Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 10, 2023

Original research article

Role of fine needle aspiration cytology and frozen section in the diagnosis of thyroid swelling: A retrospective study

[1]Dr. Vinila Belum Reddy, [2]Dr. M Naveen Kumar, [3]Dr. S Vanajakshi, [4]Dr. I Hariharan, [5]Dr. B V Haricharan, [6]Dr. Manimekhala, [7]Dr. Neeti, [8]Dr. Anvi K Reddy, [9]Dr. Sakshi Kawatra

[1]Associate Professor, Department of Pathology, Apollo Institute of Medical Science & Research, Hyderabad, Telangana, India

[2,3,4,9]Assistant Professor, Department of Pathology, Apollo Institute of Medical Science & Research, Hyderabad, Telangana, India

[6]Professor, Department of Pathology, Apollo Institute of Medical Science & Research, Hyderabad, Telangana, India

[7,8]MBBS Student, Apollo Institute of Medical Science & Research, Hyderabad, Telangana, India

Corresponding Author:
Dr. Vinila Belum Reddy

Abstract

Introduction: Fine Needle Aspiration Cytology (FNAC) has for long been a useful, cheap and safe procedure in preoperative evaluation of thyroid lesions. Frozen sections on the other hand can confirm the FNAC diagnosis and it also serves as an intraoperative guide to decide the extent of the thyroid surgeries. The choice of the diagnostic method used is vital because of its implications on the medical and surgical management and the quality of the outcome.

Aim: The purpose of this study will be to compare the result obtained by FNAC and frozen section of the thyroid to the final histopathological diagnosis, in order to establish their role in evaluation of thyroid lesions and their role in surgery.

Materials and Methods: This four year retrospective study was conducted between Jan 2019 to July 2023. All patients undergoing both FNAC and frozen sections for thyroid lesions.
were included in the study. Descriptive statistics was applied to draw conclusions. Sensitivity, specificity, and diagnostic accuracy were calculated for both FNAC and frozen sections.

Results: A total of 30 patients met the inclusion criteria with 26 females (86.67%) and 4 males (13.33%). The average age was 42.2 ± 14.4 years. The overall malignancy rate among the nodules included in the study was 20% (n=6). The sensitivity and Accuracy in our study was similar to available literature with FNAC having a sensitivity of 71.43% and accuracy of 93.3%, whereas the Frozen section showed a sensitivity of 85.7% and accuracy of 96.67%.

Conclusion: In the present study, frozen sections had better sensitivity and accuracy compared to FNAC in thyroid lesions. Better sample size will give us a better insight regarding the advantage and added benefit of the Frozen section over FNAC.

Keywords: Needle aspiration cytology, frozen section, diagnosis of thyroid swelling

Introduction

Thyroid swellings are very common in the general population, affecting women more commonly than men. Although palpable thyroid nodules concern 4 to 7% of the general population, this prevalence can exceed 50% on high-resolution neck ultrasound. Only 10% of these nodules correspond to thyroid carcinoma, which is detected two to four times more frequently in women [1-2]. The annual incidence of thyroid carcinoma is 0.5 to 10 cases per 100,000 inhabitants, corresponding to papillary carcinoma in 70 to 85% of cases, follicular carcinoma in 5 to 10% of cases, medullary carcinoma in 5% of cases, and poorly differentiated or undifferentiated carcinoma in less than 5% of cases [1]. The 10-year relative survival ranges from 98% for papillary carcinoma to 13% for undifferentiated carcinoma. The recurrence rate increases with the size of papillary carcinoma. Classical favorable prognostic factors are: women under the age of 40, well differentiated papillary carcinoma with a lesion less than 2 cm strictly confined to the thyroid with no metastases [1].

According to recent population studies conducted in South India, thyroid swellings are detected in 12% of adults [3]. In India, thyroid carcinoma was found to account for 2% of all male carcinoma and about 5-6% of carcinomas in women [4]. Thyroid glands' superficial location makes it easily amenable to direct physical examination, Fine Needle Aspiration, and surgical biopsy. However, the aim of appropriate investigations and management is not only to evaluate for the cause of the swelling but more importantly, to rule out malignancy of the thyroid gland [4, 5].

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 10, 2023

The importance of classification of thyroid swellings into benign and malignant swellings is to decide the best approach for management of the patient. Accurate screening and diagnostic tools are needed to correctly diagnose these patients with malignancy. The importance of finding the best suited investigatory methods lies in the fact that not all patients with thyroid swelling require surgery. Among the patients that do require surgery, the results of the investigations play a large role in determining the extent of thyroid removal surgery. Hence, these tests play a large role in deciding the management plan for the patient [6, 7].

Fine needle aspiration cytology (FNAC) is a useful tool to detect the pathology of the thyroid gland as it is a simple, quick, and affordable procedure that can be done in the outpatient setting. This has become a standard compulsory procedure before any thyroid surgery. The main utility of FNAC is in its ability to distinguish between benign and malignant lesions, as well as classify the swelling in terms of its etiology [6, 7, 8]. FNAC is found to be a highly specific test, but it may not be the most sensitive test as it has a large number of false negatives. A larger number of false negatives can mean that clinicians may miss out on potentially malignant cases leading to higher rates of mortality due to thyroid malignancies. Furthermore, patients who are found to have a false positive result will have unnecessarily undergone extensive surgical procedures associated with an increased risk of complications. On several occasions it may report results which may be indeterminate or suspicious [9,10]. Shortcomings of FNAC can be frequently noticed in its inability to differentiate follicular lesions into benign and malignant pathology [2, 6]. It is found that Hashimoto thyroiditis is one of the most commonly misdiagnosed swelling in the thyroid, and follicular and hurthle cell adenomas are wrongly classified as papillary carcinomas on numerous occasions [10, 11, 12].

Also, FNA has limitations in diagnosing cystic lesions with malignancy, lymphomas occurring in the background of Hashimoto's thyroiditis, focal lesions, conditions where dominant non-neoplastic lesions obscures a small carcinoma.

To overcome the limitation of FNA, to differentiate benign lesions from malignant lesions and to determine the extent of surgery many surgeons perform intra operative frozen sections. Since its introduction in 1891 by William H. Welch, and use of cryostat in the 1960s FS is one of the popular methods for rapid diagnosis to guide the surgeon in intra operative decision making. The intra operative frozen section involves careful gross examination and microscopic analysis. Intraoperative Frozen sections are justified when the diagnosis of malignant neoplasm will alter the course of surgery and when the operating surgeon intends to perform a more extensive surgery. A frozen section can aid in the differentiation of benign and malignant swellings in situations where FNAC results were found to be inconclusive, hence enabling the surgeon to decide whether to follow through with a complete thyroidectomy or not [13, 14]. This can benefit the patient as it reduces the need for a follow-up surgery if diagnosed as malignant.

As far as the frozen section in thyroid is concerned it can reliably diagnose papillary, medullary and anaplastic thyroid carcinoma. Its utility in follicular neoplasm is most debatable. The cost effectiveness of FS has been debated much in literature. Though it is a valuable tool in the diagnosis of the thyroid lesion and determining the extent of thyroid surgery, still in certain cases diagnosis can be incorrect or inconclusive, so histopathology of the excised specimen remains the most reliable test. Histopathology can undoubtedly identify basic tumor features required for staging of thyroid carcinoma. It also gives valuable information regarding the status of the resected lymph node status and can provide definitive proof regarding the type of tumors affecting the gland [13, 14, 15, 16, 17].

The diagnostic accuracy of frozen sections and FNA varies in various studies. The accuracy of FS in various studies ranges from 87% to 97% in western countries and in Indian studies, accuracy was up to 96%. Published data on accuracy of FNAC from 65% to 96% and to 100% if papillary microcarcinomas are excluded. In Indian studies accuracy of FNAC ranges from 84 to 94.1% [15, 16, 17, 18, 19, 20, 2].

The purpose of our study is to review our own experience with FNAC and frozen section in thyroid nodules at our institution and to study diagnostic utility of frozen section and also assess if it had any added benefit in cases in which preoperative FNAC was performed

Aims and Objectives

Aim

To study the diagnostic utility of frozen section and fine needle aspiration cytology in accurately categorizing thyroid lesions utilizing final histopathology diagnosis as gold standard.

Objectives

To Compare Fine needle aspiration cytology wherever available with frozen sections and assess if frozen section offered additional diagnostic advantage over fine needle aspiration cytology.

Material and Methods

Study location: Apollo Institute of Medical Sciences and Research, Hyderabad.

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 10, 2023

Study duration: 4 years (2019-2023).

Study population: Included all patients with preoperative FNAC, Intraoperative Frozen sections and final pathology performed in Department of Histopathology, Apollo Institute of Medical Sciences and Research, Hyderabad during the study period.

Study design: Retrospective, Cross Sectional study.

Study inclusion criteria

1. All cases of Thyroid lesions received at the histopathology department on which frozen section was performed and also had a preoperative FNAC done.

Study exclusion criteria

1. Thyroid samples for which frozen section was not done.
2. All the cases which did not have a preoperative FNAC.
3. History of Irradiation to head and neck.

Study procedure

The present study was conducted on 30 cases of Thyroid tissue submitted after thyroid surgery, who had intraoperative frozen section done and also preoperative FNAC done.

FNAC Procedure

The procedure is explained to the patient and informed consent is taken. After a brief history and physical examination, the patient is made to lie down in a supine position with a pillow under neck to maximize the visualization of the gland. 24 gauge needles are used for the procedure which provide adequate material while causing less bleeding. The non-aspiration technique provides a better and less hemorrhagic material and is the preferred method to perform the FNAC in our department. If the lesion is cystic, with the help of syringe fluid is evacuated. If any solid area is palpable after fluid is aspirated, a re-aspiration is performed.

Conventional smears, both air dried and fixed are prepared from each aspirate. If fluid is aspirated, the physical details are recorded and the fluid is centrifuged, processed and stained. Fixed smears are stained with H&E, Papanicolaou stains. Air dried smears are stained with Giemsa.

Frozen section procedure

All the thyroid specimens which are subjected to the frozen section included a careful gross examination to look for abnormal areas of generalized pathology. Minimum two representative samples are taken in encapsulated nodules, with the section representing the tumor, capsule and the adjacent non-neoplastic tissue.

Tissue is placed on a chuck containing OCT Medium. It is quickly frozen in a cryostat with a closed refrigerator system, with a rotary type microtome and anti-roll plate all maintained at temperature of -23^0 C to -30 ^oC (LEICA/D). Two or three frozen sections (5 micron thick) are placed on a glass slide and stained with rapid H&E. The average time required for frozen section diagnosis in our institute is 15-30 min. The report is informed verbally over telephone to the operating surgeon within the time frame and at the same time a written frozen section report is dispatched.

Permanent-HPE Method

Once the frozen section diagnosis is done, the specimen is fixed in10% neutral buffered formalin overnight. Multiple sections are then taken from the representative areas. In encapsulated nodules, tumor capsule interface is thoroughly sampled. These sections are processed in an automated tissue processor (LEICA), embedded in paraffin. Sections of 3-4 microns are cut with rotary microtome (LEICA 2) and stained with hematoxylin and eosin using automated slide stainer (LEICA-ST-5)

Study definition and study analysis

FNAC were classified into 6 categories-Criteria of BSRTC [22]:

i) Non-diagnosis
ii) Benign
iii) Atypia of undetermined significance
iv) Follicular neoplasm
v) Suspicious for Malignancy
vi) Malignancy

Frozen section was classified into 3 categories [21]:

- Benign.
- Malignant.

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 10, 2023

- Indeterminate.

The final histopathology samples were classified into 3 categories
- Benign.
- Malignant.

Results

A total of 30 patients met the inclusion criteria with 26 females (86.67%) and 4 males (13.33%). The average age was 42.2 ± 14.4 years. The overall malignancy rate among the nodules included in the study was 20% (n=6). Among the malignant nodules 4 were Papillary carcinoma Thyroid and 2 were Follicular variants of papillary thyroid carcinoma.

Table 1: Stratification of Fine needle aspiration biopsies according to Bethesda System

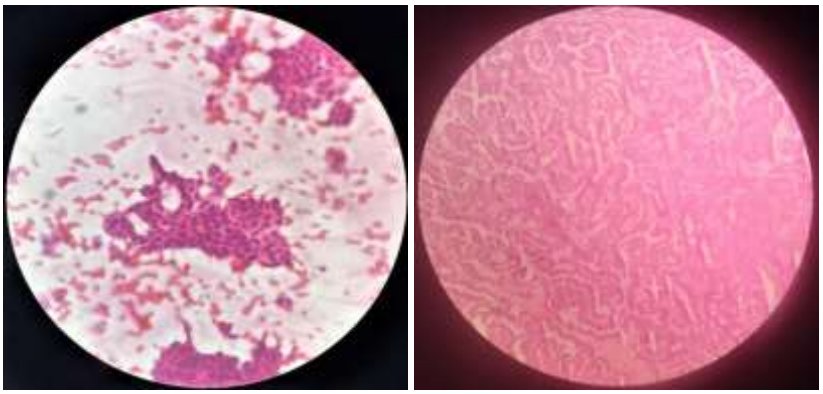
Diagnostic Category	Number of samples
Non-diagnosis	0
Benign	19
Atypia of undetermined significance	2
Follicular neoplasm	4
Suspicious for Malignancy	5
Malignancy	0

Table 2: Frozen Section performance for each Bethesda category and the final histopathological diagnosis

FNAC	iFS Performance	Final Diagnosis
Bethesda II (19)	Correctly diagnosed 18 benign	18 benign
	Misdiagnosed 0 benign	
	Correctly diagnosed 1 malignant	1 malignant
	Misdiagnosed 0 malignant	
Bethesda III (2)	Correctly diagnosed 2 benign	2 benign
	Misdiagnosed 0 benign	
	Correctly diagnosed 0 malignant	0 malignant
	Misdiagnosed 0 malignant	
Bethesda IV (4)	Correctly diagnosed 3 benign	3 benign
	Misdiagnosed 0 benign	
	Correctly diagnosed 1 malignant	1 malignant
	Misdiagnosed 0 malignant	
Bethesda V (5)	Correctly diagnosed 0 benign	0 benign
	Misdiagnosed 0 benign	
	Correctly diagnosed 4 malignant	5 malignant
	Misdiagnosed 1 malignant	

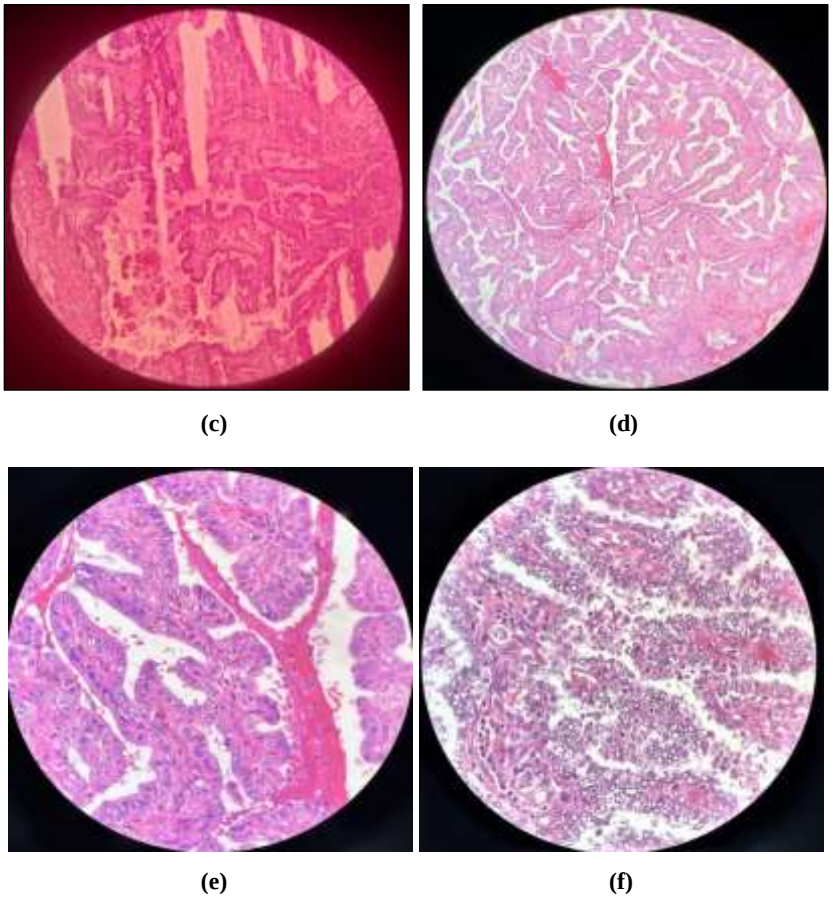
Table 3: FNAC & Frozen section performance in classifying thyroid nodules as benign or malignant

Test	Sensitivity	Specificity	Accuracy
FNAC	71.43%	100%	93.3%
iFS for all nodules	85.7%	100%	96.67%
iFS for BC II nodules	100%	100%	100%
iFS for BC III IV and V nodules	83.33%	100%	90.9%



(a) **(b)**

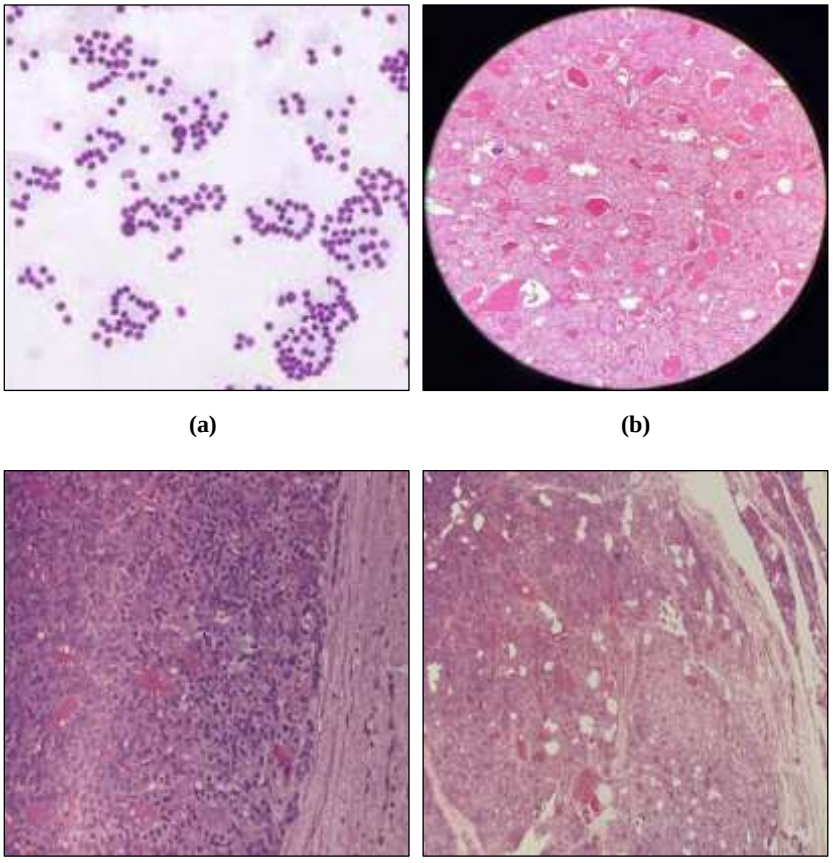
ISSN:0975 -3583,0976-2833 VOL14, ISSUE 10, 2023



(c) (d)

(e) (f)

Fig 1: Papillary Carcinoma Thyroid a) FNAC, b & c) Frozen Section, d, e & f) H&E section



(a) (b)

(c) (d)

Fig 2: a) FNAC-Follicular neoplasm, b) Frozen section-Follicular neoplasm, c) H&E-Follicular Adenoma, d) H&E-Follicular Carcinoma

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 10, 2023

Discussion

The present study is a four year retrospective study done during a period of 2019-2023, done at the Department of Histopathology, Apollo Institute of Medical Sciences and Research, Hyderabad. This study included 30 cases of Thyroid section for which a frozen section was requested and also had a preoperative FNAC done. A female predominance was noted with a median age of 40yrs. This is similar to other studies done. Also, malignant nodules were noted in 20% and Papillary carcinoma was the most common similar to previous studies.

In the last decade FNAC has become the most useful method to assess preoperative malignancy risk in thyroid nodules. Intra operative frozen section has been historically proposed as a tool for tailoring surgical extension of thyroidectomies. Due to increasing thyroid cancer screening and diagnosis rates, dependency on reliable preoperative and intraoperative histological data is the requirement of the day.

Among the 19 cases diagnosed as Type II Bethesda (benign) by FNAC, the Frozen section could diagnose one malignant nodule accurately. The diagnosis of follicular lesions can be challenging. According to previous literature, the follicular lesions can only be distinguished as benign or malignant based on the capsular or vascular invasion. Such findings, especially in minimally invasive follicular carcinoma, are only clearly picked up on histopathological diagnosis [20]. Most of the studies have shown that neither FNAC nor frozen section was proficient enough to detect follicular carcinoma correctly. In our study the Frozen section could detect one malignant case among the 4 classified as Type IV Bethesda by FNAC. On the contrary the Frozen section misdiagnosed one malignant nodule diagnosed by FNAC as benign. It was a case of Nodular goiter with papillary carcinoma.

In this study, we found that the frozen section was slightly more sensitive and had slightly more accuracy than FNAC in detecting malignancy in the thyroid gland. Published data on accuracy of FNAC varied from 65% to 96%. In Indian studies accuracy of FNAC ranges from 84 to 94.1%. The accuracy of the Frozen section in various studies ranges from 87% to 97% in western countries and in Indian studies, accuracy was up to 96%. The sensitivity and Accuracy in our study was similar to available literature with FNAC having a sensitivity of 71.43% and accuracy of 93.3%, whereas the Frozen section showed a sensitivity of 85.7% and accuracy of 96.67% [15, 16, 17, 18, 19, 20].

Main limitation of our study is the sample size. Although the Frozen section had shown better sensitivity when compared to FNAC, better sample size would have given us a better insight regarding the advantage and added benefit of the Frozen section over FNAC. However, even though FNAC has its limitations, i.e. the results heavily depend on how the sample has been taken, experience of the interventional radiologist or pathologist taking the FNAC, taking multiple aspirations. Performing the procedure under ultrasonographic guidance can substantially improve the capability of the interventional radiologist or pathologist to get an aspirate of the best quality to get a diagnosis.

Conclusion

Our study concludes that fine needle aspiration cytology is a good screening tool to detect malignancy in thyroid carcinoma. Frozen section has slightly better Sensitivity and accuracy when compared to FNAC and might give an added advantage in planning treatment options in certain subset of patients. More detailed study with adequate sample size are required.

Conflict of Interest: None.

Funding Support: Nil.

References

1. Chan JKC. Tumors of the thyroid and parathyroid glands. In: Fletcher 3rd CHDM, editor. Diagnostic histopathology of tumors. 2 Churchill: Livingstone Elsevier, 2007, 997-1079.
2. Alexander EK. Approach to the patient with a cytologically indeterminate thyroid nodule. J Clin Endocrinol Metab. 2008;93:4175-82.
3. Usha Menon V, Sundaram KR, Unnikrishnan AG, Jayakumar RV, Nair V, Kumar H. High prevalence of undetected thyroid disorders in an iodine sufficient adult south Indian population. J Indian Med Assoc. 2009;107:72-77.
4. Unnikrishnan AG, Menon UV. Thyroid disorders in Indian epidemiological perspective. Indian J Endocr Metab. 2011;15:S78-S81.
5. Belfiore A, La Rosa GL, La Porta GA, Giuffrida D, Milazzo G, Lupo L, *et al*. Cancer risk in patients with cold thyroid nodules: relevance of iodine intake, sex, age, and multi nodularity. Am J Med. 1992;93(4):363-369.
6. Yeung MJ, Serpell JW. Management of the solitary thyroid nodule. Oncologist. 2008;13(2):105-112.
7. Hegedus L. Clinical practice: the thyroid nodule. N Engl J Med. 2004;351:1764-71.
8. Dean DS, Gharib H. Fine-needle aspiration biopsy of the thyroid gland (updated 2015 Apr 26). In: De Groot LJ, Chrousos G, Dungan K, *et al*., (eds) Endotext. South Dartmouth (MA), 2000. MD Text.com, Inc. https://www.ncbi.nlm.nih.gov/books/NBK285544/.

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 10, 2023

9. Liu FH, Liou MJ, Hsueh C, Chao TC. Thyroid follicular neoplasm: analysis by fine needle aspiration cytology, frozen section, and histopathology. Diagn Cytopathol. 2010;38(11):801-805.
10. Mates˘a N, Tabain I, Dabeliæ N, Petric V, Kusiæ Z. Diagnostic relevance of fine needle aspiration cytology for follicular lesions of the thyroid: retrospective study. Croat Med J. 2002;43(5):606-609.
11. Seningen JL, Nassar A, Henry MR. Correlation of thyroid nodule fine-needle aspiration cytology with corresponding histology at Mayo Clinic, 2001-2007: an institutional experience of 1945 cases. Diagn Cytopathol. 2012;40(1):E27-32.
12. Baier ND, Hahn PF, Gervais DA, *et al*., Fine-needle aspiration biopsy of thyroid nodules: experience in a cohort of 944 patients. AJR Am J Roentgenol. 2009;193:1175-9.
13. Almeida JPA, *et al*., The role of intraoperative frozen sections for thyroid nodules. Rev Bras Otorrinolaringol. 2009;75(2):256-260.
14. Cetin B, Aslan S, Hatiboglu C, Babacan B, Onder A, Celik A, *et al*. Frozen section in thyroid surgery: is it a necessity? Can J Surg. 2004;47(1):29-33.
15. Chang HY, Lin JD, Chen JF, *et al*., Correlation of fine needle aspiration cytology and frozen section biopsies in the diagnosis of thyroid nodules. Clin Pathol. 1997;50:1005-9.
16. Lumachi F, Borsato S, Tregnaghi A, Marino F, Polistina F, Basso SMM, *et al*. FNA cytology and frozen section examination in patients with follicular lesions of the thyroid gland. Anticancer Res. 2009;29:5255-5258.
17. Mayooran N, Waters PS, Kaim Khani TY, Kerin MJ, Quill D. FNAC and frozen section correlations with definitive histology in thyroid diseases. Eur Arch Otorhinolaryngol. 2016;273(8):2181-2184.
18. Gerhard F, Huber F, Dziegielewski P, Matthews TW, Warshawski SJ, Kmet LM, *et al*. Intraoperative frozen-section analysis for thyroid nodules-a step toward clarity or confusion? Arch Otolaryngol Head Neck Surg. 2007;133(9):874-881.
19. Batra C, Singh S, Katra R, Marwah N, Atreja A. Role of fine needle aspiration and frozen section in the diagnosis of thyroid lesions. Internet J Pathol., 2010, 11(1).
20. Kahmke R, Lee WT, Puscas L, Scher RL, Shealy MJ, Burch WM, *et al*. Utility of intraoperative frozen section during thyroid surgery. Int J Otolaryngol., 2013. Article ID 496138.
21. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, *et al*. American thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer. Thyroid, 2015, 26(1).
22. Han M, Fan F. Bethesda System for Reporting Thyroid Cytopathology-An Updated Review. J Clin Transl. Pathol. 2023;3(2):84-98. Doi: 10.14218/JCTP.2023.00005.