

# Could there be Targeting of the Thyroid Stimulating Hormone towards the Thyroid Gland? Thyroid Stimulating Hormone Levels Differences in the Thyroid Artery, Femoral Artery and a Peripheral Vein

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**Abstract:** *Introduction:* The hypothalamic hormones are secreted in very small amount and directly targeting to the pituitary gland. All stimulating hormones are secreted in the general circulation to reach their target glands. Could there be targeting of these stimulating hormones to their specific glands? If so then there would be differences between TSH level in thyroid artery, femoral artery and peripheral veins. No previous data was available concerning this question. *Objectives:* This study was designed to investigate the possibility of targeting the thyroid stimulating hormone towards the thyroid gland by evaluating the level of TSH in the thyroid artery and femoral artery, a peripheral vein and see if there is any difference. *Methods:* A cross sectional hospital based study was conducted in 2016 in the National Ribat Hospital in adult Sudanese. Blood Samples were taken from three euthyroid patients during thyroidectomy from the inferior thyroid artery, a peripheral vein and the femoral artery. Then the samples were analyzed by I chroma (blood chemistry analyzer) for TSH level. *Results:* There is a clear difference, in TSH levels between the thyroid artery ( $1.46 \pm .78$ ) uIU/ml and the femoral artery ( $.47 \pm .16$ ) uIU/ml and the peripheral vein ( $1.85 \pm .9$ ) uIU/ml. *Conclusions:* This pilot study showed that there is a difference in TSH levels between thyroid artery and femoral artery which might indicate that TSH is targeted towards the thyroid gland. Further studies are recommended to study the level of TSH in thyroid artery, femoral artery and a peripheral vein in animals and then investigate the possible mechanisms.

## 1. Introduction

The thyroid gland is an endocrine gland in the neck, consisting of two lobes connected by an isthmus. It is found at the front of the neck. The thyroid gland secretes thyroid hormones ( $T_4$  and  $T_3$ ), which primarily influence the metabolic rate and protein synthesis. The hormones also have many other effects including those on development.

The thyroid hormones triiodothyronine ( $T_3$ ) and thyroxine ( $T_4$ ) are synthesized from iodine and tyrosine. They are primarily regulated by thyroid-stimulating hormone (TSH), released by the anterior pituitary gland. Circulating levels of Thyroid Hormones (THs) are maintained within a relatively narrow range<sup>(1)</sup>. They appear to exert their effects by acting on one subtype of the Thyroid hormone receptor (TR). TRs are encoded by two separate genes,  $\alpha$  and  $\beta$ , the primary transcripts of which are alternatively spliced to generate three major products capable of mediating the response to TH; these transcripts – TR $\alpha$ 1, TR $\beta$ 1, and TR $\beta$ 2 – exhibit a very selective spatial and temporal pattern of expression in the developing and adult brain<sup>(2-3, 4)</sup>. Interestingly, TR $\beta$ 2 is expressed in the pituitary gland<sup>(5)</sup> and in the hypothalamic Para ventricular Nucleus (PVN),<sup>(6)</sup> and appears to be the predominant mediator of the negative feedback action of TH on TSH.<sup>(7)</sup> Pituitary TSH secretion regulates  $T_4$  (thyroxine) and  $T_3$  (triiodothyronine) secretion, which exert log linear

negative feedback on pituitary thyrotropes<sup>(8, 9)</sup> due to this relationship, small changes in the concentration of free thyroid hormone (TH) result in large changes in the serum concentration of TSH; therefore, the thyroid-stimulating hormone (TSH) is the most reliable test for diagnosing primary hypo and hyperthyroidism,<sup>(10, 11)</sup>

Thyroid functions tests (TFT) are commonly used to assess thyroid function. It includes measuring the level of thyroid hormones  $T_3$  and  $T_4$ , as well as TSH. The blood sample for TFT is usually taken from venous blood.<sup>(12)</sup> Elevated TSH generally indicates hypothyroidism, while low TSH generally indicates hyperthyroidism. However, when TSH is measured by itself, it can yield misleading results, so additional thyroid function tests must be compared with the result of this test for accurate diagnosis. As high ( $T_3$  and  $T_4$ ) may reveal hyperthyroidism and low  $T_3$ ,  $T_4$  may reveal hypothyroidism, or subclinical hyperthyroidism (normal  $T_3$  and  $T_4$  with a low TSH). Reference ranges for TSH may vary slightly. In the UK, guidelines issued by the Association for Clinical Biochemistry suggest a reference range of (0.4-4.5  $\mu$ IU/mL).<sup>[12]</sup> TSH is secreted directly to the circulation, although it is control by TRH from the hypothalamus by the hypothalamohypophyseal portal system, and TRH has no role in the investigation, the main function of TSH is on the thyroid gland and few receptors for the feedback control in

the pituitary. As TRH is anatomically targeting of pituitary gland could there be targeting of TSH to the thyroid gland. If there is targeting of TSH to thyroid gland then its level in thyroid artery will be expected to be high, this study aims at measuring TSH in thyroid artery and compare it to the femoral artery and venous blood.

## 2. Methods

A cross sectional hospital based pilot study was conducted in the National Ribat Hospital in Khartoum Sudan in three euthyroid patients undergoing thyroidectomy.

The consent was taken from the hospital and the patients before surgery. Samples were collected ( 5cc of blood ) from the inferior thyroid artery, a peripheral vein and the femoral artery during thyroidectomy performed by a surgeon under general anesthesia with atropine (antisialagogue), fentanyl (analgesia), propofol(hypnosis), atracurium (muscle relaxant) , oxygen for induction of anesthesia, and inhaled Isoflurane and oxygen/nitrate for maintenance. Then it puts in non heparinized container in the centrifuge to separate the serum from samples in lab, and analyzed by using I chroma (chemistry analyzer) which is base on (fluorescence scanning of target analytics in human blood, urine and other specimen). After that results of TSH levels were analyzed electronically by using SPSS (statistical analyzer). But due to small sample size it did not give significant correlation, although there were significant different in there levels specially between thyroid and femoral artery. Further studies are recommended to identify the level of TSH between thyroid artery, femoral and peripheral veins in rabbit as taken samples from human is very difficult and need surgeon and special circumstance.

## 3. Results

Three adults patients were included, 2 females and 1 male, their age above 25 years.

Table1: Shows the mean value of TSH levels in thyroid artery, femoral artery and peripheral veins per international unit of enzyme activity/ Milliliter

TSH in the thyroid artery is triple that in the femoral artery and not very different from the venous blood.

**Table 1:** Shows the mean value of TSH levels in thyroid artery, femoral artery and peripheral veins per international unit of enzyme activity/ Milliliter

	Number	Mean ( uIU/ml )	Stander error
Thyroid artery samples	3	1.4630	.77724
Peripheral vein samples	3	1.8533	.92398
Femoral artery samples	3	.4733	.15948

## 4. Discussion

This study has been initiated to investigate the hypothesis that there is targeting of stimulating hormones, TSH as an example. The targeting is clearly seen of releasing hormones from the hypothalamus to the anterior pituitary, which is done anatomically by the short cut of the portal system.

These releasing hormones don't go into the general circulation as they are secreted in very minimal amount. If we consider the normal value for TSH in the venous blood is (0.4-4.5 uIU/mL)<sup>(12)</sup> and it was distributed homogenously in the whole adult blood then, how much TSH is secreted per day is not known and how much is taken by thyroid gland is also not known. If we assumed that there is targeting of TSH to thyroid gland then it is expected that TSH in thyroid artery will be higher than a peripheral artery like the femoral artery.

This is what has been shown by this pilot study where the thyroid artery TSH value was triple the femoral artery level, although it was not that different from the venous blood (table1). This indicates that TSH is possibly targeted more towards the thyroid gland. This observation is taken from the euthyroid patients who have been treated in the middle of major operation under general anesthesia and it definitely needs to be supported by animal experiments. If this proved to be true, then what could be the mechanism which target TSH to the thyroid gland? It is so far known that TSH acts only on the thyroid gland, which means that the TSH receptor combination will decrease its level close to the gland and may enhance its movement towards the gland.

In the animal the level in thyroid vein can be measured with the level in thyroid artery and the amount used by the gland can be estimated. The level in the venous blood is close to that of the thyroid vein, possibly due to the drainage of the vein from many small arteries and summation of their levels.

This can apply to all stimulating hormones, ACTH, TSH and LH, and can be investigated.

## 5. Conclusion

This pilot study has shown a higher level of TSH in the thyroid artery compared to the femoral artery and it needs further extensive investigation.

## 6. Acknowledgment

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Nil

## 8. Conflicts of Interest

There are no conflicts of interest.

## 9. Ethical Approval

The study was approved by the Institutional Ethics Committee

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