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Assessment Of Serum Progesterone and Serum Prolactin in Patients with Carcinoma Thyroid Before and After Thyroidectomy: A Pilot Study

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ABSTRACT:
Introduction: To assess the effect of total thyroidectomy on Serum progesterone and Serum prolactin present in patients with thyroid carcinoma. Method: This is a hospital-based prospective study carried out between November 2020 to November 2022 on patients diagnosed with a case of carcinoma thyroid who were admitted to J.N. Medical college and hospital. This study was done in the Department of Surgery, Jawaharlal Nehru Medical College and Rajiv Gandhi Centre of Diabetes and Endocrinology, Aligarh Muslim University, Aligarh. The patient's blood samples were collected and assessed for serum progesterone and serum prolactin (S. PRL) prior to and after 3 months postoperatively after total thyroidectomy. Result: There was an increase in the value of S. PRL. There was no change in the value of S. Progesterone. Conclusion: There was a significant change in the hormonal status after thyroidectomy. Serum PRL increased and Serum Progesterone showed no change. To our best knowledge, this was the first of a kind study to evaluate hormones following thyroidectomy in cancer patients.

keywords: thyroidectomy, carcinoma thyroid, prolactin assessment, progesterone assessment.

INTRODUCTION:

Thyroid hormones (TH) are responsible for regulating the critical cellular functions of metabolism, differentiation, proliferation, and apoptosis. Thyroid-stimulating hormone (TSH), which in turn acts at the thyroid gland to stimulate TH synthesis and secretion, is produced by the pituitary gland when hypothalamic thyrotropin-releasing hormone (TRH) activates it. [1] [2]

Tetraiodothyronine (T4), the main hormone produced by the thyroid gland, is converted to triiodothyronine by specific iodothyronine deiodinases (T3). Through the formation of complexes between T3 and nuclear thyroid hormone receptors alpha (TR-) and beta (TR-), T3 serves as the primary TH mediating metabolic activity. This nuclear T3-receptor complex regulates the transcription of specific genes by binding to thyroid hormone response areas on those genes. [3] The conditions known as hyperthyroidism and hypothyroidism are widespread and are characterized by specific clinical signs.

The impact of thyroid hormones on the development of cancer has been shown in pre-clinical research. [4] The number of thyroid cancer diagnoses has dramatically increased during the past few decades (TC).

[1] Globocan 2020 reports that there have been 586,202 cases with 43,646 deaths. The incidence rate was found to be 59.7% in Asia, with more females than males affected. [5] According to Globocan 2020, thyroid cancer was shown to be prevalent at 1.5% in India (20,432 new cases).[6]

Thyroid hormones are crucial for the healthy functioning of the female reproductive system because they control the metabolism and proliferation of ovarian, uterine, and placental tissues. In addition, they influence the release of gonadotropin-releasing hormone (GnRH) in the hypothalamic-pituitary-gonadal axis, as well as a number of other hormones and growth factors, such as estrogen, prolactin (PRL), and insulin-like growth factor (IGF). As a result, subfertility or infertility in women may be caused by variations in the blood levels of THs, such as hypo- and hyperthyroidism.[7]

Estrogen increases thyroxine-binding globulin and the requirement for thyroid hormone in hypothyroid women, which is a well-known indirect effect of oestrogen on the thyroid economy. [8] Human thyroid tissues with and without cancer have been found to contain the oestrogen receptor (ER), although the findings are inconsistent. In thyroid tumours, ER would promote apoptosis and other suppressive effects while, in contrast, oestrogen binding to ER would stimulate cell proliferation and growth. The ERα : ERβ ratio may have an impact on the pathogenesis of thyroid cancer. [9]

There isn't much research that has looked at the differences in thyroid hormone release during or after surgical treatment. [10] In order to assess the effect of hormonal variation (S.PRL & S. Progesterone) in patients before and after thyroid surgeries in those with thyroid cancer, the current study was done.

PATIENTS AND METHOD

This hospital-based prospective study was conducted between November 2020 and November 2022 on patients admitted to J.N. Medical College and Hospital who had been diagnosed with thyroid cancer. This research was conducted at the Rajiv Gandhi Centre for Diabetes and Endocrinology and the Department of Surgery at Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, UP, India

Study Design: Patients who were admitted to the surgical ward for a total thyroidectomy and had a diagnosis of thyroid enlargement were included in the study. Patients' particulars were noted. All patients with thyroid cancer who entered the hospital were evaluated, and the patient was added to the study based on the diagnosis of thyroid carcinoma.

The patient's blood samples were collected and assessed for Serum testosterone prior to surgery and after 3 months postoperatively.

Approval was obtained from the institutional ethics committee, Faculty of Medicine, Jawaharlal Nehru Medical College, A.M.U, Aligarh and Informed consent were taken from the 30 patients included in the study

Patients Included in the study:

- Patients diagnosed to be having carcinoma thyroid through clinical and histopathological or radiological examination.
- Patients are not on any hormonal medications
- The patient is ready for follow up
- Patients giving consent for their inclusion in the study

Data Collection: In the present study, patients' blood samples of around 4 ml were collected one day prior to surgery in a plain vial and sent to the Rajiv Gandhi Centre of Diabetes and Endocrinology for assessment. Patients' information was kept confidential. The patient was followed for 3 months and

another blood sample was collected (after a period of 3 months post-surgery). Both samples were analyzed for Serum testosterone and compared.

Statistical Analysis: The present study analysed all the qualitative data using the Pearson Chi-square test. Paired sample t-test was also used to check the significant difference between pre-op and post-op hormonal assessment. All the Statistical test was performed using the Statistical Package for the Social Science computer program (SPSS) version 25.0

OBSERVATION AND RESULT

Among the cases included in the study 46.7% (n;14) were from the younger age group falling under the category of 20-30 years followed by 41-50 & 51-60 years with a mean age of 37.07 years.

There was a significant pre-dominance ($p<0.001$) of females having thyroid malignancy with 93.3% (n; 28) among the cases included in the study.

Among the Ultra-Sonography (USG) findings for classifying thyroid malignancy, the score of TIRADS 5 was found to be the most common with 46.7% (n;14) followed by TIRADS 4 with 43.3% (n;13) out of the cases included in the study.

Among the Fine Needle Aspiration Cytology (FNAC) findings for thyroid malignancy, the Bethesda Category 4 (BETHESDA 4) was found to be the most common with 36.7% (n;11) followed by BETHESDA 5 with 33.3% (n;10) out of the cases included in the study.

Among the histopathology examination (HPE) for thyroid malignancy, papillary thyroid cancer (PTC) was found to be the most common with 73.3% (n;22) followed by follicular thyroid carcinoma (FTC) with 16.7% (n;5) out of the cases taken for the study.

The hormonal assessment for Serum Prolactin (PRL) showed a significant **increase** with $P <0.001$. The mean value in the pre-op was 27.30 and the mean value in the post-op was 52.52. (Table 1 and graph 1)

For the hormonal assessment for Serum Progesterone there was **almost no change** with $P <0.01$. The mean value in the pre-op is 2.27 and the mean value in the post-op is 2.01. (Table 2 and graph 2)

DISCUSSION

This entire study was designed to compare the pre-operative and post-operative value of serum testosterone at an interval of 3 months after total thyroidectomy. So, it could be supplemented; which in turn, would alter the lifestyle and make the life of the patient better.

1. Distribution of Age and Gender

In our study, the mean age of patients was 37.07 years among which 28 (93.3%) were female and 2 (6.7%) were male. All the cases underwent total thyroidectomy. A retrospective study on 359 patients diagnosed with thyroid malignancy. Sixty-four out of the 359 included patients were men (18%), and 295 (82%) were women [11]. In a retrospective study at a single tertiary care institution, 370 consecutive patients with low-or intermediate-risk DTC were submitted to total thyroidectomy [12]. The mean age at diagnosis was 47 years. 257 out of 359 were female 70% and 61 were male (30%).

Our study is in accordance with most papers where females are usually way more affected than males regarding thyroid carcinoma. In all the studies, females are more in number than males.

2. Ultra-Sonography findings

Ultrasonography (USG) provides better visualisation of the thyroid in the case of diagnosing thyroid malignancy. the most common USG-based classification used is the thyroid image reporting and data system (TIRADS). In our study, the most common TIRADS score was TIRADS 5 which was found among 14 (46.7%) and was followed by TIRADS 4 (43.3%). A study on 24 pediatric patients under the age of 18 years with thyroid nodules attended in the last 15 years. It was concluded of the overall 31 nodules, the distribution by EU-TIRADS the TIRADS 4 score was the most common which was different from our study where TIRADS 5 was the most common [13]. A prospective study in a sample of 1097 nodules using TIRADS based on the concepts of the Breast Imaging Reporting Data System of the American College of Radiology. They concluded that TIRADS had an accuracy of 94% in predicting malignancy related to thyroid nodules [14]. Which means TIRADS 4 (5-80% malignancy), and TIRADS 5 (>80% malignancy).

3. Fine Needle Aspiration Cytology

The other pathological investigation used in our study for diagnosing thyroid malignancy was fine needle aspiration cytology (FNAC) which uses the BETHESDA category system for classification. A retrospective study on all patients with thyroid nodules who presented to the hospital in Lahore Pakistan, from January 2011 to September 2018. It was found that the most common BETHESDA category for malignancy was category IV which was about 47.1% [15]. It is in accordance with our study where BETHESDA IV is the most common (36.7%) which is followed by BETHESDA V (33.3%). A study to determine the value of FNAC in thyroid nodules in Victoria Australia and found an accuracy of 67.2% in predicting thyroid neoplasia. FNAC of the higher grade was an indicator of malignancy [16]. This was consistent with our study as well where BETHESDA categories IV and V were on the higher side.

4. Histopathological Findings

The most common histopathological finding found in our study was papillary thyroid carcinoma which came out to be 73.3% followed by Follicular carcinoma which was about 16.7%. A study in Malaysia on the genetic alteration of thyroid cancer. It stated that papillary thyroid carcinoma is the most common prevailing thyroid cancer which was also found in our study [17]. A study of 3,241 patients on characteristics of thyroid nodules and conducted that papillary thyroid cancer (PTC) is the most common. This is in accordance with our study where PTC is the most common [18]. An article published in modern pathology stated that papillary thyroid carcinoma is the most common thyroid malignancy. It is consistent with our study [19].

5. Serum Prolactin

To our best knowledge, this is the first study to document the changes in female hormones after total thyroidectomy. In our study, we found a significant increase in serum PRL. A prospective study on 113 women in a tertiary hospital in western Uttar Pradesh, India. In this study, they compared the effect of hypothyroidism on the female reproductive hormones which showed hypothyroidism is associated with hyperprolactinemia. [20]

6. Serum Progesterone

In our study, there was almost no difference in the progesterone level pre-operative and post-operatively with P<0.001. To our best knowledge, this is the first study to document changes in progesterone levels after thyroidectomy in humans. A study was conducted on the effect of thyroidectomy on the production of progesterone in the adrenal cortex of rats. they concluded that it did not have any effect on the production of the hormone.[21]

CONCLUSION

This prospective study was carried out at a tertiary hospital in India. the study sample included patients with high suspicion of thyroid malignancy, later confirmed through Histopathological examination. There was a significant change in the hormonal status after thyroidectomy. Serum PRL increased (P<0.001) and Serum Progesterone showed no change (P<0.001). To our best knowledge, this was the first of a kind study to evaluate S. PRL and S. Progesterone following thyroidectomy in cancer patients. Further study is definitely required in this field.

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Ethics approval and informed consent: There is ethical clearance from the local ethical committee, JNMCH, AMU, Aligarh, UP, India and informed consent were taken from all the patients.

Conflict of interest: There is no conflict of interest.

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