Original Article

Association of Age with Thyroid Hormone Status and Ischaemic Heart Disease (IHD)

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Abstract

Background: *Aging is associated with increased prevalence of thyroid function abnormalities including hypothyroidism. A meta-analysis showed an increased prevalence and incidence of cardiovascular mortality only in a relatively younger population.* ***Objective:*** *To compare the thyroid function status in IHD patients of different age groups.* ***Methods:*** *This cross sectional study was carried out on 31 IHD subjects aged 35-59 years (Group B_1) and 19 IHD subjects aged 60-85 years (Group B_2) in the Department of Physiology, Dhaka Medical College, Dhaka from July 2009 to June 2010. For comparison 24 healthy subjects aged 35-59 years (Group A_1) and 26 with age 60-85 years (Group A_2) were studied. The IHD subjects were selected from coronary care unit of cardiology department and OPD of Dhaka Medical College Hospital, Dhaka. Serum FT_3, FT_4 and TSH of all subjects were measured by radioimmunoassay. Statistical analysis was done by unpaired Student's 't' test.* ***Results:*** *The mean ± SD of FT_3 and FT_4 were significantly lower and TSH was significantly higher in Group B_1 IHD patients than that of Group A_1 healthy subjects, but no difference was found between Group A_2 and Group B_2 and between Group B_1 and Group B_2.* ***Conclusion:*** *Thyroid hormone levels are significantly lower in younger IHD population (age 35-59 years) than the age-matched normal controls.*

Key wards: *Age, Thyroid hormone, Ischaemic heart disease (IHD)*

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Introduction

Cardiovascular disease is the foremost cause of premature death in men and women in western communities; these diseases also have major impact on health care and can be a great economic burden, being the most common cause of hospital admission.[1,2]

Ischaemic heart disease (IHD) has become a global health problem of 21st century.[3] IHD results from myocardial ischaemia due to imbalance between the supply and demand of the heart for oxygenated blood. There are also reduced supply of nutrients and inadequate removal of metabolites.[4] The aetiology and pathogenesis of coronary heart disease (CHD) are multifactorial, with progression being influenced by hyperlipidaemia, hypertension, glucose intolerance, smoking, circulatory procoagulants and sex hormones.[3,5] Thyroid hormone levels are suggested to be observed in all middle aged population for early diagnosis of cardiac involvement as hypothyroidsm was found to be associated with IHD.[6]

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Hypothyroidism, with its accompanying hypercholesterolaemia and hypertension has been found to be associated with cardiovascular disease. Moreover subclinical hypothyroidism is a strong indicator of risk for atherosclerosis and myocardial infarction.[7-12] Hypothyroidism may also protect the heart muscle by reducing its workload and oxygen consumption.[5]

Aging is associated with increased prevalence of thyroid function abnormalities including hypothyroidism.[13,14] An increased prevalence of overt hypothyroidism (OH) and subclinical hypothyroidism (SH) has been consistently reported with frequency ranges from 0.5% to 5% for OH and 5% to 20% for SH in women older than 60-65 years.[13,15]

Many similarities between signs and symptoms of hypothyroidism and the aging process can be observed, such as bradycardia, hypertension, hypercholesterolaemia, weight gain, cold intolerance, constipation, muscle weakness, lethargy, cognitive dysfunction, depression, impotence and dry skin.[15] An age dependent decline of the thyroid function has been documented in the oldest old population.[1] A meta-analysis of 15 studies showed an increased prevalence and incidence of cardiovascular mortality only in a relatively younger population. Cardiovascular as well as all-cause mortality was also increased in studies involving subjects younger than 65 years.[16] At a younger age, hypothyroidism may synergize (through dyslipi-daemia, endothelial dysfunction or direct effect on the heart) with other genetic or environmental factors to increase the risk of IHD. In contrast, older subjects represent population with longer survival and lower cardiovascular risk, who might rather benefit from the energy sparing effects of mild hypothyroidism.[14] From these literatures it can be assumed that discrepancy in thyroid function status may exist in IHD patients of different age groups. However, such issue has not yet been properly addressed in our IHD patients. For this reason we designed this cross-sectional comparative study to compare the thyroid function status in IHD patients of different age groups.

Materials and Methods

This cross sectional study was carried out in the Department of Physiology, Dhaka Medical College, Dhaka from July 2009 to June 2010. Total 100 subjects aged 35 to 85 years of both sexes were included in this study. Out of this 100, 50 apparently healthy subjects were controls (Group A) and 50 diagnosed and documented IHD patients were the cases (Group B). Group A was further divided into Group A_1 and Group A_2 on the basis of age. Subjects of 35-59 years were included in Group A_1 and subjects of 60-85 years were included in Group A_2. Similarly Group B was also divided into Group B_1 (35-59 years) and Group B_2 (60-85 years).

The IHD subjects were selected from coronary care unit of cardiology department and OPD of Dhaka Medical College Hospital, Dhaka and control subjects were selected from Dhaka city by personal communication. Subjects with history of thyroid disease, chest pain for other causes or pregnancy were excluded. Ethical consideration for the subjects was taken into account before inclusion into the study. The aims and benefits of the study were explained to each subject and informed consent was taken. A detailed history regarding medical, personal, family and socio-economic condition was recorded in a preformed questionnaire. With all aseptic preparations 5 mL of venous blood was drawn and serum was separated. Serum FT_3, FT_4 and TSH of all subjects were measured by radioimmunoassay in the laboratory for Nuclear Medicine and Ultrasound, Bangladesh Atomic Energy Commission, Dhaka Medical College Campus, Dhaka. Statistical analysis was done by unpaired Student's 't' test using SPSS version 12. Data were expressed as mean ± SD.

Results

Thirty six male and 14 female IHD patients and 34 male and 16 female healthy subjects participated in this study. Among healthy subjects 24 were in Group A_1 and 26 were in Group A_2. Among IHD patients 31 were in Group B_1 and 19 were in Group B_2.

The comparison of anthropometric parameter and thyroid hormone status between Group A_1 and Group B_1 are shown in Table I. The Group A_1 and Group B_1 were matched in terms of age and BMI ($p>0.05$). Although the mean serum FT_3, FT_4 and TSH levels of both Group A_1 and Group B_1 were within normal reference value, but mean serum FT_3 and FT_4 were significantly lower and TSH level was significantly higher in Group B_1 than that of Group A_1 ($p<0.05$).

Table I: Comparison of different variables between Group A_1 amd Group B_1

Variables	Groups		P values
	A_1 (n=24) Mean±SD	B_1 (n=31) Mean±SD	
Age (year)	47.13 ± 4.13	45.94 ± 4.94	0.347^{NS}
BMI	22.64 ± 3.56	22.25 ± 3.82	0.701^{NS}
FT_3 (pmol/L)	4.79 ± 1.89	3.85 ± 1.56	0.049*
FT_4 (pmol/L)	19.48 ± 3.74	15.69 ± 4.75	0.002**
TSH (mIU/L)	1.88 ± 1.15	8.50 ± 13.89	0.024*

Unpaired Student's 't' test was performed to compare between groups. P value <0.05 was accepted as significant. *= significant, **= highly significant, NS = not significant

The comparison of anthropometric parameter and thyroid hormone status between Group A_2 and Group B_2 are shown in Table II. The Group A_2 and Group B_2 were matched in terms of age and BMI ($p>0.05$). Although the mean serum FT_3, FT_4 and TSH levels of both Group A_2 and Group B_2 were within normal reference value, but mean serum FT_3 and FT_4 were lower and TSH level was higher in Group B_2 than that of Group A_2, the differences between two groups did not reach the level of significance ($p>0.05$).

Table II: Comparison of different variables between Group A_2 amd Group B_2

Variables	Groups		P value
	A_2 (n=26) Mean±SD	B_2 (n=19) Mean±SD	
Age (years)	66.69 ± 7.32	68.89 ± 8.89	0.368^{NS}
BMI	21.76 ± 5.63	21.40 ± 2.28	0.798^{NS}
FT_3 (pmol/L)	4.36 ± 1.18	3.77 ± 0.96	0.083^{NS}
FT_4 (pmol/L)	18.44 ± 4.65	16.37 ± 3.83	0.119^{NS}
TSH(mIU/L)	3.37 ± 2.34	6.90 ± 10.41	0.100^{NS}

Unpaired Student's 't' test was performed to compare between groups. P value <0.05 was accepted as significant, NS = not significant

The comparison of anthropometric parameter and thyroid hormone status between Group B_1 and Group B_2 are shown in Table III. The mean ± SD of age of Group B_1 was 45.94 ± 4.94 years and Group B_2 was 68.89 ± 8.89 years ($p<0.001$). No significant differences were observed in age and BMI between two groups ($p>0.05$). The mean serum FT_3, FT_4 and TSH levels were almost similar in Group B_1 and Group B_2 ($p>0.05$).

Table III: Comparison of different variables between Group B_1 and Group B_2

Variables	Groups		P value
	B_1 (n=31)) Mean±SD	B_2 (n=19) Mean±SD	
Age (years)	45.94 ± 4.94	68.89 ± 8.89	0.000**
BMI	22.25 ± 3.82	21.40 ± 2.28	0.385^{NS}
FT_3 (pmol/L)	3.85 ± 1.56	3.77 ± 0.96	0.841^{NS}
FT_4 (pmol/L)	15.69 ± 4.75	16.37 ± 3.83	0.600^{NS}
TSH (mIU/L)	8.50 ± 13.89	6.90 ± 10.41	0.668^{NS}

Unpaired Student's 't' test was performed to compare between groups. P value <0.05 was accepted as significant. **= highly significant, NS = not significant

Discussion

In the present study we intended to evaluate the influence of age on the thyroid hormone status in IHD patients. The mean ± SD of FT_3 and FT_4 were significantly lower and the mean ± SD of TSH was significantly higher in Group B_1 than that of Group A_1 ($p<0.05$). However, Group B_2 did not show such difference with the Group A_2 ($p>0.05$). No significant difference in any general characteristics and thyroid hormone status was observed between Group B_1 and Group B_2 ($p>0.05$). Several studies agree with the present findings.[14-20]

Some investigators reported that mild hypothyroidism is associated with a significant increase of IHD risk only in middle aged (<65 yrs old) subjects, whereas mild thyroid failure may be harmless or beneficial in advanced age.[14,17]

It has been suggested that at a younger age hypothyroidism may synergize (through dyslipidaemia, endothelial dysfunction or direct effect on the heart) with other genetic or environmental factors to increase the risk of IHD. On the other hand older subjects represent population with longer survival

and lower cardiovascular risk, who might rather benefit from the energy sparing effects of mild hypothyroidism.[14] Razvi et al explained the effect of age on vascular risk in subjects with hypothyroidism. First, it is possible that at a younger age, lack of thyroid hormones has a profound pathophysiological effect, resulting in accelerated vascular disease, perhaps through dyslipidaemia, endothelial dysfunction, or a direct effect on the myocardium in a proportion of susceptible individuals. As age of the subjects increases, they become relatively resistant to the adverse vascular effects of low thyroid activity.[16] Clinical manifestations of subclinical hypothy-roidism include abnormal lipid metabolism, cardiac dysfunction, elevated risk of atherosclerosis and coronary heart disease.[19] Overt hypothyroidism, with its accompanying hypercholesterolaemia and hypertension, has been found to be associated with cardiovascular disease. Subclinical hypothyroidism is strongly and independently associated with aortic atherosclerosis and myocardial infarction.[10] Reduced serum T_3 is a strong predictor of all-cause and cardiovascular mortality and, in fact, is a stronger predictor than age, left ventricular ejection fraction, or dyslipidaemia.[18] A meta-analysis found that mild hypothyroidism is associated with a significant increase of IHD risk only in middle-aged (<65 yrs old) subjects. This finding supports the concept that mild thyroid failure is detrimental in young to middle-aged subjects, whereas may be harmless or perhaps beneficial at advanced age.[14]

However, data on the associations with coronary heart disease (CHD) events and mortality are conflicting among several large prospective cohorts.[11] Elderly normal population may have low thyroid hormone status. Some researchers reported that thyroid abnormality is more common in older age group than middle age group.[7,21,22] The prevalence of subclinical hypothyroidism approaches about 15% in women who are over 60 years of age.[19]

It was also reported by Mariotti and Cambuli that the oldest subjects with lower cardiovascular risk might be benefited from the energy sparing effects of mild thyroid failure. The physiological function of thyroid hormone is to increase the O_2 consumption of all cells of the body. Mild thyroid failure in turn decreases O_2 consumption of the cells and thus reduces the cardiac workload. This is the possible mechanism by which mild thyroid failure plays a cardioprotective role in old age. An increased prevalence of overt hypothyroidism has been consistently reported with frequencies ranging from 0.5% to 5% for OH and from 5% to 20% for SH in women older than 60-65 years.[15]

From the findings of the present study it can be concluded that thyroid hormone levels are significantly lower in younger IHD population compared with age-matched normal controls. There is no significant difference between the elderly IHD patients and age-matched normal controls and between younger IHD population and elderly IHD population regarding thyroid hormone status.

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