in our study by the fact that 45.3% of the experimental individuals had elevated anti-TPO antibodies ($P = 0.015$). As expected, the odds ratio test showed that the risk of subclinical hypothyroidism in individuals with elevated serum anti-TPO was 19.9 times higher than in those with negative anti-TPO. According to the results of the Pearson correlation test, there was a significant relationship between anti-TPO and TSH levels in the case and control groups ($P = 0.001$ and $P = 0.006$, respectively).

**DISCUSSION**

The present study provides evidence of an association between $A2095C$ (rs121908087) and $A2173C$ (rs732609) genetic variations in the $TPO$ gene with anti-TPO levels in patients who have subclinical hypothyroidism (SCH). The results showed that these polymorphic regions have a significant correlation with subclinical hypothyroidism. In addition, as expected, the serum anti-TPO titer had increased significantly in the patient group, especially in those who have the C allele in the $A2173C$ polymorphic region. Furthermore, we detected the presence of amino acid substitutions, such as Asn698Thr for $A2095C$ and Thr725Pro for the $A2173C$ polymorphism, on performing bioinformatics studies.

Autoimmune thyroid disease (AITD) is thought to arise from a combination of genetic and environmental factors. Since the protein structure of thyroid peroxidase is related to genetic variations in the $TPO$ gene, TPO appears to play a critical role in thyroid hormone synthesis; however, genetic variations may lead to changes in its structure, thus the TPO enzyme is recognized as a foreign body and antibodies are produced against it. Hashimoto’s thyroiditis (HT), an autoimmune disease in which the thyroid gland is gradually destroyed by lymphocyte invasion and antibody-mediated immune processes, is the most common cause of hypothyroidism and may occur as a result of subclinical hypothyroidism.

Since the TPO enzyme structure and/or its activity is defective in autoimmune thyroid disease, for the first time the hypothesis is being proposed that genetic variations of the $TPO$ gene may contribute to the occurrence of these diseases. Based on the results of the present study, in the presence of the C allele of $A2173C$ SNP, anti-TPO antibody levels would increase in patients with subclinical hypothyroidism, although we did not observe any correlation between increased anti-TPO levels and the C allele of $A2095C$.

Because of the high prevalence of subclinical hypothyroidism and its associated metabolic risk factors such as hyperlipidemia, the American Thyroid Association recommends screening tests by measurement of serum TSH after the age of 35 at 5-year intervals.

To date, several studies have found evidence of the association of $TPO$ gene polymorphisms with anti-TPO levels in patients with hypothyroidism; however, the genetic variations in the $TPO$ gene and their correlation with anti-TPO antibodies levels have not been investigated in patients with subclinical hypothyroidism who do not have overt hypothyroidism and its symptoms.

In line with studies which indicated that $TPO$ gene variations such as polymorphisms are associated with anti-TPO levels, as well as with some studies in patients with overt hypothyroidism in the Tehran population, the present study also indicates the association of genetic characterization of the $TPO$ gene with anti-TPO levels. However, the novelty of our study was to investigate exon 12 $TPO$ gene polymorphisms in patients with subclinical hypo-