



EPIDEMIOLOGICAL CHANGES IN DIAGNOSIS OF LUNG CANCER BY IHC IN THE PRESENT ERA

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ABSTRACT **BACKGROUND:** Lung cancer is currently the most frequently diagnosed major cancer in the world and the most common cause of cancer mortality worldwide. Lung cancers are broadly classified into Small cell carcinoma and Non-small cell carcinoma of lung. Non-small cell carcinoma is further subdivided into Squamous cell carcinoma, Adenocarcinoma, Neuroendocrine-large cell and Undifferentiated carcinoma of lung. Maximum incidence of lung cancers occurs in 40 to 70 years of age with peak incidence in 50 to 60 years.

MATERIALS AND METHODS: Present study is a prospective study conducted at a Tertiary Care centre, Department of Pathology in a duration of 22 months from September 2018 to July 2020. This study was conducted on total 120 cases. Prepared cytological smears and lung biopsy specimen were received after CT guided procedure from department of pulmonary medicine. After fixation and staining procedure, diagnosis, typing and subtyping was done which was further confirmed by immunohistochemistry techniques using the expression of P63, TTF 1, CK 7 and Napsin A.

RESULT: Out of total 120 cases, history of smoking was present in total 94 patients including male and female. 58 (48.33%) were confirmed as adenocarcinoma of lung, 42 (35%) cases as squamous cell carcinoma, 11 (9.16%) as small cell carcinoma and 8 (6.66%) cases were inconclusive for diagnosis.

CONCLUSION: Each of the subtypes of lung cancers are clinically, morphologically, genetically and therapeutically distinct and hence it is important to accurately classify them by Immunohistochemistry technique. Present study shows that incidence of adenocarcinoma was seen to be highest amongst patients with history of smoking.

KEYWORDS : Biopsy, FNAC, Immunocytochemistry/histochemistry, Lung carcinoma, smoking

INTRODUCTION:

Lung cancer is currently the most frequently diagnosed major cancer in the world and the most common cause of cancer mortality worldwide. According to the studies conducted till recent past, Small cell carcinoma and squamous cell carcinoma are found to be highly associated with exposure to tobacco smoke. The relative proportions of major histologic variants of lung carcinoma are: Adenocarcinoma (38%), Squamous cell carcinoma (20%), Small cell carcinoma (14%), Large cell carcinoma (3%). Cancer of the lung occurs most often between the ages of 40 and 70 years with a peak incidence in the 50s or 60s. Only a small number of cases appear before the age of 40. Lung malignancies are largely due to carcinogenic effects of cigarette smoke. It was predicted that changes in smoking habits will greatly influence lung cancer incidence and mortality as well as the prevalence of various histologic types⁽¹⁾. About 80% of lung cancers occur in active smokers or those stopped recently along with other genetic and environmental factors. Incidence trends and geographical patterns are different for men and women and primarily reflect historical, cultural and regional differences in tobacco smoking⁽²⁾. However, the significance of all these factors pales by comparison with the role played by cigarette smoking, both in males and in females⁽³⁾. Worldwide, rates of female lung cancer are increasing⁽⁴⁾. In some regions, particularly Asia, indoor air pollution and occupational exposures play a greater role in female lung cancer⁽⁵⁾. About 80% of lung cancers occur in active smokers. Older age is associated with cancer development due to biologic factors that include DNA damage over time and shortening telomeres. Accordingly, the median age of lung cancer diagnosis is 70 years for both men and women⁽⁶⁾. The relationship of cigarette smoking with malignant, dysplastic and metaplastic alterations of the tracheobronchial tree has also been thoroughly documented by the meticulous histologic observations of Auerbach et al⁽⁶⁾.

AIMS & OBJECTIVES:

- To study the incidence of lung carcinoma amongst smokers and

non-smokers in Saurashtra region

- To assess the role of smoking in pathogenesis of lung malignancy
- To assess the histopathological type of lung carcinoma in smokers and non-smokers, confirmed by IHC

MATERIALS AND METHODS:

METHOD:

Present study is a prospective study conducted at a Tertiary Care centre, Department of Pathology in a duration of 22 months from September 2018 to July 2020. This study was conducted on total 120 cases. Prepared cytological smears and lung biopsy specimen were received after CT guided procedure from department of pulmonary medicine. After fixation and staining procedure, diagnosis, typing and subtyping was done which was further confirmed by immunohistochemistry techniques using the expression of P63, TTF 1, CK 7 and Napsin A. Immunocytochemistry and Immunohistochemical staining was done following standard procedures using DAKO-Antibody with Positive and Negative controls for each case.

RESULTS:

Table no. 1: Age and Sex distribution

Age group	Male	Female	Total
0 to 40 years	05	01	06 (5%)
41 to 60 years	45	04	49 (40.83%)
>60 years	55	10	65 (54.16%)
Total	105 (87.5%)	15 (12.5%)	120

Table no. 1 shows Age and sex wise distribution of the cases. Maximum number of patients were in the age group of more than 60 years of age with highest incidence in male patients.

Table no. 2: Gender wise distribution of Smokers and Non smokers

Age Group	Male		Female		Total
	Smoker	Non smoker	Smoker	Non smoker	
0 to 40 years	04	01	00	01	06 (5%)
41 to 60 years	39	06	02	02	49 (40.83%)
>60 years	44	11	05	05	65 (54.16%)
Total	87 (72.5%)	18 (15%)	07 (5.83%)	08 (6.66%)	120

Table no.2 shows the age and sex wise distribution amongst smokers and non-smokers. Male preponderance was seen in total number of cases along with highest association with smoking.

Table no.3: Incidence of carcinoma according to age groups

Age group	Small cell Ca.	Non-small cell carcinoma		Inconclusive	Total
		Squamous cell Ca	Adenocarcinoma		
0 to 40 years	00	02	03	01	06 (5%)
41 to 60 years	07	17	21	03	48 (40%)
>60 years	04	23	34	04	65 (54.16%)
Total	11 (9.16%)	42 (35%)	58 (48.33%)	08 (6.66%)	119 (99.16%)

One case was diagnosed as Adeno-squamous carcinoma of lung after confirmation by Immunohistochemistry

Table no.3 shows the age group wise incidence of confirmed lung malignancy. Maximum number of patients were diagnosed with Non-small cell carcinoma of lung with higher occurrence of Adenocarcinoma, followed by Squamous cell carcinoma (42 cases) and Small cell carcinoma of lung (08 cases). 08 cases were inconclusive for diagnosis due to lack of diagnostic material.

Table no. 4: Incidence if carcinoma amongst Smokers and Non smokers

Age group	Smoker			Non-Smoker			Inconclusive	Total
	Small cell Ca	Squamous Cell	Adenocarcinoma	Small cell ca	Squamous cell ca	Adenocarcinoma		
0 to 40 yrs	00	01	02	00	01	01	01	06
41 to 60 yrs	06	11	21	00	04	02	03	47
>60 yrs	04	15	28	00	09	06	04	56
Total	10 (8.33%)	27 (22.5%)	52 (43.33%)	00	14 (11.66%)	09 (7.5%)	08 (6.66%)	120

Table no 4 shows type of carcinoma with highest association with smoking. It was observed that in smokers Adenocarcinoma was most common to occur whereas Squamous cell carcinoma was common to occur in Non-smokers. Maximum number of patients being in age group of >60 years of age.

DISCUSSION:

Ahrendt Et al (2001) (7) classified their total 106 patients into two age groups i.e. <65 years (49 patients/46.22%) and >= 65 years (57 patients/48.11%). Noronha Et al (2012) (8) classified their 489 patients into three age groups. 11% belonged to 0 to 40 years of age group, 57% in 40 to 60 years and 32% patients were above 60 years of age. According to Groot Et al (2018) (9), 53% of cases were between 55 to 74 years of age while 37% were over 75 years of age. Present study shows similarity in age group classification with Noronha Et al. We classified patients into <40 years: 06 cases (5%), 41 to 60 years: 49 cases (40.83%) and > 60 years: 65 cases (54.16%).

Study by Ahrendt Et al (2001) included total 106 patients of which 55 (51.88%) were male and 51 (48%) were female. Noronha Et al (2012) carried out study on total of 489 patients of which majority i.e. 380 (77.7%) were male and 109 (23.3%) were female. Groot Et al (2018)

did not mention any details about total number of cases as well as incidence amongst the respective gender. Present study was conducted on 120 cases of which 105 (87.5%) were male and 15 (12.5%) were female. All the studies conducted showed maximum incidence in male population.

Study by Ahrendt et al shows that 92/106 patients (87%) were smokers. Amongst the non-smokers (14/106 i.e. 13%) majority patients were female i.e. 11/14 (79%). According to Noronha et al, out of 489 patients, 255 (52.1%) had no history of smoking while 234 (47.9%) had positive history for smoking. Study by Groot et al (2018) covered the overall epidemiology of lung cancer with its incidences worldwide. It considered the occurrence of lung cancer with relation to various risk factors such as tobacco and smoking, Other smoking products like cannabis sativa, Environmental risk factors such as Radon, Asbestos, Pollution and air quality, Infections and Genetic risk factors as well. Since it covers a vast dimension, there is no specific data available regarding the exact number of smokers and non-smokers. Present study (2020) shows total 94/120 (78.33%) patients with positive history of smoking. Of these 94 smokers, 87 (72.5%) were male whereas 07 patients (5.83%) were female. Smoking habits in female also included Chronic chulha exposure and bajar/masala consumption. Remaining 26/120 patients (21.66%) were non-smokers. Of these 26 non-smokers cases, 18 (15%) were male and 08 (6.66%) were female.

Ahrendt et al (2001) states that incidence rates of squamous cell, large cell and small cell lung carcinoma among women have leveled off or started to decrease, the incidence of adenocarcinoma continues to increase. Adenocarcinoma of lung has become the most common type of lung carcinoma in the US (10).

According to Noronha et al (2012), small cell carcinoma was diagnosed in 8% of patients while 92% of the patients had non-small cell lung (NSCLC). Within NSCLC, the most common histology was Adenocarcinoma (43.8%) followed by squamous cell carcinoma (26.2%), large cell carcinoma (2.1%) and other (8.3%). In 19.6% of patients, only cytology was performed and hence only a diagnosis of Non-small cell lung carcinoma was made. On other hand, study by Groot et al (2020), states about the overall smoking prevalence and lung cancer incidence, with no emphasis on the histological type diagnosed. Present study observed that of the total 120 cases, amongst smokers, 52 patients were diagnosed with adenocarcinoma, 27 with Squamous cell carcinoma and 10 with Small cell carcinoma lung. Whereas, amongst the non-smokers, 14 were diagnosed with Squamous cell carcinoma and 09 with Adenocarcinoma lung. Total 08 cases were inconclusive for confirmatory diagnosis due to lack of diagnostic material to perform Immunocytochemistry/ Immunohistochemistry.

Image:

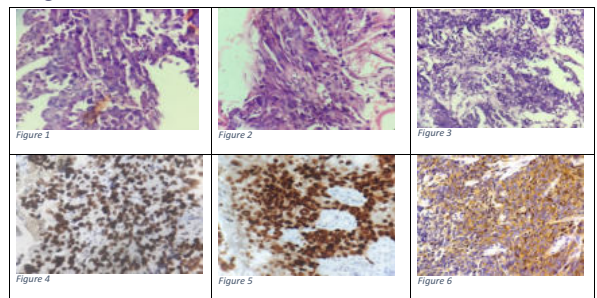


Fig.1: H&E stained (40x) section of Adenocarcinoma of lung showing sheet of cells with mild to moderate nuclear pleomorphism, round nuclear contour, vesicular chromatin, at places prominent nucleoli and vacuolated cytoplasm.

Fig.2: H&E stained section (40x) of Squamous cell carcinoma lung, shows sheet of malignant epithelial cells showing nuclear pleomorphism, high N:C ratio, hyperchromatic nuclei and moderate amount of dense eosinophilic cytoplasm.

Fig.3: H&E stained section (40x) of Small cell carcinoma lung, shows small sheets and clusters of small round cells showing nuclear molding, nuclear overlapping, scant cytoplasm and crushing artifact.

Fig.4: IHC (40x)- section of Adenocarcinoma lung, showing nuclear positivity for TTF-1.

Fig.5: IHC (40x)- Section of Squamous cell carcinoma lung, shows nuclear positivity for P63. TTF-1 and CK-7 were negative.

Fig.6: IHC (40x)- Section of Small cell carcinoma lung, shows cytoplasmic Positivity for Synaptophysin in Small cell carcinoma of Lung.

CONCLUSION:

Present study aimed at studying the incidence of lung carcinoma amongst smokers and Non-smokers in Saurashtra region along with emphasis on the histopathological type and confirmation by IHC. Smoking is a crucial risk factor in the pathogenesis of lung malignancy. Our observations show that maximum patients had a positive history for chronic duration of smoking. Of these patients, highest incidence was of Adenocarcinoma (43.33%), followed by Squamous cell carcinoma (22.5%) and Small cell carcinoma lung (8.33%). On the other hand, Non-smoking category of patients showed maximum incidence of Squamous cell carcinoma (11.66%) whereas Adenocarcinoma was diagnosed in 7.5% of patients. The present study hence shows that overall, Adenocarcinoma of lung has currently the highest prevalence in patients especially in those who are exposed to chronic Tobacco smoke/Bidi smoking/Chulha smoke exposure (major risk factor in women) in contrast to earlier prevalence of squamous cell carcinoma. Immunocytochemistry/Immunohistochemistry is seen to play a significant role in making a confirmatory diagnosis in adjunction to Gold standard Histopathological examination as well as aid in the treatment protocol.

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Conflicts of Interest: None

Ethical Approval: This study was approved by Institutional Ethical Committee (IEC)

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