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Association between Atherogenic Index and Thyroid Status in Hypothyroid Patients

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Abstract

Objective: To find out the association between atherogenic index and thyroid status in hypothyroid patients. ***Method:*** This case control study was conducted in the Biochemistry Department of National Institute of Kidney Diseases and Urology during the period of 2018 and 2019. 100 subjects aged between 20-50 were selected by purposive sampling from the patients and attendants attending to the outpatient department of NIKDU. Among them 55 subjects were diagnosed case of hypothyroidism with TSH >4ng/dl and FT4<0.9 ng/dl and 45 subjects were age and gender matched healthy euthyroid controls. Here student unpaired t-test, Chi-square test and Pearson's correlation test were used to determine the association of atherogenic index and hypothyroidism. SPSS version 23 was used for the level of significance and p value <0.05 was considered statistically significant. ***Result:*** A total 100 subjects were included in the study without subjects with hypertension, diabetes mellitus and renal failure. All the variables were compared between the two groups. Out of 55 cases, 20 were males and 35 were females. Out of 45 control subjects, 12 were males and 35 were females. There was no statistically significant difference in case and control group in term of gender and Chi-square test was done to measure the level of significance. Among case and control, highest percentage were in the range of 20-30 years with 43.6% and 55.5% respectively. The mean age of case group was higher than the control group, but the difference was not statistically significant ($p<0.05$). Mean AIP level was 0.75±0.27 in case group and 0.35±0.20 in control group and was statistically significance difference (<0.05) between the two groups. ***Conclusions:*** From this study, it may be concluded that high atherogenic index is associated with Hypothyroidism. Hypothyroid patient with increased AIP is prone to develop cardiovascular diseases. So, to decrease the incidence of cardiovascular diseases in hypothyroid individuals, regular monitoring of serum lipid profile should be done by clinician.

Keywords: Atherogenic index of plasma (AIP), Hypothyroidism, Thyroid stimulating hormone (TSH), free thyroxine (FT_4).

INTRODUCTION

Hypothyroidism is defined as a deficiency of thyroid activity, which results from reduced secretion of both T_3 and T_4 irrespective of cause (Sheik, 2008). Hypothyroidism may be due to primary diseases of thyroid gland itself or lack production TSH in pituitary gland (Galesanu *et al.*, 2004).

The incidence of hypothyroidism varies, depending on geographical and environmental factors such as iodide, goitrogen intake, the genetic characteristics and the age distribution of population. Hypothyroidism affects the cardiovascular, renal, neuromuscular, nervous and the reproductive system (`de Castro *et al.*, 2001).

Subclinical hypothyroidism was defined as a TSH level greater than 4.0 mU/L in presence of a

normal free thyroxin level (11to 25pmol/l [0.9 to 1.9 ng/dh]). Clinical hypothyroidism was defined as a TSH level greater than 4.0 mU/L and a decreased free thyroxin level (<11pmol/L [0.9ng/dl]) (Helfand & Redfern, 1998). Euthyroidism was defined as a normal TSH level (0.4 to 4.0mU/L).

Overt hypothyroidism is a clinical condition when TSH levels are more than 20mU/L (Morris *et al.*, 2001). Overt hypothyroidism disturbances, characterised by symptoms and/or clinical signs with abnormal serum levels of thyroid hormone, are generally associated with disturbance in lipid profile (Deschampheleire and Scheen, 1999).

Hypothyroidism occurs in 0.4% women and 0.1% men. Thyroid failure is more common in women and its prevalence rises with age (Canaris, Manowitz, Mayor & Ridgway 2000). Thyroid hormone significantly affects lipoprotein metaboilism as well as some cardiovascular disease risk factors thus influencing overall CVS risk (Duntas, 2002, Friis & Pedersen, 1987, Canaris, Manowitz, Mayor & Ridgway, 2000). With long standing, hypothyroid patients may develop various cardiac manifestations. Patients may present with dyspnoea on exertion, fatigue and oedema that may be results of either pericardial effusion or congestive failure (Gomberg-Maitland & Frishman, 1998)

Hypothyroid patients also have an increased incidence of hypercholesterolemia (Watanakunakorn, Hodges & Evans, 1965) and hypertriglyceridemia (Klein, 1990; Valdemarsson, Hansson, Hedner & Nilsson, 1983). Hypothyroid patients have an increased LDL, VLDL, HDL-C, apoprotein (ApoB) and lipoprotein a (Mohr & Meyer, 1996).

Ahterogenic index of plasma (AIP) is the new marker of atherogenecity since the AIP is related directly to the atherosclerosis risk. AIP is the ratio calculates as log of (TG/HDL-C) (Dobiásová & Frohlich,2001). Triglyceride and HDL-cholesterol in AIP reflect the balance between the atherogenic and antiatherogenic lipoprotein respectively (Dobiásová, 2004).

Existence of hypertriglyceridemia will increase the activity of hepatic lipase (HL) which results in the increase of HDL-C catabolism (degradation of HDL-C). Each degradation of 1mg HDL-C will correlate with 2% increase in the risk of coronary heart diseases (CHD) (Susanti, Donosepoetro, Patellong & Arif, 2010).

AIP values less than 0.1 are associated with low risk, 0.1 to 0.24 with medium risk, and above 0.24 with high risk of cardiovascular diseases (Ceska, 2007). There is a medium risk of cardiovascular diseases with increased AIP values in hypothyroid patients (Rajab, 2012).

Certain investigator has suggested that subjects with hypothyroidisms have an increased risk for coronary artery diseases, which may be related to atherogenic changes in lipid profile. In patients with hypothyroidism, there is often an increase in the serum cholesterol due to raised level of serum low density lipoprotein (LDL) and intermediate density lipoprotein (IDL) and occasionally fasting chylomicronaemia (Catargi *et al.*,1999).

The present study was carried out to evaluate the association of plasma atherogenic index with hypothyroidism.

METHODS

This was a case control analytical study conducted in the department of Biochemistry, National Institute of Kidney Diseases and Urology (NIKDU), Sher-E-Bangla Nagar, Dhaka, between January 2018 to December 2019.

A total of 100 subjects aged between 20-50 years were included in this study. Among of 55 subjects whose TSH value >4 IU/L and FT_4 value <0.9 ng/ml (Helfand and Redfern, 1998) were grouped into case and 45 subjects were grouped into control (euthyroid) on the basis of TSH and FT_4.Patients with hypertension, DM and renal failure were not included into the study.

With all aseptic precaution 5 ml of Venus blood were collected from all the study subjects after overnight fasting of at least 12 hours and measured plasma triglyceride, HDL-C, TSH and FT4.

Atherogenic index of plasma is the log of (TG / HDL-C) (Dobiásová & Frohlich, 2001).

$$AIP = log\left(\frac{TG}{HDL} - C\right)$$

AIP was calculated of all study subjects.

AIP <0.11, < (0.11-0.21) and >0.21 considered low risk, intermediate risk and increased risk of cardiovascular diseases respectively.

All data were analysed by using SPSS version 23. The results were expressed as mean±SD. Level of significance was tested by using unpaired t test for quantitative data and the Chi-square test for qualitative data and p value <0.05 was considered statistically significance. Pearson correlation test was done to see the association between AIP and TSH and AIP and FT_4

RESULTS

Table 1: Distribution of study subject according to sex

Gender	Group		P value
	Case	Control	
Male	20 (36.4)	12 (26.7)	
Female	35 (63.6)	33 (73.3)	0.301
Total	55 (100.0)	45 (100.0)	

Chi-square test was done to measure the level of significance.
Figure within parenthesis indicates the percentage.

Table 1 shows the sex distribution of study subjects. A total 100 subjects were included in the study and out of them 55 hypothyroid patients were grouped into cases and 45 were grouped as normal control. Out of 55 cases for study, 20 were males and 35 were females. Out of 45 control subjects, 12 were males and 33 were females. There was no statistical difference ($p<0.05$) in case and control group in terms of sex.

Table2: Distribution of study subject according to age

Age	Group		P value
	Case	Control	
20-30	24 (43.6)	25 (55.5)	0.281
31-40	21 (38.2)	13 (28.9)	
41-50	10 (18.2)	7 (15.6)	
Total	33.31±8.77	31.42±8.51	

Unpaired T test was done to measure the level of significance
Figure within parentheses indicates in percentage.

Table 2 shows the age distribution of study subjects. The mean age of case and control group were 33.31±8.77 and 31.42± 8.51 years respectively ranging from 20-50 years. Among case and control group highest percentage were in the range of 20-30 years with 43.6% and 55.5% respectively. The mean age of case group was higher than control group but the difference was not statistically significant ($p<0.05$).

Table 3: Comparison of AIP between case and control

Biochemical parameter	Group		P value
	Case	Control	
Atherogenic index of Plasma	0.75±0.27	0.35±0.20	**0.001**

Unpaired T test was done to measure the level of significance.

Table 3 showing AIP level of study subjects. Mean AIP level was 0.75±0.27 in case group and 0.35±0.20 in control group. Regarding biochemical parameters there was statistically significance differences (<0.05).

Table 4: Correlation between plasma FT_4 & AIP in hypothyroid case (N=55)

		FT_4	AIP
FT_4	Pearson Correlation	1	**-.416****
	Sig. (2-tailed)		**.002**
AIP	Pearson Correlation	**-.416****	1
	Sig. (2-tailed)	**.002**	
**. Correlation is significant at the 0.01 level (2-tailed).			

Table 4 showing Pearson correlation between plasma FT_4 and AIP in hypothyroid cases.

r=-.416**, which was significant at the 0.01 level. The result indicates that there was negative association between FT_4 and AIP, meaning decrease FT_4 level increases AIP in hypothyroid cases.

Table 5: Correlation between plasma TSH & AIP in hypothyroid case (N=55)

		TSH	AIP
TSH	Pearson Correlation	1	**.793****
	Sig. (2-tailed)		**.000**
AIP	Pearson Correlation	.793**	1
	Sig. (2-tailed)	.000	
**. Correlation is significant at the 0.01 level (2-tailed).			

Table 5 showing Pearson correlation between plasma TSH and AIP in hypothyroid cases. r=.793, which was significant at the 0.01 level. The result indicates that there was positive association between TSH and AIP, meaning decrease TSH level increases AIP in hypothyroid cases.

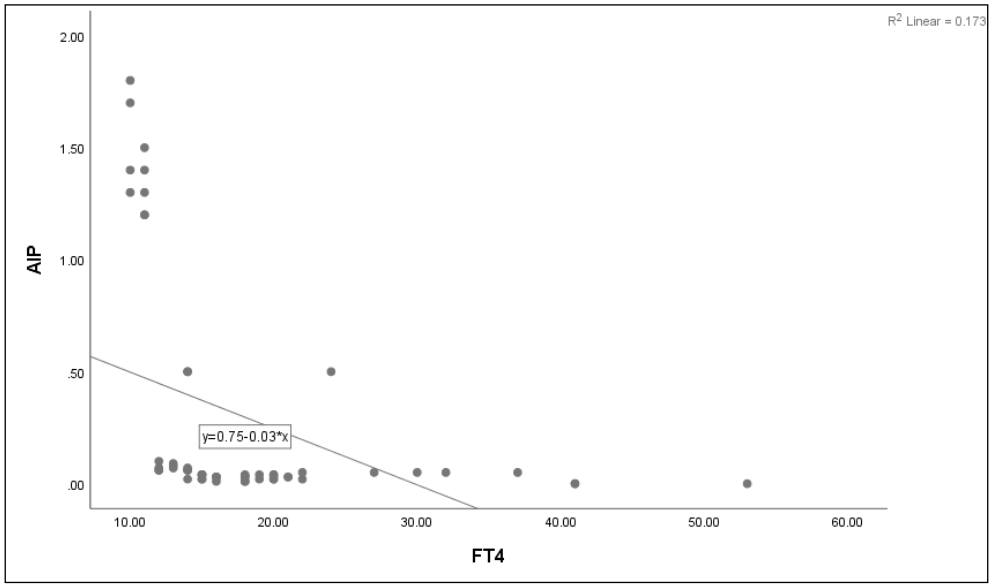

Figure 1: Scatterplot FT_4 with AIP

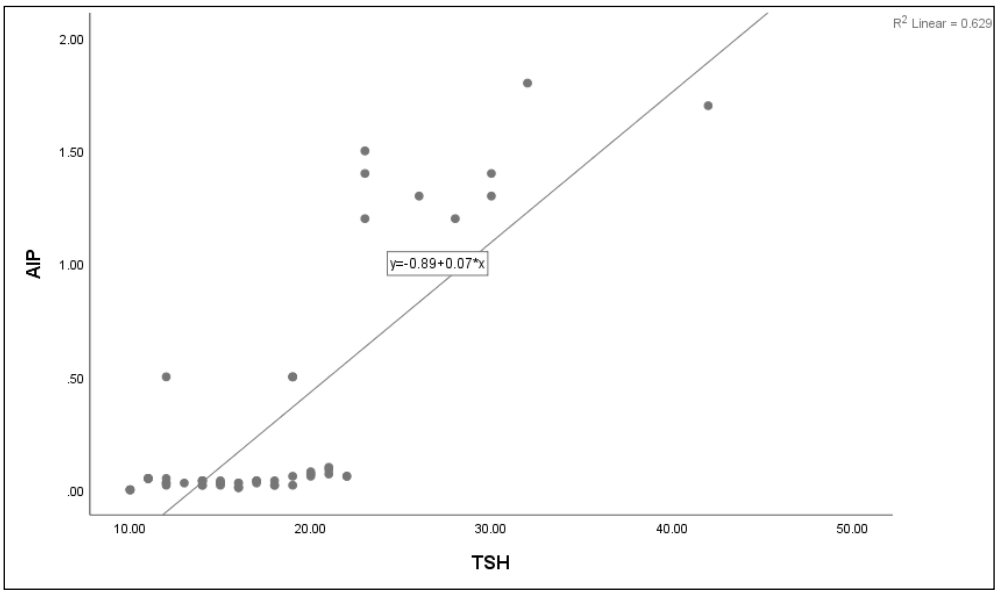

Figure 2: Scatterplot TSH with AIP

Figure 1 showing correlation of plasma FT_4 level with AIP of hypothyroid cases.

Figure 2 showing correlation of plasma TSH level with AIP of hypothyroid cases.

DISCUSSION

Hypothyroidism is a common metabolic disorder. It is a commonly encountered health problem in Bangladesh and morbidity and mortality due to cardiovascular diseases resulting from hypothyroidism is quite high. Hypothyroidism and dyslipidaemia are recognised risk factor for atherosclerosis and cardio-vascular diseases (Saber, Hossain, Alam, & Hossain, 2021; Haque, 2013). In this case control study, our aim was to evaluate if there is any association between plasma atherogenic index and hypothyroidism.

Females are more vulnerable to thyroid dysfunction, typically overt and subclinical hypothyroidism in Karve area of Nepal (Aryal *et al.*, 2010). Overall prevalence of hypothyroidism was 4.8% in men and 12.8% in women in an iodine sufficient area of Iran (Aminorroya *et al.*, 2009). In this study number of hypothyroidism is more in female subjects than male subjects which was consistent with the previous studies.

Present study showed that mean age of the case and control group were 33.13±8.77 years and 31.42±8.51 years respectively ranging from 20-50 years. In a similar study conducted by Sunanda, Sangeeta and Rao (2012), the age range was 20-60 years. Same study also done by Saini *et al.*, (2013) which were in agreement with the present study in respect of mean age and age range.

In a study conducted by Rajab (2012) showed that, mean atherogenic index was higher in hypothyroid individual (0.20±0.03) compared to euthyroid (0.11±0.02) with $p<0.05$. Shivarkishna *et al.*, (2013) also found that atherogenic index was higher in hypothyroid than euthyroid subjects. In this present study the atherogenic index was o.27±0.20 in overt hypothyroid case and 0.07±0.10 in euthyroid control subjects (p value <0.01). The atherogenic index was 0.75±0.27 in case group and 0.35±0.20 in control group (p is 0.001) and this finding was similar to the previous studies.

A study done by Saini *et al.*, (2013) showed positive correlation between AIP and TSH and negative correlation between FT_4 and AIP in hypothyroid patients. Present study was in agreement with the study above mentioned.

CONCLUSION

From this study, it may be concluded that high atherogenic index associated with hypothyroidism. As increased AIP are associated with cardiovascular diseases. So, it is advocated that regular monitoring of atherogenic index that can be calculated from TG and HDL-C component of lipid profile can be used as predictor for the early detection of development of cardiovascular complications related to hypothyroidism. This will help in more effective treatment of hypothyroid patients to reduce the risk of cardiovascular diseases.

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