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Efficiency of Fine Needle Aspiration Cytology of Thyroid Nodule in Diagnosing Malignancy  

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Dedication

To all who asked God for my success, who helped me to continue especially Mam, Dad...

Dear husband “Nasir”,

little daughters “Aalia and Ethar...”
Acknowledgment

Great thanks to my kind supervisor Dr Mohammed Mohammed Osman for his patient help, continuous support and excellent guidance.

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ABSTRACT

Introduction: A thyroid nodule is a common presentation of thyroid disease; the estimated incidence of solitary palpable thyroid nodules in the adult population of the United States varies between 1% and 10%. Fine needle aspiration cytology (FNAC) is the first line diagnostic tool in both solitary and dominant thyroid nodules.

Objectives: This study aimed to evaluate the role of FNAC in diagnosing malignancy in solitary thyroid nodule.

Methodology: This descriptive pro and retrospective study about the role of fine needle aspiration cytology examination in the diagnosis of solitary thyroid nodule and it’s co-relation with the final histopathological results.

The study was carried out during the period June 2009-August 2010, in the three main histopathology laboratories in Khartoum.

Fifty cases of thyroid nodules were studied, thirty eight of them were retrospective and twelve were prospective. Sensitivity, specificity and efficiency of the fine needle aspiration cytology in diagnosing malignancy were determined.

Results: The age of the patients ranged between 18 -84 years with a mean of 47.56 years. The commonest age group was 30 – 40 years (24%). The M: F ratio was 1:2. The fine needle aspiration cytology results were malignant in 64% while histopathology results were malignant in 76% with 78% results showing co-relation. In addition to that, cell block results showing 100% correlation with histopathology results. Fine needle aspiration cytology sensitivity was 78.3%, specificity 84%, efficiency 80%. The study showed that follicular carcinoma was the most common
diagnosis by fine needle aspiration cytology, it accounts for 32% followed by papillary carcinoma 24%. The histopathology results were 24% and 22% for follicular and papillary carcinoma respectively.

**Conclusion:** When all the findings in the study were compared together, the efficiency, sensitivity and specificity of the fine needle aspiration cytology tend to be comparable with other studies, in Sudan and elsewhere.
مستقبل البحث

مقدمة: ورم العقدة الورمية هو من أكثر الأعراض لأمراض الغدة الورمية، حدوث ورم العقدة الورمية العقدة الملفس لدى البالغين من المواطنين الأمريكيين يتفاوت ما بين 1% و10%. عادة ما يطلب أطباء الباطنية والجراحون عمل فحص الخزعة الإبرية الدقيقة كوسيلة أولى في فحص المرض لجميوعة كبيرة من مرضى ورم العقدة الورمية.

الأهداف: هدف هذه الدراسة تقييم دور اختبار الخزعة الإبرية الدقيقة في تشخيص الورم الخبيث في العقدة الورمية.

منهجية الورم: هذه دراسة توضيحية وصفية أجريت لمعرفة دور فحص الخزعة الإبرية الدقيقة في تشخيص ورم العقدة الورمية وتم مقارنتها مع نتائج السينسي المرمية بعد استئصال الورم. الدراسة أجريت في الفترة من يونيو 2009 وحتى أغسطس 2010. تم الدراسة بصورة عامة في أكبر ثلاثة معامل من امرأة بولاية الخرطوم. شملت الدراسة 50 مريضاً لديهم ورم العقدة الورمية لديهم نتائج خزعة الإبرية الدقيقة (FNA)، بعضهم تعرض لفحص (ناف الخلية)، وتحصل على النتائج النهائية لفحص السينسي الورمي.

النتائج: تجاوزت أعمار المرضى ما بين 18-84 سنة بوسط عمر بلغ 47.5 سنة. العمر الأكثر تواجداً لدى مجموعات الدراسة كانما ما بين 30-40 سنة (24%). نسبة المذكور لإناث كانت (2:1). فحص الخزعة عند اختيار الخزعة الإبرية الدقيقة أظهرت وجود ورم خبيث في 64% من مجموعات الدراسة بينما نتائج التسنيم المرمية أثبتت وجود الورم الخبيث لدى 76% منهم، فقط 78% أظهروا وجود ارتباط. بالإضافة إلى ذلك فإن نتائج فحص الخزعة أقل الخلايا أظهرت وجود ارتباط مع نتائج التسنيم المرمية بنسبة 100%. فيما يخص اختبار الخزعة الإبرية الدقيقة وجد أن الحساسية كانت 78% والخصوصية 84% والفعالية كانت 80%. أوضحت الدراسة أن سرطان النسيج الطلائي الفصي أو أكثر تشخيصاً بواسطة فحص الخزعة الإبرية الدقيقة لخلايا، حيث تمت 32%، ثم يتبع سرطان النسيج الطلائي الخلبي (24%) كما تكررت نفس النتائج فيما يخص نتائج الأنسجة المرمية حيث مثلت 24% و22% لكل من الفصي والخليبي على التوالي.

الخلاصة: عند مقارنة كل نتائج الدراسة فإنه نقص إلى أن الفعالية، الحساسية والخصوصية لاختبار الخزعة الإبرية الدقيقة جميل إلى إعطاء نتائج مماثلة لنتائج الدراسات المماثلة التي أجريت في السودان ودول أخرى.
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1.1. INTRODUCTION

A thyroid nodule is a common presentation of thyroid disease; the estimated incidence of solitary palpable thyroid nodules in the adult population of the United States varies between 1% and 10% although it is higher in endemic goiterous regions. They are four times common in females and tend to increase with age, history of radiation and diet containing goiterogenic material. It is 5, 3 % female and 0, and 8% male.\(^{(1)}\) Majority of them prove to be non neoplastic and benign neoplasm, malignant neoplasm constitutes about 5% or less of all solitary nodules. It is therefore important to identify these malignant tumors which require more immediate surgical intervention. Malignancy is found in about 8-10% of these nodules, The incidence of malignancy in the clinically solitary nodules was 14% compared to 10% for the dominant nodules\(^{(31)}\). The chance of malignancy in the solitary cold thyroid nodule is 15-20 %.\(^{(2)}\) The rate of malignancy in the solitary thyroid nodule in other studies in Sudan was 8.7% (out of 56 patients) in Sinnar Hospital and 14% (12 out of 94 patients) in Khartoum Teaching Hospital also In a third study they did find that 11.1% of the solitary thyroid nodule were malignant,\(^{(31,32,33)}\)

Thyroid cancer accounts for 1% of all malignancies, (0.5 % of cancer in men, 1.5 % in women). Particularly elevated in Iceland and Hawaii.\(^{(3)}\)

There is an increase in incidence (1973 _2002) by 2, 4 fold in (USA), this Increase attributed to increase in diagnosing tumors < 2 cm, although there is no associated increase in mortality.\(^{(3)}\)

Thyroid nodules are uncommon in childhood and adolescence; their prevalence ranges between 0.2–1.4% and is 5–10 times lower than in adults. However, the frequency of malignancy among thyroid nodules is higher than in adults; different studies have reported a 15–20% incidence, with up to 50% in some series. Furthermore, in the U.S.A. and other western countries, thyroid cancer is the third most common solid tumor in
childhood and adolescence, with an incidence of 1.75 in 100,000. Although it is usually a slow-growing tumor, a prompt diagnosis is recommended, because greater tumor size, distant spread, and greater atypia are associated with increased cumulative mortality.¹⁴

**FNAC of thyroid gland** is firstly used in 1952 by Söderström,¹ it is now firmly established as an important first line diagnostic test for the evaluation of goiter and the single most effective test for the preoperative diagnosis of solitary thyroid nodule. There is a large body of world literature attesting to its accuracy and advantages, although the need for caution in interpretation, meticulous attention to technique, and the limitation of diagnosis are also well documented.² They usually used in studies to compare the FNAC findings after interpretation with the final histopathology results and determine the accuracy of this test.

In Philippine they found that a False negatives of 2.3%, false positives 1.1% and overall accuracy exceeding 95%. Also determined sensitivity of only 53.4% in diagnosis malignancy in thyroid while over all accuracy for benign and malignant reaching 93.1 %.⁵ In Pakistan the overall results are of sensitivity of 98%, specificity of 70%, and positive predictive value of 91%, negative predictive value of 93% and diagnostic accuracy of 91%.⁶ In study from USA they found that the Sensitivity 65 – 98 % (mean 83 %) and Specificity 72 – 100 % (mean 92 %).⁷

In childhood and adolescence, the data to be found in the literature about FNAC accuracy in diagnosis of malignancy are scanty and often in disagreement. In Italia, they showed that the sensitivity, specificity, and accuracy of fine needle aspiration biopsy were 95%, 86.3%, and 90.4%, respectively. A multiple regression analysis showed that only fine needle aspiration biopsy (β coefficient = 0.963; P< 0.0001) significantly contributed to detecting malignancy (multiple r = 0.973; P < 0.0001).⁴
Other study about thyroid FNA studied FNA of 50 patients with thyroid nodules, 97% had satisfactory aspirations, 78% of cancer diagnoses were correct and 94% of benign diagnoses were correct. There is increased percent of malignant nodules excised by 60-100% with decreased percent of benign nodules excised by 34-70% leading to dramatic reduction of unnecessary operations.\(^{(8)}\).

In Britain they studied FNAC of 250 patients before they went to surgery because of thyroid malignancy they found sufficient material for diagnosis in 96% of them with sensitivity (73%); specificity (85%), accuracy (82%), PPV (54%), NPV (92.7%).\(^{(9)}\).

Other study compared the different types of thyroid malignancy and the results as follows: \(^{(10)}\)

<table>
<thead>
<tr>
<th>Diagnosis</th>
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<tr>
<td>Papillary carcinoma</td>
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<td>Follicular carcinoma</td>
<td>50%</td>
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In one Sudanese study they did find the overall sensitivity, specificity and accuracy of FNA were 95.5%, 99.5% and 99.4% respectively, and for papillary cell carcinoma is 83.3%, 100% and 99.6% as the same sequence\(^{(11)}\). Another Sudanese study showed a low positive predictive value for follicular neoplasm in particular with fine needle aspiration cytology (FNAC) (44%).\(^{(31)}\)

This study attempted to show to what extent the FNAC of 50 patients with solitary thyroid nodule suspecting to have cancer are related to the actual histopathology obtained from the whole nodule after surgery.
1.2. LITERATURE REVIEW

1.2.1. Epidemiology:

Thyroid cancers occur mostly in young and middle aged adults, elderly people also affected but it is rare in children, the mean age of presentation of papillary carcinoma is 40 years, 50 years for follicular carcinoma and medullary carcinoma and 60 years for poorly differentiated or undifferentiated carcinoma, in Sudan the commonest age group affected by thyroid cancer was 30 to 40 years followed by the age group 20 years to 30 years.\(^{11}\) Many studies have demonstrated that thyroid cancer is two to four times more frequent in females than in males. The lifetime risk of developing thyroid cancer in the United States is about 1: 120 for females.

Among United States females, thyroid cancer accounts for about 3% of all cancers and is the eighth most common malignancy. In contrast, in Kuwait, thyroid cancer ranks second comprising 8% of all female cancers, also same figures in other Gulf countries. In Sudan the reporting of epidemiological data is very poor especially demographic data and those data concerning the risk factors, only we have the prevalence of thyroid cancers among histopathology samples was 0.4%, this is in three centers NHL, RICK and SOH.\(^{12}\)

Differentiated carcinoma (papillary and follicular) made up to 94% of all thyroid cancers in Cypriots, Jordan and United States, while in Egypt was only 73%.\(^{13}\) In Sudan the most common thyroid tumor was follicular adenoma 72.2% followed by papillary carcinoma 12.4% then follicular carcinoma 9.3% and medullary carcinoma and anaplastic carcinoma of 3.1% for each.\(^{12}\)
1.2.2. Embryology:

The thyroid gland is the first endocrine gland to develop in the embryo. It begins to form about 24 days after fertilization from a median endodermal thickening in the floor of the primordial pharynx which soon form a small out pouching- thyroid primordial. The gland then passing down as a component of the thyroglossal duct along the midline to reach its final position in the midneck anteriorly to the hyoid bone, in the normal course of events the thyroglossal duct obliterated and disappears, at the same time the thyroid analog expands laterally to form the thyroid lobes. Microscopically cords and plates of follicular cells are formed by the ninth week, small follicular lumina appear by the tenth week, and colloid secretion by the twelfth week, well developed follicles lined by follicular cells and containing thyroglobulin-positive colloid by fourteenth week.\(^{(14)}\)

1.2.3. Normal Anatomy and Histology:

The normal adult thyroid gland consists of two symmetrical lobes joined by the isthmus which lies in the front of the second, third and fourth tracheal rings; the gland possesses its own capsule. Separate masses of thyroid tissues are not uncommonly found near the hyoid bone, in the superior mediastinum, or beneath the sterno-mastoid muscle.

**Blood supply:**

It is endowed with a rich lymphatic network that coalesces in the subcapsular region to give rise to collecting trunks that drain into the following nodes: (1) pericapsular; (2) internal jugular chain; (3) pretracheal (Delphian node), pretracheal, and prelaryngeal (4) recurrent laryngeal nerve chain (5) retropharyngeal and retroesophageal.

Microscopically the gland is made of round and oval follicles that are variably sized with average diameter 200 µm. They are lined by a single layer of flat to columnar follicular cells, the cytoplasm has a pale acidophilic or amphophilic staining quality; the greater the activity the
greater its amount. Ultrastructurally features of follicular cells are abundant granular endoplasmic reticulum, well developed Golgi apparatus, lysosomes and numerous microvilli in the luminal border.

The interluminal colloid is pale staining with scalloped borders in active follicles and densely eosinophilic in an inactive ones.

In addition to follicular cells, the thyroid gland contains neuroendocrine cells known as c cells and found mainly in intrafollicular position, their number varies with age; very prominent in infancy and old age.

Follicular cells with abundant granular acidophilic cytoplasm are known as Hurthle cells. Ultrastructurally, this granularity is due to accumulation of mitochondria.

Regarding the immunohistochemistry thyroglobulin is the most useful one, it is positive in colloid and cytoplasm of follicular cells, also T3 and T4.

Thyroid transcription factor 1 (TTF) is extremely useful marker but is also expressed in alveolar epithelium of the lung. Epithelial membrane antigen (EMA), low molecular weight keratin and vimentin are positive.

C cells are immunoreactive for calcitonin and NSE.\(^{(13)}\)

1.2.4. Physiology:

Thyroid gland synthesizes and secretes T3, T4 after stimulation by TSH coming from pituitary gland by means of feedback mechanism. It maintains the level of metabolism in the tissues that is optimal for their normal function. The gland is not essential for life, but in its absence there is mental and physical slowing, poor resistance to cold, in children mental retardation and dwarfism.

In mammals, the thyroid gland also secretes calcitonin, a calcium-lowering hormone.
Excess thyroid secretion leads to body wasting, nervousness, tachycardia, tremor and excess heat production.\textsuperscript{(15)}

\textbf{1.2.5. Risk factors and pathogenesis:}

Environmental, genetics and hormonal factors all are contributed in thyroid cancer development.

1- \textbf{Genetic:} Activating mutations of the TSH-R in autonomously functioning nodules, C-MYC oncogene expressed in adenomas, Carcinomas. H-RAS over expression in adenomas, carcinomas BRAF-mutations are frequent in papillary cancers.

2- \textbf{Age:} Cancer rate is higher over 60 and under 30 years so a nodule in a child doubles risk of cancer.

3- \textbf{Gender:} Cancer rate is higher for men.\textsuperscript{(13)}

4- \textbf{Thyroid irradiation:} The thyroid is one of the most sensitive tissues to carcinogenic effects of radiation in addition to breast and bone marrow, Exposure to 400-1500 rads = cancer prevalence of 5-10%.

Especially childhood irradiation to head, neck and chest increases frequency of thyroid cancer even up to 100 times for lymphoid neoplasm, thymus hypertrophy and hemangiomas.

Risk coefficient is 3.0/year/million exposed to 1 Rad, it continues through 40 years after exposure and the latent period averages 10 – 20 years, they did find that treatment for Hodgkin’s disease increases, thyroid cancer by 1.7%.

In Chernobyl: Highest risk in children < 5 years at the time of exposure with Shorter latent period for development of thyroid cancer 6-7 years and they are relatively aggressive tumors.\textsuperscript{(16,23)}

5- \textbf{Iodine deficiency:} follicular carcinoma is particularly linked to iodine deficiency, the relative frequency of papillary carcinoma is greater in geographic regions of adequate or high dietary iodine intake compared to region of iodine deficiency.\textsuperscript{(1)}
1.2.6. Clinical course:

Most patients presented with solitary thyroid nodule. The solitary thyroid nodule is defined as a discrete palpable swelling in an otherwise impalpable gland. It is a clinical diagnosis. Many of these cases prove to be multinodular but presenting as a single thyroid nodule. This nodule could be cystic thyroid nodule, Most are degenerating benign adenomas with just 0.5 – 3% risk of cancer which is more likely if the cyst is large or fluid recurs or is bloody, and here aspiration is usually indicated. Possible causes of solitary thyroid nodule:

**Benign lesion:**

1- Multinodular goiter
2- Hashimoto (chronic lymphocytic) thyroiditis.
3- Cysts: colloid, simple or hemorrhagic.
4- Follicular adenoma:-
   - Macro follicular adenoma
   - Microfollicular or cellular adenoma
5- Hurthle cell adenoma.

**Malignant lesions:**

1- Papillary carcinoma
2- Follicular carcinoma minimally or widely invasive oxyphilic (Hurthle cell) type.
3- Medullary carcinoma.
4- Anaplastic carcinoma.
5- Primary thyroid lymphoma.
6- Metastatic carcinoma (Breast, renal cell carcinoma and others)(24)

There are some clinical signs make the diagnosis of malignancy in the solitary thyroid nodule is more likely:
High suspicion with:
1- Family history of medullary carcinoma or multiple endocrine neoplasms.
2- Rapid tumor growth.
3- Firm hard nodule
4- Fixation of the nodule to adjacent structure
5- Paralysis of vocal cords
6- Regional lymphadenopathy.
7- Distant metastases.

Moderate suspicion with
1- age less than 20 years or more than 70 years
2- male sex
3- history of head and neck irradiation
4- a nodule more than 4 cm or partially cystic
5- Symptoms of compression like dysphagia, dysphonia, hoarseness, dyspnea and cough.\(^{(10)}\)

1.2.7. Diagnosis:

The diagnostic tools of solitary thyroid nodules are:
1- Clinical examination.
2- Laboratory studies.
3- Radiological studies:  A- neck ultra sound.
   B- Isotopes scanning of thyroid.
   C- CT scan.

And other imaging modalities:
- MRI, MIBI scan: lack of specificity
- PET / CT-scan.

4- Histopathological studies:
   A- Fine needle aspiration cytology.
   B- Cell block.
C- Frozen section.
D- True cut biopsy.
E- Final histopathological examination.

1.2.8. Classification of thyroid tumors:

The tradition separation of thyroid carcinoma into the major groups of papillary, follicular medullary and undifferentiated (anaplastic) carcinoma based on morphology and clinical features is strongly supported by advances in molecular studies showing the involvement of distinct genes in these four groups, with little overlap however some areas still need further classification, squamous and mucoepidermoid carcinomas cannot be regarded as subgroups of any of the major types, therefore treated separately, also poorly differentiated carcinomas best treated separately because of their clinical significance. Oncocytic thyroid tumors were used to be put with follicular family of thyroid neoplasm, they also classified as papillary carcinoma if they displays the nuclear features of that tumor, no gene specific to these tumors identified yet. So they were put in separately for further molecular studies.\(^{(12)}\)

We have WHO classification:\(^{(1)}\)

**WHO Classification Thyroid carcinoma:**

- Papillary carcinoma.
- Follicular carcinoma.
- Poorly differentiated carcinoma.
- Undifferentiated anaplastic carcinoma.
- Squamous cell carcinoma.
- Mucoepidermoid carcinoma.
- Sclerosing mucoepidermoid carcinoma with eosinophilia.
- Mucinous carcinoma.
- Medullary carcinoma.
- Mixed medullary and follicular cell carcinoma.
- Thyroid adenoma and related tumors.
- Follicular adenoma.
- Hyalinizing trabecular tumor.

**Other thyroid tumors:**
- Teratoma.
- Primary lymphoma and plasmacytoma.
- Thymoma.
- Angiosarcoma.
- Smooth muscle tumors.
- Peripheral nerve sheath tumors.
- Paraganglioma.
- Solitary fibrous tumors.
- Follicular dendritic cell tumor.
- Langerhans cell histiocytosis.
- Secondary tumors.

Also **TNM classification of thyroid carcinoma:**

The TNM system is endorsed by the International Union against Cancer (UICC), and the American Joint Commission (AJCC):\(^{(1)}\)

**T- Primary tumor:**

Tx primary tumor cannot be assessed.
To no evidence of primary tumor.
T1 tumor ≤ 2 cm limited to thyroid.
T2 tumor (2_4) cm limited to thyroid.
T3 tumor > 4 cm limited to thyroid or any tumor with minimal extra thyroid extension.
T4a tumor any size invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve.
T4b tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels.
- Multifocal tumors are designated (m). Diameter of the largest determines the classification
- All anaplastic (undifferentiated) tumors are considered T4.

Regional Lymph Nodes (N):

They are the central compartment, lateral cervical and upper mediastinal lymph nodes.

Nx Regional nodes cannot be assessed.
No No regional lymph nodes metastasis.
N1 Regional lymph node metastasis.
N1a Metastasis to level VI (pretracheal, paratracheal and prelaryngeal/ Delphin) lymph nodes.
N1b Metastasis to unilateral, bilateral or contra lateral cervical or superior mediastinal lymph nodes

Distant Metastasis (M):

Mx Distant metastasis cannot be assessed.
Mo No distant metastasis.
M1 Distant metastasis.

1.2.9. Treatment:

The treatment of most types of thyroid tumors is surgical. Lobectomy in cases in which the tumor is confined to one thyroid lobe with subsequent therapy depending on the nature of the nodule, it is used in follicular adenoma, including Hurthle cell adenoma.

Subtotal thyroidectomy constitutes adequate therapy for most minimally invasive follicular carcinoma including the minimally invasive Hurthle cell carcinoma, and papillary carcinoma. However this issue remains controversial, with several groups recommending total thyroidectomy followed by the administration of radioactive iodine.

**Total thyroidectomy:** should be reserved for the high risk group of papillary carcinoma, widely invasive follicular carcinoma including widely
invasive Hurthle cell carcinoma, poorly differentiated carcinomas, and medullary carcinomas.

**Radical surgery:** sometimes carried out in undifferentiated carcinoma, some of these tumor treated just palliative.\(^{(13)}\)

1.2.10. **Prognosis:**

1- Pathologic classification has prognostic significance; some thyroid cancers have indolent, benign behavior.

2- Age.

3- Sex.

4- Tumor microscopic grade and clinical staging.

Challenge is to define patient and tumor characteristics influencing prognosis to avoid unnecessary aggressive or inadequate treatment.\(^{(13)}\)

**Fine needle aspiration cytology:**

It is now firmly established as an important first line diagnostic test for the evaluation of goiter and the single most effective test for the preoperative diagnosis of solitary thyroid nodule. Abulcasim, a 10\(^{th}\) century Arabian physician, was credited with using the technique by Anderson and Webb but Scandinavian workers pioneered the modern use of FNA some decades ago.\(^{(17)}\) So it used since 1952 as an Initial procedure of choice for evaluating a solitary thyroid nodule before taking surgery, it decreases the size of unneeded surgery, it is safe, simple, office procedure and 90-97% yield in experienced hands.\(^{(2)}\) Got off to a good start until one case report of needle track seeding of renal cell carcinoma from thyroid metastasis brought thyroid FNA to a virtual halt.\(^{(18)}\)

**Indication for FNAC:**

1- The diagnosis of solitary or dominant Thyroid nodule.

2- The diagnosis of diffuse non-toxic goiter.

3- Confirmation of a clinically obvious thyroid malignancy.
4- To obtain materials for ultra structural study and clinical research
5- Therapeutic value (Thyroid cyst).
6- Intraoperative surgical guidance (IOC).\(^{(2)}\)

**Contraindication of FNAC:**

There are no contraindications to aspirate thyroid gland if the patient is cooperative.\(^{(2)}\)

**Thyroid FNA techniques are:**

1- Manual.

2- Guided by ultrasound or other imaging modalities, ultrasound guidance improves accuracy but increases cost. Of patients with one palpable nodule 16% will have no nodules found on ultrasound\(^{(19)}\) also palpable solitary nodule is a part of multinodular thyroid gland on ultrasound in 50% of patients, the size of the other nodules is usually less than 1 cm in the majority but 10-15% of patients will have a second non palpable nodule of more than 1 cm in size.\(^{(20)}\)

**Indications of using ultrasound guided FNAC:**

1- Cytology Inadequate
2- Partially cystic nodule
3- Nodule increases in size

US guided FNAC leads to decrease inadequate sampling and decrease the false negatives (in non representative lesion) so it leads to decrease number of thyroidectomised patients, lastly it increases the yield of thyroid cancer.\(^{(18,20)}\)

**Aspiration Technical consideration:**

- The patient should be lying in the supine position, placing a pillow under the neck tends to expose the gland more. During the procedure the patient is asked to lie still and to refrain from swallowing to prevent trauma to surrounding structures. Needling should take only 5-
10 seconds, children may need general anesthesia if the aspiration is absolutely essential
- At least three aspirations are performed during a session, we use 25-gauge needles; 22 or 23-gauge needle do not cause significantly greater trauma, 25 gauge needles provide perfectly adequate material, in diffuse goiter both sides are sampled and in nodules, material from several areas should be aspirated to reduce the number of indeterminate and false negative results, use of 22 or 21 gauge needle allows preparation of cell block samples which may be particularly valuable in the diagnosis of follicular lesions.
- Extremely vascular; blood contamination is a common problem.\(^{(2)}\)

**Complications of FNA procedure:**

Are rare if any:-
1- Pain.
2- Transient hematoma.
3- Infarction of the nodule.
4- Fainting.
5- Track seeding. (Unknown).
6- Transient Laryngeal nerve paresis.
7- Tracheal puncture.\(^{(2)}\)

**Preparing a thyroid FNA:**

Four types of smear preparation:
1- Direct Smears:
   – Air-dried, Diff Quick stained.
   – EtOH-fixed, Pap stained
2- Cytospins.
3- Cell block.
4-Liquid based preparation: \(^{(21)}(30)\)

This type of preparation is now used widely in developed countries and it is an area of many studies, it has an optimal cellular preservation, clear background and residual material can be used for ancillary technique but it has major morphological changes and artifacts beside that it is expensive and needs long training. \(^{(30)}\)

**Staining Methods:**

- **Tulodine blue stain:** for the adequacy test.
- **Pap stain:** the best for appreciation of:
  - Nuclear features; chromatin texture, nucleoli, nuclear inclusions, and nuclear grooves.
- **Romanowsky’s stain:** is useful for:
  - Evaluation of extracellular materials; colloid & amyloidal.
  - Evaluation of cytoplasmic details; cytoplasmic granules.

**Normal structures found in the FNA of the thyroid are:**

1. Small clusters and sheets of epithelial cells.
2. Small amounts of thin colloid.
3. C- cells.
5. Tracheal epithelium.
6. Skeletal muscles. \(^{(2)}\)

**Specimen Adequacy in Thyroid FNAs:**

- At least 6 clusters of follicular cells each containing 10 cells.
- Predominantly colloid, with scant follicular epithelium.
- Satisfactory, but limited by scant follicular epithelium.
- Abundant colloid, but few follicular cells, consistent with an adenomatous nodule, but interpretation limited by paucity of follicular cells. \(^{(21)}\)
**Recommend repeat FNA:-**

- Numerous macrophages but few follicular cells, c/w thyroid cyst contents, but interpretation limited by paucity of follicular cells.
- Recommend repeat FNA. (Particularly if lesion is large (>4 cm) and Hemorrhagic.)
- A non-diagnostic rate of >15% may represent a procurement or interpretation problem.\(^{(21)}\)

**In proposed Bethesda terminology for reporting thyroid FNA results**

there are 8 categories:-

- Non-diagnostic Specimen.
- Cyst Fluid Only.
- Benign.
- (Atypical) Follicular Cells of undetermined Significance.
- (Suspicious for) Follicular Neoplasm.
- Suspicious for Malignancy.
- Malignant.
- (Suspicious for) Hurthle Cell neoplasm.\(^{(21)}\)

**The criteria of British Thyroid Association in interpretation of results from Thy1 to Thy5:**

Thy 1 Material non diagnostic.
Thy 2 Cytological benign.
Thy 3 Examination unable to distinguish between benign and malignant cytology.
Thy 4 Suspicion of malignancy.
Thy 5 Examination diagnostic for malignancy.\(^{(21)}\)
There are different criteria in Sudan to classify the FNAC results, no agreed policy but most used to classify the results as below:

1-Carcinoma
Papillary carcinoma, medullary carcinoma, undifferentiated carcinoma, and malignant lymphoma can often be diagnosed based on fine-needle aspiration samples because they exhibit distinctive cytologic and sometimes architectural features

2- Suspicious for carcinoma
justified in the presence of cytologic features suggestive but not diagnostic of malignancy

3- Follicular neoplasm
Follicular neoplasm It is not possible to make a distinction between follicular carcinoma and follicular adenoma based on fine-needle aspiration cytology

4- Benign.
(e.g., nodular goiter, cyst, Hashimoto’s thyroiditis) Nodular goiter can usually be recognized by features such as abundant thick colloid, low cellularity, large follicles, and honeycombed arrangement of nuclei in the epithelial fragments

5- Inadequate.
With the exception of cyst (which can be hypocellular, with only macrophages being identified), the minimum criterion for adequacy of specimen is presence of 5 to 6 groups of thyroid follicular epithelium with >10 cells per group

6- Undeterminant.
Includes all cases that do not fulfill the diagnostic criteria of the previous described categories
The European Federation of Cytology Societies recommended using updated criteria for classification depending on findings in conventional smears and liquid based cytology into:

1* Malignant category
   - Papillary carcinomas
   - Medullary carcinoma
   - Poorly differentiated carcinoma
   - Anaplastic carcinoma
   - Lymphoma
   - Metastases
   - Hurthle cell carcinoma and well-differentiated follicular carcinomas are excluded from this category

2* Lesions suspicious for malignancy
   All cases previously described in the «Malignant category» for which the cytological criteria of malignancy are insufficient to assert the diagnosis

3* Follicular neoplasm category
   Includes all cases for which it is impossible to distinguish a benign follicular lesion (follicular adenoma, hyperplastic adenoma, benign nodule in a multinodular thyroid) from a follicular carcinoma

4* Follicular neoplasm / Hurthle cell type category
   Includes all cases with exclusively or almost exclusively oncocytes.

5* Benign category
   Includes all the benign nodules (colloid nodules, nodular goiter, hyperplastic nodules, Grave’s disease nodules)+Follicular adenoma+ All thyroiditis
6* Follicular lesion of undetermined significance or Atypia of undetermined significance
Includes all cases that do not fulfill the diagnostic criteria of the previous described categories
Therefore it includes many different situations
7* Non diagnostic category
Include FNA with less than 6 well-preserved follicular cells groups with ten cells each, poorly prepared or stained cells and cyst fluid with or without histiocytes and with less than six groups of ten benign cells.

Indications of surgical resection of thyroid nodule influenced by FNAC:
1. All proven malignant nodules.
2. All cytologically diagnosed follicular neoplasms.
3. All lesions exhibiting an atypical but non-diagnostic cellular pattern on cytology.
4. Cystic nodules which recur following aspiration.
5. When on clinical grounds, suspicion of malignancy is high even if the cytology report suggests benign lesion.

Thyroid FNA reports format:-
– Adequacy
  • Unsatisfactory (15%)
  • Less than optimal
  • Satisfactory
– Diagnostic categories:
  1- Benign (70%)
  2- Indeterminate/Suspicious (10%)
    • Cellular lesion, cannot r/o Follicular Neoplasm
- Follicular Neoplasm
- Suspicious for Malignancy

3- Malignant (5%).

- Diagnosis.
- Comment/Recommendation.\(^{(21)}\)

**Papillary carcinoma:**

It is a malignant epithelial tumor showing follicular cell differentiation and characterized by distinctive nuclear features. Most tumors manifest in adult aged 20 – 50 yrs with female to male ratio of 4:1, most of them are young. Also it is the most common paediatrics thyroid malignancy. 5% to 10% of them have history of radiation and they found that it increases in incidence with Hashimoto’s thyroiditis. The relation with Grave’s is still controversial subject. The cardinal molecular alteration is occurred in RET in form of somatic rearrangement RET/PTC3 and RET/PTC.\(^{(13)}\)

Patient presented with solitary thyroid nodule or as diffuse neck swelling, sometimes patient presented with lymph nodes metastasis or other metastatic area with no obvious thyroid swelling.\(^{(13)}\) In diagnosis of papillary carcinoma the nodule is typically cold on radioactive iodine, **FNAC** is an effective method in diagnosis papillary carcinoma, the criteria for diagnosis:-

1- Cellular smear.
2- Papillary clusters of cells.
3- Monolayer sheets of cells with dense cytoplasm and distinct intercellular borders.
4- Pale nuclei, indistinct nucleoli, intranuclear cytoplasmic invaginations (inclusions) (considered as pathognomic of papillary carcinoma ), nuclear grooves, irregular nuclear outlines
5- Variation in cell size and Askanazy cell like changes.
6- Viscous colloid. chewing gum –like.

7- Psammoma bodies.

8- Macrophages and debris ( evidence of cystic degeneration

9- Multinucleated giant cells.(2)

Logistic regression analysis of the various criteria for the diagnosis of papillary carcinoma suggested that a combination of intranuclear inclusions, papillary structure and dense met plastic cytoplasm were the three most important variables .a combination of two gave 100% predictive value.(2)

The problems in diagnosis are:-
1- Cystic changes , the fluid aspirated is looking as the materials from simple and degenerative cysts, cytologically , there is risk of overlooking papillary carcinoma if macrophages and debris are predominate, large atypical cells with enlarged nuclei and foamy cytoplasm may sometimes be the only indicator of neoplasm; however , similar cells may also be seen in benign cysts. The sensitivity of FNA diagnosis in cystic neoplasm may be as low as 40%.

2- Lymphocytic infiltration, it interferes with thyroiditis diagnosis.

3- Mixed pattern of growth.

4- Askanazy cell like change.

Macroscopic appearance is variable, most lesions are grey white firm masses with irregular borders or evenly infiltration; size ranges from microscopic to huge, multicentricity is common, marked cystic changes are seen in 10% of cases.

Microscopic appearance, the typical papillary carcinoma contains numerous true papillae usually they are complex, branching and randomly oriented with a fibro vascular core and single or stratified lining of cuboidal cells in an edematous or hyaline may contain lymphocytes foamy
macrophages, these papillae associated with follicles formation, the cells of papillary carcinoma have characteristic nuclear features:-

1- **Intranuclear cytoplasmic inclusions**, they have been regarded as pathognomic of papillary carcinoma and are seen in up to 90% of these carcinomas and in up to 5% of the cells. However, they are occasionally seen in anaplastic carcinoma, medullary carcinoma and follicular carcinoma, and have been described in non neoplastic conditions, in lesions seen near the thyroid such as paraganglioma and in metastatic renal cell carcinoma within the thyroid. Intranuclear inclusions manifest as areas of nuclear clearing with sharp well defined margins. Inclusions are similar in color and texture to cytoplasm, although they are sometimes paler. They can be mimicked by artifacts in both Pap and MGG stained material, however, artifactual vacuoles appear empty and have less distinct outlines.

2- **Nuclear grooving**, they are easily visible in alcohol fixed materials and difficult to discern in MGG preparations. It could be found in other thyroid malignancies.\(^2\)

3- **Ground glass appearance** of the nuclei (Orphan Annie) which is not actually appeared in smears.\(^{22}\)

Histochemical and immunohistochemical features: the cells are reactive for pan-keratin stains. Their usual profile is CK 7+/CK20, CK19, HMWK, thyroglobulin, thyroid transcription factor (TTF-1); they are negative for synaptophysin, and chromogranin. Candidate markers are S100, estrogen receptor and CK19. Electron microscopy shows the highly indented nuclear membrane, with formation of pseudoinclusions and multilobulation. The use of RET staining to identify expression of RET/PTC rearrangement.\(^{13}\)

**Variants of papillary carcinoma** are:

1- Papillary microcarcinoma.
2- Follicular variant.
3- Macrofollicular variant.
4- Oncocytic variant.
5- Clear cell variant.
6- Diffuse cell variant.
7- Diffuse Sclerosing variant.
8- Tall cell variant.
9- Combined papillary and medullary carcinoma

Prognosis: excellent, 10 years survival is over 90%, younger are better.\(^{(22)}\)

**Follicular carcinoma:**

(Follicular carcinoma; oncocytic carcinoma; Hurthle cell carcinoma)

It is a malignant epithelial tumor showing evidence of follicular cell differentiation and lacking the diagnostic nuclear features of papillary carcinoma. It is the second common cancer after papillary carcinoma and accounting for 10% -15% of thyroid malignancies, common in female on their fifth decade rare in children. Related mainly to iodine deficiency and irradiation, studies suggested that involvement of chromosome 2 in follicular carcinoma, also RAS mutation is found in 50% of cases\(^{(12)}\) present as a neck mass, could be with lymphadenopathy, hoarseness, bone and even subcutaneous swelling (frontal mass). Diagnosis mainly made by histopathology not by cytology, \textbf{FNAC of follicular carcinoma} lesions yielding a follicular neoplasm and it needs the histopathology result to reach definite diagnosis; the criteria for diagnosis follicular neoplasm:-

1- Cellular smear.
2- Many equal sized cell clusters scattered through out the smear (microfollicles).
3- Scanty colloid.
4-disorgnized syncytial cell aggregates.
5-askanazy cell change/clear cell change.

So cytopathology of the follicular neoplasm needs more interpretation, and the differential diagnosis are like this; in a macro follicles with abundant colloid it mostly be nodular goiter or macro follicular adenoma, with small micro follicles and scant colloid it mostly microfollicular adenoma or follicular carcinoma, in cellular smears with scant colloid with clusters and clumps with varying pleomorphism it mostly follicular carcinoma, microfollicular adenoma or trabecular adenoma. When cells have intranuclear inclusions and clefts, it is mostly papillary variant of follicular carcinoma. So the features suggestive of carcinoma in follicular neoplasm are:

- More cellular aspirate.
- Crowded disorganized clusters.
- Larger nuclei.
- More prominent nucleoli.
- More irregular chromatin pattern.\(^2\)

Macroscopically they are usually encapsulated lesion especially the minimally invasive one, it’s round to ovoid with solid and fleshy cut surface microscopically ranging from well formed follicles with colloid to solid or trabecular patterns, we depend in diagnosis on demonstration of capsular or vascular invasion. The vessels should be of venous caliber, be located in or immediately outside the capsule rather than within the tumor and contain one or more clusters of tumor cells attached o the wall and protruding into the lumen, regarding the invasion this tumor has been divided into minimally and widely invasive follicular carcinoma.

Immunohistochemistry of follicular carcinoma is as follows: reactive for thyroglobulin, TTF-1, low molecular weight keratin, EMA.\(^{13}\)

**Histopathological variants:-**

- Oncocytic variant (Hurthle cell and oxyphilic carcinoma).
- Clear cell variant.
- Signet ring variant.

**Prognosis:**

More aggressive than papillary carcinoma, but minimally invasive one has good prognosis; the oncocytic variant behaves aggressively, Metastasize to the lung, bones, and others.\(^{22}\)

**Poorly differentiated carcinoma:**

Are a group of tumors that falls between well differentiated follicular carcinoma and Undifferentiated anaplastic carcinoma in term of both morphologic appearance and behavior, it is still controversial entity. One type under the descriptive name of insular carcinoma. it is commonly occurs in older population\(^{13}\) account for 4-7% of all the clinically evident thyroid carcinomas in Italy and some Latin American countries, more common in female and over 50 years.\(^{12}\)

FNA findings are of high cellularity, necrotic background, low grade atypia, nests, trabeculae, microfollicles and cytoplasmic vacuoles.\(^2\)

Macroscopically it is a gray white mass grossly invasive with extensive necrosis, some of them are encapsulated, microscopically the distinguishing features are a nesting (insular) pattern of growth, solid to microfollicular arrangement, small uniform cells, variable mitotic activity and fresh tumor necrosis so we need to differentiate it from medullary carcinoma.\(^{13}\)

Immunohistochemically, there is reactivity for thyroglobulin and TTF-1 but not for calcitonin. Genetic alterations are intermediate between well-differentiated and undifferentiated carcinoma. The mean 5 years survival rate is about 50%.\(^{22}\)

**Undifferentiated (Anaplastic carcinoma):**
It is one of the most rapidly fatal human cancer, accounts for 10% of thyroid cancer. Occurring in elderly as fast growing mass associated with hoarseness, dysphagia and dyspnea, extra thyroidal extension is encountered at the time of initial presentation in most cases.

**Fine needle aspiration cytology** findings are:-

Highly cellular aspirate showing bizarre, large malignant cells with macrophage like appearance with mononuclear and multinucleated tumor cells (osteoclast-type), the nuclei are pleomorphic with coarse chromatin and macronucleoli. There could be malignant spindle cells with mesenchymal appearance, all the above on necrotic cell fragments, and dirty background.\(^{(2)}\)

Macroscopically it is solid tumor mass replacing most of the organ, showing massive hemorrhage and necrosis, they are typically infiltrative with invasion of surrounding structures.

Microscopically it divided into two categories; squamoid pattern and spindle (giant cell) pattern.

Immunohistochemistry indicated that all anaplastic carcinomas are indeed epithelial in nature, so it is positive for cytokeratin in 50% to 100% of them, vimentin, scattered laminin, focal EMA and CEA reactivity, thyroglobulin and TTF-1 is negative in the truly undifferentiated tumor. Metastatic tumors should be considered in diagnosis.

This tumor has poor prognosis with mortality rate over 95%, the mean survival rate is less than 6 months.\(^{(13)}\)

Palliative treatment is the mode of treatment usually used.

**Squamous cell carcinoma (epidermoid carcinoma):**

Is a malignant epithelial tumor composed of cells with squamous cell differentiation, squamous cells can be found in thyroid as a result of persistence of thyroglossal duct or structures derived from branchial pouch
or as expression of squamous metaplasia in Hashimoto thyroiditis, papillary carcinoma and other conditions.\(^{(13)}\)

Pure squamous cell carcinoma are exceptional could be as a variant of anaplastic carcinoma occurring in older ages and tends to be aggressive also could be metastasis from adjacent tissues. It account for 1 % of all thyroid cancer with female to male ratio of 2:1.

**FNAC** is useful in diagnosis of these tumors with apparent squamous cells. They are strongly positive to CK19.\(^{(22)}\)

**Medullary carcinoma:**

Arises from parafollicular C cells, 5–10% of all thyroid malignancies, 70 -80% of them are sporadic.

Medullary carcinoma comprises 5-10% of all malignancy with mean age at diagnosis 44 -50 years, and 41-43 years for familial cases. With male to female ratio for sporadic 1:1.4 and that for familial 1:1.1\(^{(22)}\) chronic hypercalcemia and Hashimmoto and radiating iodine are all researched now as associate to this tumor. About 90 % secrete calcitonin which is used as tumor marker for this carcinoma.

**Fine needle aspiration cytology findings** are of hypercellular dispersed cell pattern, cuboidal cells with eccentric pleomorphic hyperchromatic nuclei (plasmacytoid features), abundant gray cytoplasm bi and multinucleated forms may be seen. Spindle cells form also may appear. Fragments of amorphous pink background materials (amyloid).

There are problems in diagnosing it cytologically for example medullary carcinoma variants, Askanazy cell neoplasms and follicular neoplasms.\(^{(2)}\)

Macroscopically solid, firm grey, circumscribed mass but not encapsulated located in the mid portion of the upper half of the gland (greater concentration of C cells).\(^{(13)}\)
Microscopically sheets, nests and trabeculae of polygonal round or spindle cells separated by varying amount of fibrovascular stroma (looks like Carcinoid), hyalinized collagen and amyloid. The nucleoli are not prominent and mitotic figures are scant, usually they used Congo red stain for demonstration of amyloid.\(^{(13)}\)

Immunohistochemistry showing positive reactivity for keratin, TTF1, NSE, chromogranin and calcitonin.\(^{(22)}\)

Treated surgically, not responsive to radioactive iodine or radiation or chemotherapy but local recurrence occurred in 355 of patients, 5 years survival rate between 70%- 80%, good prognostic factors like young age, female sex, familial setting and small size. Poor prognostic factors older age and high mitotic activity and necrosis and decreased reactivity for calcitonin.

**Primary Lymphoma:**

Defined as primary lymphoma arising within the thyroid, uncommon less than 5% of all thyroid carcinoma, more in older females. Patients with Hashimmmoto are more prone to develop this cancer. Macroscopically it is of different sizes with multiple nodules and fish flesh cut surface. Microscopically the majority of the cases are of diffuse large B-cell lymphoma, the second category are marginal zone B-cell lymphoma, Maltoma and follicular lymphoma, an important diagnostic finding is the packing of follicular Lumina by lymphoid cells (lymph epithelial lesions) this differentiates it from thyroiditis.\(^{(13)}\)

**FNAC findings** are of hypercellular with non cohesive cells showing the features of large cell lymphoma cells anywhere.\(^{(2)}\) Immunohistochemistry, all types of thyroid lymphoma exhibit positivity for CD45 and other B cell markers.
Treated by thyroidectomy then followed by adjuvant therapy. Prognosis of thyroid Maltoma is good while of diffuse large B cell lymphoma is poor.\textsuperscript{(22)}

**Secondary Tumors of thyroid:**

Thyroid is relatively a common site for metastasis from direct extension from adjacent structures, like larynx, pharynx, trachea and esophagus or blood born metastasis from melanoma, breast, kidney and lung. FNAC is useful in diagnosis these lesions. Stains for TTF1 is reliable here except in that it is also positive in lung carcinoma metastasis.\textsuperscript{(13)}
1-3- OBJECTIVES

1.3.1. General objectives:

To determine the efficiency of FNAC as a diagnostic procedure in thyroid cancer.

1.3.2. Specific objectives:

1- To determine sensitivity, specificity and accuracy rate of FNAC in diagnosis thyroid malignancy.
2- To know the most common thyroid malignancy.
3- To enumerate the primary indications for surgery in patients included in the study group.
2- MATERIALS AND METHODS

2-1- Study design:

This is descriptive pro and retrospective cross sectional study.

2-2- Study field:

The study was carried out at The National Health Laboratory (NHL), Suba University Hospital, Khartoum Teaching Hospital, Faidel Hospital and Bahri Teaching Hospital in addition to 4 private laboratories the most important one is Almobark laboratory.

2-3- Study population and Duration of study:

All cases (50) of thyroid nodules suspected to have thyroid tumor and they underwent fine needle aspiration cytology and then histopathology examination. At the above mentioned laboratories on period from June 2009 till August 2010.

2-4- Inclusion criteria:

Patients with thyroid nodule whom having FNAC with results: follicular neoplasm, suspicious and malignant aspirate. Then having histopathological examination from cell block, true cut biopsy and the specimen itself.

2-5- Exclusion criteria:

1- Patients with FNAC results: benign and inadequate.
2- Patients without histopathological examination.
3- Poorly stained slides.

2-6- Materials and methodology:

Data collected from the request forms of the fine needle aspiration cytology and the histopathology in the different places and all the slides related to them are collected and reviewed with the supervisor and the co-supervisor. Patients who were not undergo the FNAC yet the procedure was obtained with neck hyper extended with the patient either lying down or sitting, the skin was cleaned with antiseptic, 22 gauge needle attached to
a 20 cc disposable syringe was introduced through the skin into the nodule varying the direction of insertion. Section was applied by withdrawing the plunger of the syringe and maintaining using the external thumb, the needle was advanced and withdrawn within the nodule three or four times at various angles and the suction gently released by detaching the syringe from the needle, the needle was withdrawn, the materials expelled onto glass slides, smears are made and fixed using 95% alcohol. Some patient underwent U/s guided FNA. Then stained according to laboratory policy either by Romanowsky’s stain or Pap stain or H & E. Using a microscope and with the help of the cytopathologists we reviewed the diagnosis of all the slides which were collected. Then reviewed the histopathology slides and correlate both of them for the 50 patients.

Cytological diagnoses were grouped into:

1- Carcinoma.
2- Suspicious for carcinoma
3- Indeterminate.
4- Benign.
5- Inadequate.

Only 1+2+3 are Included in this study.

Then looking for the histopathological examination of each one and correlate them to determine:

1- Sensitivity.
2- Specificity.
3- +ve predictive value
4- –ve predictive value
5- Accuracy Index.

2-7- Data processing and statistical analysis:

The data were electronically processed and analyzed using computer SPSS program, version 11.
3- RESULTS

The results of FNAB (cytologic diagnosis) in the study group of 50 patients are compared with their final histopathology results in different centers.

From above results we calculated the following:

- **Efficiency (Accuracy)** = \( \frac{TP + TN}{\text{total number of tests}} \times 100 = \frac{29 + 11}{50} \times 100 = 80\% \)
- **Sensitivity** = \( \frac{TP}{TP + FN} \times 100 = \frac{29}{29 + 8} \times 100 = 78.3\% \)
- **Specificity** = \( \frac{TN}{FP + TN} \times 100 = \frac{11}{2 + 11} \times 100 = 84.6\% \)
- **+ve Predictive Value** = \( \frac{TP}{TP + FP} \times 100 = \frac{29}{29 + 2} \times 100 = 93.5\% \)
- **–ve Predictive Value** = \( \frac{TN}{TN + FN} \times 100 = \frac{11}{11 + 8} \times 100 = 57.8\% \)

True Positive TP=29, True Negative TN=11, False Negative FN=8. False Positive FP=2
The results of the study are shown in the following tables and graphs:

Table 1: Total number of the FNAC samples in different laborites

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Frequency</th>
<th>Percentage%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bahri</td>
<td>1</td>
<td>2.0</td>
</tr>
<tr>
<td>Almobark</td>
<td>14</td>
<td>28.0</td>
</tr>
<tr>
<td>Other private lab.</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>Khartoum</td>
<td>9</td>
<td>18.0</td>
</tr>
<tr>
<td>NHL</td>
<td>11</td>
<td>22.0</td>
</tr>
<tr>
<td>Suba</td>
<td>9</td>
<td>18.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>50</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>
Table 2: Age distribution of the 50 patients included in the study

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Frequency</th>
<th>Percentage%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 _ 10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>11 _ 20</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>21 _ 30</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>31 _ 40</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>41 _ 50</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>51 _ 60</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>61 _ 70</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>71 _ 80</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>81 _ 90</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>More than 90</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>50</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>
Table 3: Sex distribution of the 50 patients with thyroid nodule in the study

<table>
<thead>
<tr>
<th>Gender</th>
<th>Frequency</th>
<th>Percentage%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>33</td>
<td>66</td>
</tr>
<tr>
<td>Male</td>
<td>17</td>
<td>34</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

Graph 1: Sex distribution of the 50 patients with thyroid nodule in the study group
Table 4: frequency and percentage of patients presented with thyroid nodule:

<table>
<thead>
<tr>
<th>Presented by Thyroid nodule</th>
<th>Frequency</th>
<th>Percentage%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>40</td>
<td>80.0</td>
</tr>
<tr>
<td>No</td>
<td>10</td>
<td>20.0</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 5: frequency and percentage of patients who have had history of goiter

<table>
<thead>
<tr>
<th>Pt. has had history of goiter</th>
<th>Frequency</th>
<th>Percentage%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>32</td>
<td>64.0</td>
</tr>
<tr>
<td>No</td>
<td>18</td>
<td>36.0</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Table 6 clinical presentation of the thyroid nodules:

<table>
<thead>
<tr>
<th>Item (sign, symptom)</th>
<th>Frequency</th>
<th>Percentage%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck swelling</td>
<td>46</td>
<td>92</td>
</tr>
<tr>
<td>Pain</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Cystic lesion</td>
<td>5</td>
<td>10.0</td>
</tr>
<tr>
<td>obstruction</td>
<td>1</td>
<td>2.0</td>
</tr>
<tr>
<td>Frontal swelling</td>
<td>1</td>
<td>2.0</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>5</td>
<td>10.0</td>
</tr>
<tr>
<td>Mediastinal mass</td>
<td>1</td>
<td>2.0</td>
</tr>
<tr>
<td>Toxic manifestation</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fixed thyroid swelling</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>U/S detected nodule</td>
<td>2</td>
<td>4.0</td>
</tr>
</tbody>
</table>
Table 7: Frequency of patients who undergo cell block

<table>
<thead>
<tr>
<th>Pt. did a cell block</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>34</td>
<td>68.0</td>
</tr>
<tr>
<td>Yes</td>
<td>16</td>
<td>32.0</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Graph 2: Frequency of patients who undergo cell block
Table 8: Frequency of benign and malignant results in cell block

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percent%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>5</td>
<td>31</td>
</tr>
<tr>
<td>Malignant</td>
<td>11</td>
<td>69</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>100.0</td>
</tr>
</tbody>
</table>
Table 9: Frequency of benign and malignant results in FNAC of the 50 pts included in the study

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Percentage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>18</td>
<td>36.0</td>
</tr>
<tr>
<td>Malignant</td>
<td>32</td>
<td>64.0</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Graph 3: Frequency of benign and malignant results in FNAC of the 50 patients included in the study
### Table 10: Frequency of FNAC results in FNAC in 50 patients included in the study

<table>
<thead>
<tr>
<th>FNAC result</th>
<th>Frequency</th>
<th>Percentage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign aspirate (colloid)</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>Follicular neoplasm</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>Suspicious aspirate</td>
<td>11</td>
<td>22</td>
</tr>
<tr>
<td>Malignant aspirate</td>
<td>19</td>
<td>38</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>50</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

### Table 11: Frequency of different diagnosis by FNAC in 50 patients included in the study

<table>
<thead>
<tr>
<th>FNAC diagnosis</th>
<th>Frequency</th>
<th>Percentage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaplastic carcinoma</td>
<td>3</td>
<td>6.0</td>
</tr>
<tr>
<td>Colloid cyst</td>
<td>3</td>
<td>6.0</td>
</tr>
<tr>
<td>Follicular carcinoma</td>
<td>12</td>
<td>24.0</td>
</tr>
<tr>
<td>Follicular neoplasm</td>
<td>12</td>
<td>24.0</td>
</tr>
<tr>
<td>Colloid goiter</td>
<td>5</td>
<td>10.0</td>
</tr>
<tr>
<td>Hurthle carcinoma</td>
<td>1</td>
<td>2.0</td>
</tr>
<tr>
<td>Medullary carcinoma</td>
<td>2</td>
<td>4.0</td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>11</td>
<td>22.0</td>
</tr>
<tr>
<td>Secondaries</td>
<td>1</td>
<td>2.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>50</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>
Table 12: Indications for surgery in 50 patients with thyroid nodule after FNAC results

<table>
<thead>
<tr>
<th>Indication</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical suspicious of malignancy</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>FNAC diagnosis of malignancy</td>
<td>42</td>
<td>84</td>
</tr>
<tr>
<td>Obstructive symptoms</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Others</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>50</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>
Table 13: Frequency of pts undergo total thyroidectomy depending on FNAC results

<table>
<thead>
<tr>
<th>Pts did total thyroidectomy</th>
<th>Frequency</th>
<th>Percentage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>15</td>
<td>30.0</td>
</tr>
<tr>
<td>No</td>
<td>35</td>
<td>70.0</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100.0</td>
</tr>
<tr>
<td>Hospital</td>
<td>Frequency</td>
<td>Percentage%</td>
</tr>
<tr>
<td>----------</td>
<td>-----------</td>
<td>-------------</td>
</tr>
<tr>
<td>Bahri</td>
<td>2</td>
<td>4.0</td>
</tr>
<tr>
<td>Almobark</td>
<td>2</td>
<td>4.0</td>
</tr>
<tr>
<td>Faidel</td>
<td>5</td>
<td>10.0</td>
</tr>
<tr>
<td>Khartoum</td>
<td>5</td>
<td>10.0</td>
</tr>
<tr>
<td>NHL</td>
<td>25</td>
<td>50.0</td>
</tr>
<tr>
<td>SUBA</td>
<td>11</td>
<td>22.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>50</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>
Table 15: Frequency of benign and malignant results in histopathology of the 50 patients included in the study:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>12</td>
<td>24.0</td>
</tr>
<tr>
<td>Malignant</td>
<td>38</td>
<td>76.0</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Graph 4: Frequency of benign and malignant results in histopathology of the 50 patients included in the study
Table 16: Histological diagnosis in 50 patients included in the study

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Frequency</th>
<th>Percentage%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaplastic carcinoma</td>
<td>4</td>
<td>8.0</td>
</tr>
<tr>
<td>colloid goiter</td>
<td>5</td>
<td>10.0</td>
</tr>
<tr>
<td>Follicular adenoma</td>
<td>6</td>
<td>12.0</td>
</tr>
<tr>
<td>Follicular carcinoma</td>
<td>16</td>
<td>32.0</td>
</tr>
<tr>
<td>Hashimimoto thyroiditis</td>
<td>1</td>
<td>2.0</td>
</tr>
<tr>
<td>Hurthle cell carcinoma</td>
<td>2</td>
<td>4.0</td>
</tr>
<tr>
<td>Medullary carcinoma</td>
<td>2</td>
<td>4.0</td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>12</td>
<td>24.0</td>
</tr>
<tr>
<td>Secondaries</td>
<td>2</td>
<td>4.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>50</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>
Table 17: Correlation between FNAC and histopathology results in general

<table>
<thead>
<tr>
<th>Correlation</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>11</td>
<td>22.0</td>
</tr>
<tr>
<td>Yes</td>
<td>39</td>
<td>78.0</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 18: Reliability of FNAC in the Diagnosis of Thyroid Nodules

<table>
<thead>
<tr>
<th>FNAC results</th>
<th>Benign histology</th>
<th>Malignant histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign aspirate (8)</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Follicular neoplasm (10)</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Suspicious aspirate (13)</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Malignant aspirate (19)</td>
<td>0</td>
<td>19</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>12</strong></td>
<td><strong>38</strong></td>
</tr>
</tbody>
</table>
Table 19: Correlation between FNAC and histopathology result

<table>
<thead>
<tr>
<th></th>
<th>Benign histology</th>
<th>Malignant histology</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant aspirate</td>
<td>2</td>
<td>30</td>
<td>32</td>
</tr>
<tr>
<td>Benign aspirate</td>
<td>10</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>12</strong></td>
<td><strong>38</strong></td>
<td><strong>50</strong></td>
</tr>
</tbody>
</table>

Table 20: Correlation between cellblock results and histopathology

<table>
<thead>
<tr>
<th></th>
<th>Benign histology</th>
<th>Malignant histology</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant aspirate</td>
<td>5</td>
<td>11</td>
<td>16</td>
</tr>
<tr>
<td>Benign aspirate</td>
<td>0</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>5</strong></td>
<td><strong>0</strong></td>
<td><strong>5</strong></td>
</tr>
</tbody>
</table>
Table 21: Correlation between FNAC results and histopathology in different types of thyroid carcinoma

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>FNAC results</th>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papillary carcinoma</td>
<td>11</td>
<td>12 91%</td>
</tr>
<tr>
<td>Follicular carcinoma</td>
<td>13</td>
<td>16 81%</td>
</tr>
<tr>
<td>Anaplastic carcinoma</td>
<td>4</td>
<td>4 100%</td>
</tr>
<tr>
<td>Medullary carcinoma</td>
<td>2</td>
<td>2 100%</td>
</tr>
<tr>
<td>Hurthle cell carcinoma</td>
<td>1</td>
<td>2 50%</td>
</tr>
<tr>
<td>Metastatic carcinoma</td>
<td>1</td>
<td>2 50%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>32</strong></td>
<td><strong>38</strong></td>
</tr>
</tbody>
</table>
4-1- DISCUSSION

Thyroid nodule is a common presentation of thyroid illness and many surgeons and physicians requesting fine needle aspiration cytology as a first line diagnosis, there are many available laboratories which can do the test, governmental and private laboratories with different guidance to perform the needling, preparation and interpretation of diagnosis, pointing to lack of a unique policy. Still thyroid biopsies constitute the major bulk of patient’s requests in cytopathology laboratories, other notice is that most of the laborites are histopathology laboratories and they give this service beside their work. The fine needle aspiration cytology slides and data of this study were gathered from different places as table_1 showed, mainly from Almobark private laboratory, NHL, Khartoum hospital laboratory and Suba hospital Laboratory. Unfortunately the histopathology specimens are processed in different places. In other studies they compared the FNAC results and histopathology results at same center and with large number of cases.(6,9,11)

The commonest age group affected by thyroid cancer is 31 to 40 years with percentage of 24 % followed by 41 to 50 years with 20 % then 18% in age group 20 -30 years, no thyroid tumor is occurred in less than 10 years or more than 90 years. In other studies the same common age group (30_40) but followed by the age group (20_30).\(^{(12)}\) Based on these finding we can conclude that young and middle aged adults were the most commonly affected by the thyroid tumors. Children were rarely affected.

Female patients constituted 66 % of cases while male patients constituted 34 %, with female to male ratio of 1.9: 1, which indicates that the females are more prone to thyroid nodules and then to thyroid cancer,

Fourty six patients presented with thyroid swelling with percentage of 92% of whole population studied who suspected to have thyroid tumor, so it is a very common presenting symptom, in addition to that 40 patients
of them presented with a solitary thyroid nodule rather than diffuse swelling with a percentage of 80%, and the solitary nodule are more likely to be a neoplasm rather than a diffuse swelling. 64% of cases have history of nodular goiter which is strong indicator to its association with thyroid tumors and then malignant tumors giving the clue that some diseases and causes that give rise to thyroid swelling can give rise also to some cancers for example iodine deficiency and Hashimmo’ts thyroiditis, 4 cases have a cystic lesion and it constitute 8 %, which occurring in benign and malignant conditions and giving a thyroid swelling or nodule but is usually disappear after aspiration, they require more attention in interpretation, 2 of them are diagnosed wrongly.\(^\text{27}\) One case with thyroid nodule appeared to be cold in scanning and proved to be cancer\(^\text{28}\).

Also notice that the fastly growing nodule, the hard one and that being recurrent are finally diagnosed as cancer, also FNAC has a great help in diagnosing obviously malignant tumor in which no role for surgery and only palliative treatment is valuable, mostly being anaplastic carcinoma and high grade lymphoma.\(^\text{2}\)

Ultrasounds can detect impalpable nodules and tow of the cases proved to have thyroid cancer in thyroid nodule which detected by ultrasound, strangely thyroid cancer presented with metastatic symptoms just like frontal and mediastinal swelling.\(^\text{24}\)

Just 16 patients underwent cell block procedure represented 32% of all patients it is helpful especially in follicular neoplasms; great value in distinguishing follicular adenomas from colloid nodules.\(^\text{25}\) Beside that ancillary studies can be done on it; the study showed that the diagnosis of cell block is consistent with the final histopathology diagnosis.

FNAC results of the 50 pts yield 32 pts as malignant and highly suspicious aspirates, these are of 64% and here results differ between different cytopathologists in diagnosing the case as highly suspicious or
malignant aspirate. 2 results of suspicious aspirate are proved to be benign lesions after thyroidectomy. 15 patients underwent total thyroidectomy depending on the FNAC results, all of them proved to have thyroid cancer.

Twelve cases (24%) of whole cases were diagnosed as follicular neoplasms which could be a benign hyperplastic goiterous nodule, follicular adenoma or even carcinoma and here it is limited in see capsular or vascular invasion, so positive predictive value of 84% was found for the follicular carcinoma in particular compared to 44% in a previous Sudanese study, and this is due to the fact that reports of suspicious follicular pattern is agreed not to imply definite malignancy\(^{(31)}\), and they are still a problem in diagnosis by FNAC, some cytological features that strongly suggested cancer are seen by cytopathologist.\(^{(2,26)}\)

In table 11 we categorized the highly suspicious results in the malignant type of suspiciousness, there are 12 cases diagnosed as follicular neoplasm waiting for histopathology to give the final diagnosis while another 12 cases, we can categorize them as follicular carcinoma or suspicious for follicular carcinoma, 11 cases as papillary carcinoma, colloid cyst is represented in 3 cases also colloid goiter in 5 cases. Medullary carcinoma demonstrated 2 cases while 1case for Hurthle cell carcinoma and 1 case for Secondaries. From these results we can conclude that follicular neoplasms (follicular adenoma and follicular carcinoma) are predominant thyroid tumor with 24 cases and 48%.

FNAB diagnosis is an indication for thyroidectomy in almost 42 of the 50 patients, means about 84%. The diagnosis here included carcinoma, suspicious of carcinoma and follicular neoplasm.

Histopathology examination took place in different places, 25 cases were studied in NHL, less variability in places than FNAC.

Malignant biopsies in 38 of cases with percentage of 76% compared with 32 malignant results in FNAC in the same 50 pts with about 6 pts
missed by FNAC as benign, one case of them delayed the surgical treatment for about one year and by that time she had distant metastasis, 2 of the missed cases are cystic in consistency when applied FNAC.

Follicular carcinoma is the most common thyroid cancer found in the study with 16 pts and percentage of 32% followed by papillary carcinoma with 12 cases and percentage of 24%, then Follicular adenoma in 6 cases with percentage of 12%.

Correlation between FNAC results and Histopathology results is seen in 39 cases out of 50 cases with percentage reaching 78%, this occurred by finding the malignant and suspicious aspirate in FNAC results yielding a malignant result in final histopathology results, furthermore by yielding the specific type of cancer which is suggested by the FNAC

Detailed comparison shows that FNAC results giving diagnosis of 32 malignant aspirates while really they are just 30 malignant biopsies with 2 cases over diagnosed as malignant by FNAC with consequence of total thyroidectomy in one of them. While it gives 8 results (16%) as benign aspirate and the real diagnosis is that all the 8 specimens are malignant so 8 cases with malignancy were missed by FNAC, 10 cases (20%) were diagnosed as follicular neoplasm proved to be benign in form of follicular adenoma and hyperplastic nodule of colloid goiter or even colloid goiter.

The cell block which is done in only 16 cases giving the results of 11 malignant aspirate and 5 benign aspirates, when these compared with the histopathology results it correlated 100%, so it is valuable technique. (25)

Regarding the individual difference in diagnosis of different types of malignancies we concluded that papillary carcinoma FNAC missed multifocal papillary carcinoma in a huge goiter and it is able to detect 91% of the papillary carcinoma, (29) while in follicular carcinoma it missed 19% of them. Cystic changes in Hurthle cell carcinoma and follicular carcinoma were missed as benign goiterous cyst, also missed metastatic carcinoma in
a huge goiter, we concluded that FNAC detected all the cases of medullary and anaplastic carcinoma 100% followed by papillary carcinoma in which FNAC detected 11 out of 12 cases of papillary carcinoma with percentage of 91%, in follicular carcinoma FNAC missed 3 out of 16 cases with percentage of 81%, FNAC of Hurthle cell carcinoma and metastatic tumors missed 1 case out of 2 for each, representing 50%.

Manually from the collected data Efficacy, Sensitivity, Specificity, Positive predictive value and Negative predictive value of FNAC were calculated. Sensitivity was found to be 78% which is not very well accepted and it is not consistent with a similar study in Sudan which showed sensitivity of 95%, and also not consistent with worldwide similar studies with a very low sensitivity 53%. Overall accuracy in detecting benign and malignant lesions reached 80% which is midway between similar studies in and outside Sudan. 93, 5% is the positive predictive value with great ability to detect malignant tumors in thyroid. For follicular neoplasms; we found that a positive predictive value of 79% compared to a Sudanese study they found a low positive predictive value for follicular neoplasm with fine needle aspiration cytology (FNAC) (44%), this is due to the fact that reports of suspicious follicular pattern is agreed not to imply definite malignancy. From all this we think that FNAC of thyroid could be used as screening test for thyroid cancer and can detects majority of them but has some limitations of the procedure include sampling errors, indeterminate cytology and experience of the cytopathologist. It was a good adjuvant to management and there is a great possibility to improve it.
When all the findings in the study are considered together, it can be said that the results are corresponding to most of studies in other places outside Sudan, and not correspond so much to the study done in Sudan, also we conclude to have these measures:

- Sensitivity = 78.3 %
- Specificity = 84.6 %
- PV +ve = 93.5%
- PV –ve = 57.8 %
- Efficiency = 80 %

The accuracy of FNAB in the diagnosis of Thyroid cancer is accepted. It is an adjuvant to the management to thyroid nodules but is not a definitive diagnostic test and in particular negative results do not exclude neoplastic disease.

Also cytological diagnosis of malignancies and suspicious of malignancy are the main indications for surgery in thyroid nodule so proper diagnosis is mandatory in management to achieve good prognosis.

Follicular carcinoma is the most common thyroid malignancy in Sudan, constituting 32% of them followed by papillary carcinoma 24% then anaplastic carcinoma 8%. Fine needle aspiration cytology detected all the cases of the anaplastic carcinomas and missed one out of twelve papillary carcinoma and also missed three out of sixteen of follicular carcinomas.
4-3- RECOMMENDATIONS

• To established a reference cytopathology laboratory with agreed policy for interpretation and diagnosis of thyroid diseases.
• Other diagnostic methods should be employed for pro operative evaluation of Thyroid nodules.
• Careful interpretation for cystic lesions
• Further prospective studies are indicated with larger number of cases to define an optimum management policy in the evaluation of thyroid nodules.
• The technique of FNAB should also be improved to maximize its diagnostic usefulness taking into account the known limitations of the procedure.
• Ultrasound guided biopsies are highly recommended to decrease the percentage of false negative results.
• Cell block procedure is easy and safe and helps much in diagnosis.
REFERENCES

4. Corrias, S. Einaudi, E. Chiorboli, G. Weber, A. Crinò, M. Andreo, G. Accuracy of Fine Needle Aspiration Biopsy of Thyroid Nodules in Detecting Malignancy in Childhood: Comparison with Conventional Clinical, Laboratory, and Imaging Approaches Division of Pediatric Endocrinology, Regina Margherita Children Hospital (A.C., S.E., M.A., L.d.S.), 10100 Turin, Italy; Pediatric Unit)
9. Cochand-Priollet B, Guillausseau PJ, Chagnon S, et al. The diagnostic value of fine-needle aspiration biopsy under ultrasonography in


18. Michael Patmas, MS, MD, MMM, FACP, FACPE, CPE. Thyroid Nodules: A Practical Approach. General Internal Medicine Faculty – PPMC, OHSU.

20. Zubair W. Baloch, MD, Phd, Martha Bishop Pitman, MD: Thyroid fine needle aspiration indications and techniques- Papaniclaou Society of cytopathology.

21. Douglas P. Clark, M.D: Thyroid Cytopathology: from morphology to molecules The Johns Hopkins School of Medicine Baltimore, MD USA dclark@jhmi.edu http://pathology2.jhu/cytopath.


Questionnaire

Name (  )
age (  ) sex (  )
Residence (  ) tribe (  )
c/o:
thyroid nodule: yes (  ) no (  )
history of goiter: yes (  ) no (  )
history of radiation: yes (  ) no (  )
others (  )
FNAC (  ) date (  ) hospital (  )
Cell block (  )
Histopathology (  ) date (  ) hospital (  )
FNAC result: adequate (  ) inadequate (  )
  benign aspirate (  )
  Follicular lesion (  )
  Suspicious of malignancy (  )
  Malignant aspirate (  ) from thyroid (  ) mets (  )
Cell block: benign (  )
  Malignant (  ) from thyroid (  ) mets (  )
They underwent surgery because of .................................................................
Histopathological result: colloid goiter (  )
  Follicular adenoma (  ) Hurthle cell adenoma (  )
  Papillary carcinoma (  ) Follicular carcinoma (  )
  Anaplastic carcinoma (  ) Hurthle cell carcinoma (  )
FNAC and histopathological results correlated yes (  ) no (  )