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Identifying malignant pleural effusion from tubercular pleural effusion by study of cancer ratio and cancer ratio plus

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ABSTRACT

Background: Early detection of malignant pleural effusions (MPE) through routine biochemical tests will go a long way in improving morbidity and mortality of these patients. **Aims and Objectives:** The current study was aimed to observe the usefulness of cancer ratio (CR) and CR plus to diagnose malignant effusions early in disease evolution. **Materials and Methods:** The study was a cross-sectional comparative observational study conducted at the indoor and outdoor facility of Respiratory Medicine department of Institute of Post Graduate Medical Education and Research, Kolkata. **Results:** Sixty-one patients were included in the study. The overall mean CR in our patients was 40.50 ± 19.83. In MPE, tuberculous pleural effusions (TPE) and "Others", the mean CR were 49.1839 ± 14.698, 19.2874 ± 16.354, and 30.6107 ± 17.342, respectively. CR with levels above 20 showed very strong statistical association with MPE diagnosis in patients of pleural effusion ($P < 0.001$). The mean CR plus in all patients was found to be 54.58 ± 28.14. According to diagnosis, the means were 65.5645 ± 22.576, 27.3255 ± 24.356, and 43.1169 ± 25.622 in MPE, TPE, and "Others," respectively. Levels above 30 had shown strong association with MPE diagnosis ($P < 0.001$). Both CR and CR plus had sensitivity of 95.12% (95% CI 80.03–98.64), specificity of 80% (95% CI 60.80–91.16), positive predictive value of 90.69, and negative predictive value of 88.88 in diagnosing MPE. **Conclusion:** CR and CR plus which are easily obtained by routine testing can be used for early detection of MPE.

Key words: Pleural effusion; Exudative effusion; Malignant pleural effusion; Tubercular pleural effusion; Pleural fluid biomarkers; Cancer ratio; Cancer ratio plus

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INTRODUCTION

Pleural effusion (PE) is collection of excess amounts of fluid in the pleural space. The first step of diagnosis and management of PE is to determine the nature of effusion whether it is exudative or a transudative. It is done according to light's criteria.[1] According to Light's criteria, exudative PE is defined when any one of the three criteria will satisfy. Light's criteria-Pleural fluid protein/serum protein >0.5 and Pleural fluid Lactate dehydrogenase (LDH)/Serum LDH >0.6. To detect the etiology of PE, thoracentesis is a baseline diagnostic procedure.[2] Pleural fluid obtained from the procedure is analyzed for biochemical; microbiological, malignant cell smear and cell block study. Among exudative PE, three conditions are very common: Tuberculous PE (TPE), Para pneumonic PE, and malignant PE (MPE). The common causes of MPE are lung cancer (CA), breast CA, lymphoma, ovarian CA, sarcoma, gastric CA, and colon CA. Due to late presentation, diagnostic delay, socioeconomic condition, and delay in starting treatment leads to poor survival in India. In ambiguous cases, pleural biopsy is carried out to detect malignancy. TPE can be easily diagnosed with the estimation of Adenosine Deaminase (ADA),[2,3] but there is no such biomarker available for

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diagnosis of MPE. Therefore, it is necessary to search a novel marker to improve the accuracy of MPE diagnosis. Biomarkers like serum LDH, pleural ADA, and pleural fluid lymphocyte may provide clues to diagnose MPE and TPE.[4-6] Serum LDH is raised in MPE whereas pleural ADA and pleural fluid lymphocyte count remain comparatively low. Inversely, serum LDH is low in TPE whereas pleural ADA and pleural fluid lymphocyte count is raised. This inverse correlation provides us with an opportunity to develop a ratio with the diagnostic power to differentiate MPE from other exudative PEs in a cost-effective, easy, early, and universally applicable manner.[7,8] New biochemical marker, "Cancer ratio (CR)" (serum LDH: Pleural ADA ratio), and "Cancer ratio plus" (CR plus) (CR: Pleural fluid lymphocyte percentage) emerged as early, easy, and cost-effective tool for diagnosis of MPE. "Cancer ratio" at the cutoff level of >20 yielded high sensitivity and specificity, for identifying MPE. Addition of "Cancer Ratio Plus" further enhanced the diagnostic accuracy when cutoff level >30 is used.[9] Hence in this study, the utility of CR and CR plus to discriminate between MPE and other causes of exudative PE will be evaluated.[9,10]

Aims and objectives

Our study objective is to evaluate the usefulness of cancer ratio and cancer ratio plus in diagnosing MPE with minimal invasive procedure like thoracentesis.

MATERIALS AND METHODS

The study was a cross-sectional comparative observational study conducted at the indoor and outdoor facility of Respiratory Medicine department of Institute of Post Graduate Medical Education and Research (IPGME and R), Kolkata. Patients with suspected PE were evaluated with proper history and thorough clinical examination. Adult patients (>18 years of age), with ultrasound thorax showing >1 cm thickness of PE and pleural fluid satisfying Light's criteria for exudative effusion were included in the study. Transudative PE, empyema, hemothorax, patients with coagulopathy or local site infection were excluded from the study. Routine blood examinations, chest X-ray, and computed tomography scan of thorax was done. Pleural fluid was sent for cell type and count, pleural fluid protein/glucose/LDH/ADA estimation, gram stains, and culture sensitivity, Acid fast bacilli (AFB) stain, BACTEC culture for mycobacterium, malignant cell smear, and cell block. All patients with negative malignant cell smear or cell block were undergone pleural biopsy to confirm diagnosis. CR is the ratio of serum LDH and pleural fluid ADA. CR plus is the ratio of CR to the percentage of differential pleural lymphocyte. Confirmation of malignancy done by presence of malignant cell in the smear or malignant tissue in cell block from pleural fluid or malignant tissue in closed pleural biopsy.

RESULTS

A total of 61 patients were included in our study. 23.0%, 16.4%, 19.7% and 36.1% patients were in 31–40 years, 41–50 years, 51–60 years and 61–70 years age group respectively with only 4.9% patients were ≥70 years of age. Around 54% were males and rest were females Table 1.

We have found that 35 (57.37%) patients were smoker and rest 42.63% patients were non-smoker. About 22.87%, 60.66% and 11.48% patients reported sick for ≤3 months, 4–6 months, and >6 months, respectively. Only 12 (19.67%) patients had shortness of breath Table 2.

Table 2 show the compiled data on signs and symptoms of the recruited patients. In our study, 16 (26.2%) patients had straw color pleural fluid and 45 (73.8%) patients had hemorrhagic pleural fluid. The mean serum protein (mean±SD) and the mean serum LDH (mean±SD) of patients were 3.80±0.44 and 820.08±127.873, respectively. The mean pleural fluid cell lymphocyte (mean±SD) count of patients was 75.05±9.90. The mean pleural fluid protein, LDH, and ADA (mean±SD) of patients were 4.28±0.39, 928.05±108.392, and 26.36±68, respectively Table 3a.

Table 3a shows the distribution of biochemical parameter. Sputum AFB was detected in 6 (9.8%) of patients. Sputum Cartridge-based nucleic acid amplification test was positive in 10 (16.39%) patients. About 14 (23%) patients were diagnosed with TPE. About 7 (11.5%) patients had pleural fluid malignant cell smear result positive. About 11 (18%) patients had pleural fluid malignant cell block result positive. For confirmation of diagnosis in ambiguous cases 39 (63.9%) patients had undergone pleural biopsy. Total 41 (67.2%) patients were diagnosed with MPE. Patients over 60 years of age are more likely to be diagnosed with MPE (P=0.0059). About 23 (56.1%) MPE, 7 (50.0%) TPE, and 5 (83.3%) patients with others diagnosis had smoking status (P=0.369). Among 41 MPE patients, 36 (87.8%) had hemorrhagic and 5 (12.2%) had straw colored fluid whereas in TPE patients, 8 (57.14%) had hemorrhagic, and 6 (42.86%) had straw colored pleural fluid. In others' category, 50% had straw colored and rest 50% had hemorrhagic fluid. Hemorrhagic fluid was strongly associated with likely diagnosis of MPE (P=0.002). In MPE, TPE and other' patients mean serum protein (mean±SD) were 3.9229±0.4022, 3.5164±0.4379, and 3.6667±0.4274 g/dL, respectively. Distribution of serum protein with diagnosis was statistically significant. (P=0.007). Mean serum LDH (mean±SD) in MPE,

Table 1: Demographic distribution of patients (n=61)

Age group (years)	n	%
31–40	14	23.0
41–50	10	16.4
51–60	12	19.7
61–70	22	36.1
>70	3	4.9
Sex		
Male	33	54.10
Female	28	45.90

Table 2: Signs and symptoms

SOB	N	%
Present	12	19.67
Absent	49	80.33
Chest pain		
Present	14	22.95
Absent	47	77.05
Haemoptysis		
Present	5	8.20
Absent	56	91.80
Clubbing		
Present	42	68.85
Absent	19	31.15
Cervical lymphadenopathy	**Frequency**	**Percentage**
Present	6	9.84
Absent	55	80.16

SOB: Shortness of breath

Table 3a: Distribution of biomarkers among patients (n=61)

Biomarkers	Mean	Median	SD	Min	Max
Serum protein	3.8	3.8	0.44	2.9	4.6
Serum LDH	820.1	840	127.9	436	1024
Pleural fluid lymphocyte	75.05	75	9.9	57	95
Pleural fluid protein	4.28	4.24	0.39	3.46	5.08
Pleural fluid LDH	928.1	920	108.4	719	1243
Pleural fluid ADA	26.36	21	14.68	11	68

LDH: Lactate dehydrogenase, ADA: Adenosine deaminase

TPE and others were 962.71±83.914, 754.86±131.2, and 681.0±212.385 U/L, respectively. Distribution of mean serum LDH had statistically significant (P=0.001) association with likely diagnosis. The mean pleural fluid lymphocytes (mean±SD) in MPE, TPE, and others were 76.66±10.603, 71.93±7.61, and 71.33±7.737 respectively with no statistical association (P=0.192). The mean pleural fluid protein (mean±SD) in MPE, TPE, and "others" patients were 4.4263±0.35964, 3.9836±0.22595, and 3.9933±0.43976 g/dL, respectively, strong association with likely diagnosis (P<0.001). The mean pleural fluid LDH in MPE, TPE, and "Others" was 960.17±107.513, 827.86±74.366, and 837.33±85.271 U/L, respectively. LDH levels had statistical association with likely diagnosis (P<0.002). Average ADA levels in pleural fluids of MPE, TPE, and "Others" were 19.27±6.652, 47.86±13.626, and 24.67±6.218 U/L, respectively. These levels were strongly associated with likely diagnosis (P<0.001) Table 3b.

Table 3b shows distribution of serum and pleural fluid biomarkers according to the diagnosis. The overall mean CR was 40.50±19.83. In MPE, TPE, and "Others", the mean CR was 49.1839±14.698, 19.2874±16.354, and 30.6107±17.342, respectively. Total non-MPE (TPE+Others) mean was 22.6844±17.0437. CR with levels above 20 showed very strong statistical association with MPE diagnosis in patients of PE (P<0.001). Similarly, the mean CR plus in all patients was found to be 54.58±28.14. According to diagnosis, the means were 65.5645±22.576, 27.3255±24.356 and 43.1169±25.622 in MPE, TPE, and "Others" respectively. The mean of CR plus in non-MPE patients was 32.0629±25.1750. Levels above 30 had shown strong association with MPE diagnosis (P<0.001) Table 4.

Table 4 shows the distribution of mean CR and CR plus with statistical association. Both CR and CR plus had sensitivity of 95.12% (95% CI 80.03–98.64), specificity of 80% (95% CI 60.80–91.16), positive predictive value of 90.69, and negative predictive value of 88.88 in diagnosing MPE. Both have a positive likelihood ratio of 4.756 suggesting PE patients having values higher than 20 for CR or values >30 for CR plus are 4 or more times like to have malignant effusion.

DISCUSSION

In suspected PE, we have to determine amount, etiology and type of effusion. In 1972, Porcel and Light,[1] developed criterion for the diagnostic separation of transudates from exudates. Subsequently, other study used modified Light's criteria using new cut-off values.[10] In accordance with Ren and Xu,[9] and Han et al.,[10] study, where CR, and CR plus and other parameters were compared between patients with MPE and those with TPE in two age groups (≤50 and >50 years). They concluded that >50 years age is a very important parameter for diagnosing MPE. Similar findings were reported by Verma et al.,[11] and a study in Lebanon. Ibrahim et al.,[12] study showed that Malignant effusions were more frequent among the older age groups, 73.6% patients with malignant effusions were older than 50 years of age. This study shows MPE was more common in males but was not statistically significant due to small sample size. High number of female patients with MPE diagnosis might be due to increasing smoking habit and adenocarcinoma is more common in female and most MPE was due to adenocarcinoma. This correlated with the study done by Korczyński et al.,[13] in which the men were 54.3% and

Table 3b: Distribution of biomarkers according to diagnosis (total n=61)

Biomarkers	Diagnosis	n	Mean	SD	Min	Max	P-value
Serum protein	MPE	41	3.9229	0.40220	3.01	4.60	0.007
	TPE	14	3.5164	0.43793	2.90	2.90	
	Others	6	3.6667	0.42740	3.10	3.10	
Serum LDH	MPE	41	962.71	83.914	641	1024	<0.001
	TPE	14	754.86	131.200	530	976	
	Others	6	681.00	212.385	436	967	
Pleural fluid lymphocyte	MPE	41	76.66	10.603	57	95	0.192
	TPE	14	71.93	7.610	60	85	
	Others	6	71.33	7.737	60	82	
Pleural fluid protein	MPE	41	4.4263	0.35964	3.82	5.08	<0.001
	TPE	14	3.9836	0.22595	3.56	4.51	
	Others	6	3.9933	0.43976	3.46	4.68	
Pleural fluid LDH	MPE	41	960.17	107.513	746	1243	<0.002
	TPE	14	872.86	74.366	719	988	
	Others	6	837.33	85.271	735	975	
Pleural fluid ADA	MPE	41	19.27	6.652	11	44	<0.001
	TPE	14	47.86	13.626	13	68	
	Others	6	24.67	6.218	16	33	

MPE: Malignant pleural effusions, TPE: Tuberculous pleural effusions, LDH: Lactate dehydrogenase, ADA: Adenosine deaminase

Table 4: Cancer ratio and cancer ratio plus in study subjects

Ratio	Diagnosis	Number	Mean	SD	Min	Max	P-value
Cancer Ratio	All	61	40.50	19.83	9.26	77.27	<0.001
	MPE	41	49.1839	14.6989	18.85	77.27	
	TPE	14	19.2874	16.3544	9.26	75.07	
	Others	6	30.6107	17.3420	17.44	60.43	
Cancer ratio plus	All	61	54.58	28.14	12.87	111.89	<0.001
	MPE	41	49.1839	14.6989	18.85	77.27	
	TPE	14	19.2874	16.3544	9.26	75.07	
	Others	6	30.6107	17.3420	17.44	60.43	

MPE: Malignant pleural effusions, TPE: Tuberculous pleural effusions

women 45.7%. Smokers have higher risk of TPE. Tewatia et al.,[14] showed that smoking cigarette, beedi or either of the two have Odds ratios (OR) of 19.22 (P<0.0001), 2.89 (P=0.0006) and 4.57 (P<0.0001) respectively. ORs for developing TPE increased with an increase in beedi or cigarette consumption, duration and pack years of smoking (P<0.001 each). This study also showed 60% of MPE patients are smoker. Out of 61 patients 41 (67.2%) are MPE, 14 (23%) were TPE and 6 (9.8%) had PE due to different etiology. Among 41 MPE almost 23 cases were due to adeno carcinoma, and mostly it is among females, 15 cases were due to squamous cell carcinoma and small cell carcinoma. Other 3 cases were due to metastatic malignancy from breast, thyroid, testes. In a similar study by Reddy et al.,[15] over distribution of PE cases were tuberculosis (38%), followed by parapneumonic effusion (28.5%) and MPE (22.2%). 73.8% patients had hemorrhagic and 23.2% had straw color as we have exclusively recruited patients with exudative effusion. Major diagnosis in our cases is MPE of which 87.8% were hemorrhagic. This corroborates with findings of Assawasaksakul et al.,[16] and Tian et al.,[17] studies. MPE had higher serum and pleural fluid protein. This level correlated with the pleural fluid levels in the study by Romero-Candeira et al., studies.[18] Mean pleural fluid LDH value was 960.17 U/L in case of MPE and for TPE is 872.86 U/L. It was statistically significant (P<0.05). Similar findings were corroborated by Zhang et al.[8] Cell smear positivity for malignant cell were around 17%. It does not corroborate with findings of similar studies by Porcel and Light,[1] and Assawasaksakul et al.[16] All these studies showed that malignant cell smear positivity between 45% and 60% and its diagnostic yield increases with subsequent sampling.[14,15] In this study cell block positivity for MPE is around 26.8%. It is very low compared to study results by Porcel and Light, Assawasaksakul et al.[16] All these studies showed that malignant cell Block is superior than cell smear. And diagnostic yield increases when combination of this two is used. Low yield in our study is probably attributed to small sample size and less dependence on these methods as majority of the patients undergone pleural biopsy for confirmation. The mean pleural ADA levels was 19.67±6.65 U/L in MPE and in TPE it is 47.86±13.62 U/L (P<0.001). These levels correlated with the studies done by Mehta et al.,[2] Helmy et al.,[3] which showed only tuberculous effusion had ADA value more than 40 U/L and MPE had below 40U/L. In this study, the mean serum LDH in MPE

was 960.17±107.513, that of TPE was 827.86±74.366 and "Others" was 837.33±85.271 with a P<0.002. This correlated with the studies done by Malhotra et al.,[19] and Lee et al.,[20] where they stated that there was high chance malignancy when serum LDH >450. Higher values for MPE were statistically significant (P<0.001) when cut off of CR was 20. Studies by Verma et al.,[11] and Han et al.,[10] has found sensitivity and specificity of CR in diagnosing MPE is around 90% similar to our study. But the sensitivity of CR in Korczyński et al.,[13] was 94% but specificity was around 70%. In the Study Zhang et al.,[8] took the cut off 14.97 for CR and get around 90% accuracy in diagnosing MPE. In this study the mean value of CR plus was much higher than other two categories. Taking cut off value of 30, level of CR plus found to be statistically significant. Ren et al.,[9] took the cut off value for CR Plus was 41 and found more than 90% accuracy in diagnosing MPE. Verma et al.,[11] also found similar type of result as this study when cut of CR Plus taken 30. Specificity was 94.1 and 95.6% respectively. Ren et al.,[9] also found that CR plus had high diagnostic accuracy for MPE.

Limitation of the study

The sample size was small, and no randomization was done. The study was done in the tertiary care hospital in a metro city, so we missed the category of patients attending the primary and secondary care hospitals. We exclusively chose exudative effusion which may lead to selection bias. Further larger studies will prove helpful in selecting cutoff values for both CR and CR plus in clinical application.

CONCLUSION

In conclusion, it can be said that the patients with MPE had significantly higher level of CR and CR Plus value than the non-MPE group. Due to lack of infrastructure and efficient human resources, diagnosis of MPE is delayed in most of the cases and that increases morbidity and mortality of the patients. This study was picked up with the aim of finding a fastest, reliable, cost-effective and easily available marker to identify the MPE.

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REFERENCES

1. Porcel JM and Light RW. Diagnostic approach to pleural effusions in adults. Am Fam Physician. 2006;73(7):1211-1220.
2. Mehta AA, Gupta AS, Ahmed S and Rajesh V. Diagnostic utility of adenosine deaminase in exudative pleural effusions. Lung India. 2014;31(2):142.
   https://doi.org/10.4103/0970-2113.129842
3. Helmy NA, Eissa SA, Masoud HH, Elessawy AF and Ahmed RI. Diagnostic value of adenosine deaminase in tuberculous and malignant pleural effusion. Egypt J Chest Dis Tuberc. 2012;61(4):413-417.
   https://doi.org/10.5588/ijtld.22.0514
4. Soh J, Toyooka S, Aoe K, Asano H, Ichihara S, Katayama H, et al. Usefulness of EGFR mutation screening in pleural fluid to predict the clinical outcome of gefitinib treated patients with lung cancer. Int J Cancer. 2006;66(10):78.
   https://doi.org/10.1002/ijc.22190
5. Banerjee AK, Willetts I, Robenson JF, Robertson JF and Blamey RW. Pleural effusion in breast cancer: A review of the Nottingham experience. Eur Surg Oncol. 1994;20(1):33-36.
6. Antonangelo L, Sales RK, Corá AP, Acencio MM, Teixeira LR and Vargas FS. Pleural fluid tumour markers in malignant pleural effusion with inconclusive cytologic results. Curr Oncol. 2015;22(5):e336-e341.
   https://doi.org/10.3747/co.22.2563
7. Drent M, Cobben NA, Henderson RF, Wouters EF and Van Dieijen-Visser M. Usefulness of lactate dehydrogenase and its isoenzymes as indicators of lung damage or inflammation. Eur Respir J. 1996;9(8):1736-1742.
   https://doi.org/10.1183/09031936.96.09081736
8. Zhang F, Hu L, Wang J, Chen J, Chen J, Wang Y. Clinical value of jointly detection serum lactate dehydrogenase/pleural fluid adenosine deaminase and pleural fluid carcinoembryonic antigen in the identification of malignant pleural effusion. J Clin Lab Anal. 2017;31:e22106.
   https://doi.org/10.1002/jcla.22106
9. Ren Z and Xu L. Role of cancer ratio and other new parameters in the differential diagnosis of malignant pleural effusion. Clinics (Sao Paulo). 2021;76:e2515.
   https://doi.org/10.6061/clinics/2021/e2515
10. Han YQ, Zhang L, Yan L, Ouyang PH, Li P and Hu ZD. Diagnostic accuracy of cancer ratio for malignant pleural effusion: A systematic review and meta-analysis. Ann Transl Med. 2019;7(20):554.
    https://doi.org/10.21037/atm.2019.09.85
11. Verma A, Abisheganaden J and Light RW. Identifying malignant pleural effusion by a cancer ratio (serum LDH: Pleural fluid ADA ratio). Lung. 2016;194(1):147-153.
    https://doi.org/10.1007/s00408-015-9831-6
12. Ibrahim A, Rida A, Malass I and Tayara I. Etiology of pleural effusion among adults in three university hospitals in beirut: A one-year retrospective cross sectional analytical study. Int J Respir Pulm Med. 2021;8:149.
    https://doi.org/10.23937/2378-3516/1410149
13. Korczyński P, Mierzejewski M, Krenke R, Safianowska A and Light RW. Cancer ratio and other new parameters for differentiation between malignant and nonmalignant pleural effusions. Pol Arch Intern Med. 2018;128(6):354-361.
    https://doi.org/10.20452/pamw.4278
14. Tewatia P, Kaushik RM, Kaushik R and Kumar S. Tobacco smoking as a risk factor for tuberculous pleural effusion: A case-

control study. Glob Health Epidemiol Genom. 2020;5:e1.
https://doi.org/10.1017/gheg.2020.1

15. Reddy SL, Varaprasad K, Narahari N, Bhaskar K, Varma GR and Paramjyothi GK. Clinical and etiological profile of an exudative pleural effusion in a tertiary care center. Indian J Respir Care. 2019;8(1):22-26.
https://doi.org/10.4103/ijrc.ijrc_8_18
16. Assawasaksakul T, Boonsarngsuk V and Incharoen P. A comparative study of conventional cytology and cell block method in the diagnosis of pleural effusion. J Thorac Dis. 2017;9(9):3161-3167.
https://doi.org/10.21037/jtd.2017.08.52
17. Tian P, Shen Y, Wan C, Yang T, An J, Yi Q, et al. Diagnostic value of survivin for malignant pleural effusion: A clinical study and meta-analysis. Int J Clin Exp Pathol. 2014;7(9):5880-5887.
18. Romero-Candeira S, Hernández L, Romero-Brufao S, Orts D, Fernandez C and Martin C. Is it meaningful to use biochemical parameters to discriminate between transudative and exudative pleural effusions? Chest. 2002;122(5):1524-1529.
https://doi.org/10.1378/chest.122.5.1524
19. Malhotra P, Sidhu LS and Singh SP. Serum lactate dehydrogenase level in various malignancies. Neoplasma. 1986;33(5):641-647.
20. Lee DS, Park KR, Kim SJ, Chung MJ, Lee YH, Chang JH, et al. Serum lactate dehydrogenase levels at presentation in stage IV non-small cell lung cancer: Predictive value of metastases and relation to survival outcomes. Tumor Biol. 20161;37(1):619-625.
https://doi.org/10.1007/s13277-015-3776-5

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SS- Prepared first draft of manuscript, data collection, data analysis; **AM**- Interpreted the result, reviewed the literature; **AKD**- Concept, coordination, review of literature and manuscript preparation; **RKH-** Concept and design of the study, statistically analyzed and interpreted, preparation of manuscript and revision of manuscript and submission; **SP-** Co-ordination and manuscript revision.

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