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# A STUDY ON TSH (THYROID STIMULATING HORMONE) LEVELS IN SMOKERS AND NON– SMOKERS - A CASE CONTROL STUDY

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**ABSTRACT**

Background: Smoking is the most common addiction in general population. Tobacco smoking is considered as the commonest source of toxic chemical exposure and chemically mediated illness in humans. It has varied effects on thyroid function. The effect of smoking on thyroid is believed to be due to the compound thiocyanate, a potent inhibitor of iodide transport, potentially capable of affecting the thyroid function. 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. 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. The result of most of the studies have shown that smokers have higher prevalence of hyperthyroidism than hypothyroidism. . Thus, this study may be instrumental in early detection and management of thyroid disease in smokers. The aim of this study is to evaluate and compare TSH thyroid stimulating hormones status in smokers and non smokers. Methods: A case control study is done with 82 patients divided into 2 groups. Group 1 (healthy male non-smokers) as control and Group 2 (healthy male smokers) as cases with inclusion and exclusion criteria. Fasting blood samples were collected and serum TSH levels were estimated. The data was analyzed using unpaired t test. Results: In the present study significant decrease in TSH observed in the cases compared to the controls. Mean±S.D of TSH in Group 1 is 2.712±0.8386 and Group 2 is 1.003±1.123, there is a significant decrease in serum TSH levels in Group 2. Interpretations & Conclusion: The finding in this study indicates that smoking is associated with biochemical hyperthyroidism. Hence evaluating thyroid hormone status in smokers might help in identifying occurrence of thyroid disorders and appropriate measures could be taken to prevent severity of morbidity and mortality associated with smoking.

**Key words:** Thiocyanate, hyperthyroidism, TSH, smoking.

## INTRODUCTION

Cigarette smoking is the second most popular smoking form of tobacco used in India [1]. Cigarettes are considered as the commonest source of toxic chemical exposure and chemically mediated illness in humans [2]. Tobacco smoke contains numerous compounds, the important substances of medical significance being the carcinogens (such as polycyclic aromatic hydrocarbons), irritant substances, nicotine, carbon monoxide and other gases [3]. Chemicals in cigarettes and cigarette smoke are known to cause not only cancer but also other serious health problems. Many of the chemicals are poisonous [4]. Three of the most widely known chemicals are nicotine, tar, and carbon monoxide [4].

Smoking has a particularly large impact in the developing world and annually accounts for 1.17 million deaths worldwide Tobacco is a serious threat to health and a proven killer and ranks second as a cause of death in the world, taking its toll by killing some 5 million people globally [5,6]. Tobacco use is an emerging pandemic marching forward relentlessly [7, 8]. Youth in general and adolescents in particular fall prey to this deadly habit with severe physical, psychological, and economic implications.

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In India tobacco kills 8–10 lakhs people each year and many of these deaths will occur in people who are very young [9, 10].

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 4.2mU/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 150mU/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 [11].

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.

This present study will contribute to the existing knowledge of the detrimental effects of tobacco smoking on thyroid function. Thus, the study was planned to analyse the alteration in thyroid profile of smokers in comparison with non-smokers and thus may be instrumental in early detection and management of thyroid disease in smokers.

## Materials and methods

### Settings:

A case control study was conducted in the Department of Biochemistry, Osmania General Hospital, Hyderabad.

### Sources of samples and data

The cases and samples were collected from Department of General Medicine, Osmania General Hospital, Afzalgunj and Department of Biochemistry, Osmania General Hospital.

### Cases

Healthy male smokers, a brief history was taken and samples were collected.

Investigations were performed at the Department of Biochemistry, Osmania Medical College / Osmania General Hospital.

### Controls

Healthy male non-smokers, a brief history was taken and samples were collected and investigations were performed at the Department of Biochemistry, Osmania Medical College / Osmania General Hospital.

In the present study the individuals were divided into two groups.

| | | |
|---|---|---|
| Group 1 | Healthy male non - smokers | N = 41 |
| Group 2 | Healthy male smokers | N = 41 |

Informed oral and written consent was taken from all individuals who took part in the study.

### Inclusion criteria

1) Smokers 2) No history of thyroid disease 3) Healthy males 4) No history of any steroids medication 5) No history of liver disease 6) Age between 25 to 50 years 7) No pituitary disorders.

### Exclusion criteria

1) Non – smokers 2) History of thyroid disease 3) History of consumption of steroids medication 4) History of liver disease 6) Age less than 25 years and above 50 years 7) Patients with pituitary disorder

### SPECIMEN COLLECTION

4ml of Fasting venous blood were collected in a vacutainer (RED CAP). Sample was centrifuged at 3000 r.p.m for 10 minutes and serum was separated for analysis within two hours of collection of blood. Grossly haemolysed and lipemic samples were excluded.

### Ethical clearance

The ethical issues involved in this study were reviewed and approved by the ethics scientific committee of Osmania Medical College.

### Statistical analysis

The data was analysed using Graph Pad prism 6.0

### Methodology

**TSH (**Thyroid stimulating hormone**)** ELISA (CAL BIOTECH KIT) – TS227T [12].

## RESULTS

The present study was undertaken in the department of Biochemistry Osmania General Hospital. A total of 82 male subjects of 41 subjects were smokers and 41 were non-smokers. The results were expressed in µIU/ml for serum TSH. The Mean ± SD of all the

parameters studied in the total cases were significantly different from those of controls. The significance of different mean values of different groups is represented by P values and P values < 0.05 is considered as significant.

**Table 1: Mean ± SD of TSH levels in smokers and Non smokers**

| Parameter | Group 1 (CONTROL) | | | Group 2 (CASES) | | |
|---|---|---|---|---|---|---|
| | Mean | ±S.D | SEM | Mean | ±S.D | SEM |
| TSH* | 2.712 | 0.8386 | 0.1310 | 1.003 | 1.123 | 0.1754 |

**Table 2: Unpaired t test of TSH in 2 groups**

| P Value | T | df | Mean ± SEM of Group 1 | Mean ± SEM of Group 2 |
|---|---|---|---|---|
| <0.0001 | 7.809 | 80 | 2.712 ± 0.1310 | 1.003 ± 0.1754 |

**Table 3: Age of total study population (N = 82) i.e Group 1 and 2**

| MINIMUM AGE | MEDIAN AGE | MAXIMUM AGE |
|---|---|---|
| 25.00 | 31.50 | 48.00 |

Thus the age range of the total study population is between 25 – 48 years

**Table 4: Age of smokers in the smoking population study i.e Group 2**

| MINIMUM AGE | MEDIAN AGE | MAXIMUM AGE |
|---|---|---|
| 25.00 | 32.00 | 48.00 |

**Table 5: Age of non-smokers in the non-smoking population study i.e Group 1**

| MINIMUM AGE | MEDIAN AGE | MAXIMUM AGE |
|---|---|---|
| 25.00 | 30.50 | 45.00 |

**Table 6: Number of cigarettes smoked per day in a study population**

| MINIMUM | MAXIMUM | MEAN ± SD |
|---|---|---|
| 3.00 | 40.00 | 12.17 ± 7.836 |

**Table 7: Duration in years of cigarette smoking in a study population**

| MINIMUM | MAXIMUM | MEAN ± SD |
|---|---|---|
| 3.00 | 25.00 | 12.02 ± 5.360 |

**Table 8: Abnormal thyroid Results among smoker population**

| | No. of Positive cases | Percentage % | 95% Confidence interval |
|---|---|---|---|
| TSH Abnormal | 24 | 58.54 | 42.11 – 73.68 |

**RESULTS**

Non-smokers had TSH within normal limits. In this study we analyzed data on 82 men, of whom 41 were smokers and 41 were non-smokers.

In this study the age range for the study population was 25 to 48 years. The minimum age is 25.00 years, median age is 31.50 years and the maximum age is 48.00 years of the total study population respectively. The numbers of cigarettes smoked in a smoking population is minimum 3 per day and maximum 40 per day and the duration of smoking was minimum of 3 years and maximum of 25 years.

In this study the Mean ± SD of TSH was lower for smokers than non-smoker. The mean and median of TSH value in this study population is 2.712 (Group 2 Non smokers) and 1.003 (smokers) respectively.

Among 41 smokers (Group 2) 24 cases were positive for abnormally low TSH with a percentage of 58.54% (95% CI 42.11 – 73.68%) and is statistically significant.

Thus this study shows that is TSH is lower whereas T3 and T4 levels are higher among the smokers hence indicating hyperthyroidism.

**Discussion**

Thyroid gland is important in human body because of its ability to produce T3 and T4 hormones which are necessary for normal development of body organs, to maintain appropriate energy levels and an active life. These hormones are required for normal growth, development and function of nearly all the tissues, with major effects on oxygen consumption and metabolic rate [13]. Thyroid hormone synthesis and secretion is regulated by a negative feedback system that involves the hypothalamus, pituitary and thyroid gland. The release of TSH causes the thyroid to stimulate the expression of the sodium/iodide symporter (NIS), which is responsible for iodide transport and therefore iodine uptake, the enzyme thyroid peroxidase, and thyroglobulin [14].

Within the thyroid gland, thyroid hormone synthesis requires iodine and the enzyme thyroid peroxidase to turn thyroglobulin (Tg) into thyroxin and triiodothyronine, T4 and T3, respectively. Thyroxine and triiodothyronine are then released into the bloodstream, where they are part of protein synthesis and metabolic processes in a multitude of cells and tissues. The regulation of thyroid hormones is a complex process. In a person with

healthy thyroid function, the presence of excess or lack of iodine, for example, leads the thyroid gland to make and release more or less of its hormones. The level of hormone in circulation signals the suppression or the synthesis of other hormones like TRH and TSH that in turn help maintain thyroid hormone balance [15].

Cigarettes are considered as the commonest source of toxic chemical exposure and chemically mediated illness in humans. Globally, tobacco use is one of the commonest elicit substances of abuse and is projected to kill 50% more people than HIV/AIDS by 2015, and to be responsible for 10% of all deaths by 2030 [2].

Inhibition of iodide transport by thiocyanate is independent of TSH concentration but competitive with iodine concentration [16]. Because of this competitive inhibition, iodine deficiency enhances the antithyroid action of thiocyanate, whereas iodide excess diminishes its harmful effect. Thereby, thiocyanate may be responsible for the goitrogenic effect of cigarette smoking seen at least in iodine deficient areas [17].

Several other mechanisms have been forwarded to explain the effect of tobacco smoke on thyroid. Tobacco smoke can cause hypoxia and formation of oxygen-free radicals which may result in free radical injury [18].

Due to multiple contrasting pathways in which tobacco smoke can effect in the functioning of thyroid gland, individual cross sectional studies have reported a decrease and increase or no effect of smoking on peripheral thyroid hormones [19].

In the present study we studied the effects of smoking on thyroid hormones. The subjects were divided into 2 groups. Group 1 included healthy non-smokers as controls, Group 2 healthy male smoker's as cases. We estimate the concentration of TSH.

In this study we analysed data on 82 men, of whom 41 were non-smokers (Group 1) and 41 were smokers (Group 2). The age of the total study cases (Group 1 and Group 2) is between 25 – 48 years. The minimum age being 25 years and maximum age is 48 years. The number of cigarette smoked among the study population in this study is minimum 3 cigarettes per day and maximum 40 cigarettes per day (Mean ± SD 12.17 ± 7.836) and the minimum duration of smoking is 3 years and maximum duration is 25 years (Mean ± SD 12.02 ± 5.360) in the smokers.

In the present study, we compared the Mean ± SD of serum TSH levels between the two groups. Serum TSH in Group 1 was 2.712 ± 0.8386 and Group 2 was 1.003 ± 1.123. The decrease in TSH levels in group 2 was significant ($p < 0.0001$). This implies that the males who smoke have low levels of serum TSH as compared to non-smoking males. Due to multiple contrasting pathways in which tobacco smoke can effect in the functioning of thyroid gland. The decrease in serum TSH was probably due to thiocyanate, 2,3-hydroxypyridine, 3,4-benzpyrene and hydroxyquinones, present in tobacco smoke $SCN^-$ inhibits iodide transport into the thyroid gland. This may cause a relative ID state in the gland which may be responsible for the goitrogenic effect of cigarette smoking. However, nicotine-dependent stimulation of the sympathetic nervous system, which in turn stimulates the thyroid gland and enhances the secretion of thyroid hormones, might also be responsible for the lower TSH levels in smokers.

These finding were in concordance with the following studies. Study conducted by L. Mehran et al, [21] found that tobacco smoking is associated with lower serum TSH values and Pontikides et al, have found Thyrotropin stimulating hormone (TSH) levels to be decreased or unaltered [20]. The mechanism behind lower serum TSH levels in smokers could be due to nicotine induced sympathetic stimulation, or increased evolution of thyroid autonomy, caused by the iodine depletion effect of thiocyanate in the thyroid. Another study done by Utiger et al., [21] found that Nicotine induces sympathetic activation which can increase thyroid hormone secretion and it may also have a direct thyroid stimulatory action along with other components of tobacco smoke like benzpyrene. A study done by Jorde et al showed that serum TSH levels were significantly lower in the smokers than in the non-smokers this is because nicotine is known to induce sympathetic activation which could enhance the secretion of thyroid hormones [22]. Similar findings were reported from Belin et al study show that smoking may be associated with thyro-regulatory changes resulting in lower TSH levels [23].

Their data was consistent with the hypothesis that decreased thyroid iodide transport and organification in smokers protect against development of auto antibodies, but predispose iodine-deficient individuals to hypothyroidism. In contrary to our study L. Hegedus et al found slight difference in serum TSH level between smokers and non-smokers which probably had no physiopathological significance [17].

In the present study there is decrease in TSH levels in male smokers with non-smokers. These findings indicate that there is a state of biochemical hypothyroidism in smokers as compared to non-smokers.

In addition to TSH, T3 and T4 for predicting thyroid disorders in smokers, other biomarker such as thyroid peroxidase antibody (TPO-Ab) thyroglobulin antibody (Tg-Ab) and thiocyanate ($SCN^-$) can be used for predicting thyroid disorder in smokers.

## CONCLUSION

Our study was a case control study involving 41 cases and 41 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 non-smokers group. There was more percentage of abnormally low TSH in smokers group with a significant p value. Thus in this study, smoking was found to be associated with lower TSH levels.

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**CONFLICT OF INTEREST:** The authors have no any conflict of interest in this study.

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