

## Thyroid Dysfunction and Their Relation to Cardiovascular Risk Factors such as Lipid Profile, hsCRP, and Waist Hip Ratio in Korea

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**Background :** Thyroid abnormalities affect a considerable portion of the population, and overt hypothyroidism is associated with an elevated risk of cardiovascular disease and adverse changes in blood lipids. Subclinical hypothyroidism is also associated with an increase risk of cardiovascular disease. So, we undertook this study to investigate the prevalence of overt and subclinical thyroid disorders and their associations with cardiovascular risk factors.

**Methods :** This study involved 66260 subjects (43588 men, 22672 women ; between 20~80 years of age, mean age 41.5±9.6). Serum free thyroxine (FT4), thyroid stimulating hormone (TSH), total cholesterol, low density lipoprotein cholesterol (LDL-C), and high density lipoprotein cholesterol (HDL-C) were measured by RIA using commercial kits. High sensitivity C-reactive protein (hsCRP) levels were determined by nephelometry.

**Results :** The prevalences of overt thyrotoxicosis, subclinical thyrotoxicosis, overt hypothyroidism and subclinical hypothyroidism were 5/1000 (334 subjects), 6.4/1000 (426 subjects), 1.6/1000 (108 subjects), and 6.4/1000 (375 subjects). Mean plasma total cholesterol and LDL-C were elevated in overt hypothyroidism than in normal controls (202.1 mg/dL and 121.8 mg/dL versus 197.1 mg/dL and 120.1 mg/dL, respectively) ( $p < 0.05$ ). In subclinical hypothyroidism, mean total cholesterol and LDL-C levels were also elevated (201.9 mg/dL and 123.7 mg/dL) ( $p = 0.015$ ,  $p = 0.047$ ). Waist-to-hip ratio (WHR) was lower in overt thyrotoxicosis and higher in hypothyroidism.

**Conclusion :** The prevalence of thyroid dysfunction in Korea is not significantly different from that reported by other countries. It was also age dependent and higher in women, but this elevation in women was lower than expected. Patients with hypothyroidism exhibited higher waist-to-hip ratios, an index of obesity. Patients with subclinical hypothyroidism exhibited elevated atherogenic parameters (Total cholesterol, LDL-C). Therefore screening and treatment for subclinical hypothyroidism may be warranted due to its adverse effects on lipid metabolism.

**Key Words :** Prevalence, thyroid dysfunction, Cardiovascular risk factors

### INTRODUCTION

Thyroidism is a relatively common disease but its reported incidence varies, being dependent upon the research subject groups and the diagnostic criteria used. The prevalences of

overt hyperthyroidism or overt hypothyroidism and subclinical thyrotoxicosis have been reported to be 5%, 5% and 1% respectively<sup>1-7</sup>. Subclinical hypothyroidism has been reported to have prevalences from 4-10% in the general population to 7-26% in the geriatric population<sup>8-11</sup>. Such thyroid dysfunctions

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cause changes in the lipoprotein metabolism. It is generally accepted that overt hypothyroidism accelerates the progress of cardiovascular diseases by increasing the total cholesterol and low density lipoprotein cholesterol, LDL-C, levels. Also, hypercholesterolemia caused by hypothyroidism is known to be a reversible phenomenon that can respond to thyroid hormone therapy<sup>12-15</sup>. However, many contradictory results have been reported on the relationship between subclinical hypothyroidism and abnormal plasma lipids. As a result of comparing patients with subclinical hypothyroidism and normal controls, no significant difference was found in plasma lipids, nor did thyroid hormone therapy cause a significant difference in this respect<sup>2, 15-18</sup>. Whereas recent studies have reported that total cholesterol and low-density lipoprotein cholesterol are more elevated in subclinical hypothyroidism than in normal controls<sup>19-22</sup>. These are crucial risk factors and are the basis of thyroid hormone therapy. However, since many studies on the relationship between subclinical hypothyroidism and hyperlipidemia have been performed using selected groups of subjects of 55 years or older, they do not represent the subject group of interest in terms of cardiovascular diseases prevention<sup>23</sup>. Thus, we examined the prevalence of thyroid dysfunctions in Korea, and used a large number of subjects covering a wide age range. These subjects had visited hospital for medical check-ups.

## MATERIALS AND METHODS

### 1. Subjects

The subjects were 66,260 individuals (43,588 males and 22,672 females) who resided mainly in the Seoul and Kyunggi areas, and had received medical check-ups at the Kangbuk Samsung Hospital, College of Medicine in Sunggyungwan University from January of 1999 to December of 2001.

### 2. Methods

Serum FT4, TSH, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, hsCRP, neutral fat, and blood pressure were measured.

The circumferences of the subjects' waists and hips were measured and their ratios calculated. Their mean serum FT4 was 0.7–2.0 ng/dL and their serum TSH 0.25–5.0 uIU/mL. Cholesterol was determined using an automatic analyzer, (ADVIA1650, Bayer). High sensitivity C-reactive protein (hsCRP) was measured using immunonephelometers (Nephelometry; Behring Nephelometer II, Dade Behring Marburg GmbH, Germany) up to a level of 0.175 mg/L. Overt hyperthyroidism was defined to have a serum TSH of 0.25 uIU/mL or lower, and a serum FT4 of 2 ng/dL or higher. Subclinical thyrotoxicosis

was defined as a normal density of serum FT4, but a serum TSH of 0.25 uIU/mL or lower. Overt hypothyroidism was defined as a serum TSH of 5.0 uIU/mL or higher with a serum FT4 of 0.7 ng/dL or lower. Subclinical hypothyroidism was defined as a normal density of serum FT4 with serum TSH of 5.0 uIU/mL or higher.

### 3. Statistical Analysis

SAS version 8.0 and SPSS version 10.0 were used for the statistical analysis, and the sequential variable data are presented as means±standard deviation. Dunnett's multiple comparison test was used to determine differences between the groups, and multiple multinomial logistic regression analysis was used to adjust for age and gender. A *p* value of 0.05 or lower was taken to be statistical significance.

## RESULTS

### 1. Clinical traits of the subjects

The 66,260 subjects included 43,588 males and 22,672 females, a ratio of 1.92:1 and of average age 41.5±9.6. 31,270 were in their 30's (30–39) which predominated, and subject frequencies by decade followed in the order 40's, 50's, 60's, 20's (or younger) and 70's (or older). The average systolic blood pressure of the subjects was 119.86 mmHg, and diastolic blood pressure was 76.73 mmHg, while the fasting blood sugar was 90.75 mg/dL. The average serum FT4, TSH, total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol were 1.31±0.29 ng/dL, 2.08 ±1.59 uIU/mL, 196.8±36.4 mg/dL, 51.7±12.6 mg/dL, and 120.1±31.2 mg/dL respectively. The hsCRP was 1.22±1.47 mg/L, and the waist-hip ratio was 0.84±0.24 (Table 1).

### 2. Prevalence of thyroid dysfunction

Overt hyperthyroidism was found in 334 (referred to as patients) (5/1,000) of the 66,260 subjects. Among these, 152 patients (3.5/1,000) were males (out of 43,588 males), and 182 patients (8.0/1,000) were females (out of 22,672 females) and thus, the condition is more prevalent in females (sex ratio was male:female=1:2.5) (Table 2). The prevalence of overt hyperthyroidism showed a tendency to rise with age to plateau in the 50's (Figure 1). Subclinical thyrotoxicosis was found in 426 patients (6.4/1,000) and 213 of these were males (4.9/1,000 male prevalence), while 213 were females (9.4/1,000 female prevalence), and thus, prevalence of subclinical thyrotoxicosis is more likely to occur in the females (ratio of male:female=1:2) (Table 3). The prevalence of subclinical thyrotoxicosis showed... tendency to increase with age, and this markedly increased in the 70's and beyond (Figure 1).

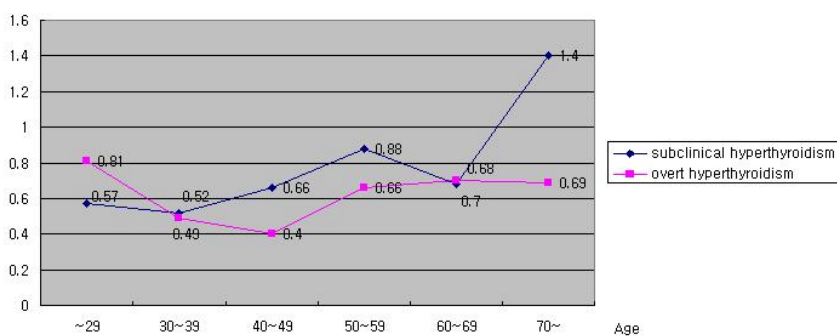
**Table 1.** Basal characteristics of subjects

	Total Mean±SD	MEN Mean±SD	women Mean±SD
age (yr)	41.54±9.62	41.33±8.77	41.96±11.07
body mass index (kg/m <sup>2</sup> )	23.44±2.98	23.90±2.79	22.56±3.12
waist to hip ratio	0.84±0.24	0.87±0.22	0.78±0.20
SBP (mmHg)	119.86±15.31	121.13±14.25	117.40±16.91
DBP (mmHg)	76.73±10.60	78.59±10.03	73.15±10.76
FBS (mg/dL)	90.75±19.92	91.27±20.72	89.75±18.24
Uric acid (mg/dL)	5.22±1.38	5.84±1.18	4.04±0.91
Total cholesterol (mg/dL)	196.89±36.42	198.92±35.50	192.97±37.7
LDL-C (mg/dL)	120.00±31.27	122.97±30.73	117.30±31.680
HDL-C (mg/dL)	51.74±12.61	48.76±11.11	57.47±13.34
Triglyceride (mg/dL)	128.50±92.14	144.29±99.06	98.13±67.40
hsCRP (mg/L)	1.22±1.47	1.26±1.47	1.14±1.48
Lipoprotein-a (mg/dL)	22.81±16.44	22.50±16.70	23.37±15.97
Apolipoprotein-A1 (g/L)	126.57±22.21	124.27±21.67	131.02±22.55
Apolipoprotein-B (g/L)	96.45±2.38	98.99±24.28	91.54±26.70
FreeT4 (ng/dL)	1.31±0.29	1.35±0.27	1.23±0.31
FreeT3 (pg/mL)	3.36±0.66	3.46±0.64	3.18±0.66
TSH (uIU/mL)	2.08±1.59	1.93±1.35	2.38±1.93

SBP, systolic blood pressure; DBP, diastolic blood pressure; FBS, fasting blood sugar; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; hsCRP, high sensitivity C-reactive protein; TSH, thyroid stimulating hormone.

**Table 2.** Prevalence of overt thyrotoxicosis according sex and age

Age (years)	men			women			total		
	subjects	affected	n/1000	subjects	affected	n/1000	subjects	affected	n/1000
≤29	769	2	2.6	1806	18	10	2567	20	7.8
30-39	21394	79	3.7	9813	73	7.4	31207	152	4.9
40-49	14949	41	2.7	5506	40	7.3	20455	81	4.0
50-59	4033	41	10.2	3437	32	9.3	7470	49	6.6
60-69	2105	12	5.7	1870	16	8.6	3975	28	7.0
≥70	338	1	3.0	240	3	12.5	578	4	6.9
total	43588	176	4.0	22672	182	8.0	66260	334	5.0

**Figure 1.** Differential prevalence of overt and subclinical hyperthyroidism according to age (percent).

Overt more likely to occur in females (ratio of male:female=1:6) (Table 4). The prevalence of overt hypothyroidism showed a hypothyroidism was found in 1.6/1,000 of total subjects. Among these, with a prevalence 0.6/1,000 for males, and 3.6/1,000 for females, and thus overt hypothyroidism is

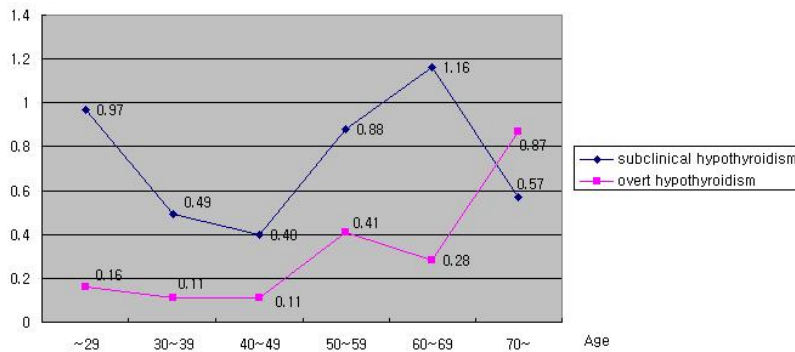
tendency to rise with age, and was highest in the 70's and higher with a prevalence of 8.7/1,000 (Figure 2). Subclinical hypothyroidism was found in 375 patients (5.7/1,000), and 129 were males (male prevalence 3/1,000) while 246 were females (female prevalence 10.9/1,000), and thus the condition is more

**Table 3.** Prevalence of subclinical thyrotoxicosis according to sex and age

Age (years)	men			women			total		
	subjects	affected	n/1000	subjects	affected	n/1000	subjects	affected	n/1000
≤29	769	2	2.6	1806	12	6.6	2567	14	5.5
30-39	21394	83	3.9	9813	93	9.5	31207	176	5.6
40-49	14949	87	5.8	5506	48	8.7	20455	135	6.6
50-59	4033	87	21.6	3437	39	11.3	7470	66	8.8
60-69	2105	13	6.2	1870	14	7.5	3975	27	6.8
≥70	338	1	3.0	240	7	29.2	578	8	13.8
total	43588	273	6.3	22672	213	9.4	66260	426	6.4

**Table 4.** Prevalence of overt hypothyroidism according to sex and age

Age (years)	men			women			total		
	subjects	affected	n/1000	subjects	affected	n/1000	subjects	affected	n/1000
≤29	769	0	0	1806	4	2.2	2567	4	1.6
30-39	21394	6	0.3	9813	28	2.9	31207	34	1.1
40-49	14949	8	0.5	5506	15	2.7	20455	23	1.1
50-59	4033	8	1.99	3437	43	12.5	7470	31	4.1
60-69	2105	3	1.4	1870	8	4.3	3975	11	2.8
≥70	338	3	8.9	240	2	8.3	578	5	8.7
total	43588	273	0.6	22672	100	4.4	66260	108	1.6



**Figure 2.** Differential prevalence of overt and subclinical hypothyroidism according to age (percent).

**Table 5.** Prevalence of subclinical hypothyroidism according to sex and age

Age (years)	men			women			total		
	subjects	affected	n/1000	subjects	affected	n/1000	subjects	affected	n/1000
≤29	769	6	7.8	1806	18	10	2567	24	9.3
30-39	21394	6	0.3	9813	115	11.7	31207	153	4.9
40-49	14949	38	2.5	5506	37	6.7	20455	81	4.0
50-59	4033	44	10.9	3437	24	7.0	7470	66	8.8
60-69	2105	14	6.7	1870	32	17.1	3975	46	11.6
≥70	338	4	11.8	240	1	4.2	578	5	8.7
total	43588	68	1.6	22672	227	10.0	66260	375	5.7

**Table 6.** Mean levels of lipid profiles, hsCRP, WHR and BMI in thyroid abnormalities

	Overt hypothyroidism	Subclinical hypothyroidism	Normal	Subclinical hypothyroidism	Overt hyperthyroidism
Total-C	202.1 ±45.9*	201.9 ±39.9*	139.1 ±36.3	188.6 ±33.8 <sup>†</sup>	163.6 ±33.5 <sup>†</sup>
LDL-C	121.8 ±37.0*	123.7 ±31.5*	120.1 ±31.2	114.4 ±30.1 <sup>†</sup>	100.0 ±28.4 <sup>†</sup>
HDL-C	5.3 ±14.6	53.5 ±13.0	51.8 ±12.6	52.1 ±12.5	49.2 ±12.5
BMI	23.4 ±3.00	22.8 ±3.10	23.5 ±3.0	23.4 ±3.1	22.6 ± 3.0
hsCRP	1.45±1.77	1.72±1.70	1.21±1.47	1.76±1.78	1.06±1.77
WHR	0.85±0.08*	0.84±0.08	0.84±0.07	0.83±0.07	0.82±0.07

Total-C, Total cholesterol(mg/dL); LDL-C, Low density lipoprotein cholesterol(mg/dL); HDL-C, High density lipoprotein cholesterol (mg/dL); BMI, body mass index (kg/m<sup>2</sup>); hsCRP, high sensitivity C-reactive protein (mg/L); WHR, waist to hip ration. Values are expressed as mean±S.D.

\* age, sex adjusted,  $p < 0.05$ ; Significant difference from normal group.

<sup>†</sup> age, sex adjusted,  $p < 0.0001$ ; Significant difference from normal group.

likely to occur in the females (ratio of male:female in the study population =1:3.6) (Table 5). The prevalence of subclinical hypothyroidism showed a tendency to increase with age, and reached a maximum in the in the 60's (Figure 2).

### 3. The relationship between thyroid dysfunction and risk factors for cardiovascular disease

For patients with overt hypothyroidism, the total cholesterol was 202.1±45.9 mg/dL vs. 197.1 36.3 mg/dL, for the group that showed normal thyroid functions, and similarly the low-density lipoprotein cholesterol level was 121.8±37.0 mg/dL vs. 120.1±31.2 mg/dL. Both values were significantly higher than the normal group, but the differences were small ( $p < 0.05$ ). In the patients with subclinical hypothyroidism, the total cholesterol was 201.9±39.9 mg/dL, which was higher than 197.1±36.3 mg/dL of the normal group, and this was statistically significant even when they were matched for age and sex ( $p = 0.015$ ). The low-density lipoprotein cholesterol levels also showed a statistically significant increase in subclinical hypothyroidal patients (123.7±31.5 mg/dL vs. 121.5 ±31.2 mg/dL ( $p < 0.0001$ )). The normal group showed a significantly higher level of high-density lipoprotein cholesterol compared to the overt hyperthyroidism ( $p < 0.0001$ ). No statistically significant difference was found between the normal group and the group that showed thyroid dysfunction in by hsCRP. The body mass indices did not show any significant difference between the normal group and the thyroid dysfunction group, but the ratio of waist/buttocks was significantly lower in the overt hyperthyroidism group than in the normal group, whereas this was higher result in the overt hypothyroidism group than in the normal group ( $p = 0.043$ ,  $p = 0.049$ ) (Table 6).

The determination of the prevalence of thyroidism in a population can produce different results, according to the subject groups or diagnostic criteria chosen. In this study, the average prevalence of overt hyperthyroidism in Korea for all age levels was 5/1,000 (3.5/1,000 in males and 8.0/1,000 in females), and was highest in the 60's age group. In 1997, in the English Whickham survey<sup>2)</sup>, the prevalence of thyroidism, including past medical history, was higher than that of the present survey with 19 female patients per 1,000 female patients, and 1.6 male patients per 1,000 male patients, and though it also found a higher prevalence in females, no association was found with age. In a Colorado study<sup>3)</sup>, thyrotoxicosis showed a prevalence of 0.1%, which is lower than that found in the present study, and a study in Spain<sup>11)</sup> also showed a prevalence rate of 0.2%, which again is lower than that found by the present study. We found that the average prevalence of overt hypothyroidism in Korea is 1.6/1,000 (0.6 males and 3.6 females). In terms of age, those in their 70's showed the highest with 9.4/1,000, and this was higher than that found in the Whickham or Colorado studies, with 1.9% and 0.4%, respectively. In the present study, the average prevalence of subclinical thyrotoxicosis in Korea was found to be 6.4/1,000 (4.9 in males and 9.4 in females), which is much higher than the prevalences of 0.09% in males, and 0.46% in females found in Norway<sup>6)</sup>, but lower than the 2.1% found in Colorado, and much lower than the 7.3% in males and the 5.9% in females found in Germany<sup>7)</sup>. In the present study, the average prevalence of subclinical hypothyroidism was 5.7/1,000 (3 in males and 10.9 in females), and the condition was found to be significantly more likely to occur in females. Age related prevalence showed a tendency to increase, and the 60's showed the highest prevalence at 11.6/1,000. In Norwegian study<sup>6)</sup>, the prevalence of subclinical hypothyroidism was 0.37% in males, and 0.9% in females, and the prevalence was highest in the 60's, which agrees

## DISCUSSION

**Table 7. Mean values of TSH and Free T4 in thyroid abnormalities**

	Free T4			TSH		
	Men	Women	Total	Men	Women	Total
Overt hyperthyroidism	3.39±1.72	3.30±1.63	3.34±1.67	0.04±0.04	0.04± 0.02	0.04± 0.03
Subclinical hyperthyroidism	1.43±0.29	1.42±0.26	1.42±0.28	0.11±0.08	0.09± 0.07	0.10± 0.07
Subclinical hypothyroidism	1.11±0.26	1.07±0.22	1.09±0.23	13.01±7.38	10.83± 4.10	11.58± 5.53
Overt hypothyroidism	0.58±0.11	0.56±0.13	0.56±0.12	23.38±13.30	19.54±12.07	20.50±12.44

Free T4 (ng/dL); TSH (uIU/mL), thyroid stimulating hormone values are expressed as mean±SD.

with the results of the present study<sup>4)</sup>. In the Wickham survey, the prevalence of subclinical hypothyroidism was three times higher in females than in men.

The Colorado, Danish<sup>5)</sup> and Spain Spanish surveys have showed higher prevalences of subclinical hypothyroidism respectively (9%, 7.2% and 5.6%). In view of these results, the prevalence of subclinical hypothyroidism in Korea seems lower than in other countries, but significantly higher in females than in man and is increase with age. Compared to the study of Jung et al.<sup>38)</sup>, who studied the prevalence rates in a population that had received medical check-ups, the present study shows a lower prevalence of thyroid dysfunction. The reasons for this difference are probably due to the different age profiles of the subject groups, and the different diagnostic criteria and tests used to diagnose thyroid dysfunction. In other words, the present study showed that the 30's predominate, and that the average age of this study was 41.5, whereas though the study by Jung et al. did not state the average age the 40's predominated. In addition, Jung et al. measured the concentrations of T3, T4, and TSH whereas we measured the concentrations of FT4 and TSH to evaluate the thyroid function. In addition, the concentration of TSH for diagnosing thyrotoxicosis was applied differently, with 0.25 uIU/mL in the present study, and 0.30 uIU/mL in the study by Jung et al. However, the fact that the thyroid dysfunction was more commonly observed in women than in men, and that hypothyroidism is more commonly observed as age increases, are common findings. The limitation of the present study is that patients who were receiving treatment for thyroid dysfunction could have been included in the normal group due to the lack of an investigation into the medical and treatment histories of subjects with respect to thyroidism. To counterbalance the effect of such a limitation, our study involved over 60,000 subjects, which allowed cardiovascular risk factors such as, blood pressures, blood sugar, level of obesity, dyslipidemia, lipoprotein (a), and hsCRP to be analyzed. Thyroid hormones and serum lipids are known to be closely<sup>14, 24, 25)</sup>. Moreover, it has been verified that overt hypothyroidism can cause cardiovascular diseases and arteriosclerosis by increasing the total cholesterol and

low-density lipoprotein cholesterol. Its mechanism has been attributed to the fact that the concentration of low-density lipoprotein cholesterol receptors falls in fibroblasts, the liver and in other tissues that the diseased thyroid cannot absorb low-density lipoprotein cholesterol as well as the normal thyroid. Thus, this material accumulates in the blood. With thyroid hormone therapy, adverse effects can be controlled and total cholesterol and low-density lipoprotein cholesterol values can be decreased<sup>26)</sup>. However, there is no clear evidence that subclinical hypothyroidism can cause cardiovascular disease, as results are contradictory<sup>20-23, 26)</sup>. Recently, several studies have found that an increase in total cholesterol and low-density lipoprotein cholesterol levels are a primary cause of arteriosclerosis and cardiovascular diseases in subclinical hypothyroidism<sup>19, 27, 28)</sup>. Various mechanisms are involved in the relationships between subclinical hypothyroidism arteriosclerosis and cardiovascular diseases. Thyroid auto-immunity is one such mechanism, which is related to cardiovascular diseases. This is an abnormal immunoreactivity, which is related to vascular injuries mediated by immune-complex<sup>29-31)</sup>.

In a Rotterdam study<sup>19)</sup>, the incidence of arteriosclerosis or hyperlipidemia was found to be higher in subclinical hypothyroidism in the presence of antibodies for thyroid peroxidase. Moreover, the low-density lipoprotein cholesterol level was found to fall by approximately 12% on thyroid hormone therapy<sup>19)</sup>.

When subclinical hypothyroidism patients, who show hyperlipidemia, receive thyroid hormone therapy, it causes the total cholesterol and low-density lipoprotein cholesterol to drop, and can decrease the incidence of cardiovascular diseases. In addition, it has been reported that this occurs more so when thyroid auto-antibodies are present<sup>19-21, 32)</sup>. On the other hand, thyroid hormone therapy causes serum lipid response to changes with TSH level<sup>17)</sup>. It has also been reported that when TSH>10 mU/L, total cholesterol and low-density lipoprotein cholesterol decrease, but when TSH<10 mU/L, there is no effect<sup>15, 17, 26)</sup>. In other words, the higher the severity of hypothyroidism, the larger the effects of the thyroid hormone therapy upon hyperlipidemia, when thyroid auto-antibodies are benign. There have not been many systematic

studies on the relationship between thyroid function and high-density lipoprotein cholesterol, and studies have shown different results, though many have been reported as statistically insignificant. Some studies have reported that the high-density lipoprotein cholesterol level reduces in thyrotoxicosis and increases in hypothyroidism<sup>24, 25</sup>. Although Carantoni et al.<sup>33</sup> reported that the high-density lipoprotein cholesterol level decreases with hypothyroidism and contributes to the risk of cardiovascular diseases. In the present study, the total cholesterol was lower in overt and subclinical thyrotoxicosis (i.e., by 34 mg/dL and 9 mg/dL respectively,  $p < 0.0001$ ), compared to the normal group, while low-density lipoprotein cholesterol was lower (by 20 mg/dL and 6 mg/dL, respectively ( $p < 0.0001$ )). Similarly, in cases of subclinical hypothyroidism, the total cholesterol was higher by 5 mg/dL and 4 mg/dL, respectively, ( $p < 0.05$ ,  $p = 0.015$ ), as was the low-density lipoprotein cholesterol, by 2 mg/dL and 3 mg/dL ( $p < 0.05$ ,  $p = 0.047$ ). As a result of analyzing the TSH and lipid levels in 279 subjects of  $\geq 65$  in America, the total cholesterol was reported to have increased by 8% at high TSH versus the normal group, and the low-density lipoprotein cholesterol to have increased by 13%. Thus, though increases in the total cholesterol and low-density lipoprotein cholesterol shown in the present study are statistically significant, their degrees are small. In the present study, total cholesterol and low-density lipoprotein cholesterol did not increase in the men with only overt hypothyroidism. However, in women, the difference in the lipid levels of the subclinical and overt hypothyroidism groups was large. Therefore, screening tests for lipids are considered necessary for women. As a result of comparing hsCRP<sup>34</sup>, which has been reported as a strong independent prognostic factor for the risk of arteriosclerosis and cardiovascular diseases, with thyroid dysfunction itself, no significant difference was found. This is considered to be due to the relatively smaller number of the subject patients involved and a study is now being planned to complement address this. Thyroid hormones are known to play an important role in controlling the energy metabolism and obesity genes<sup>35</sup>. Therefore, body mass may change in cases of thyroid dysfunction. According to the study by Mehta et al.<sup>36</sup>, 14% of obese people with a body mass index of 30–40 kg/m<sup>2</sup> showed hypothyroidism, 8% of these were reported to be overt, and 6% had subclinical hypothyroidism. In this study, body mass index (BMI) and waist-hip ratio were measured as indicators of obesity, which is an important risk factor for cardiovascular diseases. However, thyroid function and BMI did not show any significant correlation, but the waist-hip ratio was found to be significantly higher in the hypothyroidism than in the normal group. Thus central obesity, which is a risk factor for cardiovascular diseases, was found to be significantly

higher, especially in the hypothyroidism group. In conclusion, the prevalence of thyroid dysfunction in Korean people who are seemingly healthy was found to be lower than in the West, while the findings that its prevalence was higher in the aged and much higher in women concurred with findings published in West. In subclinical hypothyroidism especially, total cholesterol and low-density lipoprotein cholesterol, which are risk factors for cardiovascular diseases, were significantly elevated even after adjusting the age and gender ratio.

Therefore, we recommend that screening tests and treatment for subclinical hypothyroidism should be undertaken, and that further prospective studies should be initiated on determining the actual incidence of cardiovascular diseases in the subclinical hypothyroidal group.

#### List of abbreviation

SBP, systolic blood pressure  
 DBP, diastolic blood pressure  
 FBS, fasting blood sugar  
 LDL-C, low density lipoprotein cholesterol  
 HDL-C, high density lipoprotein cholesterol  
 hsCRP, high sensitivity C-reactive protein  
 TSH, thyroid stimulating hormone

## REFERENCES

- 1) Wiersinga WM. *Subclinical hypothyroidism and hyperthyroidism. Prevalence and clinical relevance. Neth J Med.* 46:197–204, 1995
- 2) Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, Grimley Evans J, Young E, Bird T, Smith PA. *The spectrum of thyroid disease in a community: The Wickham survey. Clin Endocrinol.* 7:481–493, 1977
- 3) Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. *The Colorado thyroid disease prevalence study. Arch Intern Med.* 160:526–534, 2000
- 4) Bjoro T, Holmen J, Kruger O, Midthjell K, Hunstad K, Schreiner T, et al. *Prevalence of thyroid disease, thyroid dysfunction and thyroid peroxidase antibodies in a large, unselected population. The Health Study of Nord-Trøndelag(HUNT). Eur J Endocrinol.* 143:639–647, 2000
- 5) Andersen-Ranberg K, Jeune B, Hoier-Madsen M, Hegedus L. *Thyroid function, morphology and prevalence of thyroid population-based study of Danish centenarians. J Am Geriatr Soc.* 47:1238–1243, 1999
- 6) Brochmann H, Bjoro T, Gaarder PI, Hanson F, Frey HM. *Prevalence of thyroid dysfunction in elderly subjects. A study in a Norwegian rural community(Naeroy). Acta Endocrinol* 117:7–12, 1998
- 7) Seck T, Scheidt-Nave C, Ziegler R, Pfeilschifter J. *Prevalence of*

- thyroid gland dysfunction in 50- to 80-year old patients. An epidemiologic cross-sectional study in a southwestern community. *Med Klin.* 15:92:642-646, 1997
- 8) Ayala C, Cozar MV, Rodriguez JR, Silva H, Pereira JL, Garcia-Luna PP. Subclinical thyroid disease in institutionalised healthy geriatric population. *Med Clin.* 117:534-535, 2001
  - 9) Bindels AJ, Westendorp RG, Frolich M, Seidell JC, Blokstra A, Smelt AH. The prevalence of subclinical hypothyroidism at different total plasma cholesterol levels in middle aged men and women: a need for case-finding? *Clin Endocrinol.* 50:217-220, 1999
  - 10) Lindeman RD, Schade DS, LaRue A, Romero LJ, Liaug CL, Baumgartner RN et al. Subclinical hypothyroidism in a bi-ethnic, urban community. *J Am Geriatr Soc.* 47:703-709, 1999
  - 11) Fardella C, Poggi H, Gloger S, Rojas A, Velasquez CG, Barroileth S, Figueroa R, Alvarez C, Salgado C, Gajardo C, Foradori A, Montero J. High prevalence of subclinical thyroidal disease among individuals attended in health control. *Rev Med Chil* 129:155-160, 2001
  - 12) Bastenie PA, Vanhaelst L, Bonnyns M, Neve P, Staquet M. Preclinical hypothyroidism : a risk factor for coronary heart disease. *Lancet.* 203-204, 1971
  - 13) Gomberg-Maitland M, Frishman WH. Thyroid hormone and cardiovascular disease. *Am Heart J.* 135:187-196, 2000
  - 14) Deschamphelleire M, Luyckx FH, Scheen AJ. Thyroid disorders and dyslipidemias. *Rev Med Liege.* 54:746-750, 1999
  - 15) Diekman T, Lansberg PJ, Kastelein JJ, Wiersinga WM. Prevalence and correction of hypothyroidism in a large cohort of patients referred for dyslipidemia. *Arch Intern Med.* 155:1490-1495, 1995
  - 16) Miura S, Iitaka M, Suzuki S, Fukasawa N, Kitahama S, Kawakami Y, Sakatsume Y, Yamanaka K, Kawasaki S, Kinoshita S, Katayama S, Shibosawa T, Ishii J. Decrease in serum levels of thyroid hormone in patients with coronary heart disease. *Endocr J.* 43:657-663, 1996
  - 17) Efsthadiadou Z, Bitsis S, Milionis HJ, Kukuviitis A, Bairaktari ET, Elisaf MS, Tsatsoulis A. Lipid profile in subclinical hypothyroidism: L-thyroxine substitution beneficial? *Eur J Endocrinol.* 145:705-710, 2001
  - 18) Vierhapper H, Nardi A, Grosser P, Raber W, Gessel A. Low-density lipoprotein cholesterol in subclinical hypothyroidism. *Thyroid.* 10:981-984, 2000
  - 19) Hak AE, Pols HA, Visser TJ, Drexhage HA, Hofman A, Witteman JC. Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: The Rotterdam study. *Ann Intern Med.* 132:270-278, 2000
  - 20) Feld S, Dickey RA. An Association Between Varying Degrees of Hypothyroidism and Hypercholesterolemia in Women: The Thyroid-Cholesterol Connection. *Prev Cardiol.* 4:179-182, 2000
  - 21) Tanis BC, Westendorp GJ, Smelt HM. Effect of thyroid substitution on hypercholesterolaemia in patients with subclinical hypothyroidism: a reanalysis of intervention studies. *Clin Endocrinol.* 44:643-649, 1996
  - 22) Pirich C, Mullner M, Sinzinger H. Prevalence and relevance of thyroid dysfunction in 1922 cholesterol screening participants. *J Clin Epidemiol.* 53:623-629, 2000
  - 23) Bauer DC, Ettinger B, Browner WS. Thyroid Function and Serum Lipids in Older Women: A Population-based Study. *Am J Med.* 104:546-551, 1998
  - 24) Diekman MJ, Angheliescu N, Endert E, Bakker O, Wiersinga WM. Changes in plasma Low-Density Lipoprotein (LDL)- and High-Density Lipoprotein Cholesterol in Hypo- and Hyperthyroid Patients Are Related to Changes in Free Thyroxine, Not to Polymorphisms in LDL Receptor or Cholesterol Ester Transfer Protein Genes. *J Clin Endocrinol Metab.* 85:1857-1862, 2000
  - 25) Aviram M, Luboshitzky R, Brook JG. Lipid and lipoprotein pattern in thyroid dysfunction and the effect of therapy. *Clin Biochem.* 15:62-66, 1982
  - 26) Kahaly GJ. Cardiovascular and Atherogenic Aspect of Subclinical Hypothyroidism. *Thyroid.* 10:8, 2000
  - 27) Kyoung Ah Kim, Jae Hoon Chung, Yeun Sun Kim, Kyu Jeung Ahn, Eun Mi Koh, Yong Ki Min, Myung-Shik Lee, Moon-Kyu Lee, Jong Hun Lee, Kwang Won Kim. Serum Lipoprotein(a) and Lipid Concentration in Patients with Subclinical Hypothyroidism. *Journal of Korean Society of Endocrinology.* 12:11-15, 1997
  - 28) Michael T, McDermott MT, Ridgway EC. Subclinical hypothyroidism is mild thyroid failure and should be treated. *J Clin Endocrinol Metab.* 86:4585-4590, 2001
  - 29) Tiche M, Lupi GA, Gutzwiller F, Grob PJ, Studer H, Burgi H. Borderline low thyroid function and thyroid autoimmunity. Risk factors for coronary heart disease? *Br Heart J.* 46:202-206, 1981
  - 30) Bastenie PA, Vanhaelst L, Golstein J, Smets P. Asymptomatic autoimmune thyroiditis and coronary heart disease. Cross-sectional and prospective studies. *Lancet.* 2:155-158, 1977
  - 31) Mathews JD, Whittingham S, Mackay IR. Autoimmune mechanisms in human vascular disease. *Lancet.* 2:1423-1427, 1974
  - 32) Meier C, Staub JJ, Roth CB, Guglielmetti M, Kunz M, Miserez AR, Drewe J, Huber P, Herzog R, Muller B. TSH-controlled L-thyroxine therapy reduces cholesterol levels and clinical symptoms in subclinical hypothyroidism: a double blind, placebo-controlled trial (Basal Thyroid Study). *J Clin Endocrinol Metab.* 86:4860-4866, 2001
  - 33) Carantoni M, Vigna GB, Stucci N, Zanca R, Fellin R. Low level of HDL cholesterol in hypothyroid patients with cardiovascular diseases. *Minerva Endocrinol.* 22:91, 1997
  - 34) Ridker PM. High-Sensitivity C-Reactive Protein : Potential Adjunct for Global Risk Assessment in the Primary Prevention of Cardiovascular Disease. *Circulation.* 103:1813-1818, 2001
  - 35) Korischoner NP, Alvarez-Dolado M, Kurz SM, Heikenwalder MF, Hacker C, Vogel F. Thyroid hormone regulate the obesity gene tub. *EMBO J.* 2:499-504, 2001
  - 36) Mehta S, Mathur D, Chaturvedi M, Devpura G, Jat VS. Thyroid hormone profile in obese subjects-a clinical study. *J Indian Med Assoc.* 99:260-272, 2001
  - 37) Jae Hoon Chung, Kwang Won Kim, Byoung Joon Kim, Sung Hoon Kim, Myung Sik Lee, Moon Gyu Lee. Prevalence of Thyrotoxicosis and Hypothyroidism in the Subjects for Health Check-Up. *Journal of Korean Society of Endocrinology.* 14:301-313, 1999