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Editorial

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Benefit of Targeted Therapy of Lung Cancer Treatment

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Abstract

Lung cancer is the second most common cancer and the leading cause of cancer deaths worldwide, with most deaths in Asia. By 2045, global deaths from lung cancer are expected to rise by 78%, reaching 3.24 million. Non-small cell lung cancer (NSCLC) makes up 85% of cases, and most are diagnosed at a late, metastatic stage. Traditional chemotherapy helps but has limited long-term benefits. Recent advances in genomics have led to new targeted therapies. These treatments, like osimertinib, alectinib, and lorlatinib, work by targeting specific genetic mutations. They have shown better results in controlling the disease and improving survival rates. Early drugs like gefitinib had limited success, but newer options now offer better outcomes in both advanced and early stages of the disease. FDA-approved therapies now target mutations in eight key genes. These treatments are changing the way we manage and treat lung cancer, offering hope for improved survival and quality of life.

Keywords: *Lung cancer, Targeted therapies, Non-small cell lung cancer (NSCLC), Precision medicine.*

Lung cancer is the second most common cancer worldwide and a leading cause of cancer-related deaths.[1] The majority (1,122,517; 61.9%) of lung cancer-related deaths were in the continent of Asia, and the four countries with the highest numbers of deaths from lung cancer were China (733,291 deaths, accounting for 39.7% of all deaths globally), the United States (138,225 deaths, 7.7%), Japan (83,369 deaths, 4.7%), and India (66,279 deaths, 3.7%).[1,2] By 2045, global deaths from lung cancer are anticipated to rise by 78.0%, reaching 3.24 million. Among continents, Asia is expected to experience the second-highest percentage increase in fatalities (+89.4%; 2,163,499 deaths), following Africa, which is projected to see a 122% rise (100,951 deaths).[3]

Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all new lung cancer cases, and more than two-thirds of these cases are metastatic at the time of diagnosis.[4] For many years, the standard treatment for advanced-stage lung cancer involved cytotoxic chemotherapy using a platinum-based doublet. Although these treatments contribute to better survival rates and enhanced quality of life, their effectiveness is limited, providing only modest responses and lacking long-term clinical benefits.[5] Advances in genomics leading to the identification of oncogenic driver gene aberrations have revolutionized the practice of thoracic oncology.[6]

Significant improvement in response rate and greater than three-year median survival in metastatic settings is now seen in subsets of patients. Molecular targeted therapies, including gefitinib and epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs), were first introduced in the 1990s for treating NSCLC. However, the initial response rate for unresectable

NSCLC was merely 10%.[6] The IPASS (Iressa Pan Asia Study) demonstrated an important outcome when oral gefitinib was compared with carboplatin-paclitaxel in patients with EGFR-mutant NSCLC; the objective response rate was 71% versus 1% between EGFR-mutant and wild-type patients, respectively.[7]

Drugs like osimertinib, alectinib, lorlatinib, and crizotinib work by blocking protein phosphorylation or inhibiting the proliferation of oncogenic signaling pathways.[8] A different mechanism is exhibited by the KRAS G12C inhibitor, such as sotorasib, which binds covalently to KRAS-mutated cysteine 12 residues at the switch II pocket.[9]

Currently, oncogenic aberrations in eight genes (EGFR, ALK, ROS1, BRAF, KRAS, NTRK, MET, and RET) have US Food and Drug Administration (FDA)-approved therapies.[10] These agents have typically been used in metastatic settings. However, the use of these agents in earlier stages of the disease has gained recent interest.[11]

Osimertinib is approved by the FDA as a first-line therapy for the treatment of EGFR-mutated NSCLC with good progression-free survival.[7] These agents are also approved for use in combination with platinum-based chemotherapy.[12] Only osimertinib for the treatment of EGFR-mutated NSCLC has been approved for use after chemoradiation. This agent also shows significant response in adjuvant settings.[12]

Among all the approved targeted therapies for the treatment of ALK-mutated NSCLC, alectinib is approved for both adjuvant and first-line settings with significant response.[13] At the ESMO Congress 2024, it was shown that alectinib offers significantly better disease-free survival (DFS) benefits over chemotherapy in adjuvant settings. The disease-free rate at two years was 93.8% in the alectinib group and 63.0% in the chemotherapy group among patients with stage II or IIIA disease.[13] The ALINA study also demonstrated a manageable safety profile of alectinib in adjuvant settings.[13]

Multiple studies have shown that second- and third-generation ALK TKIs, such as alectinib, brigatinib, and lorlatinib, outperform first-generation ALK TKIs like crizotinib and ceritinib in treating ALK TKI-naïve patients with ALK-positive NSCLC.[14,15] Included in these is the updated five-year follow-up of the randomized phase III CROWN study, which investigated lorlatinib compared with crizotinib in patients with ALK-positive NSCLC. The median progression-free survival (PFS) for patients in the lorlatinib group had not been reached compared with a median PFS of 9.1 months for those in the crizotinib group.[16] Furthermore, among patients with brain metastases at baseline, the five-year PFS rate was higher for the lorlatinib group (63%) compared with the crizotinib group, and the median time to intracranial progression was not reached in the lorlatinib group compared with 16.4 months in the crizotinib group.[16]

The European randomized phase III ALUR study compared the second-generation ALK inhibitor alectinib with pemetrexed or docetaxel in 107 patients with ALK-positive NSCLC who had progressed on prior platinum-based doublet chemotherapy and crizotinib treatment. The median investigator-assessed PFS was 9.6 months for patients in the alectinib arm compared with 1.4 months in the chemotherapy arm.[17] Globally, the most frequently used guideline, ESMO, recommends the use of either selpercatinib or pralsetinib for the treatment of RET fusion-positive NSCLC. Pralsetinib has received approval from the EMA for first-line treatment of advanced RET fusion-positive NSCLC and from the FDA for managing mNSCLC in adults with RET fusions. However, its availability in the future remains uncertain.[18]

References:

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-249.
2. World Health Organization. Lung cancer. [Internet]. [cited 2025 Jan 1]. Available from: https://www.who.int/news-room/fact-sheets/detail/lung-cancer
3. World Cancer Research Fund International. Lung cancer statistics. [Internet]. [cited 2025 Jan 1]. Available from: https://www.wcrf.org/preventing-cancer/cancer-statistics/lung-cancer-statistics/
4. Mok TS, Wu YL, Thongprasert S, Yang CH, Chu DT, Saijo N, et al. Gefitinib or carboplatin–paclitaxel in pulmonary adenocarcinoma. N Engl J Med. 2009;361(10):947-957.
5. Fukuoka M, Wu YL, Thongprasert S, Sunpaweravong P, Leong SS, Sriuranpong V, et al. Biomarker analyses and final overall survival results from a phase III, randomized, open-label, first-line study of gefitinib versus carboplatin/paclitaxel in clinically selected patients with advanced non-small-cell lung cancer in Asia (IPASS). J Clin Oncol. 2011;29(21):2866-2874.

6. Paz-Ares L, Tan EH, O'Byrne K, Zhang L, Hirsh V, Boyer M, et al. Afatinib versus gefitinib in patients with EGFR mutation-positive advanced non-small-cell lung cancer: a phase 2B, open-label, randomized controlled trial. Lancet Oncol. 2015;16(2):145-155.

7. Soria JC, Ohe Y, Vansteenkiste J, Reungwetwattana T, Chewaskulyong B, Lee KH, et al. Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer. N Engl J Med. 2018;378(2):113-125.

8. Camidge DR, Kim HR, Ahn MJ, Yang JC, Han JY, Lee JS, et al. Brigatinib versus crizotinib in ALK-positive non-small-cell lung cancer. N Engl J Med. 2018;379(21):2027-2039.

9. Shaw AT, Bauer TM, de Marinis F, Felip E, Goto Y, Liu G, et al. First-line lorlatinib or crizotinib in advanced ALK-positive lung cancer. N Engl J Med. 2020;383(21):2018-2029.

10. Novello S, Mazieres J, Oh IJ, de Castro J, Migliorino MR, Helland Å, et al. Primary results from the ALINA study: a phase III, open-label, randomized study of alectinib versus platinum-based chemotherapy in early-stage resected ALK-positive non-small cell lung cancer. Presented at: ESMO Congress 2024; 2024 Sep 13-17; Madrid, Spain.

11. Peters S, Camidge DR, Shaw AT, Gadgeel S, Ahn JS, Kim DW, et al. Alectinib versus crizotinib in untreated ALK-positive non-small-cell lung cancer. N Engl J Med. 2017; 377(9):829-838.

12. Hida T, Nokihara H, Kondo M, Kim YH, Azuma K, Seto T, et al. Alectinib versus crizotinib in patients with ALK-positive non-small-cell lung cancer (J-ALEX): an open-label, randomized phase 3 trial. Lancet. 2017;390(10089): 29-39.

13. Shaw AT, Gandhi L, Gadgeel S, Riely GJ, Cetnar J, West H, et al. Alectinib in ALK-positive, crizotinib-resistant, non-small-cell lung cancer: a single-group, multicentre, phase 2 trial. Lancet Oncol. 2016;17(2):234-242.

14. Solomon BJ, Kim DW, Wu YL, Nakagawa K, Mekhail T, Felip E, et al. First-line crizotinib versus chemotherapy in ALK-positive lung cancer. N Engl J Med. 2014;371(23): 2167-2177.

15. Gadgeel SM, Shaw AT, Barlesi F, Felip E, Goto Y, Leal TA, et al. CROWN: a phase III study of lorlatinib versus crizotinib in advanced anaplastic lymphoma kinase (ALK)-positive non-small-cell lung cancer. J Clin Oncol. 2020;38(15_suppl):9501.

16. Novello S, Mazieres J, Oh IJ, de Castro J, Migliorino MR, Helland Å, et al. ALINA: a phase III, open-label, randomized study of alectinib versus platinum-based chemotherapy in early-stage resected ALK-positive non-small cell lung cancer. J Thorac Oncol. 2024;19(1):S1-S2.

17. Novello S, Mazieres J, Oh IJ, de Castro J, Migliorino MR, Helland Å, et al. ALINA: a phase III, open-label, randomized study of alectinib versus platinum-based chemotherapy in early-stage resected ALK-positive non-small cell lung cancer. J Thorac Oncol. 2024;19(1):S1-S2.

18. Drilon A, Oxnard GR, Tan DSW, Loong HH, Johnson M, Gainor J, et al. Efficacy of pralsetinib in RET fusion–positive non–small-cell lung cancer: updated data from ARROW, a phase 1/2 study. J Clin Oncol. 2022;40(17_suppl):9009. Available from: https://ascopubs.org

Original Article

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Effect of Concurrent Chemoradiotherapy with Temozolomide and Radiotherapy Alone for Treatment of Brain Metastases

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Abstract:

Introduction: *Brain metastases are the most common neurologic complication of cancer. The aim of this study was to compare the efficacy, tolerability, and safety of concurrent chemoradiotherapy with temozolomide and radiotherapy alone in patients with previously untreated brain metastases from solid tumors.* ***Methods:*** *A total of 82 patients who met the inclusion and exclusion criteria were purposively included in this study. They were then randomly assigned by lottery into two groups, A and B. Patients in group A were treated with whole brain irradiation once daily at 3 Gy per fraction, 5 days a week, for a total dose of 30 Gy, along with a fixed dose of oral temozolomide, administered 1 hour before each daily fraction. Patients in group B were treated with the same dose of radiotherapy. The first follow-up visit occurred 2 weeks after completion of treatment, and subsequent follow-ups were scheduled at the 4th and 8th weeks after treatment. Patient follow-up was conducted via clinical evaluation, brain MRI, and a standard biochemical profile.* ***Results:*** *The objective response rate in the TMZ+WBRT arm (65%) was significantly (*p*=0.0327) superior to that achieved with radiotherapy alone (41.01%). Among 40 patients evaluable for response in the TMZ+WBRT arm, 27 responded, including 9 (22.5%) patients with a complete response, and 17 (42.5%) patients with a partial response. Eleven (27.5%) patients remained stable, and 3 (7.5%) patients showed progression. In the WBRT-only arm, 16 (41.01%) of 39 patients responded. Four (10.25%) patients had a complete response, and 12 (30.8%) had a partial response. Sixteen (41.01%) patients had stable disease, and 7 (17.19%) patients experienced progression. The most common treatment-related Grade 2 or Grade 3 toxicities in Arm A versus Arm B were as follows: skin reaction (17.5% vs. 12.82%), fatigue (12.5% vs. 7.69%), anemia (22.5% vs. 7.68%), neutropenia (15% vs. 10.25%), and thrombocytopenia (15% vs. 10.24%). None of the p-values were <0.05.* ***Conclusion:*** *The objective response rate for concurrent chemoradiotherapy with temozolomide was significantly higher than for radiotherapy alone. The toxicities associated with this regimen were well tolerated.*

Keywords: *Brain, concurrent, chemo-radiotherapy, metastasis.*

Introduction:

Brain metastases affect many cancer patients, with historically poor outcomes. However, advances in neuroimaging, neurosurgery, radiation oncology, medical oncology, and supportive care have enabled earlier detection, better local treatments, and strategies to reduce complications, improving survival and quality of life.[1] The cumulative incidence of brain metastases is 50% for lung cancer, 15-20% for breast cancer, 7-10% for renal cell carcinoma, 7% for melanoma, and <2% for colorectal cancer.[2] The prognosis remains poor, with median survival of untreated patients around one month and, with treatment, an overall median survival of less than one year.[3]

The Recursive Partitioning Analysis (RPA) by the Radiation Therapy Oncology Group (RTOG) classifies patients treated with whole brain radiation therapy into three prognostic groups: RPA class 1 (younger than 65, Karnofsky Performance Status [KPS] e" 70, controlled primary tumor, single brain metastasis) has a median survival of 7.1 months. RPA class 3 (KPS < 70) has a median survival of 2.3 months, and RPA class 2 includes all other patients, with a median survival of 4.5 months. The Graded Prognostic Assessment (GPA) system further divides patients into four categories, with median overall survival ranging from 2.6 to 11 months based on age, KPS, number of brain metastases, and disease status outside the CNS.[4] Accurate evaluation of brain metastases, including size and primary tumor histology, is crucial for determining the best treatment strategy.

Treatment options, including surgery, stereotactic radiosurgery (SRS), and whole brain radiotherapy (WBRT), continue to evolve. Solitary metastases in RPA class 1 patients may be treated with surgery followed by WBRT, though solitary metastases are rare. For multiple metastases, WBRT has been the standard treatment for decades to alleviate symptoms and prevent further intracranial metastases. Temozolomide (TMZ), a second-generation oral alkylating agent with excellent CNS bioavailability, has proven activity against primary brain tumors and may enhance the cytotoxic effects of radiation.[5] TMZ can be safely administered concurrently with radiation therapy.[6]

A randomized phase II trial involving 52 patients with brain metastases from solid tumors showed that daily low-dose TMZ (75mg/m²/day) with WBRT (40 Gy in 20 fractions over 4 weeks) followed by up to 6 cycles of TMZ (200mg/m²/day) significantly improved the objective response rate (ORR) compared to WBRT alone.[7] A subsequent phase III trial tested WBRT (30 Gy in 3-Gy fractions for 2 weeks) alone or with concurrent TMZ (75mg/m²/day during WBRT, followed by 6 cycles of TMZ) in 123 patients. Among 103 evaluable lung cancer patients, WBRT plus TMZ showed a significant improvement in response rate (48% vs. 27%; $p = 0.03$) and a non-significant improvement in median overall survival (7.9 months vs. 4.3 months; $p = 0.06$). Based on these findings, the present study aims to further evaluate the benefit of concurrent WBRT plus TMZ vs. WBRT alone in patients with brain metastases.

Materials & Methods

This quasi-experimental study was conducted from January 2018 to June 2019 in the Department of Oncology, Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka, and the Department of Radiation Oncology, National Institute of Cancer Research and Hospital, Mohakhali, Dhaka. Eighty-two patients were selected from the outpatient department (OPD) and the emergency department of these hospitals. The patients had histopathologically or cyto-pathologically confirmed primary malignant diseases with radiologically proven brain metastases.

A convenient, purposive sampling method was used for this clinical study. Patient history was documented using a prescribed datasheet. Written informed consent was obtained from each patient before their participation in the study. Clinical examinations and necessary investigations were performed. The patients were divided into two arms: Arm A and Arm B, with 41 patients in each arm.

- Arm A: Whole brain radiotherapy (30 Gy in 10 fractions over 2 weeks) concurrent with daily fixed-dose temozolomide (100 mg).
- Arm B: Whole brain radiotherapy (30 Gy in 10 fractions over 2 weeks) without temozolomide.

After completing the treatment, patients were carefully followed up weekly for two weeks, then at the fourth and eighth weeks, respectively. The follow-up included history-taking, clinical examination of the neurological system, and relevant laboratory and imaging tests. The findings were recorded in a prescribed data collection form (attached herewith).

The collected data were tabulated separately for Arm A and Arm B. Efforts were made to minimize potential biases in the study. The data were checked, edited, manually coded, and saved in a computer. Data analysis was performed using SPSS for Windows (Version 24.0) software. Statistical analyses included two-sample mean tests and Chi-square tests to compare the objective response rates and treatment toxicities between the two therapeutic arms.

The results were presented in tables, figures, and diagrams. A *p*-value of <0.05 was considered statistically significant in two-tailed tests.

Result:

Table 1: *Socio-demographic characteristics of the respondents*

Variables	Group	
	Arm A (n=41) Frequency (%)	Arm B (n=41) Frequency (%)
Age group		
18-29	0 (0)	0 (0)
30-39	6 (14.6)	5 (12.1)
40-49	8 (19.5)	9 (21.9)
50-59	12 (29.2)	10 (24.3)
60-70	15 (36.5)	17 (41.4)
Sex		
Male	25 (61)	16 (39)
Female	24 (59)	17 (41)
Economic status		
Poor	10 (24.4)	12 (29.3)
Middle	22 (53.6)	25 (60.8)
Rich	9 (21.9)	4 (9.7)
Performance status		
KPS 70	16 (39)	14 (34.1)
KPS 80	20 (48.7)	23 (56)
KPS 90	5 (12.1)	4 (9.7)

Table I presents the socio-demographic characteristics of the patients. It is evident that most of the patients belonged to the 60–70-year age group. In terms of sex distribution, 59% of patients in Arm A and 41% in Arm B were male. Most of the patients in this clinical study were from a middle-class socioeconomic background.

Regarding performance status, all patients had a Karnofsky Performance Status (KPS) between 70 and 90. Most patients had a KPS of 80, accounting for 48.78% in Arm A and 56.09% in Arm B.

Table II presents the distribution of patients based on their signs and symptoms. The majority of patients in both Arm A and Arm B reported nausea (75.60% in Arm A and 70.73% in Arm B), headache (63.41% in Arm A and 65.85% in Arm B), and vomiting (78.04% in Arm A and 73.17% in Arm B). Convulsions were less common but were observed in 26.82% of patients in Arm A and 34.41% in Arm B.

The most frequent non-hematologic adverse events were hair loss, reported in 30% of patients in the temozolomide and WBRT arm compared to 23.07% in the WBRT-only arm; skin reactions, reported in 47.5% of patients in the temozolomide and WBRT arm compared to 38.46% in the WBRT-only arm; and fatigue, reported in 42.5% of patients in the temozolomide and WBRT arm compared to 33.3% in the WBRT-only arm (Table III).

Table 2: *Distribution of patients according to sign and symptoms*

Clinical presentation	Group		χ^2 test	*p*- value
	Arm A (n =41) n (%)	Arm B (n=41) n (%)		
Headache	26 (63.41)	27 (65.85)	0.5101	0.9166
Nausea	31 (75.60)	29 (70.73)		
Vomiting	32 (78.04)	30 (73.17)		
Convulsion	11 (26.82)	14 (34.14)		

Table 3: *Distribution of patients according to non-hematological toxicity*

Toxicity		Group		χ^2 test	*p*- value
		Arm –A (n=40) n (%)	Arm-B (n=39) n (%)		
Hair loss	Grade-0	28 (70)	30 (76.92)	0.485	0.486
	Grade-1	12 (30)	9 (23.07)		
Skin reaction	Grade-0	21 (52.5)	24 (61.53)	0.702	0.703
	Grade-1	12 (30)	10 (25.64)		
	Grade-2	7 (17.5)	5 (12.82)		
Fatigue	Grade-0	23 (57.5)	26 (66.66)	0.853	0.6528
	Grade-1	12 (30)	10 (25.64)		
	Grade-2	5 (12.5)	3 (7.69)		

Table 4: *Responses of treatment between two arms*

Variables (level of response)	Arm-A (n=40)n (%)	Arm-B (n=39)n (%)	χ^2 test	*p*- value
Complete response (CR)	9 (22.5)	4 (10.25)	4.55	0.0327
Partial response (PR)	17 (42.5)	12 (30.76)		
Objective response (CR+PR)	26 (65)	16 (41.01)		
Stable disease (SD)	11 (27.5)	16 (41.01)		
Progressive disease (PD)	3 (7.5)	7 (17.94)		

As shown in table**,** the objective response rate

Table 5: *Distribution of patients according to Haematologic toxicity.*

Toxicity		Group		χ^2 test	*p*-value
		Arm –A*(n=40) n (%)	Arm-B**(n=39) n (%)		
Anemia	Grade-0	18 (45)	26 (66.66)		
	Grade-1	13 (32.5)	10 (25.64)		
	Grade-2	6 (15)	2 (5.12)	4.83	0.184
	Grade-3	3 (7.5)	1 (2.56)		
Neutropenia	Grade-0	23 (57.5)	25 (64.10)		
	Grade-1	11 (27.5)	10 (25.65)		
	Grade-2	4 (10)	3 (7.69)	0.703	0.87
	Grade-3	2 (5)	1 (2.56)		
Thrombocytopenia	Grade-0	25 (62.5)	27 (69.23)		
	Grade-1	9 (22.5)	8 (20.51)	0.740	0.86
	Grade-2	4 (10)	2 (5.12)		
	Grade-3	2 (5)	2 (5.12)		

*1 patient discontinue treatment; **1 patient died & 1 patient lost to follow up

Regarding hematologic adverse events, neutropenia was reported in 42.5% of patients in the temozolomide and WBRT arm compared to 35.9% in the WBRT-only arm. Thrombocytopenia was reported in 37.5% of patients in the temozolomide and WBRT arm compared to 30.75% in the WBRT-only arm. Anemia was reported in 55% of patients in the temozolomide and WBRT arm compared to 33.32% in the WBRT-only arm (Table V).

Discussion

The treatment of patients with brain metastases from solid tumors continues to evolve. Radiotherapy (RT) is the current treatment of choice for patients with multiple lesions or inoperable solitary lesions, demonstrating improvement in neurologic functions in up to 90% of patients. However, whole brain radiotherapy (WBRT) is associated with brain atrophy and necrosis, endocrine dysfunction, and dementia. Although WBRT is effective regarding the improvement of neurologic symptoms in patients with brain metastases, systemic disease may require additional therapies to achieve meaningful improvements in overall survival.

This study was carried out with the aim of comparing the efficacy, tolerability, and safety of concurrent chemoradiotherapy with temozolomide (TMZ) and radiotherapy alone in patients with previously untreated brain metastases from solid tumors during the period of January 2018 to June 2019. The study findings are discussed and compared with previously relevant studies.

In this study, all the patients were above 18 years of age. The mean age was 55.4 years, with a standard

deviation of ±9.7 and an age range of 33–68 years. Most patients, 27 (65.85%) in Arm A and 27 (65.85%) in Arm B, were in the age group of 50–70 years, which is consistent with the findings of a previous study that showed the peak incidence occurred in the age range of 40–60 years.

Regarding sex, male patients were found to be dominant in both arms, with percentages of 61% (25 patients) in Arm A and 59% (24 patients) in Arm B. The percentages of female patients were 39% (16 patients) in Arm A and 41% (17 patients) in Arm B, respectively.[8]

Regarding economic status, most of the patients were found to be in the middle-class group, accounting for 53.65% in Arm A and 60.97% in Arm B.

Regarding performance status, all patients were within the Karnofsky Performance Status (KPS) range of 70–90. The majority had a KPS of 80, accounting for 48.78% in Arm A and 56.09% in Arm B. Additionally, a KPS of 70 was observed in 39.02% and 34.14% of patients in Arm A and Arm B, respectively.

In this study, the most common symptoms associated with brain metastases were headache, nausea, vomiting, and convulsions. The outcome of treatment was found to be similar in both arms. Among 40 patients accessible for response in the TMZ+WBRT arm, 27 responded, including 9 (22.5%) patients with a complete response and 17(42.5%) patients with a partial response, 11(27.5%) patients remained stable and 3(7.5%) patients were progressive. In the only WBRT arm, 16 (41.01%) of 39 patients responded. Four patients (10.25%) showed a complete response and 12 (30.8%) showed partial response. Sixteen (41.01%) patients had stable diseases, and 7 (17.19%) patients were in progress. The outcome of treatment was found to be similar in both the arms.

It was found that fatigue, skin reactions, and hair loss were common acute toxicities of whole brain radiotherapy. The frequency of these acute toxicities was similar in both arms and could be managed with adequate supportive measures.

The addition of TMZ concurrent with RT was well-tolerated in this study, with no reported grade 4 hematologic toxicity. Although cumulative myelosuppression is a well-documented dose-limiting side effect associated with alkylating agents, only mild to moderate myelosuppression developed in a small number of TMZ-treated patients, and it was completely reversible and non-cumulative. TMZ demonstrated an acceptable safety profile in patients with brain metastases.

In addition, this schedule did not cause the toxic effects associated with the protracted schedule of TMZ, such as opportunistic infections, increased transaminase levels, and especially cumulative lymphopenia, which has been seen in up to 91% of patients receiving 10 cycles of protracted low-dose TMZ. These encouraging results regarding temozolomide's radio sensitizing and cytotoxic effects when added to WBRT did not differ greatly from the results of Addeo et al. (2008), a single-institution phase II trial that used a dose-intensified, protracted course of temozolomide after WBRT.[9]

In this study, patients with extracranial metastases, an uncontrolled primary tumor, or both conditions were able to start or resume chemotherapy specific to their neoplasms in a shorter time. This may have been particularly important for 34% of the patients in this study who had not received chemotherapy before the diagnosis of brain metastases. As patients with brain metastases have a short life expectancy, this treatment regimen appeared to be quite appropriate for them.

Conclusion:

The objective response rate of concurrent chemoradiotherapy with temozolomide was significantly higher than that of radiotherapy alone. The toxicities observed with this treatment schedule were well tolerated.

References:

1. Platta CS, Khuntia D, Mehta MP, Suh JH. Current treatment strategies for brain metastasis and complications from therapeutic techniques: a review of current literature. Am J Clin Oncol. 2010 Aug 1;33(4):398-407.
2. Schouten LJ, Rutten J, Huveneers HA, Twijnstra A. Incidence of brain metastases in a cohort of patients with carcinoma of the breast, colon, kidney, and lung and melanoma. Cancer. 2002 May 15;94(10):2698-705.
3. Kaal EC, Niël CG, Vecht CJ. Therapeutic management of brain metastasis. Lancet Neurol. 2005 May 1;4(5):289-98.
4. Agboola O, Benoit B, Cross P, Da Silva V, Esche B, Lesiuk H, Gonsalves C. Prognostic factors derived from recursive partition analysis (RPA) of Radiation Therapy Oncology Group (RTOG) brain metastases trials applied to surgically resected and irradiated brain metastatic cases. Int J Radiat Oncol Biol Phys. 1998 Aug 1;42(1):155-9.

5. Ortiz R, Perazzoli G, Cabeza L, Jiménez-Luna C, Luque R, Prados J, Melguizo C. Temozolomide: an updated overview of resistance mechanisms, nanotechnology advances and clinical applications. Curr Neuropharmacol. 2021 Apr 1;19(4):513-37.

6. Krauze AV, Myrehaug SD, Chang MG, Holdford DJ, Smith S, Shih J, Tofilon PJ, Fine HA, Camphausen K. A phase 2 study of concurrent radiation therapy, temozolomide, and the histone deacetylase inhibitor valproic acid for patients with glioblastoma. Int J Radiat Oncol Biol Phys. 2015 Aug 1;92(5):986-92.

7. Koukourakis GV, Kouloulias V, Zacharias G, Papadimitriou C, Pantelakos P, Maravelis G, Fotineas A, Beli I, Chaldeopoulos D, Kouvaris J. Temozolomide with radiation therapy in high grade brain gliomas: pharmaceuticals considerations and efficacy; a review article. Molecules. 2009 Apr 16;14(4):1561-77.

8. Kim BS, Seol HJ, Nam DH, Park CK, Kim IH, Kim TM, Kim JH, Cho YH, Yoon SM, Chang JH, et al. Concurrent chemoradiotherapy with temozolomide followed by adjuvant temozolomide for newly diagnosed glioblastoma patients: a retrospective multicenter observation study in Korea. Cancer Res Treat. 2017 Jan;49(1):193-203.

9. Addeo R, Caraglia M, Faiola V, Montella L, Del Prete S, Parlato C, et al. Phase II trial of temozolomide using protracted low-dose and whole-brain radiotherapy for non-small cell lung cancer and breast cancer patients with brain metastases. Cancer. 2008;113:2524-31.

Original Article

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Risk Factors Associated with Lung Cancer in Bangladeshi Women

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Abstract

Background: *Lung cancer remains the leading cause of cancer mortality in both men and women. Tobacco use causes most of the lung cancer in women, but it does not explain all cases, as about one in five women who develop lung cancer have never smoked.* ***Aim:*** *The current study was conducted to identify risk factors associated with lung cancer in Bangladeshi women.* ***Methods:*** *This was a case-control study conducted at the Department of Medical Oncology of NICRH. Thirty-six cases and 36 matched controls were selected based on the selection criteria.* ***Results:*** *The mean age of the case patients was 53.39 (SD ± 11.29) years, while the mean age of the control subjects was 48.17 (SD ± 12.13) years. Regarding marital status, educational status, and occupational status, no statistically significant differences were noted. Most of the patients were from the Dhaka Division (12, 33.3%) and Chittagong Division. Significantly more respondents in the case group (10, 30.5%) were current smokers compared to the control group (2, 5.6%), but there was no difference in passive smoking exposure. Most of the case patients (33, 91.7%) used wood burners for cooking, while 21 (58.3%) respondents in the control group used the same. Heavy fume exposure was reported by 22 cases (61.1%) and 6 control respondents (16.7%). Almost equal numbers of respondents in each group had arsenic exposure in their drinking water (9, 25% and 8, 22.2%, respectively). More respondents in the control group (18, 50%) reported a very active childhood compared to the case group (7, 19.4%). Case patients consumed more rice and less wheat than control subjects, while more respondents in the control group (91.7%) consumed vegetables daily compared to case patients (66.7%).* ***Conclusion:*** *Binary logistic regression analysis showed that heavy fume exposure during cooking was associated with an increased risk of lung cancer among women. This was also true for smoking, use of wood burners, less childhood activity, lower vegetable intake, higher rice intake, and lower wheat intake.*

Key words: *Bangladeshi Women, lung cancer, risk factor, association.*

Introduction:

Lung cancer is the leading cause of cancer death among men in both developed and developing countries and has surpassed breast cancer as the main cause of cancer death among women in developed countries.[1,2] It was the leading cancer in male patients (1684, 27.5%) at NICRH and in females, it ranked 4th (299, 6.0%) in 2014 (HBCR 2015). An interesting observation was reported

in a poster presentation in 2018, where 12% of all female patients in the Medical Oncology department of NICRH were suffering from lung cancer.[3]

Several studies have highlighted that lung cancer has different features in women compared to men, including etiology, pathophysiology, histology, risk factors, prognosis, and treatment outcomes, thus defining a distinct entity in female patients.[4-6] Lung cancer in women accounted for 26% of estimated cancer deaths in 2012, a higher percentage than the combined mortality from breast and colon or rectum cancer.[7,8] Women have a 1 in 16 lifetime risk of developing lung cancer regardless of smoking status; 47% are diagnosed above the age of 70, and 50% are diagnosed at advanced stages.[9,10]

Incidence rates in women began to increase significantly in 1973 and reached a plateau in the late 1990s, over a decade later than men, and mortality in women stabilized for the first time in 2003, two decades later than men, and has yet to decline.[7,9] The five-year survival rate remains poor, but is higher in women compared with men (less than 18% vs. less than 14%, respectively).[10]

Tobacco remains the largest risk factor for lung cancer in women, responsible for 80%-90% of cancer-related deaths and contributing to at least 50% of the worldwide lung cancer burden.[9-11] Trends in lung cancer incidence and mortality among women reflect changing trends in cigarette smoking, the prevalence of which peaked among women in the United States nearly 20 years later than men.[7,9,11,12]

The four major types of lung cancer are broadly categorized as small-cell lung cancer, originating from neuroendocrine cells, and non–small cell lung cancer (NSCLC), originating from bronchial epithelial cell precursors. NSCLC is further subdivided into squamous cell carcinoma, adenocarcinoma, and large cell carcinoma. Large-cell carcinoma is poorly or undifferentiated compared to the other cancers, and criteria for diagnosis vary widely.[14]

All histologic subtypes of lung cancer have been associated with smoking, with the strongest association being with small-cell and squamous cell carcinoma, and a less robust association for adenocarcinoma.[13] Adenocarcinoma is the most common histologic subtype of lung cancer in both smoking and nonsmoking men and women; 41.4% of lung cancer in women is adenocarcinoma, compared with 34.1% in men.[8,14,15] In women, the incidence of adenocarcinoma is slowly increasing, squamous cell carcinoma is slowly decreasing, and small-cell carcinoma has remained relatively stable. In Asian populations, 60%-80% of women with lung cancer, compared to 10%-15% of men with lung cancer, have never smoked.[9,14]

Environmental exposures known to be carcinogenic to the lungs include second-hand smoke (SHS), asbestos, arsenic, and other chemicals.[8,11,12] SHS was classified as a human carcinogen by the Environmental Protection Agency in 1993, and globally, women and children are disproportionately affected.[8,12] Women married to men who smoke have been shown to have a 25%-29% increased risk of developing lung cancer.[12,14]

Indoor burning of cooking oil and other biomass fuels in poorly ventilated areas produces polycyclic aromatic hydrocarbons, which are associated with lung cancer. This effect is particularly observed in East and South Asian women but is significant in all developing countries.[8,12,14] Additionally, in 2013, the International Agency for Research on Cancer (IARC) ranked outdoor air pollution as a Group 1 carcinogen, i.e., a known human carcinogen.

Genetic Factors: Family history is an independent risk factor for the development of lung cancer, regardless of smoking status, with women at higher risk than men, suggesting a role for heritable factors.[8,14,16] Estrogen receptors (ERá and ERâ) are expressed on lung cancer cells of both men and women, with ERâ being the more common haplotype.[8,17] In vitro, estrogen promotes the growth of both healthy and malignant lung tissue, and antiestrogen treatments have suppressed tumor growth, suggesting a hormonal role in tumorigenesis.[13]

Physical activity (PA) may be an important modifiable factor influencing lung cancer risk and incidence.[18] In general, both male and female smokers tend to engage in less PA than non-smokers.[19,20]

HPV was found in 43%-49% of adenocarcinomas, compared with 24%-29% of squamous cell carcinomas, in a study conducted in Taiwan.

The aim of this study is to identify the risk factors associated with lung cancer, to evaluate the demographic and socio-economic status of patients, to investigate the histological characteristics of lung cancer, and to

determine the risk factors responsible for the development of lung cancer among Bangladeshi women.

Materials and Methods

It was a case-control study done at National Institute of Cancer Research and Hospitals, Mohakhali, Dhaka during June 2019 to April 2020.Histological or cytological confirmed cases of primary lung cancer who attended Medical Oncology department of NICRH during data collection period. Age and socio-demographic characteristics matched control were randomly selected from the patients' attendants.

Data were processed by editing and post-coding and analyzed by SPSS for windows (IBM SPSS statistics for windows, version 22.0, Armonk NY: IBM crop.) software.

Results:

Demographic characteristics of the respondents are shown in Table 1. It was found that the case group was older (53.39 years) than the control group (48.17 years), but the difference was not significant ($p = 0.064$). Most participants in both groups were married and housewives, with no significant differences in marital status, education, or occupation.

Distribution of the case patients by histopathology is depicted in figure 1. Majority of the patients were suffering from adenocarcinoma (21, 58.3%) followed by squamous cell carcinoma (10, 27.8%).

Table 2 shows the distribution of respondents by different risk factors. Smoking was more common in the case group (27.8%) than the control group (5.6%) with a significant difference ($p = 0.024$). There were no significant differences in passive smoking, chewing tobacco consumption, arsenic in drinking water, or family history of lung disease. The case group had more exposure to heavy fumes while cooking (61.1%) and used wood burners more often (91.7%), both of which were significantly different from the control group ($p< 0.001$). Physical activity levels differed significantly, with more control group participants being very active (50.0%) compared to the case group (19.5%, $p = 0.009$). OCP use showed no significant difference between the groups ($p = 0.615$).

Table 3 shows the binary logistic regression analysis of factors associated with lung cancer risk in women. Heavy fume exposure during cooking (OR = 7.857), smoking (OR = 6.538), and use of wood burners (OR = 4.480) were identified as significant risk factors. Less physical activity (OR = 3.251) was also a notable risk factor. While less vegetable intake, frequent rice intake, and less bread intake showed weaker associations, they were not as strongly linked to lung cancer risk.

Table 1: *Demographic characteristics of the respondents*

Demographic Variable	Category		Fisher's Exact Test	*p*-value
	Case n (%)	Control n (%)		
Mean age in yrs. (±SD)	53.39 (11.29)	48.17 (12.13)	1.89*	0.064
Marital status				
Married	34 (94.4)	35 (97.2)	1.191	1.00
Divorced	01 (2.8)	01 (2.8)		
Widow	01 (2.8)	0 (0.0)		
Level of education				
Illiterate	23 (63.9)	14 (38.9)	6.472	0.092
Primary	10 (27.8)	17 (47.2)		
Secondary	02 (5.6)	04 (11.1)		
Higher secondary	01 (2.8)	0 (0.0)		
Graduate and above	0 (0.0)	01 (2.8)		
Occupation				
Housewife	34 (94.4)	31 (86.1)	1.424	0.429
Service	02 (5.6)	05 (13.9)		

* t-test

Table 2: *Distribution of the respondents by risk factors*

Variables	Category		χ^2	*p*-value
	Case n (%)	Control n (%)		
Smoking status				
Yes	10 (27.8)	2 (5.6)	6.40	0.024
No	26 (72.2)	34 (94.4)		
Passive smoking status				
Yes	26 (72.2)	22 (61.1)	1.00	0.454
No	10 (27.8)	14 (38.9)		
Chewing tobacco consumption				
Yes	25 (69.4)	16 (44.44)	0.056	0.429
No	11 (30.6)	20 (55.56)		
Type of Burner				
Wood	33 (91.7)	21(58.3)	10.66	<0.001
Gas	3(8.3)	15(41.7)		
Fume while cooking				
Heavy	22 (61.1)	06 (16.7)	16.052	<0.001
Moderate	12 (33.3)	21 (58.3)		
Less	2 (5.6)	9 (25.0)		
Heavy	22 (61.1)	06 (16.7)		
Arsenic in drinking water				
Yes	9 (25.0)	8 (22.2)	0.77	1.00
No	27 (75.0)	28 (77.8)		
Environmental pollution				
Yes	5 (13.9)	5 (13.9)	0.00	1.00
No	31 (86.1)	31 (86.1)		
Family h/o lung disease				
Asthma	08 (22.2)	6 (16.7)	3.999*	0.282
COPD	08 (22.2)	03 (8.3)		
TB	01 (61.1)	03 (8.3)		
No disease	19 (52.8)	24 (66.7)		
Physical activity				
Very active	7 (19.5)	18 (50.0)	9.295*	0.009
Moderately active	26 (72.2)	18 (50.0)		
Inactive	3 (8.3)	0 (0.0)		
OCP use				
Yes	25 (69.4)	23 (63.9)	0.25	0.615
No	11 (30.6)	13 (36.1)		

* Fisher's Exact test

Table 3: *Binary logistic regression analysis of risk for lung cancer in women*

Risk for women lung cancer	Odds Ratio (OR)	95% Confidence Interval (CI)	
		Lower	Upper
Heavy fume during cooking	7.857	2.607	23.682
Smoking	6.538	1.318	32.44
Use of wood burner	4.480	1.22	19.206
Less physical activity	3.251	1.218	8.676
Less vegetable intake	1.636	0.511	4.633
Frequent rice intake	1.231	0.212	3.881
Less bread intake	1.187	0.693	3.975

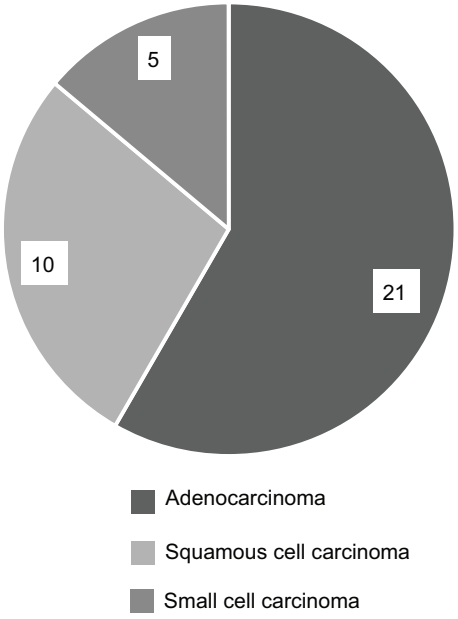

Figure 1: *Distribution of the case by histopathology*

Discussion

Over the past two decades, there has been a growing recognition of gender differences in health and disease, particularly in the context of lung cancer. Historically, lung cancer was considered a disease predominantly affecting men, as its incidence among women was much lower. However, with changing social patterns, including increased smoking among women, particularly after World War II, the epidemiology of lung cancer has evolved. Studies have shown that lung cancer behaves differently in women, with a higher proportion of cases occurring in non-smoking women compared to non-smoking men, indicating distinct risk factors and pathophysiology for women.[9] These findings align with studies suggesting that lung cancer in women is influenced by various factors such as histology, risk factors, treatment outcomes, and prognosis. [9, 16]

The current study identified several significant risk factors for lung cancer among Bangladeshi women, including smoking, exposure to heavy cooking fumes, and use of wood-burning stoves. Smoking remains one of the most significant risk factors, responsible for a large proportion of lung cancer-related deaths.[9, 10] Additionally, indoor air pollution from burning biomass fuels, such as wood, in poorly ventilated areas is a well-documented risk factor for lung cancer, particularly in women from East and South Asia.[8, 10] This is consistent with findings from other studies conducted in China and Taiwan, where prolonged exposure to cooking fumes was associated with an increased risk of lung cancer in non-smoking women.[21-23]

In terms of environmental factors, the study found a similar prevalence of arsenic exposure in the drinking water between the case and control groups, which aligns with global studies highlighting the carcinogenic potential of environmental pollutants like arsenic.[8, 12] However, no significant association was found between family history of lung disease and lung cancer risk in this study, which contrasts with some previous research suggesting that a family history may be a stronger risk factor for women than men.[8, 14]

Hormonal factors have also been implicated in lung cancer risk in women, but no statistically significant association was found in this study, which is in line with some other studies suggesting that hormonal influences on lung cancer are still not fully understood.[5, 6] Physical activity was found to be a protective factor, with less physical activity being associated with higher lung cancer risk, which is consistent with previous research indicating that a sedentary lifestyle may increase the risk of lung cancer.[18-20]

Dietary factors such as vegetable and rice consumption also showed varying degrees of association with lung cancer risk in this study. While vegetable intake was found to be a protective factor, rice consumption was higher among case patients, suggesting that dietary

habits may play a role in lung cancer risk, but more research is needed to draw definitive conclusions.[24]

In conclusion, this study highlights several important risk factors for lung cancer in Bangladeshi women, including smoking, cooking fumes, wood-burning stoves, and physical inactivity. These findings contribute to the growing body of evidence that suggests lung cancer in women is influenced by both environmental and lifestyle factors. Further research, particularly in low-income countries, is needed to identify additional risk factors and improve prevention strategies for lung cancer among women.

References

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Bray F. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359–E386.
2. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin. 2015;65(2):87–108.
3. Islam MR, Rahman M, Khan AA, Alam MJ, Siddiqua SM. Female lung cancer: Emerging issue in Bangladesh. Ann Oncol. 2019;30(9):ix133-ix134.
4. Alberg AJ, Wallace K, Silvestri GA, Brock MV. Invited commentary: The etiology of lung cancer in men compared with women. Am J Epidemiol. 2013;177(7):613–616.
5. Nakamura H, Ando K, Shinmyo T, Morita K, Mochizuki A, Kurimoto N. Female gender is an independent prognostic factor in non small cell lung cancer: A meta analysis. Ann Thorac Cardiovasc Surg. 2011;17(5):469–480.
6. Otsuka S, Klimowicz AC, Kopciuk K, Petrillo SK, Konno M, Hao D. CXCR19 overexpression is associated with poor outcome in females diagnosed with stage IV non small cell lung cancer. J Thorac Oncol. 2011;6(7):1169–1178.
7. Siegel LR, Naishadham D, Jemal A. Cancer statistics 2012. CA Cancer J Clin. 2012;62:10-29.
8. Kligerman S, White C. Epidemiology of lung cancer in women: Risk factors, survival, and screening. Am J Roentgenol. 2011;196:287–295.
9. Egleston BL, Meireles SI, Flieder DB, Clapper ML. Population-based trends in lung cancer incidence in women. Semin Oncol. 2009;36:506–515.
10. Marshall AL, Christiani DC. Genetic susceptibility to lung cancer—light at the end of the tunnel? Carcinogenesis. 2013;34:487–502.
11. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin. 2011;61:69–90.
12. Paulus JK, Christiani DC. Women and Health. 2. Waltham, MA: Academic Press; 2012. p. 641-677.
13. Paulus JK, Zhou W, Kraft P, Johnson BE, Lin X, Christiani DC. Haplotypes of estrogen receptor beta and risk of non-small cell lung cancer in women. Lung Cancer. 2011;71:258–2563.
14. Sun S, Schiller JH, Gazdar AF. Lung cancer in never smokers—a different disease. Nat Rev Cancer. 2007;7:778–790.
15. Fu JB, Kau Y, Severson RK, Kalemkerian GP. Lung cancer in women: Analysis of the national surveillance, epidemiology, and end results database. Chest. 2005;127:768–777.
16. Thomas L, Doyle LA, Edelman MJ. Lung cancer in women: emerging differences in epidemiology, biology, and therapy. Chest. 2005;128:370–381.
17. Berardi R, Verdecchi L, Di Pietro Paolo M, Giamperi R. Women and lung cancer: Clinical and molecular profiling as a determinant for treatment decisions: A literature review. Crit Rev Oncol Hematol. 2009;69:223–236.
18. deRuiter W, Faulkner G. Tobacco harm reduction strategies: the case for physical activity. Nicotine Tob Res. 2006;8(2):157–168.
19. Chiolero A, Wietlisbach V, Ruffieux C, Paccaud F, Cornuz J. Clustering of risk behaviors with cigarette consumption: a population-based survey. Prev Med. 2006;42(5):348–353.
20. Kvaavik E, Meyer HE, Tverdal A. Food habits, physical activity and body mass index in relation to smoking status in 40–42 year old Norwegian women and men. Prev Med. 2004;38(1):1–5.
21. Gao YT, Blot WJ, Zheng W, Ersnow AG, Levin LI, Zhang R, Fraumeni JF Jr. Lung cancer among Chinese women. Int J Cancer. 1987;40:604–609.
22. Koo LC, Ho JH. Worldwide epidemiological patterns of lung cancer in nonsmokers. Int J Epidemiol. 1990;19(suppl 1):S14–S23.
23. Seow A, Poh WT, Teh M, Eng P, Wang YT, Tan WC, Yu MC, Lee HP. Fumes from meat cooking and lung cancer risk in Chinese women. Cancer Epidemiol Biomarkers Prev. 2000;9:1215–1221.
24. Vieira AR, Abar L, Vingeliene S, Chan DS, Aune D, Navarro-Rosenblatt D, Stevens C, Greenwood D, Norat T. Fruits, vegetables and lung cancer risk: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):81–96.

Original Article

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Incidence and Risk Factors for Hypertension During Induction Chemotherapy for Childhood Acute Lymphoblastic Leukemia

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Abstract

Background: *Hypertension is a common but underreported side effect in patients with acute lymphoblastic leukemia (ALL) undergoing chemotherapy. The incidence of hypertension in childhood ALL varies widely, ranging from 10-67%. Despite numerous studies, the etiology, risk factors, and natural history of hypertension in this context remain poorly understood.* ***Objective:*** *This study aimed to detect the incidence and identify risk factors for hypertension during induction chemotherapy in children with acute lymphoblastic leukemia.* ***Methodology:*** *This prospective observational study was conducted from July 2017 to July 2018 at Bangabandhu Sheikh Mujib Medical University, Dhaka. It involved children aged 1 to 17.9 years newly diagnosed with acute lymphoblastic leukemia (ALL). Exclusions included those under 1 year, over 18 years, with pre-existing hypertension, or relapsed ALL. Informed consent was obtained from parents or guardians. Baseline tests measured WBC count, serum creatinine, electrolytes, uric acid, inorganic phosphate, and calcium levels before chemotherapy, following the modified UKALL 2003 protocol. Patients were categorized into standard and intermediate-risk groups and monitored for hypertension throughout the 35-day induction phase.* ***Results:*** *Hypertension developed in 16 patients (17.2%) during chemotherapy induction, all of whom required antihypertensive treatment. Tumor lysis syndrome (TLS) was present in 12.5% of hypertensive patients, significantly associated with hypertension (OR 10.857,* p *=0.021). Induction toxicities, including febrile neutropenia (*p*=0.004), convulsion (*p *=0.002), and coagulopathy (P=0.028), were strongly associated with hypertension. The median age for the onset of hypertension was 4.5 years. Hypertension was most frequent between the first and second weeks of chemotherapy, peaking at 75.25% in the second week and decreasing to 31.25% by the end of induction.* ***Conclusion:*** *The incidence of hypertension during induction chemotherapy was 17.2%, with the highest frequency in the second week of treatment. Younger age, TLS, and induction toxicities were significant risk factors for developing hypertension.*

Keywords: *Hypertension, Induction Chemotherapy, Acute Lymphoblastic Leukemia*

Introduction

Acute lymphoblastic leukemia (ALL) is the most common pediatric malignancy. It represents 25%-30% of all childhood cancers and approximately 75% of all cases of childhood leukemia.[1] In the Department of Paediatric Hematology and Oncology, BSMMU 58% of cases of ALL among 455 newly diagnosed children with malignancy were recorded in one year.[2] The 5-year survival rate for children with ALL has greatly increased over time and is now more than 85% overall Chemotherapy and stem cell transplantation (HSCT) are the established therapeutic options for these patients.

Typically, ALL is treated by chemotherapy in different phase induction therapy, consolidation, CNS-directed therapy, and maintenance.[3] The aim of treatment is the elimination of the neoplastic cell clone and the restoration of normal hematopoiesis.[4] Although contemporary treatments cure more than 80% of children with acute lymphoblastic leukemia (ALL), some patients require intensive treatment and many patients still develop serious acute and late complications owing to the side effects of the treatments.[5] Treatment-related toxicity cannot only be life-threatening but is also a major reason for the interruption or discontinuation of chemotherapy.[6] Hypertension is frequent, but under recognized and undertreated, a complication of chemotherapy for Acute lymphoblastic leukemia (ALL).[7] Although hypertension is a common complication of Acute lymphoblastic leukemia (ALL), its true incidence in this disease is unknown.[8] Little has been published on the rate of prehypertension and hypertension (HTN) in children with hematologic malignancies.[9] Glucocorticoids are used universally in remission induction therapy for Acute lymphoblastic leukemia (ALL).[6] Glucocorticoids form the backbone of induction and re-induction phases of ALL therapy and hypertension is an important though often under-reported non-hematological toxicity associated with its use.[10-15]

Hypertension is one of the adverse effects in patients undergoing chemotherapy, especially those who receive high dose corticosteroids. Corticosteroid treatment induces apoptosis of leukemic cells, therefore, it is the backbone of induction-phase chemotherapy for Acute lymphoblastic leukemia (ALL).[16] When daunomycin was included in treatment regimens, toxicity was greater among patients receiving dexamethasone.[17] The incidence of hypertension was 10 times higher than in the general pediatric population, and this hypertension was not associated with renal infiltration, hyper leukocytosis, or corticosteroid use but had an association with patients receiving dexamethasone.[16] Although hypertension (HTN) is a known possible complication of high-dose corticosteroids, the actual incidence and risk factors for this adverse event are poorly understood.[18] Hypertension causes several morbidities like headache, nausea, vomiting, visual disturbances, seizure, and focal neurological deficits and so on which also change health-related quality of life. Thus, the purpose of this study is to see the incidence and risk factors for hypertension during induction chemotherapy for childhood acute lymphoblastic leukemia.

Materials and Methods:

This prospective observational study was conducted at the Department of Pediatric Hematology and Oncology, BSMMU, Dhaka, from July 2017 to July 2018, including 120 newly diagnosed acute lymphoblastic leukemia (ALL) patients aged 1 to 17.9 years. Patients were enrolled consecutively, excluding those with pre-existing hypertension, cases of relapse, or ages outside the defined range. Data on demographics, family history, clinical findings, and investigations were collected using a questionnaire, and baseline parameters like BMI, white blood cell count, electrolytes, and renal function were recorded. Chemotherapy was administered using a modified UKALL 2003 protocol, with hypertension monitored daily using age-specific blood pressure tables. Statistical analysis, including univariate and multivariate methods, was performed using SPSS version 22. Ethical approval was obtained from the BSMMU ethics committee, and informed consent was provided by guardians, with confidentiality maintained throughout.

Results

The present single-centered, prospective observational study was conducted for a period of one year from July 2017 to July 2018 in the Department of Pediatric Hematology and Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. All patients admitted to the Department of Pediatric Hematology and Oncology, and 1 to 17.9 years with both sexes diagnosed newly with Acute Lymphoblastic Leukemia were the study

population. A total of 120 children with ALL were included in this study, among them 19 patients died, and 8 patients left against medical advice. So data were analyzed among 93 patients. All the admitted patients had received the UKALL 2003 protocol (modified).

Table 1: Shows initial characteristics of the study population. In this study, most of the patients were in the age group of <10 years 76 (81.7%), remaining were in the age group of e"10 years. The mean age was 6.0±3.78 years, median age was 4.5 years, and range was between 1.30 to 15.0 years. Among 93 patients, 59 (63.4%) were male and 34 (36.6%) were female patients. Male children were predominant in number. Male: Female ratio was 1.7:1. On BMI category of study subjects, among 86 patients 43 (50.0%) were normal, 36 (41.8%) were underweight, 6 (7.0%) were overweight and 1 (1.2%) was obese. Only 8 (8.6%) patients had a positive family history of hypertension. 52 (55.9%) were treated with regimen A, whereas 41(44.19%) were treated with regimen B. Age under 2 years was not included in the BMI calculation. There were 7 patients below 2 years of age. So, the number of patients was 86 while calculating BMI.

Table-1: *Initial characteristics of the study patients (n=93)*

Variables	Frequency (%)
Age (in years)	
<10	76 (81.7)
≥10	17 (18.7)
Sex	
Male	59 (63.4)
Female	34 (36.6)
BMI category (n=86)	
5th. 85th percentile	43 (50.0)
<5th percentile	36 (41.8)
85th-95th percentile	6 (7.0)
> 95th percentile	1 (1.2)
Family history of HTN	
Yes	8 (8.6)
No	85 (91.4)
Treatment regimen	
A	52 (55.9)
B	41 (44.1)

Table-2 Demonstrates incidence of hypertension among the 93 children with ALL included in this study. Out of 93 patients, hypertension was observed in 16 (17.2%) patients. 77 (82.8%) patients had no hypertension during induction chemotherapy.

Table 2: Incidence of hypertension among the children with ALL during induction chemotherapy (n=93)

Hypertension	Frequency (%)
Yes	16 (17.2)
No	77 (82.8)
Total	93 (100.0)

Table-3 Shows stages of hypertension, among 16 cases 7 (43.8%) patients had Stage 1 hypertension, while 9(56.2%) had Stage II hypertension.

Table-3: Stages of hypertension (n=16)

Stage of HTN	Frequency (%)
Stage 1	07 (43.8)
Stage 11	09 (56.2)
Total	16 (100.0)

Figure 1 Percentage of hypertension during induction period, hypertension present in 9(56.25%) patients at week-1, 12 (75.25%) patients at week-2, 10 (62.5%) patients at week-3, 8 (50%) patients at week-4, 5 (31.25%) patients at week5; indicating percentage of hypertension reaches its peak at week-2, then gradually decreasing.

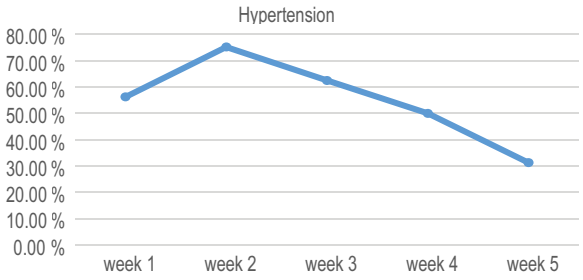

Figure-1: *Graphical presentation of percentage of hypertension at different weeks of remission induction (n-16).*

Table-4 shows measurement of risk factors for hypertension in children with ALL. There were 7 patients below 2 years of age. So, the numbers of patients were 86 while calculating BMI (**) odds ratio could not be calculated because cell frequency was 0.Table-4 Shows association of hypertension with age, gender, family history of hypertension, treatment regimen, BMI category, cannot be considered as risk factor, because those factors had no statistical significant relation with having hypertension. However, the table shows patients having induction toxicity had higher percentage (68.8%) of hypertension, which was statistically significant

Figure 2 Changes of serum creatinine level of hypertensive patients, at diagnosis, at the onset of hypertension and at the end of hypertension. There was no obvious difference of serum creatinine level except one patient who had GBS followed by AKI.

Table-4: Measurement of risk factors for hypertension in children with ALL (n=93)

Factors		Patients with HTN (n=16) f (%)	Patients without HTN (n=77) f (%)	OR (CI 95%)	*p*-value
Gender	Male	11 (68.8)	48 (62.3)	0.133 (0.42-4.21)	0.628^{ns}
	Female	5 (31.3)	29 (377)		
Age (years)	<10	13 (81.3)	63 (81.8)	0.963 (0.24-3.84)	0.957 ^{ns}
	≥10	3 (18.8)	14 (18.2)		
Treatment regimen	Regimen A	7 (43.8)	45 (58.4)	0.553 (0.19-1.64)	0.281^{ns}
	Regimen B	9 (56.3)	32 (41.6)		
Family h/o HTN	Yes	3 (18.8)	5 (6.5)	3.32 (0.71-15.63)	0.112^{ns}
	No	13(81.3)	72 (93.5)		
BMI category*	>95 percentile	0 (0.0)	1 (1.3)	**	0.499^{ns}
	<95th percentile	16 (100.0)	76 (98.7)		
Induction toxicities	Yes	11(68.8)	23(29.9)	5.17 (1.61-16.55)	0.003
	No	5(31.3)	54(70.1)		

Chi-square test was done, ns- not significant. HTN Hypertension; *Age under 2 years was not included in BMI calculation; f= Frequency

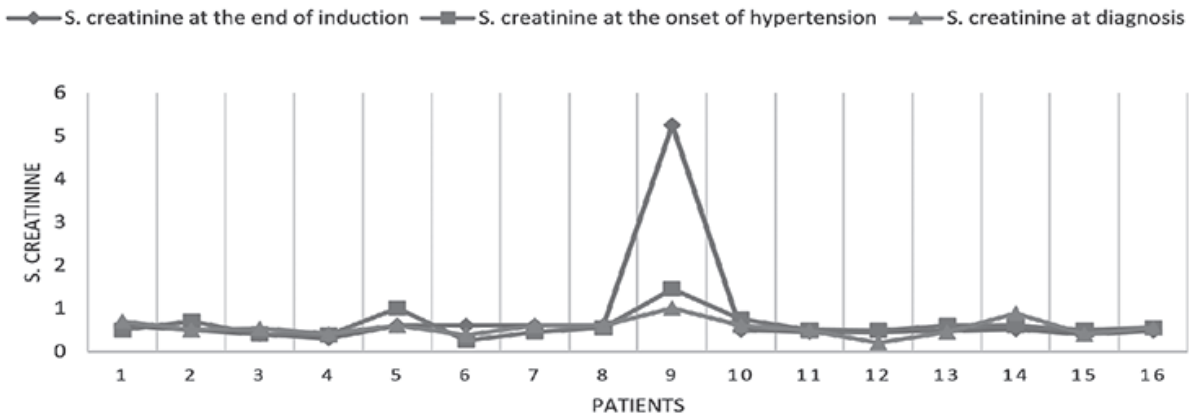

Figure-2: *Changes of serum creatinine level of hypertensive patients, at diagnosis, at the onset of hypertension and at the end of hypertension (n-16)*

Table-5 Shows the outcome of hypertension among the study population at the end of induction. Among a total of 93 patients hypertension was observed in 16 cases. 12 (75%) patients became normotensive after certain period during induction remission and hypertension persists at the end of induction remission in 4 (25%) patients.

Table-5: *Outcome of hypertension at the end of induction (n=16)*

Outcome	Frequency (%)
Improved	12 (75.0)
Persistence	04 (25.0)
Total	16 (100.0)

Table-6: *Multivariate logistic regression analysis of risk factors for the development of hypertension (n=16)*

Variables	B	*p*-value	OR	95% CI	
				Lower	Upper
Induction toxicities	1.057	1.319	2.879	2.17	38.17
TLS	2.104	0.123	0.122	0.008	1.772
Febrile neutropenia	1.008	0.123	0.365	0.101	1.313
Coagulopathy	1.218	0.216	0.296	0.043	2.035
Convulsion	22.544	0.999	-	-	-

Table-6 Shows multivariate logistic regression analysis of risk factors for the development of hypertension. In multivariate logistic regression analysis no factor was found statistically significant.

Discussion

Acute lymphoblastic leukemia (ALL) is the most common pediatric malignancy, accounting for one-quarter of all childhood cancers. The cure rate has significantly improved due to advancements in supportive care. Hypertension is a common complication during induction therapy, leading to morbidity and potential relapse.[6] It is believed that steroids, a key component in induction therapy, cause a dose-dependent increase in blood pressure, which typically resolves after cessation of steroids.[9] This study found hypertension in 17.2% of patients, which aligns with previous reports, [16, 18] though lower than others.[8] Transient hypertension was found in 23.8%, while persistent hypertension was observed in 76.2%. Hypertension peaked in the second week of chemotherapy (75.25%) and gradually decreased over time. Most patients were asymptomatic, with one patient developing hypertensive encephalopathy. The median time to detection of hypertension was day 8, and the mean duration was 13.5 days, with most cases resolving spontaneously without changing steroid therapy. The findings suggest that hydration and chemotherapeutic agents may unmask latent hypertension.[8] Age under 10 years was an important predictor, consistent with other studies.[19-21] Tumor lysis syndrome (TLS) was more prevalent in hypertensive patients, suggesting a significant relationship between TLS and hypertension.[17] Renal derangement was noted in 25% of hypertensive patients, but was not statistically significant. The study also found a higher incidence of hypertension in patients with B-cell lineage ALL compared to T-cell lineage, though this was not statistically significant.

Hypertension was strongly associated with TLS, febrile neutropenia, convulsions, and coagulopathy. The frequency peaked in the second week of induction therapy and decreased thereafter. Regular blood pressure monitoring, particularly in the first two weeks of chemotherapy, is crucial. Further studies are needed to assess the long-term impact of hypertension on survival and the progression to renal or cardiovascular diseases.

References

1. Lanzkowsky P, Lipton JM, Fish JD. Lanzkowsky's manual of pediatric hematology and oncology. 5th ed. London: Elsevier Academic Press; 2011.
2. Islam A, Jamal CY, Nahar K, Siddique R, Begum F, Begum M, et al. Paediatric Oncology Data Based Network (POND) Registry initiated in Bangladesh. Pediatr Blood Cancer. 2013;60:144-5.
3. Pieters R, Hunger SP, Boos J, Rizzari C, Silverman LB, Baruchel A, et al. L-asparaginase treatment in acute lymphoblastic leukemia: a focus on Erwinia asparaginase. Cancer. 2011;117:238-49.
4. Arceci RJ, Hann LM, Smith OP. Pediatric hematology. 3rd ed. Hoboken: John Wiley & Sons; 2007.
5. Pizzo PA, Poplack DG. Principles and practice of pediatric oncology. Philadelphia: Lippincott Williams & Wilkins; 2006.
6. Kamdem LK, Hamilton L, Cheng C, Liu W, Yang W, Johnson JA, et al. Genetic predictors of glucocorticoid-induced hypertension in children with acute lymphoblastic leukemia. Pharmacogenet Genomics. 2008;18:507-14.

7. Osterweil N. Treatment-related hypertension, kidney injury are undertreated in kids with leukemia. MDedge. 2017 Apr 29.

8. Attard-Montalto SP, Saha V, Ng YY, Kingston JE, Eden OB. High incidence of hypertension in children presenting with acute lymphoblastic leukemia. Pediatr Hematol Oncol. 1994;11:519-25.

9. Louis CU, Butani L. High blood pressure and hypertension in children with newly diagnosed acute leukemia and lymphoma. Pediatr Nephrol. 2008;23:603-9.

10. Kamdem LK, Hamilton L, Cheng C, Liu W, Yang W, Julie A, et al. Genetic predictors of glucocorticoid-induced hypertension in children with acute lymphoblastic leukemia. Pharmacogenet Genomics. 2008;18:507-14.

11. Louis CU, Butani L. High blood pressure and hypertension in children with newly diagnosed acute leukemia and lymphoma. Pediatr Nephrol. 2008;23:603-9.

12. Attard-Montalto SP, Saha V, Ng YY, Kingston JE, Eden OB. High incidence of hypertension in children presenting with acute lymphoblastic leukemia. Pediatr Hematol Oncol. 1994;11:519-25.

13. Bakk I, O'Brien S, Reed S, Koch T. Steroid-induced hypertension during induction chemotherapy for acute lymphoblastic leukemia in US children's hospitals. Blood. 2014;124:3651.

14. Juliansen A, Andriastuti M, Sudung OP, Sekartini R. Hypertension, high-dose corticosteroids, and renal infiltration in children with acute lymphoblastic leukemia. Paediatr Indones. 2014;54:324-9.

15. Belgaumi AF, Al-Bakrah M, Al-Mahr M, Al-Jefri A, Alusa A, Saleh M, et al. Dexamethasone-associated toxicity during induction chemotherapy for childhood acute lymphoblastic leukemia is augmented by concurrent use of daunomycin. Cancer. 2003;97:2898-903.

16. Juliansen A, Andriastuti M, Pardede S, Sekartini R. Hypertension, high-dose corticosteroids, and renal infiltration in children with acute lymphoblastic leukemia. Paediatr Indones. 2014;54:372-6.

17. Belgaumi AF, Al-Bakrah M, Al-Mahr M, Al-Jefri A, Al-Musa A, Saleh M, et al. Dexamethasone-associated toxicity during induction chemotherapy for childhood acute lymphoblastic leukemia is augmented by concurrent use of daunomycin. Cancer. 2003;97:2898-903.

18. Bakk I, Koch T, Stanek J, O'Brien SH, Reed S. Steroid-induced hypertension during induction chemotherapy for acute lymphoblastic leukemia in US children's hospitals. J Pediatr Hematol Oncol. 2018;40:27-30.

19. Malhotra P, Kapoor G, Jain S, Garg B. Incidence and risk factors for hypertension during childhood acute lymphoblastic leukemia therapy. Indian Pediatr. 2018;55:877-9.

20. Olger S, Yetgin S, Cetin M, Aras T. Can renal leukemic infiltration cause hypertension in children? J Pediatr Hematol Oncol. 2006;28:9.

21. Yetgin S, Olgar [a], Aras T, Cetin M, Düzova A, Beylergil V, et al. Evaluation of kidney damage in patients with acute lymphoblastic leukemia in long-term follow-up: value of renal scan. Am J Hematol. 2004;77:132-9.

Original Article

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Histomorphological Pattern of Ovarian Tumor in A Tertiary Level Hospital

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Abstract

Background: *Ovarian tumors are one of the most common malignancies in females worldwide, affecting all age groups. They have become increasingly important due to the wide variety of neoplastic entities. The aim of this study was to explore the histomorphological patterns of ovarian tumors in a population group from Bangladesh.* ***Methods:*** *This study was conducted at the Department of Pathology, Dhaka Medical College, Dhaka, between July 2017 and December 2017, and included 100 cases. The patients were clinically and sonographically diagnosed with ovarian tumors. Samples from these patients were received at the pathology department for analysis.* ***Results:*** *In this study, most patients (28.0%) were aged 31-40 years, with a mean age of 36.3 ± 12.7 years. Most patients (63.0%) presented with abdominal discomfort and occasional pain. The majority (89.0%) had a unilateral lump. A cystic tumor was found in 56.0% of the patients, and omental deposits were identified in six (6.0%) cases. Most tumors were benign (69.0%), with one (1.0%) borderline tumor and 30 (30.0%) malignant tumors. Surface epithelial tumors were the most common (65.0%), followed by germ cell tumors (32.0%), sex cord-stromal tumors (2.0%), and metastatic tumors (1.0%).* ***Conclusion:*** *It is not possible to definitively distinguish benign ovarian tumors from their malignant counterparts based solely on clinical behavior. Accurate pathological evaluation is essential for determining the appropriate therapeutic management of ovarian tumors. Histopathological examination remains the gold standard in diagnosing most ovarian tumors.*

Keywords: *Ovarian malignancy, histomorphology.*

Introduction

Ovarian cancer is the most lethal gynaecological cancer. Worldwide, 239,000 new cases of ovarian cancer and an estimated 152,000 deaths were recorded in 2014.[1] It is the fourth most common cancer in women in India.[2,3] In Bangladesh, ovarian cancer ranks 12th in newly diagnosed cancer cases. The prevalence rate in Bangladesh is about 4.4 per 100,000.[4] The National Institute of Cancer Research and Hospital (NICRH) cancer registry data revealed that about 20-25% of cancers are diagnosed at a localized stage.[5]

In developed countries, more than 90% of ovarian cancers are epithelial in origin, with the remainder composed of germ cell tumors (2–3%) and sex cord-stromal tumors (5–6%). Germ cell tumors account for 10–15% of ovarian

cancers in Asian and African populations. Dysgerminoma accounts for more than 70% of germ cell tumors, whereas granulosa cell tumors are the most common sex cord-stromal tumor. Most epithelial ovarian cancers are diagnosed in postmenopausal women, whereas germ cell tumors occur in young women of childbearing potential, often in their twenties.[6]

Ovarian tumors require immediate diagnosis and management. Early diagnosis can make a significant difference in treatment modality and outcomes. Histopathological examination plays a crucial role in definitive diagnosis and patient management. Understanding the existing disease pattern and health-seeking behavior is essential for effective healthcare delivery to any population. The aim of this study is to identify the histopathological patterns of ovarian tumors and to examine the association between clinical parameters, gross morphology, and risk factors among these patients.

Materials and Methods:

This was an observational cross-sectional study conducted at the Department of Pathology, Dhaka Medical College, Dhaka, from July 2017 to December 2017. The study included clinically and sonographically diagnosed ovarian tumor samples from patients received at the department. The sample size was determined to be 100 cases, and sampling was done using the purposive sampling method. The inclusion criteria were resected ovarian masses from all age groups, and the exclusion criteria were a) non-neoplastic cysts of the ovary and b) patients who were unwilling to participate. Ethical assurance for protection of human rights in compliance with the Helsinki declaration for medical research involving human subjects (1964), participation in this study was entirely voluntary. Consent was obtained after explaining the study in Bengali to all respondents.

Results:

Most patients (28.0%) belonged to the age group of 31-40 years. The mean age was 36.3±12.7 years. Among them, only 3.0% of patients had a family history of ovarian tumors. The majority (64%) of patients did not use contraceptives, while 13 patients used injectable contraceptives, 10 used oral contraceptive pills (OCP), 8 used barrier methods, 3 underwent tubal ligation, and 2 used IUCDs. Abdominal discomfort and occasional pain were the most common symptoms (63%), followed by loss of body weight, abdominal lump, back pain, loss of appetite, dyspepsia, etc. (Table 1).

Table 1: Distribution of the study patients by symptoms of ovarian tumour (n=100)

Symptoms of tumour	Percentage
Abdominal lump	47.0
Abdominal heaviness	31.0
Abdominal discomfort andOccasional pain	63.0
Severe abdominal pain	9.0
Abnormal vaginal bleeding	11.0
Urinary symptom	21.0
Loss of appetite, dyspepsia	41.0
Loss of body weight	53.0
Shortness of breath	17.0
Back pain	46.0
Incidental diagnosis	9.0

Regarding sonographic findings, most patients had a unilateral lump (89.0%). Fifty-six patients had cystic tumors, while the remaining 44% had solid or partly solid/cystic tumors. Ascites was found in 19 patients on ultrasound.

Table 2 shows that most patients (53.0%) had tumors within the size range of 10-20 cm, and most tumors had an intact capsule (81.0%). The majority of tumors were cystic (56.0%), with 59.0% being unilocular. Most of the cystic tumors contained thin serous fluid (36.0%).

Table 2: Distribution of the study patients by macroscopic findings of ovarian tumors (n=100)

Macroscopic findings	Percentage
Size of tumor	
<10 cm	39.0
10-20 cm	53.0
>20 cm	8.0
Capsule	
Intact	81.0
Ruptured	19.0
Cosistancy	
Cystic	56.0
Solid	13.0
Cystic and solid	31.0
Cut section	
Unilocular	59.0
Multilocular	41.0
Content	
Thin serous fluid	36.0
Thick mucoid fluid	15.0
Sebaceous material/hair	26.0
Haemorrhage/necrosis	14.0
Omental deposit	6.0

Table 3: Percentage distribution of surface epithelial tumors (n=65)

Type of surface epithelial tumors	Number of patients	Percentage
Serous cystadenomas	26	40.00
Serous cysadenofibroma	02	3.08
Mucinous cystadenomas	09	13.85
Mucinous cysadenofibroma	03	4.62
Brenner tumor	01	1.54
Serous cystadenocarcinoma	15	23.08
Mucinous cystadenocarcinomas	06	9.23
Endometrioid carcinoma	01	1.54
Microinvasive Mucinous carcinoma	01	1.54
Mucinous borderline tumor	01	1.54

A total of 100 cases of ovarian tumors were documented during this study period. Of these, the majority (69) were benign, 1 was borderline, and 30 were malignant.

In this study, surface epithelial tumors were the most common (n=65), followed by germ cell tumors (n=32), sex cord-stromal tumors (n=2), and metastatic tumors (n=1).

Table 3 shows that, of the 65 cases of surface epithelial tumors, serous cystadenomas comprised 26 cases (40.0%), serous cystadenocarcinoma comprised 15 cases (23.08%), mucinous cystadenomas comprised 9 cases (13.85%), and mucinous cystadenocarcinomas comprised 6 cases (9.23%).

On the other hand, germ cell tumors showed the distribution according to subtypes (Table 4). Table 5 shows that 56 tumors were cystic in consistency, of which 44 (78.6%) were surface epithelial tumors. Thirteen were solid in consistency, of which 7 (53.8%) were surface epithelial tumors. Thirty-one tumors had both cystic and solid consistency, of which 16 (51.6%) were germ cell tumors.

Table 4: *Distribution of germ cell tumors*

Type of Germ cell tumors	Number of patients	Percentage
Mature cystic teratoma	22	68.75
Mature cystic teratoma with serous cyst adenoma	01	3.13
Mature cystic teratoma with mucinous cyst adenoma	03	9.38
Immature teratoma	01	3.13
Dysgerminoma	04	12.50
Yolk sac tumor	01	3.13

It was found that, out of 69 benign tumors, 41 (59.4%) were surface epithelial tumors. One borderline tumor was identified, which was a surface epithelial tumor. Malignant tumors were found in 30 patients, of which 23 (76.7%) were surface epithelial tumors (Table 6).

Table 5: Distribution of histomorphological pattern of ovarian tumors according to consistency (n=100)

Histomorphological pattern	Consistency		
	Cystic(n=56)	Solid (n=13)	Cystic and solid(n=31)
	n (%)	n (%)	n (%)
Surface epithelial tumors	44(78.6)	7(53.8)	14(45.2)
Germ cell tumors	12(21.4)	4(30.8)	16(51.6)
Sex cord-stromal tumors	-	2(15.4)	-
Metastases	-	-	1(3.2)

Table 6: Distribution of histomorphological pattern in type of tumor (n=100)

Histomorphological pattern	Type of tumor		
	Benign (n=69) n(%)	Borderline (n=1) n(%)	Malignant (n=30) n(%)
Surface epithelial tumors	41(59.4)	1(100.0)	23(76.7)
Germ cell tumors	26(37.7)	0(0.0)	6(20.0)
Sex cord-stromal tumors	2(2.9)	0(0.0)	0(0.0)
Metastases	0(0.0)	0(0.0)	1(3.3)

In relation to grading, it was observed that four patients had low-grade serous cystadenocarcinoma and 11 had high-grade serous cystadenocarcinoma. Four patients had low-grade mucinous cystadenocarcinomas, and 2 had high-grade mucinous cystadenocarcinomas.

Omental deposits of malignant tumors were found in 3 (10.0%) cases of serous cystadenocarcinoma, 2 (6.7%) cases of mucinous cystadenocarcinomas, and 1 (3.3%) case of endometrioid carcinoma.

Figure 1: *Gross picture of mature cystic teratoma. Cut surface shows unilocular cyst with sebaceous material and hair shafts (case No.5).*

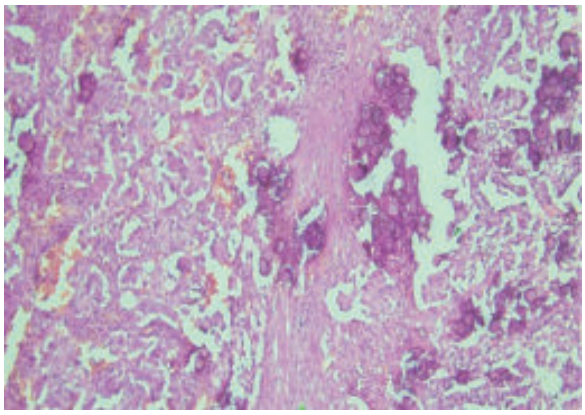

Figure 1: *Gross picture of mature cystic teratoma. Cut surface shows unilocular cyst with sebaceous material and hair shafts (case No.5).*

Discussion:

Incidence

A total of 100 cases of ovarian tumors were documented during this study period, of which the majority (69.0%) were benign, 1 was borderline, and 30 were malignant. Similar results were observed in studies conducted by Kanya[7] and Sawant and Mahajan[8]. Kanya[7] found that out of 154 ovarian tumors, 75.3% (116/154) were benign, 3.2% (5/154) were borderline, and 21.4% (33/154) were malignant. The study by Sawant and Mahajan8 reported that among 70 neoplastic ovarian lesions, 52 (75.7%) were benign, 2 (6.1%) were borderline, and 6 (18.2%) were malignant.

Age Distribution

In this study, the age range was from 9 to 80 years, with 28 (28.0%) patients in the 31-40 years age group, which constituted the largest proportion. The mean age was 36.3±12.7 years. The youngest patient in our series was a 9-year-old girl with dysgerminoma, and the oldest patient was an 80-year-old woman with mucinous cystadenocarcinoma of the ovary.

Nature of the Tumors

This study revealed that surface epithelial tumors were the most common (65.0%), followed by germ cell tumors (32.0%), sex cord-stromal tumors (2.0%), and metastatic tumors (1.0%). Similar results were observed in other studies. Thakkar and Shah [9] found that among all tumor types, serous tumors formed the largest group (65.4%), followed by germ cell tumors (17.8%) and mucinous tumors (8.5%). Sex cord-stromal tumors constituted 6.1% of the total cases in their study.

In the present study, of the 32 cases of germ cell tumors, 22 (68.75%) were mature cystic teratomas, 4 (12.50%) were dysgerminomas, and 3 (9.38%) were mature cystic teratomas with mucinous cystadenoma.

Clinical Presentation

It was observed that most patients had abdominal discomfort and occasional pain (63.0%), followed by

loss of body weight (53.0%), abdominal lump (47.0%), back pain (46.0%), loss of appetite and dyspepsia (41.0%), and abnormal vaginal bleeding (11%). The present study is consistent with the findings of Pilli et al.[10], where abdominal pain was the most common symptom. Thakkar and Shah[9] revealed that abdominal pain was the most common presenting symptom, followed by menorrhagia. In non-neoplastic lesions, menorrhagia was the most common symptom.

In the present study, serum CA-125 was elevated in 13 cases of serous cystadenocarcinoma and 3 cases of mucinous cystadenocarcinoma. Serum CA 19-9 was elevated in 5 cases of serous cystadenocarcinoma and 4 cases of mucinous cystadenocarcinoma. Serum alpha-fetoprotein was elevated in cases of immature teratoma and yolk sac tumor. Engelen et al.[11] found that in patients with mucinous tumors, preoperative CA 19-9 was more frequently elevated (8/14, 57%) than CA 125 (3/20, 15%) or CEA (2/18, 11%).

Site of Involvement

Most patients had a unilateral lump (89.0%). The majority (56.0%) had cystic tumors. Ascites was found in 19 patients, and metastasis to pelvic lymph nodes was found in 5 patients.

Histomorphological features

In this study, most patients had tumor sizes ranging from 10-20 cm (53.0%). An intact capsule was observed in 81 cases. Most patients had cystic tumors (56.0%), with 59 patients having unilocular cysts. Thin serous fluid was found in 36 cases, and omental deposits were found in 6 cases. Omental deposits in malignant tumors were found in 4 cases of serous cystadenocarcinoma (13.0%) and 2 cases of mucinous cystadenocarcinoma (6.7%). Kanya[7] observed that, on gross examination, most tumors were cystic (55.1%, 85/154), followed by solid tumors (24.6%, 38/154), and 20.21% (31/154) showed both solid and cystic areas. In the study by Panchal et al.[12], most tumors were cystic (44.5%, 37/83), followed by solid (13.2%, 11/83) and mixed (42%, 35/83). Sawant and Mahajan[8] found that, on gross examination, 44.78% of cases were cystic, 22.39% were solid, and 32.83% were partly solid and partly cystic. Pradhan et al.[13] observed that, on gross examination, most tumors were cystic (44.5%), followed by solid (13.2%) and mixed (42%).

In this study, 56 cases had cystic consistency, of which 44 (78.6%) were surface epithelial tumors. Thirteen were solid in consistency, of which 7 (53.8%) were surface epithelial tumors. Thirty-one cases had both cystic and solid consistency, of which 16 (51.6%) were germ cell tumors. Garg et al.[14] in their study observed that, out of 60 epithelial tumors, 50 (83.3%) were cystic in nature, followed by cystic to solid consistency (15%, 9/60), and solid tumors (1.7%, 1/60). Most germ cell tumors were cystic in nature (75%, 12/16), followed by solid tumors (18.8%, 3/16). The majority of sex cord-stromal tumors (57.1%, 4/7) and all metastatic tumors were partly solid to cystic in consistency.

In this study, out of 69 benign tumors, most were surface epithelial tumors (41, 59.4%), followed by mature cystic teratomas (26, 37.7%) and sex cord-stromal tumors (2, 2.9%). One patient had a borderline surface epithelial tumor. Malignant tumors were found in 30 patients, of which 23 (76.7%) were surface epithelial tumors, followed by dysgerminomas (4, 13.3%). Garg et al.14 observed that the most common benign tumor was serous cystadenoma (37.64%, 32/85), followed by mucinous cystadenoma (15.29%, 13/85) and mature cystic teratoma (14.12%, 12/85). Serous cystadenocarcinoma was the most common malignant tumor (5.88%, 5/85), followed by adult granulosa cell tumor (4.7%, 4/85). The only borderline tumor was mucinous tumor. There were 2 cases of metastatic ovarian tumors, one of which was a Krukenberg tumor and the other an extra-ovarian primary peritoneal carcinoma. In the study by Patil et al.[15], out of 109 surface epithelial tumors, 84.4% were benign, 0.91% were borderline, and 14.67% were malignant. Benign surface epithelial tumors comprised 74.2% (92/124) of all benign tumors, while their malignant counterparts formed 61.5% (16/26) of all malignant ovarian tumors.

Patil et al.[15] observed that serous cystadenoma (41.93%) was the most common benign tumor, followed by mucinous cystadenoma (32.25%). Serous cystadenocarcinoma (38.46%) was the most common malignant tumor. Pradhan et al.[13] observed that the most common malignant tumors were from the surface epithelial tumors (40%, 6/15), followed by germ cell tumors (33%, 5/15), metastatic tumors (20%, 3/15), and sex cord-stromal tumors (7%, 1/15). Sawant and Mahajan[8] reported that, out of 6 malignant cases, 4 were serous cystadenocarcinomas, 2 were endometrioid carcinomas, and 2 were borderline serous tumors.

Conclusion:

This study found that surface epithelial tumors were the most common type of ovarian tumor in the perimenopausal age group, with a higher incidence of malignancy, followed by germ cell tumors. The most common benign tumor was serous cystadenoma, and the most common malignant tumor was serous cystadenocarcinoma. However, the sample size was too small to draw definitive conclusions. Among malignant ovarian tumors, delayed diagnosis was common, as most patients presented with abdominal discomfort and occasional pain, often at a late stage of the disease.

References:

1. World Cancer Report 2014. World Health Organization. 2014. Edited by Bernard W. Stewart and Christopher P. Wild, Chapter 5.12:465.
2. Saranath D, Khanna A. Current Status of Cancer Burden: Global and Indian Scenario. Biomed Res J. 2014;1(1):1-5.
3. Gangaraju S, Sarella LK, Chaveli L, Gurugubelli S. Scenario of ovarian mass lesions at a teaching hospital in Andhra Pradesh, India. Int J Reprod Contracept Obstet Gynecol. 2015 Aug;4(4):982-989.
4. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C. Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 11. Lyon, France: International Agency for Research on Cancer, 2014. Available from: http://globocan.iarc.fr.
5. Hospital Cancer Registry, NICRH, Annual Report 2005. Directorate General of Health Services, Ministry of Health and Family Welfare; supported by WHO.
6. Sankaranarayanan R, Ferlay J. Worldwide burden of gynaecological cancer: The size of the problem. Best Pract Res Clin Obstet Gynaecol. 2006;20(2):207-225.
7. Kanya K. Study of histomorphological patterns of ovarian tumors. J Sci Innov Res. 2015;4(3):117-120.
8. Sawant A, Mahajan S. Histopathological Study of Ovarian Lesions at a Tertiary Health Care Institute. MVP J Med Sci. 2017;4(1):26-29.
9. Pilli GS, Suneeta KP, Dhaded AV, Yenni VV. Ovarian tumours: a study of 282 cases. J Indian Med Assoc. 2002 Jul;100(7):420-424.
10. Thakkar NN, Shah SN. Histopathological Study of Ovarian Lesions. Int J Sci Res. 2015 Oct;4(10):1745-1749.
11. Engelen MJA, et al. Serum CA 125, CEA, and CA 19-9 as tumor markers in borderline ovarian tumors. Gynecol Oncol. 2000;78:16-20.
12. Panchal N, Parikh U. Histopathological patterns of ovarian tumors. Int J Sci Res. 2015;4(1):335-337.
13. Pradhan A, Sinha AK, Upreti D. Histopathological patterns of ovarian tumors at BPKIHS. Pradhan A, et al. 2012 May-August;10(2):87-97.
14. Garg N, Anand AS, Annigeri C. Study of histomorphological spectrum of ovarian tumours. Int J Med Health Res. 2017;3(10):12-20.
15. Patil RK, Bhandari BJ, Kittur SK, Haravi RM, Aruna S, Jadhav MN. Histomorphological Study of Ovarian Tumors at a Tertiary Care Centre. Ann Pathol Lab Med. 2017;4(6):639-645.

Case Report

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Rare Tumour of Lung in A Child: The Diagnostic Dilemma

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Abstract

Background*: Benign fibrous histiocytoma of lung in a child is an unusual case. This benign tumour may recur and make the treatment difficult for the patient if he is not properly followed up.* ***Materials and method****: Patient's physical, clinical, radiological findings are reviewed, and the report was issued in time.* ***Results****: The sample was collected for histopathological procedures, correlated with the clinical findings and diagnosed the case.* ***Conclusions****: Benign fibrous histiocytoma in lungs in a child is a very rare disease; there have been a few such cases reported and to our knowledge, this is the first documented case in lung in the National Institute of Diseases of the Chest and Hospital, Mohakhali, Dhaka.*

Key words: *BFH: Benign Fibrous Histiocytoma MT: Mantoux Test, S.: Serum, Z-N (Ziehl-Neelsen),*

Introduction:

Benign fibrous histiocytoma (BFH) in the lung is extremely rare in children. Although it is a non-cancerous tumor, it can come back if not properly treated and monitored. This case report highlights a unique diagnosis of BFH in a child at the National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka. It shows how clinical, radiological, and lab tests were used to identify the condition and stresses the importance of regular follow-ups to manage the disease effectively and prevent future complications.

A 17-year-old boy from Kishoreganj was admitted to the medicine unit of NIDCH with complaints of recurrent episodes of fever lasting one month, accompanied by a non-productive cough and occasional hemoptysis. He was otherwise healthy and asymptomatic. For these symptoms, he had been treated as a case of pneumonia by local physicians. On physical examination at admission, the patient was tachypneic, with a respiratory rate of 34 breaths per minute and blood pressure of 110/70 mm Hg. No lymphadenopathy was observed, except for palpable cervical lymph nodes.

Systemic Examination:

Examination of the respiratory system revealed restricted chest movement on the left side, with absent breath sounds in the upper part of the left lung. The rest of the systemic examination was unremarkable.

Investigations:
Initial investigations showed hemoglobin levels of 15.4 g/dL, with total and differential counts within normal limits, and a platelet count of 167,000/cu mm. The erythrocyte sedimentation rate (ESR) was 59 mm at the end of the first hour. Serum electrolytes were within normal limits, and prothrombin time was 14 seconds. Other findings included normal electrocardiography (ECG), random blood sugar of 11.1 mg/dL, normal echocardiogram, serum creatinine of 0.7 mg/dL, and serum bilirubin of 2.1 mg/dL. SGPT was 33 U/L, albumin was 5.7 g/dL, and total protein was 9.5 g/dL. The Mantoux test was negative, and sputum analysis for acid-fast bacilli (using Z-N staining) showed no evidence of infection.

Imaging Findings:
A chest X-ray revealed an opaque shadow in the left hemithorax. Bronchoscopy demonstrated a mitotic lesion in the left lung, with an endobronchial growth located at the left principal bronchus, approximately 2 cm from the carina. A computed tomography (CT) scan of the chest showed a mediastinal shift to the left side, with segmental collapse and consolidation in the left upper and lower lobes. The heart and great vessels appeared normal, and there was no pleural effusion or lymphadenopathy. The bony thorax was also normal.

Clinical Progression and Surgical Intervention:
The patient was transferred to the Thoracic Surgery Unit with a clinical diagnosis of a left-sided collapsed lung of uncertain etiology. He underwent a left-sided bronchotomy, which revealed a well-encapsulated, soft tissue mass arising from the principal bronchus of the left lung. The mass was excised, and the tissue was sent for histopathological examination.

Histopathological Examination:
The specimen consisted of an endobronchial growth from the left principal bronchus and a hilar lymph node. On gross examination, the tissue was greyish-white and measured 1.5 × 1.0 × 1.0 cm, processed as a single block. Another fragmented piece of greyish-white tissue, of similar dimensions, was also processed. Microscopically, the sections showed a benign neoplasm composed of short and long fascicles with uniform cellularity, displaying two types of cells with transitional forms. Most cells were fibriform, with vesicular, elongated nuclei and amphophilic cytoplasm. Some were rounded, with small, darkly stained nuclei, open chromatin, inconspicuous nucleoli, and foamy cytoplasm. These cells were arranged in storiform and herringbone patterns. Focal areas of necrosis, hyalinized stroma, dilated blood vessels, and infiltration of lymphocytes, plasma cells, foamy histiocytes, and giant cells within a fibrovascular stroma were noted. Additionally, a cyst wall lined by tall columnar epithelium was observed. There was no evidence of malignancy.

Diagnosis:
The case was diagnosed as a primary benign fibrous histiocytoma of the lung (cellular type), with a differential diagnosis of solitary fibrous tumor. Immunohistochemistry for CD68 and CD34 was recommended for further evaluation.

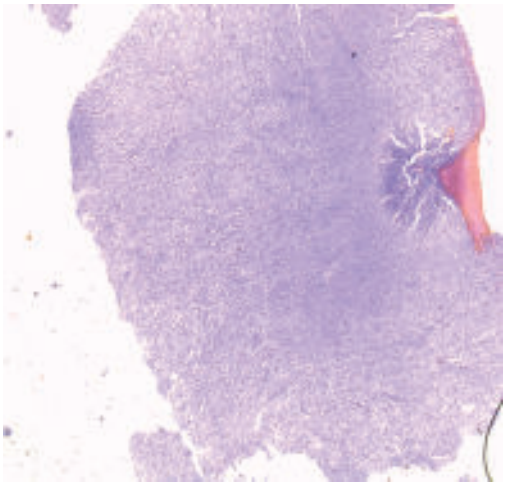

Figure 1: *Hyalinized stroma and dilated blood vessels*

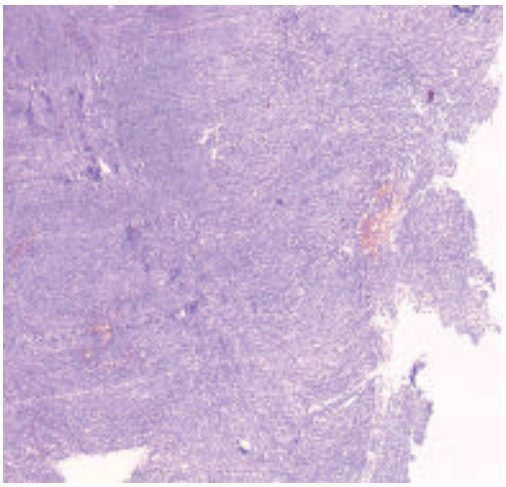

Figure 2: *Infiltration of lymphocytes, plasma cells, foamy histiocytes and giant cells*

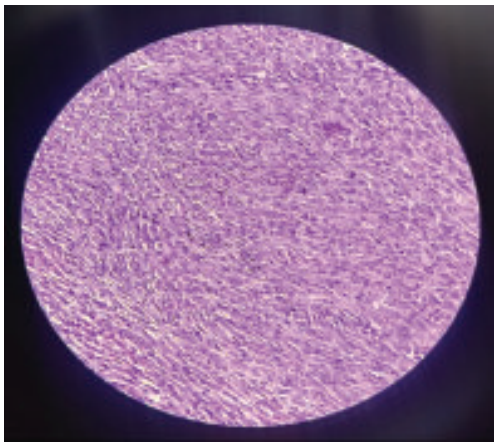

Figure 3: *Short and long fascicles of uniform cellularity*

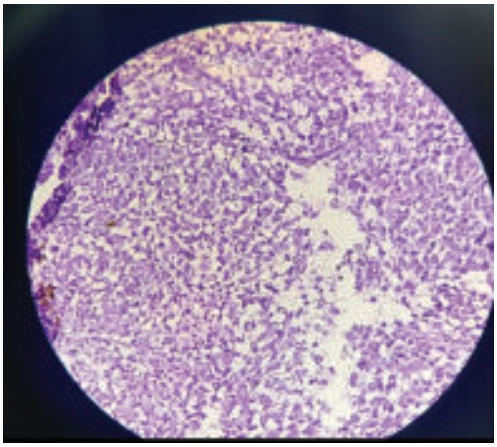

Figure 4: *Rounded cells with small darkly stained nuclei, open chromatin with inconspicuous nucleoli and foamy cytoplasm.*

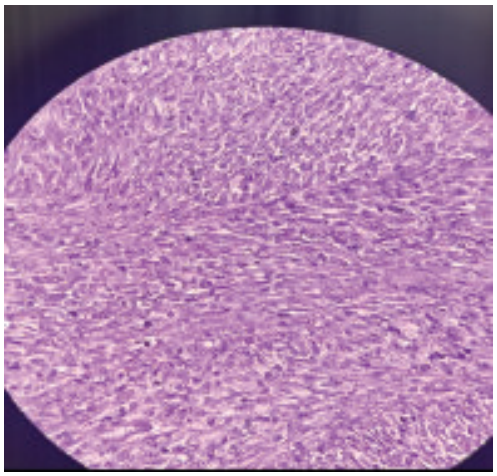

Figure 5: *Fibriform cells with vesicular, elongated nuclei and amphophilic cytoplasm. Storiform as well as herring bone patterns arrangement.*

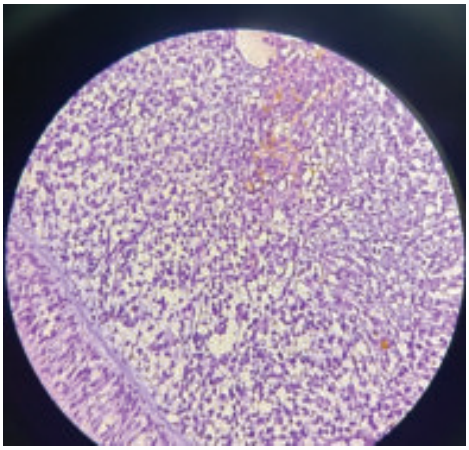

Figure 6: *Cyst wall lined with a tall columnar lining epithelium in the lower left.*

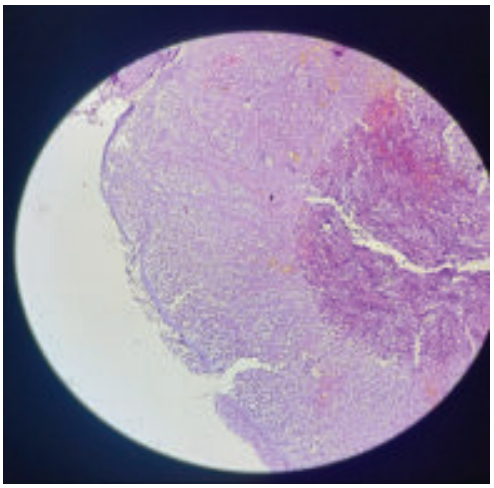

Figure 7: *Necrotic areas*

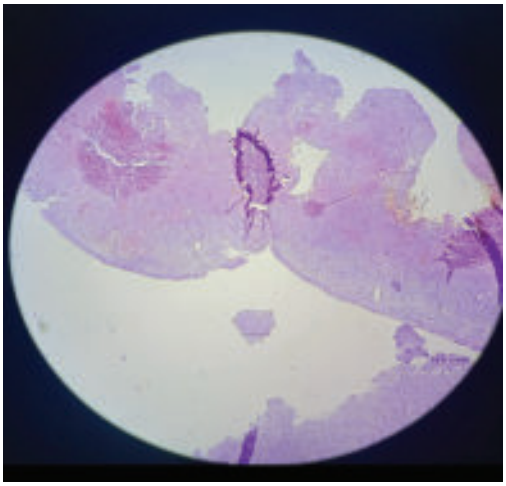

Figure 8: *Focal areas of necrosis*

Discussion:

Benign fibrous histiocytoma (BFH) is an extremely rare mediastinal tumor, with a few cases reported in the 20–40-year age group, primarily in women, and predominantly located in the posterior mediastinum. BFH is a tumor of mixed origin, involving fibroblastic and histiocytic components, with an unknown etiology. The most common sites of presentation are the lower extremities, head, and neck regions.

In this case, the tumor was found during surgery to arise from and be completely confined to the lung. BFH tumors are typically well-circumscribed and pseudo-encapsulated, with central hemorrhage or occasional cystic changes. They display a characteristic biphasic pattern of histiocytes and fibroblasts, as well as myofibroblasts and undifferentiated mesenchymal cells. Occasionally, focal areas of necrosis are observed. BFH tumors located in deeper body parts are generally larger and better circumscribed than their cutaneous counterparts.

The diagnosis of BFH should be supported by CD68 positivity on immunohistochemistry. Nearly half of BFH tumors in the lung measure 5 cm or greater at excision, compared to most cutaneous fibrous histiocytomas, which are typically less than 3 cm. The benign nature of the lesion supports cure through surgical excision alone, which is associated with an excellent prognosis. Immunohistochemistry was advised for diagnostic exclusion based on tumor location, radiographic findings, microscopic characteristics, and to rule out other benign lesions. Further immunohistochemistry for markers such as Vimentin, CK, Desmin, Calretinin, SMA, S100, EMA, CD45, and Ki67 is usually performed for confirmatory diagnosis.

Risk factors for metastasis may include large tumor size, high cellularity, local recurrence, and aggressive behavior. The recurrence rate for ordinary fibrous histiocytoma, even when incompletely excised, is less than 2%, whereas the recurrence rate for cellular variants is approximately 26%. Although BFH may carry a low potential for malignancy, complete surgical resection has been reported to reduce recurrence. An adequate resection margin and close clinical follow-up are mandatory.

In this case, the postoperative course of the patient was uneventful. No postoperative radiotherapy or chemotherapy was administered. At one year of follow-up, the child remains healthy and symptom-free.

Conclusion:

The diagnosis of benign fibrous histiocytoma (BFH) of the lung is a diagnosis of exclusion. Its rarity, benign nature, and excellent prognosis underline the need for precise diagnosis and proper management. The cause of BFH remains uncertain, with ongoing debate among pathologists about whether it represents a true tumor, a reactive process, or a defect in cell development. The diagnostic and therapeutic approach should focus on minimizing pitfalls in management to ensure the best outcomes for the patient. Regular follow-up is essential to monitor for potential recurrence and to provide effective care.

References:

1. Enzinger FM, Weiss SW. *Soft tissue tumor*. 4th ed. Mosby; 2001. p. 441–55.
2. Sajjad SM, Begin LR, Dail DH, Lukeman JM. Fibrous histiocytoma of lung: a clinicopathological study of two cases. *Histopathology*. 1981;5(3):325–34.
3. Fletcher CD. Benign fibrous histiocytoma of subcutaneous and deep soft tissue: clinicopathologic analysis of 21 cases. *Am J Surg Pathol*. 1990;14(8):801–9.
4. Sood N, Singhal VS. Benign fibrous histiocytoma of the mediastinum. *Indian J Chest Dis Allied Sci*. 1992;34:33–7.
5. Lago JV, Pujol JL, Reboiras SD, Larrauri J, Schacke M. Fibrous histiocytoma of the lung. *Thorax*. 1976;31(4):475–9.
6. van Giffen NH, van Rhijn LW, van Ooij A, Cornips E, Robben SG, Vermeulen A, et al. Benign fibrous histiocytoma of the posterior arch of C1 in a 6-year-old boy: a case report. *Spine*. 2003;28(18):E359–63.
7. Fletcher CD. *Diagnostic histopathology of tumors*. Churchill Livingstone; 2000. p. 1014–505.
8. Prieto VG, Reed JA, Shea CR. Immunohistochemistry of dermatofibromas and benign fibrous histiocytomas. *J Cutan Pathol*. 1995;22(4):336–41.
9. Calonje E, Mentzel T, Fletcher CD. Cellular benign fibrous histiocytoma: clinicopathological analysis of 74 cases of a distinctive variant of cutaneous fibrous histiocytoma with frequent recurrence. *Am J Surg Pathol*. 1994;18(7):668–76.

10. Colome-Grimmer MI, Evans HL. Metastasizing cellular dermatofibroma: a report of two cases. *Am J Surg Pathol*. 1996;20(12):1361–7.

11. Doyle LA, Fletcher CD. Metastasizing 'benign' cutaneous fibrous histiocytoma: a clinicopathologic analysis of 16 cases. *Am J Surg Pathol*. 2013;37(4):484–95.

12. Fletcher CDM, Calonje E. Cutaneous fibrohistiocytic tumors: an update. *Adv Anat Pathol*. 1994;1(1):2–15.

13. Matsubara O, Tan-Liu NS, Kenney RM, Mark EJ. Inflammatory pseudotumors of the lung: progression from organizing pneumonia to fibrous histiocytoma or to plasma cell granuloma in 32 cases. *Hum Pathol*. 1988;19(7):807–14.

14. Bhat A, Geethamani V, Vijaya C. Soft tissue giant cell tumor of low malignant potential: a rare tumor at a rare site. *J Clin Diagn Res*. 2013;7(12):2960–1.

15. Cerfolio RJ, Allen MS, Nascimento AG, Deschamps C, Trastek VF, Miller DL, et al. Inflammatory pseudotumors of the lung. *Ann Thorac Surg*. 1999;67(4):933–6.

Case Report

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Amputation of Forearm – A Dreaded Complication of Chemotherapy Extravasation in Cervical Cancer Patients

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Abstract:

Chemotherapeutic drugs can cause toxic local tissue injury due to extravasation and are classified as irritants, vesicants, and non-vesicants. Extravasation (EV) of some drugs can cause severe tissue destruction and be potentially devastating if not managed effectively. Compared to irritants, vesicant-induced extravasation occurs at a higher rate. Here, we report two cases of forearm amputation due to severe necrosis and devascularization resulting from chemotherapy extravasation. Two patients with advanced-stage cervical cancer who received chemotherapy with 5FU and cisplatin experienced grade IV toxicity, i.e., extravasation of chemotherapy. Both patients developed this complication during their second cycle of chemotherapy. The diagnosis was delayed, and ultimately, forearm amputation was performed. Amputation of the arm due to severe necrosis following 5FU and cisplatin-based chemotherapy in cervical cancer is extremely rare and constitutes a devastating complication.

Key words: *Extravasation, Amputation, Carcinoma cervix*

Introduction

Extravasation is a rare complication of chemotherapy, with an incidence ranging from 0.1% to 6.5%.[1] It can induce localized injury, necrosis, and nerve damage, and may ultimately cause permanent and potentially disfiguring damage that may require surgical intervention for management.[2,3] Chemotherapeutic agents are classified as vesicants, irritants, and non-vesicants according to their potential to cause tissue injury.[4] The severity of tissue injury depends on the type, concentration, and quantity of the chemotherapeutic agent injected.[5] Irritant anticancer agents may cause transient inflammation with swelling, redness, and pain at the site of extravasation but rarely lead to necrosis.[6] According to the ESMO-EONS classification of cytotoxic drugs, cisplatin and 5-fluorouracil (5FU) are classified as irritants based on their ability to cause tissue damage.[7] These drugs (cisplatin and 5FU) form a standard combination regimen used in the treatment of cervical carcinoma patients.[8]

Several factors are responsible for the extent of injury following extravasation, including the type of drug that extravasates, the concentration and volume of the drug in the tissue, the location of the extravasation, and patient comorbidities and other factors.

The severity of extravasation injury was graded using the CTCAE v4.3 grading scale, with symptoms ranging from pain, erythema, and mottling of the skin to tissue necrosis.[9,10] The Millam classification is one of the most widely used tools to assess the severity of skin lesions following extravasation.[11]

- Class I: Painful infiltrated region, no erythema, no oedema, difficulty in perfusion.
- Class II: Painful infiltrated area, small oedema (0-20%), no pallor, pulse downstream of the infiltrated area present, capillary pulse (recoloration time less than three seconds).
- Class III: Painful infiltrated area, significant oedema (30-50%), pallor, decreased local heat, downstream arterial and capillary pulses present.
- Class IV: Painful infiltrated region, very significant oedema (30-50%), pallor, decreased local heat, decreased or absent arterial pulse, skin recoloration time greater than 3 seconds, ulceration, or skin necrosis.

Cisplatin is a platinum-containing drug, and extravasation of high concentrations of cisplatin (e"0.75 mg/dL) can aggravate tissue damage and lead to necrosis.[5] Reports of 5FU-induced grade III extravasation are minimal. The intensity of the reaction after extravasation can vary widely, from mild redness and oedema to intense, irreversible ulceration, necrosis, and severe pain, most often requiring surgical treatment.[12]

Fogure 1: *A 50-year-old woman known case of carcinoma cervix III B with blackish discoloration of arm*

Despite some avoidance measures, such as secure administration, the presence of local policies and protocols, and the training of appropriate staff members, extravasation still occurs.[13]

Case 1:

A 50-year-old lady presented to the Gynaecological Oncology OPD in January 2022, diagnosed with cervical cancer (ca-cervix), stage IIIB. She had profuse per vaginal bleeding. According to the Multidisciplinary Tumor Board, she was advised to undergo urgent CCRT and ICRT. Due to a long waiting time for CCRT at the National Institute of Cancer Research & Hospital, she sought treatment at a private institution. During the third week of chemotherapy, she developed burning, pain, and swelling in the forearm. Two to three days later, the skin of the forearm gradually became blackish, with blistering, moist desquamation, and some areas of skin shedding. A duplex study of the right arm was performed, which revealed occlusion of the right subclavian, axillary, brachial, radial, and ulnar arteries. A decision was made to amputate the arm.

Case 2:

A 55-year-old lady attended the Gynaecological Oncology OPD in March 2023 with complaints of post-coital bleeding occurring three times in one month. On examination, her cervix was broad and barrel-shaped (3.5 cm), with an endophytic growth. The left parametrium was involved, while the right parametrium was free, and the clinical stage was determined to be IIB. According to the tumor board decision, CCRT and ICRT were planned. However, due to long waiting times, induction chemotherapy with cisplatin and 5-fluorouracil was administered. During her second cycle of chemotherapy, she experienced burning, pain, and swelling in the forearm. Upon inquiry, she revealed that the chemotherapy infusion had been administered earlier than the previous cycle due to a large number of patients waiting and a shortage of available beds. Two to three days later, the skin of the forearm became blackish, blistering, and moist, with some areas of desquamation. A duplex study of the left upper limb vessels was performed, which revealed occlusion of the left subclavian, axillary, brachial, radial, and ulnar arteries by an organized thrombus, while the venous system of the left upper limb appeared normal. A decision was made to amputate the left arm.

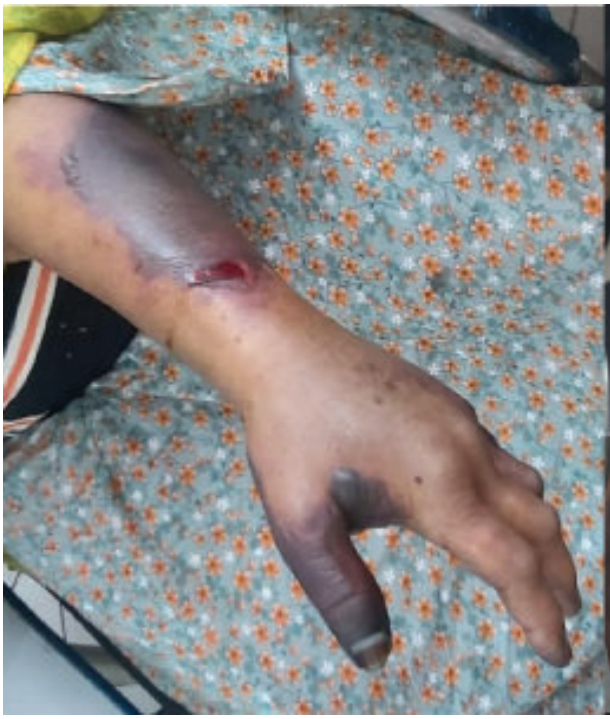
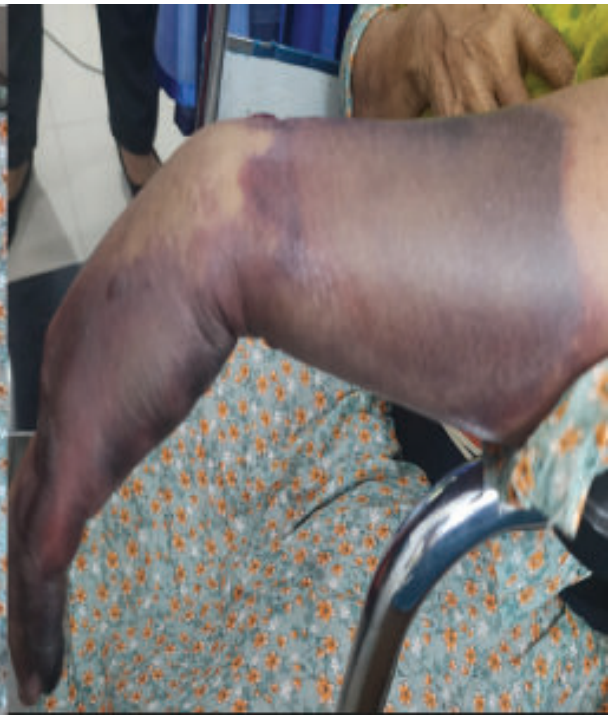


Figure 2



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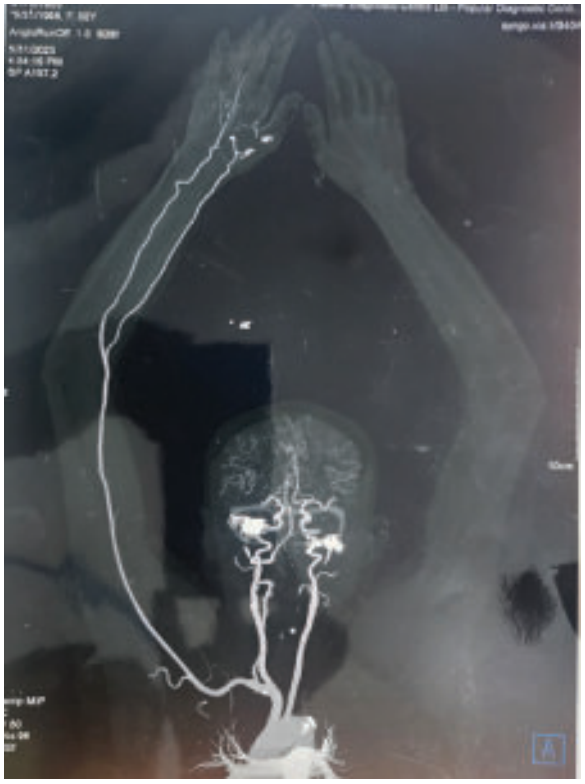

Figure 3

Discussion:

Extravasation of chemotherapy is one of the most dreaded complications and is considered a medico-surgical emergency. The effectiveness of treatment is time-dependent; after 24 hours, the treatment is no longer curative, but the aim is to limit further damage.[11] Extravasation refers to the unintentional escape of a chemotherapeutic agent from a vessel into the surrounding tissues, either by leakage or due to involuntary injection of the drug into the tissues.[14] The incidence rate of extravasation is 0.6% to 6%.[14] Elderly individuals, children, those with thin or fragile venous lumens, recurrent interventions, certain chemotherapy drugs, radiotherapy, hypertension, venous occlusion, and neurological diseases all increase the risk for extravasation.[12] The antecubital area and areas where the skin is thin, such as the hands, are preferable sites for intravenous infusion, and extravasation injuries are more frequent in these areas of the body.[12]

There is no clear relationship between age or gender and the occurrence of extravasation. The ages of our patients were 50 and 55 years. In both cases, extravasation developed in the upper extremity, and both patients had received 5FU and cisplatin chemotherapy

prior to radiotherapy for advanced-stage cervical carcinoma.

According to the ESMO-EONS classification of cytotoxic drugs, chemotherapy drugs are classified as vesicants, irritants, or non-vesicants based on their ability to cause tissue damage.[7] 5FU is an antimetabolite, and cisplatin, an alkylating agent, are both irritant chemotherapy drugs.[14]

Irritants can cause an inflammatory reaction, including aching, swelling, pain, and phlebitis at the injection site or along the vein. They may cause sclerosis, hyperpigmentation along the vein, burning, local warmth, discomfort, erythema, or tenderness. These local inflammatory reactions are self-limiting and do not typically cause long-term sequelae.[14] When continuous infusion of large amounts of the drug is required, appropriate selection of the vein is crucial to prevent extravasation and permanent damage.[13] The dorsum and wrist areas of the hand should preferably be avoided.[8] In these two cases, chemotherapy was administered in the wrist area of the hand. In our institute, peripheral lines are used more frequently, while central lines are preserved for patients with inaccessible peripheral sites. Swelling is the most common symptom of extravasation, followed by erythema. In both of our patients, swelling, blistering, erythema, and blackish discoloration were the presenting symptoms. Peripheral pulses were also absent.

Early detection of extravasation is essential for a good patient outcome. Extravasation requires the immediate discontinuation of chemotherapy to treat the symptoms and prevent further complications. The offending drugs should be removed by aspiration, followed by hot and cold compresses if necessary.[7] In the present cases, extravasation developed during the second cycle of chemotherapy with 5FU and cisplatin.

These two patients were unfortunate enough to require amputation of the forearm. Normally, irritants do not cause permanent and devastating injury. The treatment of extravasation from large quantities of irritant anticancer agents is often managed with local steroid injections. However, an unknown amount of the drug was extravasated in these cases, and the patients were not given any local injection of steroids. A local injection of a specific antidote, sodium thiosulfate, is considered effective for treating extravasation from cisplatin.

Conclusion:

Consistent training and knowledge among all members of the healthcare team regarding chemotherapy administration are critical factors for the effective prevention of chemotherapy-induced extravasation.

Recommendation: A chemo port and peripherally inserted central catheter (PICC) can be used during chemotherapy to avoid extravasation. Appropriate treatment, including the specific antidote, should be administered as early as possible in the event of extravasation.

References:

1. Hisashi T, Yasuhisa I, Tomoki I, et al. Regimen of 5-fluorouracil and cisplatin increases the incidence of extravasation in patients undergoing chemotherapy. *In Vivo*. 2021;35(2):1147-1150.
2. Kreidieh FY, Moukadem HA, El Saghir NS. Overview, prevention, and management of chemotherapy extravasation. *World J Clin Oncol*. 2016;7(1):87-97.
3. Jackson-Rose J, Del Monte J, Groma et al. Chemotherapy extravasation: establishing a national benchmark for incidence among cancer centers. *Clin J Oncol Nurs*. 2017;21(4):438-455.
4. Pluschnig U, Haslik W, Bartsch R, Mader RM. Extravasation emergencies: state-of-the-art management and progress in clinical research. *Memo*. 2016;9(6):266-270.
5. Hiroto O, Asako M, Takako S, Rie A. Skin necrosis due to the extravasation of irritant anticancer agents. *Intern Med*. 2018;57(7):757-760.
6. Egu J, Moldovan K, Herman P, et al. Prevention of extravasation by the local application of hybrid aerogel microparticles as drug delivery systems for cervical cancer chemotherapy. *Eur J Hosp Pharm*. 2022. Available from: https://doi.org/10.1136/ejhpharm-2022-eahp.362.
7. Fidalgo JAP, Fabregat LG, Cervantes A, et al. Management of chemotherapy extravasation: ESMO-EONS clinical practice guidelines. *Ann Oncol*. 2021;23:Vii167-173.
8. Reddy SS, Somayaji S, Munthy MK, Maka VV. 5-fluorouracil-induced extravasation injury. *Indian J Cancer*. 2020;57(4):280-282.
9. CTCAE Files [Internet]. Available from: https://evs.nci.nih.gov/ftpl/CTCAE/About.html [last cited 2019 Apr 21].
10. Boulanger J, Ducharme A, Dufour A, Fortier S, Almanric K. Management of extravasation of antineoplastic agents. *Support Care Cancer*. 2015;23(5):1459-1471.
11. Asmaa C, Sara K, Amal J, Ahmed J, et al. Extravasation: surgical management and prevention. *Eur J Med Health Sci*. 2022;4(4):180-185.
12. Hasan G, Serdar U, Aiper C, et al. Management of extravasation injuries in the upper extremity. *Hand Microsurgery*. 2017;6(2):81-86.
13. Hassan DS, Hasary HJ. Chemotherapy-induced extravasation injury: classification and management. *Al-Rafidain J Med Sci*. 2022;2(1):81-92.
14. Schrijvers DL. Extravasation: a dreaded complication of chemotherapy. *Ann Oncol*. 2003;14(Suppl 3):iii26-iii30.

Review Article

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Cancer Epidemiology: Global Trends, Prognosis, and Future Directions

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Abstract

Cancer remains one of the greatest public health challenges globally, impacting millions of lives each year. This review examines the latest GLOBOCAN 2022 data, comparing it with data from 2018, to shed light on evolving trends in cancer incidence, mortality, survival rates, and future projections. While lung, breast, and prostate cancers continue to be the most diagnosed cancers worldwide, notable shifts in mortality patterns have been observed. For instance, lung and liver cancers have emerged as increasingly deadly cancers, highlighting the urgent need for renewed global strategies to address these growing threats. In addition to trends in incidence and mortality, the review also highlights the impact of groundbreaking advancements in cancer treatment. Technologies such as liquid biopsy, immunotherapy, and personalized medicine are beginning to transform the way cancer is diagnosed, treated, and monitored, offering hope for better outcomes and more tailored approaches to cancer care. These innovations are especially significant as cancer rates continue to rise globally.

Keywords*: Cancer, epidemiology, GLOBOCAN, frequency, mortality, survival, global trends.*

Introduction

Cancer remains a leading cause of morbidity and mortality worldwide, with rising incidence rates primarily attributed to aging populations, urbanization, and lifestyle factors.[1] Accurate and timely cancer epidemiological data is essential for formulating effective prevention, screening, and treatment strategies. The purpose of this review is to present an updated analysis of cancer epidemiology using the latest GLOBOCAN 2022 data[2], comparing it with GLOBOCAN 2018[3] to assess shifts in the global cancer burden.

The GLOBOCAN database, managed by the International Agency for Research on Cancer (IARC), provides global estimates for cancer incidence, mortality, and prevalence. These estimates form the foundation of national and international cancer control policies and help shape the priorities for cancer research and healthcare interventions. In this review, the most prevalent and deadly cancers, their epidemiological trends, and projections for cancer incidence and mortality up to 2060 are analyzed.[2,3]

Global Cancer Incidence: Comparison of 2018 vs. 2022

In 2018, there were approximately 18.1 million new cancer cases worldwide, with the top three most frequent cancers being lung (2.09 million cases), breast (2.09 million cases), and prostate (1.28 million cases). The

most notable findings from GLOBOCAN 2018 were the dominance of lung cancer in men and breast cancer in women.[3]

The GLOBOCAN 2022 data presents an updated global cancer incidence of approximately 19.9 million new cancer cases, representing an increase of 9.95% from 2018.[2] The most frequently diagnosed cancers in 2022 were still lung cancer (2.48 million cases), breast cancer (2.29 million cases), and prostate cancer (1.46 million cases), with small increases in both lung and breast cancer incidence.[2]

Lung cancer remains the leading cancer globally, with 2.48 million cases in 2022, about an 18.6% increase from 2.09 million cases in 2018.[2] Lung cancer incidence has slightly increased among both men and women, though men continue to have the highest incidence. [2]

Breast cancer incidence has risen, from 2.09 million cases in 2018 to 2.29 million cases in 2022, further consolidating its position as the most frequently diagnosed cancer in women.[2]

Prostate cancer incidence also saw an increase, from 1.28 million cases in 2018 to 1.46 million cases in 2022, reflecting a rising burden, particularly in regions with aging populations.[2]

Notably, the incidence of colorectal cancer also showed an increase, rising from 1.8 million cases in 2018 to approximately 1.93 million cases in 2022.[2]

Table 1: Comparison of Global Cancer Incidence – GLOBOCAN 2018 vs. 2022

Rank	Cancer site	Number of cases	
		2018 n (%)	2022 n (%)
1st	Lung	2,093,876 (11.6)	2 480 675 (12.4)
2nd	Breast	2,088,849 (11.6)	2 296 840 (11.5)
3rd	Colorectum	1,800,977 (10.0)	1 926 425 (9.6)
4th	Prostate	1,276,106 (7.1)	1 467 854 (7.3)
5th	Stomach	1,033,701 (5.7)	968 784 (4.8)

Cancer Mortality: Comparison of 2018 vs. 2022

In 2018, cancer accounted for 9.55 million deaths globally, with the deadliest cancers being lung cancer (1.76 million deaths), stomach cancer (0.782 million deaths), and liver cancer (0.781 million deaths).[3] According to GLOBOCAN 2022, the global cancer death toll has risen to 9.74 million deaths, reflecting a 1.98% increase in cancer-related mortality over the four years.[2]

In 2022, the leading causes of cancer death were lung cancer (1.80 million deaths), colorectal cancer (0.90 million deaths), liver cancer (0.76 million deaths), breast cancer (0.67 million deaths), and stomach cancer (0.66 million deaths).[2] Lung cancer remained the deadliest cancer, causing 1.80 million deaths in 2022, an increase from 1.76 million deaths in 2018.[2] Liver cancer showed a slight decrease in mortality, falling from 0.781 million deaths in 2018 to 0.758 million deaths in 2022.[3,2] Stomach cancer also remained a significant cause of death, though the number of deaths decreased slightly from 0.782 million in 2018 to 0.660 million in 2022.[3,2] The overall cancer mortality rate continued to rise, reflecting the increasing global burden, particularly in lower- and middle-income countries where access to early detection and treatment remains limited.[2, 4]

Table 2 : Comparison of Global Cancer Mortality – GLOBOCAN 2018 vs. 2022

Cancer Site	Number of deaths	
	2018 n (%)	2022 n (%)
Lung (Trachea and Bronchus)	1,761,007 (18.4)	1 817 469 (18.7)
Colorectal	861,663 (9.0	904 019 (9.3)
Stomach	782,685 (8.2	660 175 (6.8)
Liver	781,631 (8.2)	758 725 (7.8)
Breast	626,679 (6.6)	666 103 (6.8)

Cancer Survival and Prognosis: Trends from 2018 to 2022

Survival rates for common cancers have seen some improvement over the past few years due to advances in early detection and treatment, but disparities remain, particularly between high-income and low-income countries. According to the CONCORD-3 study[5] and GLOBOCAN 2022,[2] the five-year relative survival rates for major cancers are as follows:

- **Prostate cancer**: Survival rates continue to be high, with 5-year survival ranging from 70% to 100%.[4] This is consistent with the data from 2018.
- **Breast cancer**: The 5-year survival rate for breast cancer remains high at 80–85%, showing a modest increase compared to 2018.[2]

- **Lung cancer**: Survival rates for lung cancer remain low at 10–20%, with only slight improvements due to better treatment options and early detection programs, particularly in high-resource settings.[2]
- **Liver cancer**: The survival rate for liver cancer remains low, with 5-year survival rates typically <20%.[4]
- **Pancreatic cancer**: Pancreatic cancer remains one of the deadliest cancers with a 5-year survival rate of 5–15%.[4]

Table 3: *Global 5-Year Relative Survival Rates – GLOBOCAN 2022*

Cancer Type	5-Year Survival Rate (%)
Prostate	70–100
Breast	80–85
Rectum	60–70
Colon	50–70
Cervix Uteri	50–70
Stomach	20–40
Lung (Trachea and Bronchus)	10–20
Liver	<20
Pancreas	5–15

Future Projections and Strategies

The GLOBOCAN 2022 projections suggest a substantial rise in cancer incidence and mortality by 2060, with an estimated 30 million new cancer cases and 18 million cancer deaths annually.[2] This underscores the urgent need for continued investment in cancer prevention, early detection, and treatment.

Advancements in cancer research, particularly in personalized medicine, immunotherapy, and digital epidemiology, offer hope for better treatment outcomes. For instance, liquid biopsies are being explored for their potential to detect cancer at earlier stages and monitor treatment responses.[6,7] Immunotherapies, especially immune checkpoint inhibitors, have shown promising results in treating cancers such as melanoma, lung cancer, and some gastrointestinal cancers.[8]

Public health strategies must focus on reducing cancer risk factors, improving access to screening programs, and ensuring equitable access to the latest treatment modalities.[2]

Conclusion

Cancer remains one of the most significant global health challenges, with rising incidence and mortality rates, particularly in low- and middle-income countries. The GLOBOCAN 2022 data highlights critical trends and emphasizes the need for enhanced prevention, screening, and treatment strategies. Advances in personalized medicine and immunotherapy hold promise for improving survival outcomes, but the global cancer burden is set to increase in the coming decades. Immediate action is required to curb this growing public health crisis.

References

1. Bray F, Laversanne M, Weiderpass E, et al. The changing global burden of cancer. *Nature Reviews Cancer*. 2021;21(3):88-101.
2. Global Cancer Observatory. GLOBOCAN 2022: Estimated cancer incidence, mortality, and prevalence worldwide in 2022. Lyon: International Agency for Research on Cancer; 2022.
3. Global Cancer Observatory. GLOBOCAN 2018: Cancer incidence and mortality worldwide in 2018. Lyon: International Agency for Research on Cancer; 2018.
4. Global Burden of Disease Cancer Collaboration. Global burden of cancer and trends in 2017: The global burden of disease study 2017. *Lancet Oncol*. 2019;20(9):1–14.
5. Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of cancer survival 1995–2009: analysis of individual data for 25,676,887 patients from 279 population-based cancer registries in 67 countries (CONCORD-3). Lancet Oncol. 2018;19(11):1427-1439.
6. Tumeh PC, Harview CL, Yearley JH, et al. PD-1 blockade induces responses by inhibiting adaptive immune resistance. *Nature*. 2014;515(7528):568-571.
7. Salathe M. Digital epidemiology: The new frontier in public health surveillance. *Lancet*. 2018;392(10152): 2117-2119.
8. Rassy E, Kattan MW. Personalized cancer treatment: From genomics to immunology. *Lancet Oncol*. 2020;21(4):426-439.

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