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Study on primary non-small cell lung cancer with special reference to immunohistochemistry, EGFR mutation and K-RAS mutation in a tertiary care hospital

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Abstract---Background: In lung cancers the use of immunohistochemistry is recommended for those cases in which diagnosis is unclear between adenocarcinoma and squamous cell carcinoma. This study is to know the different mutations in NSCLC of the lungs in our tertiary care centre. Aims & Objectives: To study clinical and radiological correlation with different histological types of primary lung cancer with reference to immunohistochemistry TTF-1 and p63 and to detect EGFR, KRAS mutation. Material & Methods: The study was conducted in a tertiary care centre of Odisha during the period from Sept. 2019 to Sept. 2021. 40 patients of age >18yrs with strong clinical suspicion and/or chest radiographic diagnosis of primary lung cancer are included in this study from IPD of Pulmonary Medicine Department, SCB MCH, Cuttack after taking into account inclusion and exclusion criteria. Results: Most of the cases were in the

5th & 6th decade of age with mean age of 58.8yrs. Most males (57.5%) in the study were smoker and all females were Never-Smokers. EGFR mutation found in 7 cases out of 20 Adenocarcinoma (35%) and 2 cases out of 19 Squamous cell carcinomas (10.5%). K-RAS mutation was detected in 1 adenocarcinoma patient (5%).

Keywords--NSCLC- non-small cell lung cancer, adeno carcinoma, squamous cell carcinoma, EGFR- epidermal growth factor receptor, K-RAS- Kristen rat sarcoma.

Introduction

Lung cancer is one of the most common cancers diagnosed worldwide. According to GLOBOCON 2020 on December 14, worldwide an estimated 19.3 million new cancer cases and almost 10 million cancer deaths occurred in 2020. ^[1]This is the second most frequently diagnosed cancer and the leading cause of cancer death in 2020, representing approximately 1 in 10 cancers diagnosed and 1 in 5 deaths due to cancer.^[2,3] In males, it ranked second while in females it was sixth in terms of cancer incidence.^[4,5]

Aims and Objectives

- To study clinical and radiological correlation with different histological types of primary lung cancer using different diagnostic modalities.
- To study the role of immunohistochemistry TTF-1 and p63 to establish the sub type of lung cancer.
- To detect EGFR, KRAS mutation for targeted therapy for primary NSCLC.

Material and Methods

The study was conducted in the Department of Pulmonary Medicine, SCB Medical College and Hospital, Cuttack in collaboration with Department of Pathology during the period from September 2019 to September 2021^[6,7]. 40 patients of age >18years with strong clinical suspicion and/or chest radiographic diagnosis of primary lung cancer are included in this study from IPD of Pulmonary Medicine Department.^[8,9]

Inclusion criteria

Patient with Clinical &/or radiological presentation of primary non-small cell lung cancer and the same diagnosed by bronchoscopy & USG / CT guided biopsy.

Exclusion criteria

Any contraindication to invasive procedures like bronchoscopy, USG/ CT guided biopsy & Non-consenting patients.

Results

Demographic Profile

DEMOGRAPHIC PROFILE			
MALE	AGE GROUP	18-40	0(0%)
		41-60	15(50%)
		>60	15(50%)
	Smoking Status	Never Smoker	7
		Current Smoker	22
		Ex Smoker	1
FEMALE	AGE GROUP	18-40	0(0%)
		41-60	8(80%)
		>60	2(20%)
	Smoking Status	Never Smoker	0
		Current Smoker	0
		Ex Smoker	0

4.2 Radiographic Findings		
Ct Thorax Findings	NO. OF PATIENTS	PERCENTAGE
MASS	26	65%
MULTIPLE NODULES	5	12.5%
COLLAPSE	9	22.5%
CONSOLIDATION	7	17.5%
MEDIASTINAL NODES	26	65%
SVC INVOLVMENT	3	7.5%
PLEURAL INVOLVEMENT	21	52.5%
CHEST WALL INVASION	7	17.5%
ASSOCIATED EMPHYSEMA	10	25%

Relationship between histological subtypes and molecular diagnostic methods

Histological Subtypes	EGFR Mutation Positive	Percentage	K-Ras Mutation Positive	Percentage
ADENO CARCINOMA	7	35%	1	5 %
SQUAMOUS CELL CARCINOMA	2	10.5 %	0	0 %

Discussions

In this study 57.5% are in the age group of 40-60 years with Mean age of 58.8yrs. Patients with smoking history was 57.5% which is lesser than the study by Jindal et al., Jagdish Rawat et al & Viswanath Sundaram et al who reported Lung cancer in smokers that of 69%, 81.77% & 71% respectively. The ratio of male to female is 3:1 and it correlates with the study by Anurag Agrawal et al. & R.

Prasad et al. All the female patients in our study are Never-smoker & 90% of them had history of biomass fuel exposure as the probable risk factor for lung cancer. J. Rawat et al (2005) showed most frequent symptom was cough (72.9%). In our study cough (75%) was the most common symptoms followed by breathlessness (67.5%) and chest pain (65%). Pallor was seen in 35% cases, clubbing in 27.5% & lymphadenopathy in (10%) which is similar to report by Guleria et al(1971).

Omer S. Almoudi(2010) reported lung mass in 82% followed by mediastinal adenopathy in 51% and pleural effusion in 36%, collapse in 33% and consolidation in 27% of cases in a study with 114 patients. Similarly in our study CT revealed mass lesion in 65% of cases followed by mediastinal adenopathy in 65% of cases & pleural effusion in 52.5% of cases. Pleural effusion incidence are higher in our study which may be due to the late presentation. Yield by CT/USG guided transthoracic needle biopsy and endobronchial biopsy was comparable with the study by Jayant b. Chauhan et al, Agrawal et al and Rateesh Sareen et al. Most common pathological subtype is Adenocarcinoma followed by squamous cell carcinoma. Adenocarcinoma is the predominant subtype among smokers while adenocarcinoma and squamous cell carcinoma are found equally among non-smokers.

40 biopsy samples were submitted for immunohistochemical study and out of which 20 cases have been morphologically diagnosed as adenocarcinoma and 19 cases as squamous cell carcinoma, 1 case as large cell carcinoma. After application of TTF-1 and p-63 IHC for diagnosis 19 cases of adenocarcinoma (90%) were found to be TTF-1 positivity and 17 cases of squamous cell carcinoma (89.5%) are P-63 positive. 1 case was negative for TTF-1 and 2 cases are negative for P63. Among all the patients subjected to Immunohistochemical study, TTF-1 positivity were found in 13 male patients (43.3%) and 5 female patients (50%). Similarly P-63 positivity were detected in 12 male patients (40%) and 5 female patients (50%). Most of the studies conducted have found that approximately one third of NSCLC patients harbour an EGFR mutation (32.9%) and among the sub types it is most commonly associated with adenocarcinoma and patients who are non-smokers. In our study EGFR mutation was detected in 9 cases out of 39 cases (23%) and among them 35% cases of adenocarcinoma and 10.5% cases of squamous cell carcinoma patients harbour EGFR mutation which is similar to most of the studies. However, K-RAS mutation was detected in 1 adenocarcinoma patient (5%).

Conclusion

Clinico-Radiological examination, histopathological evaluation and molecular study of primary NSCLC is always needed for accurate diagnosis and targeted therapy. Unsatisfactory and benign lesions with high degree of suspicion needs clinical correlation and close follow up where a re-biopsy may be necessary. NSCLC characterization was performed using combination of morphology and immunohistochemistry from samples and subsequently EGFR, K-RAS mutations in clinico-radiologically suspected primary non -small cell lung cancer.

There is no conflict of interest.
No funding done.

Limitations

Our study was conducted with a relatively small number of cases in a single centre. However further multi-centric studies may be carried out to strengthen the above study.

References

1. Clinic pathologic profile of bronchogenic carcinoma among female in north india: R Prasad et al 2015
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3. Guleria JS, Gopinath N et al. Bronchial carcinoma an analysis of 120 cases, J .Ass. Phy .India 1971; 19:251-55.
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INSTITUTIONAL ETHICS COMMITTEE
ACHARYA HARIHAR POST GRADUATE INSTITUTE OF CANCER,
Medical Road, Mangalabag, CUTTACK-753007

Re-Regd. No. ECR/297/Ins/DG/2019/RR-19 issued under New Drugs and Clinical Trials Rules, 2019
and NECRB/R of Department of Health Research, Govt. of India

Letter No : 046-IEC-AHPGIC

Date : 06.09.2021

To

Dr. Biswabikash Mishra,
Post Graduate Resident,
Guide: Prof. Jyoti Patnaik,
Department Of Pulmonary Medicine,
S.C.B Medical College,
Co-Guide: Prof. Surendra Nath Senapati,
Dept. Of Radiation Oncology, AHPGIC.

Dear Dr. Mishra,

The Institutional Ethics Committee, AHPGIC reviewed your research proposal for your thesis titled: "A study on primary non small cell lung cancer with special reference to immunohistochemistry EGFR mutation and K-RAS mutation in a tertiary care hospital".

The following documents were reviewed:

- a) Study Protocol : "A study on primary non small cell lung cancer with special reference to immunohistochemistry EGFR mutation and K-RAS mutation in a tertiary care hospital".
- b) Patient Information Sheet and Informed Consent Form in English & Odia.
- c) Investigator's Synopsis.
- d) Proposed methods for patient accrual.
- e) Principal Investigator's current CV.
- f) Investigator's undertaking.

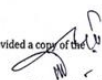
The following members participated in Institutional Ethics Committee meeting of AHPGIC by Online Process through zoom platform on 4th September 2021 at 4.00PM.

Sl. No	Name	Role in IEC	Official Capacity
1.	Dr. Asoka Kumar Das	Scientist	Chairman
2.	Prof. Kailash Chandra Mohapatra	Clinician	Member
3.	Dr. Sanghamitra Pati	Clinician	Member
4.	Dr. Kaushik Mishra	Clinician	Member
5.	Dr. Kall Prasad Pattanaik	Basic Medical Scientist	Member
6.	Dr. Narmada Kumari Parida	Social Scientist	Member
7.	Sri Manoj Kumar Mishra	Legal Expert	Member
8.	Mrs. Mrinalini Padya	Lay Person	Member
9.	Dr. Manoranjan Mahapatra	Clinician & Oncologist	Member-Secretary

We approve the study to be conducted in its presented form

The Institutional Ethics Committee should be informed

- (a) about the progress of the study
- (b) any Serious Adverse Events occurring in the course of the study
- (c) any changes in the protocol and patient information or informed consent and to be provided a copy of the final report


Member Secretary
Institutional Ethics Committee,
AHPGIC, Cuttack



INSTITUTIONAL ETHICS COMMITTEE
S.C.B. MEDICAL COLLEGE & HOSPITAL, CUTTACK - 753007,
ODISHA

Email id: icescb19@gmail.com

Ethics Committee Regd. No. ECR/84/Insu/OR/2013/RR-20
 Issued under New Drugs and Clinical Trials Rules, 2019 by DCGI (Central Licensing Authority)

CHAIRPERSON
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 Retired Judge, Odisha High Court,
 Cuttack.

DEAN & PRINCIPAL
 Prof. Dattesswar Hota,
 S.C.B. Medical
 College & Hospital, Cuttack.

MEMBER SECRETARY
 Prof. Prasenjeet Mohanty
 Prof. & HOD SKIN & VD,
 SCBMCH, Cuttack, Mob: 7381231102

IEC Appln. No:- 846

Date. 04.06.2021

Communication of Decision of the Institutional Ethics Committee [IEC]

To
 Dr. Biswabikash Mishra, PG, Pulmonary Medicine, SCBMCH.

Protocol title: **A STUDY ON PRIMARY NON SMALL CELL LUNG CANCER WITH SPECIAL REFERENCE TO IMMUNOHISTOCHEMISTRY AND EGFR MUTATION AND K-RAS MUTATION IN A TERTIARY CARE HOSPITAL**

Investigators: Dr. Biswabikash Mishra, PG, Pulmonary Medicine, Dr. Jyoti Patnaik, Prof. Pulmonary Medicine, Dr. Surendra Nath Senapati, Assoc. Prof. Oncology, AHRCC
 Dr. Dilleswari Pradhan, Assoc. Prof. Pathology, Dr. Roma Rattan, Assoc. Prof. Biochemistry, SCBMCH
 Name & Address of Institution: S.C.B. Medical College, Cuttack

Expedited review Full Committee Review Revised Review

Date of Review [D/M/Y]: 04.06.2021 / 11.06.2021

Decision of the 42nd IEC meeting held on 04.06.2021.

Approved Revision with Minor Modification
 Not Approved Revision with Major Modification for Resubmission

Suggestions (if any):

Recommended for a Period: 3 (Three) years

Please note:

- > Inform IEC immediately in case of any Adverse Drug Reactions/Adverse Events.
- > Inform IEC in case of any change of study procedure, site and investigator.
- > In case of Clinical Trial, the Annual Reports to be submitted to IEC and the Members of IEC have right to monitor the trial with prior intimation.


 Signature of Member Secretary
 Institutional Ethics Committee
 Member Secretary
 Institutional Ethics Committee
 S.C.B. Medical College, Cuttack