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STUDY OF SERUM TSH LEVELS IN TOBACCO SMOKERS AND NON-SMOKERS

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ABSTRACT: INTRODUCTION: TSH is the major regulator of the morphologic and functional states of the thyroid. All steps in the formation and release of thyroid hormones are stimulated by TSH secreted by the pituitary thyrotrophs. Cigarette smoking has multiple effects on thyroid function. These include both pro- (e.g. thyroid stimulating) and anti-thyroid actions and also actions that increase susceptibility to or exacerbation of the manifestations of Graves' disease.^[1] The result of most of the studies have shown that smokers have higher prevalence of hyperthyroidism than hypothyroidism. This study will contribute to the existing knowledge of the detrimental effects of tobacco smoking on thyroid function. Thus, this study may be instrumental in early detection and management of thyroid disease in smokers. **AIM OF THE STUDY:** To compare the serum TSH levels in smokers and non-smokers. **MATERIALS AND METHODS:** A cross-sectional study was done on 150 (75 smokers and 75 non-smokers) patients at Vydehi Institute of Medical Sciences and Research Centre, Bangalore for a period of 18 months (From 1st January 2012 to 30th June 2013). Serum TSH levels were compared in the two groups. **RESULTS:** In this study 33.3% population had smoked for 6 to 10 years whereas 18.7% fell in the more than 20 years of smoking category. (Mean±SD: 12.75±8.84). Mean TSH in smokers and non-smokers was 6.27±5.83 and 5.04±5.73 respectively. **CONCLUSION:** Smoking was found to be associated with high TSH levels. **KEYWORDS:** Non-smokers, Pack-years, Smokers, Tobacco, TSH.

INTRODUCTION: TSH is the major regulator of the morphologic and functional states of the thyroid. All steps in the formation and release of thyroid hormones are stimulated by TSH secreted by the pituitary thyrotrophs. Thyroid cells express the TSH receptor (TSHR), a member of the glycoprotein G protein-coupled receptor family. It is a glycoprotein secreted by the thyrotrophs in the anteromedial portion of the adenohypophysis. In normal serum, TSH is present at concentrations between 0.4 and 4.2 mU/L. The level is increased in primary hypothyroidism and reduced in thyrotoxicosis. The plasma TSH half-life is about 30 minutes, and production rates in humans are 40 to 150 mU/day. There is a linear inverse relationship between the serum free T₄ concentration and the log of the TSH, making the serum TSH concentration an exquisitely sensitive indicator of the thyroid state of patients with an intact hypothalamic-pituitary axis.^[2]

Tobacco use is the single most important preventable health risk in the developed world and an important cause of premature death worldwide. Smoking causes a wide range of diseases including many types of cancer, chronic obstructive pulmonary disease, coronary heart disease, stroke, peripheral vascular diseases and peptic ulcer diseases. Cigarette smoking has multiple effects on thyroid function. These include both pro- (e.g. thyroid stimulating) and anti-thyroid actions and also actions that increase susceptibility to or exacerbation of the manifestations of Graves' disease.^[1] There are minor and probably physiologically unimportant alterations in thyroid hormones and thyrotropin concentrations,^[3] central (Thyroid) and peripheral antithyroid action, thyroid gland

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stimulating or goitrogenic action, carcinogenesis lowering properties and also actions that increase susceptibility to Graves' disease.^[4]

Thiocyanate (SCN⁻), a major component of smoke, derived from hydrogen cyanide, a perchlorate like goitrogen is generated from cigarette smoke as a detoxifying product of cyanide. It seems more likely that this dual mode of action of tobacco smoke (Hypo or hyperthyroid) is a result of the effects of multiple components of smoke, such as nicotine, hydroxypyridine metabolites and benzpyrenes, which may also interfere with thyroid function.^[3,5] The result of most of the studies have shown that smokers have higher prevalence of hyperthyroidism than hypothyroidism. This study will contribute to the existing knowledge of the detrimental effects of tobacco smoking on thyroid function. Thus, this study may be instrumental in early detection and management of thyroid disease in smokers.

MATERIALS AND METHODS: Patients presenting to Medicine department at Vydehi Institute of Medical Sciences and Research Centre (VIMS and RC) who satisfied the inclusion criteria were included in the study.

Duration of Study: For a period of 18 months (From 1st January 2012 to 30th June 2013).

Sample Size: 150 cases (75 smokers and 75 non-smokers).

Method of Collection of Data: It was a duration based study. Detailed clinical examination and tests for serum TSH were done on all patients. A fasting blood sample was taken. TSH levels were measured and recorded by Access Beckman Coulter instrument. It was done by Chemiluminescence method.

Normal laboratory value of TSH was taken as 0.5 to 8.9µIU/ml. The data was recorded as per the proforma and informed written consent was taken from all the patients and the data was analyzed statistically.

Inclusion Criteria: Smokers of more than 3 years duration between age group of 18 years to 65 years and who have been smoking equal to or more than 1 pack year.

Pack Year- It is calculated by multiplying the number of packs (1 pack=20) of cigarettes smoked per day by the number of years the person has smoked.^[6]

Exclusion Criteria:

1. Known case of thyroid disorder.
2. Patients on medication for thyroid disorder.
3. Smoking for less than 3 years.
4. Any other condition that will alter thyroid profile.
5. Patients with pituitary disorder.

Statistical Analyses: It was a cross-sectional study with cases and controls. Data was analyzed using chi square test and t-test.

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The following methods of statistical analysis have been used in this study. Data were entered in Microsoft Word and Excel and analyzed using the statistical software, namely SAS 9.2, SPSS (Statistical Package for Social Science) 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1

The results were averaged (Mean+standard deviation) for continuous data and number and percentage for dichotomous data. The proportions were compared using Chi-square (χ^2) test of significance. The Student's t-test was used to determine whether there was a statistical difference between groups in the parameters measured if the data is normal. The test $p < 0.05$ was accepted.

RESULTS: In our study as per different age groups, the percentage of smokers was 5.3%, 29.3%, 28%, 14.7%, 21.3%, 1.3% in age groups 18 to 20 years, 21 to 30, 31 to 40, 41 to 50, 51 to 60 and greater than 60 years age group respectively. Thus maximum prevalence of smoking was found to be in the 21 to 30 years age group followed by 31 to 40 years group and least in greater than 60 years age group.

In this study 33.3 % population had smoked for 6 to 10 years whereas 18.7 % fell in the more than 20 years of smoking category. (Mean $\pm$ SD: 12.75 $\pm$ 8.84). (Figure 1)

38.7% were in 1-2 pack year groups while 16 % were under greater than 20 pack years. None of the patients were under 11-15 pack year group. (Table 1) (Figure 2)

57.3% smokers and 82.7% non-smokers had TSH in normal range with $p < 0.009$ (Table 2, Figure 3)

Mean TSH in smokers and non-smokers was 6.27 $\pm$ 5.83 and 5.04 $\pm$ 5.73 respectively. (Table 3, Figure 4)

DISCUSSION: In our study, as per different age groups maximum prevalence of smoking was found to be in the 21 to 30 years age group (29.3%) followed by 31 to 40 years group and least in greater than 60 years age group.

Global Adult Tobacco Survey India (GATS), a standardized household survey to track tobacco use in Indian population above 15 years of age, was conducted by the International Institute for Population Sciences, Mumbai on behalf of the Ministry of Health and Family Welfare, Government of India. According to the survey, among age group of 15-24 years age group 0.3% females and 9.3 % males were tobacco smokers. Similarly female and male smokers were 2.1% and 27%, 5.7% and 37.4%, 9.9% and 31% in 25 to 44 years, 45 to 65 years and greater than 65 years age group respectively. This implied that the maximum percentage of male smokers lies in the age group of 45 to 65 years age and maximum prevalence of female smokers is in greater than 65 years age group.^[7]

In our study, 33.3 % population had smoked for 6 to 10 years whereas 18.7% fell in the more than 20 years of smoking category. 38.7% were in 1-2 pack year groups while 16 % were under greater than 20 pack years. None of the patients were under 11-15 pack year group.

In our study, 57.3% smokers and 82.7% non-smokers had TSH in normal range with $p < 0.009$. (Table 2, Figure 3). Normal TSH was more in the non-smokers group. Abnormally low and high TSH was more in the smokers group with a significant p value.

In a population based cross-sectional study by Bjorn O et al,^[8] among women, the mean thyrotropin (TSH) level was lower in current (1.33 mIU/L; 95%confidence interval [CI], 1.29-1.36 mIU/L) and former smokers (1.61 mIU/L; 95% CI, 1.56-1.65mIU/L) compared with never smokers (1.66 mIU/L; 95% CI, 1.63-1.70 mIU/L). In the same study, among men, the mean thyrotropin level

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was lower in current (1.40 mIU/L; 95% CI, 1.36-1.44 mIU/L) and former smokers (1.61 mIU/L; 95% CI, 1.57-1.6661 mIU/L) compared with never smokers (1.70 mIU/L; 95% CI, 1.66-1.75 mIU/L). These findings indicate that smoking is associated with lower TSH levels.

Offie et al ^[9] compared serum thyroid hormone and thyroid stimulating hormone (TSH) concentrations in active, passive, and non-smokers and determined their association with cigarette tobacco smoke exposure. Serum concentrations of the various hormones of active smokers, passive smokers, and non-smokers (nonexposed), respectively, were as follows. Median TSH concentrations were 1.02, 1.06, and 1.12 mIU=L ($p < 0.001$ for the comparison of each group with the other two groups), and mean TSH levels were 1.40 mIU=L, confidence interval (CI) 0.07–6.83 mIU=L; 1.30 mIU=L, CI 0.25–3.01 mIU=L; and 1.50 mIU=mL, CI 0.71– 4.00 mIU=L.

A cross-sectional study done by Jorde et al ^[10] showed that serum TSH levels were significantly lower in the smokers than in the non-smokers, both in males (1.63+/-0.88 vs. 1.95+/-1.04 mIU/L [$p < 0.01$]), and in females (1.55+/-0.86 vs. 1.86 +/-1.01 mIU/L [$p < 0.01$]). There was no association between number of cigarettes smoked and the serum TSH level. It was concluded that smokers have lower serum TSH than non-smokers.

Belin et al ^[11] in the Third National Health and Nutrition Examination Survey (NHANES III), found that fewer smokers (2.6%, 95% CI = [2.0-3.2%]) had elevated TSH compared with nonsmokers (5.5%, 95% CI = [4.7-6.3%]). Smoking was found to be associated with mild TSH decreases.

In two birth cohorts by Ericsson et al,^[12] the serum thyrotropin (TSH) concentration was significantly lower in smokers than in ex-smokers and non-smokers ($P=0.05$ and $P=0.001$, respectively).

In a study by Christensen et al ^[13] smokers were found to have TSH insignificantly lower in smokers than in non-smokers. Lower levels of TSH among smokers have generally been reported in most studies.^[3,12,14,15,16,17]

CONCLUSION: Our study was a cross-sectional study involving 75 cases and 75 controls in the form of smokers and non-smokers respectively. Serum TSH levels were compared in the two groups.

To summarize, in our study maximum prevalence of smoking was found to be in the 21 to 30 years age group followed by 31 to 40 years group and least in greater than 60 years age group.

Abnormal TSH was more in the smokers group as compared with the nonsmokers group. There was more percentage of abnormally high TSH in smokers group with a significant p value. Thus in this study, smoking was found to be associated with higher TSH levels.

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