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ATHEROGENIC INDEX OF PLASMA (AIP) AND CASTELLI RISK INDEX (CRI) IN THE PREDICTION OF CARDIOVASCULAR RISK IN POSTMENOPAUSAL WOMEN WITH SUBCLINICAL HYPOTHYROIDISM

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ABSTRACT **Background:** The frequency of subclinical hypothyroidism is substantially increased in postmenopausal women. It's a proven fact that indeed mild thyroid failure can have several clinical symptoms such as depression, memory loss, cognitive impairment, and a variety of neuromuscular complaints. There is also an increased cardiovascular threat, caused by increased serum total cholesterol and low-density lipoprotein cholesterol as well as reduced situations of high-density lipoprotein. With time, overt hypothyroidism can develop. **Objective:** To evaluate the usefulness of AIP and Castelli risk index in the assessment of cardiovascular risk in postmenopausal women with subclinical hypothyroidism. **Materials & Methods:** Present study was carried out at the Department of Biochemistry, Government Medical College, Kota, Rajasthan. Hundred and twenty-five age-matched female patients with an equal number of controls attending Medicine & Gynaecology OPD and IPD were enrolled in this study basedon the inclusion and exclusion criteria.TotalCholesterol (TC),high-densitylipoprotein cholesterol (HDL-C), and triglyceride(TG)were determined by a fully automated biochemistry analyzer.Low-densitylipoprotein cholesterol (LDL-C) was calculated byFriedewald's formula and fT3, fT4 & TSH were measured by the electrochemiluminescence immunoassay method. AIP andatherogenic indices werederivedby the calculationmethod. **Results:**There was a significant increase (P<0.001)in TC, TG, VLDL-C, LDL-C, and AIP but a significantdecrease (P<0.001) in HDL-C. The AIPand atherogenic indiceswere found to besignificantly increased in postmenopausal womenwith subclinical hypothyroidism. **Conclusion:** Subclinical hypothyroidism in postmenopausal women may cause dyslipidemia carrying a high cardiovascular disease risk.

KEYWORDS : Atherogenicindices, AIP, Cardiovascularrisk, Subclinical hypothyroidism

INTRODUCTION

Menopause is quiet a natural process that marks the cessation of a women's menstrual cycle. During this period, women experience a spread of predictable symptoms and conditions associated with changes in steroid hormone levels and aging. (Takahashi *et al*., 2015).Estrogen receptors are diminished in vascular endothelium and smooth vascular muscles with the effect of aging and atherosclerosis alongwith vascular wall damage (Nelson, 2008).

There's an adding frequency of high situations of thyroid-stimulating hormone with age- mainly in postmenopausal women and this is more advanced than in men. The symptoms of thyroid complaints can be analogous to postmenopausal complaints and are clinically delicate to separate. Coronary atherosclerosis and osteoporosis may be exacerbated in the presence of hyperthyroidism or hypothyroidism. (Schindler, 2003)

It's of significance that indeed mild thyroid failure may have several clinical features such as dejection, cognitive impairment, memory loss and different kind of neuromuscular complaints. There is also an increased cardiovascular threat, caused by increased serum total cholesterol and low-density lipoprotein cholesterol as well as reduced situations of high-density lipoprotein. In the context of the cardiac complaint, SCH is of particular interest. Subclinical hypothyroidism, like overt hypothyroidism, has been linked to an increased risk of heart failure (Rodondi *et al*., 2005; Rodondi *et al*., 2008) and atherosclerosis. (Bastenie *et al*., 1977). With SCH, studies show an elevated risk of incident coronary heart disease (CHD) events (Iervasi *et al*., 2007; Walsh *et al*., 2005). Dyslipidemia has been linked as a major threat factor for Atherosclerosis (Shen *et al*., 2015). Dyslipidemia describes as a disease of the lipids. Which mainly comprise of increased levels of TC, LDL-C, TG and low levels of HDL-C situations according to the ATP III criteria (NCEP, 2001). Various dyslipidemic studies reveals that the (AIP) atherogenic index of plasma is a significant predictive tool of Atherosclerosis and better than LDL (Dobiasova *et al*., 2000).

To evaluate changes within the lipoproteins (Tan *et al*., 2004) used the atherogenic index of plasma (AIP), calculated as:

$$Atherogenic\ index\ of\ plasma\ (AIP) = \log.\frac{[Serum\ Triglycerides]}{[Serum\ HDL\text{-}Cholesterol]}$$

TG and HDL-C present in molar concentrations (Dobiasova et al., 2001). Castelli risk index-I (CRI-I) and Castelli risk index- II (CRI-II) are good indicators of cardiovascular risk in comparison to traditional lipid parameters (Stampfer et al., 1991).They are calculated as:

$$Castelli\ risk\ index\text{-}I\ (CRI\text{-}I) = \frac{[Serum\ total\ Cholesterol]}{[Serum\ HDL\text{-}Cholesterol]}$$

$$Castelli\ risk\ index\text{-}II\ (CRI\text{-}II) = \frac{[Serum\ LDL\text{-}Cholesterol]}{[Serum\ HDL\text{-}Cholesterol]}$$

It has been proven that thyroid dysfunction has a major impact on triple D's i.e., dementia depression, and deaths, and on CAD risk in postmenopausal women, but still, to date, there is not any agreement on routine screening of thyroid profile. Likewise, AIP and Atherogenic indices can be a good predictor of earlier CAD risk if used along with lipid profile.

MATERIALS AND METHODS

The present study was carried out at the Department of Biochemistry, Govt. Medical College Kota Rajasthan. 125 age-matched female patients with an equal number of controls attending Medicine & Gynaecology OPD and IPD were enrolled in this study based on the inclusion and exclusion criteria. Informed consent was taken from all the participants, who took part in the study appraising them of the nature and objective of the study. Lipid profile measurement (Total Cholesterol, Triglycerides, HDL-C) was based on the enzymatic method, on a fully automated biochemistry analyzer, XL-640 (Transasia Bio-Medicals Ltd, Mumbai, India) based on photometric principles. Further, LDL-cholesterol (LDL-C) was calculated using the Friedewald equation [LDL Friedewald = TC – HDL – (TG/5)] (Friedewald et al., 1972). Further, atherogenic indices such as total cholesterol (TC)/high-density lipoprotein cholesterol (HDL-C) and LDL-C/HDL-C were calculated from the individual parameters of the lipid profile.

Thyroid profile included estimation of free T3, free T4, and TSH. And the method employed was electrochemiluminescence immunoassay (ECLIA) on Cobas e411 autoanalyzer (Roche Holding AG, Switzerland). Patient recruitment and study designs were according to the institutional ethical committee (IEC) recommendations. Samples were run in triplicates and the mean results obtained are represented as mean ± SD. The atherogenic index of plasma was calculated using the formula: AIP = Log (TG/HDL-C). (Dobiásová et al., 2001).

Statistical analysis

We have used a non parametric statistical tool, the student t-test for comparing one variable between independent samples (or groups). Correlation analysis was done by the Spearman rank correlation method. p-value <0.05 was considered to be significant and p-value <0.01 was considered to be highly significant for a given hypothesis testing. All the statistical analyses were performed using GraphPad Prism Ver. 6.0 (GraphPad Software, Inc., CA, USA) and Microsoft Excel, MS office 2013 (Redmond, WA, USA).

RESULTS

PARAMETERS	CONTROLS	CASES	p-value
Total Cholesterol (mg/dL)	155.18 ± 13.6	172.43 ±	<0.001
Triglycerides (mg/dL)	124.00 ± 19.9	162.88 ± 22.2	<0.001
LDL-C (mg/dL)	87.44 ± 13.2	97.76 ± 11.5	<0.001
HDL-C (mg/dL)	42.95 ± 3.18	42.04 ± 3.2	<0.05
AIP	0.101 ± 0.06	0.23 ± 0.08	<0.001
Free T3 (pg/mL)	2.61 ± 0.52	2.74± 0.54	0.053
Free T4 (ng/dL)	1.02 ± 0.12	1.0 ± 0.12	0.188
TSH µIU/mL	2.36 ± 0.85	6.57 ± 1.09	<0.001
TC/HDL-C (CRI-I)	4.13 ± 0.48	3.6 ± 0.42	<0.001
LDL/HDL-C (CRI-II)	2.35 ± 0.38	2.05 ± 0.39	<0.001

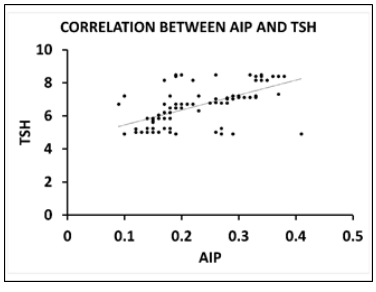

Figure 1. Correlation between serum TSH and AIP (r = 0.647).

DISCUSSION

The serum total cholesterol in cases and controls were 172.43 ± 12.02 and 155.18 ± 13.6 mg/dL respectively. There was a significant increase (p<0.001) in serum total cholesterol in the cases when compared to the controls. Similarly, the Triglycerides were significantly higher in cases (p<0.001). HDL Cholesterol was significantly lower (p<0.05), thereby intuitively suggesting that LDL-Cholesterol was significantly higher (p<0.001). Consecutively the AIP, TC/HDL-C ratio, and LDL/HDL cholesterol ratio were found to be significantly increased in postmenopausal women with subclinical hypothyroidism

These observations further attest to the finding of earlier workers Njajou et al., (2009)whoreported that AIP plays a predictive value for atherosclerosis, and may be used as an indicator for assessing cardiovascular risk, and for predicting the acute coronary events. The present study shows similarity with Khakurelet al,(2018) who found a significant increase in TC, LDL-C, and a significantly lower level of HDL-C in postmenopausal women as compared to premenopausal women. Another study by Godinijak et al., (2017) reported that the mean values of serum TC, TG, and LDL-C were elevated in subclinical hypothyroid postmenopausal women as compared to euthyroid control.In our investigation, we found a profoundly significant positive correlation between AIP and TSH in the study group and control group [Fig.1] (r = 0.647, p<0.0001). These findings are in close association with the results of Madhura et al., (2020) who found the same results, a significant correlation of AIP with S-TSH levels in the SCH group.

CONCLUSION

The present study indicates that AIP and Castelli risk indexcan be used as potential tools for predicting the risk of CAD in postmenopausal women, especially those with subclinical hypothyroidism.

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CONFLICT OF INTERESTS

The authors hereby declare that they have no conflict of interests related to this original work.

REFERENCES

1. Bastenie PA, Vanhaelst L, Golstein J, Smets P (1977). Asymptomatic autoimmune thyroiditis and coronary heartdisease. Cross-sectional and prospective studies. Lancet. 23;2(8030):155-158.
2. Dobiasova M, Frohlich J (2001).The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FERHDL). Clin Biochem. 34:583-588.
3. National Cholesterol Education Program (NCEP) (2001). Evaluation and Treatment of High Blood Cholesterol in Adults Executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) J. Am. Med. Assoc. 285:2486-2497.
4. Friedewald WT, Levy RI, Fredrickson DS (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without the use of the preparative ultracentrifuge. Clin Chem.18(6):499–502.
5. Godinjak, Amina,VelijaAsimi, Zelija, burekovic, Azra, dizdarević-bostandzić, Amela, jusufović, Selma, Iglica, Amer, gicić, Selma, kukuljacAdis (2017).Subclinical Hypothyroidism is Associated with Atherogenic Lipid Profile in Postmenopausal Women.The Turkish Journal of Endocrinology and Metabolism. 21:37-41.
6. Iervasi G, Molinaro S, Landi P,et al. (2007). Association between increased mortality and mild thyroid dysfunction in cardiac patients. Arch Intern Med.167(14):1526-1532.
7. Khakurel G, Kayastha R, Chalise S, Karki PK (2018). Atherogenic Index of Plasma in Postmenopausal Women. J Nepal Health Res Counc. 16(2):175-177.
8. Nelson HD(2008) Menopause.Lancet. 371(9614):760-70.
9. Njajou, O T., Kanaya, A M., Holvoet, P., Connelly, S., Strotmeyer, E S., Harris, T B., (2009).Association between oxidized LDL-C, obesity, and type 2 diabetes. Diabetes Metab Res Rev. 25(8):733-739.
10. Madhura NS, Shankar M, Narasimhappa S., (2020). Subclinical hypothyroidism (SH) and Atherogenic Index of Plasma (AIP) in Women: A Case-Control Study from a Tertiary Care Hospital in South India. Cureus. 24;12 (9):e10636.
11. Rodondi N, Newman AB, Vittinghoff E, et al. (2005). Subclinical hypothyroidism and the risk of heart failure, other cardiovascular events, and death. Arch Intern Med.165(21):2460–2466.
12. Rodondi N, Bauer DC, Cappola AR, et al., (2008). Subclinical thyroid dysfunction, cardiac function, and the risk of heart failure. The Cardiovascular Health studies. J Am Coll Cardiol.52(14):1152–1159.
13. Schindler AE(2003). Thyroid function and postmenopause. Gynecol Endocrinol. 17(1):79-85.
14. Shen S.W., Lu Y., Li F., Shen Z.H., Xu M., Yao W.F., Feng Y.B., Yun J.T., Wang Y.P., Ling W., et al(2015). Potential long-term effects of previous schistosome infection may reduce the atherogenic index of plasma in Chinese men. Int. J. Parasitol. 45:289–294.
15. Stampfer MJ, Sacks FM, Salvini S, Willett WC, Hennekens CH (1991). A prospective study of cholesterol, apolipoproteins, and the risk of myocardial infarction. N Engl J Med.325(6):373-381.
16. Takahashi TA, Johnson KM (2015). Menopause. Med Clin North Am. 99(3):521-534.
17. Tan MH, Johns D, Glazer NB(2004).Pioglitazone reduces the atherogenic index of plasma in patients with type 2 diabetes. Clin Chem. 50:1184-1188.
18. Walsh JP, Bremner AP, Bulsara MK, et al., (2005). Subclinical thyroid dysfunction is a risk factor for cardiovascular disease. Arch Intern Med.165(21):2467-2472.