HISTOPATHOLOGICAL PROFILE OF LUNG TUMORS ON CT/USG GUIDED CORE NEEDLE BIOPSY SPECIMENS

A DISSERTATION

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CERTIFICATE

This is to certify that this dissertation entitled **"HISTOPATHOLOGICAL PROFILE OF LUNG TUMORS ON CT/USG GUIDED CORE NEEDLE BIOPSY SPECIMENS"** is a bonafide work done by **Dr.K.KULOTHUNGAN**, in partial fulfillment of the regulations of The TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY, Chennai for the award of M.D. Pathology Degree.

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I declare that this dissertation entitled **"HISTOPATHOLOGICAL PROFILE OF LUNG TUMORS ON CT/USG GUIDED CORE NEEDLE BIOPSY SPECIMENS"** has been done by me under the guidance and supervision of **Prof.Dr.A.V.SHANTHI, M.D.,** It is submitted in partial fulfillment of the requirements for the award of the M.D., Pathology March 2008 Examination to be held under The Tamilnadu Dr. M.G.R. Medical University, Chennai. This has not been submitted by me for the award of any degree or diploma from any other University.

Dr.K.KULOTHUNGAN

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CONTENTS

INTRODUCTION

The last 100 years have seen the incidence of lung cancer transformed from it being an almost unknown disease to it far outstripping all other forms of cancer as a cause of death in many countries. In men it is responsible for about 40% of cancer deaths and in women it now rivals breast cancer as the major cause of cancer mortality.

Many developing countries have a relatively low incidence of lung cancer but are beginning to see the rises already experienced elsewhere as the inhabitants take to smoking in increasing numbers.

Lung carcinoma is largely a disease of the elderly and this tumor is very rare in children but occasional cases are encountered. It carries a very poor prognosis as spread of the tumor often results in it being inoperable at presentation while many patients with lung carcinoma have coexistent chronic obstructive lung disease that renders them unfit for surgery. Overall 5 year survival rates vary from 6-20%.

Lung carcinomas fulfill many of the following criteria for successful screening programme : the condition is common ,the population at risk is well known and premalignant changes can be detected cheaply(eg,sputum cytology).Unfortunately the premalignant changes

cannot be easily eradicated as there is no bronchopulmonary equivalent of a uterine cone biopsy. Nor does screening for early invasive growths by a combination of sputum cytology and radiography appear to reduce mortality.

Transthoracic biopsy is a safe and effective procedure in the evaluation of benign lesions, undetermined pulmonary lesions and an important tool in those patients with a peripheral mass inaccessible by bronchoscopy.

The methods that are commonly used are for obtaining materials for pathological diagnosis are:

1) Core needle biopsy by radiological intervention

2) Transbronchial biopsy

3) Transthoracic needle aspiration

Our study is based on histomorphological profile of lung tumors on CT/USG guided core needle biopsies

AIMS AND OBJECTIVES

1) To study the histomorphological variants of lung tumors on CT/USG guided core needle biopsy specimens.

2) To study the age, sex and site of prevalence of various histopathological variants of lung tumors.

3) Employing PAS and immune markers in selective cases.

4) To define morphological criteria in various subtypes of lung cancers.

REVIEW OF LITERATURE

Transthoracic biopsy is an important diagnostic tool in those patients with a peripheral mass inaccessible by bronchoscopy thus hindering the diagnosis by transbronchial biopsy.Pulmonary needle biopsy was used by Leyden in 1883 to detect microorganisms (Leyden H et al)[20].Three years later Menetrier succeeded in diagnosing pulmonary

neoplasms by transthoracic aspiration.Needle aspiration and biopsy has been in widespread use in recent years with an acceptable safety.

CT/USG guided percutaneous transthoracic biopsy is a safe and effective procedure in the evaluation of undetermined pulmonary lesions and also permits successful drainage of pulmonary abscesses(Mathis G et al) [23].According to Kardos et al and Davies et al ,this technique is particularly useful for benign lesions or tumors with pleomorphic morphological charecteristics and has better diagnostic value relative to bronchoscopic sampling in those cases where the size and location of the nodule make it inaccessible with the bronchoscopy.[4,17]

Thoracotomy in almost every case provides sufficient material for a definite diagnosis and has the added advantage that in a small percentage of patients with malignant lesions an attempt at curative curative resection can also be made.But Steal et al[30] stated that most lesions ,atleast in the older population ,can be expected to be malignant and that ,of these, the majority on clinical grounds be nonresectable at the time of presentation.In addition ,a number of patients will have benign lesions which do not require surgical treatment and also some will have small cell carcinoma for which chemotherapy is preferred.[30]

In light of these considerations and of the considerable morbidity associated with thoracotomy it is desirable in most

patients to establish a diagnosis by a closed procedure.Percutaneous needle biopsy provides a mean of accomplishing this.

The modalities commonly employed for the image guided percutaneous needle biopsy include fluoroscopy, conventional CT/USG,helical CT(which is more commonly used)(Wiscott et al).[35]CT fluoroscopy ,which was established most recently, has simplified the process and has decreased the time required for CT scan guided needle biopsies

. According to Haramati et al,the various kind of needles used are divided into the following two types: the modified trucut and modified Menghini type.[11]The Trucut type of needle consists of an outer cutting cannula and an inner trocar that contains the specimen notch. In general the following procedure is used with this type of needle. When the tip of the needle reaches the lesion ,the inner trocar is thrust forward ,followed by a forward thrusting of the outer cutting cannula.(Takuji Yamagami et al).[33]The specimen is then trapped in the notch of the trocar when the cutting cannula is advanced.

The Menghini type, which is also known as full cut type needle, consists of an inner trocar that does not have a notch and an outer cutting cannula.When the tip of the biopsy needle reaches the lesion,the outer cutting cannula is advanced ,while the inner trocar is held stationary and the tissue core is captured inside the outer cannula.The

Menghini type needle creates a vaccum in the end of the outer needle when the outer cutting cannula is thrust forward.

Biopsy is taken with Trucut disposable needle following premedication with atropine and infiltration of the chest wall with lignocaine.A tissue core of 2 by 20 mm in size is obtained and should preferably be placed in saline solution or fixative under negative pressure so that collapsed alveolar spaces may become inflated.

INDICATIONS:

1) To differentiate malignant from benign lesions
2) When the diagnosis of malignancy by FNAC is uncertain
3) More detailed characterization of the lesion is required
4) As a safe and reliable procedure in elderly with suspected chest malignancy
5) As an important diagnostic tool in those patients with peripheral pulmonary mass inaccessible by bronchoscope.

INTERPRETATION OF BIOPSY SPECIMENS:

According to Quint et al[26] the results are classified into following 4 groups:

1) Positive or suspicious for malignancy
2) Benign specific

3) Benign non specific

4) Non diagnostic

The diagnosis of benign lesion is to be made only if a) there was a complete or near complete core of tissue available and b) there was sufficient morphological detail to make a confident diagnosis of a benign process. In addition it was recognized that a very small specimen of inflammatory or necrotic tissue could not exclude a diagnosis of malignancy and such cases were included in the nondiagnostic category.[6]

Further nondiagnostic biopsy specimens were classified into 3 types:

1) No material is obtained

2) Normal lung tissue is biopsied

3) Specimen too small and distorted to make a diagnosis.

There are reasons for which a diagnosis could not be reached on the biopsy material: a) locality of the lesion: According to Yang et al,[37]the sensitivity of diagnosis of malignancy was 96.8% and accuracy was 97.5% in case of sub pleural tumors and the sensitivity of diagnosis of malignant tumors located within the lungs was 94.6% and accuracy was 95.2%.

The size of the lesion of the lesion does not influence much on the adequacy of the biopsy material. According to Laurent et al, [19the] accuracy of CT/USG guided biopsy nodules smaller than 20 mm, are comparable to those of larger lesions.

COMPLICATIONS:

1) Uncontrollable hemorrhage: There is a relatively high incidence of severe hemorrhage in diffuse pulmonary disease than in localized mass lesions as blood vessels penetrate through the lung in a normal fashion in diffuse pulmonary disease (Douglas et al)[6]
2) Pneumothorax(Halil et al)[12]
3) Emphysema(Lourenco et al)[18]
4) Hemoptysis(Galfieri et al[7]
5) Air embolism
6) Tumor implantation along the needle tract

CONTRAINDICATIONS:

1) Chronic respiratory insufficiency
2) Pulmonary arterial hypertension
3) Hemorrhagic diathesis
4) Highly vascular lesions
5) Echinococcal infections

HISTOLOGICAL CLASSIFICATION OF LUNG CARCINOMAS:

The WHO classification of lung cancers is based upon differentiation in the whole tumor, and has no provision for

making a non specific diagnosis that could be further refined if further material becomes available. Lung cancers are frequently heterogeneous and biopsy specimens provide only a small amount of tissue from which to make a preoperative diagnosis. Acccording to Edwards et al,[27]only 10-15% of patients with lung cancer will have tumor resected and the preoperative tumor classification confirmed. Therefore most patients"treatment will be based upon the diagnosis from preoperative specimens alone.

Though there is a spectrum of different histological types of lung cancers like squamous cell, small cell,adeno,adenosquamous ,large cell neuroendocrine carcinomas etc,it is imperiative to classify lung cancers as small cell carcinomas(SCLCS) and non small cell carcinomas(NSCLCS) as treatment protocol is different for SCLCS and NSCLCS.(Delik Erman et al).[6]

SMALL CELL CARCINOMAS:

Small cell carcinoma occurs generally in major airways, grows rapidly, metastasis early and initially at least is sensitive to chemotherapy. According to Betticher et al[1], small cell carcinoma cells have

1) Small uniform round or spindle cells arranged in sheets/ribbons/rosettes

2) Nucleus with fine stippled chromatin and inconspicuous nucleoli

3) Thin nuclear membrane

4) Ill defined cell borders

5) High mitosis and necrosis may be present.

Small cell carcinoma is liable to be mistaken for large cell carcinoma

.The main differentiating points are:

	small cell ca	large cell ca
cell shape	Fusiform	polygonal
N/C ratio	High	low
chromatin	Fine	coarse
Nucleoli	Indistinct	prominent

A study conducted by Delik Erman et al[6] of 571 cases of lung carcinomas between 1994-99 revealed that small cell carcinoma constituted only 31 % of cases and most of the cases had extensive disease at presentation.

Undifferentiated carcinoma of small cell type is composed of small tumor cells with

1) hyper chromatic ,coarsely granular or vesicular nucleus,

2) small but distinct nucleoli

3) scant but identifiable cytoplasm

4) Distinct cell border.

Tumors of this cell type may be classified as squamous cell carcinoma of small cell type.

NON SMALL CEL CARCINOMAS:

This entity composes about 70 % of lung cancers and includes all categories except small cell carcinomas. They are:

1) Squamous cell carcinoma

2) Adenocarcinoma

3) Large cell carcinoma

4)Adenosquamous carcinoma

5) Bronchial gland carcinoma-adenoidcystic carcinoma and mucoepidermoid carcinoma

6) Miscellaneous tumors

SQUAMOUS CELL CARCINOMA:

Squamous cell carcinoma most often involves the central portion of the lung, arising from the large bronchi. Approximately one third however are peripheral tumors. There is a strong relationship with cigarette smoking and other carcinogens. It usually has a

long natural history and evolves from gradually accumulating epithelial changes throughout the bronchial tree over many years.

As the tumor progresses, it forms an endobronchial mass causing bronchial obstruction.Squamous cell carcinomas occurring in the periphery of the the lung are usually cavitary due to extensive necrosis.

According to Suprun et al, [32] a high accuracy of diagnosis can be achieved for squamous cell carcinoma by adhering to criteria like

1) Keratin formation

2) Intercellular bridges

3) Coarse, diffuse chromatin

4) Dense shrunken nucleus

5) Less conspicuous nucleoli

6) Geographic necrosis uncommon

In cases where these features were absent,squamous cell carcinoma has intraepithelial insitu like extensions along the bronchus and neither small cell carcinoma nor adenocarcinoma replaces the bronchial epithelium to any considerable extent and most of the cases are either well or moderately differentiated. This feature is useful in histological typing of lung cancers in small biopsy specimens.[31]

Variants of squamous cell carcinomas have been described that have prognostic significance.

1) Papillary variant- this variant tends to be well differentiated and has an excellent prognosis.

2) Small cell variant-this variant reveals areas that contain small tumor cells with little cytoplasm and without intercellular bridges gradually blending with more clear cut evidence of squamous differentiation.

3) Basaloid variant-nodular or trabecular growth pattern with peripheral palisading of the basal layers of malignant squamous cells along the basement membrane reminiscent of basal cell carcinoma.

Both small cell and basaloid variants carry a poor prognosis. Other rare variants are clear cell, giant cell and spindle cell variants have been observed. The grading of squamous cell carcinoma could not be done from small biopsy specimens.[3]

ADENOCARCINOMA:

Adenocarcinoma is an invasive tumor showing varying morphology with papillary,acinar and solid patterns. They are more common in women than men and tend to be more often peripheral in location than squamous cell carcinoma or small cell carcinoma. These tumors show an increase in its incidence that cannot be ascribed solely to

changes in histological typing. There is also an increased proportion of adenocarcinoma in non smokers and in the young

The individual cells exhibit features like

1) Enlarged nuclei

2) Peripheral clumping of chromatin

3) Prominent nucleoli

Histologically adenocarcinoma is a heterogeneous group of tumors that shows variation in architecture, hence the mixed type is the most common pattern observed. The other common patterns are

1) Acinar pattern

2) Papillary pattern

3) Micro papillary pattern

4) Bronchi alveolar pattern

5) Solid pattern.

Multicentricity of the tumor may be seen in approximately 20% of cases with tumor nodules present in other areas of the lung tissue.

The diagnosis of adenocarcinoma seems to be more of a challenge as mucin and gland formation are frequently not present in small biopsy .They require the demonstration of glandular elements by using special stains like PAS.Thomas et al, [34] advocated the use of non small cell category (NSCLC) in cases where definite features of differentiation were absent, but the lesion lacked the features of small cell carcinoma.

According to Delik Erman et al,[6]among NSCLC, squamous cell carcinoma constituted the predominant group with 60%,adenocarcinoma with 30% and large cell carcinoma comprising about 5% and others 5%.NSCLC occurred predominantly in 50-80 years. Only 3% of cases presented before 30 years.Yutaka Mizushima[38] et al stated that under the age group of 30 years, a high incidence of female gender, low incidence of squamous cell carcinoma and adenocarcinoma constituted the predominant histological type with favorable prognosis.

LARGE CELL CARCINOMA:

This tumor is charecterised by sheets of large cuboidal cells without evidence of cytoplasmic differentiation on routine stains.This tumor shows the greatest degree of interobserver variability among the pathologists.[29]

A diagnosis of large cell carcinoma cannot be diagnosed on small biopsy as they are considered poorly differentiated forms of either squamous,adeno or neuroendocrine carcinoma and all major histological types of lung carcinomas may contain foci of features of large cell carcinoma .So the diagnosis of large cell carcinoma is based on the resected specimens.(Edwards et al).[27]

ADENOIDCYSTIC CARCINOMA:

Adenoidcystic carcinoma is a rare lung malignancy that occurs in a wide age range .Hilal Alunoz et al[10] stated that it occurred predominantly in the trachea where it constituted the most common malignancy next to squamous cell carcinoma. Only 10 -15 % of cases occurred in the periphery. Most common histological pattern is cribriform with many microcystic spaces containing PAS positive eosinophilic secretions.

MUCOEPIDERMOID CARCINOMA:

Mucoepidermoid carcinoma is a very rare entity that predominantly occurs in younger age group with equal sex incidence. Xiuli et al [36]stated that it commonly arises from the sub mucosal glands of bronchi and it is usually well differentiated usually composed of mucinous cells,squamoid and intermediate cells. The occurrence of this particular tumor in young patients is due to recurrent translocations like t (1; 11), t (11:19).

CARCINOID:

They are neuroendocrine tumors of low grade malignancy which comprises <1% of lung tumors. The mean age of presentation is 55 years with equal sex incidence. About 8% of cases develop in the second decade where it is considered the most common pulmonary tumor of childhood.[3]They are not related to smoking or other pollutants. They do not appear to dedifferentiate into small cell or large cell neuroendocrine

carcinoma. Several histological patterns are recognized, the most common being insular pattern.

Microscopically, the tumor cells are:

1) uniform and generally polygonal
2) moderate amount of eosinophilic cytoplasm
3) round nuclei with fine granular chromatin
4) And inconspicuous nucleoli.
5) Mitosis is occasional and if present, <2/10 hpf.
6) If necrosis and or mitosis more than 2 /10 hpf,the alternate diagnosis of small cell carcinoma or atypical carcinoid to be diagnosed.

INFLAMMATORY MYOFIBROBLASTIC TUMOR:

Inflammatory myofibroblastic tumor is a benign tumor of undetermined etiology that occurs in the age of less than 40 years with female predominance .Mahele et al[21] stated that it

commonly presented as an asymptomatic solitary nodule with systemic features like fever, increased ESR due to the cytokines secreted by the tumor.Histologically it is composed of three basic patterns1)organizing pneumonic pattern in which airways are filled with plump fibroblasts and histiocytes and parenchyma replaced with histiocytes ,fibroblasts and mononuclear cells.2)fibrohistiocytic pattern which is the most common pattern in which myofibroblasts are arranged in whorls(Hiroyuki Sakurai et al)[13] 3)lymphohistiocytic pattern ,the least common pattern in which polymorphs,,plasma cells, vacuoloted histiocytes and fibroblasts occupy the predominant cell types.

ADENOSQUAMOUS CARCINOMA:

Adenosquamous carcinoma is a distinct tumor entity that carries a poor prognosis compared to conventional squamous cell and adenocarcinoma.It is a relatively rare entity with a frequency of 1 -4 %.The diagnosis is based on the light microscopy which should reveal that both the adeno and squamous cell component exhibiting malignant features and both components should constitute more than 10%.according to Takamari et al.[28]The prognosis is not based on the relative proportions of adeno or squamous components but due to the increased inherent potential of this tumor to metastasis to regional lymph nodes. The most common age group is 60 -70 years with increased male incidence and most of these tumors occur in the periphery of the lung. The histology of

this tumor is uncertain .It may arise from adenocarcinoma with squamous metaplasia, collision tumor, high grade mucoepidermoid carcinoma and bipotential undifferentiated cell origin.

BRONCHIOALVEOLAR CARCINOMA:

Bronchioalveolar carcinoma is a tumor that commonly occurs in females of middle to late age group .It is a variant of adenocarcinoma which lacks stromal, vascular and pleural invasion(Hiroyuki et al)[13].It commonly occurs in the periphery of the lung. Therefore this category is reserved for adenocarcinomas that show a non invasive, non destructive pattern of mural growth throughout. Microscopically it is divided into two types

1) Mucinous type

2) Nonmucinous type

Mucinous type:

The tumor is formed by well differentiated mucin containing columnar cells that line respiratory spaces without invading the stroma.The cells are relatively monomorphic,show little atypia,and produce large amounts of mucin leading on to bronchorroea. Continuity between the tumor cells lining alveoli and the epithelium of respiratory bronchioles or alveolar spaces can be demonstrated. A sharp demarcation is often between the neoplastic and the normal cells, an useful diagnostic feature. It carries a worst prognosis compared to non mucinous type.

Nonmucinous type:

They comprise 70% of cases of bronchioalveolar carcinoma. The tumor cells(clara cells or type 2 pneumocytes) are cuboidal rather than columnar and contain bright eosinophilic cytoplasm. The degree of nuclear atypia and nucleolar prominence is greater than mucinous variety. Hob nail cells may be present. Apical snouts may be present as indicator of clara cells. Cilia are characteristically absent and their presence should suggest the possibility of reactive condition. Incontrast to mucinous variant, various degrees of interstitial fibrosis and chronic inflammatory cells are present.

It carries an excellent prognosis and local excision may be curative.

CHARECTERISTICS OF LUNG CARCINOMA ACCORDING TO AGE GROUP AND SEX:

Age is considered as a risk factor for the development of lung cancer with a high percentage of cancers found older than 65 years. In this age group, there is a high percentage of non smokers and females.

Squamous cell carcinoma is the most predominant tumor in all age groups but the proportion of adenocarcinoma is higher in patients <60 years (de Parot et al)[5]that is adenocarcinoma is mainly observed in patients less than 60 years. Guntulu et al[9] noted that adenoarcinoma and small cell carcinoma were predominant in the younger

age group whereas squamous cell carcinoma occurred predominantly in the old age group. Michaela et al[24] also pointed out that young patients were significantly found to have adenocarcinoma more when compared to old patients.

Also the proportion of female cases was increased due to the changing pattern in the female smoking habit. A study was conducted by Yutaka Mizushima et al [38] to analyze various histological types and prognosis of lung carcinomas <30 years with those of older patients. Under the age group of 30 years ,a high incidence of female gender ,a low incidence of squamous cell carcinoma, preponderance of adenocarcinoma with more favorable prognosis were observed. Adenocarcinoma composed of 46% of all tumors, squamous cell carcinoma 4%,small cell carcinoma4%,large cell carcinoma 15% and bronchial gland carcinoma like mucoepidermoid and adenoidcystic carcinoma accounted for 19% .

In the age group of 30 -49 years, adenocarcioma constituted the predominant category accounting for 61%,squamous cell carcinoma 13%,small cell carcinoma 9%,large cell carcinoma 13%,and adenosquamous carcinoma4%.Delik Erman [6]stated that under the age group of 45 years NSCLC occurs infrequently.

In the age group of 50-69 years, again adenocarcioma constituted the predominant histological type with 37%, small cell carcinoma 27%,

squamous cell carcinoma24%, large cell and adenosquamous carcinoma constituted 5% each.Brambilla et al [2]stated that adenocarcinoma constituted the predominant histology under the age group of 50 years

In the age group of >70 years squamous cell carcinoma constituted the predominant type with 43%,adenocarcinoma 30%,small cell carcinoma17%,large cell carcinoma constituted 5%,adenosquamous 4% and carcinoid 2%.

ROLE OF IHC:

The expression of cytokeratins (CK) in human lung cancers is studied using monoclonal antibodies to cytokeratins 4,5,7,8,10,18 and 19.(Jos LV Broers et al)[16].When applied to adenocarcinoma,high level of cytokeratins 7,8 and and 18 are detected with higher concentrations of cytokeratin 7.Thus monoclonal antibody specific for cytokeratin 7 can therefore be helpful to distinguish adenocarcinoma from other non small cell carcinoma.Masahika[22] too stated that positivity of staining of cytokeratin 7 was found in 95.4% of adenocarcinomas.

Squamous cell carcinoma expresses cytokeratin 4,5 and 14 .Further Masahika et al[22] stated that squamous cell carcinoma of lung are usually well to moderately differentiated and IHC is usually not required to arrive at the diagnosis .Further he stated transbronchial and CT guided biopsy are often performed to obtain a pathological diagnosis but the

material obtained may be insufficient for immunophenotyping to be performed .

These staining patterns are not absolutely specific as squamous cell carcinomas tend to express cytokeratins 8 and rarely cytokeratin 7.Some small cell carcinoma and carcinoid tend to express cytokeratin 18. (Johansson et al).[15]

The neuroendocrine tumors express a panel of markers like NSE (neuron specific enolase),chromagranin ,synaptophysin etc but none of the antibodies are totally specific .Moreover Brambilla[2] stated that in small biopsy specimens NSE appeared to the first screening marker for neuroendocrine tumors.

Therefore because of considerable overlapping, immunophenotyping should not be used alone for histopathological classification of lung tumors but only to an adjuvant to light microscopy.

MATERIALS AND METHODOLOGY

The core material forming the basis of this study comprised of 140 cases of CT/USG guided core needle biopsy lesions of the lung from the Institute of pathology, Madras Medical College, Chennai .The study period is from May 2005 to May 2007.

The biopsy specimens were subjected to meticulous microscopic examinations. The specimens were fixed in 10% neutral buffered formaldehyde, processed routinely and embedded in paraffin**.**

Histological Sections (5 to 6 μm) were routinely stained with Hematoxylin and Eosin stains and special stains like PAS (periodic acid - Schiff) was done in selected cases. Additional sections were cut from paraffin embedded tumor tissue for immuno histochemistry. Due to the cost restriction, IHC could not be done for all the cases in the present study.

I. HEMATOXYLIN AND EOSIN

1. Dewax Sections. Hydrate through graded alcohols to water.
2. Stain in Harris hematoxylin for 5 minutes.
3. Wash well in running tap water.

4. Differentiate in 1% acid alcohol.
5. Wash well in tap water until sections are again blue for 10 to 15 minutes.
6. Stain in 1% eosin for 1 to 2 minutes.
7. Wash in running tap water for 1 to 5 minutes.
8. Dehydrate through alcohols, clear in xylol and mount is DPX.

II. PAS TECHNIQUE

1. Dewax sections and bring to distilled water.
2. Treat with periodic acid for 5 minutes.
3. Wash well with several changes of distilled water.
4. Cover with Schiffs solution for 15 minutes.
5. Wash in running tap water for 5 – 10 minutes.
6. Stain nuclei with Harris hematoxylin differentiating as appropriate in acid-alcohol and blueing as usual.
7. Wash in water.
8. Rinse in absolute alcohol.
9. Clear in xylene and mount.

Result:

Glycogen of cytoplasm of tumor cells stain magenta and the nucleus stains blue

IMMUNO HISTOCHEMICAL TECHNIQUE

This test was done for selected cases like poorly differentiated carcinoma, small cell carcinoma and adenocarcinoma which had no histological features in light microscopy.

The test was based on Avidin biotin complex (ABC) technique (Heat mediated antigen retrieval)

STAINING PROTOCOL

REAGENTS

1. 2% Hydrogen peroxide solution

H_2o_2	-	2 ml
Methanol	-	70 ml
Tris buffer	-	30 ml

2. Antigen Retrieval Solution

A. Citrate Buffer (stock)

Citric acid	-	5.25 gm
Distilled Water	-	500 ml

B. Sodium Citrate (stock)

Sodium Citrate	-	7.35 gm
Distilled water	-	500 ml

Citrate buffer working solution

A Solution	-	9 ml
B Solution	-	41 ml

made upto 500 ml at PH - 6.0

v

3. TRIS Buffer

Tris	-	3.025 gm
Sodium Chloride	-	40 gm
Ammonium Choloride	-	22 ml

Made upto 5 litres at PH of 7.6.

4. Primary Mouse antibody against inhibin

5. Secondary biotinylated antibody to mouse immuno globulin6. Substrate to the enzyme

7. **Chromogen Diamino benzidine (DAB)**

8. **Harris Hematoxylin Counterstain**

9. **DPX mountant**

10. **Grades of alcohol and xylene**

STAINING PRINCIPLE

In the Peroxidase anti-peroxidase (PAP) method, the PAP reagent consists of antibody against horse radish peroxidase and horse radish peroxidase antigen in the form of stable immune complexes. This is linked to the primary antibody against the antigen to be demonstrated (cytokeratin or synaptophysin in this case) through a secondary antibody. This secondary antibody is specific to the antigenic determinant present on the primary antibody. The presence is visualized by a substrate to the peroxidase linked to a chromogen

STEPS OF THE PROCEDURE

1. This technique is done on formalin fixed and paraffin embedded sections. Four micron sections to be taken on salanized slides.

2. Paraffin wax is removed from the slides mounted tissue sections by xylene I, xylene II, xylene III, each 5 minutes.

3. Dewaxed sections are then rehydrated by sequentially placing in absolute alcohol, 90% and 70% alcohol, 3 minutes each.

4. The slides are placed in running tap water for 10 minutes.

5. Then slides are transferred to distilled water - 5 minutes.

6. Endogenous peroxidase in the tissue sections is blocked using 3% H_2O_2 in methanol for 30 minutes.

7. Slides are washed in running tap water - 15 minutes

8. Then slides are rinsed in distilled water for 10 minutes.

9. About 3 litre of sodium citrate buffer is brought to boil in the pressure cooker without sealing the lid.

10. The slides with sections attached are placed in metal racks and lowered into the boiling citrate solution.

11. The pressure cooker is sealed and brought to full pressure. Heat timing begins when full pressure is reached, wait for 3 whistles.

12. Immediately, the cooker is placed in a sink containing cold tap water for 5-10 minutes, then rinsed in running tap water.

13. Slides are placed in distilled water for 5 minutes.

14. The slides are then washed with 3 rinses of Tris buffer solution, PH 7.6 for 5 minutes each.

15. The sections are covered with normal human serum for monoclonal (1/10) dilution, swine serum for polyclonal 1/10 dilution.

16. The blocked serum solution is tipped off the slide and replaced with 100-200 micro litres of primary anti body for 45 minutes.

17. The slides are then washed with 3 changes of TBS for 5 minutes.

18. Sections are covered with second layered antibody biotinylated mouse immunoglobulin 1/400 dilution for 45 minutes at room temperature.

19. The slides are then washed with 3 changes of TBS, 5 minutes each.

20. Sections are then covered with streptavidin 1/800 dilution for 4 minutes at room temperature.

21. The slides are then rinsed with 3 charges of Tris buffer solution, 5 minutes each.

22. Sections are covered with DAB solution for (Substrate Chromogen) 10 minutes at room temperature.

23. The slides are then rinsed with distilled water for 5 minutes, then in running tap water for 5 minutes.

24. The sections are counterstained with Harris haematoxylin for 30 seconds, then washed in running tap water.

25. The slides are placed in Scott's solution for 3 minutes.

26. Slides are rewashed with distilled water, the dehydrated taking through 90% alcohol, absolute alcohol and xylene.

27. Slides are mounted with DPX.

SUMMARY OF THE PROCEDURE

Preparation Protocol :

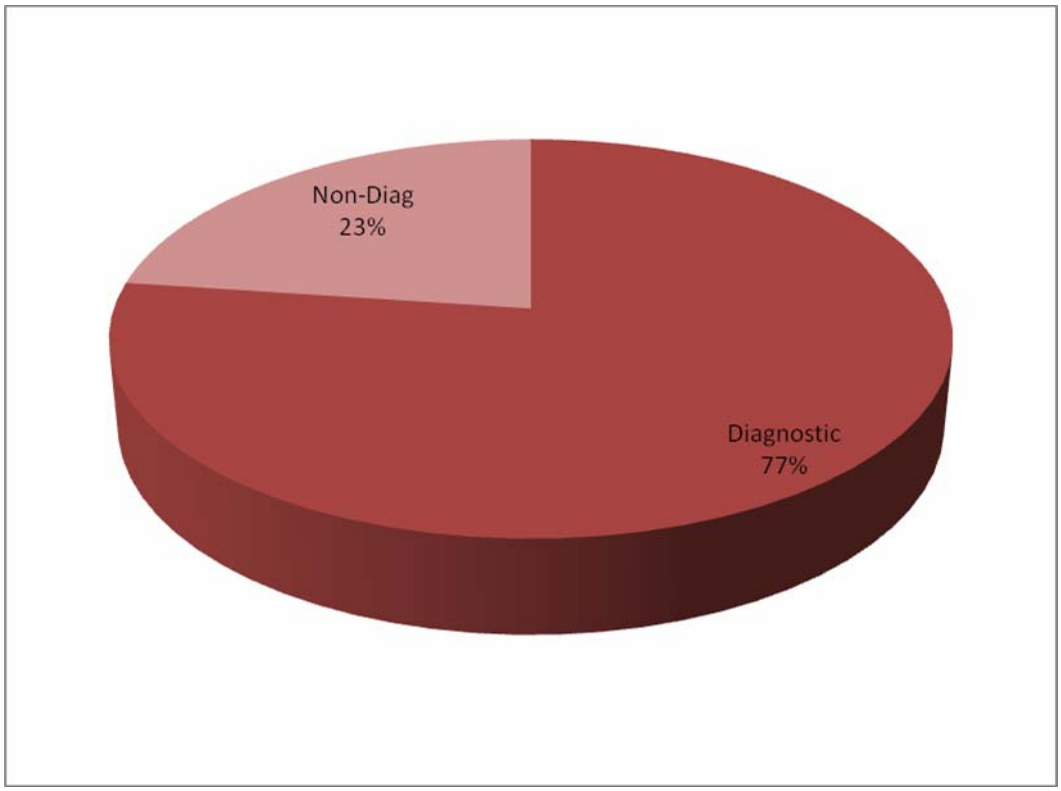
* Prepare wash buffer solution
* Deparaffinise and rehydrate specimens
* Epitope retrieval
* Prepare substrate chromogen solution
* Apply peroxidase blocking reagent.

DISCUSSION

This study deals with the various types of lung tumors diagnosed on CT/USG guided core needle biopsies obtained from

patients in the age group of 13 to 80 years in the period between may 2005 to may 2007.

A total of 140 cases have been studied .Of those 140 cases 32 cases have been reported as inadequate samples due to the various reasons being due to materials containing normal lung parenchyma, specimens too small and distorted to make a diagnosis, no material in the specimen and the presence of necrotic , inflammatory and fibrotic material.(Figs 32,33,34).



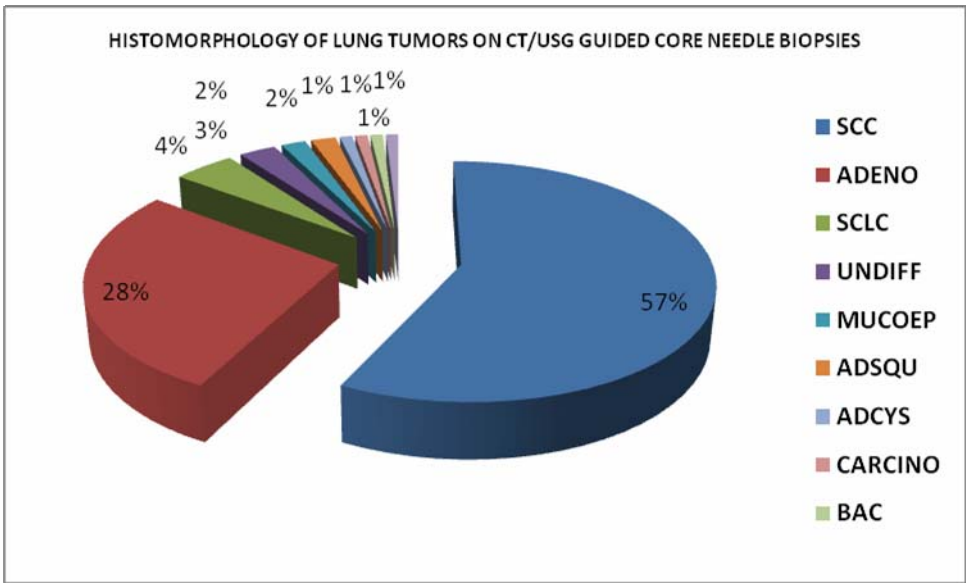
Of the remaining 108 cases 62 cases were diagnosed as squamous cell carcinoma(57%),30 cases diagnosed as adenocarcinoma(28%),5 cases

diagnosed as small cell carcinomas(4%),3 cases diagnosed as undifferentiated carcinomas ,2 cases diagnosed as mucoepidermoid carcinoma,1 case each of an adenoid cystic carcinoma, inflammatory myofibroblastic tumor, bronchioalveolar carcinoma and carcinoid was diagnosed.

Regarding the sex incidence, out of 108 cases 88 cases were males(81%),and 20 cases were females(19%).Of 62 cases diagnosed as squamous cell carcinomas, 60 cases were males (96.8%) and 2 cases were females(3.2%) with male female ratio of 4.4:1.Of 30 cases of adenocarcinomas, 17 cases were males(56.6%) and 13 cases were females(44.4%) with male female ratio of 1.3:1. All the 5 cases diagnosed as small cell carcinomas were males.1 case of adenoid cystic carcinoma reported was a male whereas out of 2 cases of mucoepidermoid carcinoma reported,1 case each of a male and a female was found. 1 case of bronchioalveolar carcinoma reported was a female. The single case of inflammatory myofibroblastic tumor was a female patient.

HISTOMORPHOLOGY OF LUNG TUMORS ON CT/USG GUIDED BIOPSIES

SQUAMOUS CELL CARCINOMA	62
ADENOCARCINOMA	30
SMALL CELL CARCINOMA	5
UNDIFFERENTIATED CARCINOMA	3
MUCOEPIDERMOID CARCINOMA	2
ADENOSQUAMOUS CARCINOMA	2
ADENOIDCYSTIC CARCINOMA	1
CARCINOID	1
BRONCHIOALVEOLAR CARCINOMA	1
INFLAMMATORYMYOFIBROBLASTIC TUMOR	1
TOTAL	108

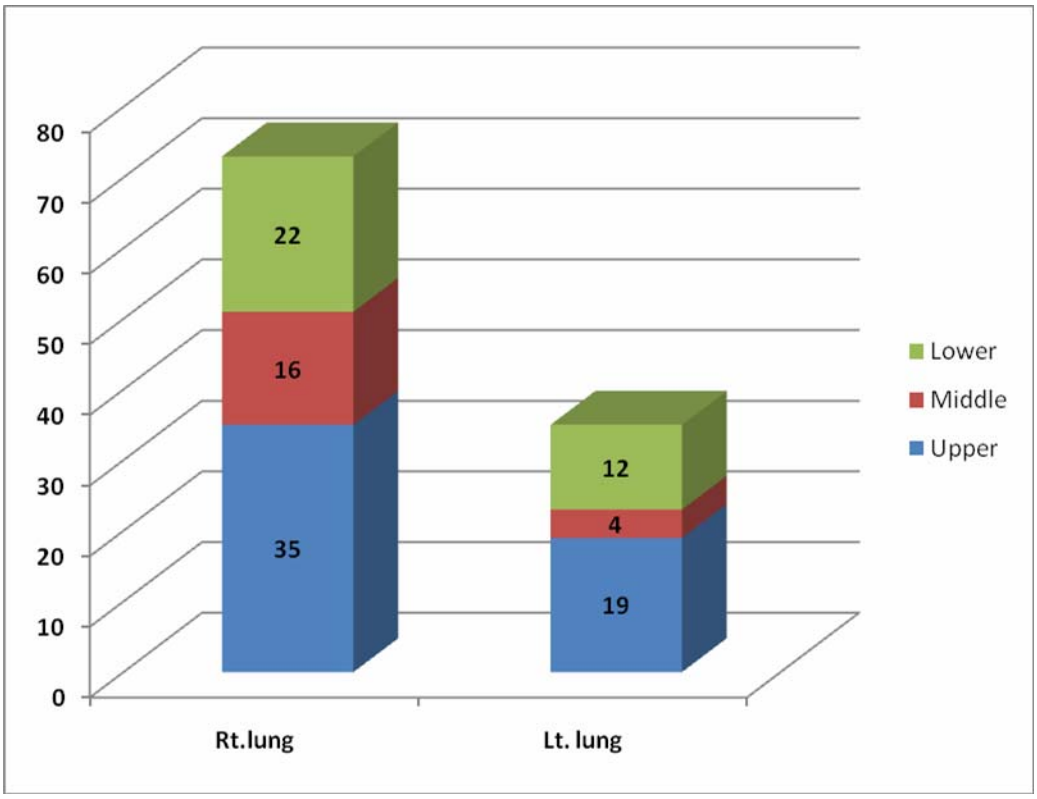


Regarding the site of prevalence of tumors out of 108 cases 73 cases were seen in the right side of the lung(67.5%) and 35 cases in the left side of the lung(32.5%).The lobar distribution was as follows:35 cases in the right upper lobe(32.4%),16 cases in the right middle lobe(15.5%), 22 cases in the right lower lobe(19.8%),19 cases in the left upper

lobe(17.5%),4 cases in the lingual(3.7%) and 12 cases in the left lower lobe(11.1%).

SITE OF PREVALANCE OF LOBES

	Upper	Middle	Lower	TOTAL
Rt.lung	35	16	22	73
Lt. lung	19	4	12	35



The age groups are divided into 4 groups and the 108 neoplastic lesions were analyzed with respect to each decade

GROUP A:	<30yrs
GROUP B:	30-49yrs
GROUP C:	50-69yrs
GROUP D:	>70yrs

GROUP A (<30 years):

In this age group,1 case has been reported(n=1).The case was a male patient aged 13 years and the histopathological diagnosis turned out to be adenocarcinoma..According to Yutaka Mizushima et al, most number of cases occurs in females with a percentage of 62% and adenocarcinoma constitutes the predominant histological type. .

GROUPB (30-49 years):

In this age group of 30 to 49 years,out of 108 cases ,29 cases had been reported(n=29).Total no of males were 19 (n=29) constituting 65% and the female cases were 10(35%).Squamous cell carcinoma constituted 15 cases (52 %), adenocarcinoma constituted 9 cases (31%) and one case each of mucoepidermoid carcinoma, undifferentiated carcinoma, adenosquamous carcinoma, bronchioalveolar carcinoma and inflammatory myofibroblastic tumor was reported(3.4%).According to Yutaka Mizushima, most of the cases occurred in males with a percentage of 61% and the predominant histological type is adenocarcinoma..

GROUPC (50-69 years):

This age group constituted the predominant group where out of 108 cases, 68 cases were seen (63%).Out of 68 cases ,58 cases were males(81.7%) and females numbered 10(19.3%) with male female ratio of 5.8:1.Out of 68 cases ,43 cases were squamous cell carcinoma(63%), adenocarcinoma numbered 17 cases (25%),3 cases of small cell carcinoma(4.4%),2 cases of undifferentiated carcinoma (2.8%) and 1 case each of adenosquamous carcinoma, mucoepidermoid carcinoma ,adenoid cystic carcinoma (1.6%)

According to Mizushima et al, 81 % percentage of cases occurred in males and the predominant histological entity was adenocarcinoma(37%)

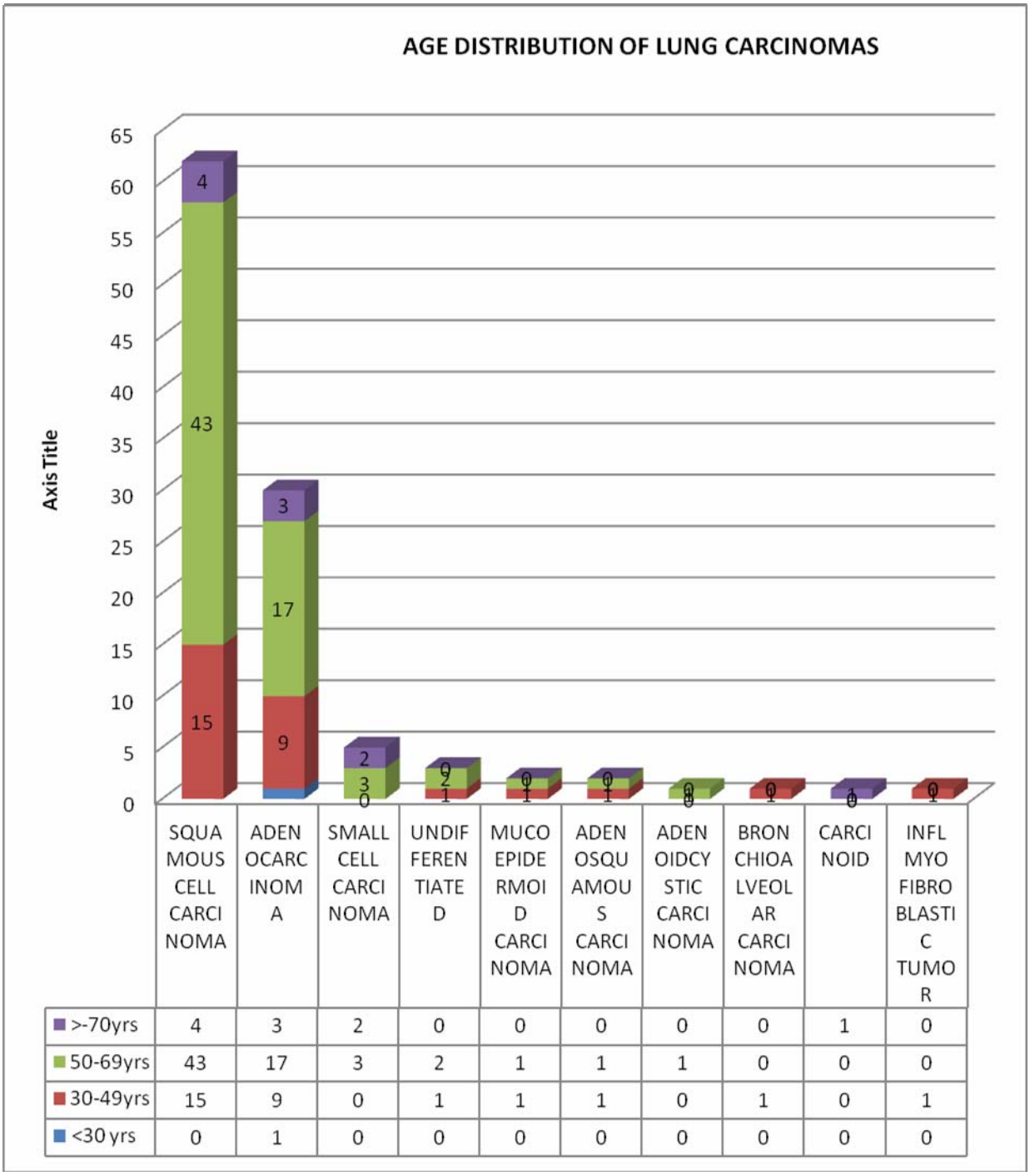
.

GROUP D (>70 years):

In this age group, 10 cases have been reported. Squamous cell carcinoma constituted 4 cases (40%), adenocarcinoma constituted 3 cases (30%) , 2 cases of small cell carcinomas(20%) and 1 case of carcinoid was reported.

AGE DISTRIBUTION OF LUNG CARCINOMAS

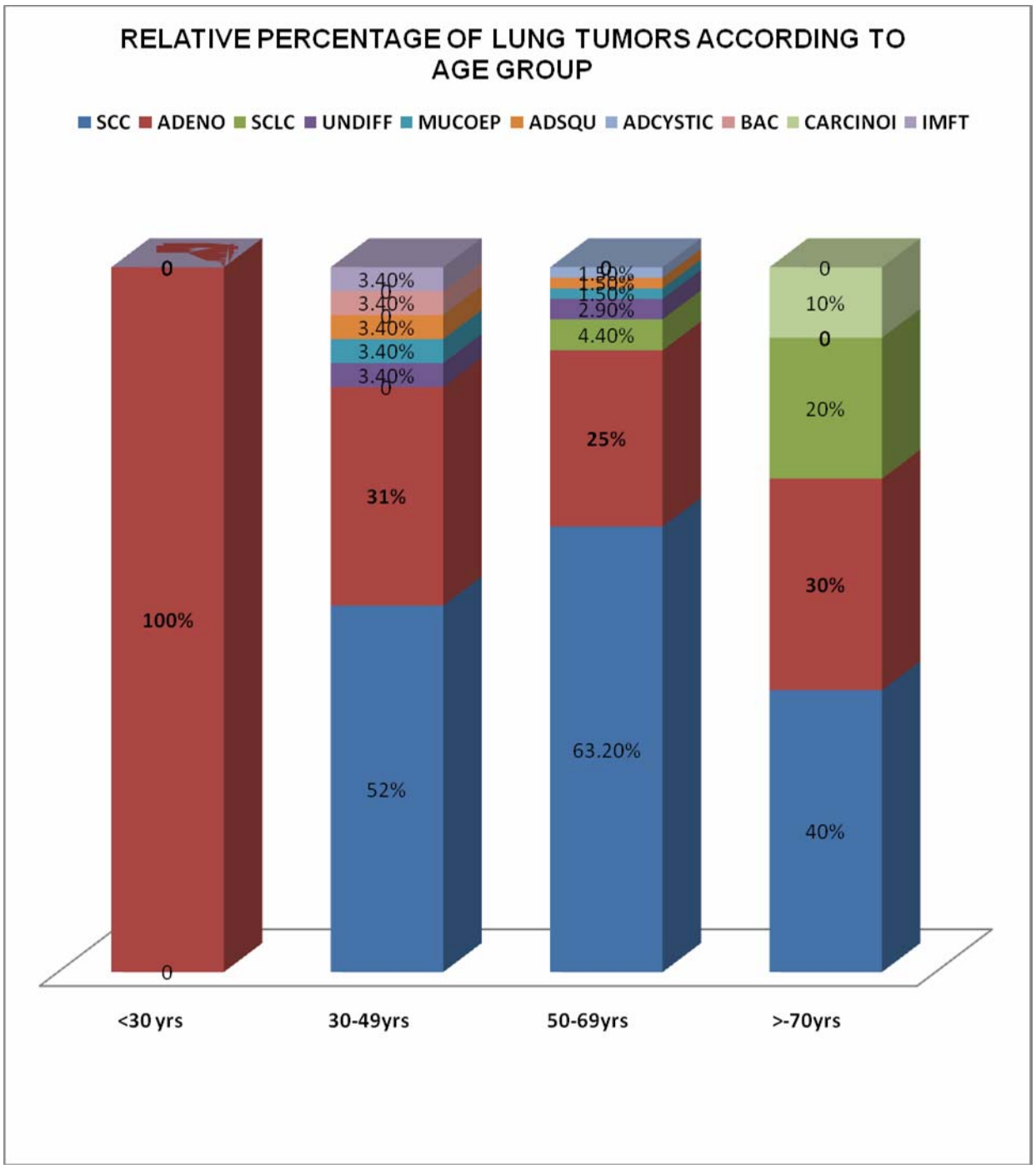
	<30 yrs	30-49yrs	50-69yrs	>-70yrs
SQUAMOUS CELL CARCINOMA	0	15	43	4
ADENOCARCINOMA	1	9	17	3
SMALL CELL CARCINOMA	0	0	3	2
UNDIFFERENTIATED CARCINOMA	0	1	2	0
MUCOEPIDERMOID CARCINOMA	0	1	1	0
ADENOSQUAMOUS CARCINOMA	0	1	1	0
ADENOIDCYSTIC CARCINOMA	0	0	1	0
BRONCHIOALVEOLAR CARCINOMA	0	1	0	0
CARCINOID	0	0	0	1
INFL MYO FIBROBLASTIC TUMOR	0	1	0	0
TOTAL	1	29	68	10



	SQUAMOUS CELL CARCINOMA	ADENOCARCINOMA	SMALL CELL CARCINOMA	UNDIFFERENTIATED	MUCOEPIDERMOID CARCINOMA	ADENOSQUAMOUS CARCINOMA	ADENOIDCYSTIC CARCINOMA	BRONCHIOALVEOLAR CARCINOMA	CARCINOID	INFLMYOFIBROBLASTIC TUMOR
>-70yrs	4	3	2	0	0	0	0	0	1	0
50-69yrs	43	17	3	2	1	1	1	0	0	0
30-49yrs	15	9	0	1	1	1	0	1	0	1
<30 yrs	0	1	0	0	0	0	0	0	0	0

RELATIVE PERCENTAGE OF LUNG TUMORS ACCORDING TO AGE GROUP

	<30 YRS	30-49 YRS	50-69 YRS	>70 YRS
SQUAMOUS CELL CARCINOMA	0%	52%	63.20%	40%
ADENOCARCINOMA	100%	31%	25%	30%
SMALL CELL CARCINOMA	0%	0%	4.40%	20%
UNDIFFERENTIATED CARCINOMA	0%	3.40%	2.90%	0%
MUCOEPIDERMOID CARCINOMA	0%	3.40%	1.50%	0%
ADENOSQUAMOUS CARCINOMA	0%	3.40%	1.50%	0%
ADENOIDCYSTIC CARCINOMA	0%	0%	1.50%	0%
BRONCHIOALVEOLAR CARCINOMA	0%	3.40%	0%	0%
CARCINOID	0%	0%	0%	10%
INFLAMMATORY MYOFIBROBLASTIC TUMOR	0%	3.40%	0%	0%
MALE:FEMALE	1:00	19:10	58:10:00	10:00



SQUAMOUS CELL CARCINOMA:

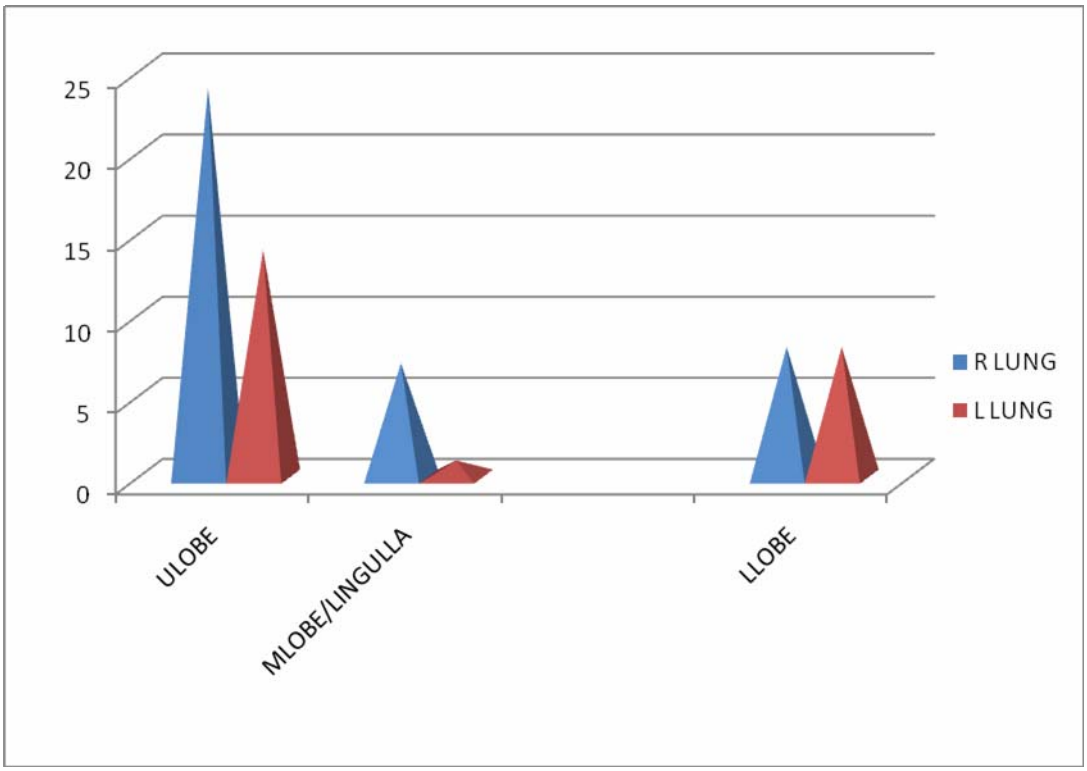
This particular pathological entity constituted the predominant neoplasm in our study .Out of 108 cases 62 cases belonged to this category(57%)showing a male predominance with 60 cases (97.1%).The predominant age group of involvement was 50-69 years (n=68) where 43 cases have been reported constituting 63%..No case was recorded under the age of 30 years. 4 cases were seen above 70 years.

Majority of squamous cell carcinomas were found in the right upper lobe constituting 39%(n=24) followed by 7 cases in the right middle lobe, 8 cases in the right lower lobe, 14 cases in the left upper lobe, 1 case in the lingual and 8 cases in the left lower lobe .This shows the prevalence of squamous cell carcinoma in the upper lobes thus correlating with the literature[3]

Squamous cell carcinoma was diagnosed based on certain features like intercellular bridges and keratin formation. (Figs 1, 2, 3) In the absence of the above features, squamous cell carcinoma can be diagnosed on small biopsies based on the intraepithelial insitu like extension along the bronchus which is not seen in adeno or small cell carcinoma[31].

SITE OF PREVALANCE OF SQUAMOUS CELL CARCINOMA

	Upper LOBE	MiddleLOBE/LINGULA	Lower LOBE
R LUNG	24	7	8
LLUNG	14	1	8

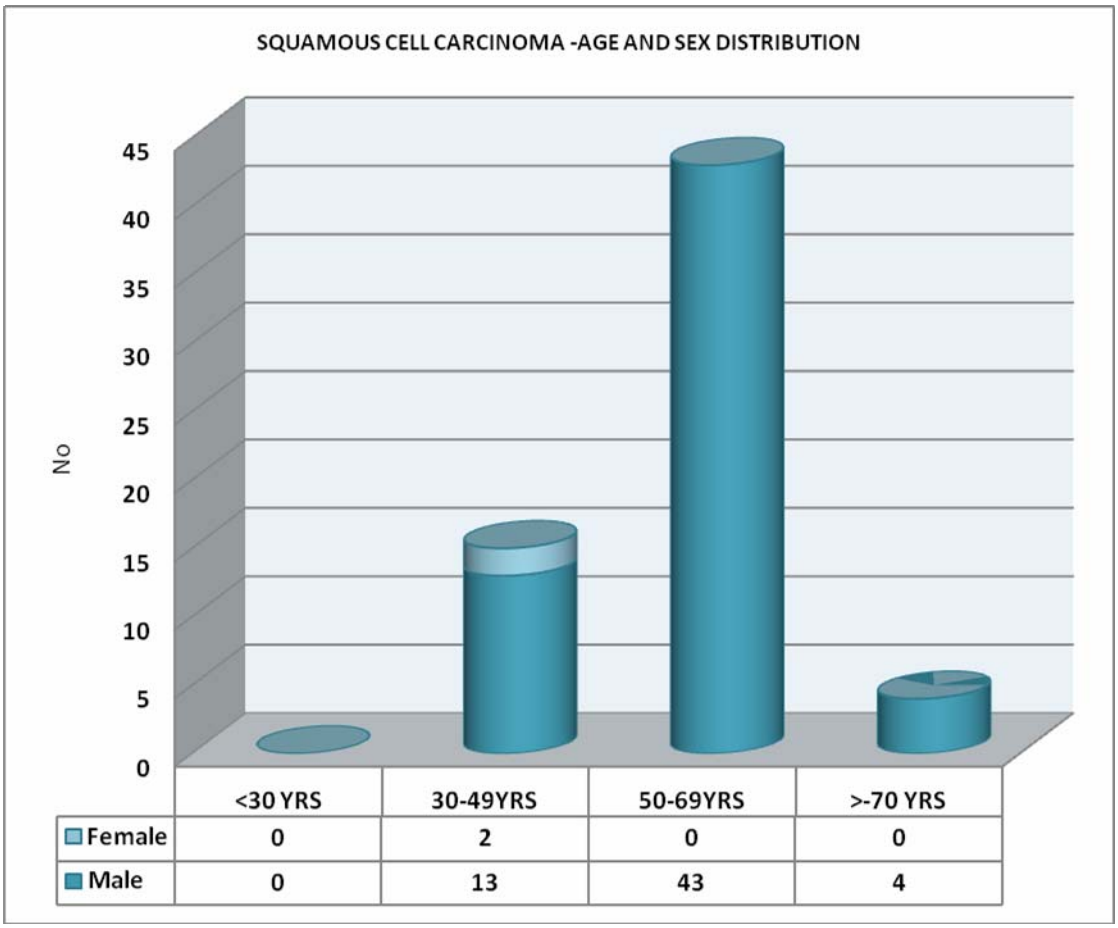


Though all our cases demonstrated keratinisation and intercellular bridges, intraepithelial insitu like extension could not be seen in any of the cases. '

SQUAMOUS CELL CARCINOMA –AGE AND SEX DISTRIBUTION

	Male	Female	PERCENT
<30 YRS	0	0	0

30-49YRS	13	2	24.1
50-69YRS	43	0	69.6
>-70 YRS	4	0	6.3
TOTAL	60	2	100



ADENOCARCINOMA:

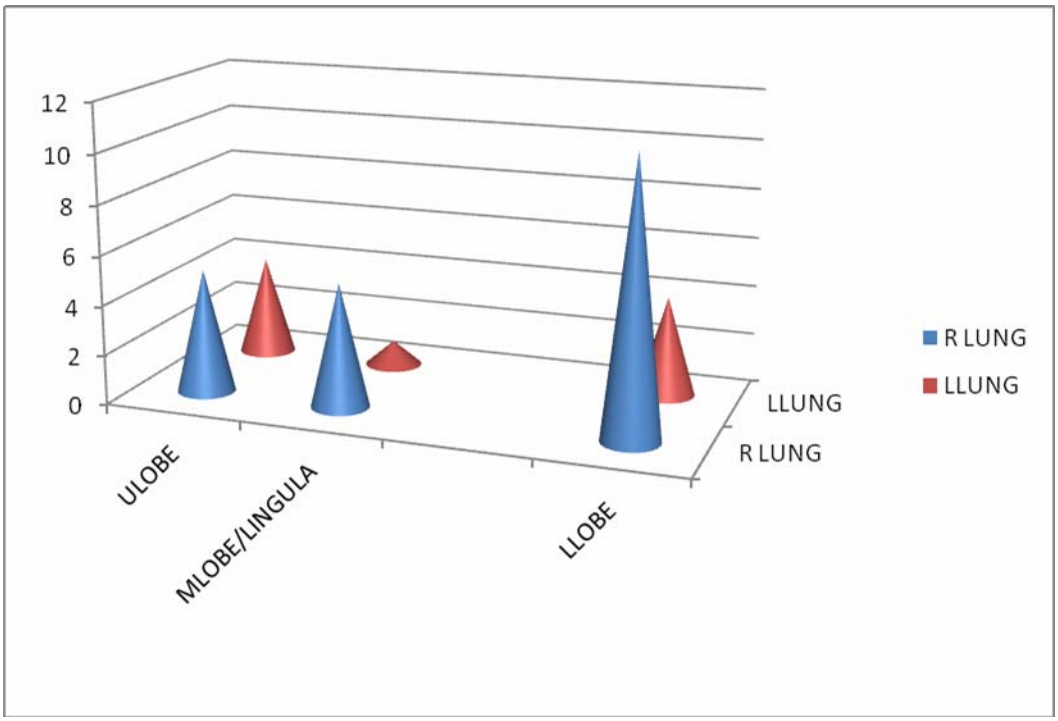
This pathological entity constituted the predominant neoplasm next to squamous cell carcinoma. Out of the total 108 cases, 30 cases belonged to this category.(28%).The predominant age

group was 50-69 years where 17 cases were noted(56.6%).In the age group of 30-49 years , 9 cases were noted. One case was seen under the age of 30 years and 3 cases above 70 years .In our study one case of adenocarcinoma was reported under the age group of 30 years .Out of 30 cases, 17 cases were males (56.6%) and females constituted 13 cases (44.4%).

Majority of adenocarcinomas were found in the right lower lobe(33.3%) followed by 5 cases each in the right middle and lower lobes,1 case in the lingula,and 4 cases each in the left upper and lower lobes.

SITE OF PREVALANCE OF ADENOCARCINOMA

	ULOBE	MLOBE/LINGULA	LLOBE
R LUNG	5	5	11
LLUNG	4	1	4

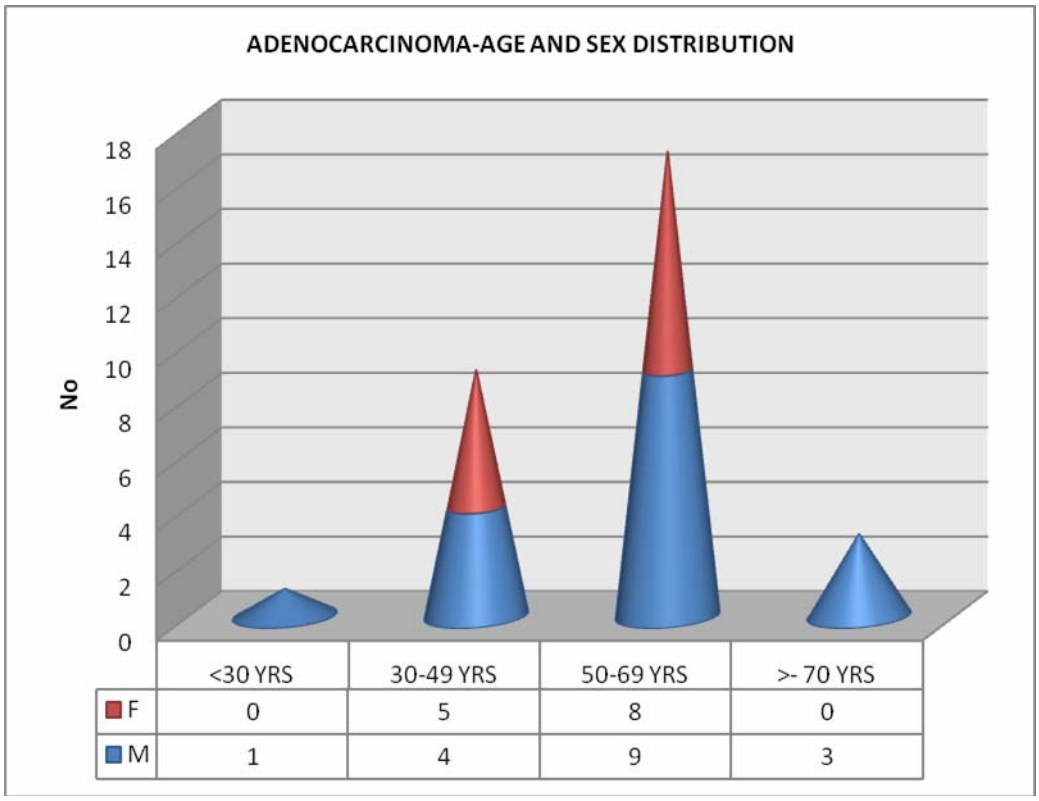


Adenocarcinoma was diagnosed base on the gland formation and mucin production. (Figs 4, 5, 6). The special stain PAS was employed for confirmation of the diagnosis in 18 cases and all of them turned out to be PAS positive.(Figs 7, 8) Cytokeratin7 immunohistochemical stain was positive in a case which did not have mucin formation and glandular differentiation in H and E sections.(Figs 9,10).

ADENOCARCINOMA AGE AND SEX INCIDENCE

	M	F	PERCENT

<30 YRS	1	0	3.3
30-49 YRS	4	5	30
50-69 YRS	9	8	55.6
>- 70 YRS	3	0	11.1
TOTAL	17	13	100



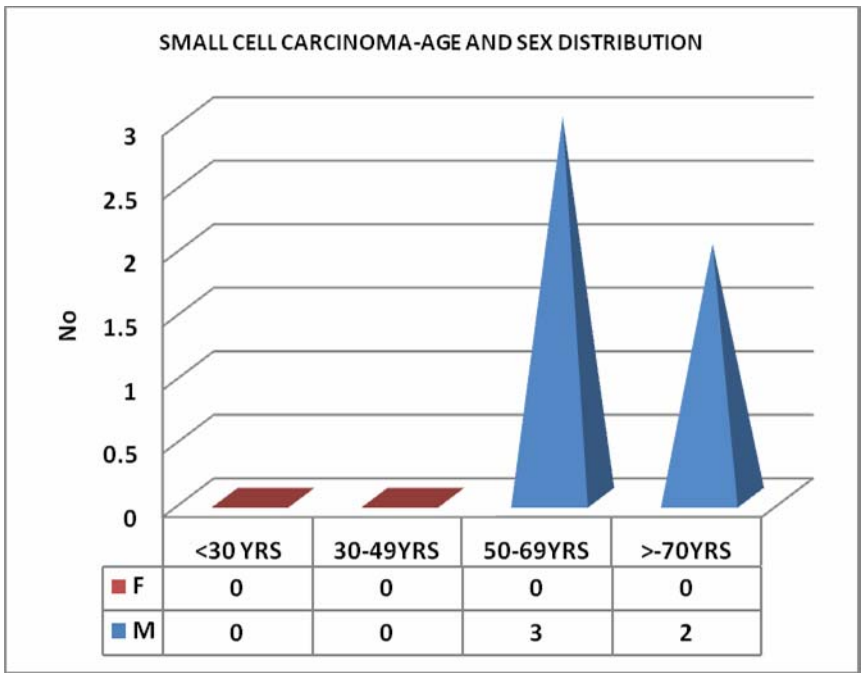
SMALL CELL CARCINOMA:

5 cases of small cell carcinoma were reported constituting 4% of the total cases.All the cases were males. The

predominant age group was 50-69 years where 3cases (60%) were seen and the remaining two cases were found in the age group of >70 years cases. All cases demonstrated histo pathological features like hyper chromatic nucleus, inconspicuous nucleoli and fine stippled chromatin which are the essential diagnostic features of this tumor[1] (Figs 11,12,) and confirmed by application of NSE to a single case.(Figs 13).

SMALL CELL CARCINOMA- AGE AND SEX DISTRIBUTION

	M	F	PERCENT
<30 YRS	0	0	0
30-49YRS	0	0	0
50-69YRS	3	0	60
>-70YRS	2	0	40
TOTAL	5	0	100

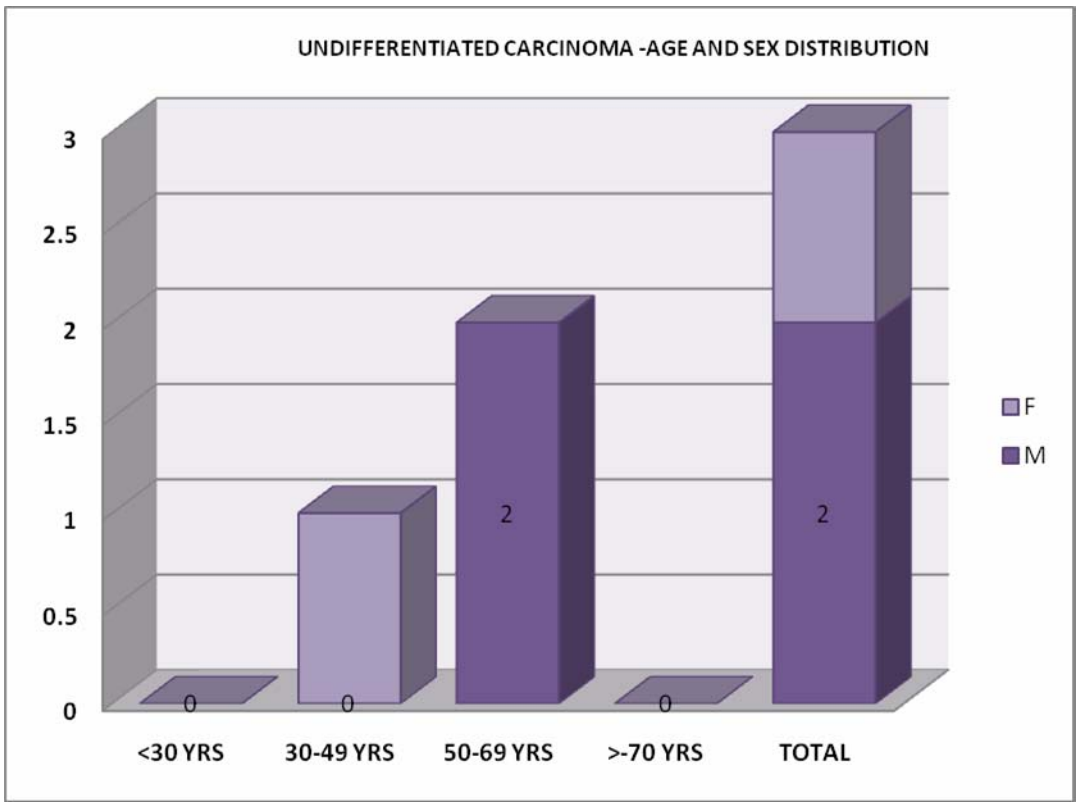


UNDIFFERENTIATED CARCINOMA:

Undifferentiated carcinoma constituted 3 cases (3%) of the total number of cases.2 cases were males and the other was a female.2 cases were found in the age group of 50-69 years and the other case was found in the age group of 30-49 years. Microscopically the cells composed of sheets of undifferentiated cells exhibiting cytological atypia. (Figs 14,15) . Immuno histochemistry of this tumor with a panel of cytokeratins and NSE was done and was found to be negative.

UNDIFFERENTIATED CARCINOMA-AGE AND SEX DISTRIBUTION

	M	F	PERCENT
<30 YRS	0	0	0
30-49 YRS	0	1	33.40%
50-69 YRS	2	0	66.60%
>-70 YRS	0	0	0
TOTAL	2	1	100%



CARCINOID:

One case of carcinoid was reported in a 70 year old male patient. It was found in the right middle lobe. Microscopically the tumor cells are polygonal with uniform round nucleus with fine chromatin and

moderate amount of eosinophilic cytoplasm. (Figs 28, 29).Immunohistochemistry could not be done to this case due to the inadequacy of the material.

ADENOID CYSTIC CARCINOMA:

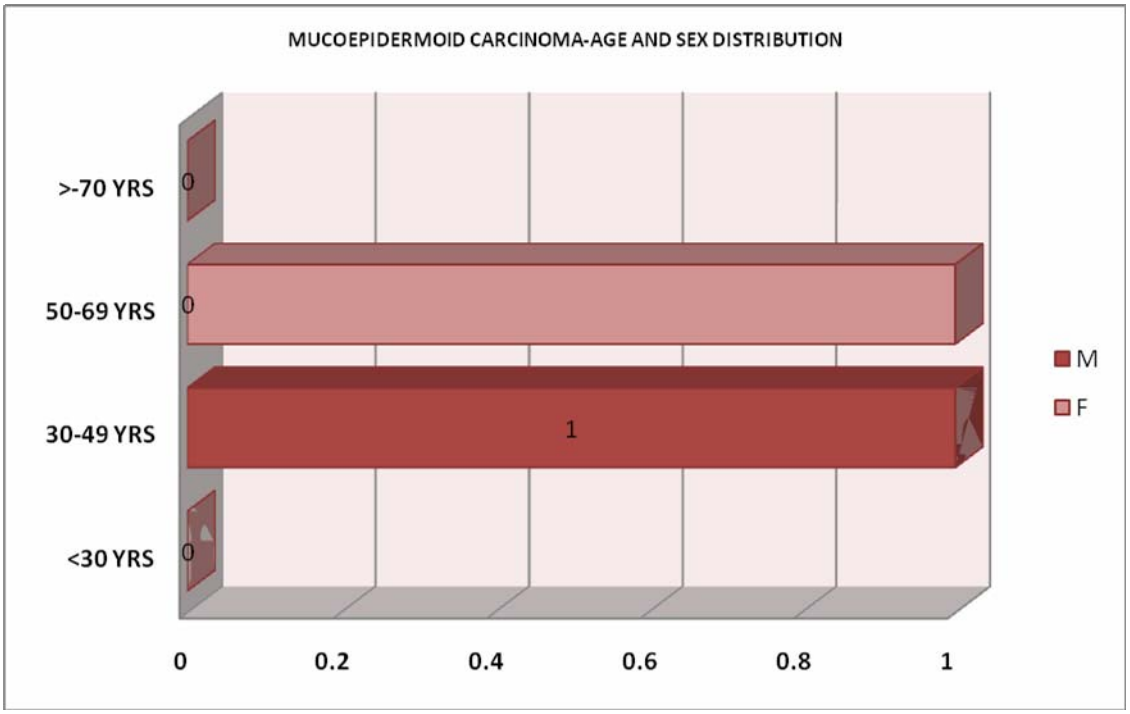
In our study one case of this entity had been reported .He was a 55 year old male patient and it is located in the right lower lobe. According to Hilal Alunoz et al, about 85% of cases occurred in the trachea with only 10 to 15%cases occurred in the periphery and the most common histological pattern is cribriform pattern. In our study, the pattern is cribriform pattern (Figs 23, 24) and confirmed by PAS stain. (Fig 25)

MUCOEPIDERMOID CARCINOMA:

In our study one case of this particular entity has been reported. She is a 47 year old female patient and the lesion is found in the right upper lobe. Microscopically the tumor demonstrated squamoid cells, mucinous cells, intermediate cells and clear cells and confirmed by PAS (Figs 16, 17, 18, 19). According to Xiuli Liu et al, these tumors predominantly occur in children and present with intra luminal bronchial mass with equal sex incidence.

MUCOEPIDERMOID CARCINOMA-AGE AND SEX DISTRIBUTION

	M	F	PERCENT
<30 YRS	0	0	0
30-49 YRS	1	0	50
50-69 YRS	0	1	50
>-70 YRS	0	0	0
TOTAL	1	1	100%



INFLAMMATORY MYOFIBROBLASTIC TUMOR:

In our study, one case of this particular entity had been reported. She was a female patient aged 39

years, presented with a solitary mass in the right middle lobe correlating with Mahale.A et al which stated that this particular tumor occurs more common in young females occurring predominantly as a solitary pulmonary lesion. Microscopically the tumor composed of spindle shaped cells, lymphocytes and plasma cells. (Figs 30,31).

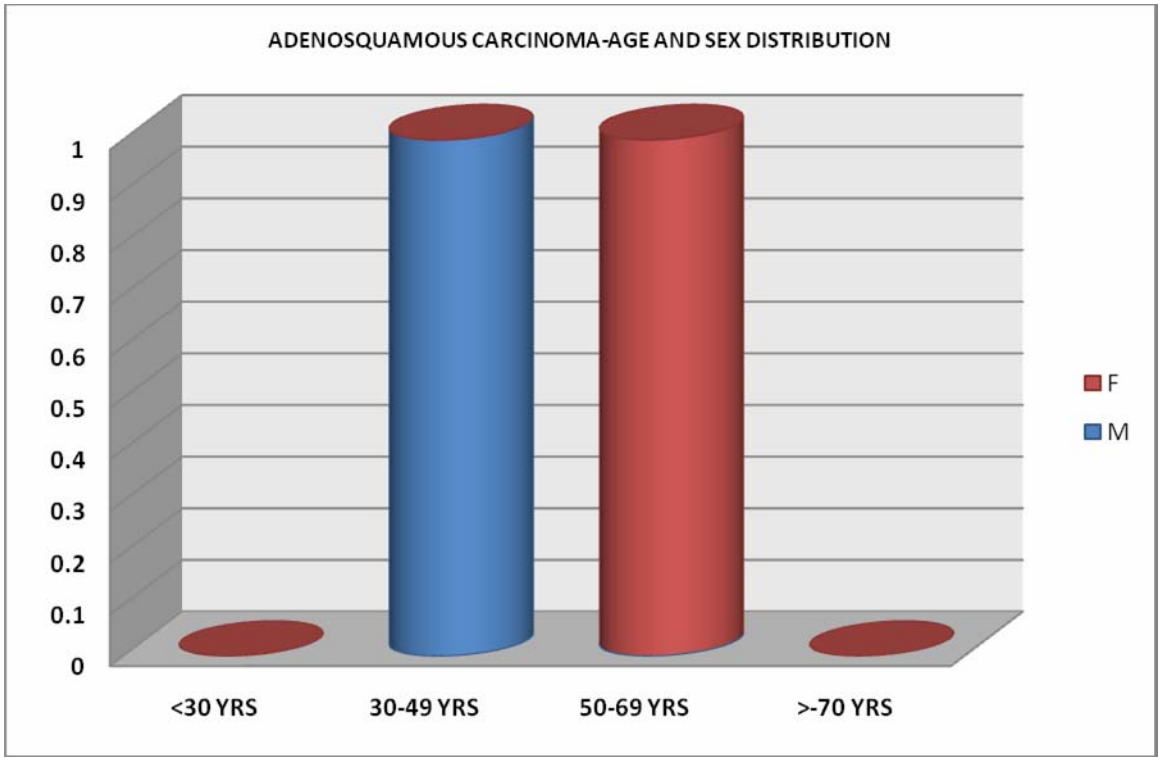
ADENOSQUAMOUS CARCINOMA:

In our study,2 cases of adenosquamous carcinoma had been reported, one being a 49 year old male and the other being a 58 year old lady. Both those cases were found in the right lower lobe .The adenocarcinomatous component composes 20% of the tumor confirmed with PAS stain. (Figs 20,21,22). These features correlated with Shin o Takamari et al who stated that for confirmation of adenosquamous carcinoma required either components accounting more than 10%.

ADENOSQUAMOUS CARCINOMA-AGE AND SEX DISTRIBUTION

	M	F	PERCENT
<30 YRS	0	0	0

30-49 YRS	1	0	50
50-69 YRS	0	1	50
>-70 YRS	0	0	0
TOTAL	1	1	100



BRONCHIOALVEOLAR CARCINOMA:

In our study, one case of bronchioalveolar carcinoma was reported in a 39 year old lady who presented with a solitary mass in the lingual. Microscopically it was composed of columnar to

cuboidal cells with mild nuclear atypia with no invasion of the surrounding stroma (Figs 26, 27) thus correlating with the literature.[13]

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SUMMARY AND CONCLUSION

This study takes into account, the available data ie,age, sex, site of involvement, histomorphological features, special stains and immunochemical methods in arriving at the following observations.

1) Out of 140 cases, 77% of cases were adequate biopsies and 23% were inadequate as far as diagnosis was concerned.
2) Regarding the age group, predominant number of cases was found in 50-69 years with the frequency of 63%.

3) Males were the predominant sex involved with the male female ratio of 4.4:1.
4) Regarding the histopathological type, squamous cell carcinoma was the most common over other types with 57%.
5) The site of prevalence of the tumors was found in the right upper lobe in 32.4% of cases. Squamous cell carcinoma showed a predilection for involving the upper lobes and adenocarcinoma involved the lower lobes.
6) The youngest age of involvement was 13 years and the oldest age was 80 years with the mean of 46.5 years.
7) Rare cases of inflammatory myofibroblastic tumor, adenoidcystic carcinoma and mucoepidermoid carcinoma were documented in our study.
8) Immunohistochemistry is useful in selected cases in arriving at the diagnosis.

To conclude, CT/USG guided core needle biopsy specimens are extremely valuable in the preoperative diagnosis of various histopathological entities especially in differentiating small cell carcinoma (SCLC) from non small cell carcinomas (NSCLCS) as treatment protocol varies between these entities, by strictly adhering to the already proposed histomorphological criteria .

The procedure been properly done and adequate material been obtained, this core needle biopsy sample will be extremely useful in a confident diagnosis thus obviating the need for thoracotomy in most cases.

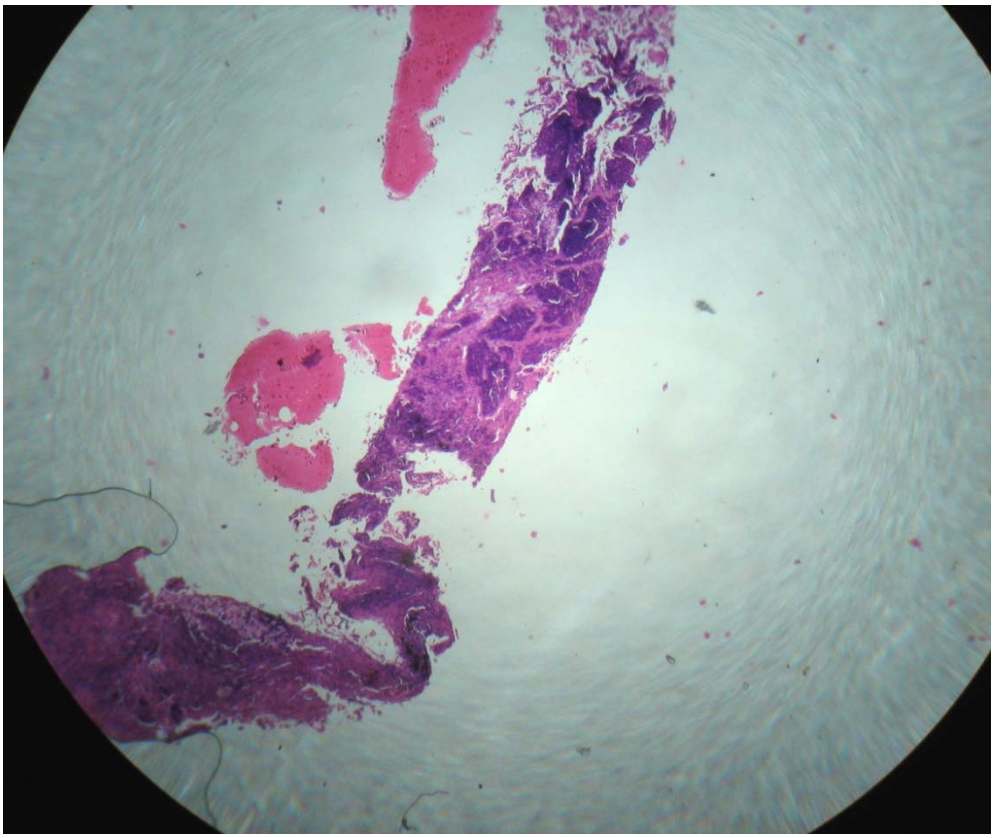

Fig 1 Squamous cell carcinoma –H&E (40 X)

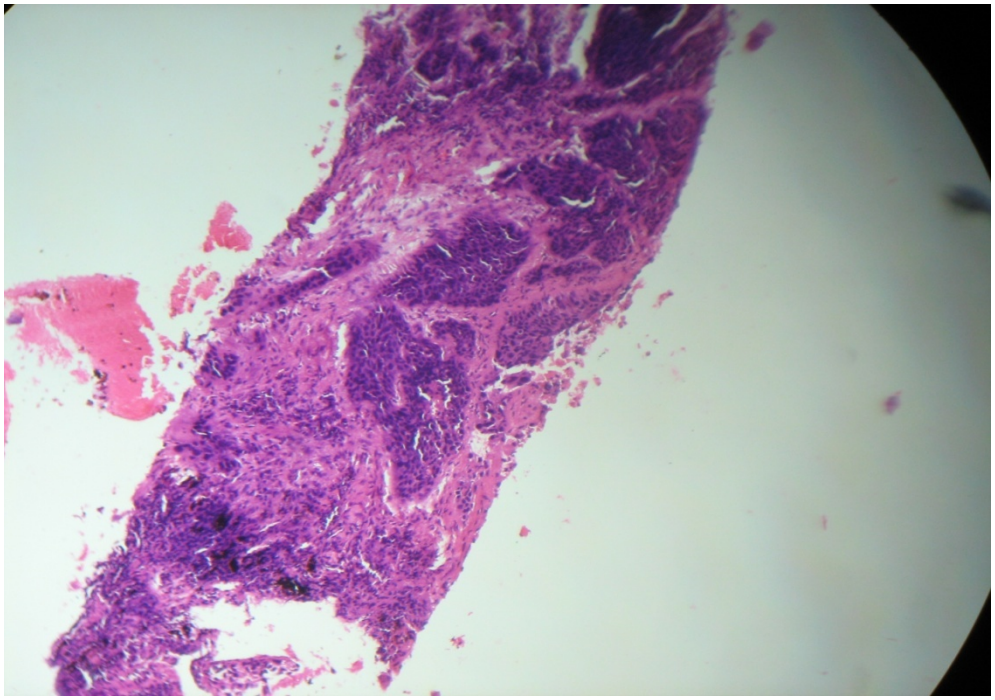

Fig 2 Squamous cell carcinoma-H&E (100X)

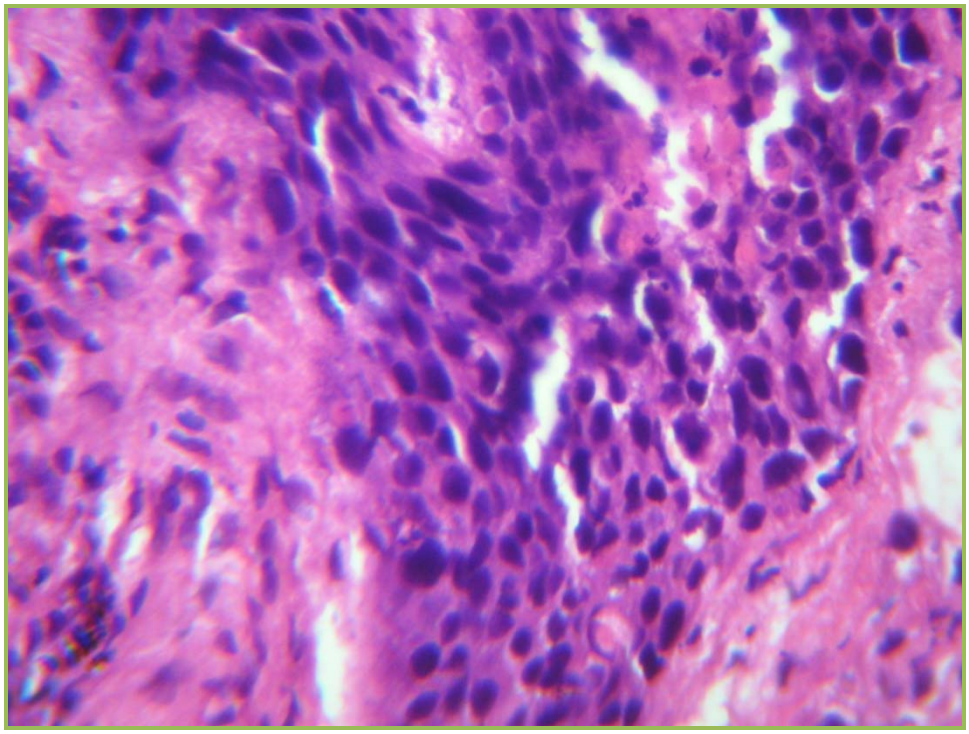

Fig 3 Squamous cell carcinoma –H & E (400 X)

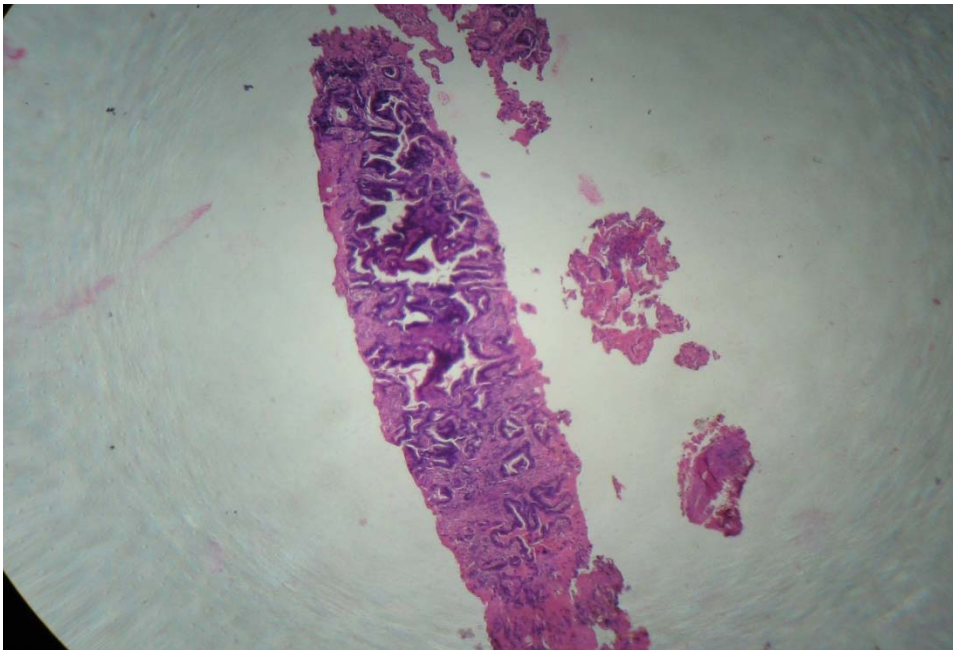

Fig 4 Adenocarcinoma-H&E (40X)

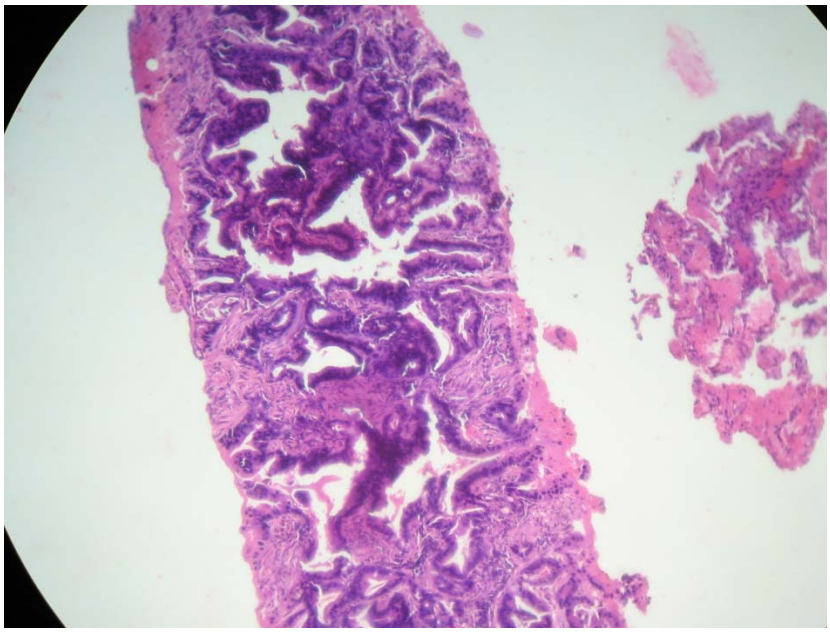

Fig 5:Adenocarcinoma –H&E(100X)

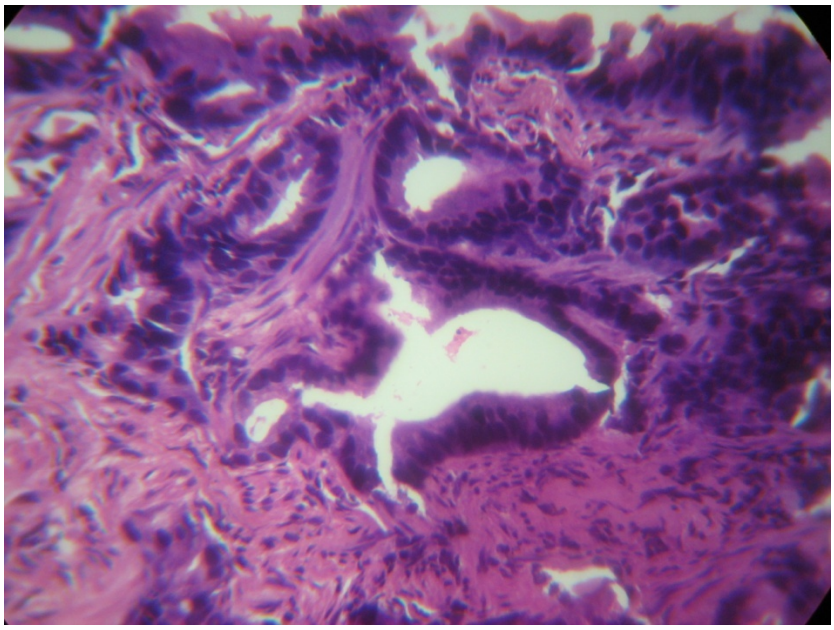

Fig 6:Adenocarcinoma-H&E(400X)

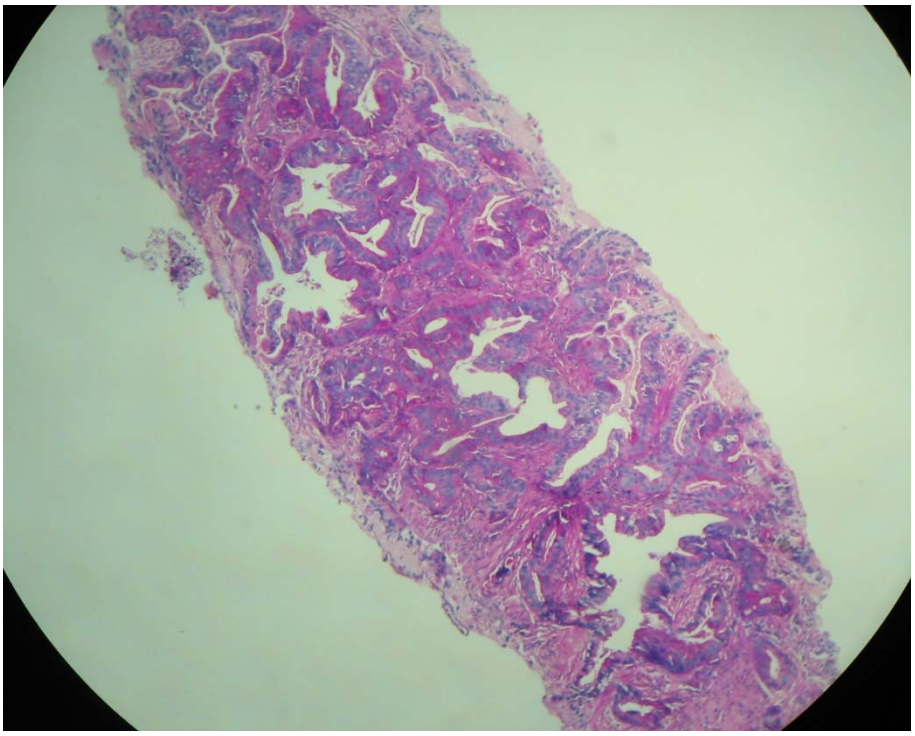

Fig 7 Adenocarcinoma –PAS (100X)

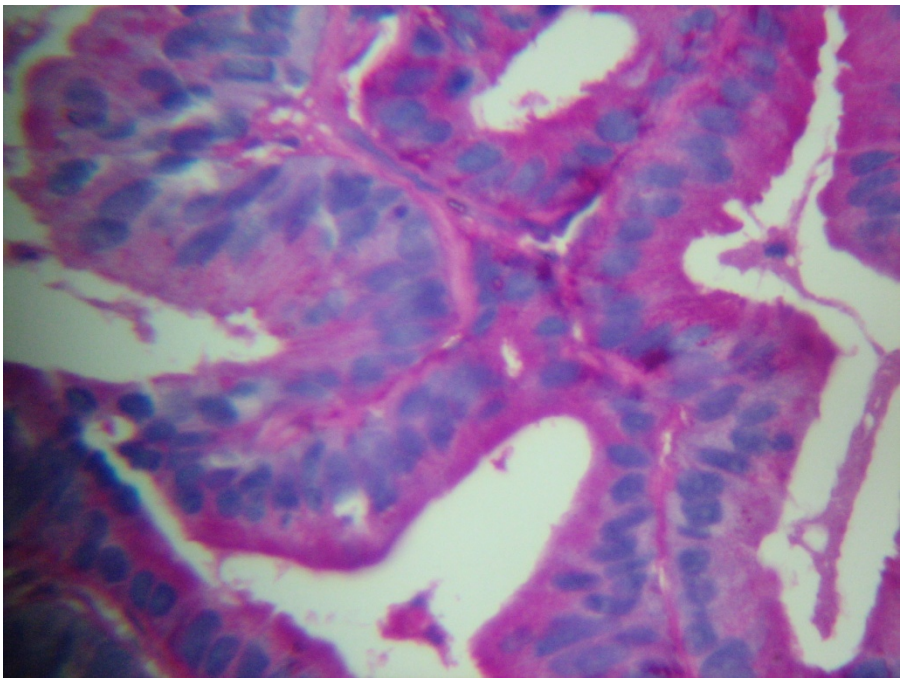

Fig 8 Adenocarcinoma –PAS (400X)

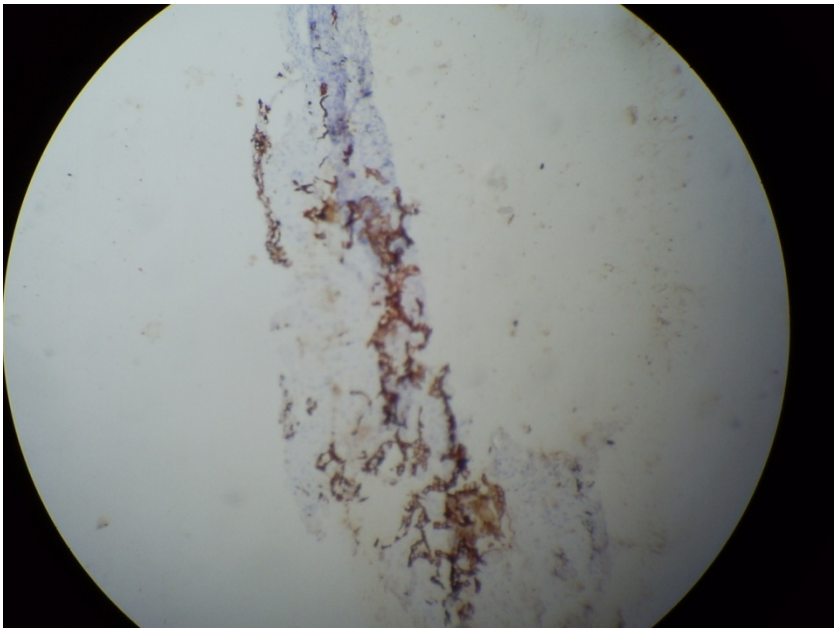

Fig 9:Adenocarcinoma positive for cytokeratin 7(100X)

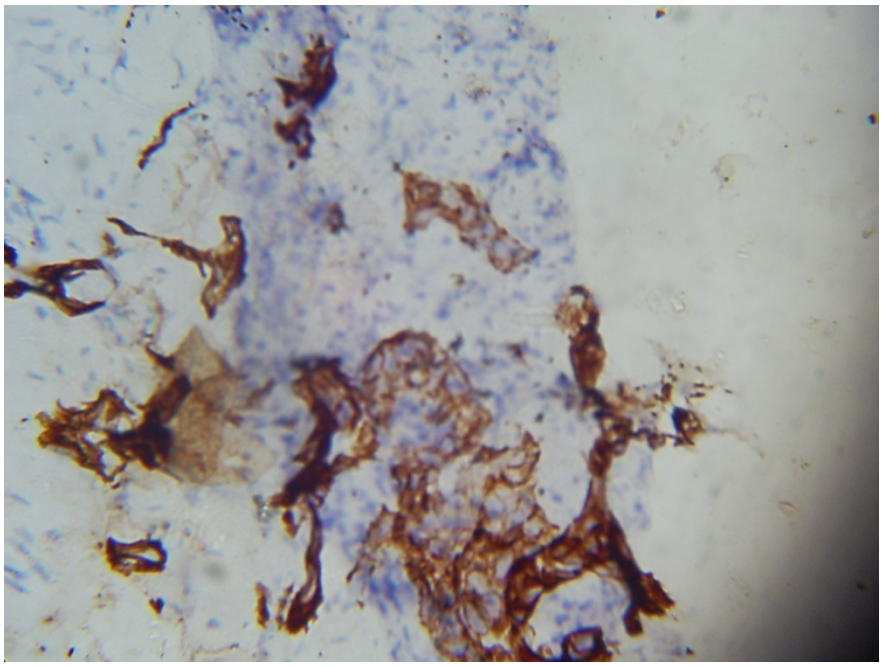

Fig 10:Adenocarcinoma positive for cytokeratin 7(400X)

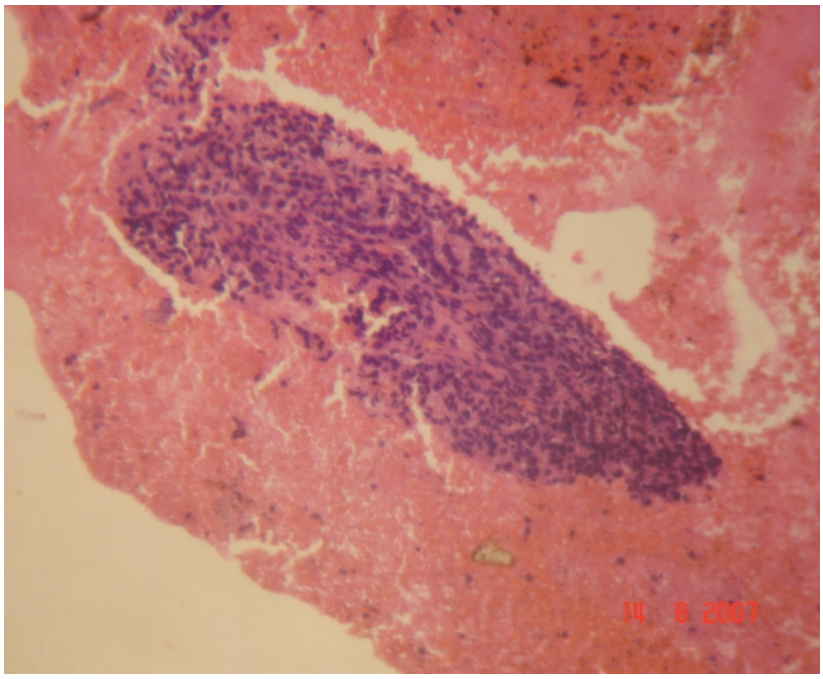

Fig 11-Small cell carcinoma H&E (100X)

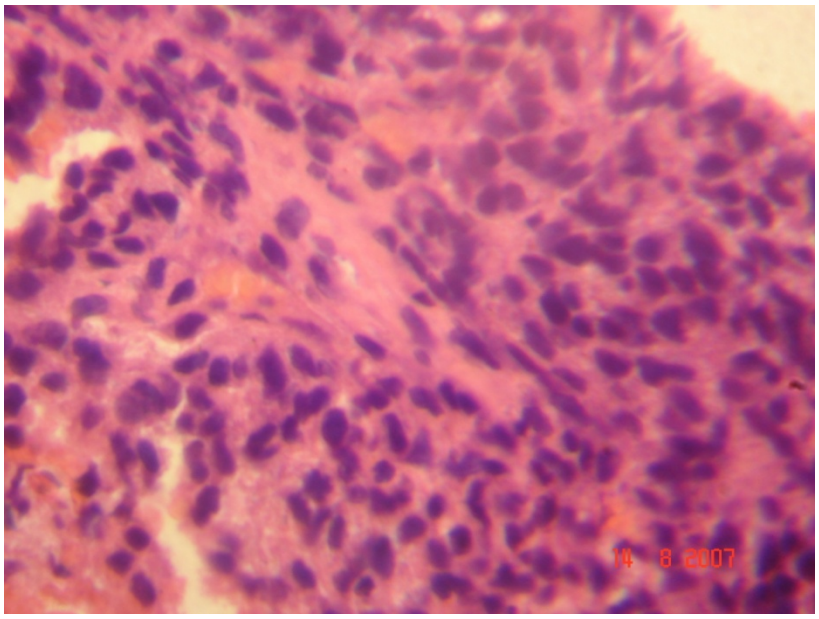

Fig 12-Small cell carcinoma H&E (400X)

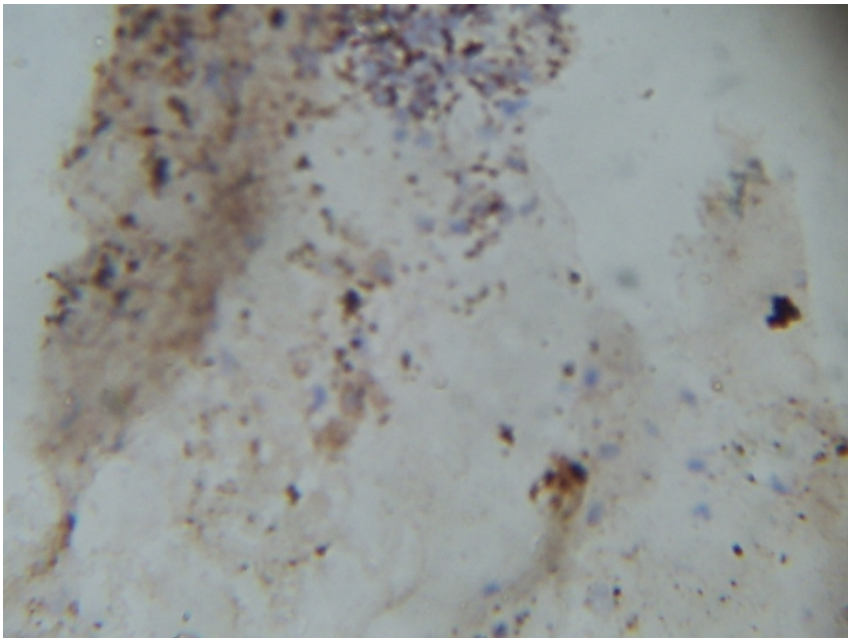

Fig 13: Small cell carcinoma positive for Neuron specific enolase (100x)

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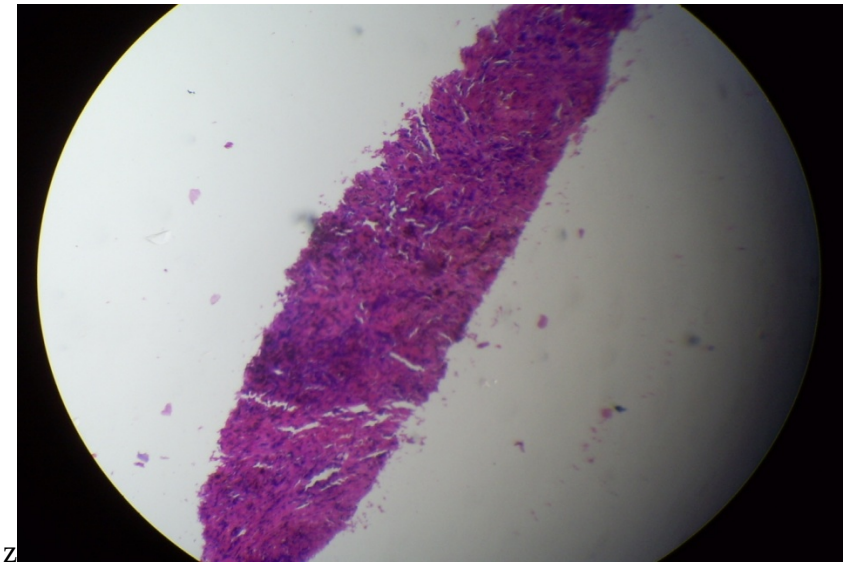


Fig 14: UndifferentiatedH &E(40X)

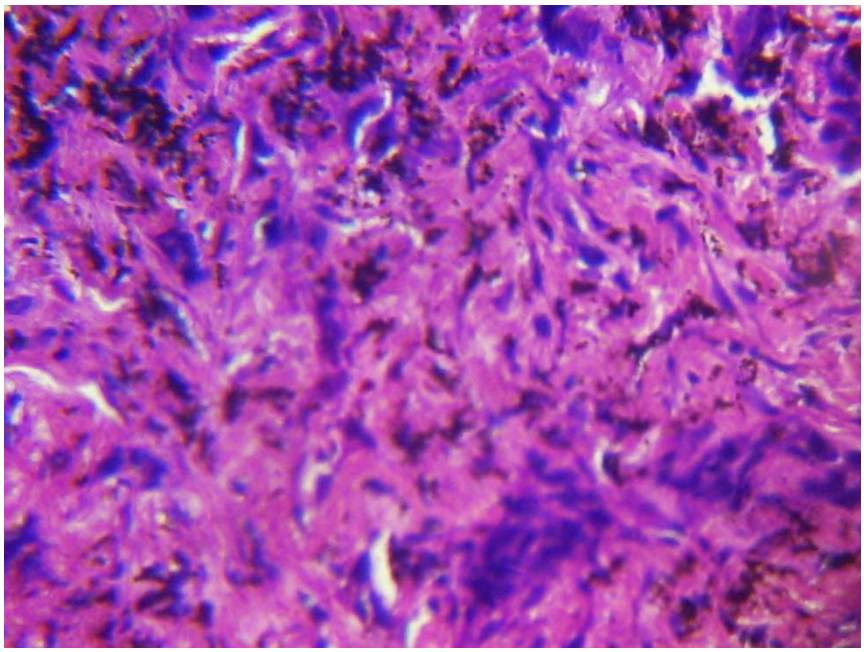


Fig 15: Undifferentiated carcinoma-H&E (400X)

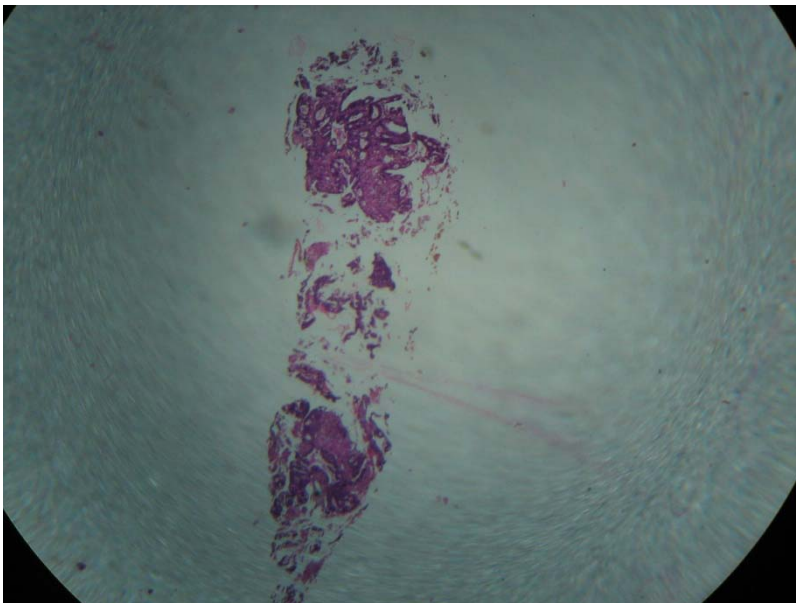


Fig 16:Mucoepidermoid carcinoma-H&E(40X)

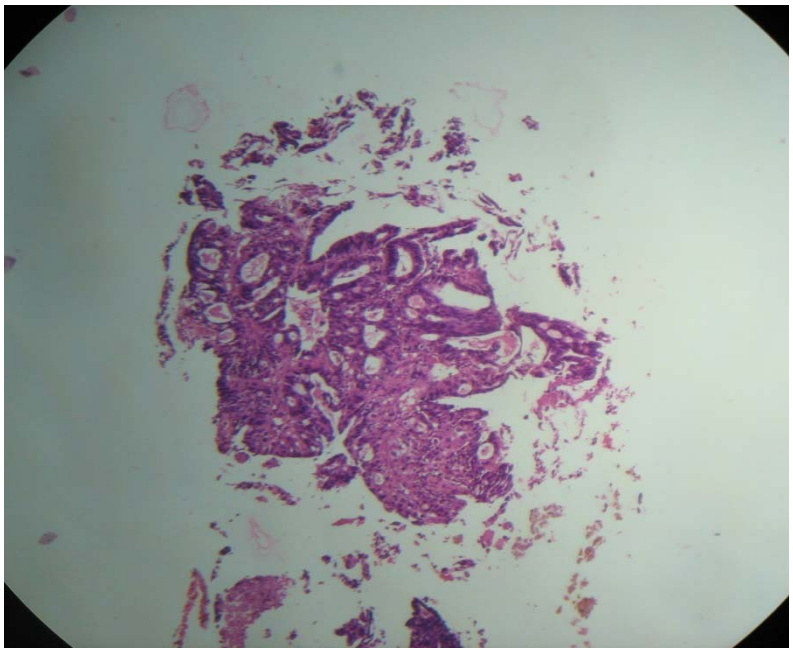


Fig 17:Mucoepidermoid carcinoma –H&E(100X)

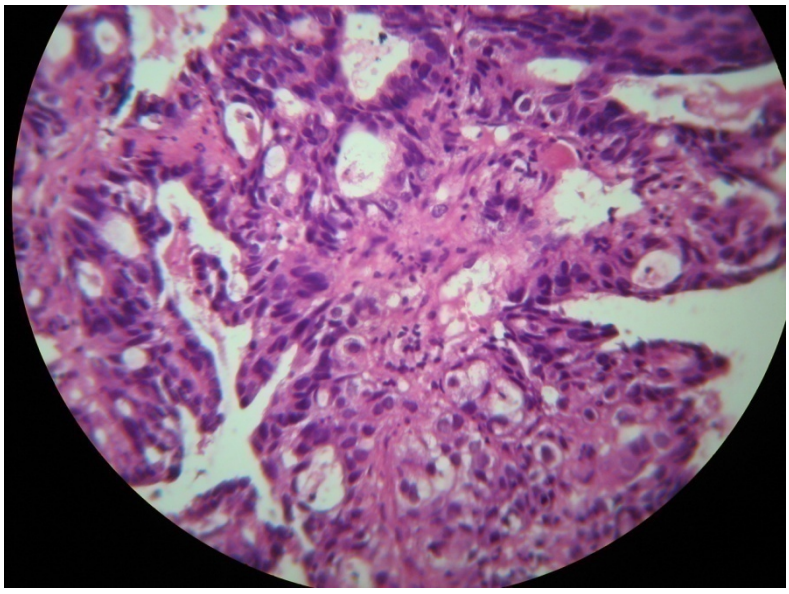


Fig 18:Mucoepidermoid carcinoma-H&E(400X)

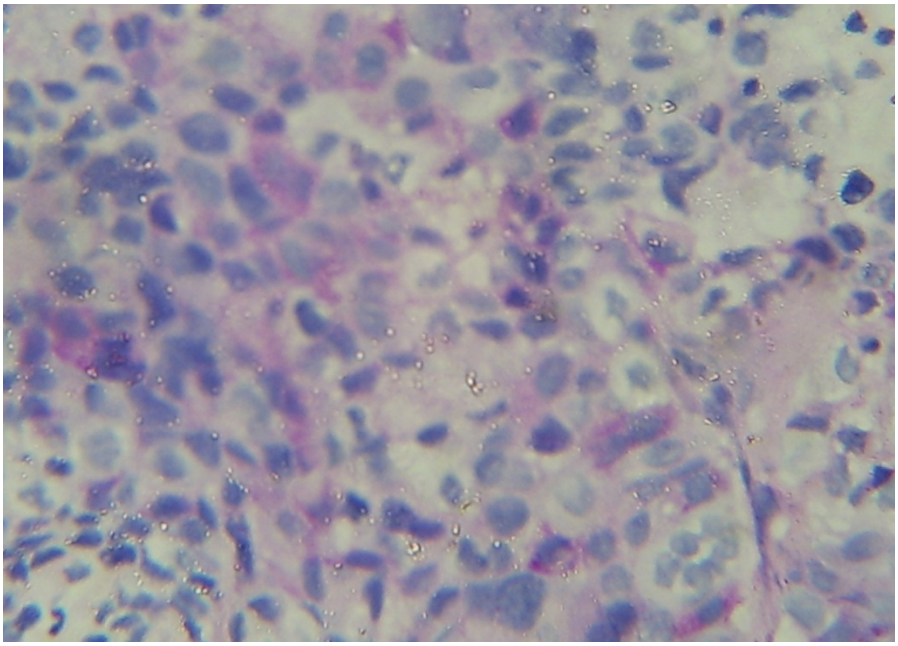


Fig 19:Mucoepidermoid carcinoma-Positive for PAS(400X)

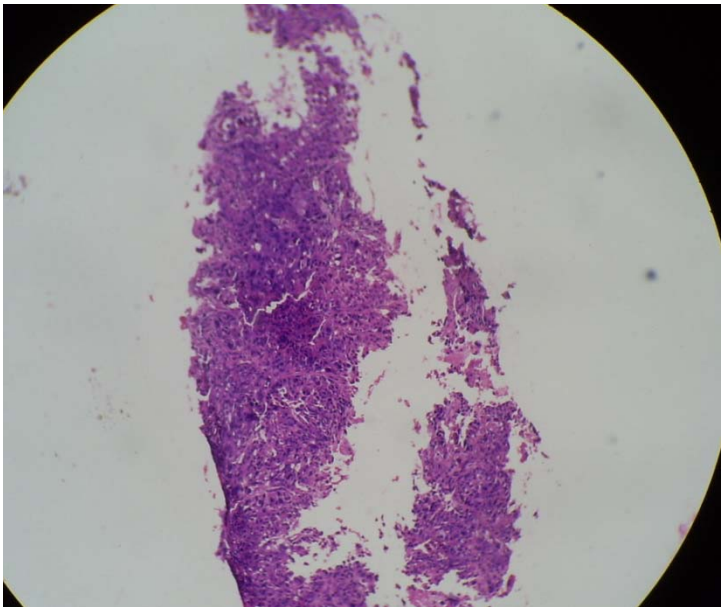


Fig 20:Adenosquamous carcinoma-H&E(100X)

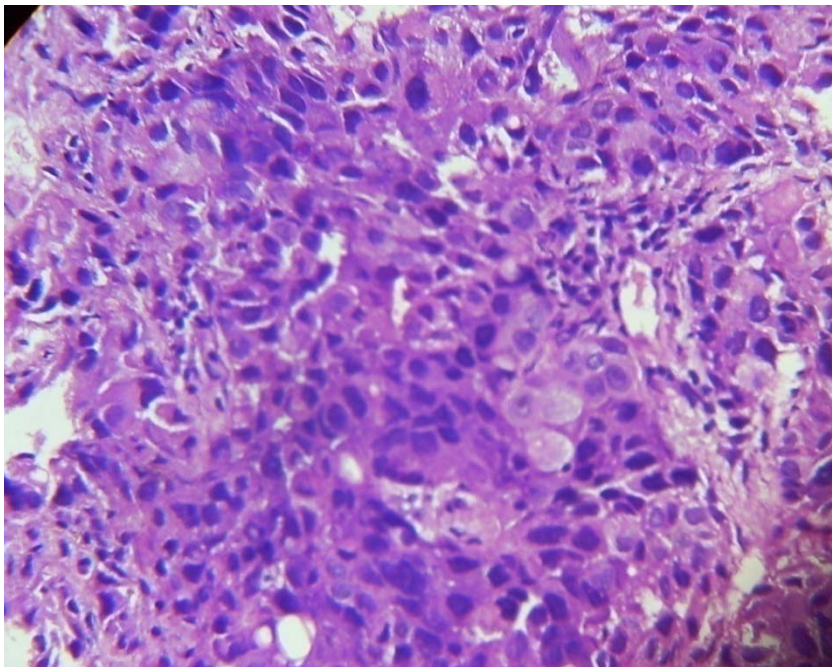


Fig 21:Adenosquamous carcinoma-H&E(400X)

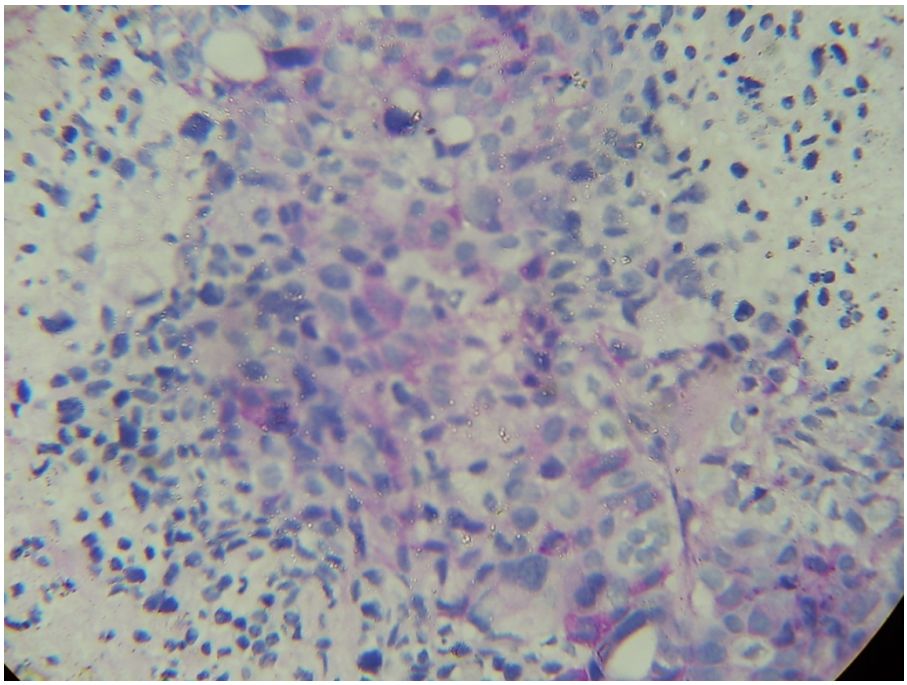


Fig 22:Adenosquamous carcinoma-H&E(400X)

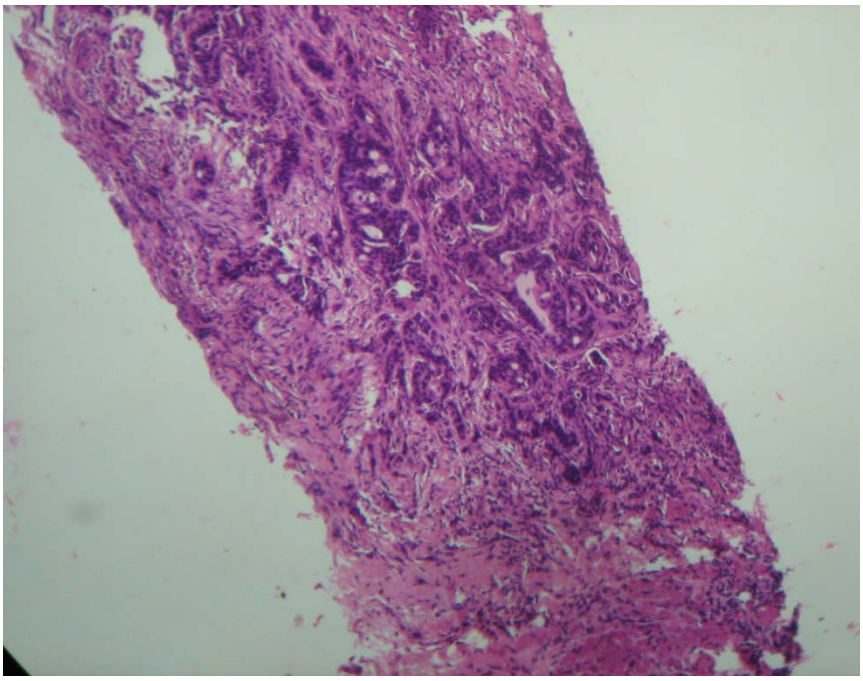


Fig 23:Adenoidcystic carcinoma-H&E(100X)

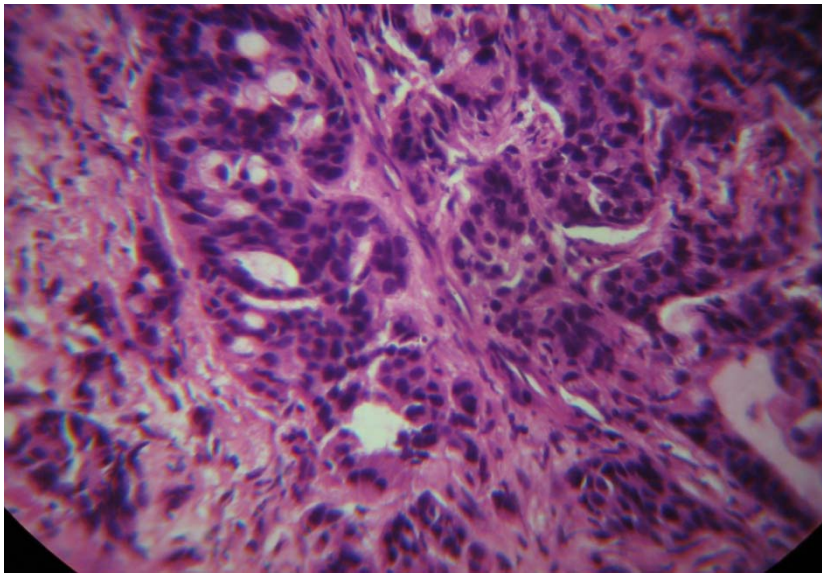


Fig 24:Adenoidcystic carcinoma-H&E(400X)

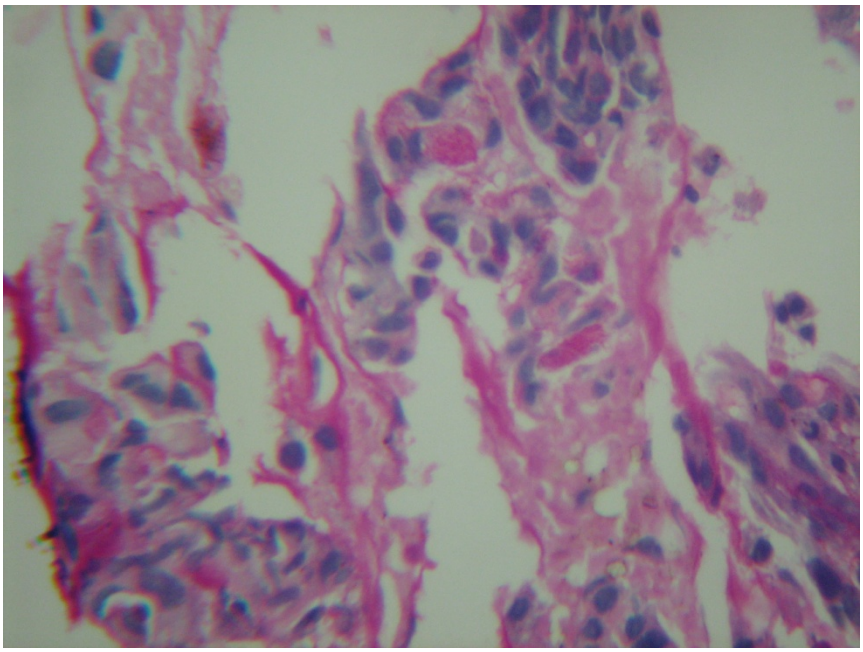


Fig 25:Adenoidcystic carcinoma-Positive for PAS(400X)

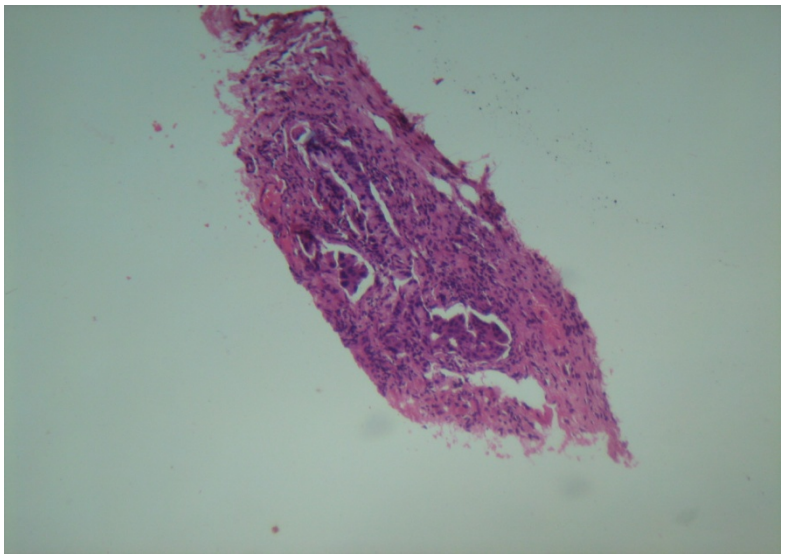


Fig 26:Bronchioalveolar carcinoma-H&E(100X)

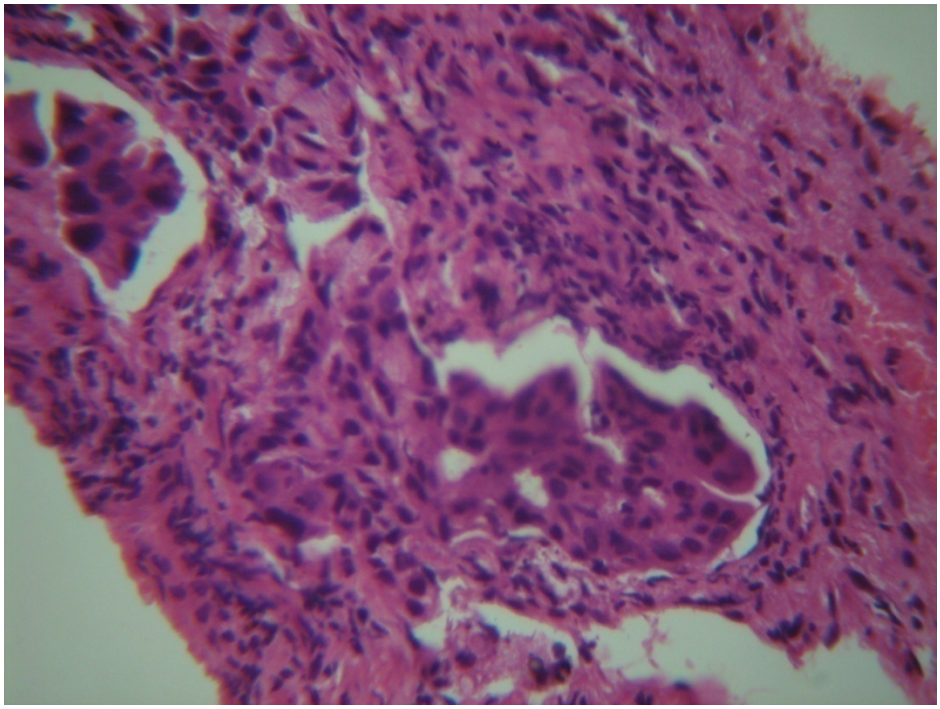


Fig 27: Bronchioalveolar carcinoma-H&E (400X)

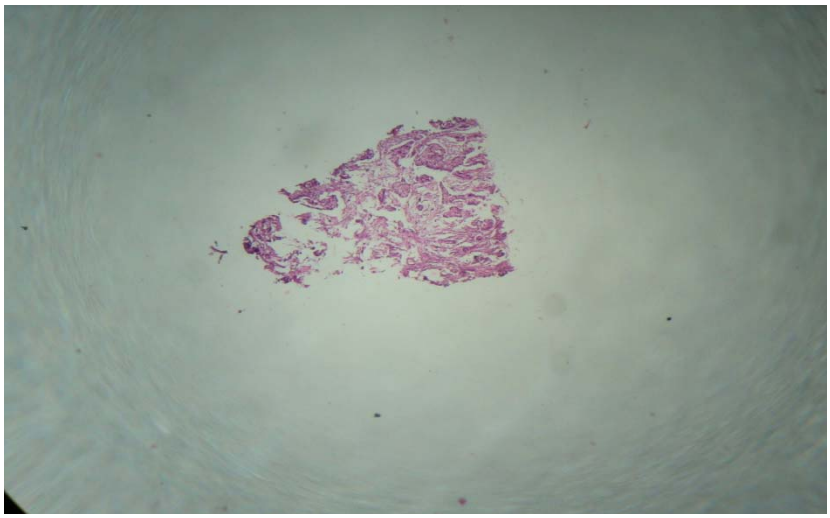


Fig 28: carcinoid –H&E (40X)

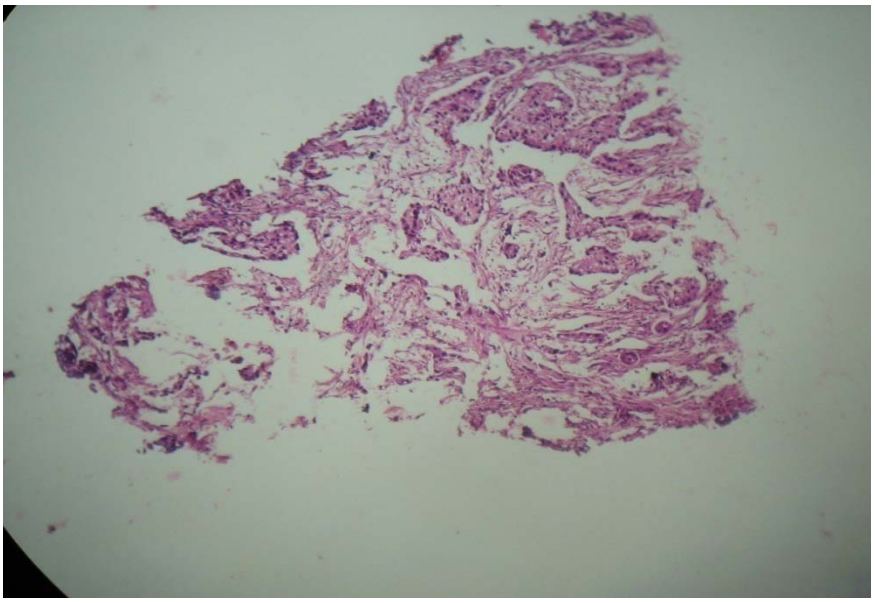


Fig 29: Carcinoid-H&E(100X)

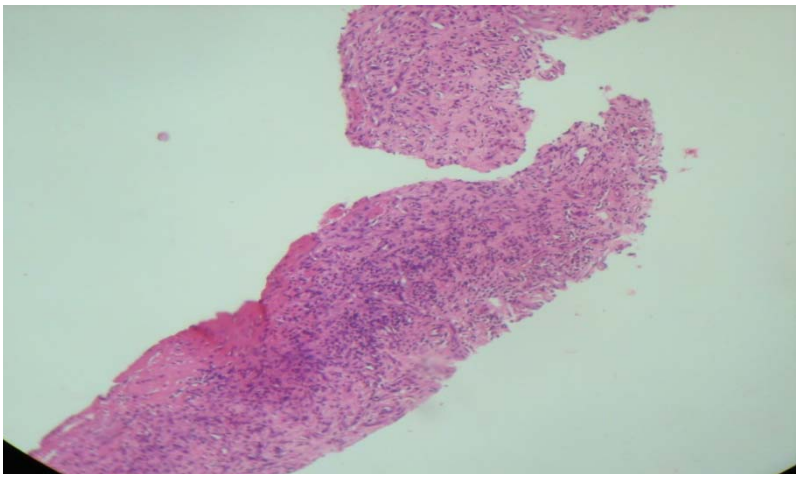


Fig 30: Inflammatory myofibroblastic tumor-H&E(100X)

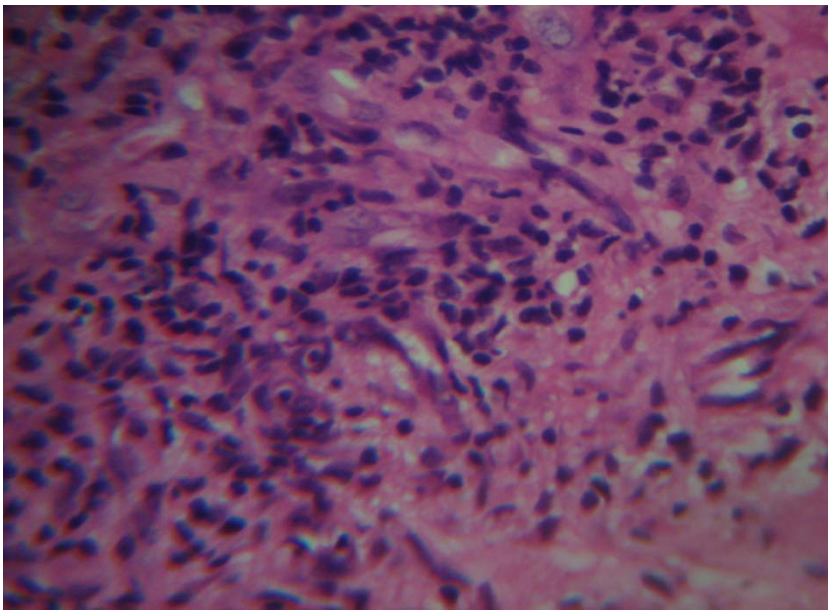


Fig 31: Inflammatory myofibroblastic tumor-H&E(400X)

NONDIAGNOSTIC BIOPSIES

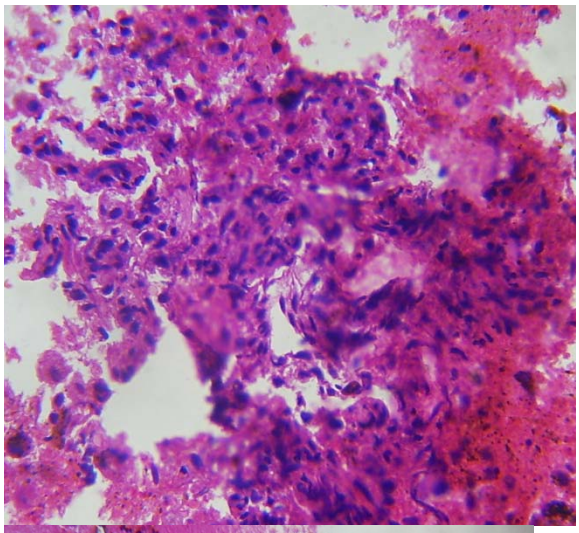


Fig 32 : Inflammation and fibrosis-H&E(100X)

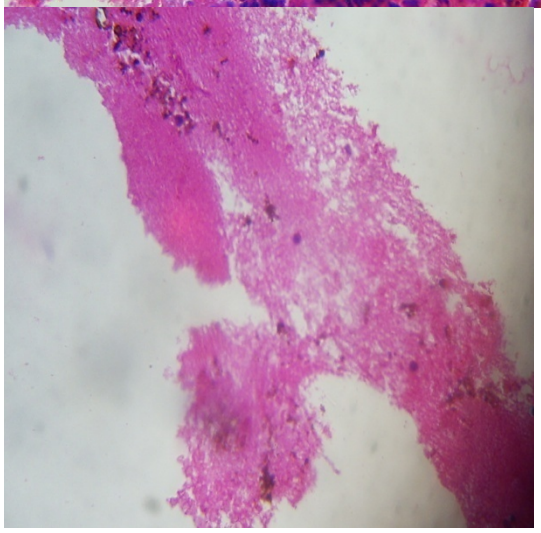
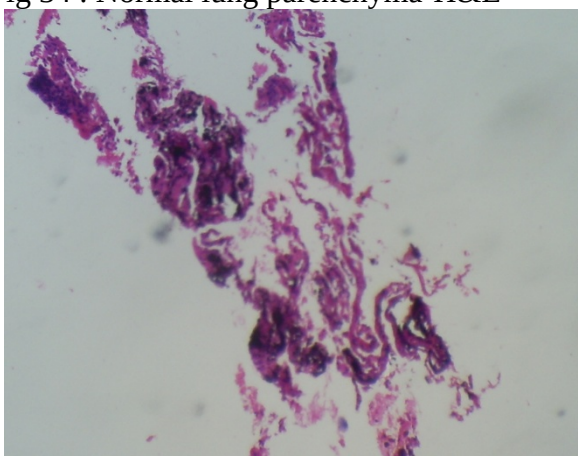


Fig 33 : Necrosis and hemorrhage-H&E(100X)

Fig 34 : Normal lung parenchyma-H&E



(100X)

S.NO	BIOP NO	AGE	SEX	SIDE	LOBE	HISTOPATHOLOGICAL DIAGNOSIS
1	27/05	67	M	L	UL	NONDIAGNOSTIC
2	45/05	60	M	R	UL	SMALL CELL CARCINOMA
3	57/05	62	M	L	LL	SQUAMOUS CELL CARCINOMA
4	144/05	65	M	L	LIN	NONDIAGNOSTIC
5	147/05	53	M	L	UL	SQUAMOUS CELL CARCINOMA
6	157/05	62	M	R	ML	SQUAMOUS CELL CARCINOMA
7	177/05	35	M	L	UL	SQUAMOUS CELL CARCINOMA
8	434/05	39	F	R	ML	INFLAMMATORY MYOFIBROBLASTTUMOR
9	550/05	72	M	R	ML	SMALL CELL CARCINOMA
10	658/05	42	M	R	UL	SQUAMOUS CELL CARCINOMA
11	1059/05	69	M	R	UL	SQUAMOUS CELL CARCINOMA
12	1114/05	60	M	R	UL	SQUAMOUS CELL CARCINOMA
13	1162/05	56	M	L	UL	ADENOCARCINOMA
14	1174/05	64	M	L	UL	ADENOCARCINOMA
15	1189/05	41	M	L	UL	SQUAMOUS CELL CARCINOMA
16	1218/05	53	M	L	UL	SQUAMOUS CELL CARCINOMA
17	1306/05	56	M	L	LL	SQUAMOUS CELL CARCINOMA
18	1416/05	55	M	R	UL	NONDIAGNOSTIC
19	1442/05	60	F	R	UL	ADENOCARCINOMA
20	1460/05	53	M	L	UL	NONDIAGNOSTIC
21	1520/05	55	M	L	LL	SQUAMOUS CELL CARCINOMA
22	1549/05	65	M	L	UL	SQUAMOUS CELL CARCINOMA
23	1757/05	60	M	L	UL	SQUAMOUS CELL CARCINOMA
24	1771/05	56	M	R	LL	SQUAMOUS CELL CARCINOMA
25	1779/05	58	M	R	UL	SQUAMOUS CELL CARCINOMA
26	1816/05	50	F	R	ML	MUCOEPIDERMOID CARCINOMA
27	2009/05	40	F	R	ML	ADENOCARCINOMA
28	2035/05	30	F	R	UL	NONDIAGNOSTIC
29	2065/05	47	M	L	UL	NONDIAGNOSTIC
30	2187/05	64	M	L	UL	SQUAMOUS CELL CARCINOMA
31	2339/05	70	M	R	ML	SQUAMOUS CELL CARCINOMA
32	2432/05	59	M	L	UL	NONDIAGNOSTIC
33	2507/05	52	M	L	LIN	NONDIAGNOSTIC
34	2546/05	66	F	L	LL	NONDIAGNOSTIC
35	2617/05	35	M	L	UL	NONDIAGNOSTIC
36	2628/05	44	M	R	ML	SQUAMOUS CELL CARCINOMA
37	4864/05	63	M	R	UL	SQUAMOUS CELL CARCINOMA
38	4872/05	73	M	L	UL	ADENOCARCINOMA
39	4901/05	32	M	R	ML	ADENOCARCINOMA

40	4994/05	70	M	L	UL	SQUAMOUS CELL CARCINOMA
41	5058/05	51	M	L	UL	SQUAMOUS CELL CARCINOMA
42	5261/05	62	M	R	UL	SMALL CELL CARCINOMA
43	5345/05	70	M	R	ML	CARCINOID
44	5747/05	46	F	L	UL	SQUAMOUS CELL CARCINOMA
45	5748/05	51	M	R	UL	NONDIAGNOSTIC
46	5789/05	67	M	R	UL	ADENOCARCINOMA
47	5807/05	60	M	L	LL	SQUAMOUS CELL CARCINOMA
48	5986/05	45	M	R	UL	SQUAMOUS CELL CARCINOMA
49	6295/05	55	M	R	ML	SQUAMOUS CELL CARCINOMA
50	6334/05	56	M	R	UL	NONDIAGNOSTIC
51	6463/05	62	M	R	ML	NONDIAGNOSTIC
52	6472/05	57	M	R	UL	SQUAMOUS CELL CARCINOMA
53	6497/05	65	M	R	UL	SQUAMOUS CELL CARCINOMA
54	6518/05	65	M	R	UL	SQUAMOUS CELL CARCINOMA
55	6622/05	60	F	L	UL	NONDIAGNOSTIC
56	6790/05	65	F	L	LL	ADENOCARCINOMA
57	6851/05	54	M	R	UL	SMALL CELL CARCINOMA
58	6911/05	13	M	R	LL	ADENOCARCINOMA
59	6950/05	45	F	R	LL	ADENOCARCINOMA
60	6994/05	66	M	R	LL	NONDIAGNOSTIC
61	64/06	45	M	R	LL	ADENOCARCINOMA
62	218/06	50	M	R	LL	SQUAMOUS CELL CARCINOMA
63	238/06	45	M	L	LL	NONDIAGNOSTIC
64	252/06	53	M	R	LL	SQUAMOUS CELL CARCINOMA
65	254/06	72	M	R	LL	SQUAMOUS CELL CARCINOMA
66	270/06	60	M	R	UL	SQUAMOUS CELL CARCINOMA
67	273/06	57	M	R	UL	NONDIAGNOSTIC
68	301/06	43	M	R	LL	SQUAMOUS CELL CARCINOMA
69	309/06	48	M	R	LL	NONDIAGNOSTIC
70	322/06	65	M	L	LL	NONDIAGNOSTIC
71	339/06	60	M	R	UL	NONDIAGNOSTIC
72	348/06	58	M	L	LL	NONDIAGNOSTIC
73	383/06	59	M	L	UL	SQUAMOUS CELL CARCINOMA
74	392/06	67	M	R	UL	SQUAMOUS CELL CARCINOMA
75	398/06	38	M	L	UL	SQUAMOUS CELL CARCINOMA
76	421/06	67	M	R	LL	SQUAMOUS CELL CARCINOMA
77	434/06	55	M	R	LL	ADENOIDCYSTIC CARCINOMA
78	477/06	45	M	L	LL	SQUAMOUS CELL CARCINOMA
79	499/06	58	F	R	UL	NONDIAGNOSTIC
80	542/06	48	F	R	LL	ADENOCARCINOMA

81	55O/06	60	M	R	LL	NONDIAGNOSTIC
82	558/06	60	M	R	LL	NONDIAGNOSTIC
83	592/06	52	M	R	LL	UNDIFFERENTIATED CARCINOMA
84	661/06	69	M	R	LL	NONDIAGNOSTIC
85	689/06	49	M	R	LL	ADENOSQUAMOUS CARCINOMA
86	731/06	60	M	L	LL	ADENOCARCINOMA
87	744/06	53	M	R	UL	NONDIAGNOSTIC
88	819/06	58	F	R	LL	ADENOSQUAMOUS CARCINOMA
89	876/06	60	M	R	LL	SQUAMOUS CELL CARCINOMA
90	879/06	54	M	R	LL	ADENOCARCINOMA
91	1080/06	40	M	L	UL	SQUAMOUS CELL CARCINOMA
92	1086/06	56	M	R	UL	SQUAMOUS CELL CARCINOMA
93	1138/06	67	M	R	LL	ADENOCARCINOMA
94	1190/06	35	F	R	LL	ADENOCARCINOMA
95	1238/06	59	M	R	UL	SQUAMOUS CELL CARCINOMA
96	1239/06	65	M	R	LL	ADENOCARCINOMA
97	1291/06	44	M	R	UL	ADENOCARCINOMA
98	1562/06	65	M	R	ML	SQUAMOUS CELL CARCINOMA
99	1716/06	64	M	R	LL	UNDIFFERENTIATED CARCINOMA
100	1808/06	67	M	R	UL	SQUAMOUS CELL CARCINOMA
101	1875/06	70	M	R	LL	SQUAMOUS CELL CARCINOMA
102	2111/06	60	M	R	LL	SQUAMOUS CELL CARCINOMA
103	2803/06	57	M	R	LL	ADENOCARCINOMA
104	2817/06	60	M	R	UL	SQUAMOUS CELL CARCINOMA
105	2938/06	60	M	R	LL	SQUAMOUS CELL CARCINOMA
106	3062/06	48	M	R&L	ALL	NONDIAGNOSTIC
107	3509/06	45	F	L	LINGULA	BRONCHOALVEOLAR CARCINOMA
108	3514/06	40	M	R	LL	ADENOCARCINOMA
109	3560/06	19	M	R	LL	NONDIAGNOSTIC
110	3631/06	20	M	R	LL	NONDIAGNOSTIC
111	3660/06	46	F	R	UL	ADENOCARCINOMA
112	3707/06	56	M	L	UL	SQUAMOUS CELL CARCINOMA
113	3715/06	68	M	L	LINGULA	ADENOCARCINOMA
114	3734/06	51	F	L	LL	NONDIAGNOSTIC
115	3805/06	58	M	R	ML	NONDIAGNOSTIC
116	3834/06	56	F	L	LL	ADENOCARCINOMA
117	3848/06	40	M	L	LINGULA	SQUAMOUS CELL CARCINOMA

118	3892/06	49	M	L	UL	SQUAMOUS CELL CARCINOMA
119	3972/06	58	M	L	LL	SQUAMOUS CELL CARCINOMA
120	3997/06	52	M	L	LL	ADENOCARCINOMA
121	4025/06	61	M	R	LL	SQUAMOUS CELL CARCINOMA
122	4074/06	30	F	R	LL	UNDIFFERENTIATED CARCINOMA
123	4104/06	60	M	R	ML	ADENOCARCINOMA
124	4122/06	56	F	R	ML	ADENOCARCINOMA
125	4187/06	55	M	R	ML	SQUAMOUS CELL CARCINOMA
126	4632/06	42	M	L	LL	SQUAMOUS CELL CARCINOMA
127	5026/06	42	M	R	UL	SQUAMOUS CELL CARCINOMA
128	5321/06	70	M	R	LL	ADENOCARCINOMA
129	6084/06	50	F	R	UL	ADENOCARCINOMA
130	6351/06	58	M	R	ML	SQUAMOUS CELL CARCINOMA
131	6364/06	50	F	R	LL	NONDIAGNOSTIC
132	8162/06	47	F	R	UL	SQUAMOUS CELL CARCINOMA
133	8213/06	80	M	R	LL	SMALL CELL CARCINOMA
134	268/07	55	M	R	UL	SQUAMOUS CELL CARCINOMA
135	351/07	53	M	L	LL	SQUAMOUS CELL CARCINOMA
136	384/07	50	F	L	LL	ADENOCARCINOMA
137	2476/07	72	M	R	UL	ADENOCARCINOMA
138	4849/07	71	M	R	UL	MUCOEPIDERMOID CARCINOMA
139	5052/07	57	M	R	UL	SQUAMOUS CELL CARCINOMA
140	5121/07	65	M	R	UL	SQUAMOUS CELL CARCINOMA

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