



EPIDEMIOLOGY OF AUTOIMMUNE THYROID DISEASE

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ABSTRACT

Most diseases involve many genes in complex interactions, in addition to physical and cultural environmental factors. If a disease is caused by genetic and environmental factors, its etiological origin can be referred to as having a multifactorial pattern. The common multifactorial diseases encompass environmental influences on the causal processes. Thyroid is a multifactorial type of origin of disease. The epidemiological studies show that if thyroid disease is caused by the interaction of both genetic and environmental factors, then mostly it is autoimmune thyroid disease. When the antibodies attack the thyroid gland, it is called Auto Immune Thyroid Disease (AITD). The present study attempts to examine whether the occurrence of thyroid disease in a micro area is due to autoimmune conditions. To prove the fact clinically, blood of thyroid patients were collected and tested in a laboratory. The result shows that most of the patients have autoimmune thyroid disease. Moreover, some environmental and genetic factors were also examined since thyroid disease is a multifactorial origin of disease.

KEYWORDS : Auto Immune Thyroid Disease (AITD); Multifactorial diseases; Thyroid Peroxidase Antibodies; Hashimoto's disease; Grave's disease; Thyroid Stimulating Hormone; Spatial analysis; Quadrat analysis

1. INTRODUCTION

Etiology is the cause of origin of diseases. Diseases can be caused by intrinsic factors, extrinsic factors or both. Extrinsic factors imply all the factors in the external surroundings in which people live. Intrinsic factors are the internal affairs and arrangement of a human body including variations in genetic makeup in the DNA of cells. Most diseases involve many genes in complex interactions, in addition to environmental influences.¹ Almost all diseases have a combination of genetic and environmental influences.²⁵ According to the World Health Organization, "the causal links between environmental change and human health are complex because they are often indirect, displaced in space and time, and dependent on a number of modifying forces".³⁰

If a disease is caused by internal and external factors, its etiological origin can be referred to as having a multifactorial pattern. The common multifactorial diseases all involve environmental influences on the causal processes. Thyroid is a multifactorial type of origin of disease. Thyroid disease is of different types on the basis of cause of origin, iodine level and thyroid gland disfunctions. The epidemiological studies show that if thyroid disease is caused by the interaction of both intrinsic and extrinsic factors, then mostly it is autoimmune thyroid disease. When the antibodies attack the thyroid gland, it is called Auto Immune Thyroid Disease (AITD).³⁴ It is mainly caused by the genetic makeup and the triggers from the physical and cultural environment. Significant epidemiological evidence indicates that autoimmune thyroid disease is caused by an interaction between so-called susceptibility genes and environmental factors.³² Genetic predisposition plays a crucial role in the loss of tolerance to self-antigens and initiation of the autoimmune process.⁸

The present study is to confirm autoimmune thyroid disease with its genetic and environmental factors. Thyroid can be considered as a life style disease and the incidence rate has been increased in recent times. The etiologic study of thyroid disease needs examination of both genetic and environmental factors.¹² It should be examined in a manner of hypothesis testing and closer to an individual level.²⁵ So, the approach of this study is micro-level to avoid generalizations. Therefore the testing would give the etiological insight of thyroid disease.

Autoimmune thyroiditis is a condition in which our immune system attacks the thyroid gland. Immune system acts as a defense against bacteria, viruses and fungi. But when it is overloaded with infections, it may attack our body parts itself. When more stress like infections or allergies in the intestinal tract the immune system attacks the healthy cells, pituitary gland, thyroid gland etc. When gets attacked by immune system thyroid gland becomes inflamed.⁴ The laboratory test for identifying auto immune thyroid disease is Thyroid Peroxidase Antibodies (TPO). Auto immune thyroid is of two types: Hashimoto's disease and Grave's disease. Hashimoto disease is the most common thyroid disease. In this disease, our immune system attacks the thyroid gland and it becomes inflamed. It cannot make enough thyroid hormone for metabolic functions. It is a disorder same as hypothyroidism caused by the attack of immune system. Grave's disease results in the abnormal stimulation of the thyroid gland and produces more hormones to the blood stream. It is same as hyperthyroidism but induced by the immune system.

2. MATERIALS AND METHODS**2.1 Data source**

The age-specific and gender-specific data were obtained by questionnaire survey conducted in the area of study. The study area is Kalady Panchayat in Ernakulam district of Kerala state, India. The geographic location of patients was obtained through GPS (global positioning System) survey. Blood samples of selected thyroid patients from the clustering area were collected. They were assembled in a diagnostic center (DDRC, Kalady) for taking blood samples. The blood test includes T3 (triiodothyronine), T4 (thyroxine), TSH (thyroid stimulating hormone), TPO (Thyroid peroxidase) and the blood group. Secondary data was collected from census report and literature review.

2.2 Data Analysis

The collected data were entered into excel worksheet and graphs were generated to analyse the gender wise and age wise distribution of thyroid patients. Data that had been kept in excel worksheet including the GPS points were transferred to ArcGIS software for analysis and map preparation. Maps were prepared to show the spatial distribution of disease by plotting the GPS points of thyroid patients. Quadrat analysis method was used to reveal the pattern of spatial distribution.

This method analyses the frequency of points occurring in different parts of an area. In this method, a set of quadrats or square cells was superimposed on the study area and the number of points in each cell is determined. This method considers the variability in the number of points per cell. If the variability of the cell frequencies is large, then the pattern would have a clustered arrangement and if the variability is moderate then the pattern of points would reflect a random spatial arrangement.¹⁰

Lastly, three thyroid patients were selected from each clustered cell of quadrats. There were eleven cells having more than or equal to ten thyroid cases. These eleven cells are called clustered cells. Therefore, in total, thirty three patients were selected for blood test. The patients were randomly selected from each cell for checking the blood to diagnose the autoimmune thyroiditis.

TPO (Thyroid Peroxidase Antibodies) is the blood test for determining the presence of antibodies against thyroid gland. These antibodies are mistakenly produced by our immune system to attack the normal tissue. The unit for TPO is IU/ml. It stands for International Units Per Milliliter, an arbitrary amount agreed upon by scientists and doctors. If the observed value of TPO in blood is >35 IU/ml, then the patient has the autoimmune thyroiditis. TSH (Thyroid stimulating hormone) level of blood has also been taken to know the type of autoimmune thyroiditis. If the TSH level in blood is < 0.5 μ IU/ml, then the patient has Grave's disease and if it is >4.5 μ IU/ml, the patient has Hashimoto's disease.

3. RESULTS AND DISCUSSION

The spatial pattern, gender wise and age wise occurrence of thyroid disease were the major concerns of the first part of the analysis. These would reveal the intrinsic and extrinsic influences of autoimmune thyroid disease. The spatial pattern would disclose the influence of any physical or socio-cultural factors (extrinsic) in the incidence of thyroid disease. The age wise and gender wise analysis of thyroid disease would show the influence of age and gender (intrinsic) in the incidence of disease respectively.

Spatial distribution shows that there is an unusual clustering of thyroid disease in kalady town and adjoining areas like Mattoor, Marottichode, Kaipattoor, Manickyamangalam and Thottakam. Road intersections, junctions and road sides are more clustered with the disease indicating air pollution due vehicle traffic. North eastern part of the study area has the maximum clustering. There are stone crushers, ricemills and timber industries are spatially distributed in these areas. Figure 1 shows the spatial distribution of thyroid disease in Kalady, figure 2 has the spatial distribution of thyroid disease superimposed by landuse and figure 3 shows the hotspot areas of disease distribution.

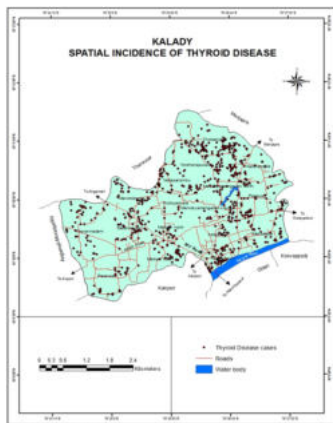


Fig.1

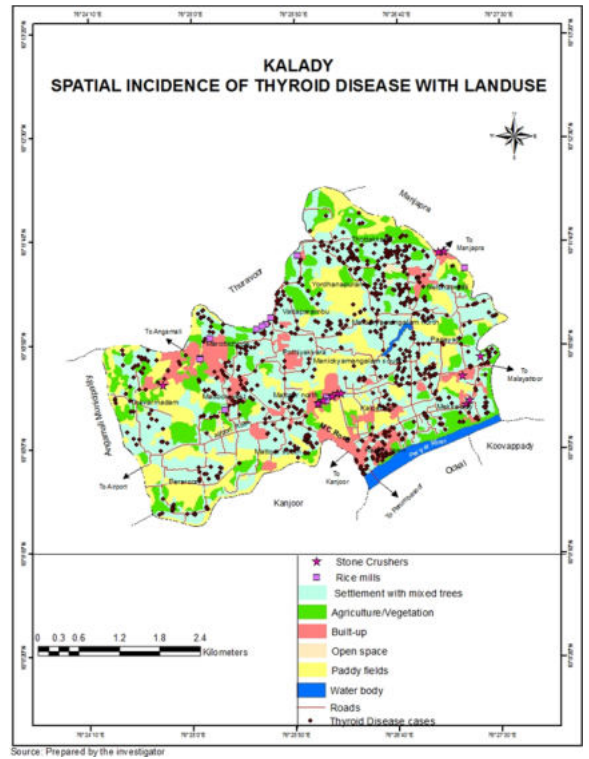


Fig. 2

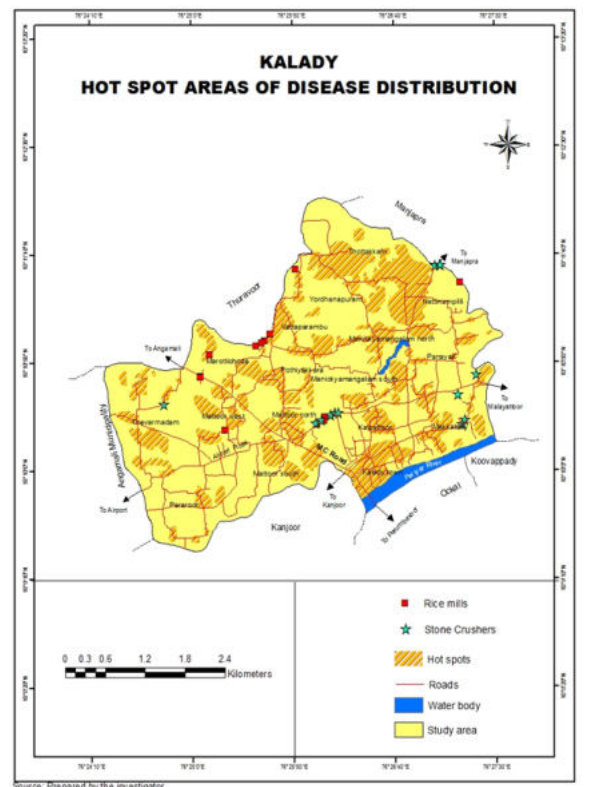


Fig. 3

The spatial distribution of thyroid disease shows that there is clustering in spatial pattern and hotspots has been identified. Disease clustering in some areas indicates the influence of physical environment like air pollution from rice mills, granite stone crushers, timber industries and vehicle engine combustion. Moreover the area has heavy vehicle traffic in peak hours since a state highway (Main Central Road) passes through it. Pollution from atmosphere is a risk factor for

triggering autoimmune conditions. Halogen from the atmosphere that imitates iodine is pulled inside the thyroid gland. Too many impurities in the atmosphere eventually lead to inflammation of thyroid gland. When it is inflamed the immune system attacks the gland results in thyroid disease.

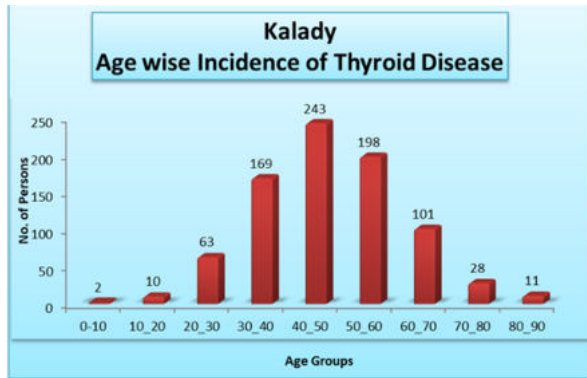


Fig. 4

As illustrated in figure 4, the age group 40-50 has the maximum number of incidence. There is an orderly increase of thyroid disease incidence from the ages 0-10 to 40-50, after that it decreases systematically down to the age group 80 - 90. There are 63 and 169 cases in the age groups of 20-30 and 30-40 respectively. Thyroid cases have been increased more than two times from 20-30 age groups to 30-40 group. This indicates genetic factors influencing the occurrence of disease along with physical and cultural environment. Out of 825 thyroid disease cases, 610 come under the ages 30-60.

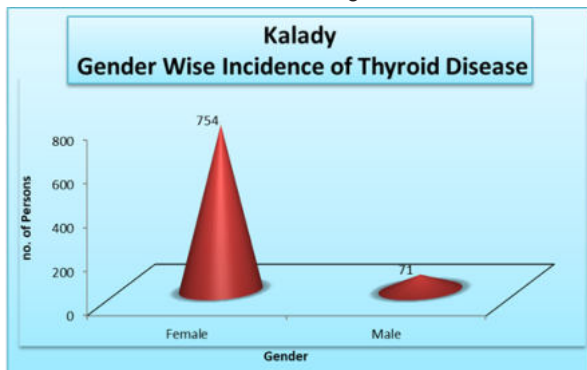


Fig. 5

When the gender wise incidence of thyroid disease is considered, females have the greatest number of incidences.²⁷ Out of 825 thyroid disease cases, 754 are females and only 71 are males. This stresses the power of intrinsic factors (internal body structure) influencing thyroid disease. Females are more vulnerable to hormonal changes and infections. Thyroid disease is closely associated with all other hormones in the body and this is the reason why females have high incidence. Gender wise distribution of thyroid cases is shown in figure 5.

From the above discussed facts, it is clear that there are environmental factors influencing the spatial pattern of thyroid disease in Kalady. If the spatial distribution showed a random pattern then there would be no environmental influence.²⁸ Since the spatial distribution has a clustered pattern, it is certain that there are some environmental factors influencing it. Environment consists of two types: physical and cultural. Environment can be defined as the sum of situation that surrounds us at a given point of time and space. It comprises of physical, biological and cultural elements that are interlinked both individually and collectively. It is the surroundings in which an organism must survive or maintain its life process. Therefore, some physical or cultural

environment is associated with the occurrence of thyroid disease. The physical and cultural environments have a great influence upon human health.⁵ Environmental factors that cause diseases are classified into four groups; physical agents, chemical agents, biological agents and nutritional factors. These are determined by the physical and cultural features of a region.¹⁵

Though environment has influence, intrinsic factors like gender and age are also strongly associated with the occurrence of thyroid disease. Gender influence in thyroid disease indicates the internal arrangement of organs. Females are more subjected to hormonal changes than men. Thyroid gland is a part of endocrine system. Any changes in other parts of endocrine system can affect the gland. Each gland in the endocrine system has separate functions in the body. But the glands in the system are interconnected. Most connected glands with thyroid are ovaries and adrenals. When there are fluctuations in hormones produced by ovaries and adrenals it will give strain to thyroid gland.

When there are changes in the production of stress hormones by adrenal glands, it gives stress to immune system and ovaries. Then immune system makes our cells not to absorb thyroid hormones and ovaries produce estrogen, which in turn causes liver to produce proteins that weaken thyroid hormones. Whenever there is major change in the ovaries it will give strain to thyroid gland including pregnancy period. This is the reason why women get more thyroid disease than men. About two thirds of thyroid cancer patients are women in USA. There the ratio of occurrence of thyroid cancer in women and men is 2:1. In Japan, the female-male ratio of thyroid occurrence is 13:1.²⁷

Females are having the chance of lack of nutrients like calcium and iron due to vitamin insufficiency. Their body is in continuous demand of nutrients. Thus the failure of supplying nutrients needed to our body may lead to immune responses. This might be one reason for the highest incidence of thyroid disease in females.

The age group 30-50 has the maximum hormonal changes and thus it is the high incidence age group. Thyroid cancer occurs in the later decades of life, even though most patients will develop thyroid disease between the ages of 25 to 55.²⁸

Thus women are more susceptible to autoimmune thyroid disease. Age group also plays role in the incidence of disease. Again the age group with more hormonal changes is more susceptible to the disease. The findings conclude the influence of both environmental and internal arrangement of the body in the incidence of thyroid disease.

Significant epidemiological evidence indicates that autoimmune thyroid disease is caused by an interaction between so-called susceptibility genes and environmental factors. Genetic predisposition plays a crucial role in the loss of tolerance to self-antigens and initiation of the autoimmune process.⁸ Gregory A. Brent, MD, professor of medicine and physiology at the David Geffen school of Medicine at the University of California at Los Angeles presented his findings about autoimmune thyroid disease as follows. "Genetic background accounts for about 70% of the risk for autoimmune thyroid disease. The remainder is likely related to a range of environmental triggers".⁴ He says that toxicants affect iodine uptake, thyroid hormone synthesis and action. But few studies are carried out to assess how this will affect humans.

In general, autoimmune thyroid disease is a complex disease with multi factorial origin. The combined effects of environmental triggers and genetic makeup result in auto

immune disease. Individuals react differently to environmental chemicals and toxins; some persons have genetic susceptibility to have auto immune disease.

To prove the fact, blood of thyroid patients were analyzed to find the presence of antibodies. Subsequently a quadrat was placed over the study area which had the spatial distribution of thyroid disease (Figure 6). The cells with more than or equal to ten thyroid cases were selected for taking the samples (Figure 7). There are eleven cells having more than ten thyroid cases. Three thyroid patients were randomly selected from each cell for testing the blood. The selected patients were diagnosed in a laboratory for the confirmation of autoimmune thyroiditis and TSH level.

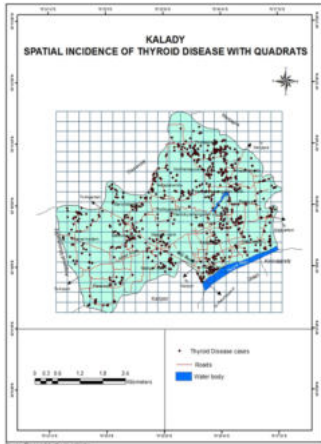


Fig.6

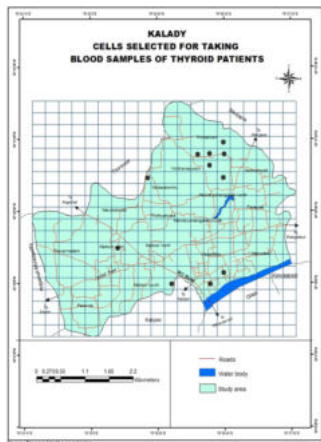


Fig.7

When the blood samples of selected thyroid patients were analyzed in the laboratory, it was confirmed that majority of the patients had autoimmune thyroiditis. Of the thirty-three patients, twenty-six patients had autoimmune thyroiditis. They had the TPO value more than 35 IU/ml of blood. About 78.8% of observed patients had thyroid disease due to autoimmunity.

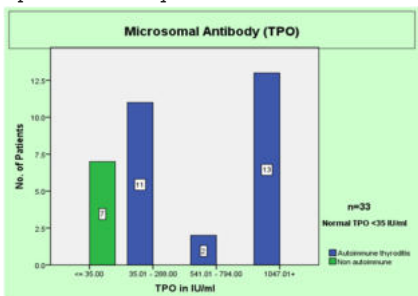


Fig.8

The microsomal antibody or TPO measures in International Unit (IU) per milliliter. If it is below 35 IU/ml, then there is a little anti-body produced against thyroid gland. Here, only seven thyroid patients had no anti bodies against their gland. But twenty-six patients had anti bodies produced by their immune system against thyroid gland. The antibodies vary in its level of production. Most of the autoimmune thyroiditis had antibodies more than 1000 IU/ml of blood (figure 8).

In the autoimmune thyroid disease, Hashimoto's disease is the most common one. It is the condition of thyroid gland not producing enough hormones due to the attack of immune system. The gland become inflamed and cannot work properly.

The spatial distribution of autoimmune thyroiditis is characterized by proximity to main roads, stone crushers and rice mills. So, it can be confirmed that air pollution from vehicles, stone crushers and rice mills are the major environmental triggers for the occurrence of thyroid disease in the study area.¹⁵

4. CONCLUSION

Even though autoimmune thyroid disease seems to be occurred due to the internal deviations of a human body, physical and cultural environment have strong influence in it. Immunity works when a foreign material enters into human body such virus, fungus or bacteria. It will be in disorder when it is overloaded with much immune response such as air pollution. In this study, the autoimmune thyroid disease could be influenced by the presence of air pollutants from stone crushers, ricemills and vehicles. This is the reason why thyroid cases are clustered near the roads, junctions, road intersections, ricemills and stone crushers.

The long-term exposure to the fine particles of air causes infection and thereby autoimmune conditions. One reason for developing auto-immune condition is the stress given to immune system. The continuous infections give over burden to immune system and thereby develop autoimmune thyroid disease. Moreover, the silica particles from stone crushers and preservatives used in timber industry can make auto immune thyroid disease.

From the study, it is inferred that environmental conditions along with the susceptible inheritances lead to autoimmune thyroiditis. The susceptible people are females having chance of hormonal changes. Furthermore, food habits of people like low level vitamins and other essential nutrients trigger autoimmune conditions. Researches show that high intake of carbohydrates and minerals like calcium and iron prompt autoimmune response. Studies were conducted in the same region revealing that water in this area has high level of iron and calcium. All these factors contribute to the occurrence of disease.

If unwanted immune responses are reduced, autoimmune thyroid diseases could be prevented. Autoimmune thyroid disease is a life style disease and if people understand the physical and cultural factors affecting disease, the incidence rate can be reduced well.

The study of casual links between environment and diseases is vital as it could prevent the incidence of many diseases. Since diseases are the result of both genetic and environmental interactions, studies related to the cause of diseases should be focused on environmental and biological factors.

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