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Serum gp91^{phox}/NOX2 Level Among Patients with Subclinical Hypothyroidism, and Its Relation to Atherogenic Indices

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Abstract

Background and objectives: Subclinical hypothyroidism is emphasized by a normal serum-free thyroxin4 concentration as well as an elevated thyroid stimulating hormone concentration, Gp91^{phox}, the catalytic key of nicotinamide-adenine-dinucleotide-phosphate-oxidase and predictor of its activation, has lately been examined as an indicator of systemic oxidative. The current study aimed to assess the level of serum gp91phox among patients with subclinical hypothyroidism.

Methods: The current case-control study included 160 participants: 80 newly diagnosed subclinical hypothyroidism patients were obtained from the Diabetic and Endocrinology Unit at Azadi Teaching Hospital, and 80 healthy individuals, lasted eight months from November 2022 to July 2023. Lipid profile and thyroid function tests have been done for. The serum soluble gp91phox level was compared between both groups.

Results: The mean serum gp91phox was higher among subclinical hypothyroidism cases (9.06 ± 4.80 ng/mL) than among healthy individuals (7.40 ±3.42 ng/mL). There was a statistically significant elevation of the mean of atherogenic-index of plasma in cases (0.39, p. value = 0.049) compared to the controls (0.30, p. value = 0.049), and the mean of Castelli Risk Index II in cases (2.18, p. value = 0.008) was significantly greater than that of the controls (1.86, p. value = 0.008) in subclinical hypothyroidism.

Conclusion: There was a significantly higher mean serum level of gp91^{phox}/NOX2 in patients with subclinical hypothyroidism.

Keywords: Atherogenic indexes, Gp91^{phox}/NOX2, SCH, Subclinical hypothyroidism

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Introduction

Subclinical hypothyroidism (SCH) is described as a combination of a normal serum free T4 concentration and a high thyroid stimulating hormone (TSH) concentration.[1] As the majority of patients with SCH are free of signs and symptoms, therefore; the diagnostic precision of those patients is entirely dependent on the laboratory test results.[2] Worldwide, Subclinical hypothyroidism has a high range of prevalence, between 3% and 15%, as well as being more common in women and elderly people.[3] The two most common causes of subclinical hypothyroidism are iodine deficiency and autoimmune thyroiditis.[3] Subclinical hypothyroidism can be regarded as a common risk factor for the development of overt hypothyroidism and cardiovascular disorder (CVD), as it is associated with the development of atherosclerosis, disturbance of blood pressure, dyslipidemia, hypercoagulability, and endothelial dysfunction.[4,5] Dyslipidemia can be defined as a disturbance of blood lipid metabolism (increase serum low-density lipoprotein cholesterol, triglycerides, and total cholesterol, and decrease high density lipoprotein cholesterol).[6] It is a major risk factor for cardiovascular diseases.[5] Moreover, various studies have shown that plasma lipid indices or factors that contribute to atherosclerosis (such as the plasma atherogenic index, the Castelli Risk Index I and II, the atherogenic coefficient, and non-HDL cholesterol) that are calculated from lipid outline parameters which was shown superior forecasting capacity in cardiovascular diseases.[7,8] Oxidative stress is described as an imbalance between free radicals (increased) and antioxidants (decreased).[9] Different studies showed different results regarding the association between Subclinical hypothyroidism and oxidative stress and its markers.[9,10] Nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (NOX) is a key oxidase in the production of reactive oxygen species (ROS) in the cardiovascular system; its activation promotes the development and advancement of atherosclerotic illnesses.[11,12] Gp91^{phox}/ NOX2, a measure of systemic oxidative stress, has been identified as the catalytic core of NADPH oxidase and a sign of its activation, as it is involved in the electron transfer from NADPH to molecular oxygen.[13] The present study was sought to evaluate the degree of serum Gp91^{phox} among subclinical hypothyroid patients compared to the euthyroid control group, and to assess the relationship between different serum TSH levels, as well as atherogenic indices of plasma among SCH patients.

Patients and methods

The current case-control study was carried out in Azadi Teaching Hospital, Duhok City, KRG - Iraq, covering a period of 8 months' interval from November 2022 to July 2023. Besides, the present study included a total of 160 respondents; 80 of them joined the endocrine and diabetes unit of the medicine department in Azadi Teaching Hospital, where they were newly diagnosed with subclinical hypothyroidism, and another 80 were healthy volunteers regarded as control euthyroid participants that had been chosen from family, friends, and relatives. They were of similar age and gender distribution. Recently diagnosed subclinical hypothyroidism depends on a serum level of TSH greater than 4.2 and free T4 within the normal range.[14] Exclusion criteria include chronic inflammation, diabetes mellitus, neoplasm, smoking, alcohol, medication, recent severe illness, and pregnancy (as this impacts the serum level of gp91^{phox}/NOX2). A meeting interview was held to fulfill the study's requirements by completing a prepared questionnaire form. The questionnaire comprised items regarding the respondent's name, age, date of birth, gender, and a history of thyroid disorders in the

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family, diabetes mellitus, and cardiovascular disease. The study collected anthropometric data encompassing height (in centimeters), body weight (in kilograms), and waist circumference, and the body mass index (BMI) is computed by dividing the weight (in kilograms) by height squared (in meters). Body mass index can be categorized as following: underweight BMI<18.5 kg/m^2, normal weight BMI 18.5–24.9 kg/m^2, overweight BMI 24.9–29.0 kg/m^2, as well as BMI ≥ 30 kg/m^2 considered obese.[15] All participants have been informed to attend Mazi Medical Complex, clinical biochemistry unit of the laboratory department, in the morning, and after an overnight fast, 5 ml of blood samples have been drawn from respondents into gel vacutainer tubes and centrifuged for 20 minutes at 3000 revolutions per minute. For further analysis, serum samples were divided into aliquots, which were organized at -80°C (thermos-fischer Scientific, USA) in a freezer.The serum-soluble gp91^{phox}/NOX2 level was measured by an enzyme-linked immunosorbent assay, depending on the antigen-antibody reaction and the enzymatic reaction. The Cobas 6000 (Hitachi, Roche) was used to measure all other parameters, employing various principles. Hormones such as thyroid stimulating hormone, fT4, fT3, and TPO had to depend upon electrochemiluminescence immunoassay, whereas the lipid profiles depended upon the enzymatic colorimetric method. The cutoff used for serum-soluble gp91phox (NADPH oxidase 2) was (6.1 ± 0.5 ng/mL), serum TSH (0.2–4.2 microIU/mL), free T4 level (12–22 pmol/ml), free triiodothyronine (3.1–6.8 pmol/ml), and anti-TPO (below 30 IU/mL).[16] The cutoff values used for lipid profiles depended on the national cholesterol education program.[17] The atherogenic indices of lipid were as stated: log TG/HDL-c is the atherogenic index of plasma (AIP), (less than 0.11 is correlated with low risk of CVD; the values between 0.11 and 0.21 and further than 0.21 are related to intermediate as well as enhanced risks, respectively), Castelli's Risk Index (CRI-I) = TC/HDL-c (risky CRI I value ≥5.0), Castelli's Risk Index (CRI-II) = LDL-c/HDL-c (risky CRI II value ≥3.0), atherogenic Coefficient (AC) = (TC-HDL-c)/HDL-c (risky AC value >2.1).[18] The data were analyzed utilizing the Statistical Package for Social Sciences (SPSS, version 26). The Chi-square test of relationship was employed to compare the proportions of the two research groups. In this regard, Fisher's exact test was employed when the anticipated frequency (value) decreased below 5 or exceeded 20% in any of the table's cells. Hence, A student's t-test (unpaired t-test). for two independent samples was used to compare the means of the two research groups. While a p-value of ≤ 0.05 was deemed statistically significant. All participants gave their written consent prior to participating, and the Ethics Committee of the Duhok Directorate of Health and the Kurdistan Higher Council of Medical Specialties approved the study (26102022-8-8, October 26, 2022).

Results

Eighty cases with SCH were involved in the present study (cases), and 80 healthy individuals. The mean age (SD) of cases was 33.4 (8.9) years, and that of the control was 32.8 (8.6) years (p = 0.659). The majority of the participants (77.5%) were aged less than 40 years. The majority (75%) of them females (p = 1.000). It is evident in Table 1 that around three quarters of the cases were either over-weight (35%) or obese (38.8%) compared with 17.9% over-weight controls (p < 0.001). More than half (53.8%) of cases were with high waist circumference, compared with 42.5% of group of control (p = 0.154) Table (1).

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Table (1): Basic features of study respondents.

	Case	Control	Total	p. value
Age (years)				
< 40	61 (76.3)	63 (78.8)	124 (77.5)	
≥ 40	19 (23.8)	17 (21.3)	36 (22.5)	0.705*
Mean (SD)	33.4 (8.9)	32.8 (8.6)		0.659†
Gender				
Male	20 (25.0)	20 (25.0)	40 (25.0)	
Female	60 (75.0)	60 (75.0)	120 (75.0)	1.000*
BMI (Kg/m^2)				
Normal	21 (26.3)	64 (82.1)	85 (53.8)	
Over-weight	28 (35.0)	14 (17.9)	42 (26.6)	
Obese	31 (38.8)	0 (0.0)	31 (19.6)	< 0.001**
Mean (SD)	28.7 (5.3)	23.6 (1.7)		< 0.001†
Waist circumference				
Normal	37 (46.3)	46 (57.5)	83 (51.9)	
High	43 (53.8)	34 (42.5)	77 (48.1)	0.154*
Mean (SD)	92.1 (13.7)	89.3 (13.0)		0.193†
Total	80 (100.0)	80 (100.0)	160 (100.0)	

Source: Authors from SPSS outputs.
*By Chi-square test. The remaining p-values were computed using the unpaired t-test.

The mean Anti-TPO of cases (54.37 IU/mL), it was significantly ($p < 0.001$) higher than that of the control group (16.52 IU/mL). More than one third (36.3%) of cases had Anti-TPO level of ≥ 30 IU/mL, compared with 8.8% of the control group ($p < 0.001$). The mean of gp91^{phox}/NOX2 was significantly ($p = 0.013$) higher among cases (9.06 ng/mL) than among the controls (7.40 ng/mL) as illustrated in Table (2).

Table (2): Biochemical measurements of study respondents

	Case		Control		
	Mean	SD	Mean	SD	p. value
TSH (microIU/mL)	7.37	2.98	2.57	0.97	< 0.001
T3 (pmol/ml)	4.21	0.82	3.67	0.34	< 0.001
T4 (pmol/ml)	14.70	3.03	16.96	2.02	< 0.001
Anti-TPO (IU/mL)	54.37	82.93	16.52	14.74	< 0.001
Anti-TPO categories No. (%)					
< 30	51	(63.7)	73	(91.3)	
≥ 30	29	(36.3)	7	(8.8)	< 0.001*
Cholesterol (mg/dl)	158.46	29.60	152.65	22.59	0.165
Triglycerides (mg/dl)	120.95	83.42	95.91	44.49	0.019
HDL (mg/dl)	43.55	9.98	45.01	14.30	0.454
LDL (mg/dl)	89.89	25.14	76.65	13.67	< 0.001
gp91^{phox}/NOX2 (ng/mL)	9.06	4.80	7.40	3.42	0.013

*By Chi-square test. The remaining p-values were computed using the unpaired t-test.

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In terms of the Atherogenic Index of Plasma (AIP) (p = 0.382) proportions, there was no statistically significant difference between the control group and cases, but it is evident in Table 3 that the mean AIP of cases (0.39) was higher than that of the controls (0.30), and the difference was significant (p = 0.049). The study did not find between in the proportions and means of CRI-I between the two groups (p = 0.127 and p = 0.513 consecutively). In table 3 shows that 12.5% of cases had CRI-II of ≥ 3 compared with 6.3% of the controls (p = 0.175), but the mean of cases (2.18) was significantly (p = 0.008) further than that of the controls (1.86). No significant differences detected between cases and controls in the proportions and means of the atherogenic coefficient (p = 0.248 and p = 0.513) as presented in Table (3).

Table (3): Atherogenic indices of study participants.

		Case	Control	Total	
		No. (%)	No. (%)	No. (%)	P. value
Atherogenic Index of Plasma (AIP)	Low risk	15 (18.8)	22 (27.5)	37 (23.1)	
	Intermediate risk	18 (22.5)	14 (17.5)	32 (20.0)	
	High risk	47 (58.8)	44 (55.0)	91 (56.9)	0.382*
	Mean (SD)	0.39 (0.29)	0.30 (0.28)		0.049**
CRI_I	< 5	64(80.0)	71 (88.88)	135 (84.4)	
	≥ 5	16 (20.0)	9 (11.3)	25 (15.6)	0.127*
	Mean (SD)	3.83 (1.18)	3.70 (1.24)		0.513**
CRI-II	< 3	70 (87.5)	75 (93.8)	145 (90.6)	
	≥ 3	10 (12.5)	5 (6.3)	15 (9.4)	0.175*
	Mean (SD)	2.18 (0.82)	1.86 (0.66)		0.008**
Atherogenic coefficient (AC)	< 2.1	25 (31.3)	32 (40.0)	57 (35.6)	
	≥ 2.1	55 (68.8)	48 (60.0)	103 (64.4)	0.248*
	Mean (SD)	2.83 (1.18)	2.70 (1.24)		0.513**
Total		80 (100.0)	80 (100.0)	160 (100.0)	

Source: Authors from SPSS outputs.
*By Chi-square test. **By unpaired t-test.

Discussion

The correlation between SCH and elevated levels of oxidative stress and oxidative stress biomarkers for this condition is well-established.[9,19] Accordingly, a significant elevation of the mean gp91^{phox}/NOX2 level among patients with SCH was greater than that of the controls have been observed. This observation can be explained by the fact that increase serum TSH level in patients with SCH will enhance the oxidative process and inflammatory reaction as it is associated with increase IL-6 and TNF-α secretion, which could potentially play a role in the modulation of vascular function through the elevation of NO metabolites.[9,20] Our results were consistent with another study that observed increased oxidative stress and levels of serum gp91^{phox}/NOX2 among patients with SCH.[9] In the present case-control study, the majority of patients with SCH were obese females younger than 40 years old, as well as one third of them had positive TPO. The relationship between SCH and obesity was mostly related to the serum TSH level as well as adipocyte-secreted leptin, the presence of thyroid autoantibodies, and an adaptive response to increase resting energy expenditure.[21,22] TSH directly stimulates preadipocyte differentiation, resulting in adipogenesis.[23,24] Our results were consistent with others, as they showed

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more prevalence of SCH among young obese females with positive TPO antibody.[21,22,25] The exact explanation was not fully understood, but various researches suggested the role of female hormones such as estrogen and a link between subclinical hypothyroidism and autoimmune thyroid disease (Hashimoto's disease).[14,26] Many studies have demonstrated an association between SCH and dyslipidemia. However, the link between SCH and atherogenic indices is less well-documented.[27,28]At the same time, the AIP is more predictive of cardiovascular disease compared to individual lipids, and CRI-II is a more accurate predictor of heart disease risk than LDL alone.[27,29] The present study showed a significantly higher mean level of AIP and CRI-II with a less significantly higher mean level of CRI-I and AC compared to healthy participants. The current results were consistent with the previous one.[30] These abnormalities can be explained by many facts, as thyroid hormones have a crucial role in the regulation of lipid metabolism (synthesis, absorption), such as the induction of the expression of hydroxymethyl glutaryl coenzyme-A reductase in the liver, the mobilization of lipids in adipose tissue, liver, and the enhancement esterification of fatty acids at the hepatic level. The study focuses on the content of fatty acids in lipids and the control of genes involved in lipogenesis and lipolysis.[17,31,32]

Conclusion

Our research revealed that SCH patients have significantly higher mean gp91^{phox}/NOX2 levels compared to euthyroid individuals. Most of the patients were young, obese females. There was a significantly higher mean level of atherogenic indexes, mainly AIP and CRI II, in SCH cases.

Conflict of interest

There is no conflict of interest.

References

1. Chaker L, Cappola AR, Mooijaart SP, Peeters RP. Clinical aspects of thyroid function during ageing. Lancet Diabetes Endocrinol. 2018 Sep;6(9):733-742. doi: 10.1016/S2213-8587(18)30028-7. Epub 2018 Jul 17.
2. Wu K, Zhou Y, Ke S, Huang J, Gao X, Li B, et al. Lifestyle is associated with thyroid function in subclinical hypothyroidism: a cross-sectional study. BMC Endocr Disord. 2021 May 28;21(1):112.
3. Gosi SY, Garla VV. Subclinical Hypothyroidism. Treasure Island (FL): StatPearls Publishing; 2024 Jan.
4. Razvi S, Weaver JU, Pearce SH. Subclinical thyroid disorders: significance and clinical impact. J Clin Pathol. 2010 May;63(5):379-86. doi: 10.1136/jcp.2008.057414/
5. Bhardwaj S, Bhattacharjee J, Bhatnagar MK, Tyagi S. Atherogenic index of plasma, Castelli risk index and atherogenic coefficient - new parameters in assessing cardiovascular risk. Int J Pharm Bio Sci. 2013 Jul-Sep;3(3):359-364.
6. Abid HA, Abid ZS, Abid SA. Atherogenic indices in clinical practice and biomedical research: A short review. BJBABS. 2021;2(2):52. DOI: https://doi.org/10.47419/bjbabs.v2i02.52/
7. Sujatha R, Kavitha S. Atherogenic indices in stroke patients: A retrospective study. Iran J Neurol. 2017 Apr 4;16(2):78–82. PMID: 28761629; PMCID: PMC5526781.
8. Abdullah BI, Salih SF. Lipoprotein (a) level among patients with type 2 diabetes mellitus and prediabetes in comparison with healthy controls. SJUOZ. 2023;11(1):996. DOI: https://doi.org/10.25271/sjuoz.2023.11.1.996/

9. Ma X, Wang F, Zhen X, Zhao L, Fang L, Dong Z, et al. gp91phox, a novel biomarker evaluating oxidative stress, is elevated in subclinical hypothyroidism. Int J Endocrinol. 2020 May 6; 2020:3161730. doi: 10.1155/2020/3161730. Epub 2020.
10. Öztürk Ü, Vural P, Özderya A, Karadağ B, Doğru-Abbasoğlu S, Uysal M. Oxidative stress parameters in serum and low density lipoproteins of Hashimoto's thyroiditis patients with subclinical and overt hypothyroidism. Int Immunopharmacol. 2012 Dec;14(4):349-352. doi: 10.1016/j.intimp.2012.08.010. Epub 2012 Aug 28.
11. Finkel T, Holbrook NJ. Oxidants, oxidative stress and the biology of ageing. Nature. 2000 Nov 9;408(6809):239-247. doi: 10.1038/35041687/
12. Sedeek M, Hébert RL, Kennedy CR, Burns KD, Touyz RM. Molecular mechanisms of hypertension: role of Nox family NADPH oxidases. Curr Opin Nephrol Hypertens. 2009 Mar;18(2):122-7
13. Cangemi R, Celestini A, Calvieri C, Carnevale R, Pastori D, Nocella C, et al. Different behaviour of NOX2 activation in patients with paroxysmal/persistent or permanent atrial fibrillation. Heart. 2012 Jul;98(14):1063-6.
14. Salih S.F. The prevalence of thyroid dysfunction among women with type 2 diabetes mellitus in Duhok. Duhok Medical J. 2015; 9(2): 52-59.
15. Weir CB, Jan A. BMI Classification Percentile and Cut Off Points. Treasure Island (FL): StatPearls; 2023 Jun 26. PMID: 31082114 Bookshelf ID: NBK541070.
16. Gokbulut P, Koc G, Kuskonmaz SM, Onder CE, Omma T, Fırat S, et al. High thyroperoxidase antibody titers may predict response to antithyroid drug treatment in Graves disease: a preliminary study. Acta Endocrinol (Buchar). 2023 Apr-Jun;19(2):195-200.
17. Rastgooye Haghi A, Solhjoo M, Tavakoli MH. Correlation Between Subclinical Hypothyroidism and Dyslipidemia. Iran J Pathol. 2017 Spring;12(2):106–111. PMCID: PMC5831065. PMID: 29515631.
18. Olamoyegun MA, Oluyombo R, Asaolu SO. Evaluation of dyslipidemia, lipid ratios, and atherogenic index as cardiovascular risk factors among semi-urban dwellers in Nigeria. Ann Afr Med. 2016 Oct-Dec;15(4):194-199. doi: 10.4103/1596-3519.194280. PMID: 27853034; PMCID: PMC5402827/
19. Cebeci E, Alibaz-Oner F, Usta M, Yurdakul S, Erguney M. Evaluation of oxidative stress, the activities of paraoxonase and arylesterase in patients with subclinical hypothyroidism. J Investig Med. 2012 Jan;60(1):23-28. doi: 10.2310/JIM.0b013e31823581dd. PMID: 21997314.
20. Wang HC, Dragoo J, Zhou Q, Klein JR. An intrinsic thyrotropin-mediated pathway of TNF-alpha production by bone marrow cells. Blood. 2003 Jan 1;101(1):119-123. doi: 10.1182/blood-2002-02-0544. Epub 2002 Jun 28. PMID: 12393601.
21. Closs C, Vargas-Uricoechea H, Schwarzstein D, Lobo M, Lagranja E, Godinez-Leiva E, et al. Relationship of Subclinical Hypothyroidism on Epicardial Adipose Tissue: A Systematic Review and Meta-Analysis. Curr Probl Cardiol. 2023 Jul;48(7):101674. doi: 10.1016/j.cpcardiol.2023.101674. Epub 2023 Feb 24. PMID: 36841317.
22. Camarena V, Sant D, Mohseni M, Salerno T, Zaleski ML, Wang G, et al. Novel atherogenic pathways from the differential transcriptome analysis of diabetic epicardial adipose tissue.

Comparative Study. Nutr Metab Cardiovasc Dis. 2017 Aug;27(8):739-750. doi: 10.1016/j.numecd.2017.05.010. Epub 2017 Jun 10. PMID: 28739185; PMCID: PMC7540222.

23. Solanki A, Bansal S, Jindal S, Saxena V, Shukla US. Relationship of serum thyroid stimulating hormone with body mass index in healthy adults. Indian J Endocrinol Metab. 2013 Oct;17(Suppl 1): S167-S169. doi: 10.4103/2230-8210.119560. PMID: 24251146; PMCID: PMC3830292.
24. Feldt-Rasmussen U. Thyroid and leptin. Review. Thyroid. 2007 May;17(5):413-419. doi: 10.1089/thy.2007.0032. PMID: 17542671.
25. Zhang J, Huang C, Meng Z, Fan Y, Yang Q, Zhang W, et al. Gender-Specific Differences on the Association of Hypertension with Subclinical Thyroid Dysfunction. Int J Endocrinol. 2019 Dec 30; 2019:6053068. doi: 10.1155/2019/6053068. PMID: 32082373; PMCID: PMC7012202.
26. Antonelli A, Ferrari SM, Corrado A, Di Domenicantonio A, Fallahi P. Autoimmune thyroid disorders. Review. Autoimmun Rev. 2015 Feb;14(2):174-180. doi: 10.1016/j.autrev.2014.10.016. Epub 2014 Oct 25. PMID: 25461470.
27. Karthick N, Dillara K, Poornima KN, Subhasini AS. Dyslipidaemic Changes in Women with Subclinical Hypothyroidism. J Clin Diagn Res. 2013 Oct;7(10):2122-2125. doi: 10.7860/JCDR/2013/5777.3448/
28. Blum MR, Gencer B, Adam L, Feller M, Collet TH, da Costa BR, et al. Impact of Thyroid Hormone Therapy on Atherosclerosis in the Elderly with Subclinical Hypothyroidism: A Randomized Trial. J Clin Endocrinol Metab. 2018 Aug 1;103(8):2988-2997. doi: 10.1210/jc.2018-00279. PMID: 29846630.
29. Sasikala T, Goswami K. Castelli risk index-1 and atherogenic coefficient are better predictors of cardiometabolic risk in patients with hypothyroidism. Int J Clin Biochem Res. 2020;7(2):254-259. doi: 10.18231/j.ijcbr.2020.055/
30. Qasim B, Arif S, Mohammed A, Abduljabbar R. Dyslipidemia in Subclinical Hypothyroidism: A Case-Control Study. J Endocrinol Diab. 2018;5(1):1-6. DOI: 10.15226/2374-6890/5/1/00192/
31. Axelband F, Dias J, Ferrão FM, Einicker-Lamas M. Nongenomic signaling pathways triggered by thyroid hormones and their metabolite 3-iodothyronamine on the cardiovascular system. Review. J Cell Physiol. 2011 Jan;226(1):21-28. doi: 10.1002/jcp.22325. PMID: 20658515.
32. Rizos CV, Elisaf MS, Liberopoulos EN. Effects of Thyroid Dysfunction on Lipid Profile. Open Cardiovasc Med J. 2011; 5:76–84. doi: 10.2174/1874192401105010076. PMID: 21660244; PMCID: PMC3109527.