Comparison of Sputum Cytology with BronchoAlveolar Lavage Cytology in Diagnosis of Lung Cancer: A Hospital Based Study In BPKIHS

Adhikari M[1], Karki S[2], Pradhan A[2], Upadhayay P[2]

ABSTRACT

Introduction: Lung cancer is one of the commonest cancers and its burden is increasing in developing countries as well. It has high mortality rate as most cases are diagnosed at late stages where there have very less therapeutic benefits. Early diagnosis of lung cancer can be done by cytology screening tools like Sputum and Bronchoalveolar Lavage Cytology study. **Aims**: To compare the diagnostic yield of Sputum cytology with Broncho-Alveolar Lavage cytology in diagnosing lung cancer by correlating with biopsy findings. **Methods**: This is a one-year hospital based prospective cross sectional study done at Department of Pathology, BPKIHS, Dharan. It included 34 cases subjected to Sputum and broncho-alveolar lavage cytology as well as Transbronchial biopsy. Diagnostic yield of Sputum and BAL cytology were calculated by correlating with biopsy findings. **Results:** Age of patients ranged from 29 to 84 years with near equal gender distribution. Biopsy was positive for lung cancer in 22 cases (65%). Sensitivity of Sputum and broncho-alveolar lavage cytology were calculated as 38.9 % and 68.4% respectively. Cigarette smoking showed statistically significant correlation with Lung cancer. Most common cancer detected in biopsy was squamous cell carcinoma followed by Adenocarcinoma. **Conclusion:** Sputum and Bronchoalveolar Lavage cytology study can serve as initial screening tools for suspected lung cancer cases, especially in limited resources settings. However, the final confirmation has to be done by the gold standard histopathology study.

Keywords: Biopsy, Bronchoalveolar Lavage, Carcinoma, Cytology, Sputum

Authors:

1. Dr. Milan Adhikari
2. Dr. Smriti Karki
3. Dr. Anju Pradhan
4. Dr. Paricha Upadhyaya

[1]Department of Pathology, Nepalgunj Medical College and Teaching Hospital, Kohalpur, Banke
[2]Department of Pathology, B.P. Koirala Institute of Health Sciences, Dharan

Address for Correspondence:

Dr. Milan Adhikari
Department of Pathology
Nepalgunj Medical College and Teaching Hospital
Kohalpur, Banke, Nepal
Email: milanadhikari011@gmail.com

INTRODUCTION

Lung cancer is one of the commonest cancers and cause of cancer related deaths all over the world.[1] In Nepal, lung cancer is the commonest cancer among male and third most common in female population with overall incidence of 16.64%.[2] Deaths by lung cancer is largely by the carcinogenic effects of cigarette smoking.[3] Lung cancer is fatal in more than 90% of diagnosed cases because most cases are diagnosed at very late stage when the disease is incurable.[4] This dismal mortality makes early diagnosis and treatment essential for improvement in the morbidity and mortality.[5] Evidences suggest screening and early detection may improve outcome in lung cancer which can be achieved by evaluation of various cytological specimen.[3] Sputum Cytology is a simple reliable, cost effective and non-invasive procedure for diagnosis of pulmonary lesions.[6] BAL is a safe and reliable sampling method from distal airways and alveoli, which has been referred to as a 'liquid biopsy of the lung'.[7] Diagnosis made by any cytological examined hence has to be verified by the gold standard- biopsy. A diagnostic TBBx may prevent the need for an open lung biopsy.[8] Therefore, this study was carried out to see the difference in the diagnostic yield of Sputum cytology with BAL cytology in the diagnosis of lung cancer and correlating them with transbronchial biopsy.

METHODS

A Hospital based comparative cross sectional study was carried out from May 2017 to April 2018 in the Department of Pathology, BPKIHS, after obtaining ethical clearance from the institutional review board (Ref. no: 333/073/074-IRC). All patients suspected of lung malignancy undergoing cytological (Sputum and BAL) as well as histopathological diagnostic procedures were included in the study after taking informed consent. Failure to give any of the three samples were excluded from the study.

A total of 34 cases were taken for the study which was calculated based on the study done by Kumar P et al which showed the sensitivity of sputum cytology as 30%. (Kumar P et al). Both BAL as well as 3 samples of sputum were processed and stained with PAP and Giemsa stains as per the standard protocol. Biopsy specimen were processed and stained with routine H and E stain as per the standard protocols. Slides were screened and reporting done by expert pathologists.

Data were analyzed using Microsoft excel 2010 and standard statistical software SPSS 20.0.

RESULTS

Age of the patients in our study ranged from 29 to 84 years with a mean age of 57.59 ±13.28 Years. Mean age of the cancer positive patients in our study was found to be 60.5 years. We received total of 34 cases out of which 19 (55.9%) were males and 15 (44.1%) were females. 13 (76.50%) out of 19 male and Nine (69.20%) out of 15 females were biopsy positive for lung cancer. But gender as such was not significant in causation of lung cancer. (p value of 0.6).

Figure 1: Biopsy Result (n=34)

Of the total 34 cases, biopsy was positive for malignancy in 22 cases (65%), negative in Eight cases (23%) and undetermined in Four cases (12%). Undetermined cases were those which were either inadequate for evaluation or suspicious for malignancy which could have either of the results.

Figure 2: Type of malignancies in biopsy positive cases

11 (50%) of the biopsy positive cases were diagnosed as SCC

while five (22.71%) cases were diagnosed adenocarcinoma. One case was diagnosed as small cell carcinoma and no specific cancer subtyping was possible in Five cases.
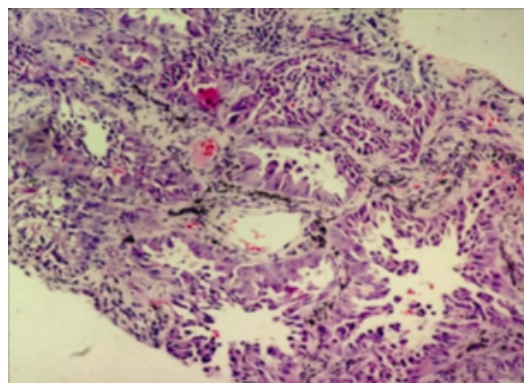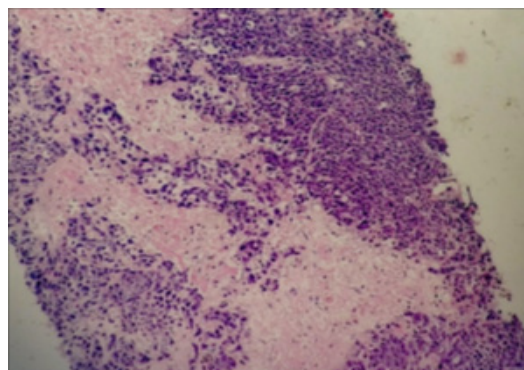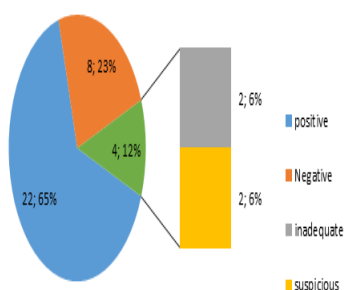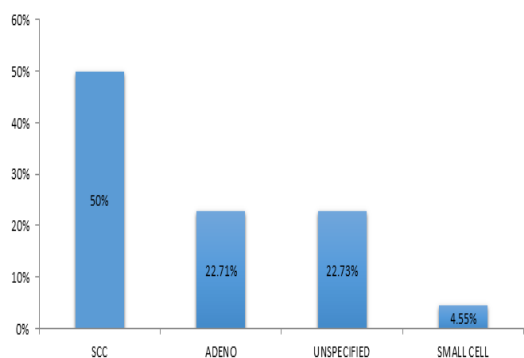

Photo1: Adenocarcinoma of lung (H &E stain, 40x)
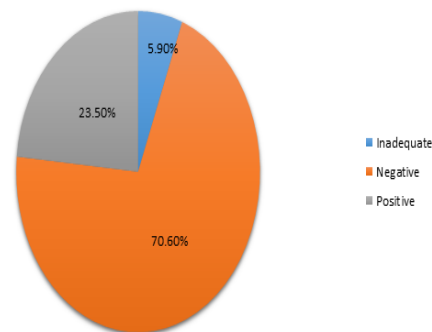

Photo 2: SCC Lung (H &E, 40x)

Figure 3: sputum cytology result (n=34)

Eight (23.5%) cases showed positive sputum cytology while 24 (70.6% cases) were cancer negative. Two cases (5.90%) were inadequate for evaluation. Six out of Eight sputum positive cases were diagnosed as squamous cell carcinoma while two cases were given a diagnosis of malignancy as definite type could not be ascertained by sputum cytology alone.
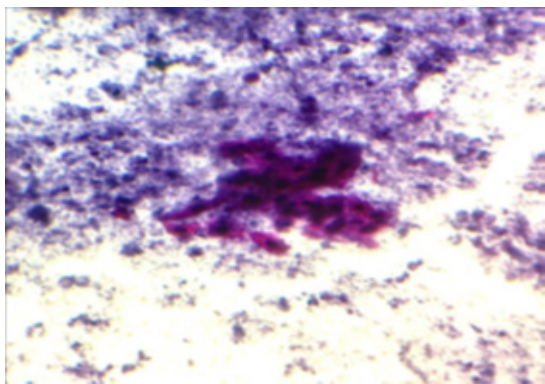
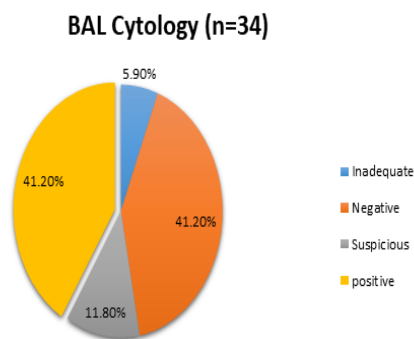*Photo 3: Squamous cell carcinoma in sputum (PAP Stain, 40x)*

Figure 4: BAL cytology

BAL cytology was positive in 14 cases (41.20%), negative in 14 cases (41.20%), suspicious of malignancy in Four cases (11.80%) and was inadequate for evaluation in Two cases. Of the positive cases detected by BAL, three cases (21.4%) were diagnosed as adenocarcinoma while the subtype of 11 cases (78.6%) could not be identified and hence were reported as malignancy only.
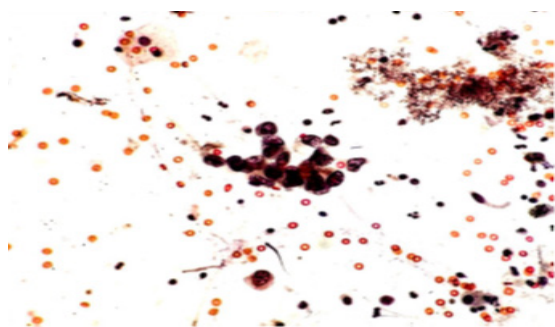

Photo 4: Adenocarcinoma in BAL cytology (PAP stain, 40x)

All the undetermined Sputum and BAL samples (inadequate and suspicious for malignancy), to which corresponding histology is either positive or negative is excluded for analysis and test results are grouped into test positive/ not-positive and test negative/ not-negative and thus sensitivity for each were calculated.

		Histopathology	
		Positive	Not positive
Sputum cytology	Positive	8	0
	Not positive	13	12
	Total	21	12

Table I: sputum sensitivity

Sensitivity of sputum cytology = (Test positive/ True positive) * 100

= 8/21 * 100

= 38.09%

		Histopathology		
		Positive	Not positive	Total
BAL cytology	Positive	13	1	14
	Not positive	6	11	17
	Total	19	12	31

Table II: Sensitivity of BAL cytology

Sensitivity of BAL cytology = (Test positive/ True positive) * 100

=13/19 * 100

= 68.4 %

Twenty four of the participants were ever smokers and 10 were never smokers. Duration of smoking varied widely from less than 10 yrs in two participants to >30 years in maximum of six patients.

The median pack years among smokers was found to be 8.
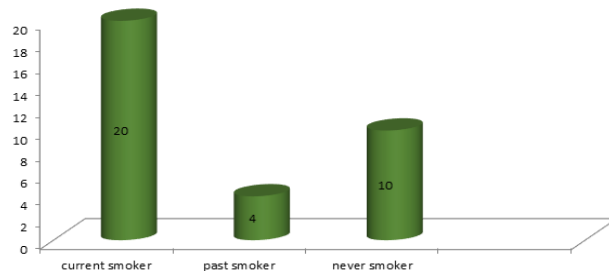
Figure 5: Smoking status among study population

Characteristic	categories	cancer		P value	Remark
		Positive	Negative		
Smoking	Never smoker	2 (25%)	6 (75%)	0.001	S *
	Ever smoker	20 (90.9%)	2 (9.1%)		
* Fisher's Exact test applied					

Table III : Association of smoking with lung cancer

Two (25%) out of Eight never smokers were lung cancer positive whereas 20 (90.90%) of the 22 ever smokers were cancer positive and the association of smoking with lung cancer was statistically significant. (P value- 0.001)

DISCUSSION

We received a total of 34 cases out of which 19 (55.9%) were males and 15 (44.1%) were females. 13 (76.50%) out of 19 male and 9 (69.20%) out of 15 females were biopsy positive for lung cancer. But gender as such was not significant in the causation of lung cancer with a p-value of 0.6. Age of the patients in our study ranged from 29 to 84 years with a mean age of 57.59 ±13.28 Years. Mean age of the cancer positive patients in our study was found to be 60.5 years and that of cancer negative patients was 53.15 years with p value of 0.2 which was statistically non-significant. A comparable study on clinicopathological evaluation of bronchogenic carcinoma by Barsky et al revealed the mean age of BAC patients as 59.2 ± 11.5 years, as compared to 64.1 ± 13.5 years for non- bronchoalveolar carcinoma.[9]

The sensitivity of sputum cytology in our study was 38.09%. Studies have shown the sensitivity of sputum cytology in diagnosing lung cancers ranged from as less as 4% to as high as 60%. comparable results were obtained from the studies done across the globe%.[3,4,10-12]

Discordent to our study, Ammanagi et al studied the value of sputum cytology in diagnosing lung cancer in which sensitivity of sputum cytology was 60%, which increased with an increase in the number of samples examined.[13]

In our study Sensitivity of BAL cytology in detecting lung cancers was found to be 68.48%. most of the studies in the past have results comparable to ours, with the sensitivity ranging from 42% to 69.6%.[3,14,15,17,18]

Among the 22 biopsy positive cases, 11(50%) cases were biopsy-proven SCC, Five (22.7%) were adenocarcinoma, one (4.5%) case of small cell carcinoma and Five cases (22.7%) were unclassified. All the cases were classified into specific subtypes based on the morphological features and some special stains. Though the current trend has suggested adenocarcinoma to be the commonest lung carcinoma, in our study Squamous cell carcinoma was the commonest one followed by adenocarcinoma.[19,20]

90% of ever smokers (current and past) had positive cancer biopsy whereas only 25% of non-smokers were cancer positive. In our study significant association is seen between smoking and lung cancer (p-value of 0.001). No of pack years of smoking is not statistically significant in our study though other studies have shown that the likelihood of getting lung carcinoma is directly proportional to the frequency and duration of smoking (pack years).[19,21,22] The non-significant result of our study might be due to the small sample size and also the history of smoking being quite common among the biopsy negative patients.

LIMITATIONS

The most important limitation of our study is a small sample size. Study on a large scale which would have better represented the study population would produce more reproducible results. Undetermined cases (inadequate for evaluation and suspicious for malignancy in biopsy) could not be included in the analysis of variables. Owing to unavailability of IHC during the study period, 2 cases had to be omitted wherein definite diagnosis of malignancy based on histopathology alone could not be made.

CONCLUSION

The overall accuracy of our sputum cytology diagnosis and BAL cytology diagnosis is similar to those reported in the literature. Few cases we missed out in our study owing to the sample inadequacy and lack of IHC in suspicious cases. Had these things been taken care of and feasible, the diagnostic yield of these cytological procedures, as well as biopsy diagnosis, would have been higher in our study.

REFERENCES

1. Malik PS, Raina V. Lung cancer: prevalent trends & emerging concepts. Indian J Med Res. 2015 Jan;141(1):5–7.

2. Piya MK, Acharya SC. Oncology in Nepal. South Asian J cancer. 2012;1(1):5–8.

3. Kumar P. Comparison of Effectiveness of Sputum Cytology With Bronchoalveolar Lavage (Bal) in the Diagnosis of Lung Cancer.International Journal of current Research 2014;6(8):8150–52.

4. Ch KM, Younus M, Rehman AU, Zafar SF, Bukhari SMH. The Importance of Sputum Cytology in the Diagnosis of Lung Cancer. 2010;16(3):198–201.

5. Shukla S, Malhotra KP, Husain N, Gupta A, Anand N. The utility of cytology in the diagnosis of adenocarcinoma lung: A tertiary care center study. J Cytol. 2015;32(3):159–64.

6. Krane JF. Koss' Diagnostic Cytology and Its Histopathologic Bases, Fifth Edition., International Journal of Gynecological Pathology. 2007.26(3) 270.

7. Wongsurakiat P, Wongbunnate S, Dejsomritrutai W, Charoenratanakul S, Tscheikuna J, Youngchaiyud P, et al. Diagnostic value of bronchoalveolar lavage and postbronchoscopic sputum cytology in peripheral lung cancer. Respirology. 1998;3(2):131–7.

8. Donato L, Tran TMH, Mihailidou E. Interventional bronchoscopy. Vol. 38, Paediatric Bronchoscopy. 2010. 64–74

9. Holmes E. Rising incidence of bronchioloalveolar lung carcinoma and its unique clinicopathologic features. Cancer. 1994 Feb 15;73(4):1163–70.

10. Agrawal R. SPUTUM CYTOLOGY IN BRONCHOGENIC CARCINOMAS. 2000;39(1):326–8.

11. Sing A, Freudenberg N, Kortsik C, Wertzel H, Klosa B, Hasse J. Comparison of the sensitivity of sputum and brush cy-

tology in the diagnosis of lung carcinomas. Acta Cytol. 1997;41(2):399–408.

12. Raab SS, Hornberger J, Raffin T. The importance of sputum cytology in the diagnosis of lung cancer: a cost-effectiveness analysis. Chest. 1997 Oct;112(4):937–45.

13. Ammanagi AS, Dombale VD, Miskin AT, Dandagi GL, Sangolli SS. Sputum cytology in suspected cases of carcinoma of lung (Sputum cytology a poor man's bronchoscopy!). Lung India. 2012 Jan;29(1):19–23.

14. Bhat N, Nazeir MJ, Bashir H, Bashir N, Farooq S, Fatima K, et al. Correlation of bronchial biopsy with bronchoalveolar lavage in lung malignancies. 2016;4(2):428–35.

15. Das SK, Das A, Saha SK, Biswas S. Diagnostic yield of broncho-alveolar lavage fluid and postbronchoscopic sputum cytology in endoscopically non-visible lung cancers. J Indian Med Assoc. 2011 Oct;109(10):730–2, 741.

16. Richa Sharma, Hemina Desai, Pankaj Malukani, R.N.Gonsai HMG. Comparison Of Bronchoalveolar Lavage Cytology And Biopsy In Lung Malignancy. Int J Curr Res Rev. 2014;6(5):43–7.

17. Binesh F, Pirdehghan A, Mirjalili MR, Samet M, Majomerd ZA, Akhavan A. Comparative assessment of the diagnostic value of transbronchial lung biopsy and bronchoalveolar lavage fluid cytology in lung cancer. Asian Pac J Cancer Prev. 2015;16(1):201–4.

18. Rennard SI. Bronchoalveolar lavage in the diagnosis of cancer. Lung. 1990 Dec;168(S1):1035–40.

19. Janssen-Heijnen MLG. Epidemiology of Lung Cancer. In: Tumors of the Chest. Springer Berlin Heidelberg; 2006. p. 3–12.

20. Lewis DR, Check DP, Caporaso NE, Travis WD, Devesa SS. US lung cancer trends by histologic type. Cancer. 2014 Sep 15;120(18):2883–92.

21. Kumar V, Abbas AK, Aster JC, editors. Robbins and Cotran pathologic basis of disease. Ninth edit. Philadelphia, PA: Elsevier/Saunders; 2015. 1391 p.

22. Boyle P, Maisonneuve P. Lung cancer and tobacco smoking. Lung Cancer 1995