

Though USG features alone cannot predict malignancy or benignity, but techniques that combine USG features and FNA cytology are most effective and most accurate for predicting malignancy^[10].

Similarly, TSH measurement can be part of the initial workup in every patient with a thyroid nodule and be used as a guide for further management. Lower levels of TSH are associated with a lower risk of papillary thyroid cancer in patients with thyroid nodular disease^[11]. Recent studies have investigated the relationship between serum TSH concentration and thyroid cancer. TSH was found to be an independent predictor of malignancy in thyroid nodules^[12]. The risk of malignancy rises in parallel with serum TSH, even within the normal range, and higher TSH levels were found to be associated with advanced-stage thyroid cancer^[11,12].

Thus, the aim of this study was to correlate cyto-histo, cyto-biochemical and cyto-radiological evaluation to give us broader and better evaluation of palpable thyroid nodules wherever these modalities were available.

Materials and Methods

This analytical study comprised of 156 cases of palpable diffuse and nodular thyroid lesions subjected to FNAC in Department of Pathology over a period of one and half year at a rural tertiary health care Institute after obtaining ethical clearance from institute Human ethics committee. Data regarding clinical features, concise history, thyroid function tests and USG features were obtained from cytology requisition forms and medical records section and analyzed.

Cytological evaluation was done on May Grunwald Geimsa (MGG) and Hematoxylin and Eosin (H&E) stained slide and reporting based on Bethesda classification.^[3] Benign group consisted of Colloid goitre, thyroiditis, cysts (colloid cyst/thyroglossal cyst), whereas the indeterminate group consisted of lesions with follicular architecture with two subgroup -atypia of undetermined significance (AUS)/ follicular lesion of undetermined significance (FLUS) and another was FN (follicular neoplasm)/SFN (suspicious for follicular neoplasm). Malignant group consists of suspicious for malignancy and malignant cytology without any overt follicular architecture.

For biochemical correlation, results of thyroid function tests were categorized as euthyroid, hypothyroid and hyperthyroid and findings were correlated with cytological diagnosis.

For radiological correlation, features of benign and malignancy were noted. In ultra-sonography, imaging features significantly associated with the incidence of

malignancy were microcalcification, hypervascularity, hypoechoic, irregular shape, ill-defined margins, absence of halo/rim and solid appearance^[13]. Conversely, predominantly cystic lesion with no microcalcifications, isoechoogenicity and spongiform appearance (defined as aggregations of multiple microcysts in more than 50% of the nodule) are features highly suggestive of benignity^[14,15].

Statistical Methods: Percentage was used for descriptive statistic to explain the distribution and simple data interpretation. To test the efficacy of FNAC against gold standard histopathology, diagnostic test like sensitivity, specificity, positive and negative predictive value and accuracy was applied.

Results

Thyroid lesions constituted 19.3% of total lesions subjected to FNAC in the study period. Age group ranged from 13 to 77 years and maximum cases belonged to 5th decade. Thyroid lesions showed female preponderance with ratio of 6.09:1 over males. Mean age for male and female were 41.6 years and 42.02 years respectively with no statistical significance. Most common clinical presentation was nodular swelling (86%). Benign lesions accounted for 75.6% on FNAC and Goitre was the most common lesion diagnosed on FNAC, accounting for 56.4% cases followed by thyroiditis (15.4%) and cystic lesion (3.8%). Indeterminate lesions which falls under grey zone area in thyroid FNAC accounted for 16(10.3%) cases – Ten were FLUS and six were FN/SFN. Malignant cases were Twelve (7.7%) on cytology. Ten cases (6.4%) were labelled unsatisfactory due to low cellularity or hemorrhagic smears. [Table 1]

Cyto-histocorrelation: [Table 2] FNAC diagnostic categories were compared with corresponding histopathological diagnosis. Out of 156 FNACs, histopathology was available in 36 (23%). In 118 benign cytology cases, histology was available in 36 cases, and cyto-histo concordance was seen in 20 (77%). Out of 6 cases of colloid goitre on cytology, two showed incidental Papillary micro-carcinoma with surrounding colloid goitre changes on histology and four were follicular variant of Papillary carcinoma on histology which accounted for false negative cases. [Fig:1,2]

In 16 indeterminate cases of cytology, histology was available in 6 cases, 4 cases of FLUS showed adenomatoid nodule with colloid goitre and two cases of follicular neoplasms turned out to be follicular carcinoma. [Fig:1,2]

In four malignant cytology cases, cyto-histo concordance was 100%. Thus, overall cyto-histo concordance was seen in 72.2% cases.

Table 3: Cyto-Biochemical correlation.

THYROID FUNCTION TESTS	No. of cases evaluated (n=118)	Percentage(%)	Cytological diagnosis n (%)
Euthyroidism	92	78%	Colloid goitre 56 (60.8%)
Hypothyroidism	22	18.6%	Thyroiditis 12 (54.5%)
Hyperthyroidism	04	3.4%	Goitre 04 (100%)

Table 4: Cyto-Radiological correlation.

Cytological diagnosis (n=156)	Radiological diagnosis available (Total n=116)	Correlated with FNAC	Not correlating with FNAC n (Radio Diagnosis)	Histopathology available
Benign(118)				
Colloid goitre (88)	72	64 (88.8%)	08 (6PTC+ goitre,	06 (PTC)
Thyroiditis (24)	18	14 (77.8%)	2Thyroiditis)	02
Cyst (06)	04	04 (100%)	04 (goitre)	02
Indeterminant (16)				
FLUS (10)	06	06(CG)	02(CG)	06 (CG)
FN/SFN/ HN (06)	04	02(FA)		02(FC)
Malignant (12)	04	04 (100%)	-	04(2PTC,2MTC)
Non diagnostic (10)	08	-	08 (CG)	-
Total	116	94(81.03%)	22(18.97%)	

FA=follicular adenoma,FC=follicular carcinoma,CG= colloid goitre,PTC=Papillary thyroid carcinoma,MTC=medullary thyroid carcinoma

Table 5: Cytological diagnosis rendered in thyroid lesions in Indian studies.

Indian studies	Nonneoplastic (%)	Malignant (including suspicious for malignancy)(%)	Indeterminant/follicular lesions (including FLUS/ Suspicious of follicular Neoplasm)(%)	Non diagnostic (%)
Handa et al ⁷	87.7	3.91	3.22	5.06
Richa etal ²²	53.16	9.56	35.10	2.12
Sunita etal ¹⁸	94.6	1.6	3.1	0.7
Bagga et al ⁵	90.5	1.2	6.7	1.6
Pande et al ⁴	72.03	4.69	18.79	4.47
Present study	75.6	7.7	10.3	6.4
AsliMuratli et al ¹⁹	59.5	20.5	9.3	10.8

Table 6: Sensitivity, specificity, Accuracy, negative and positive predictive values in thyroid lesions in Indian studies and foreign studies.

Study	Number of Patients	Sensitivity	Specificity	Accuracy	Negative Predictive value	Positive Predictive value
Sengupta etal ²¹	178	90	100	98.88	98.75	100
Gupta etal ¹⁷	75	80	86.6	84	86.6	80
Sunita etal ¹⁸	104	50	100	94.2	93.8	100
Prakash etal ²³	162	40	100	95.71	95.58	100
Pande etal ⁴	112	57.14	90	80.28	83.33	70.58
Bagga etal ⁵	32	66	100	96.2	96	100
Richa Sharma etal ²²	74	89.47	86.11	87.83	88.57	87.18
Foriegn Asli etal ¹⁹	126	87.1	64.6	77.3	79.5	76.1
Fatemeh etal ²⁰	101	95.2	68.4	85.14	89.6	83.3
Present study	36	40	100	81.3	78.6	100

Discussion

Palpable Thyroid nodules are one of the main indications of thyroid FNACs. The prevalence of palpable thyroid nodules range from 4 to 7% for adults [16]. In our study, thyroid FNACs accounted for 19.3% amongst all lesions subjected to FNACs. In present study, most common age group affected was 5th decade with mean age of 41.8 years. Female preponderance was seen with Female :Male ratio of 6.09:1. Similar findings were noted in studies from different parts of India and Asian countries [4,7,17,18,19,20,21]

In present study, majority thyroid lesions on cytology were benign accounting for 75.6% and most common benign lesion found was colloid goitre (56.4%). Similar findings were noted in other Indian studies. [4,5,7,18,22] Frequency of Malignancy in our study on cytology was 7.7%. In other Indian studies it ranged from 1 to 16% [4,5,7,17,18,21,22]. [Table 5]

Cyto-histo Correlation: FNA has become a primary diagnostic tool for evaluating thyroid nodules and a correct cytologic diagnosis obviates unnecessary thyroid surgeries. Therefore incidence of benign cytological lesions subjected for surgical excision are less over the period of time due to efficacy of cytology. This was also observed in our study where histopathology was available in 36 cases (23.07%) out of 156 cytology cases. The overall cyto-histo concordance achieved in our study was 72.2%. In other Indian studies, it ranged from 50% to 95% [4,18,22,23,24].

In our study, out of twenty two cases of goitre on cytology, six showed papillary carcinoma on histology and accounted for false negative cases. Out of six, two were incidentally detected papillary micro-carcinomas in a colloid goitre specimen. This is a common pitfall of FNAC as lesion is too small which could have missed due to untargeted FNAC. Here, USG can help to detect smaller lesions like papillary micro-carcinoma with features such as solid nodule with microcalcification. In literature, it has been mentioned that papillary micro-carcinomas (smaller than 1 cm) incidentally found at the time of surgery are much more common (up to 36%) but it is controversial whether or not a survival benefit exists with the diagnosis and treatment of such entities, given their generally benign course [15,16,17,18]. Another four case of papillary carcinoma on histology were follicular variant of PTC which was reported as adenomatoid goitre probably due to lack of high cellularity required for neoplastic lesions, follicular architecture, and inadequate or missed nuclear features lead to misdiagnosis. Strict criteria for nuclear features in lesion with follicular architecture should be followed to avoid misdiagnosis. Here also, imaging study findings can be correlated to come to conclusion.

In case of malignancies, two follicular neoplasm on cytology turned out to be follicular carcinoma. This is one of the true pitfall of cytology were criteria to diagnose follicular carcinoma is capsular and vascular invasion which can be assessed only on histology and cannot be assessed on cytology.

Four cases of follicular lesions of undetermined significance (FLUS) cytology were diagnosed due to high cellularity which was more for colloid goitre but short of suspicious follicular neoplasm turned out to be adenomatoid colloid goitre on histology. Repeat aspirates can help to clinch a definitive diagnosis on cytology in these cases which are sitting on fence and comes under grey zone, thus helping clinicians for further definitive management [3].

In present study, unsatisfactory/ non-diagnostic cases accounted for 6.4%. Six cases were unsatisfactory due to haemorrhage and low cellularity inspite of repeat aspirates. Four cases showed poor compliance and lost in follow-up. Non-diagnostic rate approximately ranged from 0.7 to 10% in the studies from different parts of India [4,5,7,18,22].

In statistical analysis, sensitivity, specificity, diagnostic accuracy, negative predictive value and positive predictive value in our study was 40%, 100%, 81.3%, 78.6% and 100% respectively. Low sensitivity was due to low number of sample subjected to histopathology examination and as well as false negative cases missed on cytology, suspicious on radiology and subjected to surgical excision. Sensitivity, specificity, diagnostic accuracy, negative predictive value and positive predictive value in other studies ranged from 40-90%, 85-100%, 77-98%, 80-98% and 70-100% in Indian studies respectively [4,5,17,18,21,22,23]. Other Asian studies show higher sensitivity but low specificity as compared to Indian studies [19,20]. [Table 6]

Cyto-Hormonal Correlation: Though FNACs are the mainstay investigation in the evaluation and diagnostication of thyroid masses, thyroid function tests and USG neck study are the next important investigations in further evaluation of thyroid nodules. In our study, majority (78%) cases were euthyroid and most of them were colloid goitre (60.8%) on cytology. Similar findings were noted in other studies were euthyroid cases ranged from 56 to 66% [18,7]. Interestingly, in our study hypothyroidism was more common (18.6%) than hyperthyroidism (3.4%) in this southern coastal iodine sufficient belt. This is in contrast with the study from northern parts of iodine deficient sub-Himalayan belt of India where hyperthyroidism cases were more frequent [7]. Interestingly, study from western India showed near equal occurrence of hypo and hyperthyroidism [18]. Majority of the cases of Hypothyroidism in our study showed thyroiditis (54.5%) on cytology. Thus, inflammation and goitrogens

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