Assessment the correlations of albumin creatinine ratio ACR and thyroid Hormones in patients with thyroid disorders and renal cell carcinoma

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Abstract
The incidence of thyroid disease has increased worldwide and the patients with thyroid disorders are also predisposed to other types of disorders including renal cell carcinoma. Human RCC is thought to arise from a variety of specialized cells located along the length of the nephron. We aimed to assess the correlations of albumin creatinine ratio ACR and thyroid hormones in patients with combined of hyper or hypothyroidism and renal cell carcinoma to the investigation of which study groups (hyper or hypo) have a risk to the incidence of RCC. This case-control study included four groups, the first group included 20 patients with hyperthyroidism, the second group of 20 patients with hypothyroidism, the third group were 20 patients with RCC, and 20 healthy subjects as a control group. We investigation of TSH, fT3, fT4, Albuminuria, Creatinine, ACR in all groups. We found that the serum level of TSH was significantly lower in patients with hypothyroidism (HPOTH) group (1.23 ± 0.43 μIU/ml) compared to hyperthyroidism (HPRTH) (13.32± 3.2 μIU/ml), RCC (10.12± 2.7 μIU/ml and control group (4.12 ± 1.3 μIU/ml), (p-value<0.05). The results of current study demonstrated that ACR (with albumin measured in milligrams and creatinine in grams) were significantly differs in HPRTH vs. HPOTH and control groups (330±16) vs. (220±11) (230±10), RCC vs. HPOTH and control groups (350±19) vs. (220±11) (230±10), this showing highly significant differences in RCC and HPRTH groups compare HPOTH and control groups (p-value<0.05). We concluded that the hyperthyroidism patients have more risk factor to the incidence of RCC rather than hypothyroidism patients according to ACR.

Keywords: Thyroid Disorders, Renal Cell Carcinoma, Thyroid Hormones

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Introduction
The incidence of thyroid disease has increased worldwide and patients with thyroid disorders are also predisposed to other types of cancer including renal cell carcinoma (1). Approximately 1 in 13 or 20 million people (7.35%) have thyroid disease in the United States and thyroid disorders are classified into hypothyroid, hyperthyroid, and subclinical cases and both hypothyroidism and hyperthyroidism account for a high level of morbidity in this region (2). The prevalence of hyperthyroidism in renal disease such as renal cell carcinoma (RCC) leads to increasing of renal blood flow, protein urea, and free radicals that acceleration in the incidence of RCC (3). Thyroid functional disorders are commonly observed in chronic kidney disease patients and various thyroid function test abnormalities are frequently seen in those patients,
resulting from alterations in thyroid hormone synthesis, metabolism, and regulation (4). Human RCC is thought to arise from a variety of specialized cells located along the length of the nephron. RCC is comprised of several histological cell types, both clear cell and papillary RCC are thought to arise from the epithelium of the proximal tubule (5). Dhote R et al (2000) were reported that cigarette smoking, obesity, hypertension and/or related medications have been implicated as risk factors although the increase in risk is relatively modest of RCC (6). The tumors of RCC arise from the cells of the proximal renal tubular epithelium. It is considered an adenocarcinoma and there are two subtypes: sporadic and hereditary. Both subtypes are associated with mutations in the short arm of chromosome 3, with the implicated genes being either tumor suppressor genes (VHL and TSC) or oncogenes (like c-Met) (7). RCC is one of the most vascularized strong malignant growths and angiogenesis assumes an urgent job in the development of renal tumors, due to the up-regulation of pro-angiogenic VEGF and platelet-determined development factor (PDGF). The up-regulation is brought about by transformation in the von Hippel-Lindau (VHL) quality, which actuates overexpression of hypoxia-inducible factor (HIF) (8). RCC is a tumor that is impervious to chemotherapy and radiotherapy. Cytokine treatment is valuable for just too few patients (without numerous troublesome prognostic factors) and is related to the event of extremely unfavorable impacts (9). The thyroid hormones (THs), thyroxine (T4) and its dynamic structure triiodothyronine (T3), are delivered by the thyroid organ. All together for the thyroid organ to create T3 and T4, iodine is required. The most widely recognized type of TH in the blood is T4 (with the proportion T4/T3 = 20/1); in any case, T4 is changed over to multiple times increasingly strong T3 by 5'-iodine inside the cell. Creation of T3 and T4 is managed by means of a shut circle criticism significant levels of T3 and T4 in blood plasma hinder the creation of thyroid-animating hormone in the pituitary organ. In spite of the way that T3 and T4 are lipophilic, they are not ready to diffuse inactively through the phospholipid layer of the cell. Rather, the T3 and T4 hormones are subject to membrane iodothyronine transporters (10). Thyroid dysfunction affects renal physiology and development, whereas kidney disease could result in thyroid dysfunction. Disorders of the thyroid and kidney may co-exist with common etiological factors (11). The aim of this study is to examine the association of hyper or hypothyroidism with increased risk of RCC by assessment of ACR and thyroid hormone levels.

Materials and methods
Study design: This case-control study included 40 patients with hypothyroidism and hypothyroidism disorders, 20 patients have RCC, and 20 subjects apparently healthy control group. Other unknown thyroid disorders and thyroid cancer were excluded from the present study, also hypertension, diabetes mellitus, renal, hepatic disorders, pregnancy, and patients receiving drugs that could interfere with thyroid function such as oral contraceptive pills were excluded.

Estimation of fT3, fT4, and TSH: This is done by ELISA kits supplied by the ElabscinceTM Company and the protocols were made by instructions provided by the manufacturer.

Estimation of Albuminuria, Creatinine, and ACR: This was performed using spectrophotometric kits provided by SpinreactTM Company.

Statistical analysis: Statistical analysis of data in this study was performed utilizing a student’s t-test and ANOVA. Comparisons between groups were made using P-values less than 0.05 significant for all data showed in the results.

Results
The serum level of TSH was significantly lower in patients with hypothyroidism (HPOTH) group (1.23 ± 0.43 μIU/ml) compared to hyperthyroidism (HPRTH) (13.32 ± 3.2 μIU/ml), RCC (10.12 ± 2.7 μIU/ml) and control group (4.12 ± 1.3 μIU/ml), (p-value<0.05), as shown in figure 1:

Figure (1): Serum levels of TSH (μIU/ml) in patients groups and control

Table 1, showing the serum TSH levels of study groups depending on age and BMI. Age and BMI were showing risk factors for RCC (p-value 0.012 and 0.01, respectively) and BMI only effects on HPOTH group:

<table>
<thead>
<tr>
<th>STUDY GROUPS</th>
<th>TSH (mean± SD) μIU/ml</th>
<th>TSH (mean± SD)μIU/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age</td>
<td>&lt; 40</td>
</tr>
<tr>
<td>HPRTH</td>
<td>12±2.7</td>
<td>13±2.9</td>
</tr>
<tr>
<td>HPOTH</td>
<td>4.11±1.3</td>
<td>4.13±1.2</td>
</tr>
<tr>
<td>RCC</td>
<td>10±2.0</td>
<td>11±2.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CONTROL</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Significant (p-value<0.05)

The results of current study demonstrated that ACR (with albumin measured in milligrams and creatinine in grams) were significantly differs in HPRTH vs. HPOTH and control groups (330±16) vs. (220±11) (230±10), RCC vs. HPOTH and control groups (350±19) vs. (220±11) (230±10), this showing highly significant differences in RCC and HPRTH groups compare HPOTH and control groups (p-value<0.05), as shown in figure 2:
The serum level of fT3 and fT4 were significantly lower in patients with hypothyroidism (HPOTH) group compared to hyperthyroidism (HPRTH), RCC and control group, (p-value<0.05), as shown in figure 2:

The results also showing a positive correlation between ACR and TSH levels in HPRTH and negative correlation between these markers in HPOTH group but we found no correlation between ACR and TSH levels in RCC group, as shown in figures 4 and 5, and 6:
Discussion
Thyroid hormones (TH) are known for their impact on metabolism, development, and normal growth mostly during fetal development. In adults, deregulation of thyroid hormone levels can cause hypo- and hyperthyroidism, which is connected with a vast number of clinical symptoms and tumor promotion or suppression (12). Hyperthyroidism results in protein breakdown and eventual renal atrophy. In addition, children with congenital hypothyroidism have a high incidence of congenital renal anomalies (13). Biochemical markers play an important role in accurate diagnosis and also for assessing risk and adopting therapy that improves clinical outcome (14, 21). The effects of hypothyroidism on the kidney are usually opposite to the effects of hyperthyroidism. The RBF is reduced in hypothyroidism by decreased cardiac output (negative chronotropic and inotropic effects) (15). Hyperthyroidism results in increased RBF and GFR (16). The effect of thyroid hormones on RBF and GFR occurs at multiple levels. Among the pre-renal factors, thyroid hormones increase the cardiac output by positive chronotropic and inotropic effects, as well as, a reduction in systemic vascular resistance (17). The GFR is reversibly reduced (by about 40%) in more than 55% of adults with hypothyroidism due to several reasons. There is decreased sensitivity to β-adrenergic stimulus and decreased renin release (18). TSH levels change and its height might be transient. Therefore, the thyroid capacity test (TFT) ought to be rehashed before diagnosing SCH, with the exception of pregnant patients. Furthermore, it is fundamental to reject different reasons for raised TSH, including the nighttime estimation of TFT, recuperation period of nonthyroidal sickness, hypothyroid period of thyroiditis, test inconstancy or on the other hand obstruction, untreated hypocortisolism (19). Meier et al (2001) were demonstrated improvement in mood, cognition and hypothyroid indications just when TSH
levels exceeded 10 mIU/L. The prevalence of hyperthyroidism in RCC patients is the same as it is with the general population; thus RCC is directly associated with hyperthyroidism. However, it is important to understand that aspects of hyperthyroidism can indeed accelerate RCC. In conclusion, Hyperthyroidism patients have more risk factors for the incidence of RCC rather than hypothyroidism patients according to ACR.

Acknowledgment

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References


