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Factors Influencing Autoimmune Thyroid Disease

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Annotation: Autoimmune thyroid disease (AITD) are among the most common diseases in recent times. Their causes and symptoms vary from one person to another. The main cause may be an immune or acquired disorder. Therefore, this article aims to focus on the causes that lead to thyroiditis, hyperactivity and lethargy. Most of these causes are known and common, and recovery can be achieved when the main cause is known. The infection may be diagnosed based on the causes in addition to the apparent symptoms and using common diagnostic methods such as X-rays, ultrasound, and laboratory testing of thyroid hormones.

Keywords: Autoimmune, Graves disease, hypothyroidism, Hashimoto's thyroiditis.

1- Introduction

Autoimmune thyroid disease (AITD), which is also referred to as Hashimoto's thyroiditis (HT) or Graves' disease (GD), is caused by an interaction between genetic susceptibility, which accounts for roughly 70–80% of thyroid autoimmunity development, and a number of environmental factors, such as selenium deficiency, increased iodine intake, alcohol consumption, smoking status, drug side effects, infections, stressful life events, and microbiota [1,2]. The etiology of AITD is complex, involving both environmental and genetic variables, and it appears that females are predisposed to the disease more than males. The two primary forms of AITD are HT and GD, both of which exhibit a substantial correlation in age groups over (45–50) years [3].

Prevalence of the two main AITDs, HT and GD, which are distinguished by hypothyroidism and

thyrotoxicosis, respectively, has been estimated at 5% [4]. Thyroid autoantibody synthesis and lymphocytic infiltration of the thyroid are two characteristics shared by both AITDs [5]. It appears that several environmental factors, like iodine, smoking, infection, and diet greatly contribute to AITD.[6] At first, it was believed that only major histocompatibility complex (MHC) class II genes predisposed people to AITD since AITD is associated with the immune system. Subsequent research, on the other hand, verified that a number of non-MHC susceptibility genes play a role in AITD etiology. A few genes are exclusive to HT or GD, others are common to both disorders, and some are common to AITD and other types of the autoimmune diseases [7]. These genes have been believed to predispose people to AITD.

Materials and Methods

2- Factors influencing autoimmune thyroid disease:

2-1- Gender differences in AITD

With female to male ratio ranging between 5:1 and 10:1, AITD is far more common in the females compared to males. With the exception of a few new clues, the biological cause for the gender disparities is not totally evident. Postpartum thyroiditis is frequently observed before permanent Autoimmune hypothyroidism [8,9], and GD [10] might start during the postpartum period. For maintaining a state of tolerance to fetal alloantigens and preventing fetus rejection, it appears that the development of maternal regulatory T-cells (Treg) early in pregnancy causes reduction in the amount of thyroid antibodies circulating throughout pregnancy [11]. Thyroid antibodies return with a brief increase following delivery. One major contributing cause to the increased likelihood of parity as an AITD risk factor is thought to be fetal microchimerism. Fetal microchimerism results from persistence of fetal cells in the maternal tissues, which start to circulate in the mother by the first trimester[12]. Autoimmune disorders such as AITD could be brought on by maternal immune responses directed against fetal antigens. Indeed, prenatal microchimerism has been observed in thyroid tissues as well as blood from women who have either Graves' or Hashimoto's disease[13]. Therefore, female preponderance of AITD can be explained, at least partially, by parity. In addition to sparity, X chromosomal inactivation may have a major role in high AITD prevalence in women. It is known that in early stages of female embryogenesis, 1 of the 2 X chromosomes is inactivated. "Skewed X chromosome in activation" (XCI) refers to inactivation of the same X chromosome in no less than 80% of cells[14]. This might cause immunological tolerance to X-linked antigens to be lost, which can then trigger autoimmunity, including AITD[15]. Given that AITD is much more widespread in women, there is a possibility that estrogens play a major role in AITD. No less than 15% of females over 60 and 2% of males have HT [16].

Results and Discussion

2-2- Environmental Factors

Out of the several environmental influences, the most significant ones seem to be diet, infection, medications, iodine, and smoking [17].

2-2-1 Nutrition: Nutritional elements include tri-iodothyronine (T3, active hormone), thyroxine (T4, pro-hormone), and iodine, which represents one of the essential components of the thyroid hormones and shows the major participants in the production of the thyroid hormone occurring in thyroid follicular cells[18]. The relationship between the intake of iodine and circulating thyroid antibodies is complicated; an increase in circulating antibodies is linked to the intake of iodine below as well as above recommended levels [19]. Both populations with a consistent high intake of iodine and those with mild to moderate iodine insufficiency (ID)[20] have circulating TPO- and Tg-antibodies. Studies in numerous nations have demonstrated that an increased thyroid autoimmunity risk results from excess intake of iodine or a rise in intake after the fortification of the iodine of iodine-deficient population[21]. Insufficient iodine intake could cause nodular goiter, a condition where thyroid antigens are released from abnormal gland and lead to presence of the thyroid antibodies in circulation,[22]. A necessary trace element for all higher animal species, such as humans,

is selenium (Se). There are not many selenoproteins in the human selenoproteome. Thus far, a biological role has been assigned to around half, while several have no known purpose [23]. Housekeeping and stress-related proteins are two general categories into which mammalian selenoproteins could be divided[24]. Antioxidative oxidoreductases, also known as thioredoxin reductases and glutathione peroxidase, are the primary functional proteins in thyroid gland. They play a crucial role in antioxidant process, regulate redox status, and guard against damage from oxygen free radicals. The local stimulation of thyroid hormones in addiction is caused by two isoforms Of all bodily tissues, the thyroid gland has maximum concentration of selenium (Se) and is home to numerous selenoproteins with distinct biological roles[25]. It has been established in the 1980s that supplementing with selenium is essential for avoiding and/or treating clinical manifestations of severe selenium deficiency[26]. A decade later, the first description of the association between severe selenium insufficiency and thyroid dysfunction in the children has been made [27]. Both GO and GD were linked to cigarette smoking[28]. On the other hand, smoking lowers thyroid antibody incidence and the likelihood of overt hypothyroidism [29]. Thyrotoxicosis produced by amiodarone may be associated with thyroid autoimmunity [30].

2-2-2-Effect of Infections:

Infectious agents are one of the etiological elements that are frequently mentioned in relation to AT. For instance, people with Graves's thyrotoxicosis have been found to be infected with *Yersinia enterocolitica*. It appears that Helicobacter pylori (Hp) is yet another significant causative factor [31]. Half of the world's population is afflicted by the pervasive HP illness. Gram-negative, microaerophilic, spiral-shaped HP is the causative agent of persistent colonization of the gastric mucosa in relation to the development of major gastric disorders, including peptic ulcer disease, adenocarcinoma, chronic gastritis, and MALT lymphoma [32], [33]. AITD and viral infections: there is substantial evidence linking the hepatitis C virus to AITD among a number of infectious agents [34, 35]. People who have HCV infection but are not yet receiving IFN-α therapy do exhibit thyroid impairment. Patients who do not have clinical thyroid impairment but have an untreated HCV infection frequently have elevated levels of thyroid antibodies [36]. Indeed, in HCV patients, IFN-α therapy could have a synergistic effect on thyroid dysfunction [37]. Enteroviruses, aside from HCV, were found in the thyroid tissue of individuals suffering from HT. Intriguingly, compared to patients infected with HBV, a much larger proportion of HCV patients, regardless of age, had positive thyroid antibodies. It was suggested that proinflammatory cytokines produced by HCV infection of human thyrocytes heighten the autoimmune response and consequent AITD. TPO[38] activity is lowered in iron deficiency (ID) to decrease thyroid hormone synthesis. Studies on humans and animals provide evidence that thyroid function depends on iron levels. In rodents, ID, without or with anemia, reduced the levels of serum T3 and T4, as well as the activity of 5′-deiodinase (DIO) and the capacity for the thermoregulation as a response to cold [39]. Serum T4 and T3 levels were considerably lower in U.S. women who have mild ID anemia (Hb, 110g/l) than in controls who had adequate iron levels [40]. Moreover, a study that has been carried out with the participation of 365 Swiss pregnant women in 2nd and 3rd trimesters with borderline ID (median urine iodine concentration 139µg/l) had found that urinary iodine, total T4, and TSH concentrations have been all assessed. ID also predicts poor maternal thyroid health throughout pregnancy. TSH and total T4 were significantly predicted by body iron reserves, which were determined by the concentration of blood Hb, serum ferritin, mean corpuscular volume, and transferrin receptor ($P<0{\cdot}0001$)[41]. Additionally, serum free T4 concentrations have been considerably lower in 3340 pregnant and 1052 non-pregnant Chinese women who have ID than in women who have normal iron levels, indicating that ID is linked to hypothyroxinaemia.[42]

2-2-3-Medication

Many drugs and medications can affect thyroid function, but only a small subset (glucocorticoids, dopamine agonists, somatostatin analogs and rexinoids) suppress TSH at the level of the hypothalamus or pituitary. Fortunately, the widely used glucocorticoids and the somatostatin analogs do not induce clinically evident central hypothyroidism even after prolonged high dose use.

Dopamine agonists do not cause clinically significant central hypothyroidism, but may have an additive effect of TSH suppression in patients with non-thyroidal illness, which may lead to a state of iatrogenic central hypothyroidism in this patient population. Rexinoids, clearly induce clinically significant central hypothyroidism in most patients, who require levothyroxine replacement and monitoring of serum free T4 levels. As this newer class of drugs may be used in more patients (advanced cancer, metabolic disorders, dermatologic disorders), clinicians need to be aware of this unique and treatable side-effect[43].

2-3-Genetic Factors

Strong genetic influences on the etiology of AITD are supported by investigations using twins as well as family members [44]. Research on twins reveals that monozygotic twins had a much greater concordance rate for both GD [45] and HT [46] than dizygotic twins do. According to these research, around 80% of the risk for GD is inherited [47]. Many important genes for AITD have been found by linkage and association studies. These genes include immune-regulatory genes as well as thyroid-specific genes like the thyroid-stimulating hormone receptor (TSHR) and thyroglobulin (Tg). AITD and other auto immune illnesses are predisposed by the same immune-regulatory genes. The following AITD genes were found using tag single nucleotide polymorphism screening as well as conventional case-control studies: PTPN22, which interacts with molecules that are necessary for T-cell receptor signaling [48], CTLA-4, which functions to inhibit T-cell signaling[49], and IL2RA, which encodes CD-25, expressed on T-regulatory cells and is considered important in the downregulation of the T cell activity [50].

Conclusions

One of the most prevalent autoimmune illnesses, thyroid disorders are influenced by a variety of genetic, environmental, and psychological variables, particularly in women. They might become more common and need to be removed at a young age. The nutritional and genetic factors are two of the most significant factors influencing it. A shortage in any of the nutrients required for producing thyroid hormones results in a functional malfunction in the gland and the organs that are functionally associated to it.

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