THYROID HORMONE PROFILE IN PATIENTS WITH GASTROINTESTINAL MALIGNANCIES
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ABSTRACT

BACKGROUND
Gastrointestinal malignancies is most frequently diagnosed life-threatening cancer in humans. Thyroid hormones play a critical role in growth and development of alimentary tract. Evidence has implicated components of thyroid hormone signaling in development and progression of various cancers of alimentary tract. There is ongoing effort geared towards developing next generation TR specific agonists and antagonists, such molecules may have applicability in gastrointestinal cancer prevention and treatment.

MATERIALS AND METHODS
Cases - 60 cases of GI malignancies were taken, 15 each of gastric, oesophageal, colorectal, pancreatic cancers. Controls- 60 age and sex matched controls. All patients were investigated for T3, T4, TSH and TPO antibodies.

RESULTS
Statistically low mean t3, t4 and high TSH in cases compared to controls and TPO antibody levels raised in cases.

CONCLUSION
In GI malignancy, thyroid dysfunction is seen. Low level of thyroid hormone is seen in cases, even though there is no overt hypothyroidism.

KEYWORDS
Thyroid Hormones, Thyroid Receptors, Gastrointestinal, Thyroid Peroxidase Antibodies.

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BACKGROUND
Given that, thyroid hormones signaling has been characterised as a major effector of digestive system growth and homeostasis, numerous investigations have examined its role in the occurrence and progression of cancers in various tissues of this organ system. The present study is to know regarding the effects of thyroid hormone signalling on cancers of oesophagus, stomach, pancreas, colorectal cancers.

Thyroid hormones bind to thyroid hormone receptors belonging to nuclear receptor super family. In addition to intracellular TRs, the integrin alpha-v beta-3 has been recently been identified as cell surface receptor for TH. Two separate binding sites for TH have been identified on this integrin. One site binds T3 to stimulate p13k pathway and other site bind T4 to activate Erk1/2 pathway.

The latter mechanism has been demonstrated to enhance mitogenesis and decrease apoptosis in tumour cells. T4 binding to this integrin has also been implicated in increased FGF-dependent angiogenesis.

<table>
<thead>
<tr>
<th>Normal Cells</th>
<th>Malignant Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue oxidation- Thyroid stimulates metabolism by increasing oxygen consumption probably by catalysing the enzyme systems, which are responsible of tissue oxidation.</td>
<td>Malignant tissues in comparison with normal tissues and benign tumours are characterised not only by having the lowest concentration of cytochrome C, but also by having the greatest disparity between the components of oxidase cytochrome system.</td>
</tr>
<tr>
<td>Growth- Thyroid promotes normal growth under physiological conditions.</td>
<td>Most carcinogenic substances, in particular the potent hydrocarbons, have a considerable growth restraining influence.</td>
</tr>
<tr>
<td>Development- Thyroid brings about development and differentiation of tissue.</td>
<td>Malignant disease tends to show a dedifferentiation or reversion towards anaplastic tissue.</td>
</tr>
</tbody>
</table>
The metabolic rate in man decreases progressively with increasing age and the incidence of malignant disease increases progressively with age. The incidence of malignant disease thus seems to be correlated with the decrease in metabolic rate. As metabolic rate is in general a rough indication of thyroid activity, there would appear to be some relationship between malignant disease and thyroid dysfunction. In the same way, the lowered metabolic rate commonly found in patients with all types of peptic ulcers maybe considered with the incidence of carcinoma of stomach still one of the commonest neoplasms of man.

This in itself commends too many idea that cancer has a chemical and probably a hormonal basis for comparatively sudden changes in the function of endocrine glands either to the plus or to the minus direction. Thyroxine encourages normal physiological tissue respiration rather than the so called anaerobic type, which appears to be the one demonstrable biochemical difference between normal and neoplastic tissue. Thyroxine in adequate amounts may reverse the process of dedifferentiation or drift towards anaplastic growth that characterises most neoplastic tissue.

**Gastric Cancer**

Substantial number of patients with gastric cancer developed antithyroid antibodies, although this was not always associated with diminished thyroid function. A higher incidence of atrophic body gastritis was observed in patients with autoimmune thyroid disease. Implementation of iodine prophylaxis has proven to be effective in decreasing the incidence rate and death for gastric cancer in iodine-deficient areas.

**Pancreatic Cancer**

Several studies showed an association between hypothyroidism and autoimmune pancreatitis, latter a potential risk factor for pancreatic cancer. Studies showed occurrence of autoantibodies in pancreatic adenocarcinoma patients. Pancreatic cancer with lymph node metastasis exhibit raised integrin alpha v-3 beta-3.

**Colorectal Cancer**

Hypothyroid patients who have used levothyroxine for five years are found to have significantly decreased relative risk of CRC. Plasma thyroid levels are found to be reduced in CRC patients with systemic metastasis suggesting that TH signaling may suppress CRC invasiveness.

**Oesophageal Cancer**

Few studies have linked TH signaling to the development of oesophageal cancer, greater incidence of hyperthyroidism was demonstrated in patients with oesophageal cancer compared to controls.

**AIMS AND OBJECTIVES**

**Aims**

1. To find out the association of thyroid hormones and gastrointestinal malignancies including oesophageal cancer, gastric cancer, pancreatic cancer and colorectal cancers.

2. To find out the association of thyroid peroxidase antibodies in gastrointestinal malignancies.

**Objectives**

Incidence of thyroid disease in patients with oesophageal cancer, gastric cancer, pancreatic cancer and colorectal cancer and incidence of thyroid peroxidase antibody positivity in patients with gastrointestinal malignancies.

**MATERIALS AND METHODS**

Cases- This study was conducted in Government Medical College, Kozhikode, and patients admitted in surgery ward with biopsy-proven cases of oesophageal, gastric, pancreatic and colorectal cancers were taken as cases. Total 60 cases were included in the study, 15 cases of each malignancies was taken for the study.

Controls- 60 age and sex-matched healthy subjects who visited for general checkup were considered. Previous and present history of any malignancies and thyroid diseases were ruled out in controlled subjects.

**Inclusion Criteria**

Patients not having pre-existing thyroid illness and diagnosed cases of oesophageal, gastric, pancreatic and colorectal malignancies.

**Exclusion Criteria**

Patients’ undergone thyroidectomy and patients having pre-existing thyroid illness.

**Methods**

All patients were asked about detailed history of GI malignancies and history suggestive of any thyroid disease such as hyperthyroidism and hypothyroidism. Detailed examination of abdomen and other systems was done and cancer is staged with help of staging investigations. All patients were investigated for serum T3, T4, TSH and thyroid peroxidase. A normal range were 0.8-2.02 ng/mL for T3, 5.13-14.06 micro g/dL for T4 and 0.2-4 micro IU/mL for TSH. Thyroid antibody levels detected by thyroid peroxidase antibody immunoassay kit. Normal value is 35 IU/mL.

**RESULTS**

Thyroid profile was done in all patients. Mean age was 56.35.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>P value</th>
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<tbody>
<tr>
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<td></td>
<td></td>
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</tr>
<tr>
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<td>1.18760</td>
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<tr>
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<td></td>
<td></td>
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</tr>
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</tr>
<tr>
<td>TPO Antibody</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>37.773069</td>
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<tr>
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Table 1. Mean T3, T4, TSH and TPO Antibody Compared
DISCUSSION

It is revealed in the present study that when comparing mean T3 T4, TSH and TPO antibody with that of controls T3, T4 values were low in cases, even though values were in normal limits. Patients with GI malignancies had a low level of T3 and T4 when compared with normal people. Mean TSH were found to be high in cases compared to controls. Levels of TPO antibodies is high in cases compared to controls.

Similar results demonstrated in few studies. Syringos et al’ studied thyroid autoantibodies and thyroid function in patients with gastric cancer. Antithyroid antibodies were raised in patients with gastric cancer, of the 8 patients with positive antithyroid antibody, only 2 patients had hypothyroidism.

Mean TSH was found to be high in cases compared to controls, even though there is no overt hypothyroidism.

Fyssas et al found that out of 33 patients with pancreatic cancer, 8 patients has positive antithyroid antibody.

Low levels of thyroid hormones are found in earlier studies in colorectal cancer. Hypothyroid patients who have used levothyroxine for 5 years are found to have significantly decreased risk of colorectal cancer.

One finding seen in all for malignancies is the positive association with antithyroid antibody. This result has to be further investigated whether this raised TPO Ab levels is due to immune regulation caused by malignant cells or whether patients with thyroid autoimmunity is prone for developing GI malignancies. As there is many autoimmune factors in the aetiology of gastric cancers like atrophic body gastritis, this result has immense value for further researches.

CONCLUSION

From this study, we can’t say whether hypothyroidism is associated with GI malignancies, but definitely patients with GI malignancies had low thyroid hormone levels and raised antithyroid antibody. Thyroid function or dysfunction maybe associated with the susceptibility or immunity to cancer. So, it is important to build up a healthy thyroid tissue during development and during adult life.

REFERENCES


