ABSTRACT

Background: Most patients with thyroid diseases present with palpable neck swelling. Accurate evaluation of thyroid nodules is crucial as they can be neoplastic. The use of fine needle aspiration and smear cytology for the detection of malignant thyroid lesions is the usual practice. However, it has its limitations and diagnostic pitfalls. Cell block analysis can be a useful adjunct to smears for establishing a more definitive cytopathologic diagnosis. This study was aimed to evaluate cytology and cell block findings in the patients of palpable thyroid lesions.

Methods: A cross-sectional, hospital-based comparative, observational study was conducted in Department of Pathology after receiving ethical approval from Institutional Review Committee. The study was conducted from 1st August 2022 to 1st August 2023. Statistical analysis of the diagnostic utility of cell block was evaluated taking into account sensitivity and specificity.

Results: Among the 50 cases diagnosed as non-neoplastic by smear cytology, 2 were found to be neoplastic by cell block and similarly among the 5 cases which were not diagnosed by cytology, 2 cases were confirmed to be non-neoplastic thyroid lesions by cell block. Sensitivity of FNAC to detect neoplastic lesions was 66.6% and specificity was 100%, while cell block had 100% sensitivity and 100% specificity to detect those lesions.

Conclusions: As both smear cytology and cell block procedures are done in a single setting, combination of two procedures has beneficial effect not only to support diagnosis but also to establish new diagnosis.

INTRODUCTION

Fine needle aspiration cytology (FNAC) is a cost-effective procedure which can confirm benign thyroid lesions and can reduce the burden of unnecessary surgery. In recent years, the pivotal role of FNAC in detecting malignant potential of thyroid nodules is also being explored.

Conventional smear cytology after FNA has limitations due to lesser availability of representative tissue and lesser possibility for adjuvant diagnostic investigations like immunocytochemistry. In contrast, the cell block technique which retrieves small tissue fragments from a FNA specimen to form a paraffin block, increases the cellular yield, improves diagnostic accuracy and also allows for multiple immunostains and other studies to be performed akin to histopathology.

In Nepal, most studies evaluating the role of FNAC for diagnosing thyroid lesions and its comparison with histopathology are only available. Our study aimed to compare the cell block technique with smear cytology in regards to diagnosing thyroid lesions.

METHODS

A cross-sectional, hospital-based, observational study was conducted in department of Pathology at KIST Medical College and Teaching Hospital, Imadol, Lalitpur during period of 8 months from 1st August 2022 to 1st April 2023. Ethical approval was taken from Institutional Review Committee (Ref no 2079/80/04) before the conduct of the study. Patients of all age groups and both sex with either incidentally detected or evident palpable thyroid lesion were included in the study. Non-consenting patients and patients in whom inadequate material was obtained were excluded. The study participants were explained about the study in detail. They were assured of confidentiality and informed written consent was taken. The study participants were explained about the study in detail.

A convenience sampling technique was used. The sample size was calculated using the formula:

Using formula, \( n = \frac{z^2pq}{e^2} \) and taking \( p = 19.2\% \), \( q = 1-p = 80.8\% \) at 5% maximum tolerable error and \( z = 1.96 \) (for 95% confidence interval), the sample size was calculated as...
59.5 Here 59 participants were included in the study.

After obtaining a written consent, initial examination of the thyroid lesion was done. Under aseptic conditions, the lesion was fixed between the thumb and the index finger and a 21G needle connected to a 10 ml disposable syringe was used to aspirate. One to two needle passes were made for each lesion. Some of the material from the syringe was expelled on to clean and dry microscopic slide, and direct smears were prepared. Staining was carried out using Papanicolaou stain and May-Grünwald Giemsa stain. Remaining material in the syringe was allowed to clot and the pellet obtained thereby was fixed in 10% formalin for 18-24 hours. Routine processing and embedding in paraffin wax was done. Thus, the cell block preparations were done and then stained with Haematoxylin and Eosin stain. Cyto-morphological features in the stained smears were studied and the diagnosis was compared with the corresponding cell block sections.

Data entry was done using Microsoft Excel 2010. Statistical analysis was done by using Statistical Package for Social Sciences (SPSS) version 16 for Windows. Statistical analysis of the diagnostic utility of cell block was evaluated taking into account sensitivity and specificity.

**RESULTS**

FNAC samples obtained from 59 patients of both sex and different age groups with corresponding cell blocks were included in the study. Ultrasound guided FNA was performed wherever indicated in the cases. In all these cases FNAC findings were correlated with cell block preparation, however histopathological correlation could be obtained in only 37 cases. Therefore, the diagnostic efficacy of cell block taking histopathology as gold standard were considered based on the 37 cases which could be followed up histologically.

The average age of the participants undergoing FNAC was 31.95 and maximum patients were in the age group 30-39 years. Male: female ratio was 1:1.68. Of all the patients who presented to the Department of Pathology, KISTMCTH, majority (n=43) were from within the valley. The chief complain among 55 patients was anterior neck swelling and the nature of swelling was solitary type in 35 patients. The consistency of the swelling was soft in maximum 46 patients. Thyroid hormone status was normal in 49 patients and the nature of aspirate was blood mixed in 44 patients. Colloid goitre was the most common diagnosis.

Using the Bethesda system, the cases were distributed as neoplastic, non-neoplastic and non-diagnostic for each technique and the results were as seen in figure 1.

| Table 1: Table comparing the results of FNAC with Cell block |
|-----------------|-----------------|-----------------|-----------------|
| **Variable**    | **Cell block diagnosis** |                  | **Total**      |
|                 | Non-neoplastic   | Neoplastic      | Non-diagnostic |
| FNAC diagnosis  |                  |                  |                |
| non-neoplastic  | 48               | 2               | 0              | 50             |
| Neoplastic      | 0                | 4               | 0              | 4              |
| non-diagnostic  | 2                | 0               | 3              | 5              |
| Total           | 50               | 6               | 3              | 59             |

On tabulating the diagnoses by FNAC and comparing them with cell block diagnoses (Table 1), we can see the advantage of cell block over FNAC. Among the 50 cases diagnosed as non-neoplastic by FNAC, 2 were found to be neoplastic by cell block and similarly among the 5 cases which were not diagnosed by FNAC, 2 cases were confirmed to be non-neoplastic thyroid lesions by cell block.

The gold standard test i.e., histopathological analysis was possible only in 37 patients. On comparing the results of FNAC with those of histopathology (table 2), we can see the sensitivity and specificity of FNAC to diagnose neoplastic cases to be 66.6% and 100% respectively.

Similarly comparing the results of cell block analysis with those of histopathology (Table 3), we found cell block analysis to have 100% sensitivity and 100% specificity to detect neoplastic lesions.

**DISCUSSION**

FNAC is regarded as the single most accurate and cost-effective procedure in thyroid lesions. But like with any other test it has its own constraints. 1,2 Cell blocks were thus introduced in order to improve the cellular yield, accuracy and interpretations. 4 Multiple studies have been done to determine the role of cell block when supplemented with routine FNAC.7,8

In the present study, a total of 59 patients presenting with thyroid enlargement underwent FNA with subsequent cell block preparation. The age of the patients ranged from nine to 64 years with a mean age of 31.95 which was comparable to
The main problem encountered was bloody smears or aspirates that could not be diagnosed. In the undertaken study, the higher rates (6%) of specimen that could not be diagnosed. Nondiagnostic category was found to be 2.22%.

Overall, the majority of patients with papillary carcinoma were female. Most of the patients in the current study resided within the valley which could be explained by the proximity of this tertiary care hospital to the patients. People living in the hilly region were more affected by thyroid abnormalities as compared to patients from Terai region. This corroborates with studies suggesting high prevalence rates of endemic goiter in mountainous and hilly regions of Nepal.

The major presenting symptom in this study was anterior neck swelling. This is similar to the study by Khan et al. In this study, 63% of the patients were female and 37% were males. The male to female ratio was found to be 1:1.68 which was comparable to the study by Hegazy RA et al (M:F = 7:10), Ahmed Z et al (M:F : F= 1:6.5) and Bhatta S et al (M:F= 1:4). Similarly, autoimmune thyroiditis like other autoimmune disorders is predominantly a disease of female. Most of the patients in the current study resided within the valley which could be explained by the proximity of this tertiary care hospital to the patients. People living in the hilly region were more affected by thyroid abnormalities as compared to patients from Terai region. This corroborates with studies suggesting high prevalence rates of endemic goiter in mountainous and hilly regions of Nepal.

Similar to our study, Ahmed Z et al in their study categorized thyroid lesions on the basis of FNA findings and noted the predominance of nonneoplastic lesions (83.33%) as compared to neoplastic lesions (14.44%). Nondiagnostic category was found to be 2.22%. One of the main limitations of thyroid FNAC was the higher rates (6%) of specimen that could not be diagnosed. The main problem encountered was bloody smears or aspirates diluted by colloid. Aspirates with insufficient cellularity were also considered nondiagnostic. Nondiagnostic smears could be attributed to the skill of the aspirator, unavailability of routine ultrasound guided FNA and sample preparation method. Onsite evaluation of the aspirates has also been found to significantly decrease the rates of non-diagnostic specimen.

Cell block preparation is known to increase cellular yield and improve diagnostic accuracy. Among the 50 cases diagnosed as non-neoplastic by FNAC, 2 were found to be neoplastic by cell block and similarly among the 5 cases which were not diagnosed by FNAC, 2 cases (40%) were confirmed to be non-neoplastic thyroid lesions by cell block. Cell blocks provided additional information and established new diagnosis in three cases. Of this one case was diagnosed as Hashimoto’s thyroiditis on cell block. The remaining two cases which were diagnosed as benign on smears (one colloid cyst, other colloid goitre) were diagnosed as follicular neoplasm and papillary carcinoma after examining the cell block. In the remaining 55 cases, cell block findings corroborated with cytological findings and thus aided in the confirmation. Morphological details were enhanced with preservation of the architectural pattern. This was of particular importance in follicular neoplasm and papillary carcinoma.

The circumstances under which smears alone are negative and cell block is positive occurs most commonly when only a small fragment of tumor is contained in the material submitted for cytological examination. Such small fragment will be missed during the preparation of smears, but will be included in the block of remaining material.

Of the 59 FNA performed, subsequent histopathological correlation could be done in only 37 cases. Based on histopathology, 16.22% cases were diagnosed as neoplastic as compared to 10.16% on cell block and 6.77% diagnosed on FNAC.

In the current study the sensitivity of cell block was 100%, specificity 100%. This was similar to the study by Cristo AP et al where sensitivity was 100%, specificity 90%. Similar findings were reported by Ahmed Z et al (sensitivity 93.75%, specificity was 93.75%).

The major contribution of cell block analysis to FNA cytology would be recognition of neoplastic lesion being diagnosed on FNAC, but missed on smears. Similarly, cell block can be useful in confirming the diagnosis of non-neoplastic lesion being diagnosed on FNAC, but missed on smears.
in the present study was to decrease the rate of unsatisfactory specimen and avoidance of repeated aspirations. Upgrading of the diagnosis from benign to malignant lesion was observed in two cases which changed the patient’s management.

CONCLUSION

The main purpose of FNAC in thyroid lesions is to confirm the disease and to triage the patients for surgery. There is a number of literatures claiming the accuracy and usefulness of thyroid cytology. However, there is also evidence showing possible limitations and pitfalls of this procedure. Cell blocks were introduced to improve the accuracy and the interpretation. FNAs can obtain sufficient material which can be diagnostically useful when processed as cell block. As both procedures are done in a single setting, combination of two procedures has beneficial effect not only to support diagnosis but also to establish new diagnosis.

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REFERENCES: