



## A PROSPECTIVE RANDOMISED STUDY OF THYROID SWELLING IN EUTHYROID PATIENTS ON THE BASIS OF CLINICO-PATHOLOGICAL PROFILE AND MANAGEMENT

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**ABSTRACT** **Background;** Thyroid swelling is common problem faced by clinicians as they cause apprehension due to their unpredictable behaviour. In this study, an attempt is made to find out the clinical spectrum of thyroid swelling, diagnostic accuracy of FNAC, appropriate surgical management and to compare it with postoperative histopathological diagnosis so as to determine its role in surgical management. **Aims and objectives;** To complete evaluation of thyroid swelling on the basis of clinical sign and symptoms, thyroid profile, USG neck, FNAC and compare it with postoperative histopathological diagnosis. **Materials and Methods;** The present study was carried out on various patients having thyroid disorder such as local enlargement of thyroid gland and different complaints admitted in wards or seen in outdoor of LLR and Associated hospitals, Kanpur, as a case of thyroid enlargement, only after their due consent during period of January 2014 to December 2015. Total 53 patients after histopathological confirmation in operated cases were included in this study. Clinical profile including estimation of thyroid hormones, fine needle aspiration cytology (FNAC) of the thyroid swellings, USG neck and management of thyroid swelling in euthyroid patient were performed for each patient. **Results;** All patients in neoplastic group had >40 years age whereas in Non-toxic only 12.24% patients had >40 years age. The distribution of patients according to gender was not significantly different in between non-toxic (colloid goiter) and Neoplastic. We observed that the consistency of the swelling in the nontoxic group the swelling were firm in 34 cases and cystic in 15 cases. In the neoplastic group 1 case was hard in consistency. The remaining 3 cases were firm. No cystic swelling was seen in this group. We observed that the swelling was mobile and moved freely on deglutition in all the groups except in the cases of neoplastic disorders where it was fixed. Cervical lymph nodes were involved in 1 cases of neoplasm. The distribution of patients according to Consistency and mobility were significantly different in between non-toxic (colloid goiter) and neoplastic. The results of estimation of hormones in the non-neoplastic group the colloid goiters were mainly in euthyroid, few were in hypo and hyperthyroid phase, while all the toxic multinodular goiters are in hyperthyroid phase. In the neoplastic disorders, 100% of cases were found to be in euthyroid phase. In all histopathology was performed in 26 cases. The 1 cases of colloid cyst underwent surgery and the tissue sent for histopathology, and confirmed colloid cyst. The 25 cases of simple colloid goiters which had been put to surgery and then histopathology, the diagnosis of 19 of them remain unchanged while only four cases was diagnosed as a toxic adenoma. Out of 4 cases of neoplastic disorder (2 papillary carcinoma, and 2 follicular neoplasm- cytologically diagnosed), none underwent surgical procedure. **Conclusions;** Study included patients ranging from 10 to 70 years in age, with the maximum number of cases belonging to the third and fourth decade and a large number of females as compared to males. The duration of thyroid enlargement was shortest in thyroiditis and longest in goiters. The clinical features in cases of Non-toxic goiters presented with pressure symptoms because of large swellings and neoplastic growths with weight loss and change in voice. Neck swellings in the non-toxic goiters they were firm and cystic. Majority of the neoplastic swellings were hard and fixed. On the basis of hormonal status (TSH, T3, T4) the nontoxic and neoplastic cases were euthyroid. In 20 cases the cytology (FNAC) diagnosis was confirmed by histopathology giving us accuracy rate of 77%

**KEYWORDS :** Thyroid swelling, FNAC, Thyroidectomy, Thyroid HPE

### Introduction

The thyroid gland disorders are not very common in clinical practice but are of great importance and they should be diagnosed with accuracy by the clinicians. Most of the thyroid disorders may be diagnosed clinically, but for establishment of definitive diagnosis we require certain investigations to be done. The thyroid diseases, usually present as enlargement of thyroid gland, known as goitre. The enlargement of the thyroid may be diffuse or nodular and firm or cystic. In order of frequency the following conditions are identified simple diffuse enlargement, hyperthyroidism, multinodular goitre, thyroiditis and a solitary nodular goitre (adenoma). The tumors of the thyroid may be benign or malignant which range from very benign follicular adenomas to one of the most fatal human carcinomas, like giant or small cell anaplastic carcinoma of the thyroid. Thyroid disorders can occur at any age but mainly it is a disease of young and middle age. There is a preponderance of females in almost all disorders of the thyroid. The patients in euthyroid state mainly present with swelling in the neck and no other complaints except in these cases where the swelling is large enough to cause pressure symptoms, like dysphagia, dyspnoea or hoarseness of voice. The patients of hyperthyroidism present with weight loss, heat intolerance, hand tremors and irritability or with eye signs in case of Grave's disease. The neoplastic disorders of the thyroid may present in various forms. The thyroid swelling can be a solitary nodule or a multinodular goiter. It has been observed by Lid et al (1988) that in a hot nodule the chances of malignancy are negligible. In contrast a cold solitary nodule should always be investigated for the presence of malignancy. Histopathological examination of removed thyroid swelling is most accurate way to determine the pathology. Laboratory investigation other than FNAC have limited role to find out the nature of thyroid swelling. Isotope scan can demonstrate the functioning capacity of the nodule but cannot predict the

histopathological characters (NR et al., 2012). USG scanning is capable of differentiating solid from cystic lesion but cannot distinguish malignant from benign one (Mavilia et al., 2018). Fine Needle Aspiration Cytology (FNAC) is the study of cells aspirated from a lesion by a fine needle under negative pressure. The specimen consists of a minute quantity of tissue or fluid is spread over a glass slide and after fixation stained by Papanicolaou (pap), Haematoxylin and Eosin (H and E). stain and studied under the microscope. The simple and inexpensive technique of fine needle aspiration cytology (FNAC) has been used as a diagnostic tool since 1920, (Betsill, 1983). The technique is simple and accurate in experienced hands, cost effective and yields rapid results. It can be practiced in the out patients department. The small sized needle used in FNAC precludes significant trauma. The procedure adopted in our study consisted of clinical examination, and management includes usg neck Fine Needle Aspiration Cytology (FNAC) of thyroid gland, treatment and histopathological examination in operated cases.

### Materials and Methods

The patients of thyroid disorder who reported to the departments of L.L.R. and Associated Hospitals were subjected to clinical examination to get a record of clinical profile. The present study was carried out on various patients having thyroid disorder such as local enlargement of thyroid gland and different complaints admitted in wards or seen in outdoor of LLR and Associated hospitals, Kanpur, as a case of thyroid enlargement, only after their due consent during period of January 2014 to December 2015. Total 53 patients after histopathological confirmation in operated cases were included in this study. Clinical profile including estimation of thyroid hormones, fine needle aspiration cytology (FNAC) of the thyroid swellings, USG neck and management of thyroid swelling in euthyroid patient were

performed for each patient. On the basis of clinical examination non-neoplastic thyroid disorders (euthyroid) was divided in three groups colloid cyst, simple and multinodular goiter. Tissue histopathology was done in cases where thyroidectomy was performed. A detailed clinical history of the patients was taken followed by physical examination and routine hematological investigation and hormonal assay. A complete history regarding complaints and symptoms of hypo/hyperthyroidism was recorded, enquiring on the following lines. The complete clinical data, hormonal status were evaluated to establish the clinical diagnosis. Fine Needle Aspiration (FNA) was performed on 53 cases and 2-4 smears were prepared in every case. Operative procedure was performed in 26 patients in which histopathological examination were done. The parameters used for final diagnosis were clinical diagnosis, Fine Needle Aspiration Cytological features and Histopathology (in operated cases).

**Results:**

The baseline characteristics of patients age (years), gender, division of cases and duration of neck swelling are shown in Table 1. All patients in neoplastic group had >40 years age whereas in Non-toxic only 12.24% patients had >40 years age. The distribution of patients according to gender was not significantly different in between non-toxic (colloid goiter) and neoplastic. The division of cases and duration of neck swelling were also significantly different in between non-toxic (colloid goiter) and neoplastic.

**Table 1: Baseline characteristics of the patients**

| Baseline characteristics  | Non-toxic (colloid goiter) (n=49) |    | Neoplastic (n=4) |   | Ch.sq. | p-value |         |
|---------------------------|-----------------------------------|----|------------------|---|--------|---------|---------|
|                           | n                                 | %  | n                | % |        |         |         |
| Age (years)               | 10-20                             | 10 | 20.41            | 0 | 0.00   | 18.20   | <0.001* |
|                           | 21-30                             | 18 | 36.73            | 0 | 0.00   |         |         |
|                           | 31-40                             | 14 | 28.57            | 0 | 0.00   |         |         |
|                           | >40                               | 6  | 12.24            | 4 | 100.00 |         |         |
| Gender                    | Male                              | 10 | 20.41            | 2 | 50.00  | 0.55    | 0.460   |
|                           | Female                            | 39 | 79.59            | 2 | 50.00  |         |         |
| Division of Cases         | Colloid cyst                      | 1  | 2.04             | 0 | 0.00   | 53.00   | <0.001* |
|                           | Colloid goiter                    | 36 | 73.47            | 0 | 0.00   |         |         |
|                           | Nodular goiter                    | 8  | 16.33            | 0 | 0.00   |         |         |
|                           | MNG                               | 4  | 8.16             | 0 | 0.00   |         |         |
|                           | Papillary                         | 0  | 0.00             | 2 | 50.00  |         |         |
|                           | Follicular                        | 0  | 0.00             | 2 | 50.00  |         |         |
| Duration of Neck Swelling | <1                                | 22 | 44.90            | 2 | 50.00  | 26.73   | <0.001* |
|                           | 1-5                               | 23 | 46.94            | 0 | 0.00   |         |         |
|                           | 6-10                              | 4  | 8.16             | 0 | 0.00   |         |         |
|                           | >10                               | 0  | 0.00             | 2 | 50.00  |         |         |

\*=Significant (<0.05)

In the nontoxic group 11 cases had no other complaint except neck swelling. The commonest complaint of patients (12 cases) of this group was tiredness and fatigue followed by dysphagia (11 cases) and dyspnoea (8 cases). These symptoms can probably be attributed to the large size of thyroid swellings. Change in voice was also present in 4 cases of colloid goitres in the neoplastic group 2 cases out of 3 complained of weight loss, tiredness and fatigue were found in all (100%) cases of neoplasm. Palpitation, irritability, and change in voice were found in 33% of cases. The weight loss was also significantly higher in between non-toxic (colloid goiter) and neoplastic. Whereas, Dyspnoea, Dysphagia, Heat intolerance, Cold intolerance, Sweating, Tiredness & fatigue, Palpitation, Irritability, Diarrhoea, Visual disturbances, Menstrual disturbances, Hand tremors. Change in voice, Eye signs, and H/o fever, sore throat were not significantly different in between non-toxic (colloid goiter) and neoplastic.

**Table 2: Distribution of cases according to presenting signs and symptoms in various thyroid disorder**

|  | Non-toxic (colloid goiter) (n=49) |   | Neoplastic (n=4) |   | Ch.sq. | p-value |
|--|-----------------------------------|---|------------------|---|--------|---------|
|  | n                                 | % | n                | % |        |         |

|                        |    |       |   |       |      |        |
|------------------------|----|-------|---|-------|------|--------|
| Dyspnoea               | 8  | 16.33 | 1 | 25.00 | 0.20 | 0.657  |
| Dysphagia              | 11 | 22.45 | 1 | 25.00 | 0.03 | 0.907  |
| Weight loss            | 3  | 6.12  | 2 | 50.00 | 3.99 | 0.046* |
| Heat intolerance       | 0  | 0.00  | 0 | 0.00  | -    | -      |
| Cold intolerance       | 6  | 12.24 | 1 | 25.00 | 0.52 | 0.469  |
| Sweating               | 3  | 6.12  | 1 | 25.00 | 0.15 | 0.697  |
| Tiredness & fatigue    | 12 | 24.49 | 2 | 50.00 | 0.27 | 0.601  |
| Palpitation            | 4  | 8.16  | 1 | 25.00 | 0.05 | 0.827  |
| Irritability           | 5  | 10.20 | 1 | 25.00 | 0.01 | 0.938  |
| Diarrhoea              | 2  | 4.08  | 0 | 0.00  | 0.17 | 0.680  |
| Visual disturbances    | 3  | 6.12  | 0 | 0.00  | 0.26 | 0.610  |
| Menstrual disturbances | 0  | 0.00  | 0 | 0.00  | -    | -      |
| Hand tremors           | 3  | 6.12  | 0 | 0.00  | 0.26 | 0.610  |
| Change in voice        | 4  | 8.16  | 1 | 25.00 | 0.05 | 0.827  |
| Eye signs              | 0  | 0.00  | 0 | 0.00  | -    | -      |
| H/o fever, sore throat | 0  | 0.00  | 0 | 0     | -    | -      |

\*=Significant (<0.05)

Table 3. shows the distribution of cases according to presenting signs and symptoms in various thyroid disorder. The local examination of swelling revealed that nontoxic goiter were comparatively larger than the other thyroid swellings. In the nontoxic and neoplastic groups the thyroid swelling was mainly diffuse, while in the toxic group the swelling were multinodular. We observed that the consistency of the swelling in the nontoxic group the swelling were firm in 34 cases and cystic in 15 cases. In the neoplastic group 1 case was hard in consistency. The remaining 3 cases were firm. No cystic swelling was seen in this group. We observed that the swelling was mobile and moved freely on deglutition in all the groups except in the cases of neoplastic disorders where it was fixed. Cervical lymphnodes were involved in 1 cases of neoplasm. The distribution of patients according to Consistency and mobility were significantly different in between non-toxic (colloid goiter) and neoplastic.

**Table 3: Distribution of cases according to presenting signs and symptoms in various thyroid disorder\***

| Signs/ symptoms    | Non-toxic disorders |    | Neoplastic disorders |   | Ch.sq. | p-value |         |
|--------------------|---------------------|----|----------------------|---|--------|---------|---------|
|                    | n                   | %  |                      |   |        |         |         |
| Nodularity         | Solitary            | 4  | 8.16                 | 0 | 0.00   | 2.88    | 0.237   |
|                    | Multinodular        | 8  | 16.33                | 2 | 50.00  |         |         |
|                    | Diffuse             | 37 | 75.51                | 2 | 50.00  |         |         |
| Consistency        | Cystic              | 15 | 30.61                | 0 | 0.00   | 13.49   | 0.001*  |
|                    | Firm                | 34 | 69.39                | 3 | 75.00  |         |         |
|                    | Hard                | 0  | 0.00                 | 1 | 25.00  |         |         |
| Mobility           | Mobile              | 49 | 100.00               | 1 | 25.00  | 26.18   | <0.001* |
|                    | Fixed               | 0  | 0.00                 | 3 | 75.00  |         |         |
| Palpable lymphnode | -                   | 0  | 0.00                 | 1 | 25.00  | 2.63    | 0.105   |

\*=Significant (<0.05)

The distributions of cases according to hormonal status are shown in Table 4. The results of estimation in the non-neoplastic group the colloid goiter were mainly in euthyroid, few were in hypo and hyperthyroid phase, while all the toxic multinodular goiters are in hyperthyroid phase. In the neoplastic disorders, 100% of cases were found to be in euthyroid phase. TSH levels were recorded and it was found to be normal in euthyroid phase, elevated in hypothyroid phase and suppressed or undetectable in hyperthyroid phase. These findings were common in all the study groups.

**Table 4: Distribution of cases according to hormonal status**

| Hormones | Non neoplastic (Toxic-non-toxic) |                  |        | Neoplastic |      |       |
|----------|----------------------------------|------------------|--------|------------|------|-------|
|          | Eu                               | Hypo             | Hyper  | Eu         | Hypo | Hyper |
|          | No. of cases =49                 | No. of cases =04 |        |            |      |       |
| TSH      | N                                | ↑                | ↓      | N          | -    | -     |
| T3       | 68%                              | 4.2%↓            | 28.8%↑ | 100        | -    | -     |
| T4       | 60%                              | 4.2%↓            | 36.8%↑ | 100        | -    | -     |

Table 5 shows the correlation of antithyroglobulin antibodies and FNAC of the thyroid disorders. In all histopathology was performed in 26 cases. The 1 cases of colloid cyst underwent surgery and the tissue sent for histopathology, and confirmed colloid cyst. The 25 cases of simple colloid goiter which had been put to surgery and then histopathology, the diagnosis of 19 of them remain unchanged while only four cases was diagnosed as a toxic adenoma. Out of 4 cases of neoplastic disorder (2 papillary carcinoma, and 2 follicular neoplasm-cytologically diagnosed), none underwent surgical procedure.

**Table 5: Correlation of antithyroglobulin antibodies and FNAC of the thyroid disorders**

| Cytological Diagnosis | No. Of Cases For HPE | No. Of Cases Verified | Histopathological diagnosis of cases not verified by HPE |
|-----------------------|----------------------|-----------------------|--|
| Colloid cyst          | 01                   | 01                    | 0  |
| Simple Colloid        | 25                   | 19                    | 0  |
| Follicular neoplasm   | 0                    | 0                     | 2  |
| Papillary carcinoma   | 0                    | 0                     | 2  |
| Total                 | 26                   | 20                    | 04   |

**DISCUSSION:**

Till the advent of Fine Needle Aspiration Cytology (FNAC), thyroid disorders were being diagnosed on clinical and surgical grounds. But now, greater reliability is being placed on this diagnostic procedure in preference to the old and classical surgical biopsy. Apart from being a quick and cheaper method, it also cuts down significantly on the risks produced by surgery and anesthesia. Martin and Ellis (1930) the pioneers of FNAC found the method superior to surgery, where there is also a danger of local spread of the disease by surgical manipulation. In the study of 150 thyroid cases Rudowsky (1958) could establish a definitive diagnosis in 49% of cases. Although clinical diagnosis coupled with FNAC has made the early diagnosis of thyroid disorders much easier, certain diagnosis pitfalls have also been observed. The present study was conducted on 53 cases of thyroid disorders. The cases comprised of nontoxic colloid goiter and colloid cysts (90%), and neoplastic disorders (10%). In the present study the cases were selected from various thyroid disorders, with a special emphasis on those suspected of malignancy. The cases showed a wide variation in age ranging from 10 years to 70 years. Most of the patients in the nontoxic group showed a greater age variation from 2<sup>nd</sup> to 5<sup>th</sup> decades with the peak in the 3<sup>rd</sup> and 4<sup>th</sup> decades i.e. 32 out of 49 cases. 4 cases of malignant nature were in 5<sup>th</sup> to 7<sup>th</sup> decades (Bailey and Love, 2000 and Robbins, 2001). The sex distribution of cases showed a preponderance of females (77%) in all the groups of thyroid disorders which correlate well with the findings of Levine (1983) and Robbins (2001). The duration of neck swelling was varying. The maximum cases in the nontoxic group presented with a swelling of one to two years duration with a few cases extending up to a period of six years. The neoplastic cases however had a shorter duration and three out of four cases presented within a year of appearance of swelling. There was a single case of papillary carcinoma in a female of 50 years, which was discovered in a thyroid swelling existing for past 15 years. Their findings are in accordance with Bailey and Love (2000) and Robbins (2001). On studying the various signs and symptoms of thyroid disorders -The patients of nontoxic group of thyroid disorders were mainly asymptomatic and their only presenting complaint was neck swelling. The symptomatic cases had constitutional symptoms like tiredness and fatigue. Eleven out of thirty six cases complained of dysphagia caused by the pressure of a large thyroid swelling. The neoplastic disorders presented with constitutional symptoms, weight loss, and change in voice in 33% of cases, because of involvement of left recurrent laryngeal nerve.

The local examination in nontoxic goiter included in our study were predominantly diffuse with only 8 out of 49 swellings being multinodular, and 4 solitary nodules. These findings are in variation with the normal occurrence of diffuse and colloid goiter. Majority of

the non-toxic goiter were firm and only colloid cysts and a few colloid goiter were cystic in consistency. The significant finding recorded in our study was that 1 out of 4 neoplastic disorders were hard in consistency whereas tree cases presented with firm consistency. The finding coincides with that of Liel et al (1988). The lymphnodes were also involved in 33% of cases. In study of hormonal status of thyroid gland in different disorders we observed that some of the colloid goiters were found in the transient phase of hyperthyroidism. The neoplastic disorders in this study were in euthyroid state that is in accordance with the observations of Liel et al (1988) but in variance with the findings of Sobel et al (1985) in case of papillary carcinoma. The 53 cases in which adequate smears were obtained on aspiration were placed in two groups on the basis of their cytological diagnosis. The first group was of non-toxic disorders consisting colloid goiters and cysts (49 cases) and the 2<sup>nd</sup> group was of neoplastic disorders (4 cases). In our study the largest number of cases (58%) comprised of nontoxic simple colloid goiter. These goiters presented as a diffuse swelling in majority of cases. Few cases were multinodular or solitary nodules. The aspirates in these cases always contained sticky colloid material. On cytological study of neoplastic group, 2 cases was diagnosed as follicular neoplasm, 2 as papillary carcinoma. Solomon (1982) and Rojeski (1985) reported that FNAC is recommended as the initial diagnostic procedure in solitary thyroid nodules. Although FNAC is limited in its ability to distinguish between benign and malignant follicular lesions. Similar observations were made by Shariff (1988). Hence the cytological diagnosis of follicular lesion is confined to the broad term 'Follicular neoplasm' instead of labeling it as benign or malignant. Thus the problem may be overcome by a planimetric study of nuclear size as was carried by Boon et al (1980). Therefore in line with the above authors we also confined our diagnosis to the term 'Follicular neoplasm'. Papillary carcinoma was another lesion included in our study of neoplastic disorders. It was discovered in a female of 45 years and male of 70 yrs. of age. The swelling was diffused and cystic in nature. The FNAC revealed moderate cellularity. The follicular cells were arranged in monolayered sheets. The characteristic psammoma bodies were observed in papillary fronds. These findings of ours are similar to that of Kini et al (1980) except that our cases did not show intranuclear cytoplasmic inclusions or multinucleated giant cells. Kini SR, Miller JM, Hamburger JI, et al. Cytopathology of papillary carcinoma of the thyroid by fine needle aspiration. *Acta Cytol* 1980;24:511-521. Out of 26, total 53 cases had undergone surgical biopsy and subsequently histopathological examination. The comparative study of histological diagnosis and cytological diagnosis showed that in 20 out of 26 cases a correct cytological diagnosis was made. In this the accuracy of FNAC study was 77%.

**CONCLUSION**

On the basis of observations of clinical profile of the cases including estimation of thyroid hormones, FNAC, USG and histopathology in the case's of operated patients following conclusion could be drawn: - This study included patients ranging from 10 to 70 years in age, with the maximum number of cases belonging to the third and fourth decade and a large number of females as compared to male. The duration of thyroid enlargement was shortest in thyroiditis and longest in goiter. The clinical features in cases of Non-toxic goiter presented with pressure symptoms because of large swellings and neoplastic growths with weight loss and change in voice. Neck swellings in the non-toxic goiter they were firm and cystic. Majority of the neoplastic swellings were hard and fixed. On the basis of hormonal status (TSH, T3, T4) the nontoxic and neoplastic cases were euthyroid. In 20 cases the cytology (FNAC) diagnosis was confirmed by histopathology giving us accuracy rate of 77%. Our study combining clinical profile, FNAC, USG features in thyroid disorders yielded a high accuracy rate of 77%.

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