Clinical and Pathological Evaluation of Patients with Nodular Goiter

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Abstract
The aim of this study is clinical and pathological evaluation of nodular thyroid Goiter Patients.

Methods :- The Present prospective study pts of nodule thyroid goiter who were treated surgically was performed over a period from February 2004 – January 2007. clinical symptoms and signs, thyroid function test and Formalin fixed, Paraffin embedded blocks from 127 patients with thyroidctomy were included in this study.

Results :- A total of 127 cases were included there is female predominance (77%), (73.1 %) cases were euthyriod, (24.2 %) cases hyperthyriedism and (3.1 %) hypothyriedism. the histopathological results of thyroid Nodules were (69.3 %) colloid nodular Goiter, (15.7%) toxic Nodules, 11.8 % thyroid tumors only (3.2 %) was hashiomito’s thyrioditis. The Papillary carcinoma is the most common malignant tumor (3 cases) followed by follicular carcinoma (2 cases).

Conclusion :- Based upon the findings of this study. It can be concluded that Most of thyroid nodules are benign, Euthyriod and more common in female. Most cases of hypothyroidism associated with hashiomates thyrioditis. Papillary carcinoma is Most common Malignant thyroid Nodule tumor. benign thyroid tumor is more common than Malignant thyroid tumor. Incidental finding of thyroid tumor was in majority of cases of thyroid Nodule while the Minority of cases were clinically suspicious

Introduction
Thyroid nodules are very common about 4% of women and 2% of men have palpable thyroid nodule.[1] A nodule is a swelling or lump which can be solid or liquid filled cyst or mass. Most of them are benign (95%) but small percentage (5%) can be cancerous.[2]
Patients should be questioned about local symptoms [pain, dysphagia, pressure or a change in voice], about duration of the nodule, and about systemic symptoms (from hyperthyroidism, hypothyroidism or other illness).[1-3]

Nodule that are truly solitary, feel firm or hard on examination, are growing rapidly or are nonfunctional on scans are likely to be malignant.[3]

The types of thyroid nodule disorder including one of two categories: [3,4]
Hypothyroidism, which involves an under active thyroid gland. Or hyperthyroidism, which involves an overactive thyroid gland symptoms of hypothyroidism includes :-[4,5]
• An enlarged thyroid (Goiter), which may appear as a swelling at the base of the neck, fatigue, weight gain, decrease appetite, depression, hoarse voice, dry, coarse skin and hair, puffiness around the eyes, felling cold increased cholesterol and slower digestion and constipation.
• Symptoms of hyperthyroidism include :- [5]
Weight loss, hair loss, nervousness and irritability, arrhythmia, feeling hot, weakness in muscles, tremors and an enlarged thyroid (Goiter)

1- Hashimoto's thyroiditis :

The most common form of hypothyroidism is a condition known as Hashimoto's thyroiditis.

Hashimoto's thyroiditis is a type of autoimmune thyroid disease in which the immune system attacks and destroys the thyroid gland.

Person with Hashimoto's thyroiditis may experience a goiter, a feeling of fullness or tightness in the throat, a person with hashimoto's thyroiditis can also exhibit no symptoms.[6]

A thyroid nodule is any abnormal growth of thyroid cells forming a lump within the thyroid gland. Although most thyroid nodules do not cause any symptoms, occasionally a nodule will cause pain, difficulty in swallowing or breathing hoarseness or hyperthyroidism. [7]

Thyroid nodules are common because of the risk of malignancy and hyper function.[8]
Evaluation of patient with nodular goiter are usually found by the patient or a family member, or during a general physical examination history and physical examination are rarely helpful in differentiating benign and malignant nodule.[9]

The biochemical assessment including the Measurement of T. S. H. level is helpful, as suppression suggests that a nodule is hyper functioning.[10]

Occasionally nodules will produce thyroid hormone, and cause hyperthyroidism, thyroid nodule can also develop in patients who have coexisting thyroid condition, this frequency occur with people who have Hasiomatos thyroiditis.

A rare form of thyroid cancer is medullary carcinoma. Which can be detected by a blood test to measure calcitonin.[11]

Common types of the benign thyroid nodules are adenomas, thyroid cysts, and hashimoto's thyroiditis uncommon types of benign thyroid nodules are due to subacute thryoiditis or Riedel's tuma.

The following features in favor a benign thyroid nodule:-[12]

Family history of hashimoto's thyroiditis, family history of benign thyroid nodule or goiter. Symptoms of hyperthyroidism or hypothyroidism, Pain or tenderness associated with nodule and a soft smooth, Mobile nodule.

Well-differentiated thyroid cancers arise from follicular cells and encompass both papillary and follicular carcinomas.
• papillary carcinoma are the most common thyroid cancer (75-85%) they are non capsulated, often multicentric and bilateral in a thyroid of cases the most common sites of metastasis are
regional lymph nodes and less commonly the lungs.[13]

- well–differentiated thyroid carcinoma has an excellent prognosis despite the presence of L.N. Metastasis in 5%-20% of patients and distant metastases in 10%-15%. 10 years survival is 80% - 95%.[12,13]

- Follicular carcinoma :- represent 5% - 10% of thyroid cancer they are encapsulated, more common in females, and the features of malignancy is invasion of the capsule, Blood vessels. Microscopically is extremely variable, ranging from well-formed follicles they almost always solitary and metastases are usually blood – borne.[14]

The prognosis of the follicular carcinoma is directly related to the degree of encapsulation.[15]

The following features increase the suspicious of a malignant nodule:- [16] age less than 20 years and more than 70 years, male gender, recent of swallowing difficulties, recent of hoarseness, History of external neck irradiation during childhood, Firm, irregular and fixed nodule, Presence of cervical lymphadenopathy and Nodule that is cold on scan.

- Anaplastic thyroid carcinoma

About 5% of thyroid cancers are anaplastic in contrast to other forms of thyroid cancer Ana plastic thyroid carcinoma is one of the most aggressive tumors in human and death occurs at a mean of 6 month after diagnosis.[18]

Symptoms of a nodule are varied some people are presented with hyperthyroidism, others have difficulty in swallowing, a felling of fullness, pain or pressure in the neck and finally, many people have nodule with no obvious symptoms related to thyroid dysfunction at all.[17]

Thyroid imaging is not a routine but used to answer a specific clinical question.[19]

The finding of hyper functioning or hot nodule excludes the malignancy in almost all patient.

- a non function or cold Nodule was thought to indicate increased risk of malignancy.[19]

Is commonly performed, but routine ultra sonographic studies rarely aid clinical decision making .[20]

Despite early suggestions that nodule in multinoduler goiter are less likely to be malignant, more recent studies show that the risk of malignancy in a dominant nodule in this condition is similar that in a solitary nodule [23]

**Patients and Methods**

This is a prospective study of 127 cases with nodular goiter who were treated by surgery in Al-hilla teaching hospital and private clinic during a period between of August 2004 and February 2007 inclusive. The patients age range was 20 – 70 years.

The clinical history includes (age and sex) and clinical signs were taken, blood samples for all patients were collected for thyroid function test by ELISA method. The specimens were obtained after subtotal thyroidectomy under general anesthesia was formalin fixed and paraffin embedded block section and followed routine ( haematoxylin and eosin ) stain was done followed by histopathological study for all cases.

**Results**

One hundred twenty seven cases in the present study, there is female predominance (77 % ) with female to male ratio 3:1 (Table 1). The age and sex distribution of patients is illustrated in table (3), the age range was (20 - 50 ) year with peaks in the third decade:The biochemical analysis of thyroid function test are recorded in table (2); which shows that euthyroid 93 (73.2 % ) is the most common biochemical result of patient with thyroid nodule followed by
hyperthyroidism 30(24.4%) and by hypothyroidism 4 (3.1%).
The histopathological result of thyroid nodule study is illustrated in table (4).
Most of cases are multi nodular goiter 77 cases (60.3%) followed by toxic nodule 31 cases (24.4%), while thyroid tumor 15 cases (11.8%), and hashiomato's thyrioditis 4 cases. 4 (3.2%)
The histopathological type of thyroid tumor shown in table (5)
The benign thyroid tumor (follicular adenoma) represent the most common tumor 8 cases (53%), while the papillary carcinoma is the most common malignant thyroid tumor 3 cases (3%) followed by follicular carcinoma 2 cases (2%), while Hurthle cell adenoma regarded as a variant of follicular adenoma but the follicular cells shows eosinophilic cytoplasm due to increase in mitochandrial number. we have 2 cases (13%) of Hurthle cell adenoma.
In this study we have one case the patient was thyrotoxic but histopathological diagnosis. Was papillary carcinoma.
- In our study, there is one case of papillary carcinoma in one lobe coexist with hurthle cell adenoma in other lobe.
- In the present study most of patients who presented clinically as hypothyroidism (4 cases) in pathological studies present as hashiomato's thyrioditis, only one cases of hypothyroidism present as follicular adenoma.

Table 1: Male \ Female Ratio

<table>
<thead>
<tr>
<th>Sex</th>
<th>Number</th>
<th>Percent</th>
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</thead>
<tbody>
<tr>
<td>F</td>
<td>98</td>
<td>77.2%</td>
</tr>
<tr>
<td>M</td>
<td>29</td>
<td>22.8%</td>
</tr>
<tr>
<td>Total</td>
<td>127</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 2 Biochemical analysis

<table>
<thead>
<tr>
<th>Type</th>
<th>Number</th>
<th>Percent</th>
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</thead>
<tbody>
<tr>
<td>Euthyrid</td>
<td>93</td>
<td>73.2%</td>
</tr>
<tr>
<td>hyperthyroidism</td>
<td>30</td>
<td>24.4%</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>4</td>
<td>3.4%</td>
</tr>
<tr>
<td>Total</td>
<td>127</td>
<td>100%</td>
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</tbody>
</table>

Table 3 Sex and age distribution of patients

<table>
<thead>
<tr>
<th>Sex / Age</th>
<th>&lt; 20</th>
<th>20 – 50</th>
<th>&gt; 50</th>
</tr>
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<tbody>
<tr>
<td>Female No. and percent</td>
<td>12</td>
<td>88</td>
<td>9</td>
</tr>
<tr>
<td>Male No. and percent</td>
<td>4</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>97</td>
<td>14</td>
</tr>
</tbody>
</table>
Table 4  Histopathological types of thyroid Nodules

<table>
<thead>
<tr>
<th>Histopathological types</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>colloid Goiter</td>
<td>77</td>
<td>60.6%</td>
</tr>
<tr>
<td>Toxic Nodule</td>
<td>31</td>
<td>24.4%</td>
</tr>
<tr>
<td>Hashiometes thyrioditis</td>
<td>4</td>
<td>3.2%</td>
</tr>
<tr>
<td>Thyriod Tumor</td>
<td>15</td>
<td>11.8%</td>
</tr>
<tr>
<td>Total</td>
<td>127</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 5 Types of thyroid tumor

<table>
<thead>
<tr>
<th>Types of thyroid tumor</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicular adenoma</td>
<td>8</td>
<td>53 %</td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>3</td>
<td>21 %</td>
</tr>
<tr>
<td>Hurthle cell adenoma</td>
<td>2</td>
<td>13 %</td>
</tr>
<tr>
<td>Follicular carcinoma</td>
<td>2</td>
<td>13 %</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>100%</td>
</tr>
</tbody>
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Discussion
In the present study, (88.2%) cases are benign and (11.8%) are malignant and this is differ from Khalil et al; [21] (37.9%) were cases are benign and (62.1%) cases are malignant , but this result agreed with Cifter C et al; 22 where (13.7%) case are malignant.
In this study there are 4(3.2%) cases of Hashiometes thyrioditis and this finding agreed with Khalil et al;[21] and Tadesse B et al;[24] 2 (2.9%) and 4 (1.9%) cases was Hasiomatos thyrioditis.
We determined (77.2%) female and (22.8%) male in different age groups between 20-70 years and this similar with Aslaner A et al;[23] and Cifter C et al;[22] was (73%) female , (27%) male and (80.8%) female, (19.2%) male.

In our study follicular adenoma 8 cases more than malignant thyroid tumor 5 cases while in Khalil et al [21] the follicular carcinoma 10 cases more than follicular adenoma 7 cases.
The medullary and anaplastic carcinomas can be recognized in asnlar et al[23] and De antoni E [25], in our study of 127 cases there is no any case of medullary and anaplastic carcinomas . 4 cases of clinicall and hormonal assay present as hypothyroidism the histopathological results
Refer to Hasiomatos thyroiditis and one case as thyroid tumor. This is agree with Tadesse et al [24] and Govt et al [26] the most important challenge for surgeon and pathologist is the diagnosis of malignancy in MNG (multinodular goiter) to prepare patient for surgery,
According to our study we suspected thyroid malignancy when there is
1- The patient with low thyroid function test, because in our study one of four cases present as hypothyroidism have thyroid tumor and this agree with tadesess et al [24] and Govt et al [26], but also the thyrotoxicosis does not exclude the possibility of malignancy, because one patient present with thyrotoxicosis features, increase in T4and T3, decrease TSH but histopathological result showing papillary carcinoma and this is differ from kaiel and ciftreic C et al . [22]
2- Age : In the reference literatures the malignancy suspected if the patient less than 20 years or more than 70 years, Kaplan BJ et al [8] and Hoang C et al [9] while in our study we found 3 cases of thyroid malignant tumor even in the third and fourth decade.

3- Rapidly increase in size during short period, 5 cases presented with rapidly increasing in size through few months and lobectomy was done for them. The histopathology reveal that only three cases have malignant thyroid tumor, other two cases are benign thyroid nodule but there are hemorrhagic changes and cystic changes, this result similar to Adelsuasoak et al [11] and cefiter C et al. [23]

4- The present of cervical lymphadenopathy in addition to thyroid nodule, was found one case only among patients with papillary carcinoma, while other case, also present with cervical lymphadenopathy but the histopathology shows only nodular goiter and this is agree with cifter C et al [23] and Govet et al [26].

**Biochemical assessment**:-
Measurement of thyroid-stimulating hormone (TSH) level is helpful, as suppression suggests that a nodule is hyper functioning, hyper functioning solitary nodules carry a low risk of malignancy,[17,18] but this is not exclude the malignancy, in this study there is one case presented as hyperthyroidism and papillary carcinoma.

**In the thyroid function test assessment the following point should be considered**
1-TSH thyroid stimulating hormone measurement is the first step in the evaluation of thyroid nodule, because is helpful, if the TSH level low, the T4 and T3 assessment indicated to confirm the diagnosis, of hyper functioning thyroid nodule in association with clinical features, hyperfunctioning thyroid nodule has low risk of malignancy, in this study only one case of papillary carcinoma associated with thyrotoxicosis, follow up after medical therapy by TSH, and the surgery indicated in recurrence thyrotoxicosis after long period in our study we did T3, T4 and TSH at same time.

**Fine – needle aspiration cytology:**
Fine needle aspiration should be the first line investigation for solitary nodule or dominant nodule in a multinodular goiter.[21, 23]. we did not use FNA as a routine investigation.

**Routine ultra sonography** (studies rarely clinical decision making ) [19]

**Conclusions and Recommendations**
Most of nodular thyroid goiters are euthyroid and benign. The thyroid nodule is more common in female than male; the toxic goiter has low risk of malignancy, most of clinically and biochemically hypothyroid nodules are found to be histopathologically was hashiomatos thyroiditis, malignancy occur in different age group, papillary carcinoma is the most common malignant tumor, Coexist thyroid tumor had been recognized in our study, Thyroid FNA cytology is indicated in all condition, thyroid function test is indicated in all nodular goiter.

**References**
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