



RESEARCH ARTICLE

ESTIMATION OF SERUM TRIIODOTHYRONINE (T<sup>3</sup>), THYROXIN (T<sup>4</sup>) AND THYROID STIMULATING HORMONE (TSH) IN CIGARETTE SMOKERS IN KHARTOUM STATE

Malak M.BakhitHamdan<sup>1</sup>, Jasim M. Adam<sup>1</sup>, Mawaheb Abdullah Sulliman<sup>1</sup>, HarithHaider<sup>1</sup>, Ahmed Mohamed<sup>1</sup>, RehamIzzaldeenAbdallah<sup>1</sup>, RanaMaaz<sup>2</sup>, Mazin S. A. Mohamed<sup>3</sup> and Mohamed Abdelgader<sup>3\*</sup>

<sup>1</sup>National University, Khartoum, Sudan

<sup>2</sup>Alyarmok College, Khartoum, Sudan

<sup>3</sup>Napata College, Khartoum, Sudan

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ABSTRACT

**Background:** Cigarette smoking has a number of effects on the thyroid gland including the development of Graves' disease and thyroid multi-nodularity. However, the effect of smoking on thyroid function is more uncertain. This study aimed to estimate the levels of thyroid hormones in cigarette smokers

**Materials and Methods:** This study was designed as a case-control on 80 participants, 40 of who were smokers as case and 40 were non-smokers as control in Khartoum State (2016-2017). Serum T<sub>3</sub>, T<sub>4</sub> and TSH were measured by ELISA (Enzyme-Linked Immunosorbent Assay) (URIT-660 micro-plate reader made in China serial number 66001674 E)

**Results:** Were expressed as: (Mean  $\pm$  SD) and sig-2 tailed Pearson:

Serum T<sub>3</sub> level in smokers was (.063 ng/ml  $\pm$  0.18); in non-smokers was (1.48ng/ml  $\pm$  0.26) and a p value of 0.0000001; T<sub>4</sub> level in smokers was (2.75 $\mu$ g/dl  $\pm$  0.67); in non-smokers was (5.79 $\mu$ g/dl  $\pm$  0.60) and a p value of 0.000000, and TSH level in smokers was (0.62  $\mu$ IU/ml  $\pm$  0.38); in non-smokers was (0.38 $\mu$ IU/ml  $\pm$  0.08) and p value of 0.009.

**Conclusion:** Serum T<sub>3</sub> and T<sub>4</sub> levels in Sudanese smokers was decreased when compared to the levels in non-smokers. Whereas TSH levels were similar

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INTRODUCTION

The thyroid gland is one of the largest endocrine glands, weighing 23 grams in neonates and 18-60 grams in adults, and is increased in pregnancy<sup>(1)</sup>. Thyroid hormones produced by thyroid gland are essential for every activity of life, including the processes of digestion, metabolism, growth, reproduction, and mood control<sup>(2)</sup>. The production of thyroxine (T<sub>4</sub>) and triiodothyronine (T<sub>3</sub>) is regulated by thyroid-stimulating hormone (TSH), released by the anterior pituitary<sup>(3)</sup>. Often referred to as an 'overactive thyroid', is a condition in which the thyroid gland produces and secretes excessive amounts of the free (not protein bound, and circulating in the blood<sup>(4)</sup>. thyroid hormones, (T<sub>3</sub>) &/or (T<sub>4</sub>). This is the opposite of hypothyroidism ('sluggish thyroid'), which is the reduced production and secretion of T<sub>3</sub> and/or T<sub>4</sub><sup>(5)</sup>. Graves' disease is the most common cause of hyperthyroidism<sup>(6)</sup>. Iodine deficiency is often cited as the most common cause of

hypothyroidism worldwide but it can be caused by many other factors. Severe hypothyroidism in infants can result in cretinism<sup>(7)</sup>. With mild elevation of thyrotropin, thyroid-stimulating hormone (TSH), with higher level and low Free T<sub>4</sub> levels, symptoms become more readily apparent in clinical (or overt) hypothyroidism<sup>(8)</sup>. Cigarette smoking has multiple effects on the thyroid gland. It has both stimulatory as well as inhibitory actions on thyroid function and is also a powerful risk factor for development of thyroid disease, Graves' disease, Graves' ophthalmopathy and thyroid hormone abnormalities have all been linked to smoking. In normal adults, smoking has either a weak stimulatory or no effect on thyroid function and size. Small increases in thyroid hormones, mainly serum triiodothyronine and thyroglobulin concentrations may occur<sup>(9)</sup>. Tobacco smoke contains numerous compounds, polycyclic aromatic hydrocarbons irritant nicotine, carbon monoxide and other gases, to name just a few<sup>(10)</sup>.

\*✉ Corresponding author: Mohamed Abdelgader  
Napata College, Khartoum, Sudan

Thiocyanate is goitrogenic which is possibly responsible for the increased prevalence of non-toxic goiter, it inhibits iodide transport and organification as well as increasing the efflux of iodide from the gland, 2, 3-Hydroxypyridine, on the other hand, inhibit thyroxine de-iodination by limiting iodothyronine deiodinase activity<sup>(11-12)</sup>.

In 1984 a study done by Sepkovic *et al*<sup>(13)</sup> found substantial decrease in serum T3 and T4 concentrations in heavy smokers when compared with non-smokers. In contrast, their observed T4 and especially T3 concentrations in heavy smokers were higher than those of non-smokers. Such changes should also affect TSH secretion; serum TSH concentrations were slightly decreased, but not significantly, reduced in heavy smokers.

In another study done in Turkey in (1987) by A. K Iar McKaya *et al*<sup>(14)</sup> documented significant differences between groups were obtained for urinary Thiocyanate levels when non-smokers were compared with each smoking category. For heavy smokers, serum T3 concentrations were significantly above the values found in non-smokers while they were not significantly altered for moderate smokers. Moderate and heavy smokers demonstrated a slight increase in T4 hormone levels. The TSH concentrations were slightly lower than in heavy smokers when compared with control values. These differences were not statistically significant. The T4:T3 ratios were also slightly changed for each group but only the difference between heavy and moderate smokers was significant.

In Europe (1995), study was done by Luigi Bartalena *et al*<sup>(15)</sup> reported that cessation of smoking was associated with a small decrease in serum T<sub>4</sub>, reverse T<sub>3</sub> (rT<sub>3</sub>) and a small increase in serum TSH levels. While serum T<sub>3</sub> concentration was not altered significantly.

In 1997, Fisher, *et al*<sup>(16)</sup> done a study regarding cigarette smoking and thyroid hormone levels in male that found current smokers have higher thyroxin levels and lower thyroid stimulating hormone levels than never smokers and former smokers. The higher thyroxin levels that they detected in smokers, compared to non-smokers, diminished when there controlled for thyroxin-binding globulin. There also found that heavy smokers had a smaller increase in thyroxin levels than did light smokers, when compared to non-smokers.

Bjorn O. Asvold, *et al*<sup>(17)</sup>, did a research between August 15, 1995, and June 18, 1997. The study subjects were 20,479 women and 10,355 men without previously known thyroid disease and they also checked how often hypothyroidism and hyperthyroidism was found in current, former, and never smokers. Among women, the average TSH level was lower in current (1.33mIU/L) and former smokers (1.61mIU/L) compared with never smokers (1.66mIU/L). Similarly, among men, the average TSH level was lower in current (1.40mIU/L) and former smokers (1.61mIU/L) compared with never smokers (1.70mIU/L). In former smokers, their TSH levels increased gradually when they stopped smoking. Among current smokers, moderate daily smoking was associated with higher TSH levels than heavier smoking the researchers concluded that the study indicated that smoking is negatively associated with hypothyroidism but positively associated with hyperthyroidism. In other words, when people smoke, it causes hyperthyroidism. They also felt that smoking may have

reversible effects on thyroid function - once people stop smoking, their thyroid levels return to normal. They reported, for the first time, that there was a lower frequency of overt hypothyroidism among current smokers.

## MATERIALS AND METHODS

This was a case control study, which recruited 40 smokers for different durations as a case group, apparently 40 individuals as a control group from Khartoum state during the period from October 2016 to March 2017. The presence of thyroid disease was a major exclusion criterion. All the procedures were explained to the participants in their native language and written informed consent was taken before the enrollment in the study. In keeping with confidentiality Participants' identities were kept anonymous.

Three milliliters of venous blood were collected using antiseptic for the skin (70% ethanol), blood was transferred into plain container to obtain serum after blood clotting (after 30 minutes), blood was then centrifuged for 5 minutes at 4000 r/m immediately Centrifuge was used for this purpose, serum were separated and kept at -20 C until analysis. Serum T3, T4 and TSH were measured by ELISA (URIT-660 micro plate reader made in china serial number 66001674E).

Data were entered and organized into Microsoft Office Excel 2007 data sheet, then transferred to IBM Statistical Package for the Social Sciences (SPSS) version 15.

## RESULTS

**Table 1** Comparison between the means of serum T3 (ng/ml) in smokers and non-smokers

Independent T-test			T3 (ng/ml)	
Variables	Number	Mean	Std. Deviation	Std. Error Mean
Smoker	40	0.63	0.18	0.04
Non smoker	40	1.48	0.26	0.06

P value = 0.000001\*\*

- \*\* P value < 0.05 that's considered as statistically significant.

**Table 2** Comparison between the means of serum T4 (µg/dl) in smokers and non-smokers

Independent T-test			T4 (µg/dl)	
Variables	Number	Mean	Std. Deviation	Std. Error Mean
Smoker	40	2.75	0.67	0.15
Non smoker	40	5.79	0.60	0.13

P value = 0.000001\*\*

- \*\* P value < 0.05 that's considered as statistically significant.

**Table 3** Comparison between the means of serum TSH (µIU/ml) in smokers and non-smokers

Independent T-test			TSH (µIU/ml)	
Variables	Number	Mean	Std. Deviation	Std. Error Mean
Smoker	40	0.62	0.38	0.08
Non smoker	40	0.38	0.08	0.02

P value = 0.009\*\*

**Table 4** Comparison between the means of serum T3, T4, TSH and duration of smoking

Independent T-test	Duration of smoking (Years)	Number	Mean	Std. Deviation	Std. Error Mean	P value
T3 (ng/ml)	(10 years)	16	0.70	0.16	0.06	0.195*
	(> 10 years)	24	0.59	0.19	0.05	
T4 (µg/dl)	(10 years)	16	2.70	0.90	0.32	0.772*
	(> 10 years)	24	2.79	0.52	0.15	
TSH (µIU/ml)	(10 years)	16	0.75	0.42	0.15	0.211*
	(> 10 years)	24	0.53	0.33	0.10	

\*. P value > 0.05 that's considered as statistically insignificant.

**Table 5** Comparison between the means of serum T3, T4, TSH and number of cigarettes per day

One Way ANOVA	Number of cigarette/day	Number	Mean	Std. Deviation	Std. Error	P value
T3 (ng/ml)	(<6)	12	0.52	0.23	0.10	0.216*
	(6-10)	16	0.68	0.18	0.06	
	(>10)	12	0.68	0.07	0.03	
T4 (µg/dl)	(<6)	12	2.40	0.91	0.37	0.165*
	(6-10)	16	3.08	0.36	0.13	
	(>10)	12	2.68	0.63	0.26	
TSH (µIU/ml)	(<6)	12	0.59	0.42	0.17	0.127*
	(6-10)	16	0.45	0.18	0.06	
	(>10)	12	0.86	0.45	0.18	

\*. P value > 0.05 that's considered as statistically insignificant.

**Table 6**

- Correlation between duration of smoking with levels of serum T3, T4 and TSH
- Correlation between number of cigarettes with levels of serum T3, T4 and TSH

Correlations		T3 (ng/ml)	T4 (µg/dl)	TSH (µIU/ml)
Duration of smoking (Years)	Pearson Correlation	0.025	0.047	-0.195
	Sig. (2-tailed)	0.916	0.843	0.41
	Number	40	40	40
	Strength	Weak	Weak	Weak
	Direction	Positive	Positive	Positive
Number of cigarette/day	Pearson Correlation	0.314	0.254	0.415
	Sig. (2-tailed)	0.178	0.28	0.069
	Number	40	40	40
	Strength	Weak	Weak	Weak
	Direction	Positive	Positive	Positive

Correlation is significant at the 0.05 level (2-tailed).

## DISCUSSION

In this community-based case control study which was carried out during the period of October 2016 to March 2017 in Khartoum State to determine Thyroid hormones and thyroid stimulating hormone levels in Sudanese Cigarette Smokers.

The current study showed significant decrease in triiodothyronine and thyroxin level in smokers when compared with non-smokers. Our study apparently agreed with previous study which was done in 1984 by Sepkovic *et al*, and disagreed with studies that were done in Turkey (1987) by A. K Iar McKaya *et al*, and Europe (1995), study was done by Luigi Bartalena *et al*, Fisher, *et al* (1997)

Thyroid stimulating hormone was normal. This result was apparently in disagreement with previous studies in a 1984 study that was done by Sepkovic *et al*, and another study that was done in turkia (1987) by A. K Iar McKaya *et al*, In

Europe(1995) , study was done by Luigi Bartalena *et al*, Fisher, *et al* (1997), Bjorn O. Asvold, *et al*.

These findings suggested that smoking directly affected thyroid growth and function, but how it might do so, it is unknown. Nicotine causes sympathetic activation, which can increase thyroid secretion. Alternatively, nicotine or some other component of tobacco smoke might have direct thyroid-stimulating actions. Despite the association with goiter and small increases in thyroid secretion, in several case-control studies smoking was not a risk factor for either non-toxic or toxic multinodular goiter, indicating that its overall contribution to these disorders must be small. (18).

This study also demonstrated that there is weak correlation between smoking and thyroid stimulating hormone level (TSH) with number of cigarette/day and duration of smoking. This note is similar to those reported by (Paola *et al* ., 2007 Neal *et al* 2009 & Gledhill *et al*., 1988)(19).

## CONCLUSION

This study concluded that the serum Tri-iodothyronine and Thyroxin levels are decreased in Sudanese smokers when compared to the control of non-smokers individuals, where Thyroid stimulating hormone activity remained normal.

The study also showed that duration of smoking had a *weak correlation* with thyroid stimulating hormone (TSH), thyroxin (T4) and tri-iodothyronine (T3).

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