Several factors may affect the prevalence of thyroid disorders such as advancing age and dietary iodine.1-4 Epidemiological data shows that thyroid disorders such as goiter, nodularity, and hyperthyroidism are more common in areas of long-standing iodine deficiency. Different prevalence rates of thyroid disorders were reported previously from different countries.5,6 Data from screening large US population samples have revealed differences in the frequency of thyroid dysfunction in different ethnic groups,6,7 whereas studies from Europe have revealed the influence of dietary iodine intake on the epidemiology of thyroid dysfunction.8-9 Also, there was a small number of prevalence studies performed in restricted areas from Turkey in the selected groups of the populations.10-12

Sonographic examination is useful for several aspects of thyroid gland investigation, including the measurement of size and finding nodularity and echogenicity.6,13,14 By using ultrasonography, goiter and nodule prevalence were found more frequent than assessing by physical examination in epidemiological studies.15 In cross-sectional surveys, the prevalence of diffuse goiter declines with age, in contrast to the prevalence of thyroid nodules that increase with age.8
Thyroid hormones affect many metabolic processes, and hypothyroidism has been associated with both hypertension and hypercholesterolemia.5,16-18

The present study aims at investigating thyroid functions, sonographic characteristics, relation of thyroid functions and (body mass index) BMI, arterial systolic and diastolic pressure, serum glucose, total cholesterol, triglycerides, and (high-density lipoprotein) HDL-C and (low-density lipoprotein) LDL-C concentrations in a large adult population living in northern Turkey.

**PATIENTS AND METHODS**

This study was conducted in 70 (12 urban and 58 rural) areas in the province of Tokat, which is located in the Black Sea region of Turkey, with about 530,000 inhabitants aged 18 years and older. All of the urban regions and some of the rural regions, selected by cluster sampling method, were included. The study population of 1095 subjects (54 male [49.4%] and 554 female [50.6%], urban 555 [50.7%], and rural 540 [49.3%]) was selected by a random sampling method among 18 years and older inhabitants. All subjects were visited at their homes. They were asked about previous thyroid diseases such as hyperthyroidism, hypothyroidism, goiter, and other thyroidal diseases. The details about the subjects who were taking medications such as thyroxin, propylthiouracil, or radioactive iodine were recorded; previous thyroid surgery histories were also recorded.

Subjects were interviewed by an internist and 2 radiologists. Demographic characteristics such as age, gender, weight, height, and BMI were recorded. Physical examination was performed and thyroid palpation findings were noted. Ultrasonographic examinations were performed in all individuals using a GE Logic 200 (GE Medical Systems, Milwaukee, Wisconsin) machine, and thyroid sonographic features were determined. Blood samples were collected for each subject. Serum glucose, total cholesterol, LDL-C, HDL-C, triglycerides, thyrotrphin (TSH), and free T4 levels were measured by a Dimension Clinical Chemistry System (Dade Behring Inc. Newark, Delaware, USA), Roche Elecsys 2010, and Modular Analytics E170 (Elecsys module) immunoassay analyzers (Roche Diagnostics GmbH, D-68298 Mannheim, Germany). The reference interval for TSH and fT4 were 0.27 to 4.2 µIU/mL and 0.9 to 1.7 ng/dL, respectively.

In the absence of hypothalamic or pituitary disease, nonthyroidal illness or ingestion of drugs that inhibit TSH secretion such as glucocorticoids, thyroid statuses were defined as euthyroid (normal TSH and fT4), overt hypothyroidism (TSH: ↑, and fT4: ↓), subclinical hypothyroidism (TSH: ↑, and fT4: N), overt hyperthyroidism (TSH: ↓, and fT4: ↑), and subclinical hyperthyroidism (TSH: ↓, and fT4:N).

**Table 1.** Baseline characteristics of the study population.

|                  | Male (n=541) | Female (n=544) | Total (n=1095) | Range | P  |
|------------------|--------------|----------------|----------------|-------|----|
| Age, y           | 41.2 (17.7)  | 41.5 (16.3)    | 41.4 (17)      | 18-95 | .701|
| Weight, kg       | 72.8 (12.9)  | 68.2 (14.4)    | 70 (13.6)      | 70.4-120 | <.001*|
| Body mass index, kg/m² | 25.7 (7.4)  | 27.9 (5.9)    | 26.8 (6.8)    | 21.7-46.2 | <.001*|
| Waist circumference, cm | 88.7 (12)  | 89.7 (14.4)  | 89.3 (13.3)  | 55-147 | .186|
| Blood pressure, mm Hg |                  |              |                |       |    |
| Systolic BP      | 128.8 (21.8) | 135.4 (28.2)  | 132.2 (25.5)   |       | <.001*|
| Diastolic BP     | 82.5 (13.9)  | 85.4 (16.9)   | 84 (15.6)      | .002* |
| Glucose, mg/dL   | 93.9 (37.3)  | 94.3 (31.3)   | 94.1 (34.4)    | 56-537 | .822|
| Total cholesterol, mg/dL | 187.2 (39.9) | 189.6 (43.4)  | 185.9 (41.9)   | 82-392 | .003*|
| Triglyceride, mg/dL | 148.1 (85.9) | 135.3 (76.9)  | 120.9 (43)     | 29-452 | .010*|
| HDL-C, mg/dL     | 38.2 (11.2)  | 43.5 (11.2)   | 40.8 (11.5)    | 1-110  | <.001*|
| LDL-C, mg/dL     | 116.3 (34.1) | 120.8 (39.2)  | 135.2 (81.9)   | 34-452 | .039*|
| TSH, µLU/mL      | 1.5 (1.6)   | 2.2 (6.6)     | 1.9 (4.9)      | 0.01-100 | .013*|
| fT4, ng/dL       | 1.2 (0.1)   | 1.2 (0.3)     | 1.2 (0.3)      | 0.12-5.09 | .003*|

HDL: High-density lipoprotein, LDL: low-density lipoprotein; *Male vs female.

Note: Values are presented as mean (SD).
Informed consents were obtained from all subjects, and the study protocol was approved by the Ethics Committee of Gaziosmanpasa University.

Statistical analysis
Data were entered and analyzed by SPSS, version 15 (SPSS Inc., Chicago). Data were represented as percentage, frequency, and mean (standard deviation, SD). Chi-square test, ANOVA test, and Mann Whitney Test were applied. The parameters affecting the TSH levels were investigated using spearman/pearson correlation. A multiple linear regression model was used to identify independent predictors of TSH. $P$ values <.05 were considered statistically significant.

RESULTS

Characteristics of study population:
A total of 1095 subjects ([urban/rural: 555/540] and [male/female: 541/554]) were selected by a random sampling method. The mean ages (SD) of subjects were 41.4 (17) (range: 18-95) years. The mean weight and BMI (SD) were 70 (13.6) kg and 26.8 (6.8) kg/m², respectively. The mean systolic and diastolic blood pressures (SD) were 132.2 (25.5) and 84 (15.6) mm Hg, respectively. Glucose levels were similar in both genders. Serum total, HDL, and LDL cholesterol levels were higher and serum triglyceride levels were lower in the women subjects than in men subjects ($P<.05$) (Table 1). Twenty-four (2.1%) subjects had thyroid disease and 16 (1.4%) subjects had previous thyroid surgery. The medications reported as 3 (0.3%) subjects with antithyroid and 3 (0.3%) subjects with thyroid hormone replacement therapy.

The mean TSH level (SD) was 1.9 (4.9) µIU/mL in the study population. The mean TSH and free T4 levels (SD) were 1.5 (1.6) µIU/mL and 1.2 (0.1) ng/dL in males, 2.2 (6.6) and 1.2 (0.3) ng/dL µIU/mL in females, respectively ($P<.05$). The thyroid function tests were measured in normal ranges in 987 (90.1%) subjects. The TSH and free T4 levels were significantly lower in the older subjects (≥70 and 60-69 years) than in the younger subjects (<20 and 20-29 years) (Figure 1). The prevalence of thyroid dysfunction among participants was 18 (1.6%) for overt hypothyroidism, 6 (0.6%) for overt hyperthyroidism, 30 (2.7%) for subclinical hypothyroidism, and 54 (4.9%) for subclinical hyperthyroidism (Figure 1). According to these findings, the most diagnosed thyroid dysfunction among the subjects was subclinical hyperthyroidism. Both of hypothyroidism and hyperthyroidism rates were significantly higher in the female subjects than in the male subjects. The mean age was higher for the subjects with subclinical hypothyroidism than for the subjects having euthyroid.

We investigated the differences of thyroid function tests among different age groups. Subclinical hyperthyroidism was found as the most frequent abnormality in the subjects with older than 60 years, whereas subclinical hypothyroidism was the most common abnormality of thyroid function among the subjects younger than 40 years (Table 2, 3).
According to thyroid ultrasonography, 421 (38.4%) subjects had normal sonographic findings (Table 3). The most common sonographic abnormality was multinodular goiter (n=352, 32.1%). The prevalence of sonographic abnormalities was significantly different between male and female subjects. About half of the males had normal thyroid sonography. The prevalence of multinodular goiter, nodular goiter, and heterogeneity of thyroid gland was 23.5, 11.6, and 14.2 % in males, respectively. Among the female subjects, the most common abnormality was multinodular goiter (n=225, 40.6%). Only 147 (26%) females had normal sonographic findings. The prevalence of multinodular goiter increased with age (P<.001). The thyroid nodule frequency under age 20 is 17%, at 20-29 ages is 22%, at 30-39 ages is 43%, at 40-49 ages is 52%, at 50-59 ages is 74%, at 60-69 ages is 65%, and over 70 ages is 71%. The mean TSH and free T4 levels were found similar in the subjects with normal parenchyma, nodular goiter, multinodular goiter, and thyroid heterogeneity. The majority of subjects with nodular and multinodular goiter had euthyroid (91.4 and 83.5%, respectively).

Cardiovascular risk factors and thyroid functions
We investigated the correlation between serum TSH levels and metabolic risk factors. We found no significant correlation between systolic blood pressure, serum glucose, total cholesterol, triglycerides, HDL-C, and LDL-C levels. There was a positive correlation between serum TSH levels and BMI, but it was not statistically significant. Significant negative correlation was observed between TSH levels and age (r=–0.092, P=.002). According to linear regression analyses (stepwise model), the age was independently associated with TSH levels from other parameters (waist circumference, BMI, glucose, lipids, blood pressure) (P<.0001). Total cholesterol, triglyceride, and LDL cholesterol levels were similar according to TSH groups. BMI was higher in the subjects with overt hypothyroidism than in the other groups (P<.001). Systolic blood pressure was measured high in the subjects with subclinical hypothyroidism and overt hypothyroidism compared to subclinical hypothyroidism (P=.019). Subclinical hypothyroid subjects were younger and subclinical hyperthyroid subjects were older than other groups (P<.001).

**DISCUSSION**
In our study, thyroid function tests were measured in normal ranges in 987 (90.1%). The prevalence of thyroid dysfunction among participants was 18 (1.6%) for overt hypothyroidism, 6 (0.6%) for overt hyper-
thyroidism, 30 (2.7%) for subclinical hypothyroidism, and 54 (4.9%) for subclinical hyperthyroidism. It was observed that the mean TSH levels were decreased by age in the present study. In contrast to our findings, the serum TSH concentrations were reported to increase with age in both men and women according to the National Health and Nutrition Examination Survey (NHANES III). Studies of elderly persons have confirmed the high prevalence of a raised serum TSH. The Framingham Study showed that 13.6% of US women older than 60 years had TSH levels greater than 5 µIU/L. On the other hand, data from Germany, where iodine supply is deficient, yielded lower TSH reference levels that declined with age.22-25 In the present study, although TSH levels seemed to be decreased in elderly subjects, the most frequent age group of both overt hypothyroidism and hyperthyroidism was found 40 to 49 years.

In this study, thyroid dysfunction and sonographic abnormalities were investigated in a large selected population in northern Turkey. The investigation was conducted in a total of 1095 subjects, and the findings of thyroid function tests and sonographic studies were obtained. Sensitive TSH measurement is the most accurate test for evaluating thyroid dysfunction and also for screening asymptomatic individuals.22,28 In the present study, thyroid function tests were recorded within normal ranges in 987 (90.1%) subjects. The mean TSH level (SD) was 1.9 (4.9) µIU/mL in the study population. The mean TSH levels (SD) were 1.5 (1.6) µIU/mL in males and 2.2 (6.6) µIU/mL in females. The mean levels of TSH is higher in females than in males (P=.013).

The prevalence of hypothyroidism in various studies from around the world shows a considerable variation, and its current prevalence ranges from as low as 1% to as high as 20% for subclinical and 1% to 2% for overt hypothyroidism. Hypothyroidism is the most common thyroid disorder in the adult population and is more common in women. Hypothyroidism is generally associated with iodine deficiency. A review published by the American College of Physicians estimated a pooled prevalence of overt hypothyroidism of 2% in women ≥70 years and of 0.8% in men ≥60 years. The prevalence of hypothyroidism was found 0.7% and 2.5% for males and females, respectively, in our study. Similarly, the investigators of HUNT study reported that the prevalence of hypothyroidism was 0.9% and 4.8% for males and females, respectively.26 Imani et al reported a higher prevalence of all thyroid dysfunctions in females, but the difference of clinical hypothyroidism rates was statistically significant between females and males.

Recently, Gussekloo et al reported prevalence for subclinical hypothyroidism in 5.1%, overt hypothyroidism in 1.2%, overt hyperthyroidism in 0.3%, and of subclinical hyperthyroidism in 2.9%. In our study, the prevalence of subclinical hypothyroidism was found 1.8% and 3.6% for males and females, respectively. Also the prevalence of total clinical and subclinical hypothyroidism was 1.6% and 2.7% in the study population. The prevalence of overt hyperthyroidism was found 0.6% (0.4% and 0.7% for male and females, respectively) and subclinical hyperthyroidism was found 4.9% (3.5% and 6.3% for males and females, respectively). In contrast to previous studies, subclinical hyperthyroidism was more common than hypothyroidism, and it seems to be affecting the elderly population (especially 60-69 years) in the present study.

A report from Colorado stated a prevalence of elevated TSH (>5.1 mU/L) of 9.5% in the adult population increasing with age from 3% to 16% in males and from 4% to 21% in females. In the HUNT study, only 1.5% of females than 30 were hypothyroid, compared with 7.5% of those in their seventh decade. In males, the prevalence of hypothyroidism also increased with age. In the present study, the females had more thyroid dysfunction than males, which is consistent with the previous reports.

The prevalence of nodular thyroid disease depends on the population characteristics and the methods for detecting nodules. Incidental thyroid nodules are increased by a widespread use of sensitive imaging procedures in clinical practice. It is known that nodule incidence is increased with age, in women, in people with iodine deficiency, and after radiation exposure. Numerous studies suggest a prevalence of 2% to 6% with palpation, 19% to 35% with ultrasound, and 8% to -65% in autopsy data. In the present study, 421 (38.4%) subjects had normal sonographic findings according to thyroid ultrasonography. The most common sonographic abnormality was multinodular goiter (n=352, 32.1%). The percentages of multinodular goiter, single thyroid nodule and heterogeneity of thyroid were 32.1%, 13.8%, and 15.6 %, respectively. In the published reports, similar results were reported; the nodule prevalence was higher in females than in males and in younger patients than in elderly patients. Similarly, the prevalence of thyroid nodules increased with age, and the nodular thyroid disease was more common in females than in males in our study.

A strong association was observed between thyroid dysfunction and cardiovascular risk factors, such as obesity, diabetes, and metabolic syndrome. Subclinical hypothyroidism was observed frequently in the females.
with metabolic syndrome. Additionally, thyroid disease, especially overt hypothyroidism, is associated with atherosclerotic cardiovascular disease. It is well known that the patients with hypothyroidism have lipid abnormalities. We investigated the correlation between serum TSH levels and metabolic risk factors. However, there was no significant correlation between TSH levels and metabolic risk factors, such as serum lipid, glucose concentration, and systolic and diastolic blood pressure.

The published reports investigating the association between anthropometric measures and serum TSH within the normal range presents conflicting results. It was widely examined in recent studies that there is influence of biological variability of the thyroid hormones on weight. However, the results were found contradictory. Recent longitudinal studies indicate that change in TSH is positively related to change in body weight or BMI. Moreover, it was known that there was a strong association between low levels of thyroid hormones, even within the normal range, and a greater BMI, in both the general population and obese persons. There was no correlation between TSH and body weight and BMI in our study. However, BMIs were significantly higher in the subjects with overt hypothyroidism than in the other groups in our study.

A few limitations of our study are as follows: first, the present study was based on routine thyroid function test, i.e., serum-free T4 and TSH measurement. Moreover, we could not measure the urine iodine output and levels of thyroid antibodies. Turkey was an iodine-deficient area until the 1990s when dietary salt was supplemented with iodine. Moreover, recent reports suggest that the intake of iodine in this region is now mildly sufficient (mean urinary iodine level: 47.6 µg/L). In the present study, the sampling fraction was quite low. However, this study yielded a reliable data about the prevalence of thyroid disorders in our region.

This study confirmed the fact about the higher prevalence of thyroid diseases than clinically apparent in a large, unselected population. In the present study, it was reported that the total prevalence of thyroid disorders was about 9.9% in the region with known borderline iodine deficiency. The prevalence of subclinical hyperthyroidism and nodular thyroid disease was higher than the previously reported prevalence from different countries. According to our knowledge, it is the first study investigating the prevalence of thyroid disorder in a large, unselected population of our region.

In conclusion, even if there is no history about thyroid diseases, we must keep in mind that especially elderly and female population, but also asymptomatic healthy adults, can have thyroid dysfunction. According to the published reports it is well known that 5% of all thyroid nodules is malignant. In our study we detected 45.9% (n=503) nodules in 1095 subjects. There was no history of thyroid malignancy in this population. These results suggest that there are many undiagnosed thyroid malignancies. We concluded that thyroid diseases must be concluded as a public health problem, and accurate and effective strategies must be identified for the prevention and early detection of thyroid diseases.
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