Thyroid nodules are fairly common in clinical practice. Palpable nodules are seen in approximately 10% of women and 2% of men.1 With the advent of high resolution ultrasonography and extensive usage of radiological modalities, there has been a rampant increase in the discovery of asymptomatic non-palpable thyroid nodules referred as thyroid ‘incidentalomas’. Consequently, the worldwide reported prevalence has become more than double, which has led to threefold increase in the frequency of diagnostic thyroid aspirates.2 Keeping in view the growing prevalence of these cases, there is a great likelihood that in recent times the number of thyroid aspirates would outnumber the cervical pap smears. There are many causes of thyroid nodules which include both benign and malignant conditions, but it is the fear of malignant causes that warrants further investigation and management of these nodules. Thyroid nodules are mostly without symptoms, however, the absence of symptoms does not rule out malignancy.

Currently, one of the most controversial areas in the management of thyroid nodules is to decide whether these incidental thyroid nodules require further investigation, since less than 5-10% of these nodules harbour malignancy.3 On the other hand, mortality associated with thyroid malignancy is extremely rare.4 This ambiguity exists because of the dearth of randomized prospective trials documenting mortality benefits owing to the ethical limitations in designing and conducting these trials.

The diagnostic evaluation consists of clinical risks assessment as these nodules are more likely to harbour malignancy at extremes of age, male gender and persons exposed to radiation in the thyroid region. In addition to clinical risk evaluation, serum TSH measurement, ultrasound features and fine needle aspiration cytology (FNAC) are the main tools to diagnose sinister nodules.

FNAC remains the most cost-effective and reliable diagnostic tool used for the assessment of thyroid nodules with enhanced efficacy under ultrasound guidance.5-7 Local studies have also documented the high sensitivity and specificity of the procedure in diagnosis of thyroid malignancy (90% and 87.5% respectively).8,9 However, the clinical efficacy of the technique mainly revolves around the expertise of the operator carrying out the procedure and histopathologist interpreting the cytology results.5 Moreover, 20-30% of the FNAC results are in the grey zone posing significant clinical dilemma among thyroidologists.10 The terminology used for such cases ranges from indeterminate to atypical cellularity to suspicious for follicular neoplasm to Hurthle cell neoplasm or suggestive of papillary thyroid carcinoma.

According to the guidelines of American Thyroid Association (ATA) and the European Thyroid Association (ETA), results should be subjected to partial or near total thyroidectomy for the patients with intermediate cytologyy.11 However, the debate continues whether these indeterminate nodules should be referred for surgery, since 25-50% of them prove to be malignant in final histopathological analysis.12

In developing countries like Pakistan, cost benefit aspects also need to be considered in making decisions regarding surgical procedure in the absence of survival or morbidity benefit. Carmeci and colleagues documented that the probability of non-diagnostic/ inadequate sampling can be reduced from 16% to 7% by using the sonographic guidance technique as compared to simple palpation.6 Conversely, there are small percentage of patients who actually harbour malignancy in the face of normal FNAC results from 1-11% documented false negative rate especially in the cases of large nodules ≥ 4 cm.13 Careful observation alone is an option for these patients until they show an increase in > 50% of volume either by simple palpation or sonographically. Reliance on FNAC has reduced the number of surgeries performed for thyroid nodules by almost 50% and has also improved the yield of malignancy in thyroid glands that have been removed surgically.

Ultrasonography has a valuable role to play in the management of thyroid nodules. There are certain sonographic features which are certainly in favour of malignancy and include presence of microcalcifications, hypoechogenicity, poorly defined margins, intermodal/ central vascularity, lack of halo sign and presence of regional lymphadenopathy.14 Moon and colleagues reported that an elongated shape in comparison to a
wide shape, defined by an anteroposterior to transverse ratio of one or greater, is extremely specific (91.4%) for malignancy. In contrast, purely cystic content in comparison to solid component in a nodule, points towards the benign nature of the nodule.

Apart from ultrasound, other imaging modalities in the form of radionuclide thyroid scan, C.T, MRI and positron emission tomography (PET) scanning are not routinely recommended. On the other hand, thyroid nodules incidentally found on PET scanning done for other reasons have 50% more likelihood of harbouring malignancy. Ultrasound elastography, a comparatively new technique used to evaluate tissue stiffness has ability to accurately predict malignancy in solid nodules, but still its use is limited in partially cystic nodules and multinodular goiter.

It is a myth that risk of malignancy is negligible in multinodular goiters. Two of the studies found that there was no statistical difference in the occurrence of malignant disease in multinodular goiter versus single nodules (48% vs. 52% respectively). A retrospective study done by the authors' team showed that majority of thyroid malignancies present as multinodular goiters rather than solitary nodules. In case of multinodular goiters, nodules ≥ 1 cm with suspicious sonographic parameters should ideally be aspirated as is recommended for solitary nodules.

With regards to the treatment to suppress the growth of nodules, there is another myth that thyroxin therapy reduces the growth of thyroid nodules. A study based on growth of thyrocyte documented that TSH suppressive therapy does not have an effect on the expression of insulin/IGF1 signaling pathways.

Management of thyroid nodule after work up is either surgery or a diligent follow-up based on FNAC results. Genetic biomarker can be used to assist in interpretation of FNAC samples and is likely to enhance the ability to distinguish benign from malignant nodules. Greater than 70% of papillary carcinoma will have mutations in BRAF, RAS on RET/PTC genes. Clinical utility of genetic biomarkers lies in helping to make the decision between thyroid lobectomy and total thyroidectomy when FNAC shows follicular or indeterminate/suspicious malignancy lesion.

Despite several guidelines, various questions remain unanswered about the management and outcome of thyroid nodules, creating some uncertainty among physicians. Interests remain strong since clinicians/surgeons look forward to definite agreement among multidisciplinary teams in the management of thyroid nodules. Most importantly, the diagnostic and therapeutic decisions should be based on patient's preference and overall risk/benefit analysis.

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