Histopathological and Cytological Efficacy in The Diagnosis of Solitary Thyroid Nodules

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ABSTRACT

Background: thyroid nodules are found in 4-7% of the population, the preferred diagnostic approach is avoidance of numerous radiologic evaluations, and early performance fine-needle aspiration.

Objectives: the aim of this study was to evaluate the efficacy of fine needle aspiration cytology (FNAC) and histopathological assessment in diagnosis of solitary thyroid nodules.

Methods: this study was done on twenty patients diagnosed as solitary thyroid nodule. All the patients' FNAC and histopathological results were reviewed, confirmed, correlated and evaluated.

Results: there were 4(20%) men and 16(80%) women, with a male-to-female ratio of 1: 4. The patients studied ranged in age from 17 to 65 years, with the majority ranging in age between 25 and 40 years (30%). According to FNAC findings, 65% were benign/non-neoplastic and 35% were malignant aspirates. The most common benign lesion diagnosed by FNAC was a colloid nodule (25%), whereas the most common malignant lesion was papillary carcinoma (30%). There were no false-positive cases (0%). A false-negative result was found in only two cases (10%). According to the histopathological findings, 60% were benign/non-neoplastic lesions and 40% were malignant. The most common benign/non-neoplastic lesions were colloid goiter (25%) and follicular adenoma (15%), whereas the most common malignant lesion was papillary carcinoma (35%). **Conclusion:** FNAC is a useful diagnostic method, but it has some limitations in the diagnosis of subtypes of solitary thyroid nodules such as follicular lesion. Histopathological study provides a more accurate diagnosis and overcomes these limitations.

Keywords: Solitary thyroid nodule, Fine needle aspiration biopsy (FNAB), Fine needle aspiration cytology (FNAC), Histopathology.

INTRODUCTION

Thyroid nodules (TNs) are very common diseases in the general population. It was found in 19-67% by ultrasound examination [(1)]. Unilateral thyroid nodules are defined as separate swelling in one stratum without any apparent defect elsewhere[(2)].

Thyroid nodules are very common. They were detected in 4% to 7% of the population by palpation and in 60% of the patients in the post-mortem examination. Thyroid complications are more common in women than in men, about 4 to 1 times more frequent Thyroid nodules throughout life. The prevalence of thyroid nodules is evident in patients younger than 21 years of age only; 0.05-1.8%. The most common cause of unilateral nodules in children is porous benign tumor [(3)].

The majority of unilateral thyroid nodules are benign. While **Attali *et al.*[(4)]** reported that 5-20% of all thyroid nodules turn out to be really malignant.

The value of fine-needle aspiration biopsy (FNAB) for diagnosis of thyroid pathologies has been established; however, in some specific situations, its reliability is debatable. This diagnostic tool is appropriate and valuable for the evaluation of single thyroid tumors, but has shown to be less effective for that of multinodular thyroid glands [(5)].

FNAB can be performed by palpation or with ultrasound guidance. (USFNA) biopsy has been shown to decrease false negative resulting from needle misplacement and reduce the rate of non diagnostic smears from 15% to 30%[(6)].

The ultrasound-guided ultrasound needle (USFNA) biopsy is widely used as a diagnostic tool to distinguish between benign and malignant thyroid nodules, the most accurate and cost-effective method available. The use of FNAB significantly enhanced the ability to detect thyroid cancer before surgery, resulting in a 25% reduction in unnecessary surgical operations and an increase in cancer yield from 14% to at least 30%[(1)].The majorities of the vesicles are benign and represent colloidal or glandular nodules or hyperplasia, simple abscesses in the thyroid gland, autoimmune thyroiditis, and lymphoid thyroiditis, while the most common malignant biopsy in FNAC is papillary gland cancer [(7)].

Histological examination of thyroid glands is the gold standard for determining the true spread and form of thyroid nodules in the population [(8)].

AIM OF THE STUDY

The aim of this study is to evaluate the efficacy of fine needle aspiration cytology (FNAC) and histopathological assessment in diagnosis of solitary thyroid nodules.

PATIENTS AND METHODS

This study was conducted on 20 patients diagnosed with solitary thyroid nodules. All patients were selected from those attending the outpatient clinics of ENT department at Bab El-Shereia Hospital, Al-Azhar University from February 2017 to December 2018. All patients had been subjected to both FNAC and surgery during this period.

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Written informed consent: An approval of the study was obtained from Al- Azhar University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation.

Patients diagnosed with multinodular goiter were not included in this work, whereas those diagnosed with colloid goiter with a predominant nodule were included. Also, patients who had not been subjected to FNAC were excluded from the study. All patients prepared for FNA by using the dominant hand, a 23- or 25-gauge 1.5-inch needle with an attached 10-mL syringe is advanced into the lesion, with the clinician noting the consistency of the nodule upon entering. We prefer the non-suction technique because it results in less traumas and bleeding. A syringe-holder aspiration device can facilitate this technique. Once the needle enters the lesion, it is rapidly moved back and forth along a single track for each aspiration until material is seen with the hub of the needle. Firm pressure is applied to the puncture site. Three to six passes are often required to obtain an adequate sample. If a cyst is encountered, the fluid is completely aspirated and sent for cytologic examination. The region of the cyst is then evaluated by ultrasound and any residual solid component reaspirated.

The needle is then detached from the syringe, and the syringe filled with air, reattached, and the contents expelled onto a glass slide. A second slide is placed on top of the first slide and the material is smeared by pulling the slides in opposing horizontal directions. Slides can be either immediately placed into alcohol or sprayed with fixative for Hematoxilin & Eosin staining. Usually at least 6 to 10 clusters of cells on two separate slides are required to make a diagnosis. On-site evaluation by a cytopathologist can significantly reduce the inadequacy rate.

The patients were hospitalized for surgery, 8 patients underwent total thyroidectomy with neck dissection according to fine needle aspiration cytology which resulted in papillary carcinoma ,while 5 patients with follicular lesion by FNAC underwent lobectomy one of them underwent Dunhill operation as the mass involving the isthmus of the thyroid gland, 5 patients with colloidal lesion by FNAC underwent lobectomy except 1 case underwent total thyroidectomy as there is suspicious of papillary carcinoma proved by FNAC, total thyroidectomy with bilateral neck dissection and mediastinal lymph node dissection in addition to removal of strap muscles for 1 case as it is shown to be medullary carcinoma by FNAC, another 1 case diagnosed by FNAC as thyroid cyst underwent lobectomy.

FNAC and histopathological slides for all 20 cases were examined by two different pathologists; each examined the slides separately and the diagnosis was confirmed. Smears were considered adequate for diagnosis if they had six or more groups of more than 10 well-preserved follicular epithelial cells in each group. The following criteria were used for diagnosis: benign, indeterminate, malignant, and non-diagnostic, to minimize the possibility of false-positive or false-negative results. Specimens after thyroid surgery sent for histopathological examination without any information for pathologist about the result of FNAC. The result of FNAC and histopathology were collected and summarized for analysis and comparison.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following:
- Probability (P-value)
- P-value <0.05 was considered significant.
- P-value <0.001 was considered as highly significant.
- P-value >0.05 was considered insignificant.

RESULTS

This study was done on 20 patients with a clinical diagnosis of solitary thyroid nodule. There were 4 (20%) men and 16 (80%) women, with a male-to-female ratio of 1: 4 (figure **1**). The studied patients ranged in age from 17 to 65years, with the majority ranging in age between 25 and 40 years (30%). Most cases were from Bab El-Sharia and Mainsheet Nasser areas. FNAC was performed in all 20 cases. A total of 13 (65%) cases were benign/non-neoplastic and seven (35%) cases were malignant (figure 2).

The 13 benign/non-neoplastic aspirates (65%) were diagnosed as follows: 5 cases (25%) were colloid nodules(Fig. 3), 4 cases (20%) were hyperplastic follicular cells (Fig. 4&5), the follicular cells were in excess, whereas the colloid was less, 3 cases (15%) were Hurthle cell tumour and the last one case (5%) were diagnosed as thyroid cyst. The seven malignant aspirates (35%) were diagnosed as follows: 6 cases (30%) were papillary carcinoma (Fig. 6) and finally, the last case (5%) was diagnosed as medullary thyroid carcinoma.

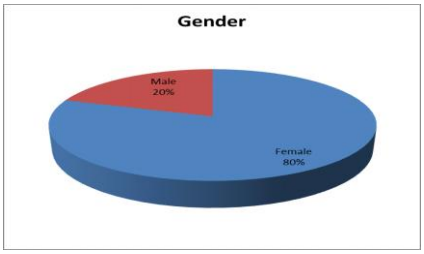

Figure (1): Pie chart gender distribution of the study group.

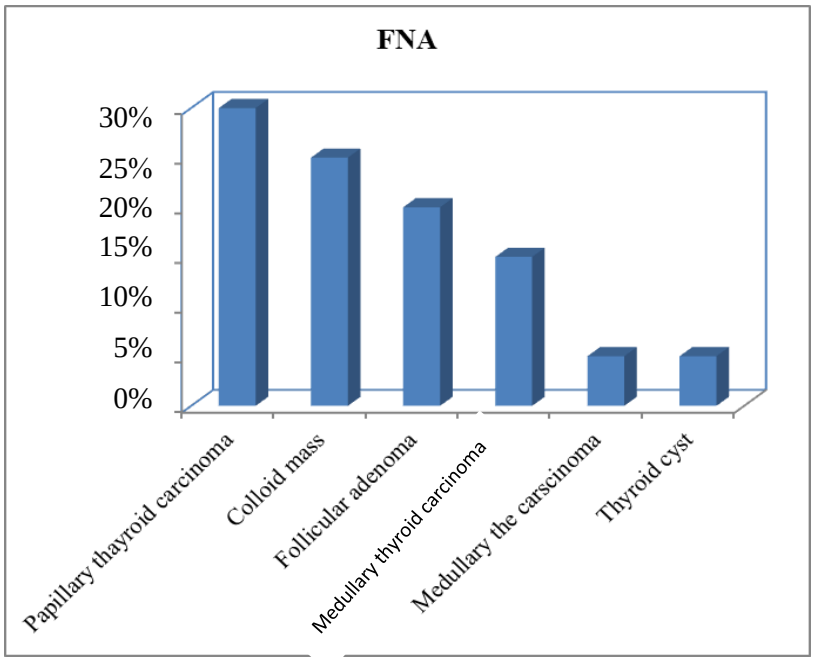

Figure (2): Bar chart FNA distribution of the study group.

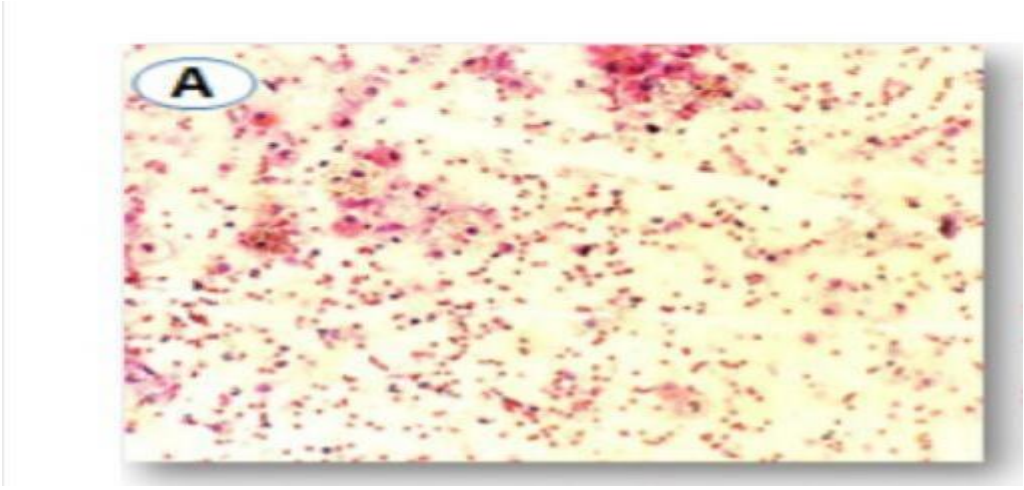

Figure (3): FNAC of thyroid nodule shows feature of colloid goiter which showed bland looking follicular cells, macrophage and colloid (H&E x200).

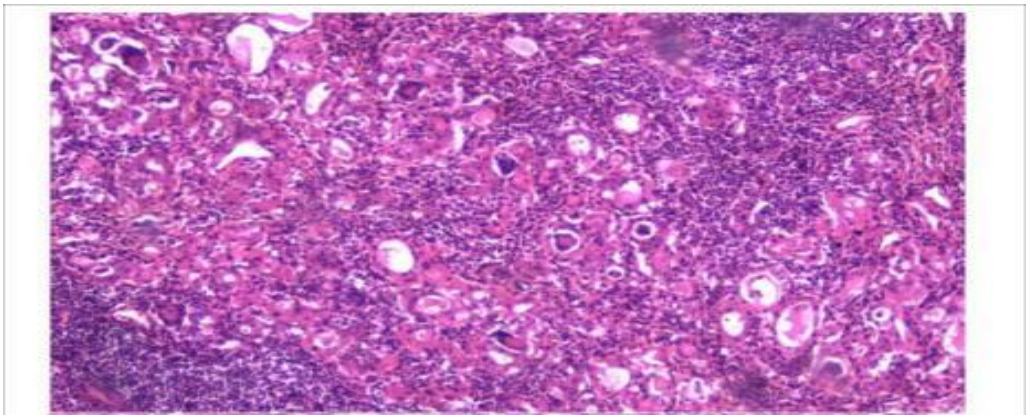

Figure (4): FNAC of follicular adenoma (H&Ex200).

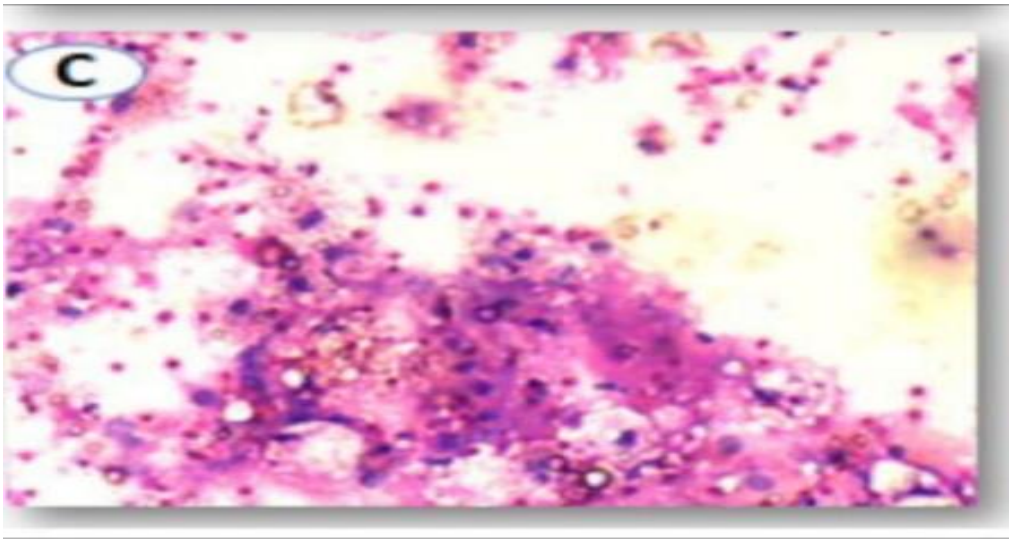

Figure (5): FNAC of solitary thyroid nodule shows feature of follicularadenoma which shows groups offollicular cells (H&E x400).

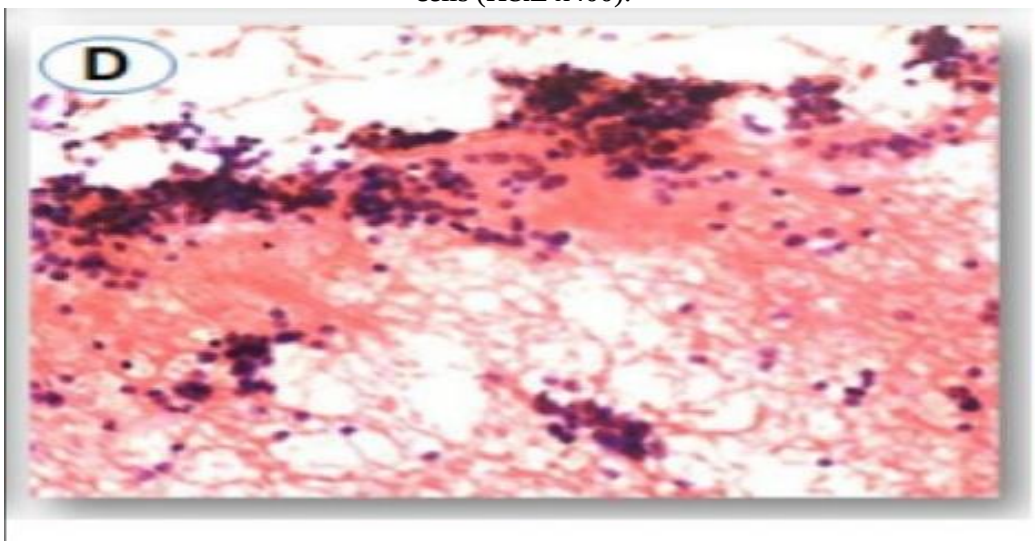

Figure (6): FNAC of solitary thyroid nodule shows feature of papillary carcinoma which shows malignant cells with hyperchromatic overlap nuclei in fugue papillary architecture (H&E x300).

Histopathological examination showed that 11 (55%) specimens were benign/non-neoplastic lesions, whereas 9 (45%) were malignant.

Benign/non-neoplastic lesions were reported as follows: A total of5 cases (25%) were colloid nodules (Fig.7), three patients (15%) had follicular adenomas: two were microfollicular, one were macrofollicular (Fig. 8), two cases (10%) had Hurthle cell tumour and finally one patient (5%) had thyroid cyst.

Malignant lesions were diagnosed as follows: Seven cases (35%) were papillary carcinoma (Fig.9), one case (5%) was a follicular variant of Hurthle cell carcinoma (Fig.10) and the last one (5%) was mudullary thyroid carcinoma. The nine malignant lesions were solid nodules.

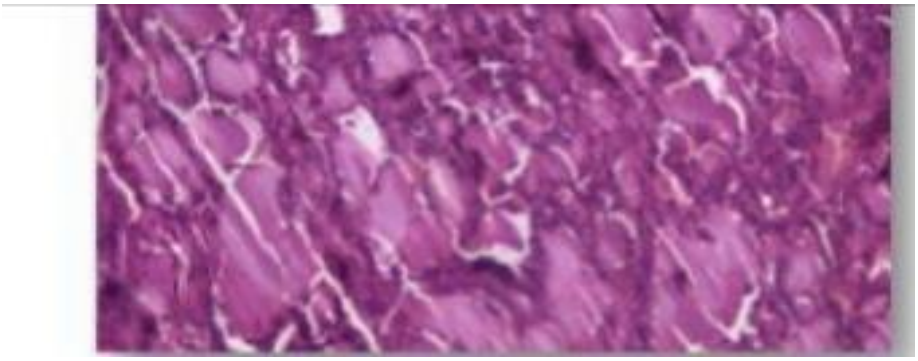

Figure (7): Histopathological examination of thyroid specimen shows colloid goiter (H&E x300).

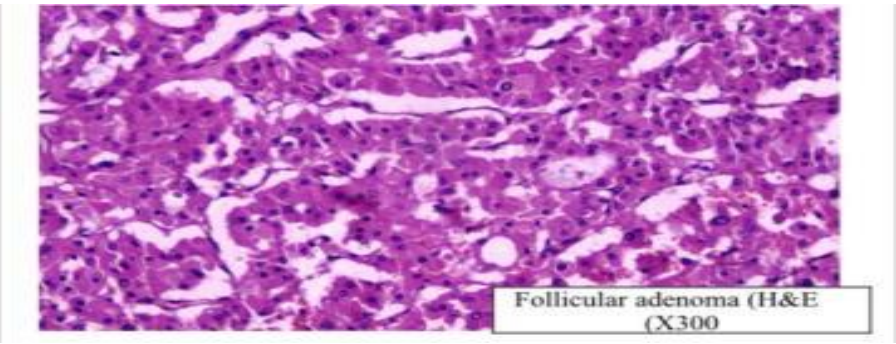

Figure (8): Histopathology of follicular adenoma.

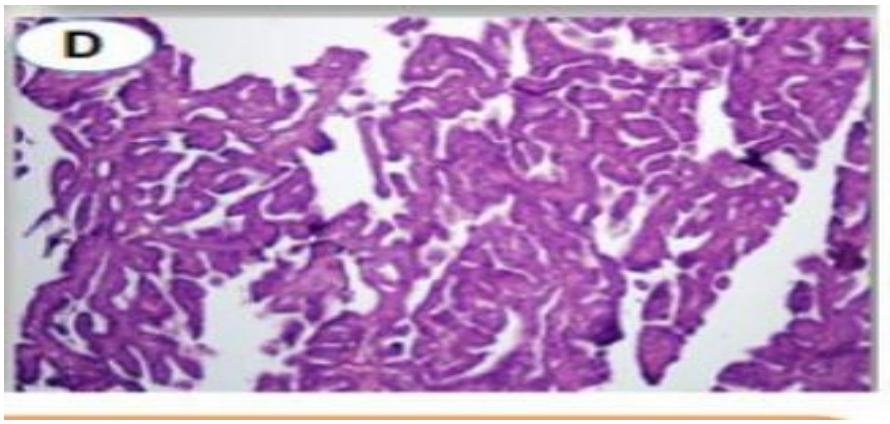

Figure (9): Histopathological examination of thyroid spicemen shows papillary carcinoma (H&E x200).

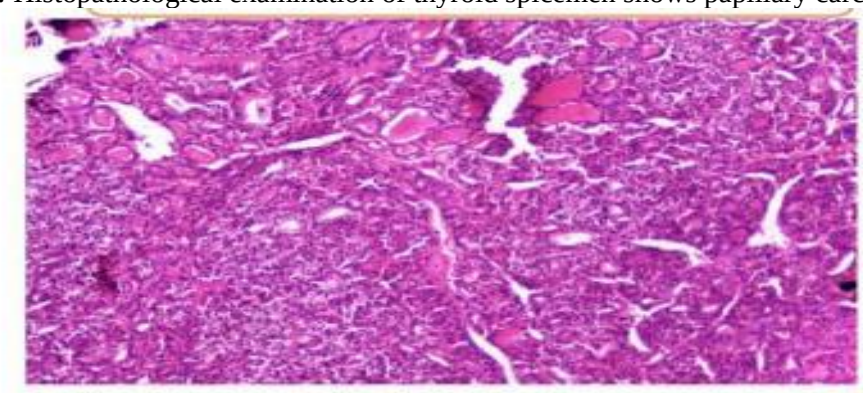

Figure (10): Histopathological examination of thyroid specimen shows follicular carcinoma which shows infiltration of capsule (H&E x 200).

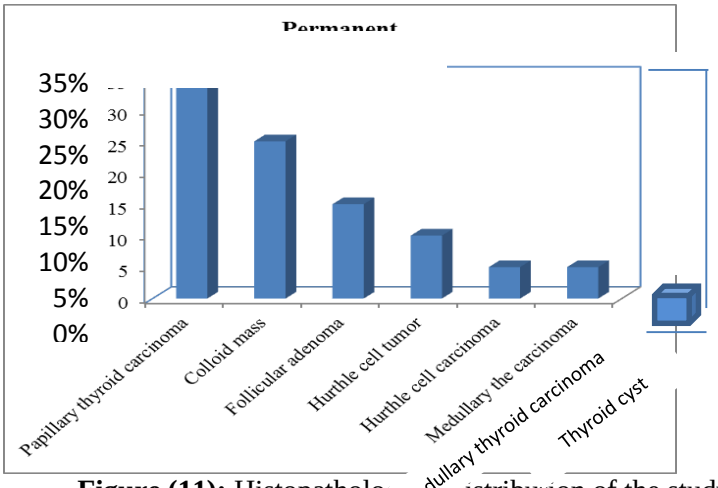

Figure (11): Histopathol distribution of the study group

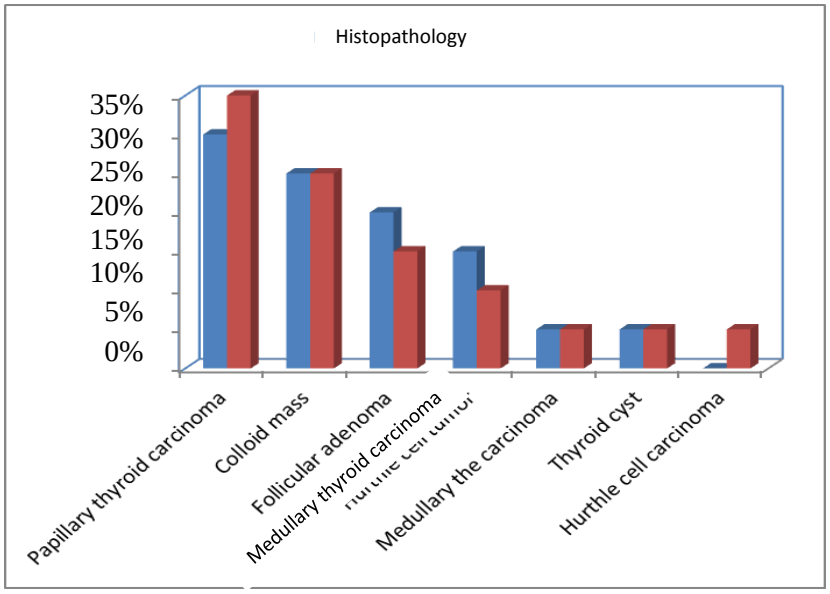

Figure (12): Bar chart between FNA and Histopathology according to histopathology.

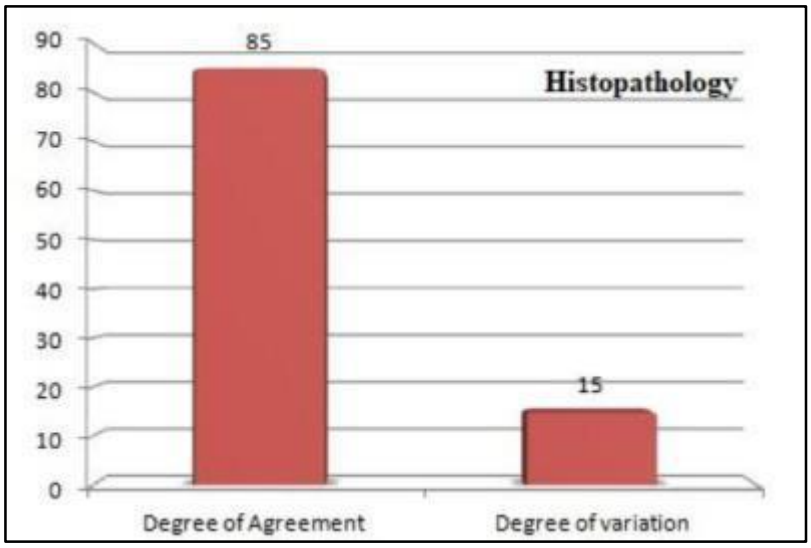

Figure (13): Agreement between FNA and histopathology according histopathology

Comparison between the results of fine-needle aspiration cytology and histopathology (figure 12): The results of FNAC are different from that of histopathological examination in 3 cases out of 20 cases (15%) as follows:

(1) Four cases were diagnosed as hyperplastic follicular adenoma by FNAC. Histopathological examination showed follicular adenoma in three cases and colloid goiter with a predominant hyperplastic nodule in one cases. So the diagnosis of follicular adenoma required histopathological examination for the assessment of capsular and blood vessel invasion.

(2) Five cases were diagnosed as colloid aspirates by FNAC. Histopathological examination showed colloid nodules in four cases and papillary thyroid carcinoma in one case.

(3) Three cases were diagnosed as hurthle cell adenoma by FNAC. Histopathological examination showed Hurthle cell adenoma in two cases and Hurthle cell carcinoma in one case.

(4) Six cases were diagnosed as papillary thyroid carcinoma aspirates by FNAC. Histopathological examination showed seven cases of papillary thyroid carcinoma due to misdiagnosis of one case of colloid aspirate by FNAC.

(5) One case was diagnosed as thyroid cyst by FNAC and histopathology.

(6) The last one case was diagnosed as medullary thyroid carcinoma by FNAC and histopathology.

(7) We obtained no false-positive results (0%); in only two cases were false-negative results obtained (10%). The first case was diagnosed as colloid nodule by FNAC and the final histological diagnosis was papillary thyroid carcinoma and the other case was diagnosed as Hurthle cell adenoma by FNAC and the final histological diagnosis was Hurthle cell carcinoma.

DISCUSSION

The incidence of thyroid disease varies between different populations and geographical locations around the world. In sufficient areas of iodine, for example, thyroid nodules are evident in about 4-7% of the population while they are more prevalent in individuals living in iodine deficiency areas [(9)].

In our study, the male-to-female ratio was 1: 4. The majority of patients were between 25 and 40 years of age (30%) with mean age (32.5 years). These results are in agreement with those of **Aimel *et al.*[(10)],** who found a male-to-female ratio of 1 : 3 The majority of patients were between 31 and40 years of age (40%). Most of the patients (68%) belonged to Azar Kashmir and other hilly areas of Pakistan. This, along with the high incidence of(65%) colloid goiter found in the study, is probably because of the dietary deficiency of iodine in hilly areas.

The numerous diagnostic procedures currently available improve the anatomic, pathologic, radiological and functional assessment of thyroid nodules but may lead to unjustified increase in cost with little practical gain, if not used rationally. As most of the hospitals lack some of these diagnostic investigations, FNAC is still regarded as the single most accurate and cost-effective procedure[(11)].

In our study, the results of FNAC were 65% benign/nonneoplastic, and 35% malignant. The benign/non-neoplastic aspirates, 65%, were colloid/toxic nodules (25%), hyperplastic follicular cells (20%), Hurthle cell tumour (15%), and thyroid cyst (5%) of total number of cases. The malignant aspirates 35 % were all diagnosed as papillary carcinoma (30%), and medullary thyroid carcinoma (5%) of cases .

In a study carried out by **Aimel *et al.*[(10)],** FNAC was performed in 60 patients. No malignant cells were found in 81.67%. A total of 10% of aspirates showed signs of malignancy, whereas 3.33% aspirates were suspicious for malignancy, which were later confirmed on histopathology as papillary and follicular carcinomas. In 5%, the aspirates were inadequate and a decision could not be made on FNAC. The benign aspirates (49) were adenomatous colloid goiter (71.5%), follicular adenoma (8.2%), toxic adenoma (8.2%), simple cysts (6.1%), Hashimoto's thyroiditis (2%), tuberculosis (2%), and abscess (2%). The malignant aspirates (six cases) were papillary carcinoma (50%), follicular carcinoma (16.7%), medullary carcinoma (16.7%), and anaplastic carcinoma (16.7%).

In this study, FNAC was uninformative in 4 out of 20 (20%) cases, which were reported as hyperplastic follicular cells (10%), colloid with cells uspicious of papillary thyroid carcinoma (indeterminate) (5%), and Hurthle cell tumour (5%). Owing to these limitations, we could not establish a definite diagnosis in follicular lesions (which required a histopathological examination for capsular and vascular invasion) or in hemorrhagic aspirates. We also could not confirm the presence of malignancy in suspicious aspirates or establish an accurate diagnosis in insufficient aspirates taken from cystic lesions as thyroglossal duct cysts and papillary cystadenoma.

In an attempt to overcome the different limitations of FNAC in this work, we considered the following: Fine-needle aspiration biopsy is the most useful diagnostic modality and is currently considered essential in the workup of any thyroid nodule. Significant experience exists in both the technical aspects and the cytological interpretation of the specimens. An accurate diagnosis useful for the physician responsible for the final management relies on a number of factors. It is vital to obtain a specimen that allows proper interpretation of the cellular and architectural contents. By the use of sonar-guided and multiple FNAC examined by two different pathologists[(12)].

Finally comparison of the results of FNAC with histopathology will eventually lead to a better understanding of the results of FNAC and a better diagnosis.

Cibas and Ali [(13)] reported that the main limitation of FNAC is hypocellular aspirates and aspirates with high follicular cellularity. Hypocellular aspirates may be observed in cystic nodules or they may be related to the biopsy technique. Aspirates characterized by high follicular cellularity suggest follicular neoplasm; however, FNAC cannot be used reliably to distinguish a benign follicular neoplasm from a malignant neoplasm [(14)].

In our work, false-positive results were obtained on FNAC examination in 0%, whereas false-negative results were obtained in 10% of cases. This false-negative cases were diagnosed as: the first case was diagnosed as colloid goiter suspicious for malignancy and the final histological diagnosis was papillary thyroid carcinoma, and the other case was diagnosed as Hurthle cell adenoma by FNAC and the final histological diagnosis was Hurthle cell carcinoma.

The rate of false-negative cytologic results ranged from1 to 6% percent in a similar study carried out by **Caruso and Mazzaferri** [(15)], and this was mainly because of sampling errors or misdiagnosis. These problems can be minimized by obtaining multiple specimens or using ultrasonographically guided needle biopsy. Three to 6% of cases may be falsely positive often because of Hashimoto's thyroiditis.

In our study, histopathological results showed benign/ non-neoplastic lesions in 55 % of cases and malignant lesions in 45 % of cases. These results are in agreement with those of **Aimel *et al.*[(10)]** who reported that86.67% benign lesions and 13.33% malignant lesions. In addition to these results, **Bakhos *et al.*[(16)]** have reported that the majority of surgically removed

thyroid nodules were nonneoplastic; only 5–30% were malignant.

In this study, benign/non-neoplastic lesions (55%) were classified as follows: colloid nodules (25%), follicular adenoma (15%), Hurthle cell tumour (10%), and simple cyst (5%) of total number of cases. Malignant lesions (45%) were classified as follows: papillary carcinoma (35%) , Hurthle cell carcinoma (5%), and medullary thyroid carcinoma (5%) of total number of cases.

Aimel *et al.*[(10)] have reported that the benign lesions(52 cases) indicated adenomatous colloid goiter (69.23%), follicular adenoma (11.53%), Hashimoto's thyroiditis(1.92%), simple cyst (5.77%), abscess (1.92%), toxic adenoma (7.69%), and tuberculosis (1.92%). The malignant lesions (eight cases) showed papillary carcinoma (50%), follicular carcinoma (25%), anaplastic carcinoma (12.5%), and medullary carcinoma (12.5%).

CONCLUSION

Fine-needle aspiration biopsy (FNAB) is the most useful investigational tool in the evaluation of solitary thyroid nodules. The four widely accepted diagnostic categories of FNAB are malignant, benign, indeterminate, or "suspicious" (i.e., suspect) for malignancy. But it has some limitations in the diagnosis of hyperplastic follicular cells, hemorrhagic aspirate, and suspicious and nondiagnostic (insufficient) aspirates. Histopathological study provides a more conclusive diagnosis and overcomes these limitations.

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