

Diagnostic accuracy of Fine Needle Aspiration Cytology of thyroid lesions along with histopathological correlation. A 3-year retrospective study

Mohammed Hussain Mohsen Al Munajjim¹, Nasher Hussein Hassan Alyami², Naif Mana Mohammed Alaqil³, Hadi Manasar Marzoq Alsalaia⁴, Fahad Ali Abdullah Al Monajam⁵, Abdullah Mohsen A Althayrayan⁶

¹*Histopathology Specialist, King Khalid Hospital, Ministry of Health, Najran Region, KSA*

²*Consultant Diagnostic Hematologist and Geneticist, Ministry of Health, Najran Region, KSA*

³*Medical laboratory specialist, Ministry of Health, Najran Region, KSA*

⁴*Laboratory Specialist, Ministry of Health, Najran Region, KSA*

⁵*Laboratory Technician, Ministry of Health, Najran Region, KSA*

⁶*Medical laboratory specialist, Ministry of Health, Najran Region, KSA*

Abstract

Background: Among endocrine malignancies, thyroid carcinoma is by far the most frequent. Approximately 5 to 15 percent of all thyroid nodules have been found to be cancerous in recent years. The results of a cytology test can help doctors determine the best course of therapy for their patients, including surgery. There has been a great deal of research into the accuracy of FNAC in diagnosing thyroid cancer.

Objectives: Diagnose thyroid FNAC lesions according to the Bethesda approach and compare them with histological diagnoses to establish diagnostic value and accuracy.

Materials and Methods: This is a three-year retrospective research conducted at the King Khalid Hospital in Najran. Data including demographics, FNAC report and histopathological diagnosis was collected from the hospital records. Thyroid cytology was classified into six categories based on the Bethesda system and histopathological correlation was done. Calculations were performed to determine the diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value.

Results: The average age was 36.6 ± 11.9 years, ranging from 16 to 83 years.. Females made up 91.5 percent of the sample, having a male-female ratio of 1:10. There were 24 (29.3%) Bethesda category II lesions, 28 (34.14%) Bethesda category IV lesions, and the least 2 Bethesda category III lesions (2.4 percent). On FNAC, 12 (14.63 %) of the lesions were malignant. There was a 92.4 percent sensitivity, 68.9 percent specificity, 84.5% positive predictive value (PPV), 83.3% negative predictive value (NPV), and an accuracy of 84.1 percent for FNAC validity.

Conclusion: This study found that in FNAC thyroid the sensitivity and specificity are both satisfactory and our findings are comparable. The Bethesda Tiered Diagnostic System is a great tool for diagnosing and managing thyroid lesions. Cytopathologists should be mindful of potential diagnostic pitfalls, which can be minimized even more if aspirates are acquired under USG supervision.

Keywords: *Fine Needle Aspiration Cytology (FNAC), Diagnostic.*

Introduction

Thyroid disorders are significant because the majority of them respond to medicinal and surgical intervention (Omer, 2020). The most prevalent type of endocrine cancer is thyroid cancer (Mistry et al., 2011). The likelihood of having a thyroid nodule is estimated to be 10%. Each year, approximately 275,000 thyroid nodules are detected, with approximately 1400 of them developing into thyroid cancer. Malignant nodules are more common in patients younger than 20 and older than 60. (Khan et al., 2012). Adults are affected by thyroid cancer, usually papillary carcinoma, with a female preponderance. In recent years, it has become more common, with 5-15 percent of thyroid nodules being confirmed as malignant (Bahaj et al., 2021). (Mistry et al., 2011). A newly found palpable nodule or a rise in the size of an existing nodule are the most prevalent symptoms of thyroid cancer (Mistry et al., 2011).

In accordance with the recommendations of the American Thyroid Association and the National Comprehensive Cancer Network, first-line diagnostics should include fine needle aspiration cytology (FNAC) due to its high diagnostic reliability and cost-effectiveness. (Omer, 2020). Thyroid FNAC is the first line of defense in any thyroid lesion due to its ability to discriminate between persons who require surgery for a malignant condition and those who have a functional/inflammatory abnormality that may be addressed medically (Raina et al., 2021).

According to studies, FNAC has a high sensitivity and specificity for predicting thyroid cancer (Mistry et al., 2011). and it delivers the most specific and clear information regarding the thyroid. Approximately 50% fewer thyroidectomies are performed when FNAC is utilized (Bhise et al., 2020).

While most benign and simple malignant lesions are straightforward to diagnose, diagnostic difficulties arise when aspirates are qualitatively or quantitatively insufficient to exclude a neoplastic process (Alshaikh et al., 2018). FNAC can't tell benign from malignant

follicular neoplasms. (Hajmanoochehri & Rabiee, 2015). FNAC has some drawbacks, including inadequate specimens, collection procedures, concerning histologic changes subsequent to thyroid fine-needle aspiration and false-negative and false-positive results (Sharma, 2016). The goal of cytologic or pathological examination reports is to offer professionals with suitable treatment guidelines for patients, including surgery (Yoo et al., 2013). Pathologists, endocrinologists, radiologists, and surgeons must communicate clearly regarding thyroid cytopathology. Consistent and reproducible diagnostic terminology is therefore of the utmost significance (Alshaikh et al., 2018)

In 2007, the Bethesda system for reporting thyroid cytopathology (TBSRTC) came into being to standardize the nomenclature used in reporting thyroid cytology (Alshaikh et al., 2018) and is comprised of six categories.

1. Unsatisfactory (UNS) or nondiagnostic
2. Benign/nonneoplastic
3. Follicular lesion of undetermined significance /Atypia of undetermined significance (AUS/FLUS)
4. Follicular neoplasm or suspicious for follicular neoplasm (FN/SFN)
5. Suspicious for malignancy(SFM)
6. Malignant

The precision with which FNAC identifies thyroid cancer has been the subject of extensive research, but the TBSRTC has been utilized in few investigations. Few research have looked into the accuracy of FNAC in cancer detection., whereas most studies have excluded some Bethesda categories from their investigations of the overall FNAC accuracy. We chose to examine the diagnostic accuracy of FNAC for all thyroid lesions.

Objectives of the study

1. To classify and evaluate thyroid FNAC lesions according to the Bethesda system and

compare them to histopathological diagnoses in order to determine diagnostic value and accuracy.

Methodology

A three-year retrospective research was conducted. A retrospective evaluation of data collected from thyroid swellings patients at King Khalid Hospital in Najran city between 2018 and 2021 was done. Najran City's Institutional Review Board (KACST) gave its clearance to the research (Protocol number 29-03-2022, registration number H-11-N-081). Before undergoing FNAC at our facility, all patients were required to provide their written informed consent in order to have the treatment. Age, gender, FNAC findings, and histopathology results were all gathered using a data collecting form. This form was also used to obtain demographic data.

Criteria for incorporation were the accessibility of records of patients with thyroid swelling between 2018 and 2021 which was conducted at King Khalid Hospital in Najran city and who had FNAC, and histopathology reports endorsed by a qualified specialist cytopathologist. We avoided all cases with incomplete data including fragmented FNAC or histopathology reports.

Fine-needle aspiration cytology: Under ultrasound guidance, a 23-gauge needle with a 20 ml disposable syringe was utilized, and a minimum of three tissue passes were performed to get adequate samples. All thyroid FNA samples were processed using standard methods, such as air-dried smears stained with a Romanowsky-type stain/diff-quick stain or 95 percent ethanol-fixed smears stained with a Papanicolaou stain. The Bethesda approach

was used to categorize thyroid cytology into six categories.

Statistical Evaluation: SPSS (Statistical Package for the Social Sciences) version 23 was used to analyze the data. Mean, standard deviations, median, and range were used to depict quantitative data. The chi-square test was used to compare categorical variables based on their absolute frequencies and percentages. The odds ratio was used to compare the occurrence of thyroid cancers in men and women. The Kappa agreement was used to assess the similarity of the two diagnostic instruments (inter-rater reliability). To compare the ages of neoplastic and non-neoplastic lesions, the Mann-Whitney test was used (non-parametric test). SPSS 23.0 was used to calculate sensitivity, specificity, accuracy, and positive and negative predictive values. The results were considered statistically significant when the significant probability was less than 0.05 (P 0.05).

Observations and Results

FNAC reviewed 85 cases, of which 82 thyroid patients with confirmed accessible histopathological diagnosis were included in the study group. The 3 cases that were excluded were categorized on FNAC as unsatisfactory or category I lesions and no surgical follow-up was available. The average age was (36.6 ±11.9) years, with ages ranging from 16 to 83. There were 7 (8.5%) men and 75 (91.5%) females, for a male to female ratio of 1:10.. Bethesda category II comprised 24 (29.3%) lesions, category IV lesions comprised 28 (34.14%), and Category III lesions comprised the least 2 (2.4%). 12 (14.63%) were malignant lesions on FNAC (Table 1).

Table 1: Descriptive data of the studied group

Characteristics	The studied group
	NO. = 82 (%)
Age (years) <i>Mean ± SD</i> <i>Range</i>	36.6 ± 11.9 (16-83)

Sex	<i>Male</i>	7 (8.5%)
	<i>Female</i>	75 (91.5%)
Bethesda system	<i>II</i>	24 (29.3%)
	<i>III</i>	2 (2.4%)
	<i>IV</i>	28 (34.15%)
	<i>V</i>	16 (19.5%)
	<i>VI</i>	12 (14.6%)

There were 19 cases of goiter, 3 cases of colloid cyst, and 2 cases of Hashimoto's thyroiditis among the benign and non-neoplastic category. Furthermore, there were two cases in the AUS/FLUS group..(Table 2, Figure 1)

Table 2: Distribution of FNAC diagnosis across Bethesda categories

FNAC Diagnosis	Bethesda category	Number	Percentage
Nodular colloid goiter	II	10	12.19 %
Multinodular goiter	II	9	10.97 %
Colloid cyst	II	3	3.65 %
Hashimoto's thyroiditis	II	2	2.43 %
Atypia of undetermined significance	III	2	2.43 %
FN/SFN	I V	28	34.14 %
SFM	V	16	19.51 %
Papillary carcinoma	VI	12	14.63 %
Total		82	100 %

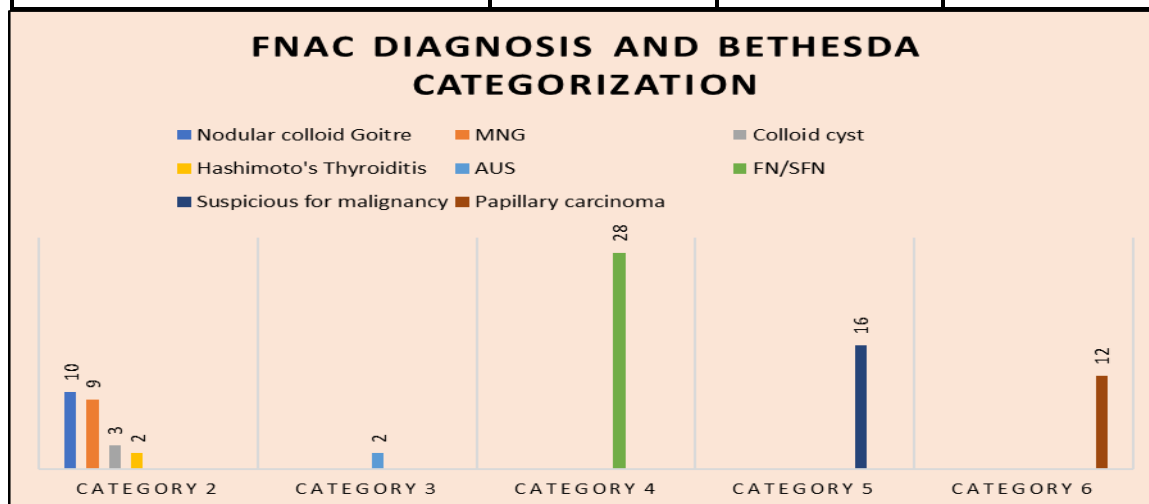


Figure 1: FNAC diagnosis and Bethesda categorization

Histo-pathological confirmation revealed overall 35 (42.68%) malignant cases, 18 (21.95%) benign neoplasms and 29 (35.36%) benign non neoplastic lesions. (Table 3; Figure 2)) Nodular Goiter was the commonest benign

non-neoplastic lesion (17.03%). The most prevalent benign neoplasm was follicular adenoma (15.85 percent), and the most common malignant neoplasm was papillary carcinoma (37.8 percent).

Table 3: Frequency distribution of histo-pathological diagnosis

Histopathological diagnosis	Number	Percentage
Colloid nodular goiter	10	12.19%
Nodular hyperplasia	11	13.41%
MNG with hyperplasia	4	4.8%
Hashimoto's thyroiditis	2	2.43%
MNG	2	2.43%
Hurthle cell adenoma	2	2.43%
Follicular adenoma	13	15.85%
Parathyroid adenoma	0	0
WDT-UMP	1	1.2%
NIFTP	2	2.4%
Follicular carcinoma	3	3.65%
Follicular carcinoma, hurthle cell variant	1	1.2%
Papillary carcinoma	31	37.80%
Total	82	100%

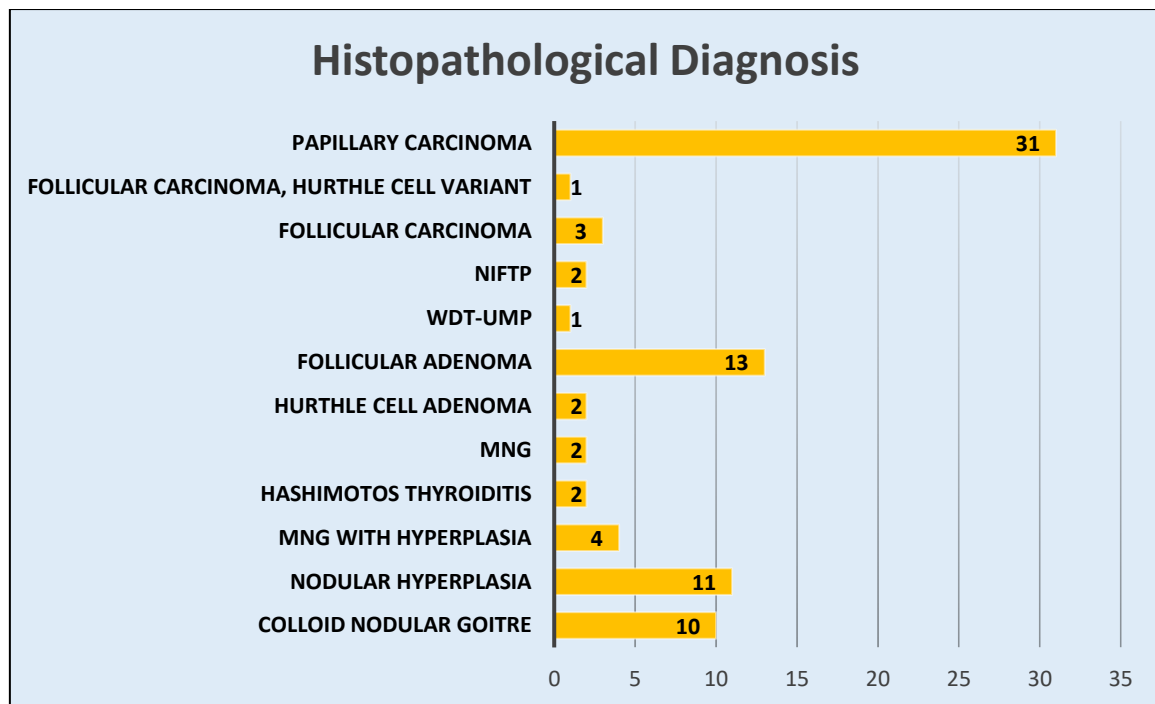


Figure 2: Histopathological diagnosis of study group lesions

Table (4) shows the correlation between FNAC and histopathological diagnosis. There were 4 (4.8%) cases of false-negative diagnoses and 9 (10.9%) cases of a false-positive diagnosis. In the category II lesions, 4 neoplastic lesions were categorized as benign and non-neoplastic. A case of Hashimoto's thyroiditis was reported

as a category III lesion. 7 benign non-neoplastic lesions were misdiagnosed as FN/SFN in category IV. In category V, all cases except one case of nodular hyperplasia showed cytological concordance with histopathology. There was 100% concordance of FNAC with histopathology in category VI.

Table 4: The outcome of thyroid lesion evaluation on histopathology

Bethesda Categories (FNAC)	Histological subtypes	Number of cases	Diagnosis type; True/False
Benign and non neoplastic (II) 24	Colloid nodular goitre	8	TN
	Nodular hyperplasia	7	TN
	Hashimotos thyroiditis	1	TN
	Multinodular goitre with nodular hyperplasia	4	TN
	Hurthle cell adenoma	1	FN
	Follicularcarcinoma	1	FN
	Papillary thyroidcarcinoma	2	FN
AUS/FLUS (III) 2	Hashimoto's thyroiditis	1	FP
	Follicular adenoma	1	TP

Follicular neoplasm/Suspicious for follicular neoplasm (IV) 28	Follicular adenoma	12	TP
	Follicular thyroid neoplasm with papillary like features	1	TP
	Nodular hyperplasia	3	FP
	Nodular goitre	2	FP
	Multinodular goitre	2	FP
	Follicular carcinoma, Hurthle cell variant	1	TP
	Hurthlecell adenoma	1	TP
	Follicular arcinoma	1	TP
	Papillary carcinoma	5	TP
Suspicious for malignancy (V) 16	Thyroid well-differentiated tumor of uncertain malignant potential	. 1	TP
	Follicular carcinoma	1	TP
	Nodular hyperplasia	1	FP
	NIFTP	1	TP
	Papillary carcinoma	12	TP
Malignant (VI) 12	Papillary carcinoma	12	TP

The non-neoplastic group had a statistically significant lower age than the neoplastic group. (P-value=0.02*) In respect to gender, there was

no statistically significant difference between the benign and malignant groups. (P-value=0.9) as shown in (table 5).

Table 5: Univariate analysis of age and sex between neoplastic and non-neoplastic cases.

Characteristics	Neoplastic (Malignant) NO=35	Neoplastic Benign and Non-neoplastic (Benign) NO=47	p-value
Age (years)	39.7 ± 14.2 36 (19-83)	33.7 ± 8.9 35 (16-54)	0.02*^
Sex Male Female	3 (8.6%) 32 (91.4%)	4 (8.5%) 43 (91.5%)	0.99^^

On microscopy, cases of colloid goiter mostly yielded colloid and showed abundant colloid with cystic macrophages. Hashimoto's thyroiditis showed hurthle cell clusters, scant colloid, and impingement of lymphocytes in the thyroid sheets and clusters, few cases however showed florid lymphocytic thyroiditis resembling lymph node. Papillary carcinoma cases revealed the characteristic nuclear changes like optically clear nuclei, nuclear grooves, and intranuclear inclusions. Histopathology shows, characteristic microscopic features with well-formed papillary structures, and nuclear changes. Immunohistochemical marker HBME1 and CK19 was used to confirm and differentiate the follicular variant.

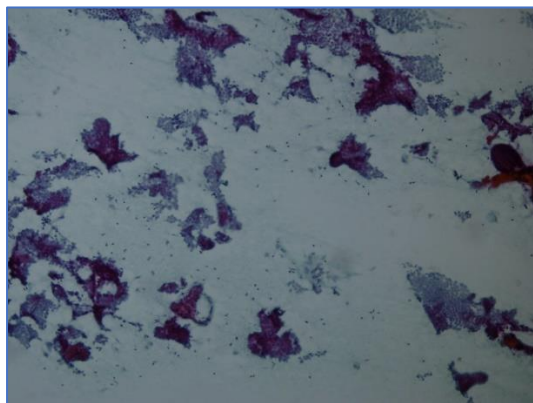


Figure 3: Papillary structures scattered in a background of minimal colloid.(pap 10X)

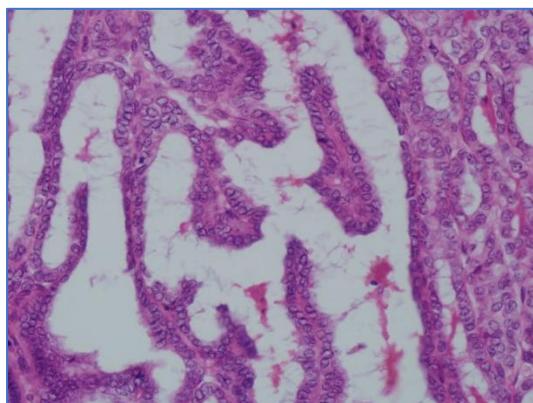


Figure 4: Histopathology of papillary carcinoma showing characteristic nuclear changes. (H & E 40X)

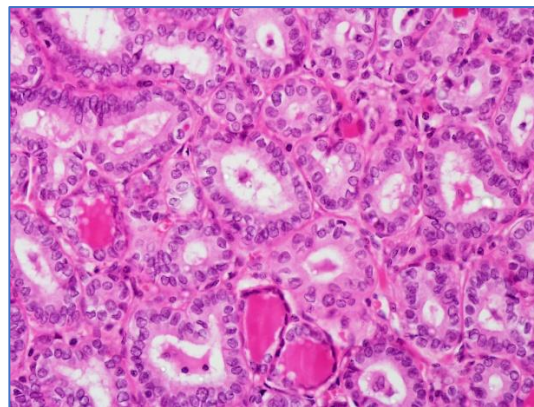


Figure 5: Histopathology of follicular variant of PTC of thyroid. (H & E. 40X)

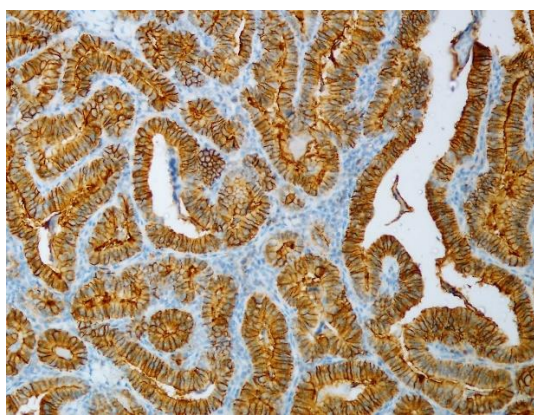


Figure 6: FVPTC showing HBME1 positivity. (40X)

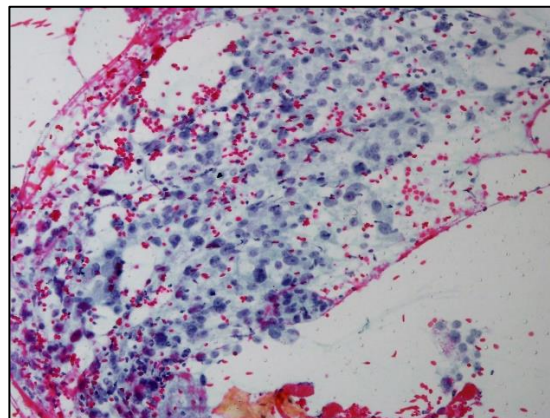


Figure 7: FNAC of thyroid showing clinging of lymphocytes to follicle epithelium and hurthle cell change. (Pap 20X)

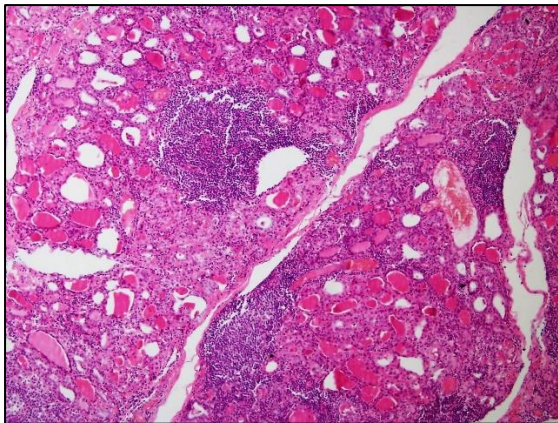


Figure 8: Histopathology of Hashimoto's thyroiditis showing lymphoid aggregates and hurthle cell change. (H & E. 20X)

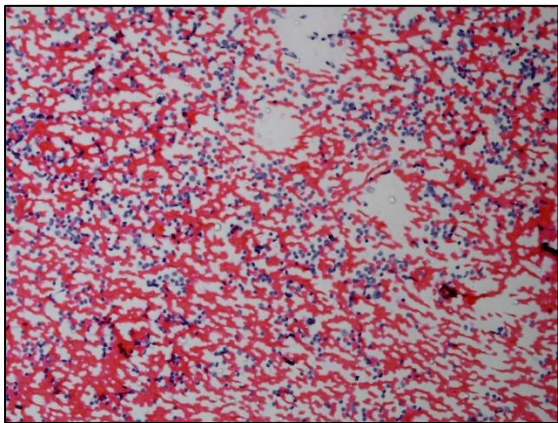


Figure 9: FNAC of Colloid goitre showing cyst macrophages with colloid and hemorrhage (Pap.10X)

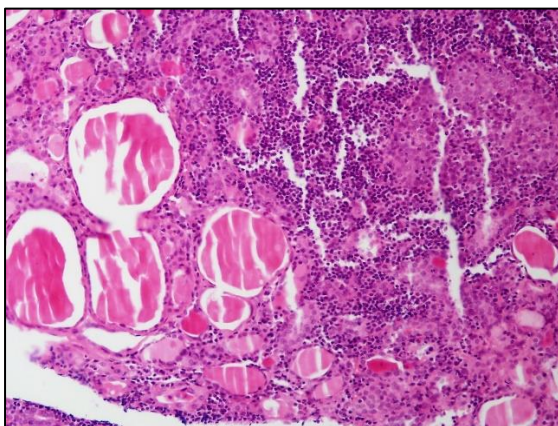


Figure 10: Histopathology of Hashimoto's thyroiditis within a colloid goitre. (H & E.20X)

Table 6 displays the number of cases that are true positive, true negative, false positive, and false negative. The sensitivity, specificity,

positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated.

Table 6: The calculated results of diagnostic accuracy

True positive	49 (59.75 %)
True negative	20 (24.39 %)
False positive	09 (10.9 %)
False negative	04 (4.8 %)
Sensitivity	92.4 %
Specificity	68.9 %
PPV	84.5 %
NPV	83.3 %
Accuracy	84.1 %

Discussion

The goal of FNAC is to find neoplastic nodules that can be surgically removed while avoiding non-neoplastic lesions. For benign categories, the risk of cancer is 0-3 percent; for malignant ones, it is approximately 100 percent (Zhu et al., 2020). 3–16% of individuals who receive a thyroidectomy for a benign condition are discovered to have an inadvertent malignancy (Poller et al., 2008). The study population's mean age was 36.6±11.9 years, with a range of 16-83 years, which is consistent with prior studies (Bahaj et al., 2021). (Bhise et al., 2020). In our analysis, there was a female preponderance, which is consistent with other data (Bhise et al., 2020).

Although category I (Unsatisfactory) lesions were not included in the study population, they accounted for 3 (3.6 percent) of the cases, which is comparable to other published studies (Bahaj et al., 2021). The majority of findings indicate that onsite adequacy assessment reduces the frequency of inadequate FNAC and clinic re-attendance rates for some patients (Poller et al., 2008). Another study recommends performing cell blocks for each instance of FNAC for thyroid lesions, as both procedures improve diagnostic yield and

facilitate precise diagnosis (Raina et al., 2021). The collection of inadequate samples may have been due to technical difficulties, aspiration of a sclerotic or calcified nodule, and nodules with substantial areas of cystic degeneration or necrosis. The introduction of ultrasound-guided FNA has improved sample collection from patients with tiny thyroid nodules that are difficult or impossible to identify on physical exam (Bagga & Mahajan, 2010).

All FNAC in this study was conducted under the supervision of USG. Borget et al. looked at the cost of FNAC as a diagnostic tool in patients with thyroid nodules and discovered that routine USG and on-site cytopathological adequacy evaluation could help reduce costs in the future. (Borget et al., 2008)

The outcome of FNA in our study was 29.3 percent benign and 14.6 percent malignant. Goiter was the most common benign lesion, whereas papillary carcinoma was the most common malignancy. Other investigations have found a similar pattern, with multi-nodular goiter being the most prevalent lesion and malignant lesions accounting for 13.5 percent to 67 percent (Kaur & Gupta 2021 ,Bahaj et al., 2021, (RAINA et al., 2020, Schlumberger, 1998).

On histological confirmation, the number of malignant lesions increased significantly. This is owing to the diagnosis of category IV and category V lesions as malignant. Papillary carcinoma was the most prevalent malignant tumor, accounting for 31 (37.80%) cases. This is consistent with prior research (Bahaj et al., 2021) (Afroze et al., 2002).

Overall, there were 9 false-positive diagnoses and 4 false-negative diagnoses (11.9% and 4.8%, respectively).. It is also known that some thyroid diseases have similar cytological features, which makes diagnosis very hard (Howlett et al., 2007). False-negative FNAC results can happen because of a mistake in the sample or a wrong interpretation of the cytology. This is very worrying because it means that a cancerous lesion could be missed (Bagga & Mahajan, 2010). Results for the false-positive rate range from 0 to 9 percent.

(Hajmanoochehri & Rabiee, 2015), (Liel et al., 2001). Other studies have found that 23 (38.1 percent) of the 62 incorrect results were due to specimen difficulties, while 39 (61.9%) were due to misinterpretation errors. (Zhu et al., 2020). 13 of the 23 specimens were incorrectly sampled, and 10 of the specimens were defective. Most false-positive diagnoses stemmed from sample errors, whereas the vast majority were caused by misinterpretation of results (80.9 %). 3-6 percent of cases may frequently be mistakenly positive due to Hashimoto's thyroiditis (Elsawy et al., 2019)

Three of the cases in category II turned out to be cancerous. They were missed because the lesions were large and multi-nodular, and malignant foci were not sampled on FNAC. Similar false-negative results have been found in previous research, with sampling error due to large-sized lesions being one of the contributing causes (Hajmanoochehri & Rabiee, 2015). (Sandhyalakshmi et al., 1998). According to the Bethesda system for reporting thyroid cytology, the predicted incidence of cancer in cytological benign nodules is 0-3 percent (Megwalu et al., 2017).

A case of Hashimoto's thyroiditis was included in AUS. Another instance of follicular adenoma classified as AUS was confirmed. Subjective cytomorphological interpretation of AUS (Kaur & Gupta, 2021). According to the Bethesda system, "the risk of malignancy for an AUS nodule is difficult to quantify". The probability of cancer is almost certainly between 5 and 15 percent (Garg et al., 2017). Cytologists should aim to better categorize "atypical follicular cells" and explain each patient's genuine risk of cancer in order to improve patient treatment and care (Garg et al., 2017). In multidisciplinary clinical settings, subclassification of AUS/FLUS might affect patient follow-up regimens and provide advise for a repeat FNA or surgery (Garg et al., 2017). If papillary microcarcinoma develops in Hashimoto's thyroiditis or in other benign lesion, the aspirated sample may not be indicative of the actual lesion because FNAC is a blind process (Sharma, 2016).

In this investigation, six cases of FN/SFN were found to be papillary carcinomas, with one of these cases being a follicular variant of papillary carcinoma. In low cellularity smears, the existence of follicular variants as well as minor or localized nucleus alterations may be to blame.

Additional research shows that 68% of patients classified as follicular neoplasm were papillary carcinoma, showing a large overlap between benign and malignant (Yang et al., 2007). The cytological diagnostic rate of Follicular neoplasm was roughly 10%, according to research (Yoo et al., 2013). Follicular carcinoma, hurthle cell variant of follicular carcinoma, and hurthle cell adenoma were all found in our study, along with 12 cases of FN/SFN adenomas. Our findings are in line with those of previous studies (Kaur & Gupta, 2021). When benign, atypical and follicular neoplasm cytology classifications require additional clinical evaluation and strict monitoring (Mayooran et al., 2016) In FVPTC, nuclear PTC features are rare (Shih et al., 2005). (1992, Harach & Zusman). Due to the absence of nuclear alterations in papillary carcinoma, the cytological diagnosis of FVPTC differs. Consequently, FNA has a low sensitivity for establishing a diagnosis of FVPTC (Kesmodel et al., 2003)

Follicular neoplasm presents two difficulties: the inability to identify the tumor's nature and the more recent difficulty in separating papillary follicular subtype (Del Rio et al., 2011). Cytology identifies neoplastic characteristics in follicular carcinoma, resulting in the suspicious diagnostic category SFN (Kaur & Gupta, 2021).

In our investigation, 16 cases (19.51 percent) were classified as SFM. There were many

papillary structures in Category 5 FNAC, as well as a few cells with nuclear grooves and inclusions, but no real papillae. They were included in SFM since it was difficult to classify them as actually malignant. Because the risk of malignancy was so high in suspicious lesions, surgical excision of the nodules should be considered in these cases (Bagga & Mahajan, 2010). (Mundasad et al., 2006). Clinicians refer to the three AUS, SFN, and SFM thyroid FNAC categories as ambiguous thyroid FNAC categories since they are associated with well-defined malignancy risk (Kaur & Gupta, 2021). Inadequate fluid collection or aspiration in cystic thyroid lesions with underlying malignancy causes false-negative diagnosis. PTC also exhibits the most hemorrhagic degenerative changes. Hemorrhagic fluid with few tumor cells could be mistaken for a benign cyst (Nguyen et al., 2005) There were 12 cases described as malignant in category VI, and histology was 100 percent consistent in this category. Naz S et al. (Naz et al., 2014) showed a 100% concordance in Bethesda 5 and 6 categories, while Park et al. (Park et al., 2016) found a 98.9% incidence of cancer in category 6.

Our analysis found that the frequency of diagnosis for each Bethesda category is within the ranges found in other studies (table 7) The comparison of thyroid histology and FNAC findings requires consistent inclusion and exclusion criteria. It is hard to compare thyroid FNAC values between institutions without this (Poller et al., 2008) In comparison to small cohorts, studies with big cohorts have revealed a higher frequency of category 1 cases (inadequate/non-diagnostic) (Alshaikh et al., 2018).

Table 7: Comparison of FNAC results across studies

Bethesda Category	Our study	Kapila et al;2015	K et Sinna EA et al; 2012	Melo Uribe MA et al;2015
I	-	4.8%	7.1%	4.1%
II	29.3%	30.5%	33.1%	23.5%

III	2.4%	15.8%	13%	2%
IV	34.14%	4.5%	16.55	16.8%
V	19.5%	21.4%	10.1%	37.2%
VI	14.6%	23%	19.5%	16.2%

A comparison of FNA cytology results against a gold standard the histopathological diagnosis provided a measure of FNAC usefulness (Jammah et al., 2012)

83.33%, and 84.14%. Our findings are comparable to a few other studies (Table 8) whereas some studies have reported a very high specificity and sensitivity.

Our study's sensitivity, specificity, PPV, NPV, and accuracy were 92.4%, 68.9%, 84.4%,

Table (8); Some studies have reported a very high specificity and sensitivity.

es	Sensitivity	Specificity	PPV	NPV	Accuracy
Hajmanoochehri et al; 2015	95.2%	68.4%	83.3%	89.6%	85.14%
Muratli A et al; 2014	87.1%	64.6%	76.1%	79.5%	77.3%
Bahaj AS et al; 2020	79.8%	82.1%	74.8%	85.9%	74.8%
Roy PK et al; 2019	81.5%	95.3%	84.6%	94.2%	99.6%
Present study	92.4%	68.9%	84.4%	83.3%	84.1%

The sensitivity and specificity of thyroid FNAC range from 65 to 99 percent, respectively (Yoo et al. 2013; BHATTI et al. 2011). (Safirullah, et al., 2004). The diagnostic accuracy of FNAC varies from series to series and partly depends on how the data are analyzed.

Pathologists' handling of the "suspect" category and their definitions of false positive and false

negative results are the primary causes of the wide range of sensitivity and specificity (Esmaili & Taghipour, 2012). Follicular lesions may be considered malignant or neoplastic by some authors. There are those who count this as a negative, but there are those who do not (Chang et al., 1997) (Mazzaferrri, 1993). In FNAC, overlapping cytological characteristics

among follicular-derived lesions and inadequate/suboptimal specimens were the most significant reasons of diagnostic misunderstanding (Yoo et al., 2013). Clinically problematic tumors should be followed and likely removed despite benign cytology (Sharma, 2016). The issue is frequently observed with follicular lesions and is consequently frequently accountable for inaccurate FNAC (Kopald et al., 1989).

FNAC's failure to discriminate follicular hyperplastic nodules and adenoma from well-differentiated follicular cancer results in a high "suspicious category" rate (Esmaili & Taghipour, 2012). FNAC was more accurate than adenoma at diagnosing invasive thyroid cancer (Vasudev et al., 2014). According to Cibas and Ali (Cibas & Ali, 2009), hypocellular aspirates and aspirations with high follicular cellularity are the primary limitations of FNAC. High follicular cellularity in aspirates suggests follicular tumor; nevertheless, FNAC cannot be utilized effectively to discriminate between benign and malignant follicular neoplasms (Raparia et al., 2009).

Limitations

Our research has some limitations. We performed a retrospective analysis at a single center, which may have resulted in a selection bias. In addition, the sample size is modest.

Conclusion

FNAC is the best way to detect benign from malignant thyroid nodules in the early stages of their development. The Bethesda technique was used to define the cytological features of thyroid lesions and histology was connected to determine diagnostic accuracy in the current study. The validity of FNAC was judged to be 92.4 percent, 68.9 percent, 84.5 percent, 83.33 percent, and 84.14 percent in terms of sensitivity, specificity, PPV, NPV, and accuracy. Our study's outcomes are consistent. FNAC is sensitive, specific, and precise for preoperative patient evaluation.

A tiered diagnostic system, such as TBSRTC, is a useful tool for thyroid lesion identification and management. Cytopathologists should be aware of potential diagnostic pitfalls, which can be reduced even further if aspirates are taken from multiple parts of the nodule using the USG guided FNA method. Future challenges will include developing simply applicable diagnostic approaches for preoperative assessment that are justified in terms of constrained consultant cytological resources and patient cost/benefit.

Reference

- [1] Afroze N, Kayani N, Hasan SH (2002). Role of fine-needle aspiration cytology in the diagnosis of palpable thyroid lesions. *Indian J Pathol Microbiol.* 45(3):241-6. PMID: 12785159.
- [2] Alshaikh, S., Harb, Z., Aljufairi, E., & Almahari, S. A. (2018). Classification of thyroid fine-needle aspiration cytology into Bethesda categories: An institutional experience and review of the literature. *Cytojournal*, 15.
- [3] Bagga, P. K., & Mahajan, N. C. (2010). Fine needle aspiration cytology of thyroid swellings: How useful and accurate is it?. *Indian Journal of cancer*, 47(4), 437.
- [4] Bahaj, A. S., Alkaff, H. H., Melebari, B. N., Melebari, A. N., Sayed, S. I., Mujtaba, S. S., ... & Alherabi, A. Z. (2020). Role of fine-needle aspiration cytology in evaluating thyroid nodules: A retrospective study from a tertiary care center of the Western region, Saudi Arabia. *Saudi Medical Journal*, 41(10), 1098.
- [5] BHATTI, S. U. Z., Malook, S. U., Tariq, M., & Zulqurnain, A. (2011). FINE NEEDLE ASPIRATION CYTOLOGY: DIAGNOSTIC ACCURACY IN THYROID NODULES. *The Professional Medical Journal*, 18(03), 386-389.
- [6] Bhise, S. V., Shaikh, A., Hippargekar, P. M., & Kothule, S. (2020). A Prospective Study of Ultrasonographic and FNAC Correlation of Thyroid Swellings with Histopathology. *Indian Journal of*

- Otolaryngology and Head & Neck Surgery, 1-7.
- [7] Borget I, Vielh P, Leboulleux S, Allyn M, Iacobelli S, Schlumberger M, et al (2008). Assessment of the cost of fine needle aspiration cytology as a diagnostic tool in patients with thyroid nodules. *Am J Clin Pathol*, 129:763-71.
- [8] Chang H. Y., Lin J. D., Chen J. F. et al, (1997). "Correlation of fine needle aspiration cytology and frozen section biopsies in the diagnosis of thyroid nodules," *Journal of Clinical Pathology*. 50(12):1005-1009.
- [9]
- [10] Cibas ES, Ali SZ (2009): The Bethesda system for reporting thyroid cytopathology. *Am J Clin Pathol.*, 132:658-665.
- [11] Del Rio, P., Minelli, R., Cataldo, S., Ceresini, G., Robuschi, G., Corcione, L., & Sianesi, M. (2011). Can misdiagnosis in pre-operative FNAC of thyroid nodule influence surgical treatment?. *Journal of Endocrinological Investigation*, 34(5), 345-348.
- [12] Elsayy, M. M., Elhabashy, H. S. E., Soliman, M. A. E., & Ahmed, A. A. M. (2019). Histopathological and Cytological Efficacy in the Diagnosis of Solitary Thyroid Nodules. *The Egyptian Journal of Hospital Medicine*, 75(4), 2653-2660.
- [13] Esmaili, H. A., & Taghipour, H. (2012). Fine-needle aspiration in the diagnosis of thyroid diseases: An appraisal in our institution. *International Scholarly Research Notices*, 2012;4.
- [14] Garg, S., Naik, L. P., Kothari, K. S., Fernandes, G. C., Agnihotri, M. A., & Gokhale, J. C. (2017). Evaluation of thyroid nodules classified as Bethesda category III on FNAC. *Journal of Cytology*, 34(1), 5.
- [15] Hajmanoochehri, F., & Rabiee, E. (2015). FNAC accuracy in diagnosis of thyroid neoplasms considering all diagnostic categories of the Bethesda reporting system: A single-institute experience. *Journal of Cytology/Indian Academy of Cytologists*, 32(4), 238.
- [16] Harach HR, Zusman SB (1992). Cytologic findings in the follicular variant of papillary carcinoma of the thyroid. *Acta Cytol*, 36:142-6.
- [17] Howlett DC, Harper B, Quante M, Berresford A, Morley M, Grant J, et al (2007). Diagnostic adequacy and accuracy of fine needle aspiration cytology in neck lump assessment: results from a regional cancer network over a one year period. *J Laryngol Otol*. 121:571-9.
- [18] Jammah, A. (2012). Evaluation of the Accuracy of Fine-Needle Aspiration Cytology in the Diagnosis of Thyroid Nodules: A Retrospective Analysis of Data From a Tertiary Care Hospital in Saudi Arabia. *Turkish Journal of Endocrinology & Metabolism*, 16(2).
- [19]
- [20] Kapila K, Qadan L, Ali RH, Jaragh M, George SS, Haji BE, et al (2015). The Bethesda system for reporting thyroid fine needle aspiration cytology: A Kuwaiti experience – A cytohistopathological study of 374 cases. *Acta Cytol*, 59:133 8.
- [21] Kaur, A., & Gupta, A. (2021). FNAC of Thyroid Lesions Based on Bethesda System: A Retrospective Cytological Study in a Tertiary Care Centre in North India. *JK Science: Journal of Medical Education & Research*, 23(4).
- [22] Kesmodel SB, Terhune KP, Canter RJ, Mandel SJ, LiVolsi VA, Baloch ZW, et al (2003). The diagnostic dilemma of follicular variant of papillary thyroid carcinoma. *Surgery*, 134:1005-12.
- [23] Khan, T. Z., Baloch, T. A., Ahmad, Z., Hafeez, A., & TASLEEM, Q. U. A. (2012). THE YIELD OF FNAC IN THYROID NODULE. *Medical Channel*, 18(3).
- [24] Kopald KH, Layfield LJ, Mohrmann R, Foshag LJ, Giuliano AE (1989). Clarifying the role of fine-needle aspiration cytologic evaluation and frozen section examination in the operative management of thyroid cancer. *Arch Surg*. 124:1201-5.
- [25] Liel Y, Ariad S, Barchana M(2001). Long-term follow-up of patients with initially benign thyroid fine-needle aspiration. *Thyroid*. 11:775-8.

- [26] Mayoaran, N., Waters, P. S., Kaim Khani, T. Y., Kerin, M. J., & Quill, D. (2016). FNAC and frozen section correlations with definitive histology in thyroid diseases. *European Archives of Oto-Rhino-Laryngology*, 273(8), 2181-2184.
- [27] Mazzaferri E. L. (1993). "Management of a solitary thyroid nodule," *The New England Journal of Medicine*, 328 (8): 553– 559.
- [28] Megwalu, U. C. (2017). Risk of malignancy in thyroid nodules 4 cm or larger. *Endocrinology and Metabolism*, 32(1), 77-82.
- [29] Melo Uribe MA, Sanabria Á, Romero Rojas A, Pérez G, Vargas EJ, Abaúnza MC, et al (2015). The Bethesda system for reporting thyroid cytopathology in Colombia: Correlation with histopathological diagnoses in oncology and non oncology institutions. *J Cytol*, 32:12 6.
- [30]
- [31] Mistry, S. G., Mani, N., & Murthy, P. (2011). Investigating the value of fine-needle aspiration cytology in thyroid cancer. *Journal of Cytology/Indian Academy of Cytologists*, 28(4), 185.
- [32] Mundasad B, Mcallister I, Carson J, Pyper P (2006). Accuracy of fine-needle aspiration cytology in the diagnosis of thyroid swellings. *Internet J Endocrinol*, 2.
- [33] Muratli, A., Erdogan, N., Sevim, S., Unal, I., & Akyuz, S. (2014). Diagnostic efficacy and importance of fine-needle aspiration cytology of thyroid nodules. *Journal of Cytology/Indian Academy of Cytologists*, 31(2), 73.
- [34] Nguyen GK, Lee MW, Ginsberg J, Wragg T, Bilodeau D (2005). Fine-needle aspiration of the thyroid: An overview. *Cytojournal*, 2:12.
- [35] Omer, J. T. (2020). Fine Needle Aspiration Cytology (FNAC) in Thyroid Gland Lesions, How Accurate is it? A Correlation with Histopathology. *Diyala Journal of Medicine*, 19(1), 95-102.
- [36] Park SY, Hahn SY, Shin JH, Ko EY, Oh YL (2016). The Diagnostic Performance of Thyroid US in Each Category of the Bethesda System for Reporting Thyroid Cytopathology. *Troncone. PLoS ONE*, 11(6).
- [37] Poller, D. N., Stelow, E. B., & Yiangou, C. (2008). Thyroid FNAC cytology: can we do it better?. *Cytopathology*, 19(1), 4-10.
- [38] RAINA, U. K., SURI, J., BHARDWAJ, S., & SAHNI, B. (2020). Diagnostic Efficacy of Fine Needle Aspiration Cytology and Cell Block Technique in Thyroid Lesions: A Hospital-based Study. *Journal of Clinical & Diagnostic Research*, 14(11).
- [39] Raina, U. K., Suri, J., Bhardwaj, S., & Sahni, B. (2021). Diagnostic utility of cell block technique as an adjunct to cytological smears in evaluation of thyroid aspirates on fine needle aspiration cytology. *Journal of Natural Science, Biology and Medicine*, 12(1), 6-6.
- [40] Raparia K, Min SK, Mody DR et al. (2009): Clinical outcomes for suspicious category in thyroid fine-needle aspiration biopsy patient's sex and nodule size are possible predictors of malignancy. *Arch Pathol Lab Med.*, 133:787–790.
- [41] Roy PK, Bandyopadhyay S, Dubey AB, Sengupta A (2019). A Comparative Study on Aspiration Cytology and Histopathology in Diagnosis of Thyroid Nodule and Its Correlation. *Indian J Otolaryngol Head Neck Surg*, 71(1):997-1001.
- [42] Safirullah, N. Mumtaz & A. Khan (2004). "Role of fine needle aspiration cytology (FNAC) in the diagnosis of Thyroid swellings," *Journal of Postgraduate Medical Institute*. 18(2):196–201.
- [43] Samreen Naz, Atif Ali Hashmi, Amnakhurshid, Naveen Faridi, Muhammad MuzzammilEdhi, Anwar Kamal, et al (2014). Diagnostic accuracy of Bethesda system for reporting thyroid cytopathology: an institutional perspective. *International Archives of Medicine*, 7:46.
- [44] Sandhyalakshmi B N, Bharath Reddy H, Srinivasamurthy V (20Schlumberger MJ (1998)). The Bethesda System of Reporting Thyroid Lesions: A Tertiary

- Care Centre Perspective. *International Journal of Contemporary Pathology*, 3(2).
- [45] Schlumberger MJ (1998): Papillary and follicular thyroid carcinoma. *N Engl J Med*.338:297-306.
- [46] Sharma, C. (2016). An analysis of trends of incidence and cytohistological correlation of papillary carcinoma of the thyroid gland with evaluation of discordant cases. *Journal of Cytology*, 33(4), 192.
- [47] Shih SR, Shun CT, Su DH, Hsiao YL, Chang TC (2005). Follicular variant of papillary thyroid carcinoma: Diagnostic limitations of fine needle aspiration cytology. *Acta Cytol*, 49:383-6.
- [48] Sinna EA, Ezzat N (2012). Diagnostic accuracy of fine needle aspiration cytology in thyroid lesions. *J Egypt Natl Canc Inst*, 24:63 70.
- [49] Vasudev, V., Hemalatha, A. L., Rakhi, B., & Githanjali, S. (2014). Efficacy and pitfalls of FNAC of thyroid lesions in children and adolescents. *Journal of Clinical and Diagnostic Research: JCDR*, 8(1), 35.
- [50] Yang J, Schnadig V, Logrono R, Wasserman PG (2007). Fine-needle aspiration of thyroid nodules: A study of 4703 patients with histologic and clinical correlations. *Cancer*, 111:306-15.
- [51] Yoo, C., Choi, H. J., Im, S., Jung, J. H., Min, K., Kang, C. S., & Suh, Y. J. (2013). Fine needle aspiration cytology of thyroid follicular neoplasm: cytohistologic correlation and accuracy. *Korean Journal of Pathology*, 47(1), 61.
- [52] Zhu, Y., Song, Y., Xu, G., Fan, Z., & Ren, W. (2020). Causes of misdiagnoses by thyroid fine-needle aspiration cytology (FNAC): our experience and a systematic review. *Diagnostic pathology*, 15(1), 1-8.