol levels increase slowly in women between the ages of 25 and 55, but this increase is slower than in men. Age-related changes in cholesterol metabolism are mainly manifested as LDL elevation; HDL levels depending on the age do not change and are generally about 10 mg/dL higher in women than men [40,41]. Therefore, the result we found in our study is due to the fact that the LDL value increases faster with age in males than in females, and the HDL values in males are lower than those in females.

Conclusion

In conclusion, dyslipidemia, one of the intervenable risk factors in the etiology of cerebrovascular disease, has an important role in the development of atherosclerosis. The fact that our study was conducted retrospectively created a limitation in our study. However, it can be emphasized that it can be a stimulant in determining the risk of stroke by knowing only the TG / HDL ratio. Regardless of the underlying etiology, there is a significant increase in t cholesterol values in cerebrovascular patients compared to the healthy population. Especially in ischemic stroke patients, TG / HDL ratio is higher than the control group. Since studies show that the lipid parameters of cholesterol triglyceride and LDL-C elevation have prognostic value in terms of recurrent stroke, the ratio of lipid parameters should be determined regardless of the etiology detected in stroke patients.

Acknowledgement

This study was produced from the master thesis of Taner ADSIZ from Firat University, Institute of Sciences, Department of Biotechnology.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

References

[1] P. Thorvaldsen, K. Asplund, K. Kuulasma, A.M. Rajakangas, M. Schroll, "Stroke incidence, case fatality and mortality in the WHO MONICA Project. World Health Organization monitoring trends and determinants in cardiovascular disease" *Stroke*, 26, 361-367, 1995.

[2] N. Ünivar, S. Mollahaliloğlu, N. Yardım, "Türkiye Hastalık Yükü Çalışması (In Turkish)", Ankara, 2004.

[3] K.S. Yew, E. Cheng, "Acute stroke diagnosis" *American Academy of Family Physicians*, 80, 33-40, 2009.

[4] B. Ovbiagele, L.B. Goldstein, R.T. Higashida, V.J. Howard, S.C. Johnston, O.A. Khavjou, D.T. Lackland, J.H. Lichtman, S. Mohl, R.L. Sacco, J.L. Saver, J.G. Trogdon, "Forecasting the future of stroke in the United States: a policy statement from the American Heart Association and American Stroke Association" *Stroke*, 44, 361-2375, 2013.

[5] C.K. Glass, J.M. Holloway, "Regulation of gene expression by the thyroid hormone receptor" *Biochimica et Biophysica Acta*, 1032, 157-176, 1990.

[6] G.A. Brent, D.D. Moore, P.R.Larsen, "Thyroid hormone regulation of gene expression" *Annual Review of Physiology*, 53, 17-35, 1991.

[7] G.S. Levey, I. Klein, "Disorders of the thyroid and Stein's textbook of medicine" 2nd edition, Brown, 1994.

[8] P.A. Masters, R.J. Simons, "Clinical use of sensitive assays for thyroid–stimulating hormone" *Journal of General Internal Medicine*, 11, 115-127, 1996.

[9] R. Bonita, "Epidemiology of stroke" *The Lancet*, 339, 342-344, 1992.

[10] R.D. Adams, M. Victor, H.A. Ropper, H.B. Brown, "Principles of Neurology" 8th ed. USA Mc Graw Hill Co. 34, 660-746, 2006.

[11] S. Balkan, "Serebrovasküler Hastalıklar (In Turkish)", Güneş Kitabevi, 2005.

[12] A.R. Folsom, W.D. Rosamond, E. Shahar, L.S. Cooper, N. Aleksic, F.J. Nieto, M.L. Rasmussen K.K. Wu, "Prospective study of markers of hemostatic function with risk of ischemic stroke. The Atherosclerosis Risk in Communities (ARIC) Study Investigators" *Circulation*, 100, 736-742, 1999.

[13] T. Ohira, E. Shahar, L.E. Chambless, W.D. Rosamond, T.H. Jr. Mosley, A.R. Folsom, "Risk factors

for ischemic stroke subtypes: The Atherosclerosis Risk in Communities study" *Stroke*, 37, 2493-2498, 2006.
[14] J. Broderick, T. Brott, R. Kothari, R. Miller, J. Khoury, A. Pancioli, J. Gebel, D. Mills, L. Minneci, R. Shukla, "The Greater Cincinnati/Northern Kentucky Stroke Study: preliminary first-ever and total incidence rates of stroke among blacks" *Stroke*, 29, 415-421, 1998.
[15] C.T. Sawin, D. Chopra, F. Azizi, J.E. Mannix, P. Bacharach, "The aging thyroid. Increased prevalence of elevated serum thyrotropin levels in the elderly" *JAMA: The Journal of the American Medical Association*, 242, 247-250, 1979.
[16] C.T. Sawin, W.P. Castelli, J.M. Hershman, P. McNamara, P. Bacharach, "The aging thyroid. Thyroid deficiency in the Framingham Study" *Archives of Internal Medicine*, 145, 1386-1388, 1985.
[17] A.R. Cappola, L.P. Fried, A.M. Arnold, M.D. Danese, L.H. Kuller, G.L. Burke, R.P. Tracy, P.W. Ladenson, "Thyroid status, cardiovascular risk, and mortality in older adults" *JAMA: The Journal of the American Medical Association*, 295, 1033-1041, 2006.
[18] V. Kotsis, M. Alevizaki, S. Stabouli, V. Pitiriga, Z. Rizos, M. Sion, N. Zakopoulos, "Hypertension and hypothyroidism: results from an ambulatory blood pressure monitoring study" *Journal of Hypertension*, 25, 993-999, 2007.
[19] I. Klein, K. Ojamaa, "Thyroid hormone and the cardiovascular system" *New England Journal of Medicine*, 344, 501-509, 2001.
[20] F. Osman, J.A. Franklyn, R.L. Holder, M.C. Sheppard, M.D. Gammage, "Cardiovascular manifestations of hyperthyroidism before and after antithyroid therapy: a matched case-control study" *Journal of the American College of Cardiology*, 49, 71-81, 2007.
[21] J. Faber, N. Wiinberg, S. Schifter, J. Mehlsen, "Haemodynamic changes following treatment of subclinical and overt hyperthyroidism" *European Journal of Endocrinology*, 145, 391-396, 2001.
[22] J.P. Walsh, A.P. Bremner, M.K. Bulsara, P. O'Leary, P.J. Leedman, P. Feddema V. Michelangeli, "Subclinical thyroid dysfunction and blood pressure: a communitybased study" *Clinical Endocrinology*, 65, 486-491, 2006.
[23] B. Biondi, S. Fazio, C. Carella, G. Amato, A. Cittadini, G. Lupoli, L. Sacca, A. Bellastella, G. Lombardi, "Cardiac effects of long term thyrotropin-suppressive therapy with levothyroxine" *Journal of Clinical Endocrinology & Metabolism*, 77, 334-338, 1993.
[24] R. Benfante, K. Yano, L.J. Hwang, J.D. Curb, A. Kagan, W. Ross, "Elevated serum cholesterol is a risk factor for both coronary heart disease and thromboembolic stroke in Hawaiian Japanese men. Implications of shared risk" *Stroke*, 25, 814-820, 1994.
[25] L.H. Duntas, "Thyroid disease and lipids" *Thyroid*, 12, 287-293, 2002.
[26] A.M. Kanaya, F. Harris, S. Volpato, E.J. Perez-Stable, T. Harris, D.C. Bauer, "Association between thyroid dysfunction and total cholesterol level in an older biracial population: the health, aging and body composition study" *Archives of Internal Medicine*, 162, 773-779, 2002.
[27] F. Monzani, N. Caraccio, M. Kozakowa, A. Dardano, F. Vittone, A. Virdis, S. Taddei, C. Palombo, E. Ferrannini, "Effect of levothyroxine replacement on lipid profile and intima-media thickness in subclinical hypothyroidism: a double-blind, placebo controlled study" *Journal of Clinical Endocrinology and Metabolism*, 89, 2099-2106, 2004.
[28] K. Sreedhar, B. Srikant, L. Joshi, G. Usha, "Lipid profile in non-diabetic stroke-a study of 100 cases" *Journal of the Association of Physicians of India*, 58, 547-551, 2010.
[29] V. Bittner, R. Hardison, S.F. Kelsey, B.H. Weiner, A.K. Jacobs, G. Sopko, "Bypass Angioplasty Revascularization Investigation. Non-high-density lipoprotein cholesterol levels predict five-year outcome in the Bypass Angioplasty Revascularization Investigation (BARI)" *Circulation*, 106, 2537-2542, 2002.
[30] P.M. Ridker, N. Rifai, N.R. Cook, G. Bradwin, J.E. Buring, "Non-HDL cholesterol, apolipoproteins A-I and B100, standard lipid measures, lipid ratios, and CRP as risk factors for cardiovascular disease in women" *JAMA: The Journal of the American Medical Association*, 294, 326-333, 2005.
[31] J.F. Meschia, C. Bushnell, B. Boden-Albala, L.T. Braun, D.M. Bravata, S. Chaturvedi, M.A. Creager, R.H. Eckel, M.S.V. Elkind, M. Fornage, L.B. Goldstein, S.M. Greenberg, S.E. Horvath, C. Iadecola, E.C. Jauch, W.S. Moore, J.A. Wilson, "American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Functional Genomics and Translational Biology; Council on Hypertension. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association" *Stroke*, 45, 3754-3832, 2014.
[32] H. Khan, A.K. Afridi, A. Saadia, "A hospital based study on stratification of risk factors of stroke in Peshawar" *Pakistan Journal of Medical Sciences*, 22, 304-307, 2006.
[33] A. Tanveer, "Localization and management in Cerebrovascular accident: a comparison of clinical assessment versus C.T scan" *Journal of the College of Physicians and Surgeons Pakistan*, 3, 5-6, 1996.
[34] A. Mahmood, M.A. Sharif, M.N. Khan, U.Z. Ali, "Comparison of serum lipid profile in ischaemic and haemorrhagic stroke" *Journal of the College of Physicians and Surgeons Pakistan*, 20, 317-320, 2010.
[35] E.K. Çoban, "Gençlerde iskemik serebrovasküler olay risk belirlemesinde Trigliserit/HDL oranı iyi bir öngörücü olabilir mi? (In Turkish)" *Medical Bulletin of Sisli Etfal Hospital*, 52, 201-205, 2018.
[36] A.C. Nirmala, T.N. Mamatha, P. Shree, B.H. Avinash, "Study of lipid profile in non-diabetic stroke in young" *Scholars Journal of Applied Medical Sciences*, 3, 1259, 2015.
[37] C.M. Ballantyne, A.G. Olsson, T.J. Cook, M.F. Mercuri, T.R. Pedersen, J. Kjekshus, "Influence of low high-density lipoprotein cholesterol and elevated triglyceride on coronary heart disease events and response to simvastatin therapy in 4S" *Circulation*, 104, 3046-3051, 2001.
[38] F. Barzi, A. Patel, M. Woodward, C.M.M. Lawes, T. Ohkubo, D. Gu, T.H. Lam, H. Ueshima, "Asia Pacific Cohort Studies Collaboration. A comparison of lipid variables as predictors of cardiovascular disease in the Asia Pacific region" *Annals of Epidemiology*, 15, 405-413, 2005.

[39] J.H. Park, J. Lee, B. Ovbiagele, "Non-traditional serum lipid variables and recurrent stroke risk" *Stroke*, 45, 3269-3274, 2014.
[40] R.A. Kreisberg, S. Kasim, "Cholesterol metabolism and aging" *American Journal of Medicine*, 82, 54-60, 1987.
[41] A. Ferrara, E. Barrett-Connor, J. Shan, "Total, LDL, and HDL cholesterol decrease with age in older men and women. The Rancho Bernardo Study 1984-1994" *Circulation*, 96, 37-43, 1997.