

Solitary Thyroid Nodule High Incidence of Thyroid Cancer

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Abstract

The Aim: The preoperative distinguish between benign and malignant in solitary thyroid nodule is important. It helps to avoid unnecessary surgery and its adverse effects, such as hypothyroidism, hypocalcemia, and recurrent nerve injury.

Methods: descriptive perspective analyzed data over a period of 6 years April 2015_April 2021 In Saudi hospital at Hajjah, Yemen. 226 thyroid operations for 207 patients ,135 patients diagnosis as Solitary thyroid nodule and 72 patients as Multi nodular goiter. the patients with a clinically as solitary thyroid nodule were included in the study group.

Results: 135 cases of clinically detected STN,126 female and 9 male patients, between 14_65 years age, median 41 years and mean 39.76 years, (94, 41) patients respectively Rt side thyroid effect more than Lt side, FNAC sensitivity, specificity and accuracy was (61%, 72%, 64%) respectively. Postoperative histopathology was reported 100(74%) patients as benign thyroid nodule and 35 patients (26%) as malignant thyroid nodule. Post operative transient hypocalcemia in 9 patients (7%), and temporary horsnese in 3 patients (2%).

Conclusion: The incidence of malignancy in STN is high. Rapid growth by history and hard fixed nodule by examination and hypoechoic, micro calcification and cervical lymphadenopathy on USG frequently in malignant nodules. Male risk factor for thyroid cancer while age, number and size of nodules were not. FNAC more helpful for diagnosis if aspiration under USG guide and reading by experience histopathologest .Type of surgery depending on preoperative evaluation including history, examination, ultrasound, FNAC result, and intraoperative assessment of the nodule .Less complications of thyroid surgery by experience surgeon.

Introduction

Solitary thyroid nodule is defined clinically as a localized thyroid enlargement with an apparently normal remaining gland, refers to an abnormal growth of thyroid cells that forms a lump within the thyroid gland. Although the vast majority of thyroid nodules are benign, a small proportion of thyroid nodules contain thyroid cancer. In order to diagnose and treat thyroid cancer at the earliest stage, most of thyroid nodules need some type of evaluation. Often these abnormal growths of thyroid tissue are located at the edge of the thyroid gland, so they can be felt as a lump in the front of neck. When they are large or when they occur in very thin individuals, they can even sometimes be seen as a lump in the front of the neck^[1]. Thyroid nodules are common. Prevalence and incidence increases with age, with spontaneous nodules occurring at a rate of 0.08% per year beginning early in life and extending into the eighth decade. Palpable Thyroid nodules are found in 5% of persons aged an average of 60 years. With the use of imaging techniques, particularly ultrasound, the chance of detection of thyroid nodules has increased many folds about 20%_60%. [2,3,4,5,6,7].

Thyroid nodules are more common in women than in men.[3,4,5,],its incidence in females is about one in 12–15 young women has a thyroid nodule, but in males is about one in 40 young men has a thyroid nodule. More than 95% of all thyroid nodules are benign (noncancerous growths). [4,5].

However, the reported incidence of thyroid cancer in general population is low, being only about 1%. Thyroid cancers occur in approximately 5_15% of all thyroid nodules independent of their size.[3,8]

The recent data suggest that the incidence of thyroid malignancy is increasing over the years. [2,3],worldwide increase incidence of thyroid cancer partly due to increased detection by US and other imaging studies but also to true increase in incidence of papillary thyroid carcinoma (PTC). [9]

The occurrence of malignancy is more in solitary thyroid nodules (STN) compared to multinodular goiter. [2,10,11].

The preoperative evaluation of thyroid nodules to distinguish between benign and malignant nodules is very important. It helps to avoid unnecessary extensive surgery and potential surgery related adverse effects, such as hypothyroidism, hypocalcemia, and recurrent laryngeal nerve injury.[2]

Preoperative diagnoses were classified as benign, suspicious or malignant based on including history, clinical examination findings (i.e. cervical lymphadenopathy, hoarseness of voice, presence of metastasis), thyroid function test, ultrasonographic features[12] and FNAC (The Bethesda system for reporting thyroid cytopathology).[13]

The ultrasound the thyroid gland is used in differentiating the true solitary thyroid nodule from those with multinodular gland. Also it classifies the nodule into solid, cystic, or mixed. However it admit a little help in determining the pathological types of the nodule[14].

Fine-needle aspiration (FNA) cytology is the first step that is performed to differentiate malignant nodules; however, 5–15% of FNA revealed inadequate nondiagnostic samples, and 15–30% of FNA result in indeterminate cytology findings category III (atypia or follicular neoplasm of undetermined significance) and category IV (suspicious for follicular neoplasm) according to the Bethesda system [15, 16].

Fine-needle aspiration cytology (FNA) is regarded as the first diagnostic step to differentiate malignant from benign nodules. FNA has served with high accuracy to diagnose papillary thyroid carcinoma which accounts for 80%–90% of all thyroid cancer because papillary thyroid carcinoma has several specific cytological nuclear features, such as optically clear elongated nuclei with nuclear grooves and intranuclear cytoplasmic pseudo inclusions [17,18,19]

Fine-needle aspiration cytology (FNAC) has become the corner stone investigation. Unfortunately, on the basis of cytological characteristic alone, the pathologist cannot reliably distinguish benign from malignant follicular thyroid lesions, ~20% of Fine-needle aspiration cytology (FNAC) will be given a final diagnosis of follicular malignancy. [20].

For benign solitary nodule hemithyroidectomy of the involved lobe is recommended and not total thyroidectomy, but in treating suspicious and false-negative (FN), Fine-needle aspiration cytology (FNAC) reports could be overcome by total thyroidectomy, Hemithyroidectomy with or without isthmusectomy is performed as the initial operation for patients with an indeterminate cytological diagnosis and no clinical evidence of regional or distant metastatic disease or any other concurrent indication for total thyroidectomy. If gross extrathyroidal tumor extension or lymph node metastasis is found at the time of operation, a total thyroidectomy is then carried out[21].

The aim of the present study was to evaluate patients with clinically detected solitary thyroid nodule for the presence of malignancy, in relation to various factors like age, gender family history, rapid growth and clinical examination hard, fixed nodule and ultrasonography (USG) findings like size of the nodule, echogenicity, micro calcification, and presence of lymphadenopathy, also Fine-needle aspiration cytology (FNAC) results. We also planned to compare the prevalence of malignancy in both solitary and multiple thyroid nodules detected by ultrasonography (USG).

Materials And Methods

This is a descriptive perspective analyzed our departmental data over a period of 6 years April 2015_April 2021. In Saudi hospital at Hajjah,Yemen. About 226 thyroid operations for 207 patients ,135 patients diagnosis as Solitary thyroid nodule and 72 patients as Multi nodular goiter. All the patients who operated in surgical department with a clinically detected solitary thyroid nodule were included in the study group. Our approach was individualized as single team. Preoperative history, examination, thyroid function test, ultrasonography (USG) and fine-needle aspiration cytology were planned in all these patients. Hemi thyroidectomy and total thyroidectomy with and without neck dissection were performed wherever appropriate. The patients and their relatives gave consent to use the information for publication purpose. The study was approved by institutional ethics committee.

For all patients the following data were recorded: Age, gender, history of radiation exposure, family history of thyroid disease ,symptoms and growth rate of nodule , and the thyroid hormone profile. The operative procedure was based on the different parameters like age of the patients, clinical examination, , Ultrasound interpretation, fine-needle aspiration cytology (FNAC) findings and indirect laryngoscopy. The decision for surgery was based on individual patient's examination and investigation findings.

In most of the patients, the plan of surgery was decided beforehand. If it was a solitary thyroid nodule, diagnosed clinically, ultrasonographically as well as fine-needle aspiration cytology (FNAC) as malignancy or high suspicion for malignancy proceed with total thyroidectomy. For others lower grad hemi-thyroidectomy of the involved side was done and the specimen was sent for routine histopathological examination (HPE). because inconclusive results no frozen section use, we preferred to wait till the final histopathology report. If result of histopathological was positive for malignancy, completion thyroidectomy was done in 4_6 weeks, The decision for other procedures, total thyroidectomy with central neck dissection, total thyroidectomy with selective neck dissection, total thyroidectomy with

modified radical neck dissection was based on the clinical, radiological, fine-needle aspiration cytology (FNAC) and histopathology findings.

During surgery, the site and type of incision were decided. Hemostasis, safeguarding of the recurrent laryngeal nerve, parathyroid, and other vital structures was taken care of during the dissection. Appropriate measures were taken to correct postoperative hypocalcemia and care of the drain was taken . Further treatment plan was decided based on the final histopathology report. If the report was benign, the patient was managed by regular monitoring of hormone levels, with or without thyroid hormone supplementation. Hypocalcemia features were managed with supplementation of calcium and Vitamin D.

If the final histopathology report was either follicular or papillary carcinoma, the patients were advised to undergo I-131 whole body scan, preferably within 4–6 weeks after surgery and radioactive iodine ablation was advised for residual tissue in the thyroid bed. All the patients were advised regular follow-up one week, one month, 6months, one year, 2years.

Statistical analysis was done using Statistical Packages for Social Sciences (SPSS), version 20.0 software (SPSS Inc; Chicago, IL, USA). Comparison of proportions between groups was done by the χ^2 test, taking P < 0.05 as significant.

Results

During our study period April 2015-April 2020 in Surgical department of Saudi Hospital at Hajjah Yemen about 226 thyroid operations for 207 patients, 135(65%) patients diagnosis as Solitary thyroid nodule and 72(35%) patients as Multi nodular goiter during period. The present study included all the patients of clinically detected Solitary thyroid nodule.

135 patients was diagnosed clinical as Solitary thyroid nodule underwent for 154 thyroid operations incidence. Solitary thyroid nodule according to the Sex to 126/135 (93%) female and 9/135(7%) male. (Table 1),135 Patients with. Solitary Thyroid Nodule b/n age 14-65 years, median age 41 years, mode 45 years, average mean age 39.76 years, ring 51 years and Stander deviation 13.98.

Result of histopathology show total 100/135 patients (74%) Develops benign thyroid nodule from patients diagnosed clinical as Solitary thyroid nodule . 95/135 was female(70%) and 5/135 male(4%),95 /100 was female(95%) and 5/100 was male(5%).

All patients Diagnosis clinical as Solitary thyroid nodule result histopathology shows benign thyroid nodule was age b/n 14_65 years, median age 31.5 years, mode 30 years and average mean age 34.72 years and stander deviation 12.40.

Result of histopathology show total 35/135 patients (26%) Develops thyroid cancer from patients diagnosed clinical as Solitary thyroid nodule . 31 /135 was female(23%) and 4/135 male(3%) and 31/35 was female(89%) and 4/35 was male(11%).

Incidence of thyroid cancer during female with solitary thyroid nodule was 31/126(25%).

Incidence of thyroid cancer during male with solitary thyroid nodule was 4/9(44.44%). this indicate high incidence thyroid cancer in male patients.

All patients Diagnosis clinical as Solitary thyroid nodule result histopathology shows thyroid cancer by age range b/n 15_62 years, median age 35 years, mode 23 years and average mean age 35.97 years, and stander deviation 11.91.

(Table 2) show Solitary thyroid nodule more Common in age group between 21-30 years old are about 50 patients and the next age group between 41-50 years old are about 29 patients.

(Table 3) show distribution according to the side that 135 Patients with Solitary Thyroid Nodule There is 94 Patients Rt Side Solitary Thyroid Nodule and 41 Patients Lt Side Solitary Thyroid Nodule, Our result, Solitary thyroid nodule appear (70%) in Rt Side of thyroid and (30%) in Lt Side of thyroid that indicated Rt side effects more than Lt side thyroid.

Benign solitary thyroid nodule distribute according to side as following Rt side 72/100(72%), and Lt side 28/100(28%),Rt side benign solitary thyroid nodule appear in 72 patients 69 female and 3 male patients ,clinical diagnosis as Rt side true Solitary thyroid nodule 49 patients, cystic Rt side solitary thyroid nodule 7 patients, 13 patients prominent Rt side solitary thyroid nodule and 3 patients Rt side solitary thyroid nodule Toxic adenoma.

Lt side benign solitary thyroid nodule appear 28 patients 26 female and 2 male patients, clinical diagnosis as Lt side true Solitary thyroid nodule 17patients, 2 patients with huge nodule 7-8 cm, cystic Lt solitary thyroid nodule 3 patients, prominent Lt Solitary thyroid nodule in 7 patients.

Solitary Thyroid Malignant Nodule appear More at Rt Side Thyroid in 22/35 patients (63%) and 13/35 patients (37%) in Lt Side of thyroid gland.

135 patients with solitary thyroid nodule distribute according to size of nodule by cm ,Most Solitary thyroid nodule even benign or malignant nodule take size between 2.1_4 Cm.(Table 4).

67/135 (50%) Patients with Solitary thyroid nodule show size of nodule b/n 2.1_4 Cm, 50/100 patients (50%) with benign Solitary thyroid nodule show size of nodule between 2.1_4 Cm and 17/35 (49%)Patients with Malignant Solitary Thyroid was Size b/n 2.1_4 CM mostly effected groups.

Before operation History and clinical examination done for all patients ,most common presentation of STN was as a swelling in the anterior aspect of the neck. The swelling was noticed by patient's relatives in most instances and in few cases, by patients themselves. Other less common symptoms were pain, hoarseness and dysphagia. The duration of symptoms ranged from one to 24 months. Rapid growth of nodule significantly last 3_6 month 20 cases, Family history of thyroid nodule was positive in 10 cases ,Hard nodule in 32 cases .

Laboratory tests including thyroid function test showed (Table 5)Thyroid function test was done in all 135 patients. 125(93%) patients were euthyroid, 6 (4%) hypothyroid and 4 (3%) patients were hyperthyroid. Before surgery, these patients were made euthyroid by supplementing thyroxin or by treatment with anti-thyroid drugs.

Benign STN According to the functional euthyroid appear clinical and para clinical before surgery in 93/100(93%) patients with Benign solitary thyroid nodule, 32/35(91%) patients with malignant solitary thyroid nodule.

hypothyroidism in 6 patients' 5 female and one male, hypothyroidism in Rt Solitary thyroid nodule in 4 patients and 2 patients Lt Solitary thyroid nodule.

by FNAC 2 cases with Benign colloid nodule with compression symptoms, one case follicular neoplasia ,one case Hurthle cell neoplasia , one case suspicious categories, one case papillary thyroid cancer . benign solitary thyroid nodule appear in 3/6 (50%)patients, with hypothyroidism, All female, 2 Lt side and one Rt side .Result of histopathology was hashimotos thyroiditis in 2 cases and one case colloid goiter with hyperplastic nodule. After became euthyroid by medical treatment underwent surgery by total thyroidectomy in 2 cases and Rt hemithyroidectomy in one case.

Malignant Solitary thyroid nodule appeared 3/6 (50%) patients was hypothyroidism before operation, results of histopathology was malignant nodule as papillary thyroid cancer on background of hashimotos thyroiditis, one of them with lymph node metastasis. That's mean high risk for malignant transformation specially Papillary Thyroid cancer than lymphoma, after became euthyroid by hormonal replacement underwent to thyroid surgery as following.

Total thyroidectomy with central lymph nodes dissection in one patient, Total thyroidectomy with Rt lymph nodes dissection in one patient and was complicated by Temporary horsness due to laryngeal edema that was improved during the first month.

Rt hemithyroidectomy followed by completion Lt hemithyroidectomy with central lymph nodes dissection done in one patient. Should be noted that all patients received post operative thyroid hormones replacement, also should be noted not all cases hypothyroidism was hashimatous thyroiditis, as one case hypothyroidism and histopathology result was colloid goiter with hyperplastic nodule.

hyperthyroidism appear in 4/100 patients All female with benign solitary thyroid nodule in the Rt side, histopathology result was 3 cases benign toxic adenoma And one case with colloid goiter hyperplastic nodule. After became euthyroid by medical treatment underwent surgery by total thyroidectomy, subtotal thyroidectomy, near total thyroidectomy and one case Rt hemithyroidectomy. That case post hemithyroidectomy become euthyroid follow up for 5years no recurrent until now and no received any replacement, but all other 3 cases received thyroid hormone therapy.

35 patients with thyroid cancer classified as histopathology result 26(74%) papillary thyroid cancer(10 classical,13 follicular variant,3 micro carcinoma), 5(14%) Follicular cancer. 1 (3%) Hurthle cell

carcinoma, 1 (3%) Medullary Thyroid cancer, 1 (3%) Non_Hodking lymphoma, 1 (3%) anaplastic carcinoma.

Findings on ultrasonography and ultrasonography predictors of malignancy

Neck Ultrasound showed solitary thyroid nodule in 135patients,85 patients (62.96%) as true solitary nodule, 4 of them big nodule with compression symptoms and trachea deviation, prominent nodule in 32 patients (23.70%), recurrent cystic 11 patients(8.14%), and two cases (1.48%) apparent thyroid nodule as supraclavicular mass. One case (0.7%) Recurrent Rt Solitary thyroid nodule after thyroidectomy 15 years ago, and 4 (2.96%) cases as Rt side toxic adenoma.

Ultrasound examination findings (Table 6) were available in 135 clinically detected Solitary thyroid nodule. Clinical diagnosis of Solitary thyroid nodule confirmed on Ultrasound in 85 (63%) patients, whereas in 32 (24%) patients, the Ultrasound revealed Prominent nodule of multinodular goiter.

On postoperative histopathology are available for 135 patients, 35 nodules were reported as malignant. 23 (66%) of true solitary thyroid nodule turned to be malignant on postoperative histopathology, while 12 patients (34%) of Prominent nodule of multinodular goiter.

Majority of the nodules (n=67, 50%) were 2–4 cm in size. However, there was no significant correlation between tumor size and the risk of malignancy .

By ultrasound hypoechoic nodule in 33/35(94%) patients with malignant nodule and 15(15%) in benign nodule.

By ultrasound nodule was solid in 30/35(86%) patients with malignant nodule, cystic nodule one patient(3%) with malignant nodule, both solid and cystic (mixed echoic) in 4(11%) patients with malignant nodule. was solid in 10(10%) patients with benign nodule, cystic nodule in 10(10%) was benign nodule, mixed solid and cystic component appeared in 80(80%) patients with benign nodule.

In addition, Ultrasound detected micro calcification in 38 patients out of which 28 turned out to be malignant while 10 nodules with micro calcification were reported as benign. Thus, 28 out of a total 35(80%) malignant case had micro calcification in contrast to 10 of 100 (10%) benign nodules, Lymph nodal enlargement was detected by Ultrasound in 26 patients. 24 of 35 (69%) malignant nodules had lymph node enlargement as against only 2 of 100 (2%) benign nodules.

fine-needle aspiration cytology

Fine-needle aspiration cytology results according to the Bethesda Categories (Table 7) was done before the surgery in all the 135 patients was reported as category 1=6 (4%), category 2=66(50%), category 3=10(7%), category 4=39(29%), category 5=11(8%), category 6=3(2%).

In(Table 8)Fine needle aspiration cytology results according to the Bethesda Categories with its subtypes. As inadequate for diagnosis 6(4%) patients, colloid nodule 28(21%), adenomatous nodule 13(10%), hyperplastic nodule 15(12%), colloid cystic nodule 7(5%), atypical cell 10(7%), follicular cell neoplasia 36(27%), Hurthle cell neoplasia 3(2%), suspicious for malignant 11(8%), malignant 3(2%).

(Table 9) and (10) correlations between FNAC and histopathology results

Performance of FNAC in diagnosis of thyroid neoplasm calculated by numerous tests is available:

- 1. True positive (TP)= the number of cases correctly identified as having thyroid neoplasm
- 2. False Positive (FP)= the number of cases incorrectly identified as having thyroid neoplasm
- 3. True Negative (TN) = the number of cases correctly identified as not having thyroid neoplasm
- 4. False Negative (FN)= the number of cases incorrectly identified as not having thyroid neoplasm
- 5. Sensitivity measures the percentage of patient who are correctly identified as having thyroid neoplasm. Thus, sensitivity = TP/(TP + FN)
- Specificity measures the percentage of patient who are correctly identified as not having thyroid.
 Thus, specificity = TN/(TN + FP)
- 7. Accuracy measures ability of fine-needle cytology to correctly identify the cases that having thyroid neoplasm and the cases that not having thyroid neoplasm. Thus, accuracy = (TP + TN)/(TP + FP + TN + FN)
- 8. Predictive value positive is the proportion of positives that correspond to the presence of the thyroid neoplasm. Thus, predictive value positive = TP/(TP + FP)
- 9. Predictive value negative is the proportion of negatives that correspond to the absence of the thyroid neoplasm. Thus, predictive value negative = TN/(TN + FN).

Table 11 Overall performance of fine Needle aspiration cytology in diagnosis of thyroid neoplasia

Sensitivity 61.33%, specificity 71.66%, accuracy 64.44%, positive predictive value 73.01% and negative predictive value 59.72%.

Histopathology findings

135 patients with solitary thyroid nodule after operation results of histopathology of them 100/135 patients (74%) diagnosis as benign thyroid nodule and 35/135 patients (26%) diagnosis as thyroid cancer(Table 12) and (13) show the post operative Histopathology was malignant solitary thyroid nodule 35(26%) and Benign solitary thyroid nodule in 100 (74%), and, of that Benign non neoplastic 60(44%)including colloid nodule 20(15%) patients, adenomatous nodule 13(10%) patients, hyperplastic nodule 12(9%),cystic nodule 5(4%)patients, chronic thyroiditis 7(5%) patients (hashimotos and lymphocytes thyroiditis)and toxic adenoma 3(2%)patients. The benign neoplastic nodule 40(30%)patients including follicular adenoma 28(21%),hurthle cell adenoma 6(4.4%) patients, and 6(4.4%) non invasive follicular neoplasia with papillary features (NIFTP).

20 patients with benign colloid goiter 4 of them with cystic degeneration and hyperplastic changes ,13 patients with benign adenomatous goiter 4 of them with cystic degenerative changes.

12 patients with benign hyperplastic nodular goiter 2 of them with cystic changes and marked fibrosis and calcification. And one them with hyperplastic papillary nodule in benign nodular goiter, 5 patients with benign cystic nodule 3 of them with hemorrhagic cystic nodule and 2cases colloid cystic nodule, 7 patients with chronic thyroiditis (hashimotos and lymphocytes thyroiditis),3 cases with hypothyroidism,3 patients with toxic adenoma and hyperthyroidism with average nodule size 4-5cm,28 patients with benign follicular adenoma 3 of them with lymphocytic thyroiditis and one case with cystic degenerative changes, 6 patients with benign hurthle cell adenoma (oncocystic neoplasm) and 6 patients with Non invasive follicular thyroid neoplasia with papillary nuclear like features (NIFTP) ,This type of thyroid tumor was previously classified non invasive encapsulated follicular variant of papillary thyroid cancer , but before few years reclassified this tumor as non malignant because character by absent capsular, vascular invasion ,tumor necrosis, high mitotic activity and have indolent behavior and may be over treatment if classify as type of cancer , All 6 patients was female ,between age 22_58 years ,mean 40.83 years ,median age 41 year, with standard deviation 12.38.

4 patients diagnosis as Lt Solitary thyroid nodule and 2 patients diagnosis as Rt Solitary thyroid nodule and Average size 2_4 cm in 3 patients, 1_2cm in 1 patients and 4_5 cm in 2 patients, Fine needle aspiration cytology benign cytology in 3 patient, Follicular neoplasia in 2 patients and Suspicious nodule in 1 patients, All 6 patients was euthyroid before operation, 3 patients underwent Lt hemithyroidectomy and 2 patients underwent Rt hemithyroidectomy.

as consider this term as benign not followed by total thyroidectomy ,only follow-up needed.

One patient underwent Total thyroidectomy because was in suspicious category ,One patient development post operative temporary horsnese was improved after few weeks .

In (Table 14) Histopathology subtype results was malignant solitary thyroid nodule in 35(26%) patients ,26(74%) papillary thyroid cancer(classical papillary thyroid cancer 10cases, papillary micro carcinoma 3 case and 13 were reported as the follicular variant of papillary carcinoma (FVPTC)) , 5(14%) Follicular cancer . 1 (3%) Hurthle cell carcinoma, 1 (3%) Medullary Thyroid cancer, 1 (3%) Non_Hodking Lymphoma , 1 (3%) anaplastic carcinoma .

Management

Depending on the interpretation of the FNAB cytological specimen, management consists of observation, levothyroxine suppression therapy, or surgery.

Patients with benign solitary thyroid nodules may undergo observation or levothyroxine suppression therapy as the initial treatment modality. Levothyroxine is typically administered for 6-12 months to determine if the solitary thyroid nodule decreases in size. If the nodule decreases in size after treatment with levothyroxine, this medication is discontinued, with follow-up examination of the thyroid nodule in 3-

6 months. However, if a benign solitary thyroid nodule increases in size, a repeat trial of levothyroxine and repeat FNAB may be indicated. Additionally, growth of a thyroid nodule during levothyroxine therapy is a strong indication for surgery.

No consensus exists regarding the degree of thyroid suppression or the efficacy of levothyroxine therapy. In fact, many endocrinologists no longer recommend thyroid suppression because of potential long-term adverse effects, such as osteoporosis and cardiac arrhythmias. Still others maintain a thyroid-stimulating hormone (TSH) level ranging from 0.1-0.3 mU/L rather than suppressing to the lowest limits of detectability to avoid immediate toxicity and long-term side effects.

Solitary thyroid nodules that are malignant, suspicious, or indeterminate on FNAB require excisional biopsy in the form of thyroidectomy. Considerable controversy exists regarding the extent of surgery for malignant, suspicious, or indeterminate solitary thyroid nodules.

Type of Surgery and operative findings

Patients with Solitary thyroid nodule According To Surgical procedures underwent for them

In (Table 15) there are 154 operation for 135 patients with Solitary thyroid Nodule 126 patients (93%)female and 9(7%)male patients age b/n 14-65 years.

100 thyroid operation for 100 patients with benign solitary thyroid nodule and 54 thyroid operation for 35 patients with malignant solitary thyroid nodule, distribute as following .

Rt hemithyroidectomy for 70 patients with Rt Solitary thyroid nodule, 60 cases was benign Solitary thyroid nodule, 9 cases followed by completion thyroidectomy after results of histopathology confirm malignant cancer and one case result of histopathology was papillary micro carcinoma 1_2cm was enough treat by Rt hemithyroidectomy.

Lt hemithyroidectomy for 32 patients with Lt Solitary thyroid nodule, of 22 cases was benign Solitary thyroid nodule and 10 cases followed by completion thyroidectomy when results of histopathology confirm malignant cancer.

19 Completion thyroidectomy after hemithyroidectomy when result of the histopathology was cancer ,10 patients completion Rt hemithyroidectomy and 9 patients Completion Lt hemithyroidectomy.

Completion Thyroidectomy with central lymph nodes dissection 17 patients (16 papillary thyroid cancer and one medullary thyroid cancer) and completion thyroidectomy with out central neck lymph nodes dissection in two patients (follicular thyroid cancer and hurthle cell cancer).

Total thyroidectomy for 22 patients, 16 patients Rt Solitary thyroid nodule and 6 patients Lt Solitary thyroid nodule, 14 patients with benign nodule and 8 patients with malignant solitary thyroid nodule (2 patients Lt Solitary thyroid nodule and 6 patients Rt Solitary thyroid nodule) treat by total thyroidectomy

and results of histopathology was 3 patients papillary thyroid cancer,4 patients follicular cancer, one anaplastic cancer. Here papillary thyroid cancer not follow by any type of neck dissection because total thyroidectomy depended on result of FNAC was false negative for Malignancy.

Near total thyroidectomy for one patient Rt Solitary thyroid nodule Toxic adenoma.

Subtotal thyroidectomy for one patient Rt Solitary prominent thyroid nodule Toxic adenoma.

Total thyroidectomy with central lymph nodes dissection 2 patients after FNAC results was malignant category 6 (papillary thyroid cancer) one of them underwent Total thyroidectomy with central lymph nodes dissection with resection underlying soft tissue infiltrated and part of strap muscle involved in patient with papillary thyroid cancer infiltrated underlying soft tissue and muscle was complicated by Temporary hypocalcemia.

Total thyroidectomy With Modified Neck dissection 4 patients ,3 cases Total thyroidectomy with Rt modified Neck dissection one case complicated by Temporary hypocalcemia,1 case Total thyroidectomy with Lt modified Neck dissection complicated by Temporary hypocalcemia and Total thyroidectomy with Selective Rt lymph nodes dissection in 3 patient one patient with papillary thyroid cancer and level 2 lymph nodes positive and 2 patients was suspicious category with Lymph nodes at level 3 by FNAC but Result of histopathology was benign hashimotos goiter .

Neck dissection was done in 26 patients, 24 patients with malignant nodule out of them 6 showed metastatic deposit in the lymph nodes.(5 patients papillary thyroid cancer, one patient non Hodgkin lymphoma in back ground of hashimatous thyroiditis), also two patients benign thyroid nodule underwent selective lymph nodes dissection because FNAC gave us false positive result. (Table 16) Patient underwent Total thyroidectomy with Rt selective lymph nodes dissection level 3 but Result of histopathology was hyperplastic nodule with marked fibrosis and calcification. Other case result of the histopathology was hashimotos thyroiditis,100 thyroid operation for 100 patients with benign solitary thyroid nodule distribute as following.

60 Rt hemithyroidectomy, 22 Lt hemithyroidectomy, 14 total thyroidectomy and 2 total thyroidectomy with Selective Rt neck lymph nodes dissection, (For these 2 cases FNAC was suspicious category with clinical Lymph nodes . One case result of the histopathology was benign hyperplastic nodule with marked fibrosis and calcification also this case complicated by Temporary hypocalcemia, Other case result of the histopathology was hashimotos thyroiditis), One case subtotal thyroidectomy for Solitary toxic adenoma and One case near total thyroidectomy for Solitary toxic adenoma .

Also cancer distributed according surgical operation (Table 15), 17 patients under went Completion thyroidectomy with central lymph nodes dissection . 16 Papillary Thyroid cancer ,1 medullary thyroid cancer, as 9 Rt solitary Thyroid nodule proved thyroid cancer after Rt hemithyroidectomy and 8 patients Lt solitary Thyroid nodule proved thyroid cancer after Lt hemithyroidectomy. all follow by completion thyroidectomy with central dissection in 17 cases.

2 patients underwent completion thyroidectomy with out central neck lymph nodes dissection after Lt hemithyroidectomy with results of histopathology one case follicular thyroid cancer and other case hurthle cell cancer.

8 patients with solitary thyroid nodule (2 patients Lt Solitary thyroid nodule and 6 patients Rt Solitary thyroid nodule) treat by total thyroidectomy. 3 papillary thyroid cancer, 4 follicular cancer, 1 anaplastic cancer. Here papillary thyroid cancer not follow by any type of neck dissection because total thyroidectomy depended on result of FNAC was false negative for Malignancy.

2 patients with solitary thyroid nodule (Rt Solitary thyroid nodule) treat by total thyroidectomy and central lymph nodes dissection. After FNAC true positive for Malignancy, One cases result of the histopathology papillary thyroid cancer on back ground of hashimatous thyroiditis, other one papillary thyroid cancer with soft tissue infiltrated was resected with part of strap muscle involved and positive lymph node.

One patients with solitary thyroid nodule (Rt Solitary thyroid nodule) treat by total thyroidectomy and selective Rt Neck lymph nodes dissection level 2. Result of histopathology was Papillary thyroid cancer of one lobe, free other lobe With Capsular and Lymph-vascular Invasions. Metastatic Deposit Of Tumor In Two Cervical Lymph Nodes(2/4). AJCC TNM STAGING [pT3, N1,Mx].

4 patients underwent thyroidectomy with modified neck lymph nodes dissection (one Lt apparently thyroid nodule) FNAC metastasis papillary thyroid cancer by total thyroidectomy with functional Lt Modified neck dissection, result of the histopathology papillary thyroid cancer with positive lymph node. (3 cases Rt Solitary thyroid nodule one of them Rt apparent thyroid nodule FNAC adenocarcinoma thyroid origin and one case Recurrence papillary thyroid cancer 20years after thyroid surgery with positive lymph node Result of histopathology was these cases (infiltrating Papillary thyroid cancer with positive lymph nod), and third one high suspicious vs follicular thyroid neoplasia Result of histopathology was (Lymphoma non hodgkin larg cell on back ground Hashimatouse thyroiditis).

One patients with solitary thyroid nodule (Rt solitary thyroid nodule) Treated by Rt hemithyroidectomy histopathology result was Papillary thyroid cancer. Intrathyroid encapsulated follicular variant for 15 years female no family history and nodule size 1_2cm was not follow by completion thyroidectomy because low risk. And follow up for 5years no recurrent until now.

In (Table 16) Types of neck lymph node surgical dissection ,Metastatic deposits in the lymph nodes were seen in 6 patients of the total 24 patients who had undergone lymph node dissection. Central node dissection was done in 19(1 positive) patients, Right side modified neck dissection (MND) in 3 (3 positive) patients, Lt side modified neck dissection in one patient(1 positive) and Rt selective neck lymph nodes dissection in 1 patients (1 positive).

<u>Complications</u>

In (Table 17) appears the Complication after thyroidectomy for Solitary thyroid nodule

12/135 patients (8.88%) ,all female patients, 7 cases post Lt Solitary thyroid nodule and 5 cases post Rt Solitary thyroid nodule .6/135(4%) and 6/100(6%) patients with benign nodule .6/135(4%) and 6/35(17%) patients with malignant nodule .6/135(4%) and .6/135(4%)

Temporary hypocalcemia 9/135 patients (7%),5/135(4%) and 5/100 (5%)patients with benign solitary thyroid nodule ,4/135(3%) and 4/35(11%)patients with malignant thyroid nodule ,4 RT Solitary thyroid nodule and 5 Lt Solitary thyroid nodule ,All patients hypocalcemia symptoms appear 24_48 hours after operation with patients still at admission with Upper limb pain and numbness most common follow by carbopedal spasm ,All response to oral calcium supplement But some time start by i.v infusion ,Completely resolved symptoms and stop treatment 1 to 8 weeks But mostly second week .

1 patient 26 years female Post total thyroidectomy diagnosed clinical as Rt Solitary thyroid nodule (Toxic adenoma) Result FNAC was suspicious category with Rt clinical lymph nodes level 3 Patient underwent Total thyroidectomy with Rt selective lymph nodes dissection level 3 but Result of histopathology was hyperplastic nodule with marked fibrosis and calcification developed temporary hypocalcemia was improved after few weeks.

3 patients post Total thyroidectomy with hashimotos thyroiditis and lymphocytic thyroiditis

One case post total thyroidectomy with follicular adenoma ,3 cases post Total thyroidectomy with central lymph nodes dissection with papillary thyroid cancer infiltrated ,One case post Total thyroidectomy with Selective Rt lymph nodes dissection with papillary thyroid cancer with lymph node metastasis and One case post Total thyroidectomy with modified Rt and Lt neck dissection.

All female between age 20-62 years ,All nodule are hard fixed with average nodule size 2_5cm .

5 cases Lt Solitary thyroid nodule and 4 cases Rt Solitary thyroid nodule.

Temporary horsnese 3 patients(2.22%),2/35(6%) patients with malignant nodule and One/100 (1%)patient with benign nodule, One RT Solitary thyroid nodule ,2 Lt Solitary thyroid nodule ,3 cases all female with age 60,40,29 mostly due to the laryngeal edema post thyroidectomy .

1 cases after total thyroidectomy for anaplastic thyroid cancer older age infiltrated tumor big tumor size 6_9 cm and 1 case after total with selective Rt Neck dissection for patients with papillary thyroid cancer with lymph node metastasis and 1 case post Lt hemithyroidectomy for patient with Noninvasive follicular neoplasia with papillary like features was 29 years old female developed temporary horsnese was improved after few weeks. All patients appear horsnese directly after operation they received Warm slin nebulizer, dexamethasone for 24_48 hours, not effective on hospital stay Completely improved 3 6 months.

Postoperative hospital stay ranged from one to 3 days, mean hospital stay being 2 days.

Follow-up ranged from one to 48 months with mean follow-up of 12.1 ± 14.2 months.

Discussion

Thyroid nodule refers to a localized lesion within the thyroid gland that is palpably or radiologically distinct from the surrounding thyroid parenchyma.[22].

Because high risk for malignant, surgeons tend to treat them with high degree of suspicion and plan treatment in a systematic manner. Clinically, STNs are common, being present in up to 50% of the elderly population. The majority of STNs are malignant. [2, 10, 11].

Therefore, it is recommended that all thyroid nodules >1 cm in size should undergo evaluation. This includes both palpable and nonpalpable nodules or detected by imaging. [22].

Benign causes of thyroid nodule include the colloid nodule and hyperplastic nodule, adenomatous nodule . Occasionally, nodularity is noticed in patients with Hashimoto's thyroiditis and toxic adenoma . Malignant causes of nodules include thyroid cancer, lymphoma as well as metastasis to the thyroid gland.[22].

In our country was different study did on thyroid cancer Al-Hureibi, Abdulmughni, Y. Thyroid FNAC .(2003) [66], Abdulmughni, Yasser A., et al. thyroid cancer (2004)[67]. Al-Jaradi, Mansour, et al. Prevalence of thyroid cancer (2005)[34],. Al-Sharafi, Butheinah A., et al.thyroid cancer (2020)[68].

During our study period, 135 patients with Solitary thyroid nodule there were 126 (93%) females with STN and 9(7%) Males patients with Solitary thyroid nodule.

Thyroid nodules are more common in females similar as noted in the previous study. [2, 6].

Solitary thyroid nodules were 10–11times more common in females as compared to males,[2, 10], Our study showed that solitary thyroid nodules were 14 times more common in female than male.

In our study 135 Patients with Solitary Thyroid Nodule b/n age 14-65 years, median age 41 years, mode 45 years, average mean age 39.76 years, range 51 years and Stander deviation 13.98. The age range and mean slightly wide, and higher compared with previous study by (Gupta).[10].

In our study Solitary thyroid nodule more Common in age group between 21-30 years old are about 50 patients and the next age group between 41-50 years old are about 29 patients. That mean second decade involved by majority of the patients (37%) this is lower than previous study by Gupta[[10] and Dorairajan and Jayashree in that third decade of life majority of the patients involved (44%).

Evaluation of solitary thyroid nodules requires the collaboration of the primary care physician, endocrinologist, pathologist, radiologist, and head and neck surgeon to provide comprehensive and appropriate management of this clinical entity.[42].

Preliminary investigation should include careful history and thorough clinical examination and thyroid function tests.combination with thyroid ultrasound and FNAC becoming relevant in the management of

thyroid nodules.[22][23].

Further investigation should be considered if the following factors are present in addition to the thyroid nodule like male gender, extremes of age (<20 or >70 years), history of neck irradiation, nodule >4 cm in size or the presence of any pressure symptoms.[22] None of our patients in the study group had history of radiation exposure.

Patients under the age of 20 or over 70 years with thyroid nodules have an increased risk of malignancy, as do men. A history of persistent hoarseness, dysphagia, or dyspnea also increases the risk, although these symptoms may also occur with benign nodules. A rapid painless growth of a solid nodule is concerning and also raises the suspicion for thyroid cancer.[25].

Numerous studies have documented that the risk of malignancy in patients with thyroid nodules is 5%–17%, whether detected by palpation or ultrasonography.

There were 135 cases of clinically detected STN with available ultrasound findings in the study group. Thirty -five (26%) (3:1)clinically detected STNs were reported as malignant in the final HPE. This high incidence of malignancy reported in our study is similar to that of Tai *et al.*[2]. 36.6% (97) of the 265 patients and also reported 20%,42.27% incidence in the papers.[10, 11] were proved to be malignant, which was higher than the general incidence of malignancy 5%. It seems that STN has a higher risk of malignancy, so in this condition we should focus on the potential danger to all these patients.

A retrospective study by Keh et al of 61 patients found 75.4% of solitary thyroid nodules to have a neoplastic pathology and 34.4% to be malignant.[51].

The rise in incidence seems to be attributable both to the growing use of diagnostic imaging and fine-needle aspiration biopsy, which has led to enhanced detection and diagnosis of subclinical nodules [52] and also early diagnosis of low-risk lesions [53].

The fact that the malignant percentages obtained in this study are higher is partly due to the pattern we used for selecting patients. In other words, we selected the cases from surgery wards, whereas other studies included in their experiments all the cases that were subjected to FNAC. As noted above, the risk of malignancy in this group has been reported to be 26% however, a higher rate has also been reported. [38, 39, 40].

In our study 35 patients diagnosed with malignant solitary thyroid nodules 31 patients was female and 4 patients was male.

Among female patients 31/126(25%) were reported as malignant in histopathology result . Also malignancy in 4 (44%) out of 9 male patients with Solitary thyroid nodule . Hence, the predominance of thyroid nodules in females .[2, 6] and increased incidence of malignant thyroid nodules in males noted in our study are similar to that of Tai *et al* (36%).[2,] [26].

Age of patients with malignant tumor range b/n 15_62 years, median age 35 years, mode 23 years and average mean age 35.97 years and stander deviation 11.91.

In our study malignant Solitary thyroid nodule more Common in age group between 21-30 years old are about 12 patients(34%).

Different studies shown different results about the role of age as a risk factor of thyroid malignancy. Pinchot et al (54) and Muratli *et al.*,[38] reported that thyroid carcinoma prevalence was higher in the elderly compared with others while Rosario and et al. did not observe a significant difference between the age of the patients (55). Nevertheless, some studies including ours, revealed that the prevalence of thyroid carcinoma is higher in the younger patients [56, 57].

In our study Most Solitary thyroid nodule even benign or malignant nodule take size between 2.1_4 Cm. Size of the nodule has no relation with the malignancy in our study which was also reported by Tai et al.[2] A study by Kamran et al. opined that the risk of follicular carcinomas and other rare thyroid malignancies increases as nodules enlarge.[27] However, no such association with size was seen in our cases.

Usually, the size of the thyroid nodule does not predict the likelihood of thyroid cancer. Only 8% of incidentally found thyroid nodules measuring <5 mm, 15% of nodules measuring 5-10 mm, and 13% of nodules measuring 10-15 mm are found to be malignant [24].

the results of this study revealed that the size of the thyroid nodules is not reliable at predicting malignancy and should not be applied in medical decision making. [58][59] was similar to the our study.

study by Valderrabano et al indicated that regardless of size, most solitary cytologically indeterminate thyroid nodules can be successfully treated with thyroid lobectomy. Comparing indeterminate tumors of less than 4 cm with those 4 cm or greater, size was not seen as a categorical or continuous variable in relation to cancer rate. Moreover, the prevalence of extrathyroidal extension, positive margins, lymphovascular invasion, lymph node metastasis, and distant metastasis did not differ by size. The investigators also found the majority of malignant tumors in both size groups to be low-risk lesions. [45].

In our study(72%,63%) Rt side thyroid more effected by either benign or malignant solitary thyroid nodules respectively. Was similar to study by Liechty et al 9 noticed that there was a predilection for benign and malignant nodules to occur in the right lobe and Robinson et al 1 also found that in 40% cases the nodules were located in the right lobe.[60].

In our study Most common results of histopathology was Benign solitary thyroid nodule in 100 (74%), of that Benign non neoplastic 60(44%)including colloid nodule 20(15%) patients, adenomatous nodule 13(10%)patients, hyperplastic nodule 12(9%),cystic nodule 5(4%)patients, chronic thyroiditis 7(5%) patients (hashimotos and lymphocytes thyroiditis)and toxic adenoma 3(2%)patients. The benign

neoplastic nodule 40(30%) patients including follicular adenoma 28(21%), hurthle cell adenoma 6(4.4%) patients, and 6(4.4%) non invasive follicular neoplasia with papillary features (NIFTP).

The malignant solitary thyroid nodule appears in 35(26%), the papillary thyroid cancer (74%) most common followed (14%) follicular thyroid cancer and followed by equal frequency (3%) hurthle, medullary, and lymphoma and anaplastic thyroid cancer.

Malignant Solitary thyroid nodule appeared 3/6 (50%) patients was hypothyroidism before operation, results of histopathology was malignant nodule as papillary thyroid cancer on background of hashimotos thyroiditis, one of them with lymph node metastasis. That's mean high risk for malignant transformation specially Papillary Thyroid cancer than lymphoma,[50].

<u>Ultrasonography</u> is the most cost-effective imaging procedure, and is highly sensitive in assessing nodule size and number. There are ultrasound patterns which suggest malignancy like irregular shape, ill-defined borders, hypoechogenicity, solid texture, heterogeneous internal echoes, micro calcification, absence of a halo, an anteroposterior to transverse diameter ratio (A/T) >1, infiltration into regional structures, and suspicious regional lymph nodes.[22].

Thyroid ultrasonography can be helpful in certain cases when it is used to guide FNAB. Data have suggested that ultrasonography-guided FNAB may be preferable to palpation-guided FNAB. [61]

Ultrasound may aid in localization and examination of nodules, but FNA or excisional biopsy is necessary to definitively determine presence of malignancy[62].

addition, high resolution ultrasound and ancillary testing in the form of molecular genetics and immunocytochemistry can improve diagnostic accuracy. [41][63].

The likelihood that the increased incidence of thyroid cancer being largely be related to early detection by high resolution ultrasound and discovery of sub-clinical thyroid nodules. [63][64] is supported by evidence suggesting survival rates for thyroid cancer have remained fairly stable. [65].

In our study 28 patients out of a total 35(80%) malignant case had micro calcification by thyroid ultrasound in contrast to 10 of 100 (10%)benign nodules, This finding suggests that in presence of micro calcification, the incidence of malignancy is more similar to study by Kuo et al indicated that on ultrasonographic examination, the presence of calcification within a thyroid lesion, nodule-like solid masses are independent factors for thyroid cancer specially follicular thyroid carcinoma instead of a follicular adenoma. [47]. Also similar to An article by Rago *et al.* suggested that atypia at cytology and spot micro calcification at ultrasound was predictive of malignancy[29].

Presence of solid echogenicity contributes to increased incidence of malignancy in comparison to either cystic or mixed echogenicity of the nodule. [2] Our study showed similar results was solid in 30/35(86%) patients with malignant nodule, The findings of our study also suggest that presence of cervical lymphadenopathy is high in presence of malignant thyroid nodule. 24 of 35 (69%) malignant nodules had lymph node enlargement as against only 2 of 100 (2%) benign nodule

Noted male gander, solid nodule, Hypoechoic, irregular borders, microcalcification, increased vascularity, and cervical lymphadenopathy are malignancy risk factors for solitary thyroid nodules study by Uyar et al([44]) and (2)(47)(29)(30)(62).

In our study By ultrasound hypoechoic nodule in 33/35(94%) patients with malignant nodule and 15(15%) in benign nodule. presence of hypoechoic is high in presence of malignant thyroid nodule was similar to study by DS Cooper - Thyroid, 2009 – Malignant lesions are found to be hypoechogenicity on ultrasound in almost 80% of cases. When the finding of a hypoechogenicity lesion is combined with microcalcifications, irregular borders, and taller than wide shape, the sensitivity for malignancy increases. Simple cysts, hyperechogenic solid nodules, and spongiform architecture are all associated with benign lesions.[62].

Papini *et al.* in their article opined that ultrasound guided FNAC should be performed on all 8–15 mm, hypoechoic nodules with irregular margins, intranodular vascular spots or micro calcification.[30]

According to literature, STN has a higher risk of malignancy than multiple nodules.[2].

In our study group, (26%)(35/135) STNs were malignant(3:1) compared to that of multinodular goiter(24/72) (22.5%). In a study from Nigeria, the authors have described malignancy in1 out of the 13 cases of STN (7.6%) and twenty four out of 160 cases of MNG (15%).[28] Hence, multinodularity does not necessarily exclude malignancy as seen by our study group.

Male gender, normal thyroid volume, single nodularity, nodule hypo echogenicity, and blurred margins were also associated with malignancy but size not significantly [29].

We have noted that male gender, micro calcification, solid echogenicity of the nodule, and presence of cervical lymphadenopathy was significantly associated with malignancy similar as noted by Tai et al.[2].

study by Yuan et al, however, indicated that the patterns of enhancement differ significantly between benign and malignant solitary thyroid nodules examined with real-time, contrast-enhanced ultrasonography, with most malignant lesions in the report demonstrating an irregular shape, an unclear boundary, and inhomogeneous and incomplete enhancement. The study involved 78 patients, including 41 with benign lesions and 37 with malignant nodules. [46]

Desjardins et al found that one half of their patients with thyroid carcinoma had a cystic component in the tumor. [49].

fine-needle aspiration biopsy (FNAB) has become the most important tool in the assessment of solitary thyroid nodules. [43].

Fine-needle aspiration cytology is recommended to be a cost-effective procedure in the initial assessment and management of thyroid nodules.[2,11] It is recommended that every patient with a palpable thyroid nodule should undergo an FNAC. USG-guided FNAC can lower the occurrence of nondiagnostic smears. Whenever we had problem in preoperative diagnosis by FNAC due to inadequate material or difficulty in aspiration by conventional method we have repeated the FNAC by USG guidance. In our study and previous study experience also noted, better yield of diagnostic cytological material with the help of the USG-guided aspirations compared to blind FNAC.[31, 32].

All our patients underwent FNAC by ultrasound guide before surgery as it helped us to decide the type of surgery to be under taken. When FNAC report was malignant or suspicious, total thyroidectomy was done. In all other cases, hemi thyroidectomy was done and subsequent plan was decided based on conclusive paraffin section report.

In a recent article, the authors have emphasized the role of USG by suggesting that nodules with a nondiagnostic FNAC result in the setting of low-risk demographics and benign appearance at ultrasound can be followed with serial ultrasound examinations, thereby avoiding repeat FNAC.[33] These findings are in contrast to the recommended current guidelines to repeat FNAC after a nondiagnostic result.[62].

Determining the nature of STN is very important as aggressive surgery may be regarded as an excessive mode of treatment. [2] We opted for surgery in all the patients as there is a high incidence of malignancy in STN patients as reported in literature. [2] The postoperative histopathology reports corroborated our findings as nearly ~1/3 of STN were reported as malignant.

study by Arul and Masilamani indicated that in cases of solitary thyroid nodules, fine-needle aspiration cytology reports using the Bethesda System for Reporting Thyroid Cytopathology correlate well with histopathologic diagnosis of these nodules, having a sensitivity, a specificity, an accuracy, a positive predictive value, and a negative predictive value of 94.4%, 97.6%, 95.8%, 98.1%, and 93.2%, respectively. [48].

Al_hureibi et al study 2003 on 196 patients with nodular goiter the fine needle aspiration

having a sensitivity, a specificity, an accuracy, a positive predictive value, and a negative predictive value of 38%, 89.9%, 72%, 66.7%, and 79.2%, respectively.[66].

In our study thyroid fine needle aspiration having a sensitivity, a specificity, an accuracy, a positive predictive value, and a negative predictive value of 61.33%, 71.66%, 64.44%, 73.1%, and 59.72%, respectively.

The sensitivity of FNA cytology in this study is low compared to published studies from outside country where The sensitivity, specificity and accuracy of FNA cytology are more than 94%. which had

adversely affected the surgical decision making as well as the outcome. We should realise that negative FNA cytology does not exclude malignancy and we have to seriously evaluate the situation and to rethink on how to raise the scale of sensitivity in FNA cytology in the diagnosis of thyroid nodules, and to improve the level of expertise in cytology.

Yemen, as any developing country, is lacking an accepted level of expertise in this field, something that makes it mandatory to continuously monitor and evaluate how valid this procedure is.

whose study reported. However, this high rate of malignancy is not surprising if we know that FNAC is nowadays routinely performed for most cases of thyroid nodules. This has led to a reduction in the number of unnecessary surgeries and consequently to a rise in the percentage reported for malignancy. [39].

The respective risk of malignancy associated with each diagnostic category is as follows:

Non diagnosed ,Benign - < 1%, Atypia (AUS) - 5-10%, Follicular neoplasm - 20-30%, Suspicious for malignancy - 50-75%, Malignant - 100% [39].

In our study risk of malignancy for each Bethesda category in following

Non diagnosed _17%, Benign - 21%, Atypia (AUS) - 50%, Follicular neoplasm - 33%, Suspicious for malignancy - 45%, Malignant - 100%.

Correlation between FNAC and histopathological diagnoses in our study shows the accuracy with which FNAC diagnosed follicular neoplasia . There were 14 cases of False Negative had been reported as benign nodule by FNAC examination and there histopathological analysis was follicular adenoma in 12 cases and hurthel adenoma in 2cases and 8 cases of False positive (FP), diagnosed as follicular neoplasm by FNAC examination and there histopathological analysis show that two of them colloid nodular goiter, one adenomatous nodule, one hyperplastic nodule, one toxic adenoma and three Hashimoto's thyroiditis (chronic lymphocytic thyroiditis). There were 31 cases True positive (TP) cases, all case were follicular neoplasm by FNAC examination, by histopathological analysis, 15 cases were follicular adenoma ,3 cases were hurthel adenoma , non invasive follicular thyroid neoplasia with Papillary features and 5 papillary carcinoma,4 cases follicular carcinoma, hurthel cell carcinoma one case and one case lymphoma

The risk of malignancy for each Bethesda category ranged from 6.9% (the "benign and nonneoplastic" category) to 100% (the "malignant" category). This wide range shows the power of the Bethesda system to differentiate and determine the probability of malignancy. The percentages obtained in our research were rather close to the figures reported in other studies: 6.9% versus 0-3% (the "benign and nonneoplastic" category), 50% versus 5-15% (AUS/FLUS), 37% versus 15-30% (FN/SFN), 81.2% versus 60-75% (the "suspicious for malignancy" category), and 100% versus 97-99% (the "malignant" category). [39].

Surgical management

154 thyroid operation for 135 patients with solitary thyroid nodule, 100 thyroid operation for 100 patients with benign solitary thyroid nodule and 54 thyroid operation for 35 patients with malignant solitary thyroid nodule, 102/154 (66%) hemithyroidectomy either Rt or Lt side thyroid for benign or malignant solitary thyroid nodules but 19 patients of hemithyroidectomy followed by completion thyroidectomy when results of histopathology was malignant thyroid nodules.

Wagana and colleagues agrees that hemithyroidectomy is the most common operation done in solitary thyroid nodule (81 operations were performed for solitary thyroid nodule, the most common operations were lobectomy and isthmectomy). They have done a retrospective review of all solitary thyroid nodules excised over a 3 years period from 1st January 1999 to 31st December 2001. A simple protocol was used to manage this condition involving history, clinical examination, fine-needle aspiration of the lesion, and excision was clinically indicated. Clinical diagnosis and operation was performed for the patients had solitary thyroid nodule over a 3-year period at Kijabe Hospital[35].

We have performed hemi thyroidectomy in benign nodules as reported by FNAC. In those cases where postoperative HPE was reported as malignant by paraffin section, completion thyroidectomy of the remaining lobe was done. Total thyroidectomy was done in those cases where FNAC was reported suspicious of malignant or malignant.

Total thyroidectomy for 22 patients, 14 patients with benign nodule and 8 patients with malignant solitary thyroid nodule (2 patients Lt Solitary thyroid nodule and 6 patients Rt Solitary thyroid nodule) treat by total thyroidectomy and results of histopathology was 3 patients papillary thyroid cancer,4 patients follicular cancer, one anaplastic cancer. Here papillary thyroid cancer not follow by any type of neck dissection because total thyroidectomy depended on result of FNAC was false negative for Malignancy.

Near total or Subtotal thyroidectomy for 2 patient Rt Solitary thyroid nodule Toxic adenoma.

Neck dissection was done in 26 patients, 24 patients with malignant nodule out of them 6 showed metastatic deposit in the lymph nodes. (5 patients papillary thyroid cancer, one patient non Hodgkin lymphoma in back ground of hashimatous thyroiditis), also two patients benign thyroid nodule underwent selective lymph nodes dissection because FNAC gave us false positive result. This Patient underwent Total thyroidectomy with Rt selective lymph nodes dissection level 3 but Result of histopathology was hyperplastic nodule with marked fibrosis and calcification. Other case result of the histopathology was hashimotos thyroiditis.

Central node dissection was done in 19(1 positive) patients, Right side modified neck dissection (MND) in 3 (3 positive) patients, Lt side modified neck dissection in one patient(1 positive) and Rt selective neck lymph nodes dissection in 1 patients (1 positive).

Decision of neck dissection was taken in those cases with either palpable lymph nodes in the neck or USG finding suggestive of lymphadenopathy. In some cases decision of lymph node dissection was taken intra operatively mainly for central nodes (level VI). Central node dissection was done in all malignant cases with USG showing lymph node enlargement and also in cases with intra operative enlarged nodes.

Prophylactic central neck dissection in clinically node-negative patients remains controversial.

Calò, Pietro Giorgio, et al. study there was no statistically significant difference in the rates of locoregional recurrence between the three modalities of treatment. Total thyroidectomy appears to be an adequate treatment for clinically node-negative differentiated thyroid cancer. Prophylactic central neck dissection might be considered for differentiated thyroid cancer patients with large tumor size or extrathyroidal extension.[36].

Study by Chen, Lawrence, et al. Was Compared with no Prophylactic central neck dissection, vs Prophylactic central neck dissection significantly reduces locoregnal recurrence but is accompanied by numerous adverse effects.

Patients who underwent Prophylactic central neck dissection had significantly lower locoregnal recurrence locoregnal recurrence (odds ratio [OR] 0.65; 95% confidence interval [CI] 0.48–0.88) but significantly higher incidence rates of transient Recurrent laryngeal nerve injury (OR 2.03; 95% CI 1.32–3.13), transient hypocalcemia (OR 2.23; 95% CI 1.84–2.70), and permanent hypocalcemia (OR 2.22; 95% CI 1.58–3.13) than that of no Prophylactic central neck dissection group. [37].

intraoperative assessment

During my study we noted that intraoperative assessment for solitary thyroid nodule was FNAC before operation was benign or follicular neoplasia should be assess for hardness and fixedity of nodule if hard and fixed nodule intraoperative best to make decisions to do total thyroidectomy instead hemithyroidectomy. Because we found hard and fixed nodule intraoperative in 32/35(91%) patients diagnosed after operation as thyroid cancer.

That means intraoperative assessment for hardness and fixedity of nodule and total thyroidectomy at that time reducing need to second operation, completion thyroidectomy and it's complication.

Complication of surgery in solitary thyroid nodules

Complications postoperatively were temporary hypocalcaemia and hoarseness of voice in 12 patients12/135 patients 9%, all female patients;; out of them 9 (7%) patient, with temporary hypocalcaemia and 3(2.2%) patient with temporary unilateral recurrent laryngeal nerve injury 7 cases post Lt Solitary thyroid nodule and 5 cases post Rt Solitary thyroid nodule .6/135(4%) and 6/100(6%) patients with benign nodule and 6/135(4%) and 6/35 (17%) patients with malignant nodule .

Temporary hypocalcemia 9/135 patients (7%),5/135(4%) and 5/100 (5%) patients with benign solitary thyroid nodule ,4/135(3%) and 4/35(11%) patients with malignant thyroid nodule.

Temporary horsnese 3 patients(2.22%) due to temporary unilateral recurrent laryngeal nerve injury and due to laryngeal edema,2/35(6%) patients with malignant nodule, One/100 (1%) patient with benign nodule.

Conclusion

The incidence of malignancy in STNs is indeed high. For that clinically detected solitary nodules should be treated with high degree of suspicion. Male patient and Rapid growth by history and hard fixed nodule by clinical examination and hypoechoic, micro calcification and cervical lymphadenopathy on USG were seen more frequently in malignant nodules. FNAC more accurate and helpful for diagnosis Solitary thyroid nodule if aspiration under USG guide and reading by experience histopathologest . Type of surgery depending on preoperative evaluation including history, clinical examination, ultrasound, FNAC result, and intraoperative assessment of the nodule . Male gender was identified as a risk factor for thyroid cancer while age, number and size of nodules were not. The most common indication of surgery was diagnosis of malignant disease when preoperative FNAC and US were inconclusive. Less complications of thyroid surgery by experience surgeon.

intraoperative assessment for hardness and fixedity of nodule and decision for total thyroidectomy at that time reducing need to second operation as completion thyroidectomy and it's complication.

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Tables

<u>Table 1:</u>
Solitary thyroid nodule according to the sex

Sex	Total (N=135)	%	Benign	%	Malignant (N=35)	%
			(N=100)			
Female	126	93%	95	95%	31	89%
Male	9	7%	5	5%	4	11%
Total	135	100%	100	100%	35	100%

Table 2:

Solitary thyroid nodule according to the age group							
Age group	Total (N=135)	%	Benign	%	Malignant (N=35)	%	
			(N=100)				
<20	13	10%	11	11%	2	6%	
21_30	50	37%	38	38%	12	34%	
31_40	25	19%	17	17%	8	23%	
41_50	29	21%	21	21%	8	23%	
51_60	16	12%	12	12%	4	11%	
>60	2	1%	1	1%	1	3%	
Total	135		100		35		

Table 3:

Solitary thyroid nodule according to Side							
Side	Total (N=135)	%	Benign (N=100)	%	Malignant (N=35)	%	
Rt side Solitary Thyroid Nodule	94	70%	72	72%	22	63%	
Lt side Solitary Thyroid Nodule	41	30%	28	28%	13	37%	

Table 4

Solitary thyroid nodule according to size of nodule (CM)							
Size	Total (N=135)	%	Benign	%	Malignant (N=35)	%	
			(N=100)				
< 1	5	4%	1	1%	4	11%	
1.0_2.0	29	21%	22	22%	7	20%	
2.1_4.0	67	50%	50	50%	17	49%	
> 4.0	34	25%	27	27%	7	20%	

Table 5

Solitary thyroid nodule according to the function							
Thyroid function	Total (N=135)	%	Benign (N=100)	%	Malignant (N=35)	%	
Euthyroid	125	93%	93	93%	32	91%	
Hyperthyroidism	4	3%	4	4%	0	0%	
Hypothyroidism	6	4%	3	3%	3	9%	

Table 6
Solitary thyroid nodule Ultrasound findings

Ultrasound findings	Benign (N=100)	%	Malignant (N=35)	%
Hypoechoic	15	15%	33	94%
Lymphadenopathy	2	2%	24	69%
Calcification	10	10%	28	80%
Solid	10	10%	30	86%
Cystic	10	10%	1	3%
Mixed	79	79%	5	11%
< 1	1	1%	4	11%
1.0_2.0	22	22%	7	20%
2.1_4.0	50	50%	17	49%
> 4.0	27	27%	7	20%

Table 7

Fine needle aspiration cytology results according to the Bethesda Categories

Preoperative FNAC results	Number of patients (N=135)	%
Bethesda Categories		
Category 1 Inadequate for diagnosis, unsatisfactory	6	4%
Category 2 Benign cytology	66	50%
Category 3 AUS/FLUS	10	7%
Category 4 FN/ SFN	39	29%
Category 5 Suspicious for Malignancy	11	8%
Category 6 Malignant	3	2%

Table 8

Fine needle aspiration cytology results according to the Bethesda Categories with its subtypes.

Preoperative FNAC	Subtypes	Number of patients N=135	%			
Bethesda Categories		N-133				
Category 1 Inadequate for diagnosis	Inadequate for diagnosis ,unsatisfactory.	6	4%			
	Colloid Nodule benign cytology	28	21%			
Category 2	Adenomatous nodule	13	10%			
Benign cytology	Hyperplastic benign nodule	15	12%			
	Colloid Cystic nodule	7	5%			
	Chronic thyroiditis	3	2%			
Category 3 AUS/FLUS	Atypical cells	10	7%			
Category 4	Follicular cell neoplasia	36	27%			
FN/SFN						
	Hurthle cell neoplasia	3	2%			
Category 5 Suspicious for Malignancy	Suspicious	11	8%			
Category 6 Malignant	Malignant	3	2%			
FNAC: Fine needle aspiration cytology, AUS/FLUS: Atypia undetermined significance (AUS) or Follicular lesion of undetermined significance (FLUS), FN/SFN: Follicular neoplasia (FN) or Suspicious Follicular neoplasia (SFN).						

Table 9

Matching between Bethesda categories and histological types used to determine FNAC accuracy

Histological types Bethesda Categories	Benign and non neoplastic	Benign and neoplastic	Malignant
Category 1,2.	TN	FN	FN
Benign and non neoplastic			
Category 3	FP	TP	TP
AUS/FLUS			
Category 4	FP	TP	TP
FN/SFN			
Category 5	FP	TP	TP
Suspicious for Malignancy			
Category 6	FP	TP	TP
Malignant			

FNAC: Fine needle aspiration cytology, AUS/FLUS: Atypia undetermined significance (AUS) or Follicular lesion of undetermined significance (FLUS), FN/SFN: Follicular neoplasia (FN) or Suspicious Follicular neoplasia (SFN), TN: True negative, TP: True positive, FN: False negative, FP: False positive.

Table 10

Correlation between FNAC and histological diagnoses together with the risk of malignancy calculated for each Bethesda category

Bethesda Category	Histopathology subtype	Number of cases	True/ False diagnosis	Risk of malignancy %
Category 1 Inadequate for diagnosis ,unsatisfactory	Hyperplastic nodule	2	TN	
	Cystic nodule	1	TN	
	Follicular adenoma	1	FN	- 1770
	Hurthle adenoma	1	FN	
	Anaplastic cancer	1	FN	
Category 2	Colloid Nodule	5	TN	
Benign and non neoplastic	Adenomatous nodule	11	TN	
	Hyperplastic nodule	7	TN	
	Cystic nodule	3	TN	21%
	Toxic adenoma	2	TN	
	Hashimatous thyroiditis	2	TN	
	Follicular adenoma	11	FN	
	Hurthle adenoma	1	FN	
	Papillary cancer	10	FN	
	Medullary cancer	1	FN	
	NIFTP	3	FN	
Category 3	Colloid Nodule	3	FP	
AUS/FLUS	Adenomatous nodule	1	FP	50%
	Cystic nodule	1	FP	— JU /o
	Papillary cancer	5	TP	

Category 4	Colloid Nodule	2	FP	
FN/SFN	Adenomatous nodule	1	FP	
	Hyperplastic nodule	1	FP	33%
	Toxic adenoma	1	FP	
	Hashimatous thyroiditis	3	FP	
	Follicular adenoma	15	TP	
	Hurthle adenoma	3	TP	
	Papillary cancer	5	TP	
	Follicular cancer	4	TP	
	Hurthle cancer	1	TP	
	Lymphoma	1	TP	
	NIFTP	2	TP	
Category 5 Suspicious for Malignancy	Hyperplastic nodule	2	FP	
	Hashimatous thyroiditis	2	FP	
	Follicular adenoma	1	TP	45%
	Hurthle adenoma	1	TP	
	Papillary cancer	3	TP	
	Follicular cancer	1	TP	
	NIFTP	1	TP	
Category 6 Malignant	Papillary cancer	3	TP	100%
FNAC: Fine needle aspiration cytolo Follicular lesion of undetermined s	ogy, AUS/FLUS: Aty ignificance (FLUS),	pia undeter FN/SFN: Fo	mined significa ollicular neoplas	nce (AUS) or sia (FN) or

Table 11

Overall performance of fine. Needle aspiration cytology in diagnosis of thyroid neoplasm

Performance	%
Sensitivity	61.33%
Specificity	71.66%
Accuracy	64.44%
Positive predictive value	73.01%
Negative predictive value	59.72 %

Table 12

Solitary Thyroid Nodule Histopathology						
Histopathology	Number of Patients (N=135)	%	Female	%	Male	%
	(14-133)		(N=126)		(N=9)	
Solitary Thyroid Benign Nodule	100	74%	95	75%	5	56%
Solitary Thyroid Malignant Nodule	35	26%	31	25%	4	44%

Table 13
Solitary Thyroid Nodule post operation Histopathology Results

Post operative histopathology	(N=135)	%
Benign non neoplastic	60	44%
Benign and neoplastic	40	30%
Malignant	35	26%

Table 14
Solitary thyroid nodule histopathology results with it's subtypes

Post operative histopathology	Subtypes	(N=135)	
Benign non	Colloid Nodule	20	15%
neoplastic	Adenomatous goiter	13	10%
	Hyperplastic nodule	12	9%
	Cystic nodule	5	4%
	Chronic thyroiditis	7	5%
	Toxic adenoma	3	2%
Benign and neoplastic	Follicular adenoma	28	21%
	Hurthle cell adenoma	6	4.4%
	Non invasive Follicular Thyroid Neoplasia with papillary like features (NIFTP)	6	4.4%
Malignant	Papillary Thyroid cancer	26	19%
	Follicular Thyroid cancer	5	4%
	Hurthle cell carcinoma	1	0.7%
	Medullary Thyroid cancer	1	0.7%
	Lymphoma	1	0.7%
	Anaplastic cancer	1	0.7%

Table 15
Solitary thyroid nodule surgical procedures

Surgical procedure	Benign	Malignant N=54	Total
	N=100	11-0-7	N=154
RT Hemithyroidectomy	60	1	61
LT Hemithyroidectomy	22	0	22
Rt Hemithyroidectomy follow by completion thyroidectomy	0	9	9
Lt Hemithyroidectomy follow by completion thyroidectomy	0	10	10
Completion thyroidectomy with central lymph nodes dissection	0	17	17
Completion thyroidectomy without central lymph nodes dissection	0	2	2
Total thyroidectomy with central lymph nodes dissection	0	2	2
Total thyroidectomy	14	8	22
Total thyroidectomy with Selective Rt lymph nodes dissection level 2	2	1	3
Total thyroidectomy with Rt Functional Modified neck dissection	0	3	3
Total thyroidectomy with Lt Functional Modified neck dissection	0	1	1
Subtotal thyroidectomy	1	0	1
Near total thyroidectomy	1	0	1
Rt: Right, Lt: Left.			

[Table 16].

Type of surgical neck dissection

Type of neck dissection	Number of patients with neck dissection(N =24)	Number of patients with positive lymph node(N=6)
Central neck lymph nodes dissection	19	1
Selective neck lymph nodes dissection	1	1
Rt Modified neck lymph nodes dissection	3	3
Lt Modified neck lymph nodes dissection	1	1

Table 17
Complications

Solitary Thyroid Nodule Common Post Operative Complication					
Complications	Total (N=12/135)	%	Benign	Malignant	
			N=6	N=6	
Temporary hypocalcemia	9	7%	5	4	
Permanent hypocalcemia	0				
Temporary Horsnese	3	2%	1	2	
Permanent Horsnese	0				
Other Complication	0				

Declarations

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