INTRODUCTION

Malignant pleural effusion (MPE) is defined as the accumulation of a significant number of exudates in the pleural space, accompanied by the presence of malignant cells or tumor tissue. Epidemiological information is limited, but an estimated 50,000 new diagnoses are made in UK each year.

The majority is due to metastatic disease most commonly lung cancer in men and breast cancer in women. These two cancers combined account for 50-60% of all malignant pleural effusion.\(^2\) Hodgkin and non-hodgkin lymphoma is the third most common cause of MPE and also the most common cause in young adults.\(^3\) Mesothelioma is the most common type of primary pleural tumor which is associated with malignant pleural effusion in more than 90% of cases.\(^4\) No primary tumor is identified in 5% to 10% of malignant pleural effusion.\(^5\)

A malignant tumor can cause a pleural effusion both directly and indirectly. Breech in the integrity of lymphatic system between the parietal pleura and mediastinal lymph nodes can result in pleural fluid formation.\(^6\) Direct tumor invasion of pleura may also contribute to the formation of pleural effusion.\(^7\)
Despite the progress in cancer treatment, the management of MPE remains palliative, with median survival ranging from 3 to 12 months. A number of factors may help to predict survival of patients including tumor characteristics, extent of disease, co-morbidities and the composition of effusion. To this, LENT score (pleural fluid LDH, Eastern Cooperative Oncology Group (ECOG) performance score, neutrophil to lymphocyte ratio and tumor type) was proposed as a tool for accurate prediction of survival. LENT prognostic score is the first validated prognostic score in MPE, which predicts survival with significantly better accuracy than ECOG. Performance status alone can be used to guide decision making in the treatment of MPE.

With the heterogeneity in the group of patients with MPE, there is a challenge to predict prognosis and survival. With improved techniques in the management of pleural effusion and better oncological options, there is an increasing need for good prognostication to tailor the most appropriate treatment. The goal of this study was to identify the prognostic factors and overall survival in patients with MPE.

**METHODS**

It is a hospital based prospective study done in department of pulmonary medicine, Guwahati medical college, Assam for the period of one year from August 2018 to 2019. Fifty-three patients of any age group with malignant pleural effusion and or thoracoscopic biopsy specimen positive for malignancy were included in the study. Informed consent was obtained from every participant before any intervention. Patients who denied consent and those with non aspirable pleural fluid were excluded from this study. Ethical committee clearance has been obtained for this study. Pleural fluid sugar, LDH, total count, differential count, malignant cytology of pleural fluid and thoracoscopy biopsy of pleura were evaluated. Performance status by ECOG score and LENT score was calculated at the time of diagnosis. Survival time was defined as the time from diagnosis to death or the last follow-up. Median survival time was calculated using Kaplan-Meier analysis curve.

**Statistical analysis**

Kaplan-Meier curves were computed for the study participants according to various parameters. Log rank (Mantel-cox) test was used to statistically determine the significant difference in survival time between the patients grouped according to the parameters, p value of less than 0.001 was taken to be significant.

**RESULTS**

Out of 53 patients in this study 34 patients were male and 19 patients were female. Age of male patients was from 24 to 75 years (56.03±12.08 years) and female age was from 22 to 82 years (50.84±15.55 years). Patients’ characteristics are presented in (Table 1).

| Characteristics                      | N  | %   |
|--------------------------------------|----|-----|
| **Gender**                           |    |     |
| Male                                 | 33 | 62.2|
| Female                               | 20 | 37.7|
| **Diagnosis**                        |    |     |
| Adenocarcinoma lung                  | 31 | 58.5|
| Breast cancer                        | 1  | 1.9 |
| Mesothelioma                         | 3  | 5.7 |
| Non-hodgkin lymphoma                 | 2  | 3.8 |
| Non-small cell lung carcinoma lung   | 10 | 18.9|
| Ovarian cancer                       | 1  | 1.9 |
| Squamous cell carcinoma lung         | 5  | 9.4 |
| **LENT score**                       |    |     |
| Low risk                             | 3  | 5.7 |
| Moderate risk                        | 35 | 66  |
| High risk                            | 15 | 28.3|
| **ECOG score**                       |    |     |
| 0                                    | 1  | 1.9 |
| 1                                    | 27 | 50.9|
| 2                                    | 13 | 24.5|
| 3                                    | 8  | 15.1|
| 4                                    | 4  | 7.5 |
| **PF side**                          |    |     |
| Right                                | 28 | 52.8|
| Left                                 | 22 | 41.5|
| Bilateral                            | 3  | 5.7 |
| **PF malignant cytology**            |    |     |
| Positive                             | 36 | 67.9|
| Negative                             | 17 | 32.1|
| **Survival status**                  |    |     |
| Alive                                | 11 | 20.8|
| Dead                                 | 42 | 79.2|
| **PF sugar category**                |    |     |
| <20                                   | 9  | 17  |
| >20                                   | 44 | 83  |

Most common cause of malignant pleural effusion was lung carcinoma (46 (86.79%), among which adenocarcinoma was the most common 31 (58.5%) followed by NSCLC 10 (18.0%) and squamous carcinoma in 5 (9.4%) of cases. MPE due to mesothelioma, ovarian carcinoma, breast carcinoma and non-hodgkin lymphoma was 3, 1, 1 and 2 cases respectively (Table 2).

LENT score was done in this study. Low risk, moderate risk and high risk was found in 3 (5.7%), 35 (66%) and 15 (28.3%) respectively (Figure 1). ECOG score was done and found highest in score-1, 27 (50.9%) followed by score-2, 13 (24.5%) (Figure 2). Out of 53 patients with MPE 28 (52.8%) of patients were having right side, 22
(41.5%) left side and 3 (5.7%) had bilateral pleural effusion.

Malignant cytology of pleural fluid was positive in 36 (67.9%) of patients and thoracoscopy biopsy positive in 17 (32.1%) patients. Pleural fluid sugar was estimated in all patients with effusion, pleural fluid sugar >20 mg/dl found in 44 (83%) and <20 mg/dl found in 9 (17%) patients. Out of 53 patients with malignant pleural effusion 42 (79.2%) died within one year of follow up.

Kaplan-Meier curves were computed for the study participants according to various parameters. Log rank (Mantel-cox) test was used to statistically determine the significant difference in survival time between the patients grouped according to the parameters.

The median survival time of patients with pleural fluid sugar less than or equal to 20 was found to be 3 months, while those with >20 was having a higher median survival time of 4.5 months. However, this difference in survival time was not statistically significant (p=0.108) (Figure 3).

### Table 2: Types of carcinoma causing MPE.

| MPE          | Type of cancer                      | Number | %   |
|--------------|-------------------------------------|--------|-----|
| Lung carcinoma | Adenocarcinoma                      | 31     | 58.5|
|              | Non-small cell lung carcinoma       | 10     | 18.9|
|              | Squamous cell carcinoma             | 5      | 9.4 |
| Outside lung | Non-hodgkin lymphoma                | 2      | 3.8 |
|              | Breast cancer                       | 1      | 1.9 |
|              | Ovarian cancer                      | 1      | 1.9 |
|              | Mesothelioma                        | 3      | 5.7 |

The median survival time of low risk LENT score patients was found to be 12 months, while medium risk LENT score patients were having a median survival time of 5.2 months and those with high risk LENT score had a median survival time of 2.5 months. This difference in survival time between the groups was statistically significant (p<0.001) i.e., as the risk increases with LENT score, the median survival time decreased (Figure 4).

The median survival time of patients with ECOG score of 1 was found to be 6.5 months, score of 2 had a median survival time of 4 months, score 3 had a median survival time of 2.5 months and score 4 had a median survival time of 1 month. The survival time gradually decreased as the ECOG score increased and this decrease was statistically significant (p<0.001) i.e., the patients with higher ECOG scores were found to be having lesser survival time (Figure 5).
Figure 4: Survival analysis according to the LENT score.

Figure 5: Survival analysis according to ECOG score.

Figure 6: Survival analysis according to the side of the pleural effusion.

The median survival time of patients with left side pleural fluid was found to be 4 months, while those with right side pleural fluid were having a higher median survival time of 4.2 months and those with bilateral pleural fluid had a mean survival time of 2 months. This difference in survival time between the sides was not statistically significant (p=0.286) (Figure 6).

DISCUSSION

In this study it was found that lung carcinoma was the most common cause of malignant pleural effusion 46 (86.79%), and among the lung carcinoma, adenocarcinoma 31 (58.5%) was the most common cause of malignant pleural effusion followed by NSCLC 10 (18.0%). According to study conducted by Saha et al, in eastern India most common etiology was lung cancer (88.9%) among which most common etiology was adenocarcinoma (52.8%), followed by squamous cell carcinoma (13). Another study by Chatterjee et al, revealed that most common etiology of MPE is lung carcinoma (44%) followed by breast carcinoma (19.8%).

In our study it was shown that pleural fluid sugar does not effects on survival of the patient. In contrast to our study Martinez-Moragon et al, showed that patients with low pleural fluid glucose (<60 mg/dl) and high LDH (>600 U/l) had poor survival and failure of pleurodesis. Zulkifli et al, conducted a study on 30 day survival of patients with MPE which showed pleural fluid sugar <60mg/dl was 22 days.

In our study LENT low risk score the median survival was 12 months and higher risk LENT score was 2.5 months. A study done by Ari et al, showed that the median survival in high risk LENT score group was 44 days. Similar to our study, a study conducted by Jenifer et al, at south India showed that median survival time of moderate and high LENT scores are 6 months and 3 months respectively.

In this study it was shown that the median survival time of patients with ECOG score of 1 was found to be 6.5 months and score 4 had a median survival time of 1 month. Similar study done by Zambani et al showed that ECOG grade 0 the median survival was 55 months and ECOG grade 4 the median survival was 1 month.

In this study it was shown that the median survival time of left sided pleural, right sided and bilateral effusion was 4 months, 4.2 months and 2 months respectively. Similar study done by Jenifer et al, showed that survival time of bilateral pleural effusion was 30 days. Biasi et al, in their analysis of a cohort of patients who underwent thoracocentesis, also reported higher mortality at 30 days in patients with bilateral MPE.

CONCLUSION

From the study it has been concluded that adenocarcinoma lung is the most common etiology of malignant pleural effusion. The median overall survival time of 4.2 months and those with bilateral pleural fluid had a mean survival time of 2 months. This difference in survival time between the sides was not statistically significant (p=0.286) (Figure 6).
time is 4 months. Higher ECOG score and LENT scores are associated with shorter survival time.

**Funding:** No funding sources

**Conflict of interest:** None declared

**Ethical approval:** The study was approved by the Institutional Ethics Committee

**REFERENCES**

1. Rahman NM, Ali NJ, Brown G. Local anaesthetic thoracoscopy: British Thoracic Society Pleural Disease Guideline 2010. Thorax. 2010;65:54-60.
2. Mongardon N, Pinton-Gonnet C, Szekely B. Assessment of chronic pain after thoracotomy: a 1-year prevalence study. Clin J Pain. 2011;27(8):677-81.
3. Antony VB, Loddenkemper R, Astoul P, Boutin C, Goldstraw P, Hott J, et al. Management of malignant pleural effusions. Eur Respir J. 2010;65:32-40.
4. Johnston WW. The malignant pleural effusion. A review of cytopathologic diagnoses of 584 specimens from 472 consecutive patients. Cancer. 1985;56(4):905-9.
5. Meyer PC. Metastatic carcinoma of the pleura. Thorax. 2119;66:437-43.
6. Andrews BS, Aroran S, Shadforth MF, Goldberg SK, Davis JS. The role of immune complexes in the pathogenesis of pleural effusions. Am Rev Respir Dis. 1981;124:115-20.
7. Antony VB, Loddenkemper R, Astoul P, Boutin C, Goldstraw P, Hott J, et al. Management of malignant pleural effusions. Eur Respir J. 2001;18(2):402-19.
8. Pilling JE, Dusmet ME, Ladas G. Prognostic factors for survival after surgical palliation of malignant pleural effusion. J Thorac Oncol. 2010;5:1544-50.
9. Bielsa S, Salud A, Martinez M. Prognostic significance of pleural fluid data in patients with malignant effusion. Eur J Intern Med. 2008;19:334-9.
10. Burrows CM, Mathews WC, Colt HG. Predicting survival in patients with recurrent symptomatic malignant effusions: an assessment of the prognostic values of physiologic, morphologic, and quality of life measures of extent of disease. Chest. 2000;117:73-8.
11. Clive AO, Kahan BC, Hooper CE. Predicting survival in malignant pleural effusion: development and validation of the LENT prognostic score. Thorax. 2014;69:1098-104.
12. Saha K, Maikap MK. Demographic, clinical, biochemical, radiological and etiological characteristics of malignant pleural effusion from Eastern India. Indian J Cancer. 2017;54:257-61.
13. Chatterjee, Kshitij MD. Etiology of malignant pleural effusion and utilization of diagnostic and therapeutic procedures. J of Bronchology and Interventional Pulmonology. 2017;24(1):10-2.
14. Moragon E, Aparicio J, Sanchis J. Malignant pleural effusion: prognostic factors for survival and response to chemical pleurodesis in a series of 120 cases. Respiration. 1998;65:108-13.
15. Amin Z, Iskandar SD, Sibli. Prognostic factors of 30 days survival of patients with malignant pleural effusion. Indian J Palliat Care. 2017;23(3):321-4.
16. Ari. LENT prognostic score for malignant pleural effusion: How does our cohort Compare. Lung cancer. 2018;115:51.
17. Jeba J, Cherian RM, Thangakunam B. Prognostic factors of malignant pleural effusion among palliative care outpatients: a retrospective study. Indian J Palliat Care. 2018;24:184-8.
18. Zambant. Important prognostic factors for survival in patients with malignant pleural effusion. BMJ Pulmonary Medicine. 2015;15:29.
19. Biass EM, Pisani MA, Murphy TE, Araujo K, Kookoools A, Argento AC, et al. Mortality among patients with pleural effusion undergoing thoracocentesis. Eur Respir J. 2015;46:495-502.

**Cite this article as:** Ramesh S, Hazarika B, Sarma J, Karwa R. Etiology and prognostic evaluation of malignant pleural effusion. Int J Community Med Public Health 2020;7:1405-9.