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# ASSESSMENT OF THYROID HORMONES STATUS IN SUB-CLINICAL THYROID DISEASE IN SELECTED ADULT PATIENTS

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**ABSTRACT**

Thyroid stimulating hormone [TSH], Tri-iodothyronine [T3], Thyroxine [T4], Free-T3 [FT3] and Free-T4 [FT4] levels of each selected patients were determined using Elecsys 2010 Chemi-luminescence automated immunoassay technology. In female group a total of 107 patients [59.44%] out of 180 showed either forms of thyroid disease. By sub-groups, forty two patients (23.33%) [n = 26; 14.44% Sub-clinical hypothyroidism, n = 16; 8.88% sub-clinical hyperthyroidism] showed sub-clinical thyroid disorders, whereas n = 65 (36.11%) exhibited true-form. In males, a total of 66 patients [55.0%] out of 120 showed either forms of thyroid diseases. As per subgroups, twenty two (18.33%) %) [n = 18; 15.0% sub-clinical hypothyroidism; n = 4; 3.33% sub-clinical hyperthyroidism] showed sub-clinical thyroid disorders, whereas 44 (36.66%) exhibited true-form. The routine screening for thyroid disease through clinical investigations would be encouraged in elderly and pregnant women.

## INTRODUCTION

Whenever elevation in serum TSH occurs above the upper limit of the reference levels with co-existing of normal serum FT4 concentration, it is known as Sub-clinical hypothyroidism; whereas a decrease in serum TSH in similar manner with normal serum FT3 and T3 concentration commonly referred to as sub-clinical hyperthyroidism (Col *et al.,* 2004; Stockli, 2007). Thus representing the early stages of thyroid dysfunction is the subclinical thyroid disease or disorder, commonly known as hypothyroidism and hyperthyroidism. For being suffering from mild or in some cases no sign of symptoms of thyroid dysfunction; it is laboratory evaluation only that a clinician can diagnose and assess the conditions from (Col *et al.,* 2004; Krysiak *et al.,* 2006; Gaby, 2004). It has been documented that initial detection and therapy of subclinical thyroid dysfunction is in-fact advantageous, when the affected population mostly comprises of children and pregnant women (Lerch *et al.,* 1999; Schlienger *et al.,* 2003; Sheth *et al.,* 1999). It was also stated that elderly and patients with progressing age are at hazard for developing sub-clinical thyroid dysfunction most commonly, sub-clinical hypothyroidism (Canaries *et al.,* 2000; Paul *et al.,* 2006; Vander pump *et al.,* 1995), which means and argued substantially that, sub-clinical hypothyroidism is much more common than hyperthyroidism. For keeping the patients conditions updated and their clinical status well-evaluated, routine assessment of TSH, FT3, T3, FT4, T4 is recommended. It was also recommended that whenever signs and symptoms that suggest a possibility of thyroid dysfunction in sub-clinical patients, the clinical condition should be evaluated through evidence based assessments and lab findings (Col *et al.,* 2004). Therefore, in present study we evaluated sub-clinical thyroid dysfunction status of several patients in our setting, inclusive of both males and females population. The study will assist in future investigation, analysis and strategic planning of treatment and management of sub-clinical thyroid dysfunctions.

## MATERIALS AND METHODS

**Patients:** Three hundred patients (120 males, 180 females) were selected from Medical, Endocrinology and General OPDs and their clinical investigations, initial diagnosis and related lab investigations were routinely collected. The study period was prospectively from Dec 2005 to Dec 2010. The patients were classified in four groups in each gender according to age; for females age groups were = 17-30 yrs, 31-45 yrs, 46-59 yrs and 60-66 yrs. In Males, age groups were = 18-30 yrs, 31-45 yrs, 45-58 yrs and 59-71 yrs. The patients were further classified according to the presence of sub-clinical dysfunction or true thyroid disorders.

**Analysis:** Blood samples were collected from each patients, serum was separated and stored at $-20^{o}$C until analyzed. Thyroid stimulating hormone [TSH], Tri-iodothyronine [T3], Thyroxine [T4], Free-T3 [FT3] and Free T4 [FT4] levels were measured on automated immunoassay analyzers (Elecsys 1010 and 2010, Roche Diagnostics, Basel) using Electro-Chemiluminescence technology (Krysiak *et al.,* 2006; 2007). Reference ranges are provided in result tables.

**Data presentations:** The results are presented in tabulated as well as percent occurrence for clarity. Where necessary comparable thyroid hormone and TSH data are presented in groups for conclusion. Statistical calculations were performed using Microsoft SPSS ver 13 (USA).

## RESULTS

Results are summarized in Tables 1-4. Briefly, 300 patients, Male n = 120, females n = 180 were included in the study, presented with suspicion and/or confirmed diagnoses of thyroid dysfunction. The subgroups were also abbreviated as MSCTD and FSCTD, males sub-clinical thyroid disease and Female sub-clinical thyroid disease, respectively.

Patients' subgroups and their respective patients were, for females = 17-30 yrs (n = 35), 31-45 yrs (n = 32), 46-59 yrs (n = 72) and 60-66 yrs (n = 41) and for males, 18-30 yrs (n = 43), 31-45 yrs (n = 48), 45-58 yrs (n = 22) and 59-71 yrs (n = 7). The patients diagnosed with subclinical thyroid dysfunction (SCTD) were; Females; 17-30 yrs (n = 5), 31-45 yrs (n = 7), 46-59 yrs (n = 10) and 60-66 yrs (n = 20) (Table 1). Results in Table 1 are expressed in each column as total number in that group and relative percentage w.r.t. main or preceding group. A total of 107 patients [59.44%] out of 180 showed either forms of thyroid disease. By sub-groups, forty two patients (23.33%) [n = 26; 14.44% Sub-clinical hypothyroidism, n = 16; 8.88% sub-clinical hyperthyroidism] showed sub-clinical thyroid disorders, whereas n = 65 (36.11%) exhibited true-form. Moreover, 73 (40.55%) subjects out of 180 exhibited normal thyroid hormone and TSH levels and devoid of any sub-clinical or true thyroid disorders.

**Table 1. Female subjects (n = 180)♠ tested for sub-clinical and true thyroid disorders (Hyperthyroidism; Hypothyroidism).**

| Groups w.r.t. age ranges | Number of subjects screened | *SCTD | SCHypo | SCHyper | *TTD | THypo | THyper | Normal |
|---|---|---|---|---|---|---|---|---|
| 17 to 30 yrs | 35 | 5 (14.28%) | 3 | 2 | 18 (51.42%) | 14 | 4 | 12 |
| 31 to 45 yrs | 32 | 7 (21.87%) | 6 | 1 | 12 (37.50%) | 8 | 4 | 13 |
| 46 to 59 yrs | 72 | 10 (13.88%) | 4 | 6 | 19 (26.38%) | 15 | 4 | 43 |
| 60 to 66 yrs | 41 | 20 (48.78%) | 13 | 7 | 16 (39.02%) | 13 | 3 | 5 |
| **Total** | **180** | **42 (23.33%)** | **26** | **16** | **65 (36.11%)** | **50** | **15** | **73** |

♠Results are expressed in each column as total number in that group and relative percentage w.r.t. main or *preceding group. A total of 107 patients [59.44%] out of 180 showed either forms of thyroid disease. By sub-groups, forty two patients (23.33%) [n = 26; 14.44% Sub-clinical hypothyroidism, n = 16; 8.88% sub-clinical hyperthyroidism] showed sub-clinical thyroid disorders, whereas n = 65 (36.11%) exhibited true-form. Moreover, 73 (40.55%) subjects out of 180 exhibited normal thyroid hormone and TSH levels and devoid of any sub-clinical or true thyroid disorders. SCTD = Sub clinical thyroid disorders, SCHypo = Sub-clinical Hypothyroid, SCHyper = Sub-clinical Hyperthyroid, TTD = True Thyroid disorders, THypo = True Hypothyroid, THyper = True Hyperthyroidism.

In males; 18-30 yrs (n = 7), 31-45 yrs (n = 6), 45-58 yrs (n = 5) and 59-71 yrs (n = 4) were diagnosed with SCTD (Table 2). Results are expressed in each column as total number in that group and relative percentage w.r.t. main or preceding group. A total of 66 patients showed either forms of thyroid diseases. As per subgroups, twenty two (18.33%) %) [n = 18; 15.0% sub-clinical hypothyroidism; n = 4; 3.33% sub-clinical hyperthyroidism] out of 120 showed sub-clinical thyroid disorders, whereas 44 (36.66%) exhibited true-form. Moreover, 54 (45.0%) subjects out of 120 exhibited normal thyroid hormone and TSH levels and devoid of any sub-clinical or true thyroid disorders. The patients diagnosed, which have true thyroid disorders were; Females (Table 1); 17-30 yrs (n = 18), 31-45 yrs (n = 12), 46-59 yrs (n = 19) and 60-66 yrs (n = 16). Males of age group (Table 2); 18-30 yrs (n = 16), 31-45 yrs (n = 11), 45-58 yrs (n = 14) and 59-71 yrs (n = 3) were diagnosed with true Thyroid disorders.

Thyroid hormone levels analyzed in female patient groups and subgroups are presented in Table 3. No significant variation was found in the levels of T3, T4, FT3 and FT4 levels in sub clinical thyroid hypo and hyperthyroidism, whereas high concentration w.r.t. to normal reference range was found in sub clinical hypothyroidism and slightly lower concentration was noted in sub-clinical hyperthyroidism. In groups of true hypothyroidism, TSH levels were analyzed to be slightly high ($p<0.01$) where as that of FT4 mildly lower ($p<0.05$) (Table 3). Furthermore patients in sub-groups of true hyperthyroidism exhibited significantly ($p<0.01$) altered TSH, FT3 and T3 levels.

Analysis of thyroid hormones in groups and subgroups of Male patients are summarized in Table 4. TSH level evaluated in sub-group-sub-clinical hypothyroidism exhibited significantly high levels ($p<0.01$) where as mildly low levels were noted in sub-clinical hyperthyroidism. Moreover, elevated levels of TSH ($p<0.001$) were

noted in true hypothyroidism patients with mildly low concentration of FT4 (Table 4). However in sub group of true hyperthyroidism, TSH, FT3 and T3 were significantly ($p<0.05$) altered w.r.t. normal reference range.

**Table 2. Male subjects (n = 120)♠ tested for sub-clinical and true thyroid disorders (Hyperthyroidism; Hypothyroidism).**

| Groups w.r.t. age ranges ⊇ 18 to 58 yrs | Number of subjects screened | *SCTD | SCHypo | SCHyper | *TTD | THypo | THyper | Normal |
|---|---|---|---|---|---|---|---|---|
| 18 to 30 yrs | 43 | 7 (16.27%) | 6 | 1 | 16 (37.20%) | 13 | 3 | 20 |
| 31 to 45 yrs | 48 | 6 (12.50%) | 4 | 2 | 11 (22.91%) | 10 | 1 | 31 |
| 45 to 58 yrs | 22 | 5 (22.72%) | 5 | --- | 14 (63.6%) | 10 | 4 | 3 |
| 59 to 71 yrs | 7 | 4 (57.14%) | 3 | 1 | 3 (42.80%) | 2 | 1 | -- |
| **Total** | **120** | **22 (18.33%)** | **18** | **4** | **44 (36.66%)** | **35** | **9** | **54** |

♠Results are expressed in each column as total number in that group and relative percentage w.r.t. main or *preceding group. Twenty two (18.33%) %) [n = 18; 15.0% sub-clinical hypothyroidism; n = 4; 3.33% sub-clinical hyperthyroidism] out of 120 showed sub-clinical thyroid disorders, whereas 44 (36.66%) exhibited true-form. Moreover, 54 (45.0%) subjects out of 120 exhibited normal thyroid hormone and TSH levels and devoid of any sub-clinical or true thyroid disorders. SCTD = Sub clinical thyroid disorders, SCHypo = Sub-clinical Hypothyroid, SCHyper = Sub-clinical Hyperthyroid, TTD = True Thyroid disorders, THypo = True Hypothyroid, THyper = True Hyperthyroid

**Table 3. Thyroid hormone (T3, FT3, FT4) and TSH levels♠ in female patients tested for sub-clinical and true thyroid disorders (Hyperthyroidism; Hypothyroidism).**

| Groups w.r.t. age ranges [17 to 66 yrs] | Sub-clinical hypothyroid | | Sub-clinical hyperthyroid | | | True hypothyroid | | True hyperthyroid | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | TSH | FT4 | TSH | FT3 | T3 | TSH | FT4 | TSH | FT3 | T3 |
| 17 to 30 yrs | 7.78 | 1.0 | 0.26 | 2.70 | 1.1 | 18.91 | 0.23 | 0.01 | 6.66 | 4.41 |
| 31 to 45 yrs | 8.01 | 1.6 | 0.33 | 2.99 | 1.2 | 22.16 | 0.34 | 0.11 | 6.12 | 4.03 |
| 46 to 59 yrs | 9.80 | 1.9 | 0.29 | 3.01 | 1.4 | 19.01 | 0.21 | 0.15 | 5.99 | 3.90 |
| 60 to 66 yrs | 9.11 | 1.7 | 0.18 | 2.78 | 1.0 | 23.45 | 0.19 | 0.18 | 7.56 | 4.10 |

♠Results are expressed as mean of values of each samples tested for required parameter. **Units:** TSH = 0.45 to 4.5 mIU/L; FT4 = 0.9 to 1.9 mg/dl; FT3 = 2.6 to 5.1 pg/ml; T3 = 0.8 to 2.0 ng/ml; T4 = 5.1 to 14.10µg/dl

**Table 4. Thyroid hormone (T3, FT3, FT4) and TSH levels♠ in Male Patients tested for sub-clinical and true thyroid disorders (Hyperthyroidism; Hypothyroidism).**

| Groups w.r.t. age ranges [18 to 71 yrs] | Sub-clinical hypothyroid | | Sub-clinical hyperthyroid | | | True hypothyroid | | True hyperthyroid | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | TSH | FT4 | TSH | FT3 | T3 | TSH | FT4 | TSH | FT3 | T3 |
| 18 to 30 yrs | 8.50 | 1.5 | 0.32 | 3.72 | 1.5 | 19.10 | 0.45 | 0.08 | 7.60 | 3.45 |
| 31 to 45 yrs | 7.60 | 1.4 | 0.31 | 3.59 | 1.3 | 19.45 | 0.43 | 0.10 | 8.15 | 4.85 |
| 46 to 58 yrs | 7.10 | 1.2 | --- | --- | --- | 21.90 | 0.51 | 0.12 | 7.87 | 3.11 |
| 59 to 71 yrs | 8.90 | 1.3 | 0.29 | 3.18 | 1.7 | 24.57 | 0.29 | 0.09 | 7.10 | 4.26 |

♠Results are expressed as mean of values of each samples tested for required parameter. **Units:** TSH = 0.45 to 4.5 mIU/L; FT4 = 0.9 to 1.9 mg/dl; FT3 = 2.6 to 5.1 pg/ml; T3 = 0.8 to 2.0 ng/ml; T4 = 5.1 to 14.10µg/dl

## DISCUSSION

It has been documented that etiological factors for sub-clinical hypothyroidism and overt hypothyroidism are the same (Biondi and Cooper, 2008; Krysiak *et al.*, 2007; Roos *et al.*, 2007), which commonly display the causative features of chronic lymphocytic thyroiditis. It is an autoimmune disorder of the thyroid gland which induces a decrease in thyroid hormone production in patients existing mild, sub-clinical, or overt hypothyroidism (Krysiak *et al.*, 2007; Roberts and Ladenson, 2004; Ross, 2005; Surks and Ocampo, 1996).

Further noteworthy etiology of primary hypothyroidism may arise from therapies resulting in destruction of thyroid tissue such as radioactive iodine treatment or external radiation therapy. Biondi and Cooper (2005) and Singer (2005) reported that after external radiotherapy of the head and neck area, mild and overt hypothyroidism is reported to be common. It may develop gradually within the first year with a risk that appears to be dose-dependent. Regarding sub clinical Hyperthyroidism the most common cause of it is exogenous, due to over dose during replacement therapy in hypothyroid patients or TSH suppressive therapy for benign or malignant thyroid disease (Anker *et al.,* 1998; Biondi and Cooper, 2008; Biondi *et al.,* 2005; Cooper, 2003; Cooper *et al.,* 2006; Papi *et al.,* 2005; Ross, 2000). Moreover, autonomous thyroid function as reported in Graves' disease, multinodular goiter, and solitary autonomously functioning thyroid nodules (AFTN) are correlated with endogenous sub-clinical hyperthyroid (Anker *et al.,* 1998; Biondi and Cooper, 2008; Biondi *et al.,* 2005; Cooper, 2003; Cooper *et al.,* 2006; Papi et al., 2005; Ross, 2000; 2005; Toft, 2001). Treatment of sub clinical hyperthyroidism (e.g Graves' disease) is mostly spontaneous without intervention. The patients with multinodular goiter and autonomously functioning thyroid adenoma, chronic sub-clinical hyperthyroidism, is associated with a progressive increase in thyroid hormone levels, thus sometimes preceding the onset of overt hyperthyroidism (Pearce and Himsworth, 1984; Ross, 2005).

The present study in this aspect describes the assessment and evaluation of sub-clinical thyroid disorders in selected population from both genders. Hence, a total of 107 female patients [59.44%] out of 180 showed either forms of thyroid disease. By sub-groups, forty two patients (23.33%) [n = 26; 14.44% Sub-clinical hypothyroidism, n = 16; 8.88% sub-clinical hyperthyroidism] showed sub-clinical thyroid disorders, whereas n = 65 (36.11%) exhibited true-form. In males, a total of 66 patients showed either forms of thyroid diseases. As per subgroups, twenty two (18.33%) %) [n = 18; 15.0% sub-clinical hypothyroidism; n = 4; 3.33% sub-clinical hyperthyroidism] out of 120 showed sub-clinical thyroid disorders, whereas 44 (36.66%) exhibited true-form.

Knowingly, the subclinical thyroid dysfunction is defined as condition where serum TSH level alternates within below and above normal levels and thus its determination is eminent. It is reported to occur in 4% to 10% of the general population, and is especially prevalent in elderly women (Canaris *et al.,* 2000; Paul *et al.,* 2006; Vanderpump *et al.,* 1995). There is sizeable ambiguity concerning the corollary of untreated subclinical hypothyroidism and hyperthyroidism, as well as the benefit of initiating therapy (Col *et al.,* 2004). It was previously reported that potential risks of subclinical hypothyroidism include progression to overt hypothyroidism, dyslipidemia, cardiovascular complications, and neurological and neuropsychiatric effects (Krysiak *et al.,* 2006). However, subclinical hyperthyroidism corresponds to a substantial risk factor for induction of atrial fibrillation in the elderly and for postmenopausal osteoporosis in females (Krysiak *et al.,* 2006). The onset of hyroid disorders varies from as low as sub-clinical hyperthyroidism (0.65%) and as high as diffuse goitre (7.35%), and sub-clinical hypothyroidism (6.59%), hypothyroidism (4.97%), hyperthyroidism (0.86%) prevailing amongst the two extremes (Paul *et al.,* 2006). Interestingly the incidence of thyroid disorders was observed to be highest in the 11-45 years age group (79.89%) (Paul *et al.,* 2006).

Regarding the management and treatments regiment for patients of thyroid disorders, the individuals with serum TSH lower than 0.1 mIU/L or higher than 10 mIU/L, the efforts may be beneficial. However, most persons found to have subclinical thyroid dysfunction with posing TSH levels between 0.1 and 0.45 mIU/L or between 4.5 and 10 mIU/L, such that the benefits of them going for treatments are not clearly ascertained (Col *et al.,* 2004). Furthermore according to the American College of Physicians' guidelines, the management regiments and proposals of patients with sub-clinical hyperthyroidism are mostly theoretical and less evidence-based, and the supervision of patients without clinical findings is irresolute (Clinical Guidelines, 1998). Henceforth, there are no extensive controlled studies comparing the efficacy of different therapies (antithyroid drugs, radioiodine or surgery) in patients with sub-clinical hyperthyroidism. Biondi and Cooper (2008) reported that small doses, i.e., 25-75 µg/day are often adequate to normalize serum TSH levels in sub-clinical hypothyroidism. However, various endocrinologists and physicians differ about the treatment of endogenous sub-clinical hyperthyroidism (Clinical Guidelines, 1998; Cooper, 1998). For concluding arguments, Col *et al.,* (2004) established that TSH determination will be superior among those populations at higher risk for developing several thyroid related disorders including to identify occult thyroid dysfunction. Amongst important ones were patients with overt disease, including women, older persons, and individuals with previous or family history of thyroid disease, type 1 diabetes mellitus, radioactive iodine treatment for hyperthyroidism, recurrent miscarriages, or administrations of medications that may affect thyroid function (Col *et al.,* 2004).

## Conclusions

It is concluded that sub-clinical thyroid dysfunction predicts future progression to overt disease. It is cautiously recommended that, if evidence backed the diagnoses, initiating treatment for sub-clinical hypothyroidism may prevent symptoms and signs of overt disease. It is also advisable that routine screening for thyroid disease through clinical investigations aided with lab findings be promoted, especially in pregnant women. Moreover, in our study, which is in its progression stages, it is premature to ascertain exact and a final percentage of sub-clinical thyroid dysfunction patients in our population. The study is in progress to evaluate sub-clinical thyroid dysfunction in lager groups including children and pregnant women.

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