Study of histopathological patterns of thyroid lesions in rural medical college

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Abstract
Aim and objectives: To study histopathological features of thyroid lesions, their age and sexwise distribution and frequency of thyroid lesions in thyroidectomy specimens in rural population along with their benign and malignant behaviour.

Materials and Methods: Present study is cross-sectional retrospective study conducted between January 2014 to December 2018 for period of five years, at the department of Pathology JIU’S IIMSR WARUDI, Rural Medical College Badnapur, Jalna in Maharashtra. All the thyroidectomy specimens received for histopathological examination during year 2014 to 2018 in Department of Pathology, were included in present study

Result: Out of 233 cases studied, 204 were females [87.55%] and 29 were males [12.45%]. Mean age of presentation was 34.68 yrs. Range of the age of presentation was 2yr-70 yr. with maximum patients [60.52%] between 21-40 yrs. There were 191 non-neoplastic lesions [81.97] and 42 were neoplastic [18.03]. Most common non-neoplastic lesions were hyperplastic lesions 149 cases [63.95%]. Multinodular goitre was most common hyperplastic lesion. [47.21%]. Second most common non-neoplastic lesions were congenital lesions 18 cases [7.72%] with most common congenital lesion being Thyroglossal cyst [6.44%]. Inflammatory lesions were found to be [6.44%], all were Hashimoto thyroiditis. Out of 42 neoplastic cases, 29 were benign [12.45%] and 13 were malignant [5.58%]. Follicular adenoma was found to be most common benign neoplastic lesion [10.73%]. Papillary carcinoma was found to be most common malignant neoplastic lesion [3%].

Conclusion: Study shows that thyroid gland lesions were common amongst rural population in Jalna district with females outnumbering males. Non-neoplastic lesions were more common than neoplastic lesions. Benign lesions out-numbered malignant lesions. Multinodular goitre was found to be commonest non-neoplastic lesion. Follicular adenoma was found to be most common benign neoplasm, while papillary thyroid carcinoma was found to be commonest malignant neoplasm. Though other modalities like, FNAC and Sonography were useful in diagnosis of most of the cases, Histopathological examination was found to be mainstay for final diagnosis.

Keywords: Rural, Thyroid lesions, Histopathology, Goitre, Adenoma, Carcinoma.

Introduction
The normal adult thyroid gland composed of two symmetrical lobes joined by “H” shaped isthmus which lies against second, third, fourth tracheal rings, situated in lower part of neck extending from the level of fifth cervical to first thoracic vertebrae.1 Histologically thyroid gland is covered by fibrous capsule underneath show thyroid follicles containing colloid lined by follicular cells that rests on basement membrane. Thyroid gland also contains C-cells [parafollicular cells] which intervene between follicular cells and basement membrane or lie in intervals between follicles. Spaces in between follicles contain stroma containing numerous capillaries and lymphatics.2

The primary hormone secreted by thyroid is Thyroxine (T4), much lesser amounts of Triiodothyronine (T3) and calcitonin [by parafollicular cells]. The primary function of the thyroid gland is to maintain the level of metabolism in the tissue that is optimal for their normal function. Thyroid hormones stimulate O2 consumption by most of the cells in body, help to regulate lipid, carbohydrate metabolism, therefore necessary for normal growth and maturation as well as proper development of the central and peripheral nervous system. Thyroid gland also secrete calcium lowering calcitonin hormone by parafollicular cells.3

Diseases of thyroid include conditions associated with excessive hormone secretion [hyperthyroidism], thyroid hormone deficiency [hypothyroidism] and mass lesion.4 Diseases of the thyroid are manifested by alterations in hormone secretion, enlargement of the thyroid gland (goitre) or both. Thyroid enlargements may be diffuse or nodular.5 Nodular lesion presents clinically as nodule and comprised of hyperplasias, benign and malignant tumours.5 Thyroid lesions can be classified pathologically as

1. Congenital abnormalities [Thyroglossal duct cyst, heterotopic thyroid tissue]
2. Thyroiditis[Acute, Granulomatous, Autoimmune, Riedel, multifocal sclerosing]
3. Hyperplasias [Dys hormonogenic goitre, Graves disease, Multinodular goitre].
4. Tumours
   a. Benign:-[Follicular Adenoma, Hurthle cell adenoma]
   b. Malignant:-[Papillary carcinoma, Follicular carcinoma, Hurthle cell carcinoma, medullary carcinoma, Poorly differentiated carcinoma, undifferentiated carcinoma, lymphomas, sarcomas metastatic lesions, etc].

There are different modalities used to evaluate and diagnose thyroid nodule, like history and clinical examination, thyroid function tests specially serum TSH, USG, FNAC, histopathological examination.8

FNAC is most appropriate investigation to define the nature of thyroid nodule and decide whether surgical intervention is needed or not.9 According to Practice
guidelines set by American Thyroid Association and National Comprehensive Cancer Network, FNAC Should be used as an initial diagnostic test because of its superior diagnostic reliability and cost-effectiveness, before both thyroid scintigraphy and ultrasonography. Though FNAC is simple, cost effective diagnostic test it has its own limitations like specimen adequacy, sampling techniques, skill of performing aspiration, interpretation of aspirate and overlapping cytological features between benign and malignant follicular neoplasm. Hence histopathological examination of thyroid tissue is needed and it is considered as final diagnostic test. Surgical excision and histopathological examination is crucial to rule out malignancy in nodules.

About 42 million people in India are suffering from Thyroid diseases. Thyroid nodules are very common in India, about 12.2% population have palpable thyroid nodule. The incidence of thyroid cancer is 8.7 per 100,000 people per year. This tends to be increasing over the years. Whenever a patient presents with a thyroid swelling, main role of clinician is to distinguish between benign and malignant nodule.

Present study was performed on rural population to know the frequency of various thyroid lesions, their histopathological features and demographic features in this population.

Materials and Methods
Present study is cross-sectional retrospective study conducted between January 2014 to December 2018 for period of five years, at the department of pathology JIiu’s IIMSR Rural Medical College, Badnapur, Jalna, Maharashtra.

Data for present study was obtained from departmental records of histopathology section for specified period of time. All the specimens of thyroid and related lesions submitted to department of pathology during specified time were included in present study.

Tissue Collection and Processing
For each case, laboratory request forms and duplicate copy of histopathological report were obtained and relevant clinical information like age, sex and histological type of thyroid diseases were noted.

Gross findings of the specimens were noted. Received specimens were fixed in 10% formalin. Sections of 3-5 micrometre were cut and taken onto slides. Routine Haematoxylin and Eosin staining was performed. Stained slides were examined under light microscope. Lesions were broadly classified into congenital, Hyperplastic lesions, inflammatory and neoplastic lesions. International guidelines set by WHO were used for further classification of neoplastic lesions.

Subsequently data was analysed and represented using bar diagram, pie diagram and frequency tables.

Observations and Result
Total 233 specimens were received over period of 5 years in dept. of pathology.

Table 1: Sex-wise and lesion wise distribution of study subjects

| Lesion               | Male | Female | Total No. | Percentage |
|----------------------|------|--------|-----------|------------|
| Hyperplastic lesions | 12   | 137    | 149       | 63.95      |
| Hashimoto thyroiditis| 0    | 15     | 15        | 6.44       |
| Thyroglossal cyst    | 7    | 8      | 15        | 6.44       |
| Ectopic thyroid      | 2    | 1      | 3         | 1.28       |
| Colloid cyst         | 2    | 7      | 9         | 3.86       |
| Follicular adenoma   | 3    | 22     | 25        | 10.73      |
| Hurthle cell adenoma | 0    | 4      | 4         | 1.72       |
| Papillary carcinoma  | 2    | 5      | 7         | 3.00       |
| Follicular carcinoma | 0    | 4      | 4         | 1.72       |
| Medullary carcinoma  | 1    | 1      | 2         | 0.86       |
| Total                | 29[12.45%] | 204[87.55%] | 233       | 100        |

Out of 233 patients, 204 were females [87.55%] and 29 were males [12.45%]. In each group, Female patients outnumbered male patients. Thyroglossal cyst and ectopic thyroid shows no sex predilection.

Table 2: Age-wise and Sex-wise distribution of study subjects

| Range of age in years | Female | %  | Male | %  | Total  |
|-----------------------|--------|----|------|----|--------|
|                       | 18     | 7.72 | 8    | 3.43 | 26[11.15%] |
| 21-40                 | 126    | 54.08 | 15   | 6.44 | 141[60.52%] |
| 41-60                 | 51     | 21.89 | 5    | 2.14 | 56 [24.03%] |
| 61-70                 | 9      | 3.86 | 1    | 0.43 | 10 [4.29%] |
| Total                 | 204    | 87.55 | 29   | 12.45 | 233[100%] |
Range of the age of presentation was 2-70 year, with maximum patients [60.52%] between 21-40 years.

Table 3: Mean age of presentation in different pathological lesions

| Lesions                  | Mean age of presentation in years |
|--------------------------|-----------------------------------|
| Hyperplastic lesions     | 36.16                             |
| Hashimoto thyroiditis    | 36.2                              |
| Thyroglossal cyst        | 18.53                             |
| Ectopic thyroid          | 12.33                             |
| Colloid cyst             | 35.77                             |
| Follicular adenoma       | 35.4                              |
| Hurthle cell adenoma     | 32                                |
| Papillary carcinoma      | 34.42                             |
| Follicular carcinoma     | 34.25                             |
| Medullary carcinoma      | 43                                |

Overall mean age of presentation was 34.68 years. Hyperplastic lesions presented with mean age of 36.16 years, Hashimoto thyroiditis presented with mean age of 36.2 years. Thyroglossal cyst presented with mean age of 18.53 years, Follicular adenoma presented with mean age of 35.4 years. Papillary carcinoma presented with mean age of 34.42 yrs. medullary carcinoma presented with mean age of 43 years.

Table 4: Distribution of Study subjects according to Pathological Lesions

| Lesions                  | Total No. | Percentage% |
|--------------------------|-----------|-------------|
| 1. Non-neoplastic lesions| 191       | 81.97%      |
| a. Hyperplastic lesions  | 149       | 63.95%      |
| b. Hashimoto thyroiditis | 15        | 6.44%       |
| c. Congenital lesions    | 18        | 7.72%       |
| - Thyroglossal cyst      | 15        | 6.44%       |
| - Ectopic thyroid        | 3         | 1.28%       |
| d. Colloid cyst          | 9         | 3.86%       |
| 2. Neoplastic lesions    | 42        | 18.03%      |
| a. Benign lesions        | 29        | 12.45%      |
| - Follicular adenoma     | 25        | 10.73%      |
| - Hurthle cell adenoma   | 4         | 1.72%       |
| b. Malignant lesions     | 13        | 5.58%       |
| - Papillary carcinoma    | 7         | 3.00%       |
| - Follicular carcinoma   | 4         | 1.72%       |
| - Medullary carcinoma    | 2         | 0.86%       |
| Total                    | 233       | 100%        |

Out of 233 cases, 191[81.97%] cases were non-neoplastic lesions and 42[18.03%] were neoplastic lesions.

Most common lesion was Hyperplastic lesion with 149[63.95%] cases. Thyroglossal cyst was found in 15[6.44%] cases and was the most common congenital lesion.

Follicular adenoma with 25 cases [10.73%] was found to be most common neoplastic lesion and second most common lesion overall.

Papillary carcinoma with 7 cases [3 %] was found to be most common malignant lesion Medullary thyroid carcinoma was found in 2 cases [0.86%].

Fig. 1: Distribution of non-neoplastic lesions
Out of 191 non-neoplastic lesions, 149 cases were found to be Hyperplastic lesions [63.95%] which comprised mainly of Multinodular goitre 110 cases [47.21%] and diffuse colloid goitre 39 cases [16.74%]. 9 cases were colloid cyst [3.86%], 15 cases [6.44%] were inflammatory lesions, comprising of Hashimoto thyroiditis. 18 cases were Congenital lesions [7.72%], commonest was Thyroglossal duct cyst with 15 cases [6.44%], 3 cases of ectopic thyroid tissue lingual, submandibular and pre-laryngeal respectively [1.28%].

Table 5: Cyto-histopathological correlation

| Cytology diagnosis                  | No. of cases | Histopathology diagnosis                           |
|-------------------------------------|--------------|---------------------------------------------------|
| Autoimmune thyroiditis             | 2            | Hashimoto thyroiditis with follicular adenoma      |
| Autoimmune                         | 1            | Papillary carcinoma in background                  |

Above table shows that 11 lesions which were not correlated on histopathology with cytology

Discussion

Diseases of the thyroid gland are among the most abundant disorders worldwide. About 300 million people in the world are suffering from thyroid disorders and about 42 million people India reside in India.¹⁴ Present study was carried out in Dept. of Pathology, JIIU’s IIMSR Rural Medical College Warudi, Badnapur, Jalna from Jan. 2014 to Dec. 2018, for period of five years. Total 233 specimens of thyroidectomy were received in Dept. of Pathology in 5years.

Table 6: Comparison of distribution of cases according to sex

| Various studies            | Female | Male |
|---------------------------|--------|------|
| Modi et al¹⁸              | 83 %   | 17 % |
| Magdalene et al¹⁶         | 89.2 % | 10.8 %|
| Solomon et al¹⁹           | 86.4 % | 13.6 %|
| Present study             | 87.55 % | 12.45 %|

In present study there were 204 females [87.55%] and 29 were males [12.45%], with female preponderance. Present study is consistent with Solomon et al and Magdalene et al studies.

Table 7: Comparison of distribution of cases according to age

| Various studies            | Mean age years | Range in years |
|---------------------------|----------------|----------------|
| Magdalene et al¹⁶         | 37.4           | ----           |
| Modi et al¹⁶              | 37.4           | 21-40          |
| Solomon et al¹⁹           | 36.3           | 30-39          |
| Present study             | 34.68          | 21-40          |

Overall mean age of presentation was 34.68 years, most common age group of presentation was 21-40 years. Present study is consistent with Solomon et al study.

Table 8: Comparison of distribution of Neoplastic and non-neoplastic lesions

| Various studies            | Non-neoplastic | Neoplastic |
|---------------------------|----------------|------------|
| Dash M et al¹³             | 73.3%          | 26.3%      |
| Magdalene et al¹⁶          | 66.7%          | 33.3%      |
| Padmavathi et al¹⁷         | 70.10%         | 29.90%     |
| Present study              | 81.97%         | 18.03%     |
Like all above mentioned studies, Non-neoplastic lesions outnumbered neoplastic lesions with 191 cases were non-neoplastic [81.97%] and 42 lesions were neoplastic [18.03%].

Table 9: Comparison of distribution of Hyperplastic lesions

| Various studies | % of Hyperplastic lesions |
|----------------|---------------------------|
| Modi et al18   | 46                        |
| Solomon et al19 | 57.2                      |
| Dwarish et al20 | 53.5                      |
| Present study  | 63.95                     |

Most common lesion in present study was hyperplastic lesion 63.95% comprised of multinodular goitre [47.21%], diffuse colloid goitre [16.74%]. 137 were females and 12 males. Most common age group of presentation was 21-40 years. Present study is consistent with Solomon et al.

Table 10: Comparison of distribution of Inflammatory lesions

| Various studies | % of inflammatory lesions |
|----------------|----------------------------|
| Magdalene et al16 | 11.7                    |
| Modi et al18     | 8                        |
| Dwarish et al20  | 7                        |
| Present study    | 6.44                     |

Inflammatory lesions were consisted of Hashimoto thyroiditis, with mean age of presentation of 36.2 years. All were females. Less no. of cases 6.44% as compared to other studies is explained by effective screening by FNAC and conservative management of these cases, lower age of presentation as compared to other studies is explained by demographic variation. Present study is consistent with Dwarish et al study.

Table 11: Comparison of distribution of congenital lesions

| Various studies | % congenital lesions |
|----------------|---------------------|
|                | Thyroglossal cyst   | Ectopic thyroid |
| Magdalene et al16 | 4.2              | -----           |
| Solomon et al19   | 6.9                | -----           |
| Present study     | 6.44               | 1.28            |

Congenital lesions in present study were consisted of thyroglossal cysts 15 cases and ectopic thyroid 3 cases lingual, submandibular and pre-laryngeal respectively. The most common congenital lesion was found to be thyroglossal cyst 15 cases [6.44%] with mean age of presentation 18.53 years, followed by 3 cases [1.28%] of ectopic thyroid lingual, submandibular and pre-laryngeal respectively with mean age of presentation 12.33 yrs. No specific female and male predilection was noted in present study for thyroglossal cyst with 8 females and 7 males and also for ectopic thyroid with 2 males and 1 female. Present study is consistent with Solomon et al study.

Table 12: Comparison of Distribution of Benign Neoplastic lesions

| Various studies | % out of total lesions |
|----------------|-----------------------|
| Modi et al18   | 27                    |
| Solomon et al19 | 17.4                |
| Dwarish et al20 | 15.5                 |
| Present study  | 12.45                 |

Total 29 cases of benign neoplastic lesions [12.45%] were there in present study. Out of which, 25 cases were follicular adenoma with mean age of presentation was 35.4 years. 22 cases were females, 3 cases were males. 4 cases of Hurthle cell adenoma with mean age of presentation was 32 years. All cases were female. Present study is consistent with Dwarish et al and Solomon et al studies.

Table 13: Comparison of distribution of Malignant Neoplastic lesions

| Various studies | % out of total lesions |
|----------------|-----------------------|
| Modi et al18   | 16                    |
| Solomon et al19 | 12.6                |
| Dwarish et al20 | 24                   |
| Present study  | 5.58                  |

Most common malignant lesion was papillary carcinoma 7 cases, 53.04% of total malignant neoplastic lesion. Out of 7 cases of papillary carcinoma, one was follicular variant of papillary carcinoma [infiltrative], two were Papillary microcarcinoma, One case presented with papillary carcinoma in the background of Hashimoto thyroiditis. Remaining three cases were papillary carcinoma classic variant. Mean age of presentation was 34.42 yrs. There were 2 males and 5 females. According to in the 4th edition WHO classification, papillary micro-carcinoma is defined as papillary carcinoma measuring 1 cm or less in diameter. Papillary carcinoma composed almost completely of follicles, with classic papillary nuclear features were classified as Follicular variant of papillary carcinoma thyroid which was sub -classified into encapsulated and non-encapsulated (infiltrative) variants. The encapsulated follicular variant PTC was further divided into invasive and non-invasive. The non-invasive encapsulated follicular variant of PTC was downgraded from carcinoma to non-invasive follicular thyroid neoplasm with papillary-like nuclear features, and cases with incomplete invasion were downgraded from carcinoma to well differentiated tumour of uncertain malignant potential.13

4 cases were follicular carcinoma with mean age of presentation 34.25 years. One case was widely invasive Follicular carcinoma [infiltrating adjacent thyroid tissue], other three cases were minimally invasive follicular carcinoma [capsular invasion only]13

2 cases were medullary carcinoma, one male and one female, with mean age of presentation was 43 years. Total malignant cases were less as compared to other studies [5.58% of total lesions], however Papillary
carcinoma was most common malignant lesion like other studies.

**Cyto-Histopathological Correlation**
From table 5, 11 lesions were not correlated on histology with cytology. Inability to hit the target lesion during FNAC was seen in first 5 cases, as many times neoplasm presents with other non-neoplastic lesions like multinodular goitre and Hashimoto thyroiditis. Interpretation problems of FNAC was seen in next 4 cases. Last two cases showed overlapping features in the case of adenomatous hyperplasia with follicular neoplasm on cytology. This indicates that though FNAC is reliable, initial diagnostic modality, has its own limitations and surgical excision and histopathological examination for final diagnosis is mandatory. Present study also correlates with other studies like Kumar et al., Bagga et al., Nandedkar et al. showing FNAC has both false positive and false negative rates.

**Histopathological characteristics of some important Thyroid Lesions**

![Fig. 4: A. Diffuse Colloid Goitre, B. Thyroglossal cyst with Respiratory lining and underneath thyroid tissue](image)

![Fig. 5: A. Gross Hashimoto Thyroiditis, B. Microscopy Hashimoto Thyroiditis](image)
Fig. 6: A. Hurthle cell Adenoma, B. Follicular Adenoma with intact capsule

Fig. 7: A. Gross Papillary Carcinoma with colloid goitre, B. Microscopy Papillary Carcinoma with orphan Annie nuclei

Fig. 8: A. Gross Follicular Carcinoma with infiltration in adjacent thyroid, B. Microscopy Follicular Carcinoma with capsular invasion tissue
Fig. 9: A. Gross Medullary Carcinoma, B. Microscopy Medullary carcinoma

Fig. 9: C. Medullary carcinoma- round to polygonal cells with salt- paper chromatin.

**Conclusion**

1. In rural population, Thyroid lesions were more common in females than in males.
2. Most common age group of presentation was 21-40 yrs.
3. Non-neoplastic lesions were more common than neoplastic lesions.
4. Most common lesions were hyperplastic lesions. Multinodular goitre was found to be commonest non-neoplastic lesion and most common lesion overall.
5. Thyroglossal cyst was most common congenital lesion.
6. Benign neoplastic lesions outnumbered malignant lesions.
7. Most common benign neoplastic lesion and second most common lesion was follicular adenoma.
8. Most common malignant lesion was found to be papillary carcinoma thyroid.
9. Though other modalities like, FNAC, Sonography were useful in diagnosis of most of the cases, Histopathological examination was found to be mainstay for final diagnosis.

**Recommendations**

1. Considering daily load of Thyroid cases to Department of Pathology in our Institute, we recommend a broad epidemiological study in this region of Aurangabad-Jalna belt.
2. Iodinization of salt should be sustained in this region as the Goitre is still the most common thyroid lesion.
3. Many times neoplasm presents with other non-neoplastic lesions like multinodular goitre and Hashimoto thyroiditis, therefore we recommend thorough clinical evaluation of any enlarged thyroid. Thyroid lesions should not be ignored just as...
multinodular goitre; effort should be made to rule out possibility of hidden neoplasm particularly malignant neoplasm.

4. As information conveyed by Pathologist is important to clinician for proper management and prognostication of case, thorough gross and microscopic evaluation of thyroidectomy specimens is mandatory, particularly Thyroid neoplasm should be categorized according to International guidelines set by WHO.

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