

FREQUENCY OF MALIGNANT PLEURAL EFFUSIONS IN BREAST CANCER PATIENTS

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Abstract

Objective:

To determine the occurrence of malignant pleural effusions in breast cancer patients.

Study Design:

Cross-sectional study

Place/ Duration of Study:

Department of Internal Medicine, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore, from 01 April 2024 to 31 January 2025.

Methodology:

The research team conducted this cross-sectional study at Shaukat Khanum Memorial Cancer Hospital and Research Centre from 01 April 2024 to 31 January 2025. The study involved 100 female breast cancer patients who were between 18 and 68 years old and who underwent thoracentesis with pleural fluid cytology. The researchers excluded patients with two different types of cancer. The diagnosis of malignant pleural effusion required cytological examination. Statistical analysis of data was conducted using SPSS version 25, and the researchers applied the chi-square test while they considered p-values reaching 0.05 as the threshold for statistical significance.

Results:

The mean age was 43.43 ± 10.83 years, BMI 25.69 ± 5.35 kg/m², and cancer duration 39.34 ± 32.80 months, with 62% cytology-positive cases and 38% negative cases. The study found important links between malignant pleural effusion and eight specific factors which included age ($p = 0.001$), cancer duration ($p < 0.001$), smoking habits ($p = 0.004$), hypertension ($p = 0.007$), family history ($p < 0.001$), cancer stage ($p < 0.001$), and treatment methods ($p < 0.001$). The examination of BMI revealed no important relationship to the study results ($p = 0.357$).

Conclusion:

MPE was significantly associated with age, duration of cancer, smoking, hypertension, family history, stage, and treatment type ($p \leq 0.007$). BMI showed no significant association ($p = 0.357$), indicating that disease-related factors are the main determinants of MPE in breast cancer patients.

Introduction:

An effusion is a collection of fluid in the body. A pleural effusion occurs when fluid accumulates in the pleural space, which exists between the lung exterior and the chest wall interior. The medical term malignant pleural effusion refers to pleural effusions that result from cancer.¹ Breast cancer is one of the most common malignancies among women throughout the world and is the major cause of most cancer-related deaths.² The data show that approximately 50% of malignant tumors can present with malignant pleural effusion. Malignant pleural effusions occur most frequently in lung cancer, breast cancer, and lymphoma, with their occurrence reaching 75% in these conditions.³ Malignant pleural effusions represent one of the typical complications that arise from advanced malignant tumors, and patients with this condition usually survive between 3 and 12 months.^{4,5}

Advanced metastatic disease produces malignant pleural effusions as a result. Patients who experience malignant pleural effusions face a poor prognosis, which leads to their death within 6 months after diagnosis. The development of new treatments for malignant pleural effusion emerged from both medical technology advancements and research studies that explored the disease's progression. These new treatments include pleurodesis and indwelling pleural catheter insertion. The medical field currently lacks effective treatment solutions for patients who experience persistent or recurring malignant pleural effusion.⁷ Malignant pleural effusions occur frequently in patients who have metastatic disease because they affect 15% of all cancer patients.^{8,10} A study found that malignant pleural effusions occurred in 1% of all cases, while 8-40% of breast carcinoma cases showed this condition.¹⁰ The study rationale is to estimate the frequency of malignant pleural effusion in female patients having carcinoma of the breast. Limited research has been conducted previously, and no local study has been carried out in this context before. Therefore, there is a need to conduct a study and get evidence for the local population. Therefore, it is important to assess the burden in the local population and determine the true magnitude of

the problem within the local context. So that in the future, we may implement more appropriate diagnostic and management protocols and also reduce the chances of malignant pleural effusions. This will help to improve our practice and knowledge.

Methodology:

The study was conducted in the Department of Internal Medicine at Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore from 01 April 2024 till 31 January 2025 after official approval of the research synopsis. The WHO calculator determines a sample size of 100 cases, which has a 95% confidence level and a 7% margin of error, and includes 15% of malignant pleural effusions, which occur in cancer patients.¹⁰

Inclusion criteria: Female patients aged 18-68 years, diagnosed with Breast cancer, undergoing thoracentesis, and undergoing Fluid cytology test on the pleural fluid sample.

Exclusion criteria: Female patients with dual primary malignancies like simultaneous Lung carcinomas, Colorectal carcinoma, or Ovarian carcinoma.

The study had included patients who had confirmed pleural effusion through chest radiographs and ultrasound examinations and who meet all study inclusion requirements from hospital wards. Detailed information, including age, BMI, presence of biopsy-proven breast cancer, and duration since cancer diagnosis, were noted. Then, patients underwent thoracentesis after ultrasound-guided marking, and samples were taken. Samples were sent to the hospital laboratory for fluid cytology testing. Reports were assessed, and malignant pleural effusions was noted. Patients were managed according to standard protocol.

Researchers entered data into SPSS version 25 for their analysis. The researchers used quantitative variables such as age, BMI, and cancer duration as their mean values and standard deviations. Frequency and percentage to present qualitative variables, which include history of smoking, hypertension (BP>160/90), family history of

cancer, stage of cancer, diabetes mellitus, treatment received for cancer, and malignant pleural effusions were included. Data was stratified for age, BMI, duration of cancer, history of smoking, hypertension, family history of cancer, cancer stage, and treatment received for cancer. The researchers used the chi-square test to compare malignant pleural effusion between MPE-positive and MPE-negative groups. Threshold of 0.05, below which P-values indicated statistical

significance. This study employed cross-sectional sampling to recruit participants.

Results:

The average patient age reached 43.43 ± 10.83 years. The average body mass index (BMI) for the study participants measured 25.69 ± 5.35 kg/m². The average cancer duration among patients reached 39.34 months, but showed wide differences in disease length throughout the patient group.

Table I: Descriptive statistics of continuous variables (n = 100)

Variable	Mean $\pm$ SD
Age (years)	43.43 ± 10.83
Body Mass Index (BMI)	25.69 ± 5.35
Duration of Cancer in Months	39.34 ± 32.80

Among 100 patients, most were non-smokers (88%), while 32% had hypertension and 25% had diabetes mellitus. 32% of the past cases were with a positive family history of malignancy. Regarding cancer stage, majority presented at Stage II (57%), followed by Stage III (20%), Stage IV (14%), and Stage I (9%). In terms of treatment, most patients

received Treatment 2 (56%), while the remaining received other modalities. Cytology was positive for malignant pleural effusion in 62% of cases and negative in 38%. Among non-malignant cytology findings, reactive mesothelial cells were most common (16%), followed by lymphocytes (11%), inflammation (9%), and hemorrhagic fluid (2%).

Table II: Frequency distribution of categorical variables (n = 100)

Variables	Category	n(%)
History of smoking	No	88 (88.0%)
	Yes	12 (12.0%)
Hypertension	No	68 (68.0%)
	Yes	32 (32.0%)
Diabetes Mellitus (DM)	No	75 (75.0%)
	Yes	25 (25.0%)
Family history of Cancer	No	68 (68.0%)
	Yes	32 (32.0%)
Stage of cancer at first presentation	Stage I	9 (9.0%)
	Stage II	57 (57.0%)
	Stage III	20 (20.0%)
	Stage IV	14 (14.0%)
Treatment receiving for cancer	1	10 (10.0%)
	2	56 (56.0%)
	3	20 (20.0%)
	4	14 (14.0%)

Fluid cytology positive for malignant cells	Yes	62 (62.0%)
	No	38 (38.0%)
Non-malignant cytology findings	Malignant	62 (62.0%)
	Lymphocytes	11 (11.0%)
	Inflammation	9 (9.0%)
	Reactive mesothelial	16 (16.0%)
	Hemorrhagic	2 (2.0%)

Statistically significant differences were observed between the patients' cytology status and age group ($\chi^2 = 16.183$, $p = 0.001$), duration of cancer ($\chi^2 = 30.611$, $p < 0.001$), history of smoking ($\chi^2 = 8.358$, $p = 0.004$), hypertension ($\chi^2 = 7.402$, $p = 0.007$), family history of cancer ($\chi^2 = 16.367$, $p < 0.001$), stage of cancer ($\chi^2 = 21.911$, $p < 0.001$), and treatment type ($\chi^2 = 18.794$, $p < 0.001$). Cytology-positive cases were more frequently observed

among patients aged 30–44 years, those with longer disease duration (13–36 months), smokers, hypertensive patients, individuals with a positive family history of cancer, advanced cancer stages (II–IV), and those receiving combination therapies. In contrast, the BMI group showed no statistically significant association with cytology status ($\chi^2 = 3.231$, $p = 0.357$), indicating no meaningful difference across BMI categories.

Table III: Association of Age Group, BMI Group, Duration of Cancer, History of Smoking, Hypertension, Family history of Cancer, Stage of Cancer, Treatment Receiving for Cancer with Malignant Pleural Effusion (MPE) (n=100)

Variables	Category	Absent	Present	Total	P-value
Age Group	18-29	14	6	20	0.001***
	30-44	17	36	53	
	45-59	5	20	25	
	60-68	2	0	2	
	Total	38	62	100	
BMI Group	<18.5	9	9	18	0.357
	18.5-24.9	15	19	34	
	25-29.9	9	22	31	
	≥30	5	12	17	
	Total	38	62	100	
Duration of Cancer group	≤12 months	22	5	27	0.001***
	13-36 months	7	32	39	
	37-72 months	5	17	22	
	>72 months	4	8	12	
	Total	38	62	100	
History of smoking	No	38	50	88	0.004**
	Yes	0	12	12	
	Total	38	62	100	
Hypertension	No	32	36	68	0.007**
	Yes	6	26	32	
	Total	38	62	100	
Family history of Cancer	No	35	33	68	0.001***
	Yes	3	29	32	
	Total	38	62	100	

Stage of cancer at first presentation	Stage I	9	0	9	0.001***
	Stage II	23	34	57	
	Stage III	5	15	20	
	Stage IV	1	13	14	
	Total	38	62	100	
Treatment receiving for cancer	Surgery Alone	9	1	10	0.001***
	Surgery + Chemotherapy	23	33	56	
	Chemotherapy + Radiotherapy	5	15	20	
	Chemotherapy + Palliative care	1	13	14	
	Total	38	62	100	

Note: Chi-square test was applied.

Discussion:

In the current study, the mean age was 43.43 ± 10.83 years, which is comparable with international studies reporting breast cancer predominantly in middle-aged women with a similar age distribution¹¹. The mean BMI was 25.69 ± 5.35 kg/m², which is consistent with regional data indicating overweight BMI in breast cancer populations; however, BMI has not shown a strong association with malignant pleural effusion in previous studies¹². The mean duration of cancer was 39.34 ± 32.80 months, showing wide variability. It is globally known that a long disease duration signifies built-up risks for pleural infiltration, possibly because the cancer has spread with time¹³.

Many patients were non-smokers (88%), while hypertension and diabetes mellitus were present in 32% and 25% of cases, respectively. A family history of cancer had been present in 32% of patients. Majority of patients presented at Stage II, which accounted for 57% of cases, while Stage III, Stage IV, and Stage I followed with 20%, 14%, and 9%, respectively. Cytology results confirmed malignant pleural effusion in 62% of cases, while 38% of cases tested negative. The study identified reactive mesothelial cells as the most common non-malignant finding, which occurred in 16% of cases, followed by lymphocytes at 11%, inflammation at 9%, and hemorrhagic fluid at 2%. The findings confirm previous research, which demonstrates that breast cancer patients develop additional health problems together with intermediate-to-advanced stage disease, which

increases their chances of developing pleural involvement^{12,13}.

The research found a significant link between age group and cytology status ($p=0.001$). In the age group of 30 to 44, the highest rate of positive-cytology cases was seen, while the 60-68 years age group showed no positive cases because malignant pleural effusion distribution differed across age groups. The finding matches earlier research, which discovered that middle-aged breast cancer patients develop pleural involvement through their active disease progression and their cancerous cells spreading to other body parts. Older patients show reduced incidence through two methods, including fewer cases in their group and surviving longer. The research discovered no significant relationship between BMI group and cytology status ($p=0.357$). The 25-29.9 kg/m² BMI group showed a higher number of cytology-positive cases, yet the overall distribution across BMI groups displayed no significant statistical distinction. This finding suggests that BMI alone is not a strong independent predictor of malignant pleural effusion in breast cancer, as outcomes are influenced more by tumor biology, disease stage, and metastatic burden. Large epidemiological studies and systematic reviews have also reported weak or inconsistent associations between BMI and advanced breast cancer outcomes^{14,15}.

There was a statistically significant association between the duration of cancer and the cytology status ($p<0.001$). Cytology-positive cases were most common among patients with 13–36 months duration of cancer, cytology-negative cases were

more common in those with <12 months disease duration, suggesting an increased likelihood of malignant pleural effusion with longer disease course. Previous studies indicate that longer disease duration is associated with increased tumor burden, higher risk of metastasis, and greater likelihood of malignant pleural effusion, with cohort studies confirming its association with advanced-stage complications^{16,17}.

Correspondence was established between history of smoking and cytology status (0.004), with all cytology-positive cases occurring among smokers. This indicates a strong association between smoking exposure and malignant pleural effusion in breast cancer patients. Large epidemiological and meta-analytic evidence shows that smoking promotes tumor progression, metastasis, and poorer outcomes, and is associated with advanced disease and pleural involvement due to systemic inflammation and tumor aggressiveness^{18,19}.

A significant statistical connection was perceived concerning the elements of smoking and cytology status ($p = 0.004$), the outcome being that all cytology-positive cases fall only among the smokers. This indicates a strong relationship between smoking exposure and malignant pleural effusion in breast cancer patients. Smoking has been consistently associated with more advanced cancer stages, increased risk of metastasis, and poorer clinical outcomes. It promotes tumor progression through systemic inflammation and biological aggressiveness. Evidence also shows that smokers with malignancy are more likely to develop pleural involvement and widespread disease dissemination compared to non-smokers^{18,19}. The study found a significant link between family cancer history and cytology results ($p < 0.001$) because more cytology-positive results occurred in patients who had cancer in their family. The genetic factors people inherit from their parents show a strong impact on how breast cancer patients develop malignant pleural effusion. The study results show that people who have a positive family history of breast cancer face higher chances of developing the disease with more severe symptoms because they carry genetic links to cancer²⁰.

The research established a statistically valid connection that linked the initial cancer presentation stage to the cytology results with a p-value below 0.001. The study found that advanced disease stages II through IV showed the highest rates of cytology-positive cases, whereas Stage I showed no positive cases, thus demonstrating that advanced disease stages lead to malignant pleural effusions. The findings support previous research, which identified cancer stage as a major factor for determining both metastasis and pleural involvement because advanced stages show increased tumor burden and systemic dissemination^{11,13}. The research established a statistically valid connection between the treatment method and the cytology results, reaching statistical significance at $p < 0.001$. The study found that patients who received combination therapies, particularly Surgery + Chemotherapy, showed higher rates of positive cytology results because these patients probably had more advanced disease, which involved their pleural space. Previous studies also show that combination treatment is typically required in advanced cancer stages, where metastatic spread and malignant pleural effusion are more frequent^{21,13}.

Conclusion:

The present study concludes that malignant pleural effusion (MPE) is significantly associated with age group, duration of cancer, smoking status, hypertension, family history of cancer, stage of disease, and treatment type ($p \leq 0.007$), indicating a strong relationship with disease progression and clinical risk factors. In contrast, BMI showed no statistically significant association with MPE ($p = 0.357$), suggesting it is not an independent predictor of cytology status in this cohort. The research results show that breast cancer patients develop malignant pleural effusion because of their advanced disease characteristics and their patient-specific clinical factors.

Limitations:

The research used data from one tertiary care hospital because it had only 100 study participants, which restricted the study's ability to

apply its results to all people. The study established a cross-sectional design which allowed researchers to find linkages between different variables but prevented them from determining which risk factors caused malignant pleural effusion (MPE). In addition, some chi-square analyses showed minor violations of test assumptions due to small expected cell counts in certain categories, which may have slightly affected the validity of the results. Furthermore, the limited availability of detailed clinical variables and the lack of long-term follow-up data may have restricted a more comprehensive assessment of disease progression and outcomes.

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