

# International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614  
ISSN (E): 2522-6622  
© Gynaecology Journal  
www.gynaecologyjournal.com  
2018; 2(4): 06-08  
Received: 02-05-2018  
Accepted: 03-06-2018

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## Evaluation of thyroid profile in gynaecological malignancies

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### Abstract

**Introduction:** Thyroid status may influence tumorigenesis of gynecologic cancer, though epidemiologic studies of this relation are limited.

**Methods:** The study included collection of a samples which was divided into two groups 100 healthy women and 144 women diagnosed with gynecological cancer (mainly ovarian cancer and endometrial cancer excluding cervical cancer), who had come to our department from May 2015 to April 2017. We evaluated thyroid profile in both the groups. **Result:** We found 16 cases of endometrial cancer (EC) and 128 cases of ovarian cancer (OC) in 2 years and out of this 4 EC patients and 37 OC patients had deranged thyroid profile i.e. 41 out of 144 (28.47%) gynecological (EC+OC) had deranged thyroid profile. However 11 out of 100 (11%) healthy patients had deranged thyroid profile. This showed significant association of deranged thyroid profile with gynecological cancer (p 0.00567). **Conclusions:** Hypothyroidism or hyperthyroidism is associated with Gynecological cancer (EC or OC) and if it is corrected in healthy women, cancer may be prevented.

**Keywords:** Endometrial cancer, gynecological cancer, ovarian cancer, thyroid profile, tumorigenesis

### Introduction

There is increasing trend of incidence of ovarian and endometrial cancer in India. Ovarian S with incidence of 6.1 per 100,000 and mortality rate of 3.8 per 100,000. Endometrial cancer is 9th most common cancer in India with incidence of 2.3 per 100,000 and mortality rate of 0.9 per 100,000 according to GLOBOCAN 2012. So to decrease the incidence and to improve the prognosis of OC and EC, various risk factor associated are studied and among them deranged thyroid profile was found as one of the important risk factor [1, 2].

In adult thyroid hormone is of decisive importance for the metabolic activity and function of nearly all organs. Various studies showed a possible interaction between thyroid function and tumor biology and prognosis in different cancers [3]. This association has recently been clarified after a membrane cell surface receptor for thyroid hormones that was characterized on rapidly dividing cells (e.g., endometrium) in contrast to the usual intracellular transport and nuclear binding in other tissues. Several *in vitro* and *in vivo* studies have implicated the role of thyroid hormones in tumor genesis and cell proliferation in glioma, gastric, and breast cancer cell lines. Blocking thyroid hormone receptors or decreasing T3 and T4 production to induce hypothyroidism has been shown to reduce tumor growth in breast, prostate and hepatocarcinoma in mouse models [4-7].

Thyroid disorders and alterations in thyroid hormone expression influence ovulation, endometrial physiology, and estrogen levels, further exploration show the possible association of risk of endometrial and ovarian cancer. In this study we evaluate thyroid profile in control group (healthy) and in EC and OC patients to analyze any association with endometrial and ovarian cancer

### Material and method

This prospective study was carried at IGIMS, from May 2015 to April 2017. During this period 16 patients were operated for endometrial cancer and 128 were operated for ovarian cancer. In the present study we evaluate pre-therapeutic serum thyroid stimulating hormone (TSH) in a group of patients which was divided into two groups (100 healthy women and 144 diagnosed cases of endometrial cancer and ovarian cancer of same age group i.e. 20-70 years). Each patient was evaluated by first general clinical examination which include mainly measurement of blood pressure and BMI (weight (kg)/height (m)<sup>2</sup>), pelvic examination and secondly serum TSH, T3,

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T4. The statistical methods used to analysis the data include number, percentage, meanwhile T-test and Anova analysis was used to compare between total control and total patients [8].

### TSH measurement

Blood samples (serum) were obtained routinely by peripheral venous puncture before therapy during pretreatment examination in cancer patients and as routine checkup in non-cancer patient.

### Statistical analysis

Values were given in number and percentage. Normal serum TSH level range from 0.5 mU/l – 5 mU/l according to Midline plus. For evaluation, patients were divided into two groups according to their pre –therapeutic serum TSH levels as follows: TSH mU<sup>-1</sup> ≤ 0.5mU/l (hyperthyroidism) and TSH >5mU/l(hypothyroidism).

Institutional ethical committee clearance was taken before study and patients were informed about this study.

### Result

**Table 1:** Distribution of patients according to age

Age(years)	OC (n=128) (%)	EC (n=16) (%)
20-30	5 (3.91%)	0(0%)
31-40	22(17.19%)	0(0%)
41-50	45(35.15%)	3(18.75%)
51-60	30(23.44%)	4(25%)
>60	26(21.03%)	9(56.25%)

**Table 2:** Showed distribution of endometrial and ovarian cancer patient and control group in relation to thyroid profile.

	EC+OC (n= 144)	Control group (n=100)
Euthyroidism	103(71.53%)	89(89%)
Hypothyroidism	38(26.39%)	10(10%)
Hyperthyroidism	3(2.08%)	1(1%)

### Discussion

In the present study serum TSH was evaluated in both case and control group. Present data demonstrates an independent association between elevated pre-therapeutic serum TSH levels and occurrence of ovarian and endometrial cancer. Thyroid disorders can present as hyperthyroidism (excessive T3 and T4 production) or more commonly as hypothyroidism (decreased T3 and T4 production) and this disorder, commonly persist especially in middle – aged and elderly women [9]. Similar result found in this study most ovarian cancer patients were of age >45yrs with mean age 47 years and endometrial cancer patients were of age >60 years with mean age 60 years (table1). In table 2, 103 EC+OC (71.53%) had normal thyroid profile while 28.47% were having deranged thyroid profile however in healthy women (control group) only 11% had deranged thyroid profile. This showed significant association between deranged thyroid profile and EC and OC (p 0.00567).

Various study suggest that TSH might be associated with systemic processes interacting with carcinogenesis [10]. But some epidemiologic studies failed to showed the impact of thyroid disorders on cancer risk [4, 11]. For total cancer risk assessment, Hercbergs *et al.* [12, 13] conducted a large prospective study of almost 30,000 people and followed their serum thyroid stimulating hormone (TSH) for over 9 years. Low levels, suggestive of subclinical hyperthyroidism, were associated with an increased risk of lung and prostate cancer but not breast or colon cancer.

The mechanism by which chronic hyperthyroidism/hypothyroidism might increase the risk of EC is not fully understood [13, 14]. The endometrium is a complex system influenced by a delicate balance of steroid hormones receptors, growth factors, and cytokines. Women with hyperthyroidism have estrogen levels 2- to 3-fold higher compared to euthyroid women due to SHBG changes and decreased clearance of estradiol [13]. Over time, chronic hyperthyroidism may indirectly increase serum estradiol levels and increase EC risk. Disordered growth of the endometrium is a precursor for endometrial hyperplasia and subsequent progression to carcinoma. In addition, the medical treatment of hyperthyroidism and the impact of thyroid blocking medications on the endometrium have not been well characterized. Previous studies have confirmed that hypothyroidism results in decreased estradiol levels and altered regulation from the hypothalamus pituitary axis (HPA). The resulting anovulation and thin endometrial lining may potentially be protective over time and balance the obesity often associated with hypothyroidism [15]. However in the study 3 cancer patients were found to be hyperthyroidism and 38 patients had hypothyroidism (table 2). This might be due to greater number of ovarian cancer in our study.

Ovarian cancer is the most lethal gynecological cancer. Risk of ovarian cancer (OC) is estrogen-linked but very little is known about the etiology or its precursor. The hypothalamic-pituitary axis (HPA) regulates the female reproductive tract not only through the regulation of estrogen and other sex hormones but also through the thyroid hormones [16]. A strong interaction between the hypothalamus–pituitary–thyroid axis and the balanced secretion of estradiol and progesterone by granulosa cells is well known. Hypothyroidism interferes with ovarian function, causing the formation of ovarian cysts and infertility [17]. Research on OC has been limited due to inability to easily access the ovaries to understand the precursors to malignant transformation. The incessant ovulation theory links ovulation to epithelial damage, inflammation, and repair that can lead to OC and is a hormone dependent process. The ovaries express estrogen, progesterone, and thyroid receptors; however, their complex interactions are not fully understood and the impact on cancer development, if any, remains unclear [16]. Only two other reports have looked into this association with conflicting results. Brinton *et al.* [18] reviewed over 2500 OC cases from a Danish tumor registry and reported no association with thyroid disease however, they were based on hospital diagnoses and only included 39 cases of thyroid disease. The other report was a population-based case-control study that suggested a significant relationship between hyperthyroidism and OC.

Another effect of TSH on adipose tissue is the release of leptin. Besides regulating energy homeostasis and neuroendocrine processes, leptin acts as a potential growth stimulator in normal and neoplastic cancer cells. Recent studies suggest a role of leptin in promoting endometrial cancer growth and invasion by regulating proangiogenic and pro-inflammatory factors [17]. As it has been shown that human endometrium expresses TSH receptors, it has been hypothesized that TSH can even directly act on uterus. Whether TSH possesses a direct biological role in tumor genesis of endometrial cancer or is indirectly promoting cancer development and progression is yet unclear. Pooled or meta-analysis studies are needed to increase power to further examine these associations.

## Conclusion

To our knowledge, very few study were present which showed significant association between deranged pre-therapeutic serum TSH levels and gynecological cancer (EC, OC). These findings, if proven by larger prospective studies, could have major clinical implications. For instance, serum TSH measurements may be used to screen women who are at high risk for endometrial cancer or ovarian cancer. Another implication may be the utilization of serum TSH measurements for determination of recurrences during the clinical follow-up. By elucidating the value of TSH as independent prognostic parameter for survival in patients with gynecological cancer, our results provide new insight in possible functional properties of TSH. Furthermore research will be needed to focused on clinical utilization of TSH for prognostic evaluation and the participation of TSH in the pathogenesis of endometrial cancer and ovarian.

We declare that this manuscript is original, it has not been published anywhere before and is not currently being considered for publication elsewhere. We also confirm that the authors do not have any conflict of interest associated with publication of this work, no significant financial support for this work has been received to influence the outcome.

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