A Clinico Pathological Study of Solitary Thyroid Nodule
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Abstract

Introduction: The thyroid disorder is the most common endocrine disorder seen in clinical practice. Lesions of thyroid are predominantly confined to females in the ratio of 5:1, and this has been attributed to variations of thyroid hormone demand during female reproductive function and physiological events such as puberty, pregnancy and lactation.

Materials and Methods: The present study of has been conducted by utilizing the cases diagnosed clinically as solitary nodule of thyroid and treated on inpatient basis in the Department of General Surgery at Bowring and Lady Curzon Hospital & Victoria Hospital, Bangalore. All patients who were clinically diagnosed to have solitary thyroid nodules from November 2012 to October 2014 were included in the study.

Results: The age of the patients with solitary nodule in the present study varied from 20 years being the youngest to 57 years being the oldest. The peak age incidence was found in 3rd and 4th decades of life. The mean age of all patients was 36.4 years. The mean age for females was 37.11 years and that for males was 31.75 years.

Conclusion: Solitary nodule of thyroid gland is a common clinical entity, more common in females than in males.

Multi-nodular goitre is the most common etiological cause for a solitary nodule of thyroid, its incidence being 57% of all solitary thyroid nodules, followed by follicular adenoma, accounting for 27% of all solitary thyroid nodules.

Keywords: Thyroid Gland, Nodule, Pathology

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Introduction

The thyroid disorder is the most common endocrine disorder seen in clinical practice. Lesions of thyroid are predominantly confined to females in the ratio of 5:1, and this has been attributed to variations of thyroid hormone demand during female reproductive function and physiological events such as puberty, pregnancy and lactation. Solitary nodule of thyroid is a common clinical entity though varying in incidence in different geographical region. It has aroused interest because of its potential to become malignant and also possibility of toxicity and complications like hemorrhage, and pressure effects etc. The solitary nodule of thyroid has been subject of controversy. The basis for this conflict stems from the fact that the thyroid nodule has different connotations when considered by thyroid clinician. The optimal management of thyroid nodule continues to be source of
controversy, and operative intervention recommended by most surgeons is not always considered divine by physicians who advocate observation or thyroid suppression. Attempts to devise a standard surgical approach for managing solitary thyroid nodule have not been successful chiefly because of marked difference in biological behavior. Historical references to what we now know as the thyroid gland arise early in medical history. In ayurvedic system of medicine, the book Sushruta Samhita written about 1500 BC, mentions the disease goitre as 'Glaganda' along with its treatment. In 1600, BC the Chinese were using burnt sponge and seaweed for the treatment of goiters. Celsus first described a bronchoceole (a tumour of the neck) in 15 AD. In 1656 Thomas Wharton named the gland the thyroid, meaning shield, as its shape resembled the shields commonly used in Ancient Greece. The credit of recognizing the significance of solitary thyroid nodule as a separate entity (because of its malignant potential, for the first time) should probably go to Warren H. Colles, who in 1949 reported results of a study of 285 cases of non-toxic nodular goitre during 1936-1948. He observed that incidence of malignancy was significantly higher i.e. 24.6% in solitary nodules than in multi-nodular goitre which is 9.8%. Ehrhardt in 1902 reported 200 cases of carcinoma thyroid. He stated that in nearly half of the cases a preexisting adenoma was present. A goitre has been recognized as a disease since earliest recorded history, consistent method of surgery of thyroid gland dates back only 100 years. Before that time, only few attempted removal of goitre for the relief of dysphagia and dyspnoea. Halsted stated that the first well documented operation was performed in 1595. But apparently successful excision was carried out in 1000AD by Albucusis and several reports sighted that, operations for the thyroid disease were performed throughout 16th century. Kocher performed the first thyroidectomy in 1872 at Bern, Switzerland. Billroth at this time had abandoned these operations because of the high mortality form sepsis and hemorrhage. Kocher through his safe and meticulous surgery served as a model for Halsted who was then studying in Europe. In 1883, Kocher reported his first 100 cases of thyroid surgery of which 30 were total thyroidectomy, in all the patients who underwent total thyroidectomy developed CACHEXIA STRUMA PRIVI which was later recognized as surgical counterpart of "MYXEDEMA". Thereafter, Kocher avoided total excision. By 1901, Kocher had performed 2000 operations including those for hyperthyroidism and carcinoma with overall mortality rate of 4.5%. In 1884, Schiff reported deaths in 60 dogs following total thyroidectomy unless animal had been provided with previous graft of thyroid tissue. Murray in 1891 and Horowitz in 1892 began clinical use of thyroid extract for the treatment of myxedema. Voneiselberg in 1830 had noted tetany in humans after operations for goitre and distinguished it from cachexia struma privi. Bley in 1891 and Voneiselberg in 1892 produced tetany in animal by excision by parathyroid glands alone. Halsted in 1906 relieved clinical tetany after thyroid operation with dietary supplements of parathyroid gland from cattle. Nobel Prize in medicine was awarded to Theodor Kocher in 1909 for his outstanding contribution to thyroid diseases and he was regarded as "Father of Thyroid Surgery". American surgeons contributed a lot in 1900's. Notable was Charles Mayo (1865-1939) of Rochester who was regarded as "Father of American Thyroid Surgery". In 1912, Mayo operated on 278 patients with exophthalmic goitre without death. Safe surgeries were performed by utilizing iodine solutions to relieve hyperthyroidism temporarily before operation, which was first reported by Plummer in 1923. The chemical description of thyroxine was isolated by Kendal in 1904 and was reported by Harrington and Berger in 1927. The
treatment of hyperthyroidism with propylthiouracil was described by Astwood and Mackenzie in 1943. Chapman in 1946 introduced radio iodine for diagnostic and therapeutic use. Thyroid carcinoma was known in 18th century and one variety was then named as MEDULLARY CARCINOMA and it was described by John Abernethy (1764-1831) of London. Butlin's review in 1887 included 50 patients, 60% of patients died soon after surgery only one survived for 4 years and none was cured. By 1901, the mortality increased to 34%, because preoperative diagnosis was rarely made and therefore advanced disease was seldom amenable to surgery. The type of lesion with better prognosis was recognized as papillary and encapsulated. In 1982, Mayo clinic published a large series, one third of whom survived between 3 and 18 years. By 1950, papillary growth was removed by total lobectomy with excision of lymph nodes or block dissection. Adenocarcinoma was treated by extended thyroidectomy with block dissection. Radio iodine therapy gave symptomatic relief with no cure. Duffy in 1950 reported the link between the childhood radiation and thyroid carcinoma and it had been instrumental in addressing the cause of thyroid carcinoma. Since 1970, FNAC as promoted by Perola Granger of Stockholm has contributed greatly in early diagnosis of carcinoma. In thyroid disease, the greatest challenge in future is to comprehend a clear appreciation of biology of disease without which logical surgical therapy cannot be designed. This fact can be appreciated in the conflict regarding extent of thyroid surgery between conservative removal of gland to total thyroidecmy in carcinoma. The thyroid FNAC has greatly altered the diagnostic and therapeutic approach to solitary thyroid nodule. With the development of techniques such as FNAC and ultrasound, the performance of thyroidecmy has become selective. 50% of the population will have one or more thyroid nodules seen on Ultrasonography. [1,2,3,4,5,6]

**Materials and Methods**

The present study of has been conducted by utilizing the cases diagnosed clinically as solitary nodule of thyroid and treated on inpatient basis in the Department of General Surgery at Bowring and Lady Curzon Hospital & Victoria Hospital, Bangalore. All patients who were clinically diagnosed to have solitary thyroid nodules from November 2012 to October 2014 were included in the study.

**Inclusion Criteria:**

All patients attending Surgical OPD with the complaints of neck swelling were screened for thyroid swelling.

1. Patients found to have solitary thyroid nodule on clinical examination including autonomous toxic nodules.
2. Age group 18 – 70 years.

**Exclusion Criteria:**

1. Patients with previous thyroid surgery.
2. Patient’s with thyroid swellings other than solitary nodule of thyroid.

**Results**

**Age Incidence:**

The age of the patients with solitary nodule in the present study varied from 20 years being the youngest to 57 years being the oldest. The peak age incidence was found in 3rd and 4th decades of life. The mean age of all patients was 36.4 years. The mean age for females was 37.11 years and that for males was 31.75 years.

| Age in Years | Females | Males | Total | Percentage |
|-------------|---------|-------|-------|------------|
| 0-9         | 0       | 0     | 0     | 0          |
| 10-19       | 0       | 0     | 0     | 0          |

**Table 1: Age Distribution in Present Study**

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The peak incidence was seen in 4th decade of life with 50% of patients. Patients in 3rd and 4th decade of life constituted 67% of total patients.

| Age Group | Number of Patients |
|-----------|--------------------|
| 20-29     | 5                  |
| 30-39     | 12                 |
| 40-49     | 7                  |
| 50-59     | 3                  |
| 60-69     | 0                  |
| Total     | 27                 |

**Chart 1: Age Distribution of Solitary Nodule of Thyroid**

Sex Incidence:
Solitary nodule of thyroid was found to be more common in females than in males. Out of 30 cases 26 were females and 4 were males. Male to female ratio was 1:6.5.

**Chart 2: Sex Incidence of Solitary Nodule of Thyroid**

Clinical Features:
Swelling in the thyroid region was the commonest complaint in all the patients. Duration of the swelling varied from 1 month to 7 years. Duration of swelling in malignancy in this study varied from 6 months to 2 years.
Table 2: Duration of Swelling in Present series

| Duration of Swelling | Number of Patients | Percentage |
|----------------------|--------------------|------------|
| 1 month              | 1                  | 3          |
| 1-3 months           | 2                  | 7          |
| 4-6 months           | 7                  | 24         |
| 7-11 months          | 6                  | 20         |
| 1-2 years            | 10                 | 33         |
| 3-5 years            | 3                  | 10         |
| More than 5 years    | 1                  | 3          |
| Total                | 30                 | 100        |

Apart from swelling, other clinical features were present as follows:

Table 3: Clinical Features in Patients with Solitary Nodule of Thyroid

| Clinical Features                      | Number of Patients | Percentage |
|----------------------------------------|--------------------|------------|
| Swelling                               | 30                 | 100        |
| Pain                                   | 0                  | 0          |
| Change in voice/Hoarseness             | 0                  | 0          |
| Pressure symptoms                      | 0                  | 0          |
| Rapid increase in size                 | 0                  | 0          |
| Tracheal deviation                     | 1                  | 3          |
| Euthyroid                              | 29                 | 97         |
| Hyperthyroid                           | 0                  | 0          |
| Hypothyroid                            | 1                  | 3          |
| Cervical lymphadenopathy               | 0                  | 0          |

Pain, change in voice/hoarseness, pressure symptoms and rapid increase in size and cervical lymphadenopathy were not present in any of the 30 cases. Tracheal deviation was found in one case but had no significant compromise of airway. One patient was hypothyroid, which was corrected with levo-thyroxine supplementation and later taken up for surgery.

Size and Site of the Nodule:
Out of 30 cases studied, in 21 cases nodule was found to be in the right lobe, in 9 cases it was found to be in the left lobe. In none of the cases the nodule was found in the isthmus.

Table 4: Distribution of Solitary Thyroid Nodule in Present Study

| Site       | Number | Percentage |
|------------|--------|------------|
| Right Lobe | 21     | 70         |
| Left Lobe  | 9      | 30         |
| Isthmus    | 0      | 0          |
| Total      | 30     | 100        |

The size of the nodules varied from 2x2 cm to a maximum of 7x4 cm. The majority of the nodules were in 3-6 cm range.
Table 5: Size of Nodules in Present Study

| Size of nodule in cm | Number of cases | Percentage |
|---------------------|----------------|------------|
| <3                  | 5              | 17         |
| 3-6                 | 22             | 73         |
| 7-10                | 3              | 10         |
| >10                 | 0              | 0          |
| Total               | 30             | 100        |

Discussion

Age Incidence:

The peak incidence in the present series was seen in 4th decade of life with 50% of patients. Patients in 3rd and 4th decade of life constituted 67% of total patients. The results in the present studies were comparable to that of other reported studies. N. R. Ananthkrishnan (1993) had reported a mean age of 37.5 years for males and 35 years for females. Most series report a peek age incidence in 3rd and 4th decades of life.

Table 6: Peek Age of Incidence of Solitary Nodule of Thyroid in different series

| SL.NO | NAME OF AUTHOR                        | YEAR | PEEK AGE OF INCIDENCE   |
|-------|---------------------------------------|------|-------------------------|
| 1     | Rojeski MT. et. Al[8]                 | 1985 | 2nd and 3rd decade      |
| 2     | N.R.Ananthkrishnan[10]                | 1993 | 3rd and 4th decades     |
| 3     | Bennedback F N[7]                     | 2000 | 4th and 5th decades     |
| 4     | Castro MR, et. Al [9]                 | 2003 | 3rd and 4th decades     |
| 5     | Present series                        | 2014 | 3rd and 4th decades     |

Females are more active reproductively in their 3rd and 4th decades of their lives. Puberty, pregnancy, abortions, child birth, lactation all increase the demand for thyroid hormones and hence affects the thyroid physiology maximally during this phase of life. This is the reason for the occurrence of thyroid diseases maximally in the 3rd and 4th decades of life.

Sex Incidence:

Out of 30 cases 26 were females and 4 were males in the present study. Male to female ratio was 1:6.5. Male to ratio quoted in various series varies but all show female preponderance.

Table 7: Male to Female Ratio in Various Series

| Sl. No | Name of Author                        | Year | M:F Ratio |
|--------|---------------------------------------|------|-----------|
| 1      | Rojeski MT. et al [8]                 | 1985 | 1: 3.5    |
| 2      | N.R.Ananthkrishnan [10]               | 1993 | 1: 3      |
| 3      | Bennedback F N [7]                    | 2000 | 1: 2      |
| 4      | Castro MR, et al [9]                  | 2003 | 1: 4.9    |
| 5      | Present series                        | 2014 | 1: 6.5    |

During and after puberty, the size of thyroid gland in females tend to vary a little during each menstrual cycles and during the pregnancy the gland enlarges throughout the period of pregnancy in view of increased demands. In males, the thyroid gland shows a tendency to regress in size after puberty and this reflects as the difference in the incidences of thyroid diseases in males and females.

Clinical Features:

Swelling in the thyroid region was the commonest complaint in all the patients.
Duration of the swelling varied from 1 month to 7 years. Duration of swelling in malignancy in this study varied from 6 months to 2 years. Pain, change in voice/hoarseness, pressure symptoms and rapid increase in size and cervical lymphadenopathy were not present in any of the 30 cases. Tracheal deviation was found in one case but had no significant compromise of airway. Pain can occur in a thyroid nodule due to hemorrhage into the nodule, infection or inflammatory conditions of thyroid and tumor infiltration into the nerves. Change in voice or hoarseness of voice occurs due to infiltration of recurrent laryngeal nerve by a malignant thyroid tumor. It can also occur as a part of myxedema due to hypothyroidism. Rapid increase in size of a thyroid nodule can occur due to hemorrhage into the nodule, rapidly growing malignant tumor (anaplastic carcinoma) or due to inflammatory thyroiditis. [3]

**Size and Site of the Nodule:**

Out of 30 cases studied, in 21 cases nodule was found to be in the right lobe, in 9 cases it was found to be in the left lobe. In none of the cases the nodule was found in the isthmus. In the series studied by N. R. Ananthkrishnan, nodule was found in the right lobe in 51% cases, in the left lobe in 34% cases and in the isthmus in 15% cases. Most of the solitary nodules occur at the junction of the isthmus and the lateral lobes. The reason for such an occurrence is not known. In the present study, the size of the nodules varied from 2x2 cm to a maximum of 7x4 cm. The majority of the nodules were in 3-6 cm range. The series studied by N. R. Ananthkrishnan showed the size distribution of the nodules as follows:

| Size in cm | N.R. Ananthkrishnan [10] series | Present Study (n=) |
|------------|---------------------------------|--------------------|
| <3         | 15.8%                           | 17% (5)            |
| 3-6        | 46.7%                           | 73% (22)           |
| 7-10       | 26.1%                           | 10% (3)            |
| >10        | 11.4%                           | 0% (0)             |

Thyroid nodules are clinically palpable only when they are >1 cm in size. Nodules lesser to 1 cm are not palpable clinically and most often detected incidentally by neck ultrasonography. Nodules of size >4 cm have a higher risk of harbouring malignancy. In cases of thyroid cancers, nodules of size >4 cm indicate poorer prognosis due to increased chances of nodal or distant metastasis [3]. Since most of the thyroid nodules that present clinically are of the size ranging from 3-6 cm, proper evaluation of the nodule has to be done to rule out malignancy. Microcarcinomas however, can occur in nodules less than 1 cm size also. [7-11]

**Conclusion**

Solitary nodule of thyroid gland is a common clinical entity, more common in females than in males. Multi-nodular goitre is the most common etiological cause for a solitary nodule of thyroid, its incidence being 57% of all solitary thyroid nodules, followed by follicular adenoma, accounting for 27% of all solitary thyroid nodules. There is a definite risk of solitary thyroid nodule of being malignant. This study shows an incidence rate of 13% of malignancy in solitary thyroid nodules, indicating that all cases of solitary thyroid nodules should be considered as important clinical entity and should be evaluated properly in order to rule out malignancy.

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