Original Research Article

Diagnostic accuracy of The Bethesda system for reporting thyroid cytopathology: A Five years Study

Nirali U Patel[1], Viral M Bhanvadia[2*], Hansa Goswami[3], Pinal Patel[4]

[1]Second Year Resident, Department of Pathology, B.J. Medical College, Ahmedabad, India
[2]Assistant Professor M.& J. Western Regional Institute of Ophthalmology affiliated to B.J. Medical College, Civil Hospital, Ahmedabad, India
[3]Professor and Head of Department, Department of Pathology, B.J. Medical College, Ahmedabad, India
[4]Third Year Resident, Department of Pathology, B.J. Medical College, Ahmedabad, India

Received: 29-11-2021 / Revised: 21-12-2021 / Accepted: 01-01-2022

Abstract

Introduction: Thyroid nodules are a common clinical problem. It is important to differentiate benign from malignant nodules. Fine needle aspiration is utilized as a preoperative diagnostic technique which is safe, simple and cost effective for triaging patients with thyroid nodules. **Methods:** The study was conducted at Histopathology department of B.J Medical college, Ahmedabad. It involved period of 5 years patients who presented with thyroid swelling and underwent FNAC and Histopathology. Out of these 1325 cases, 210 patients subsequently underwent surgical excision. Results of final histopathology were correlated with cytologic diagnosis. **Results:** Histopathologic correlation was done in 210 cases. Out of total 210 cases, 3 cases were diagnosed as Non diagnostic or unsatisfactory,199 cases were diagnosed as Bethesda II and No case was Bethesda III while 4 cases were categorized Bethesda IV and 1 case were Bethesda V and 3 cases were Bethesda VI. The incidence of malignancy in Bethesda categories through were 0%,7.53%, 0%,100%,100% and 100% respectively. Overall accuracy Of FNA cytology was 93.8% with 81.25 % sensitivity and 96.06 % specificity. **Conclusion:** Our study validated the accuracy of TBSRTC in our setup which is concordant with other studies. Therefore, we recommend routine use of TBSRTC for reporting thyroid cytopathology for initial workup. However, risk of malignancy was found to be significantly high in Bethesda IV, V and VI category to warrant further workup including ultrasound/thyroid scan in addition to repeat FNAC.

Keywords: The Bethesda system for reporting thyroid cytopathology (TBSRTC), Fine needle aspiration cytology (FNAC), Thyroid nodule

Introduction

Thyroid nodules are a common clinical problem. It is important to differentiate benign from malignant nodules. Fine needle aspiration (FNA) is utilized as a preoperative diagnostic technique which is safe, simple, and cost effective for triaging patients with thyroid nodules. Proper communication among pathologists, clinicians, radiologists, and surgeons along with cytohistological correlation is essential for reporting of thyroid FNA. Hence, consistent diagnostic terminology is vital. To achieve standardization of diagnostic terminology, morphologic criteria, and risk of malignancy for reporting of thyroid FNA, in 2007, the National Cancer Institute (NCI) organized the NCI Thyroid Fine Needle Aspiration State of the Science Conference which proposed a 6-tier system and named it The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)[1]. Although benign nodules far outnumber cancerous lesions, the risk of malignancy needs to be evaluated preoperatively to determine the extent of surgery. More over FNAC evaluation of thyroid nodules reduces load of unnecessary surgeries for benign lesion and opens the way to timely surgical intervention when there is significant risk of malignancy.Fine needle aspiration cytology (FNAC) was introduced for the same purpose and it soon gained wide acceptance among clinicians due to good patient compliance and cost effectiveness[2]. FNAC is a minimally invasive, accurate and cost-effective diagnostic tool for differentiating benign from malignant thyroid lesions thus providing basis for decisions on management options[3].

*Correspondence
Dr. Viral M Bhanvadia
Assistant Professor M.& J. Western Regional Institute of Ophthalmology affiliated to B.J. Medical College, Civil Hospital, Ahmedabad, India
E-mail: drviral2001@gmail.com

However, as some diagnoses cannot be reliably made on FNAC material like differentiation between follicular adenoma and minimally invasive follicular carcinoma, certain number of misdiagnoses are unavoidable. Inter-observer variability and inadequate aspiration are among some other limitations of this procedure. The Bethesda system for reporting thyroid cytopathology (TBSRTC) streamlined the assessment and reporting of thyroid aspirates and alleviates the inter-observer variability of this procedure. TBSRTC categorizes the FNAC diagnosis into six groups with well-defined cancer risk and clear indications for further clinical management[4]. The study aimed to evaluate diagnostic accuracy of Bethesda system for reporting thyroid cytopathology.

Methods

The study was conducted at Histopathology department of B.J Medical college,Ahmedabad.It involved period of 5 years patients who presented with thyroid swelling and underwent FNAC and Histopathology. A 22 – 23gauge needle was used for the procedure and smears and cell block preparation were made. Smears were stained with haematoxylin and eosin (H & E), giemsa and PAP stains. Repeat aspiration was done for cases with inadequate smears. FNAC were reported according to TBSRTC by 2 experienced pathologists.Out of 1325 cases 210 patients subsequently underwent surgical intervention,either excision of nodules/lobectomy or subtotal/near total thyroidectomy.Tissue specimens were grossly examined and processed according to standard guidelines and reported by senior histopathologists.Results of final histopathology were correlated with cytopathological diagnosis.

Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of FNAC, relative to the final histological diagnoses were analysed.

a. True positive (TP): Positive result in the FNA for malignancy, and confirmed in the histological study.
b. False positive (FP): Positive result in the FNA for malignancy, but not confirmed in the histological study.
c. True negative (TN): Negative result in the FNA for malignancy and no carcinoma in the histological study.
d. False negative (FN): Negative result in the FNA for malignancy, but with carcinoma in the histological study.
e. Sensitivity (S): Proportion of patients with associated carcinoma and a positive result in the FNA for malignancy, S = TP/ (TP + FN)
f. Specificity (Sp): Proportion of patients without associated carcinoma and with a negative result in the FNA for malignancy SP = TN (TN + FP).
g. Positive predictive value (PPV): Proportion of patients with a positive result and a histological confirmation of PPV = TP (TP + FP)
h. Negative Predictive value (NPV): Proportion of patients with negative results, without a carcinoma in the histological study. NPV = TN (TN + FN)
i. Diagnostic accuracy (DA): Proportion of patients diagnosed correctly by the diagnostic test, DA = (TP + TN) / (FP + FN + TP + TN)

The Bethesda System for Reporting Thyroid Cytopathology: Recommended Diagnostic Categories (2017) [4]

I. Non diagnostic or unsatisfactory
Cyst fluid only
Virtually acellular specimen
Other (obscuring blood, clotting artifact, etc.)

II. Benign
Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.)
Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context Consistent with granulomatous (subacute) thyroiditis

III. Atypia of undetermined significance or follicular lesion of undetermined significance

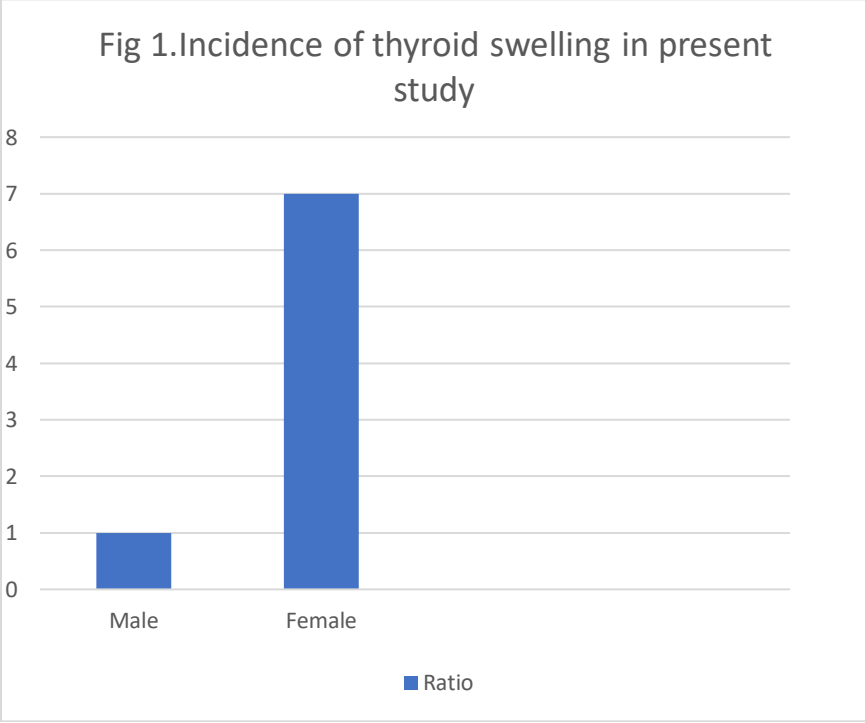
IV. Follicular neoplasm or suspicious for a follicular neoplasm
Specify if Hurthle cell (oncocytic) type

V. Suspicious for malignancy
Suspicious for papillary carcinoma
Suspicious for medullary carcinoma
Suspicious for metastatic carcinoma
Suspicious for lymphoma
Other

VI. Malignant
Papillary thyroid carcinoma
Poorly differentiated carcinoma
Medullary thyroid carcinoma
Undifferentiated (anaplastic) carcinoma
Squamous-cell carcinoma
Carcinoma with mixed features (specify)
Metastatic carcinoma
Non-Hodgkin lymphoma
Other

Result

Mean age of the patients included in the study was 40.22 years(13-66 years) and male to female ratio was 1:7. Histopathologic correlation was done in 210 cases which further underwent surgical intervention. Out of total 210 cases, 3 cases were diagnosed as Non diagnostic or unsatisfactory,199 cases were diagnosed as benign (Bethesda II) and No case was (Bethesda III) while 4 cases were categorized as Follicular Neoplasm/ suspicious for Follicular neoplasm (Bethesda IV) and 1 cases were categorized as suspicious for malignancy (Bethesda V) and 3 cases were categorized as malignant(Bethesda VI) as shown in Table 1.For Bethesda VI category, 100% concordance was found, however for Bethesda II category, 5 out of 199 cases were found to have malignant diagnosis on final histopathology. The incidence of malignancy in Bethesda categories through were 0%,7.53%, 0%,100%,100% and 100% respectively (Table 2). Overall accuracy Of FNA cytology was 93.8% with 81.25%sensitivity and 96.06% specificity (Table 3).



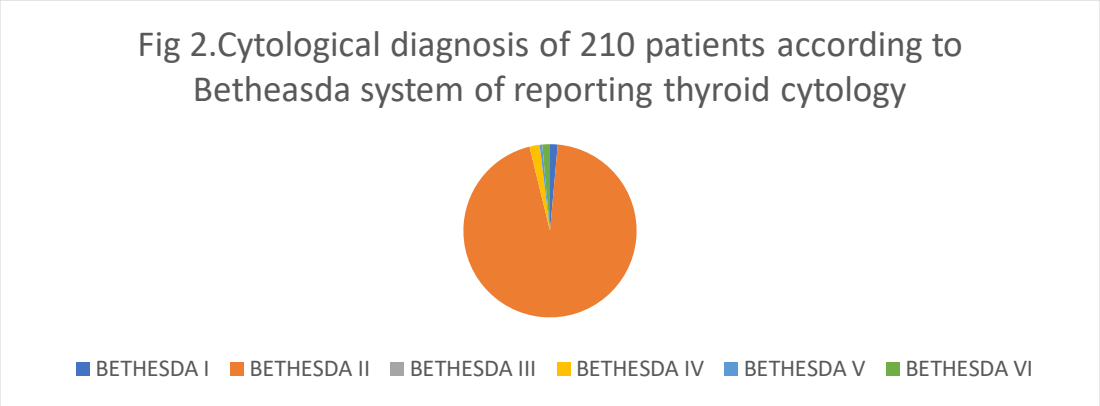


Table 1 Cytologic diagnosis of 210 patients according to Bethesda System of Reporting Thyroid Cytopathology

Bethesda category	Frequency	Percentage
Bethesda I	3	1.42%
Bethesda II	199	94.7%
Bethesda III	0	0%
Bethesda IV	4	1.90%
Bethesda V	1	0.47%
Bethesda VI	3	1.42%

Table 2Correlation of Cytologic diagnosis with final histology, with incidence of malignancy in each Bethesda category

Cytological Diagnosis	Number of cases	Percentage	Histological Diagnosis	Frequency	Percentage	Incidence of malignancy
Bethesda I	3	1.42%	Benign Cystic lesion	3	1.42%	0%
Bethesda II	199	94.7%	Colloid Goiter Nodular Goiter Bening follicular Hashimoto's thyroiditis Lymphocytic thyroiditis Diffuse toxic Goiter Adenomatous Goiter	101 53 34 4 3 3 1	50.75% 26.63% 17.08% 2.01% 1.5% 1.5% 0.5%	7.53%
Bethesda III	0					0%
Bethesda IV	4	1.90%	Suspicious of Follicular Neoplasm Follicular Neoplasm	1 3	25% 75%	100%
Bethesda V	1	0.47%	Suspicious of thyroid	1	100%	100%
Bethesda VI	3	1.42%	Poorly differentiated carcinoma of thyroid	3	100%	100%

Table 3 Diagnostic accuracy of fine needle aspiration cytology according to Bethesda system of Reporting thyroid cytopathology

True Positive	26
False Positive	7
True Negative	171
False Negative	6
Positive predictive value	78.7%
Negative predictive value	96.61%
Sensitivity	81.25%
Specificity	96.06%
Accuracy	93.8%

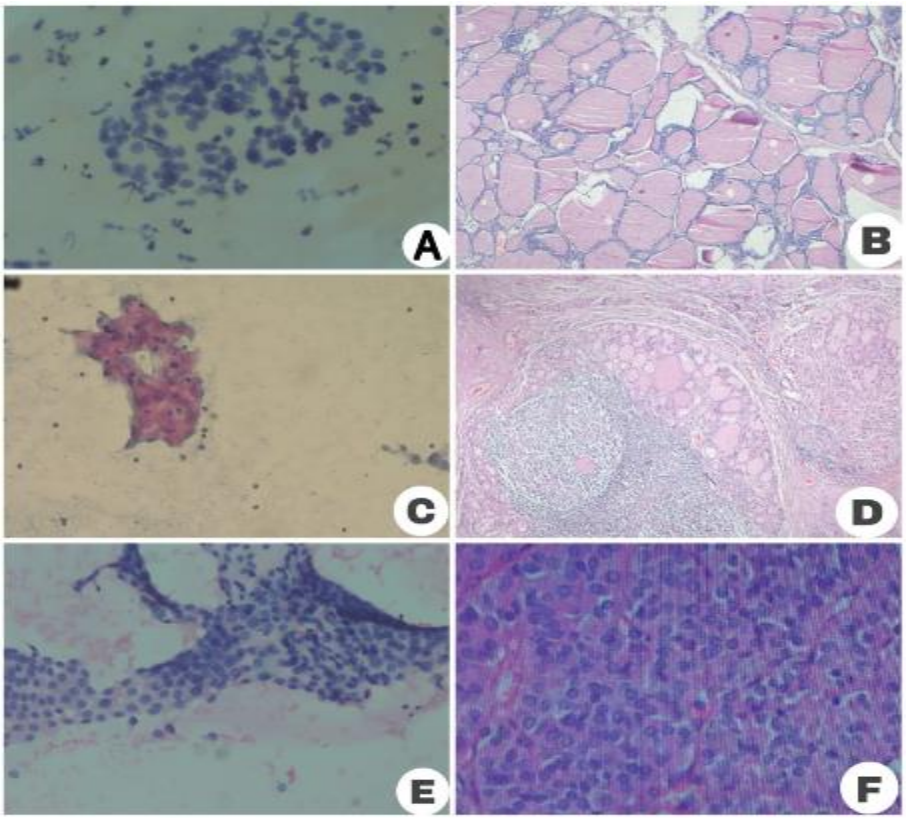


Fig 3. A.Small cluster of thyroid follicular cells in cytology of benignNodular goitre(Haematoxylin and Eosin,40X) B.Variable sized thyroid follicle filled with colloid inhistology of benign Nodular goitre(Haematoxylin and Eosin,10X) C.Hurthle cell changes in cytology of Hashimoto's thyroiditis(Haematoxylin and Eosin,40X) D.Lymphoid follicles with Prominent germinal centers in Histology of Hashimoto's thyroiditis(Haematoxylin and Eosin,4X) E.Papillary cluster of cells in cytology of papillary carcinoma of thyroid(10x)F.Nuclear features of papillary carcinoma in Histology(Haematoxylin and Eosin,40X)

Discussion

Thyroid diseases are one of the commonest health care problems in our population. B.J Medical college, Civil Hospital is one of the largest tertiary care centers of the country with a large influx of patients from both the urban and rural parts of the province. Therefore, our data is quite representative of entire population. Approximately 94.76% of thyroid swellings in our studied patients were benign on FNAC which only require surgical intervention for physical (pressure symptoms) or cosmetic reasons. Papillary carcinoma of thyroid represents the most common malignancy on final histology which is concordant with most of the national and international data[5]. The actual risk of malignancy of category III is difficult to determine, since confirmatory diagnosis is only available in a subset of patients selected for surgery who have suspicious clinical or USG features. The patients are also subjected to selection bias which overestimates the prevalence of malignancy. Patients tend to be more concerned about false positive results than false negative results, which might have pressurized cytopathologists to underdiagnose cases to avoid making false positive diagnosis[1]. The false positive rate (FPR) indicated that a patient with a malignant FNAC result was found on histological examination to have a benign lesion.The false negative rate (FNR) is defined as the percentage of patients with benign cytology in whom malignant lesions are later confirmed, after thyroidectomy.The false negative FNAC results may occur because of sampling error or misinterpretation of cytology and are of great concern because they indicate the potential to miss a malignant lesion[6].

Various researchers in different hospital and population-based studies evaluated the diagnostic accuracy of thyroid cytopathology. Bagga et al., in a hospital-based study in India involving only 32 cases found a diagnostic accuracy of 96.2% with 66% sensitivity and 100% specificity for FNAC thyroid which is concordant with our study. However, they did not follow the Bethesda system and categorized results only into benign, suspicious for malignancy and malignant categories[6].

After the introduction of BSRTC, it was rapidly adopted by most institutions.Kumar S study found sensitivity of 77%, specificity of 100%, and diagnostic accuracy of 97.7%. which is concordant with our study[7].

H Nggada study evaluated the benign diseases include 34(49.3%) nodular colloid goitre; 6(8.7%) toxic goitre; 7(10.1%) follicular adenoma; 2(2.9%) cases each of Hashimoto's and subacute thyroiditis. The malignant cases were 10(14.5%) follicular carcinoma; 3(4.3%) cases each of medullary and papillary carcinomas, and 2 (2.9%) anaplastic carcinoma. The diagnostic accuracy is 94.2%, Sensitivity, 88.9%; Specificity, 96.1%; False Negative rate, 11.1% and false positive rate, 3.9%which is concordant as compared to our study[8].

Another concordant with our study, S Bhatta study the accuracy of cytodiagnosis was 90 % with a sensitivity of 85.7 %, specificity of 92.3 %, false negative rate of 14.28% and false positive rate of 7.69%[9].

Gupta et al. evaluated 75 cases of solitary thyroid nodule. Histopathologic examination of excised specimens revealed 42 (56%) cases of colloid nodular goiter, 12 (16%) of follicular adenoma, 12 (16%) of papillary carcinoma and 3 (41%) of hurthle cell adenoma. Correlation of FNAC with histopathology revealed sensitivity, specificity, accuracy, false positive ratio and false negative ratio of 80%, 86.6 which is concordant with our study[10].

In Luck CP study the data analysed showed sensitivity of FNAC in detecting thyroid lesions is 91.6%, specificity is 97.01%. FNAC has a positive predictive value of95.6% and negative predictive value of 94.2%. which is concordant with our study.

This sampling error could have been avoided if repeat aspiration was performed. False negative diagnosis arises from inadequate samples, geographic misses of lesions, dual pathology, and errors of interpretations and also in relation to the cystic neoplasm. This is of great concern because it indicates the potential to miss the malignant lesions[11].

Himakhm et al. in a hospital-based study of 469 patients found malignancy in 179 cases, out of which 147 cases were that of papillary carcinoma. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 82%, 100%, 100%, 90% and 93% respectively which is concordant with our study[12].

TBSRTC is useful for a standardized system of reporting thyroid cytology, bridges the communication gap between cytopathologists and clinicians, and interlaboratory agreement, leading to more consistent management approaches and therapeuticinterventions. It makes the cytology report unambiguous, clear, succinct, and clinically relevant[13]. In Bethesda system, only repeat FNAC is advised in follicular lesion of undetermined significance (FLUS) category. This diagnosis (Bethesda III) is very important as cytologically unequivocal features of malignancy are absent, but few worrisome findings are present like focal nuclear enlargement/clearing or microfollicular pattern in a scanty smear which warrants repeat FNAC[14]. Ultrasound-guided FNA confirms the metastases and is often done with thyroglobulin level of the needle rinse. After surgery, in patients with total or near total thyroidectomy a serum thyroglobulin assay combined with neck ultrasonography should be performed. Rising thyroglobulin levels over time are considered suspicious for recurrence[15]. The cytopathologists should be aware of the potential diagnostic pitfalls and the interpretational errors that can be reduced further, if the aspirates are obtained from different portions of the nodule, with the use of the ultrasound-guided FNA procedure, with expert cytopathologists to perform and interpret the aspirates, and with the use of immunohistochemical and molecular markers[6].

Conclusion

Our study validated the accuracy of TBSRTC in our setup which is concordant with other studies. Therefore, we recommend routine use of TBSRTC for reporting thyroid cytopathology for initial workup of patients with thyroid nodule. However, risk of malignancy was found to be significantly high in Bethesda IV, V and VI category to warrant further workup including ultrasound/thyroid scan in addition to repeat FNAC.

Justification of study

Thyroid nodules are very common in the general population, but malignancy is relatively rare. The goal of the ultrasound guided evaluation of nonpalpable thyroid nodules by FNAC is the early detection of lesions and to save the overt spread of malignancies, while identifying and avoiding unnecessary surgery in those with benign, asymptomatic thyroid nodules. Our study showed good sensitivity, specificity for FNAC with relatively low rate of non-diagnostic or inadequate smears.

Strength of study

Our data is quite representative of entire populationand involve period of 5 years which may reduce sampling error.

Limitation of study

In our study we did not follow the patients with inadequate swellings and we could not convince the surgeons for delaying the surgery for Class II smears (Benign). Classes III and IV are the main pitfall of The Bethesda System for reporting Thyroid Cytopathology (TBSRTC).

Consent

Written informed consent was obtained from the patient for publication of this manuscript and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Conflict of Interest: Nil Source of support: Nil

References

1. Anand B, Ramdas A, Ambroise MM, Kumar NP. The Bethesda system for reporting thyroid cytopathology: A cytohistological study. Journal of thyroid research. 2020 Apr 16;2020.
2. Yassa L, Cibas ES, Benson CB, Frates MC, Doubilet PM, Gawande AA, Moore Jr FD, Kim BW, Nosé V, Marqusee E, Larsen PR. Long-term assessment of a multidisciplinary approach to thyroid nodule diagnostic evaluation. Cancer Cytopathology: Interdisciplinary International Journal of the American Cancer Society. 2007 Dec 25;111(6):508-16.
3. Barasa M, Abdallah A. Cyto-histologic discordancy in patients undergoing thyroidectomy at Aga Khan University Hospital. Pan African Medical Journal. 2019 Mar 21;32(1).
4. Cibas ES, Ali SZ. The Bethesda system for reporting thyroid cytopathology. Thyroid. 2009 Nov 1;19(11):1159-65.
5. Tabaqchali MA, Hanson JM, Johnson SJ, Wadehra V, Lennard TW, Proud G. Thyroid aspiration cytology in Newcastle: a six year cytology/histology correlation study. Annals of the Royal College of Surgeons of England. 2000 May;82(3):149.
6. Bagga PK, Mahajan NC. Fine needle aspiration cytology of thyroid swellings: How useful and accurate is it?. Indian Journal of cancer. 2010 Oct 1;47(4):437.
7. Kumar S, Aqil S, Dahar A. Role of fine needle aspiration cytology in thyroid diseases. J Surg Pak 2008;13:22-5.
8. Nggada HA, Musa AB, Gali BM, Khalil M. Fine needle aspiration cytology of thyroid nodule (s): a Nigerian tertiary hospital experience. Internet Journal of Pathology. 2006;5(1).
9. Bhatta S, Makaju R, Mohammad A. Role of fine needle aspiration cytology in the diagnosis of thyroid lesions. Journal of Pathology of Nepal. 2012;2(3):186-8.
10. Gupta M, Gupta S, Gupta VB. Correlation of fine needle aspiration cytology with histopathology in the diagnosis of solitary thyroid nodule. Journal of thyroid research. 2010 Apr 18;2010.
11. Luck CP,Srirangaramasamy J, Balamurugan M, Arumugam B, PadmavathyA.Evaluation of diagnostic accuracy of FNAC and correlation with histopathology in thyroid lesions. April - June, 2017;3 (2)
12. Himakhun W, Chansom R, Aroonroch R, Pongtippan A. Fine needle aspiration of thyroid: a cyto-histopathological correlation in Ramathibodi Hospital. J Med Assoc Thai. 2012;95(Suppl 1):S74–S78.
13. Pattnaik K, Dasnayak G, Kar A, Swain S, Sarangi CR. Implementation of the Bethesda system of reporting thyroid cytopathology in a referral center. Oncology Journal of India. 2020 Jan 1;4(1):13.
14. Naz S, Hashmi AA, Faridi N, Edhi MM, Kamal A, Khan M. Diagnostic accuracy of Bethesda system for reporting thyroid cytopathology: an institutional perspective. International archives of medicine. 2014 Dec;7(1):1-5.
15. Ali SZ. Thyroid cytopathology: Bethesda and beyond. Acta cytologica. 2011;55(1):4-12.