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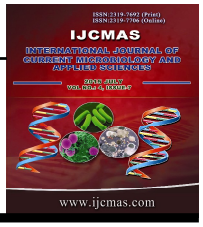

Original Research Article

The Importance of Thyroid Antibody Estimation for the Detection of Hypothyroidism: A Prospective Study

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Keywords

Clinical Hypothyroidism, Subclinical Hypothyroidism, Thyroid Stimulating Hormone (TSH), Thyroglobulin Antibody (TgAb), Thyroid Peroxidase Antibody (TPOAb)

A B S T R A C T

The present prospective study was carried out to find out the diagnostic importance of the laboratory estimation of thyroid antibodies along with TSH, to detect the hypothyroidism. The present study was carried out on 463 thyroid disorders suspected subjects who turned up to the various outpatient departments of Choithram Hospital and Research Centre, India. Thyroid antibodies (TgAb and TPOAb) and TSH were estimated using Abbott Architect i1000SR analyzer. Out of 463 screened subjects, 73 cases were detected as hypothyroid with elevated serum TSH level. Among these hypothyroid cases 34 were clinical hypothyroid and 39 were at subclinical stage. In the present study, all 34 clinical hypothyroid cases had elevated thyroid antibodies. Out of these 34 cases 27 had elevated serum TPOAb. Among 39 subclinical hypothyroid cases, 34 had elevated thyroid antibodies and out of these 34 cases, 28 had raised TPOAb levels. In the present study, total 74 cases had elevated thyroid antibodies; which were detected as thyroid disorders, including hypothyroidism and hyperthyroidism. The present study suggested that the laboratory estimation of thyroid antibodies can be a reliable adjunct for diagnosis of hypothyroidism.

Introduction

Subclinical hypothyroidism identifies a condition biochemically characterized by the association of normal free thyroid hormone levels and slight hyperthyrotropinemia (Ross DS, 2000). It represents the most frequent alteration of thyroid function and is often due to autoimmune disease. In these cases, subclinical hypothyroidism is considered a transitory condition in the evolution of autoimmune disease toward clinically overt hypothyroidism (Ross DS, 2000).

In the last decade, the diagnostic strategy for using TSH measurements in delineating thyroid status has changed as a result of the sensitivity improvements in these assays.

Currently, immunometric assays are available on a variety of automated immunoanalyser platforms. These are the third generation assays with a functional sensitivity of 0.01mIU/L. Laboratories in several countries, including India now employ such assays. WHO recommends the use of sensitive TSH assays as the first line in the assessment of thyroid function as well as free T_4, free T_3 and anti-TPO antibodies for differential diagnosis of thyroid diseases (Heuck CC *et al.,* 2000).

Because the majority of persons with subclinical hypothyroidism have few symptoms or none at all, routine population screening has been advocated (Danese MD *et al.,* 1996). Population screening has not been endorsed unanimously, because the benefits of subsequent therapy have not been established in prospective clinical trials. Using a decision and cost-effectiveness model, it was calculated that screening women older than 35 years of age every five years (Ladenson PW *et al.,* 2000).

The prevalence of subclinical hypothyroidism varies with population, age, sex, race, region, and method of TSH measurement. TSH is heterogeneous with respect to both glycosylation and biological activity (Biondi B *et al.,* 2008). A population based study showed the prevalence of subclinical hypothyroidism in the total population 4.7%. This study also showed the high prevalence of subclinical hypothyroidism in women (Rivolta G *et al.,* 1999). A study based on pregnant women of Tehran, Iran showed the prevalence of subclinical hypothyroidism, 4.15% of the study population (Yassaee F *et al.,* 2014). It is known that subclinical hypothyroidism is more prevalent in iodine-sufficient areas (Teng W *et al.,* 2006). In a study with elderly subjects in Denmark, 3.8% of subjects in the area of low iodine intake had high serum TSH, while 18% in the area of high iodine intake showed subclinical hypothyroidism (Laurberg P *et al.,* 1998). In another study with 1,061 Japanese participants, the frequency of high urine iodine correlated with hypothyroidism in the absence of autoantibodies (Konno N *et al.,* 1994).

Whilst the normal reference interval was felt to be adequately defined, the TSH range defining subclinical hypothyroidism remained elusive. An upper limit of 10 mIU/ml has been quoted in the literature (Topliss DJ *et al.,* 2004). Perhaps this is because of patients found to have an elevated TSH level, the majority (approximately 75%) have values lower than 10 mIU/ml (Canaris GJ *et al.,* 2000). However, the highest TSH quoted in the cross-sectional prevalence studies examined by the panel was 7.0 mIU/ml (Kanaya Am *et al.,* 2002). Pedersen IB *et al.,* (2003) performed a cross-sectional study of thyroid peroxidase antibodies (TPO Ab) and thyroglobulin antibodies (Tg Ab) in 4,649 Danish subjects. The presence of both antibodies was more frequent in females, and the prevalence increased with age and showed a correlation with subclinical hypothyroidism.

In Indian population, hypothyroidism is one of the major problems and there are only few population based studies on thyroid antibody tests to detect prevalence of autoimmune thyroid disorders in India. So, it was aimed to evaluate the use of the thyroid antibodies together with TSH for the diagnosis of autoimmune hypothyroidism.

Materials and Methods

A descriptive cross-sectional study carried out on 463 thyroid disorders suspected subjects in the Pathology Department of

Choithram Hospital and Research Centre, Indore, Madhya Pradesh, India from March 2008 to March 2012. For all subjects routine laboratory screening of thyroid function was done by estimation of the thyroid hormone profile. The thyroid hormone profile was evaluated in Immunoassay laboratory of Pathology Department in Choithram Hospital and Research Centre, using Abbott Architect i1000SR (Abbott Laboratories, Diagnostics Division, Abbott Park, IL, USA) analyzer based on a Chemiluminescent Microparticle Immunoassay (CMIA) for the quantitative determination of thyroid hormone profile (Kalani M *et al.* 2012). The anti-thyroid antibody tests (Anti-Thyroglobuin Antibody [Anti-TgAb] and Anti Thyroid Peroxydase Antibody [Anti-TPOAb]) were also done by Chemiluminescent Microparticle Immunoassay (CMIA) analyzer. The study proposal was reviewed by the hospital Ethical Committee, which has guidelines based on Helsinki deceleration.

The data collected were analyzed using Excel 2007, R2.8.0 Statistical Package for Social Sciences (SPSS) for windows version 16.0 (SPSS Inc.; Chicago, IL, USA).

Results and Discussion

The present study was conducted on 463 subjects and 379 (85.86%) of them had the thyroid hormone profile within normal range. Overall 73 (15.76%) cases were detected with elevated TSH and hence were considered as the cases of Hypothyroidism. Out of these hypothyroid cases 34 (46.57%) and 39 (53.42%) were Clinical hypothyroid and Subclinical hypothyroid respectively. Eleven (2.37%) cases of Hyperthyroidism were noted in this study (Fig. 1).

In the present study, the mean age of male subjects having thyroid disorders was 38.68±10.06 years, whereas for females it was 37.55±11.90 years. The ratio of male and females of overall hypothyroidism was about 1:5 (out of 73 cases, 12 were males and 61 were females) and for subclinical hypothyroid cases the ratio was about 1:4 (out of 39 subclinical hypothyroid cases 8 were males and 31 were females). In cases of hyperthyroidism it was 4:7 who have elevated serum anti-thyroid antibodies.

All 34 cases (100%) of clinical hypothyroidism in the present study had elevated levels of either TgAb or TPOAb; or both of the thyroid antibodies. Out of these 34 cases 27 (79.41%) had elevated serum TPOAb (Table1). On the other side, out of 39 subclinical hypothyroid cases 34 (87.2%) had elevated serum thyroid antibodies. Serum TPOAb elevation was seen in 71.8% (28 cases) of these subclinical hypothyroid cases (Table1). If we consider, all the cases of hypothyroidism at our end, it was seen that 93.2% cases had elevated thyroid antibodies (Table1).

In this present study, total 84 cases were detected as thyroid disorders including hypothyroidism and hyperthyroidism. Out of these total cases, 74 (88.1%) cases had elevated serum thyroid antibodies (Fig 2).

The present study showed that nearly 16% of the study population had hypothyroidism. In general, India is now considered to be in the post-iodization phase (Andersson M *et al.*, 2005). The present study suggested that, the prevalence of hypothyroidism in central Indian population and earlier recent study corroborates the same (Bose A *et al.* 2015). The high prevalence figures in central India have ascertained that thyroid disorders in India are not confined to the conventional iodine-deficient sub-Himalayan zone but also extended to the plain lands. A possible etiological role of goitrogens to interfere

with iodine nutrition has been previously suggested for, but not limited to this area (Chandra AK *et al.,* 2004 and Chandra AK *et al.,* 2004). Increasing exposure to thyroid disruptors, including industrial and agricultural contaminants and mutagens has been identified as a growing health concern throughout India (Kalra S *et al.,* 2011).

In the present study, the subclinical hypothyroid cases among the study population, was 8.42%. Unnikrishnan *et al.* (2013) conducted a study in eight major cities in India which also showed the prevalence of subclinical hypothyroidism as 8.02% in their study population. In the same study, they showed that Anti-TPO antibody is present among 21.85% of the study population. In the present study, however, the thyroid antibody prevalence was as high as 88.1%.

Table.1 Distribution of Thyroid Antibodies in Detected Cases of Hypothyroidism

Thyroid Disorders	TgAb+TPOAb (Positive)	TgAb (Positive)	TPOAb (Positive)	TgAb+TPOAb (Negative)
Clinical Hypothyroidism (n=34)	21	07	06	00
Subclinical Hypothyroidism (n=39)	15	06	13	05
Overall Hypothyroidism (n=73)	36	13	19	05

Fig.1 Distribution of thyroid disorder status in present study population

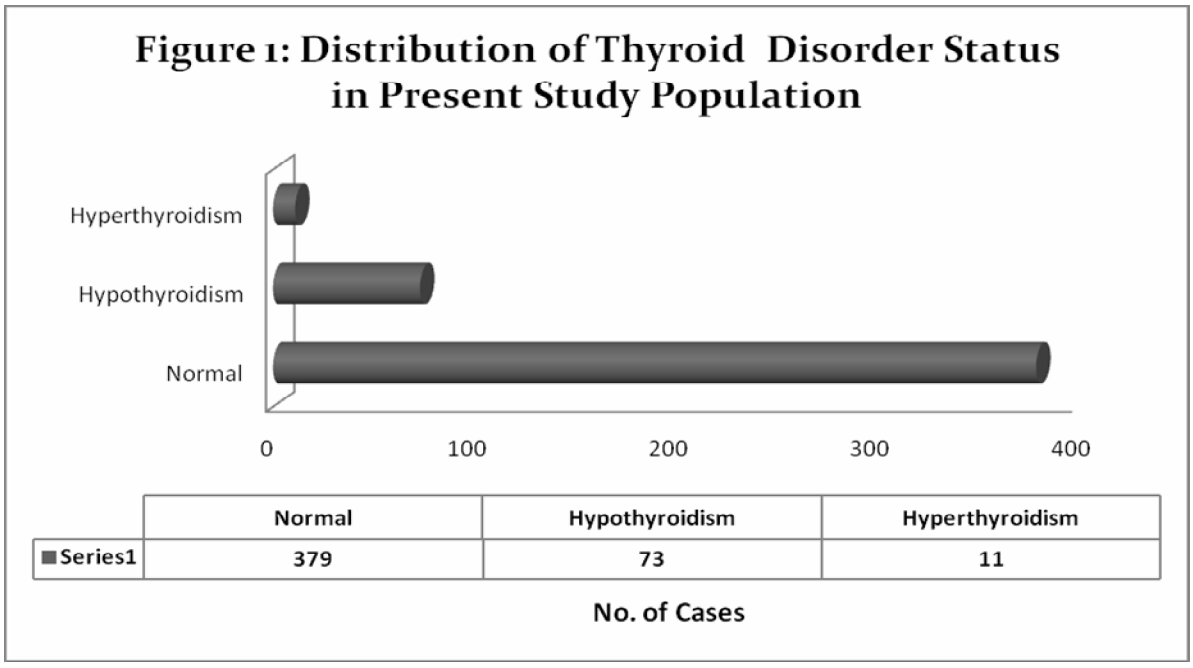
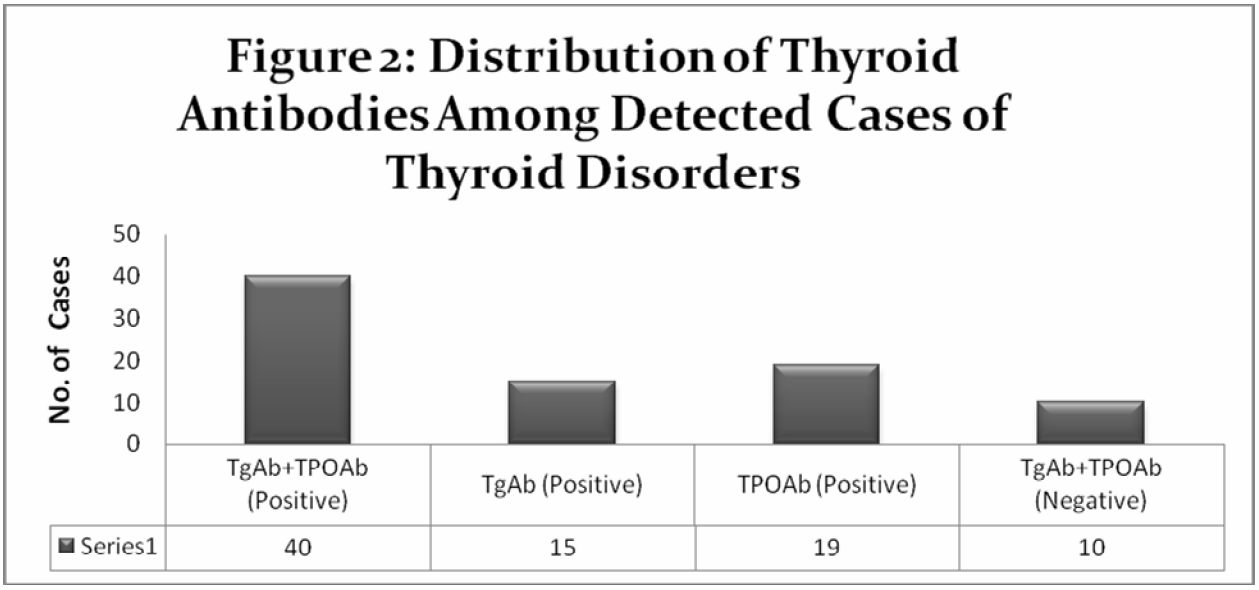


Fig.2 Distribution of thyroid antibodies among detected cases of thyroid disorder



Estimates of TPOAb prevalence depend on the sensitivity and specificity of the method employed (Vogeser M *et al.,* 2000). TPOAb prevalence is significantly higher (~11%) in dietary iodine sufficient countries like the United States and Japan as compared with iodine deficient areas in Europe (~ 6%) (Kasagi K *et al.,* 2009). The prevalence of TPOAb is higher in women of all age groups and ethnicities, presumably reflecting the higher propensity for autoimmunity as compared with men (Kasagi K *et al.,* 2009). Aging is associated with an increasing prevalence of TPOAb that parallels the increasing prevalence of both subclinical and clinical hypothyroidism (Hollowell JG *et al.,* 2002). The same study found that the odds ratio for hypothyroidism was strongly associated with the presence of TPOAb but not TgAb, suggesting that only TPOAb has an autoimmune etiology (Hollowell JG *et al.,* 2002).

Although the presence of TgAb alone did not appear to be associated with hypothyroidism or TSH elevations, the combination of TPOAb and TgAb or TPOAb alone may be more pathologically significant. In the present study, out of 73 hypothyroid cases, 26% had TPOAb elevated, whereas, approximately 50% cases had both TgAb and TPOAb elevated. If we focus on only subclinical stage of hypothyroidism at our end, almost 40% of the cases had shown the elevation of both the antibodies in serum samples.

TgAb measurement is primarily used as an adjunctive test for serum TgAb measurement when monitoring patients with differentiated thyroid cancers (DTC) (Cooper DS *et al.,* 2009). Current guidelines recommend that all sera to be processed for TgAb by a sensitive immunoassay method prior to serum Tg testing, because there appears to be no threshold TgAb concentration that precludes TgAb interference with Tg measurements (Spencer C *et al.,* 2011; Latrofa F *et al.,* 2012). Thyroglobulin appears to play a central role in a wide variety of pathophysiologic conditions affecting the thyroid gland. For example, TgAb has been implicated as a possible auto-antigen involved in the

production of thyroid autoimmune diseases (Tomer Y *et al.*, 2004).

In Western populations, the prevalence of TgAb and/or TPOAb is estimated at about 10% of the general population (Groves CJ *et al.*, 1990) , the few available studies from Africans report a much lower prevalence (0–2.7%) in healthy individuals (Okosieme OE *et al.*, 2007).

Very few studies are available from India on this issue. The present study enumerated the status of TgAb and TPOAb in Indian population and which shows high prevalence particularly among hypothyroidism.

The present findings suggest that the laboratory estimation of thyroid antibodies, both TgAb and TPOAb, can be a very reliable diagnostic tool for Hypothyroidism.

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