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Editorial

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A New Era in Bangladesh's Cancer Care Infrastructure

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Abstract

Bangladesh is entering an important phase in the development of its cancer care system. Cancer is becoming a growing public health concern, and many patients and families continue to face serious financial, physical, and emotional challenges because of the disease. For this reason, improving cancer care has become an urgent national priority. As the burden of non-communicable diseases continues to rise, especially cancer, the health system must move beyond policy promises and focus on visible improvements in access, capacity, and quality of care. Recent changes at the National Institute of Cancer Research and Hospital (NICRH) show that this shift has already begun. The extension of outpatient department services until 8:00 PM is an important step toward making services more accessible. Surgical theatres and blood transfusion services are also running during these extended hours. For patients who come from distant districts, this can make a real difference. Many of them face delays in diagnosis, surgery, and treatment. Reducing waiting time is therefore not only an administrative improvement; in cancer care, timely treatment can affect disease progression, treatment completion, and survival.

Bangladesh is entering an important phase in the development of its cancer care system. Cancer is becoming a growing public health concern, and many patients and families continue to face serious financial, physical, and emotional challenges because of the disease. For this reason, improving cancer care has become an urgent national priority.[1] As the burden of non-communicable diseases continues to rise, especially cancer, the health system must move beyond policy promises and focus on visible improvements in access, capacity, and quality of care.[2]

Recent changes at the National Institute of Cancer Research and Hospital (NICRH) show that this shift has already begun. The extension of outpatient department services until 8:00 PM is an important step toward making services more accessible. Surgical theatres and blood transfusion services are also running during these extended hours. For patients who come from distant districts, this can make a real difference. Many of them face delays in diagnosis, surgery, and treatment. Reducing waiting time is therefore not only an administrative improvement; in cancer care, timely treatment can affect disease progression, treatment completion, and survival.

At the same time, investment in modern equipment is also essential. The procurement of advanced diagnostic and treatment facilities, including high-end Linear Accelerator (LINAC) machines, is a necessary step for improving cancer treatment in the public sector. Bangladesh has long faced a shortage of radiotherapy services, which has created long waiting lists and delayed treatment for many patients.[3] The planned expansion of NICRH into a 1,200-bed facility is therefore more than an increase in hospital beds. It is an opportunity to strengthen the country's main oncology referral center and respond more effectively to the growing number of cancer patients.[1]

Another important part of the current approach is decentralization. For many years, specialized cancer services have been concentrated mainly in Dhaka. As a result, patients from rural and peripheral areas

often have to travel long distances, spend extra money, and stay away from home for treatment.[4] The planned establishment of eight specialized cancer, kidney, and cardiovascular hospitals across the eight administrative divisions could help reduce this pressure. If these regional centers are properly developed and managed, they can bring specialized care closer to patients, support earlier referral, and reduce the hardship faced by families outside the capital. This is important not only for fairness, but also for building a stronger and more sustainable cancer care system.[1]

However, infrastructure development should not be mistaken for health-system transformation in itself. New facilities and expanded services must be supported by trained professionals, effective clinical governance, and reliable maintenance systems. In particular, strengthening surgical capacity is essential to ensure that cancer surgery is delivered safely, affordably, and without unnecessary delay.[5] At the same time, radiotherapy and medical oncology services will require adequate staffing, technical support, and preventive maintenance so that advanced equipment and specialized services remain functional.

A strong cancer care system must also go beyond large hospitals. Screening, early diagnosis, proper referral, follow-up care, and palliative care are all important parts of cancer control. If community-level services are not connected with specialized hospitals, many patients may still reach care too late. Bangladesh therefore needs an integrated approach where prevention, diagnosis, treatment, and palliative care work together at different levels of the health system.

The recent progress in Bangladesh's cancer care infrastructure creates an important opportunity to address long-standing gaps in access and capacity. Extended service hours, modern equipment, institutional expansion, and regional decentralization are positive steps. The main challenge now is to implement these plans effectively. New facilities must be properly staffed, equipment must remain functional, referral systems must work smoothly, and care must be available to patients regardless of where they live. If these priorities are sustained, Bangladesh can move toward a cancer care system that is not only larger, but also more timely, accessible, and responsive to the needs of its people.

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Original Article

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Hypothyroidism Following Radiotherapy in Head and Neck Cancer Patients: A Multi-Institutional Study

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Abstract

Background: *Radiotherapy plays a pivotal role in the treatment of head and neck cancers, but it is associated with late toxicities, including radiation-induced hypothyroidism. This condition is often underrecognized and can adversely affect patients' quality of life. This multi-institutional study aimed to estimate the cumulative incidence of biochemical hypothyroidism after cervical-region radiotherapy in head and neck cancer patients and to describe the demographic, tumor, and treatment profile of the cohort.*

Methods: *This multi-institutional retrospective observational cohort study reviewed medical records of 68 head and neck cancer patients who completed radiotherapy to the cervical region between January 2020 and July 2023 at Delta Medical College, Enam Medical College and North East Medical College. Records were reviewed through July 2025 to ensure availability of 2-year thyroid-status follow-up. Patients with any documented pre-existing thyroid disorder, previous thyroid medication use, or prior thyroidectomy for any reason were excluded. Thyroid function was assessed using serum thyroid-stimulating hormone (TSH) and free thyroxine (free T4). Hypothyroidism was defined as post-radiotherapy TSH >4.5 mIU/L. Overt hypothyroidism was defined as TSH >4.5 mIU/L with free T4 <0.8 ng/dL, and subclinical hypothyroidism was defined as TSH >4.5 mIU/L with normal free T4; both were counted in cumulative incidence. Descriptive statistics were used to summarize patient characteristics and cumulative incidence.*

Results: *The mean age of the cohort was 54.6 ± 6.7 years. Forty-six patients (67.6%) were male and 22 (32.4%) were female. Laryngeal cancer was the most common primary site (18/68, 26.5%), and 42 patients (61.8%) presented with advanced disease. Definitive concurrent chemoradiotherapy was the most frequent treatment modality (42/68, 61.8%). The cumulative incidence of hypothyroidism increased over time: 11.8% at 6 months, 26.5% at 1 year, and 35.3% at 2 years after radiotherapy.*

Conclusion: *Hypothyroidism was a common and progressive late complication following radiotherapy for head and neck cancer, with more than one-third of patients developing biochemical hypothyroidism within 2 years. These findings support long-term thyroid function monitoring in head and neck cancer survivors to facilitate early detection and management.*

Introduction

Head and neck cancers represent a diverse group of malignancies, with radiotherapy being a cornerstone of treatment, either alone or in combination with surgery and chemotherapy. While radiotherapy is highly effective in achieving locoregional control, it can lead to late complications that significantly affect patients' quality of life. Among these, radiation-induced hypothyroidism is a frequently observed and often underrecognized endocrine sequela.[1] The incidence of hypothyroidism after radiotherapy for head and neck cancer has been reported to vary widely, necessitating clearer understanding of its burden and clinical implications.[2]

This multi-institutional study aimed to estimate the cumulative incidence of biochemical hypothyroidism after cervical-region radiotherapy in head and neck cancer patients and to describe the demographic, tumor, and treatment characteristics of the cohort.

Background

Hypothyroidism in Head and Neck Cancer Patients

Hypothyroidism, a condition characterized by insufficient production of thyroid hormones, is a significant concern for head and neck cancer patients following therapeutic interventions. It can manifest as either overt or subclinical disease. Overt hypothyroidism is generally defined by elevated TSH and decreased free T4, while subclinical hypothyroidism presents with elevated TSH and normal free T4.[3] Patients may experience a range of non-specific symptoms, including fatigue, weight gain, cold intolerance, dry skin, constipation, hoarseness, and cognitive dysfunction, which can impair overall quality of life.[4,5] The reported incidence of post-radiotherapy hypothyroidism in head and neck cancer patients ranges widely, from approximately 6% to 68%, highlighting variability and potential underestimation in the literature.[2,6]

Impact of Radiotherapy on Thyroid Function

Radiotherapy directed at the head and neck region can expose the thyroid gland to radiation, leading to potential damage and subsequent dysfunction. The mechanisms underlying radiation-induced thyroid injury are multifactorial, involving direct parenchymal cell damage, vascular damage, and immune-mediated reactions.[1,5] Fibrosis of the thyroid capsule and septa, as well as radiation-induced vascular injury, may also contribute to impaired thyroid function.[1]

Methods

Study Design and Population

This was a multi-institutional retrospective observational cohort study based on review of medical records. The study population comprised 68 pathologically confirmed head and neck cancer patients who completed definitive, adjuvant, or palliative radiotherapy with the cervical or neck region included in the treatment field between January 2020 and July 2023. Clinical records and thyroid function follow-up data were reviewed through July 2025; therefore, each patient included in the cumulative 2-year analysis had available thyroid status at baseline and at post-radiotherapy follow-up intervals up to 2 years.

Patient Recruitment and Data Collection

Patients were identified from institutional databases. The following clinical data were extracted from medical records:

Demographics: age and sex.

Tumor characteristics: primary site and clinical stage.

Treatment details: radiotherapy setting and treatment modality.

Thyroid function data: pre-radiotherapy thyroid status and post-radiotherapy TSH and free T4 at follow-up intervals.

Data were collected from the following institutions: Delta Medical College, Enam Medical College, and North East Medical College.

Inclusion and Exclusion Criteria

Inclusion criteria: pathologically confirmed head and neck cancer; receipt of radiotherapy involving the cervical or neck region; documented euthyroid status before radiotherapy; and availability of thyroid function tests at baseline and post-radiotherapy follow-up.

Exclusion criteria: any documented pre-existing thyroid disorder before radiotherapy, previous

thyroid hormone or antithyroid medication use, prior thyroidectomy for any reason, and incomplete thyroid function records required for the planned follow-up analysis.

Assessment of Thyroid Function

Thyroid function was assessed by measuring serum TSH and free T4. For the purpose of this study, biochemical hypothyroidism was defined as post-radiotherapy TSH >4.5 mIU/L. Overt hypothyroidism was defined as TSH >4.5 mIU/L with free T4 <0.8 ng/dL, while subclinical hypothyroidism was defined as TSH >4.5 mIU/L with normal free T4. Both overt and subclinical hypothyroidism were included in the cumulative hypothyroidism count. Patients with normal TSH and free T4 within the local laboratory reference range were classified as euthyroid.

Statistical Analysis

Descriptive statistics were used to summarize patient demographics, tumor characteristics, treatment parameters, and thyroid status. Continuous variables were expressed as mean ± standard deviation, and categorical variables were expressed as frequencies and percentages. Cumulative incidence was calculated as the number of patients meeting biochemical criteria for hypothyroidism at or before each follow-up interval divided by the total study cohort (n=68). No inferential risk-factor analysis was performed because consistently recorded thyroid dose-volume parameters and other risk-factor variables were not available in the retrospective dataset.

Results

Patient Demographics and Clinical Characteristics

The baseline characteristics of the 68 head and neck cancer patients included in the study are shown in Figure 1 to 4. The mean age of the cohort was 54.6 ± 6.7 years. The cohort included 46 male patients (67.6%) and 22 female patients (32.4%). Laryngeal cancer was the most common primary site, followed by oral cavity, oropharynx, nasopharynx, hypopharynx, and cancer of unknown primary with metastatic neck nodes. Advanced clinical stage accounted for 42 patients (61.8%). Definitive concurrent chemoradiotherapy was the predominant treatment modality.

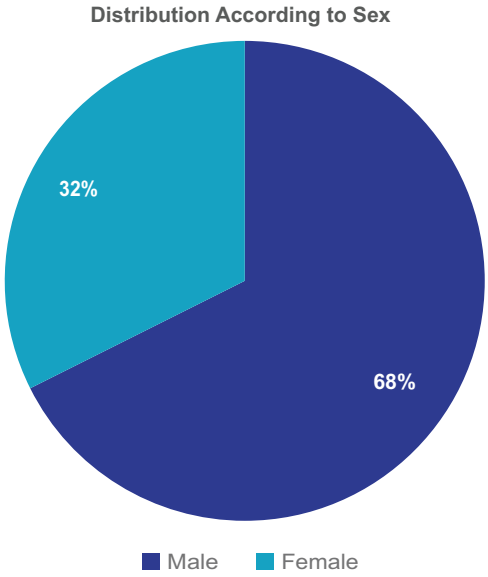


Figure 1: Distribution of respondents according to sex.

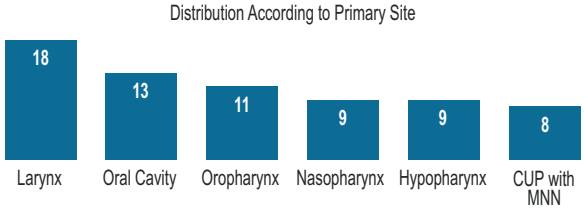


Figure 2: Distribution of respondents according to primary site.

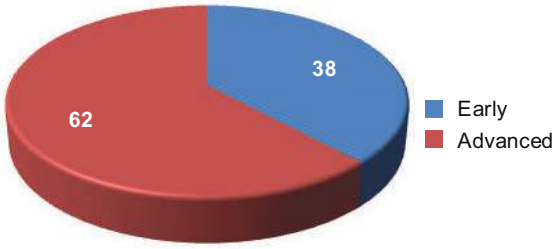


Figure 3: Distribution of respondents according to clinical stage.

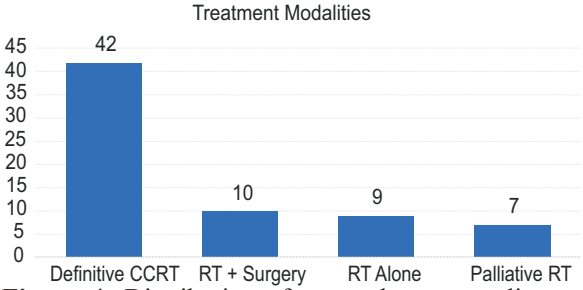


Figure 4: Distribution of respondents according to treatment modality.

Incidence of Hypothyroidism Post-Radiotherapy

At pre-treatment baseline, all 68 patients were euthyroid. The cumulative incidence of biochemical hypothyroidism increased steadily during follow-up. At 6 months post-radiotherapy, 8 patients (11.8%) had developed hypothyroidism. This increased to 18 patients (26.5%) at 1 year and 24 patients (35.3%) at 2 years after radiotherapy.

Table V: Distribution of respondents according to thyroid status

Follow-up interval	Euthyroid (n)	Hypothyroid (n)	Cumulative incidence (%)
Pre-treatment	68	0	0
6 months post-RT	60	8	11.8
1-year post-RT	50	18	26.5
2-years post-RT	44	24	35.3

Note: Hypothyroid counts are cumulative. Once a patient met the biochemical criterion for hypothyroidism at a follow-up interval, that patient was counted as hypothyroid for cumulative-incidence presentation at subsequent intervals. Reversion to euthyroid status after thyroid hormone replacement, if any, was not used to reduce the cumulative count.

Discussion

Prevalence of Post-Radiotherapy Hypothyroidism

This multi-institutional retrospective cohort study found a progressive increase in biochemical hypothyroidism after radiotherapy for head and neck cancer. The cumulative incidence reached 35.3% at 2 years, which is clinically important and falls within the broad range reported in previous studies.[1,2,6,12] These results add regional multi-centre data to the literature and reinforce that hypothyroidism is a frequent late endocrine toxicity after cervical-region radiotherapy.

The present analysis was descriptive. Formal assessment of associated factors was not performed because consistently recorded thyroid dose-volume parameters, baseline thyroid volume, and detailed systemic therapy variables were not available across all participating centres. Therefore, the manuscript has been revised to align the stated objectives, methods, results, and conclusions with the descriptive analyses actually performed.

Clinical Implications

The high and often delayed onset of hypothyroidism after radiotherapy emphasizes the need for routine and long-term thyroid function monitoring in head and neck cancer survivors.[1,8,9] Early detection allows timely initiation of thyroid hormone replacement therapy, typically with levothyroxine, which is important for symptom control and prevention of further complications.[1,8,10] Periodic TSH evaluation every 6-12 months has been recommended for these patients.[10,11] Addressing hypothyroidism can improve quality of life, which may already be compromised by cancer and its treatment.[12]

Limitations of the Study

This study has several limitations. First, its retrospective design may be associated with missing data and variability in documentation across centres. Second, thyroid function testing schedules and laboratory reference ranges may have differed between institutions, although a uniform biochemical threshold was applied for this analysis. Third, detailed radiotherapy dose-volume parameters for the thyroid gland were not consistently available, preventing risk-factor or dose-response modelling. Fourth, the cumulative-incidence table counts hypothyroidism once diagnosed and does not model possible biochemical normalization after treatment. Despite these limitations, the multi-institutional design provides useful regional data on a clinically relevant late toxicity.

Conclusion

Hypothyroidism is a prevalent and clinically important late complication following radiotherapy for head and neck cancer. In this multi-institutional retrospective cohort, cumulative biochemical hypothyroidism increased from 11.8% at 6 months to 35.3% at 2 years after radiotherapy. These findings support structured, long-term thyroid surveillance for head and neck cancer survivors and highlight the importance of multidisciplinary follow-up to detect and manage treatment-related endocrine toxicity.

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Original Article

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Correlation between the Pre-operative CT Scan Findings and Surgicopathological Staging of Ovarian Cancer in a Tertiary Care Hospital

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Abstract

Background: *Ovarian cancer (OC) is the leading cause of death from gynecologic malignancies. Accurate staging is essential for treatment planning. Due to nonspecific symptoms and early peritoneal spread, most cases present with extra-pelvic disease. Surgicopathological assessment remains the gold standard for staging and guiding decisions between primary cytoreductive surgery and neoadjuvant chemotherapy.*

Methods: *This observational cross-sectional study included 100 ovarian cancer patients at the National Institute of Cancer Research and Hospital, Dhaka, from January to December 2021. All patients underwent preoperative CT scan followed by surgery. CT findings were compared with peroperative and histopathological results. Diagnostic accuracy, sensitivity, specificity, and predictive values were calculated.*

Results: *On CT, 72% of tumors were unilateral, 78% solid, 17% had ascites, and 16% showed omental involvement. Histopathology revealed papillary serous cystadenocarcinoma (64%), mucinous cystadenocarcinoma (20%), germ cell tumors (6%), and clear cell tumors (6%). CT scan demonstrated high diagnostic performance: Stage IA (100% sensitivity, 67% specificity), Stage IIA (62.5% sensitivity, 96% specificity), Stage IIB (85.3% sensitivity, 100% specificity), and perfect metrics for Stage IIIC. Overall, preoperative CT showed good correlation with surgicopathological staging, with stronger agreement in advanced stages.*

Conclusions: *Preoperative CT scan findings correlate well with surgicopathological staging in ovarian cancer, particularly in advanced stages. Despite being a single-center study with a modest sample size, CT remains a reliable and recommended imaging modality for ovarian cancer staging.*

Keywords: *CT scan findings, Ovarian Ca, Surgicopathological staging.*

Introduction

Ovarian cancer is one of the lethal gynecologic cancers that has the highest mortality rate. The age-standardized rate of ovarian cancer (OC) incidence ranged from 3.0 to 11.4 per 100,000 women worldwide.[1] The outcome of ovarian cancer includes independent variable such as increasing age, histopathological types and grades.[2,3] Ovarian cancers belong to surface epithelial tumors that are the most common types among ovarian neoplasms. Though the etiology and history of ovarian cancer is not fully understood, it has been found from a series of investigations that certain conditions such as genetic predisposition and benign inflammatory

diseases are involved in the molecular mechanism of carcinogenesis. The pathologic studies have revealed differential background of ovarian cancers depending on histologic types. There are four representative histologic types; serous, mucinous, endometrioid and clear cell types. The ovarian surface is exposed to the peritoneal cavity. In most cases, cancer cells proliferate inward, and when thin cyst walls rupture, cancer cells spread into peritoneal cavity. Cancer cells may grow outward in papillary form, then directly expose themselves to the peritoneal cavity.[4,5]

Epithelial ovarian cancer is most commonly detected in an advanced stage, when the overall 5-years survival rate is 20-30%. Detection of early stage ovarian cancer results in improved survival. Currently, there is no effective strategy for ovarian cancer screening. Women with persistent and progressive symptoms need further evaluation.[6,7] The diagnostic decisions that have been made objectively and in a stepwise manner have reported improvement in patient outcomes. It has been shown that the pre-operative computed scan (CT scan) represents a valid tool to predict ovarian cancer staging.[8]

The goal of imaging is to help diagnose and differentiate malignant tumors from benign lesions and to stage ovarian malignancy. Cancer staging is not only a fundamental principle and one of the first and most significant steps used to predict patient outcome but also important to plan the most appropriate treatment.[9] CT scan is the recommended imaging modality for staging ovarian cancer. Clinically relevant information including size of the primary tumor, size and location of any peritoneal implants, and lymph nodes is provided by the CT scan.[10] This information can then be used to predict resectability. The overall accuracy of MDCT (Multidetector computed tomography) was reported to be as high as 89% in diagnosis of malignant adnexal masses[9]. CT findings predictive of malignancy are presence of papillary projections in a cystic lesion, necrosis in a solid mass, and peritoneal metastases.[11] Also, CT is used frequently to detect persistent or recurrent ovarian carcinoma, advanced staging of cancer and to monitor tumor response to therapy. However, CT is limited in detecting small peritoneal metastases.

With the sensitivity of 85-93% and specificity of 91-96% tumor implants larger than 1 cm can be detected by CT scan as noted by previous studies, but the sensitivity decreases to 25-50% in detecting implants that are 1 cm or smaller. Opacification of the gastrointestinal tract with oral contrast material helps to distinguish peritoneal implants from bowel and is useful for detecting bowel invasion. Some authors have advocated using water as a contrast agent because calcified metastases may be obscured by high-density contrast material.[12,13]

CT is particularly useful in patients with large amounts of ascites, which is encountered in most women with ovarian cancer. Additionally, CT has been used to predict the outcome of primary cytoreductive surgery of advanced ovarian cancer. It is crucial to determine which patients will benefit from surgery, minimizing the number of patients undergoing unnecessary surgery.[8, 9, 13] In one study, peritoneal thickening, peritoneal implants (≥ 2 cm), bowel mesentery involvement (≥ 2 cm), supra-renal paraaortic lymph nodes (≥ 1 cm), omental extension (spleen, stomach, or lesser sac), pelvic sidewall involvement, and hydroureter were most strongly associated with poor surgical outcome. On the basis of statistical probability of each factor predicting cytoreductive outcome, each radiologic parameter as well as performance status of the patients was assigned a numeric value, and total predictive index score was calculated for each patient. A predictive index score of 4 or more showed accuracy of 93%, sensitivity of 100%, specificity of 85%, positive predictive value of 87%, and negative predictive value of 100% in predicting suboptimal surgical outcome in patients with advanced ovarian cancer.[14, 15] Aim of this study was to correlate the pre-operative CT scan findings with the surgicopathological staging in ovarian cancer.

Material and Methods

This observational type of cross sectional study was conducted in the Department of Gynecological Oncology, National Institute of Cancer Research & Hospital, Dhaka, to correlate the pre-operative CT scan findings with the surgicopathological staging in ovarian cancer. Women with clinically suspected ovarian cancer of all age group were included in the study. The diagnosis was done after proper history taking, physical examination and doing some investigations. After fulfilling the inclusion and exclusion criteria, patient were enrolled with unique ID. Subjects or their relatives were briefed about the objectives of the study, risk and benefits, freedom for

participating in the study and confidentiality. Informed written consent was obtained accordingly. After taking consent, proper history was taken. Then abdominal, pelvic examination was done. Ultrasonography findings were evaluated and presumptive diagnosis of ovarian tumor noted. Different biochemical values including serum tumor marker were evaluated. CT scan was performed to find out the extent of the disease. The analyzed variables were pre-operative data (age, symptoms, CT scan findings.) Per-operative data (tumor involved one or both ovary, character of lump, ascites, peritoneal deposit, omental cake, etc.) Postoperative data (Histopthological report: tumor involves one or both ovaries with pelvic extension, omental metastasis, distance metastasis). Finally, surgical findings & histopathological findings were correlate with CT scan findings. A questionnaire was used for collection of information by interviewing patients. All the collected data were checked very carefully to identify errors in collecting data. Data processing work consisted of registration of schedules, editing, coding and computerization, preparation of dummy tables, analysis and matching data. The technical matters of editing, encoding and computerization looked by researcher.

Results:

The mean age of the patients was 43.2+17.7 years,ranging from 21 to 70 years.Most patients were from urban (66%) area and lower income(44%) class . 72.0% of tumors were unilateral, 78.0% of masses were solid, ascites present in 17.0% cases and 16.0% cases were found omental involvement. Peritoneal implant in inside of the pelvis found in 19.0% cases, outside the pelvis in 16.0% cases, liver metastasis was detect in only 6 cases and there is none of case had lympadenopathy. It was observed that 60 patients detected stage IA, 5 patients stage IB, 18 patients stage IIA, 1 patient IIB, 10 patients stage IIIB and 6 patients stage IIIC. Histopathological findings revealed, papillary serous cystadenocarcinoma 64.0%, mucinous cystadenocarcinoma 20.0%, germ cell tumour 6.0% and clear cell tumour 6.0%. Cancer involvement in one ovary was 64.0% of patients, intact capsule 95.0% cases and 22.0% cases were found omental involvement. Peritoneal implant in inside of the pelvis found in 36.0% cases, outside the pelvis in 24.0% cases, distant metastasis in 6.0% patients and lymph node involvement in 6% cases. CT scan of stage IA showed 100% sensitivity, 67.0% specificity, 68.3% PPV & 82.9% NPV. Stage IB showed 95.0% specificity, 74.9% NPV. Stage IC showed 100% specificity & 100% NPV. Stage IIA showed 62.5% sensitivity, 96.0% specificity, 83.3% PPV & 89.0% NPV. Stage IIB showed 85.3% sensitivity, 100.0% specificity, 100% PPV & 65.9% NPV. Stage IIIB showed 100% sensitivity, 96.77% specificity, 70% PPV & 100% NPV. Stage IIIC showed 100% sensitivity, specificity, PPV & NPV. Taking histopathology as the gold standard, present study shows almost similar sensitivity, specificity, PPV & NPV of pre-operative CT scan.

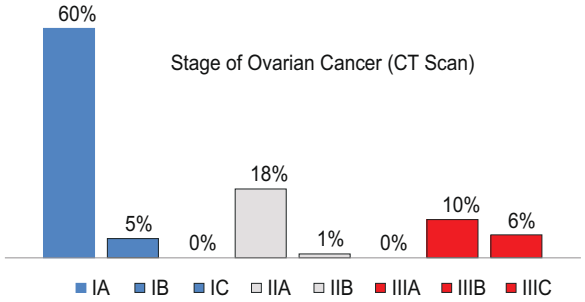


Figure 1: *Staging of ovarian cancer according to CT scan findings (n=100)*

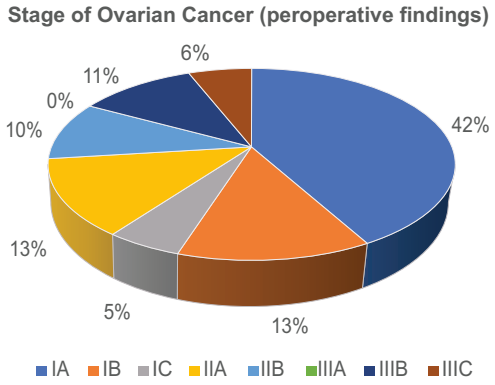


Figure 2: *Staging of ovarian cancer according to peroperative findings (n=100)*

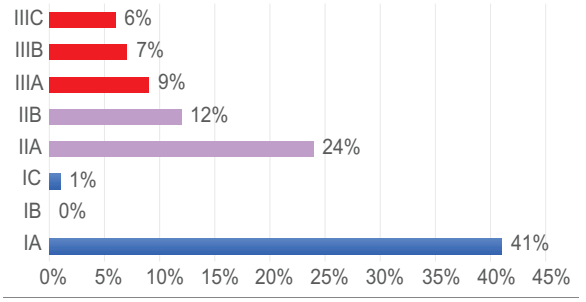


Figure 3: *Staging of ovarian cancer according to histopathological findings (n=100)*

Table I: *Correlation of CT scan findings with per-operative findings of ovarian cancer (n=100)*

CT scan findings	Per-operative findings							
	IA (n=42)	IB (n=13)	IC (n=5)	IIA (n=13)	IIB (n=10)	IIIA (n=0)	IIIB (n=11)	IIIC (n=6)
IA (n=60)	42	8	5	5	0	0	0	0
IB (n=5)	0	5	0	0	0	0	0	0
IC (n=0)	0	0	0	0	0	0	0	0
IIA (n=18)	0	0	0	8	10	0	0	0
IIB (n=1)	0	0	0	0	0	0	1	0
IIIA (n=0)	0	0	0	0	0	0	0	0
IIIB (n=10)	0	0	0	0	0	0	10	0
IIIC (n=6)	0	0	0	0	0	0	0	6

Table II: Correlation of CT scan findings with Surgocopathological staging of ovarian cancer (n=100)

CT scan findings	Surgicopathological staging							
	IA (n=41)	IB (n=0)	IC (n=1)	IIA (n=24)	IIB (n=12)	IIIA (n=9)	IIIB (n=7)	IIIC (n=6)
IA (n=60)	41	0	0	6	8	1	4	0
IB (n=5)	0	0	1	3	0	1	0	0
IC (n=0)	0	0	0	0	0	0	0	0
IIA (n=18)	0	0	0	15	3	0	0	0
IIB (n=1)	0	0	0	0	1	0	0	0
IIIA (n=0)	0	0	0	0	0	0	0	0
IIIB (n=10)	0	0	0	0	0	7	3	0
IIIC (n=6)	0	0	0	0	0	0	0	6

Table III: *Diagnostic value of CT scan for staging of ovarian cancer (n=100)*

Stages of cancer	Validity test parameters							
	TP (a)	FP (b)	FN (c)	Sensitivity (%)	Specificity(%)	PPV (%)	NPV(%)	p-value
IA (n=60)	41	19	0	100	67.0	68.3	82.9	0.275
IB (n=5)	0	5	0	0	95.0	0	74.9	0.086
IC (n=0)	0	0	1	0	100	0	100	0.064
IIA (n=18)	15	3	9	62.5	96.0	83.3	89.0	0.576
IIB (n=1)	1	0	11	85.3	100	100	65.9	0.371
IIIB (n=10)	7	3	0	100	96.77	70	100	0.893
IIIC (n=6)	6	0	0	100	100	100	100	0.982

(a) TP= true positive, (b) FP= false positive, (c) FN= false negative, (d) TN= true negative

Discussion :

This observational type of cross-sectional study was carried out in the Department of Gynecological Oncology, National Institute of Cancer Research & Hospital, Dhaka, to correlate the pre-operative CT scan findings with the surgicopathological staging in ovarian cancer. Total 100 patients were enrolled according to inclusion and exclusion criteria. According to the questionnaire, history of all the selected cases were taken, the clinical examination and relevant investigation was carried out meticulously.

CT scan was done in all patients. In this study, 72.0% of tumors were unilateral, 78.0% of masses were solid, ascites present in 17.0% cases and 16.0% cases were found omental involvement. Peritoneal implant in inside of the pelvis found in 19.0% cases, outside the pelvis in 16.0% cases, liver metastasis was detect in only 6 cases and there is none of case had lympadenopathy. Other study revealed that about 86% cases were having unilateral neoplasm, 10% cases had haemorrhagic peritoneal collection and 64% of masses were cystic.[34]

Per-operative findings revealed, 72.0% of tumors were unilateral, 78.0% of masses were solid, ascites present in 23.0% cases and 17.0% cases were found omental involvement. Peritoneal implant in inside of the pelvis found in 23.0% cases, outside the pelvis in 17.0% cases, involvement of pelvic organ in 23.0% patients, liver metastasis was detected in 6 cases and lympadenopathy in 4 cases.

In our study, correlation between the CT scan and per-operative staging found in all stages of ovarian cancer. Among the 65 CT scan stage I, 60 cases correlate with per-operative findings of stage I, but 5 cases proven stage II. In per-oprative stage II, the total number raised to 23 from 19 cases of CT scan stage II and in per-operative stage III, the total number raised to 17 from 16 CT scan stage III.

Previous study noted that CT scan depict tumor implants larger than 1 cm with sensitivity of 85–93% and specificity of 91–96%, but the sensitivity decreases to 25–50% in detecting implants that are 1 cm or smaller[12,13]. Another study showed that for the staging of ovarian cancer, the role of CT scan has largely contributed when the combination of its availability, meticulous technique, efficacy and familiarity of radiologists and physicians. This study also showed that for characterization and detection of early stage ovarian cancer, whole-body MRI with diffusion weighted sequence showed greater accuracy than CT.

In our study, histopathological findings revealed, papillary serous cystadenocarcinoma 64.0%, mucinous cystadenocarcinoma 20%, clear cell tumour 6.0% and germ cell tumour 6%. Cancer involvement in one ovary was 64.0% of patients, intact capsule 95.0% cases and 22.0% cases were found omental involvement. Peritoneal implant in inside of the pelvis found in 36.0% cases, outside the pelvis in 24.0% cases, distant metastasis in 6.0% patients and lymph node involvement in 6 cases.[5]

A prospective study[35] in Clinical Center of Serbia also revealed that from analyzing histopathological (HP) findings similar with present study. Findings are quite differing with study[34] in Australia, papillary serous cystadenocarcinoma was the most common recorded histology for ovarian cancer in 2002 with 23.2% of new cases. Serous cystadenocarcinoma, not otherwise specified was the second most common with 13.1% of cases in 2002.

Singer et al demonstrated that serous carcinoma is the most common type of ovarian cancer and is the most lethal gynecologic malignancy.[36] A prospective study in Bangladesh[37] revealed that among the malignant tumors majority 53.8% were Serous cystandenocarcinoma and Mucinous cyst adenocarcinoma 23.1%, which was similar in our study.

Cancer staging is a fundamental principle and one of the first and most important steps used to predict patient outcome as well as to plan the most appropriate treatment.[9] Ovarian cancer stages range from FIGO stage I to stage IV. In our study correlation between pre-operative CT scan findings with histopathological staging found in all stages of ovarian cancer. Among the 65 CT scan stage I, 42 cases correlate with histopathological findings of stage I, but 17 cases proven stage II & 6 cases stage III. In histopathological stage II, the total number raised to 36 from 19 cases of CT scan stage II and in histopathological stage III, the total number raised to 22 from 16 CT scan stage III.

Previous study noted that, laparotomy and histopathological diagnosis accurately correlated with CT findings.[17,18] The overall accuracy of CT reported to be as high as 89%.[9] In our study, CT scan findings of all stages correlate with histopathological findings and result is non significant. But early stages have less correlation comparatively than others. That means, CT scan findings of stage-1 transformed into upstage group.

Taking histopathology as the gold standard the sensitivity, specificity, NPV and PPV values for CT scan were in stage IA showed 100% sensitivity, 67.0% specificity, 68.3% PPV & 82.9% NPV. Stage IB showed 95.0% specificity, 74.9% NPV. Stage IC showed 100% specificity & 100% NPV. Stage IIA showed 62.5% sensitivity, 96.0% specificity, 83.3% PPV & 89.0% NPV. Stage IIB showed 85.3% sensitivity, 100.0% specificity, 100% PPV & 65.9% NPV. Stage IIIB showed 100% sensitivity, 96.77% specificity, 70.0% PPV & 100% NPV. Stage IIIC showed 100% sensitivity, specificity, PPV & NPV.

Previous study noted that taking histopathology as the gold standard ,the sensitivity, specificity, PPV & NPV for MDCT were 95.6%, 97.3%, 93.5% and 97% respectively which is almost similar with our study[31].

Additionally, CT has been used to predict the outcome of primary cytoreductive surgery of advanced ovarian cancer. It is crucial to determine which patients will benefit from surgery, minimizing the number of patients undergoing unnecessary surgery.[8,9,13] Therefore CT scan is the recommended imaging modality for staging ovarian cancer. CT provides clinically relevant information including size of the primary tumor, size and location of any peritoneal implants, and lymph nodes.[10]

Conclusion

This study has demonstrated the pre-operative CT scan findings of all stages correlate with the surgicopathological staging in ovarian cancer. But early stages have less correlation comparatively than advanced stage i.e. pre-operative CT scan findings at early stage transform into upstage group. Pre-operative CT scan can be used as a reliable tool with which we can assess staging of ovarian cancer and subsequent appropriate management of the patients can be planned.

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There is no conflict of interest

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Original Article

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Presentation and Management Outcome in Carcinoma Breast

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Abstract

Background: *Carcinoma breast is a leading cause of cancer-related morbidity and mortality among women worldwide, with a higher burden of advanced-stage presentation in developing countries. This study aimed to evaluate clinical presentation, the effect of neoadjuvant therapy, and management outcomes in carcinoma breast.*

Methods: *This observational study included 65 histopathologically confirmed carcinoma breast patients admitted to the Surgery Department of* Bangladesh Medical University *from July 2007 to December 2008. Clinical staging, FNAC findings, treatment modalities, and follow-up outcomes were analyzed. Neoadjuvant chemotherapy was administered in selected advanced cases. Patients were followed for up to 18 months.*

Results: *Most patients presented at advanced stages (Stage III: 70.77%). FNAC showed high sensitivity (95.38%) and PPV (100%). Neoadjuvant therapy was given to 40% of patients, with 50% showing clinical response ($p<0.001$). Modified radical mastectomy was the commonest procedure (86.15%). Local recurrence occurred in 33.33% and distant metastasis in 23.26%, most commonly to bone.*

Conclusion: *Late presentation remains a major challenge. Neoadjuvant therapy improves operability, while adherence to adjuvant therapy reduces recurrence. Early detection is crucial to improve outcomes.*

Keywords: *Breast carcinoma, FNAC, Neoadjuvant therapy, Mastectomy, Outcome.*

Introduction:

Carcinoma breast is the most common malignancy among women globally and a major cause of cancer-related death.[1] The burden is increasing in developing countries due to delayed diagnosis and lack of screening programs.[2] Early-stage disease has excellent prognosis, whereas advanced-stage disease is associated with poor survival.[3]

In Bangladesh, socioeconomic barriers, lack of awareness, and healthcare access limitations contribute to late presentation. This study was conducted to document clinical presentation, evaluate neoadjuvant therapy, and assess management outcomes in carcinoma breast.

Materials and Methods:

This observational study was conducted at the Surgery Department of Bangladesh Medical University from July 2007 to December 2008. A total of 65 patients with histopathologically confirmed carcinoma breast were included.

Inclusion criteria: All biopsy-proven carcinoma breast cases.

Exclusion criteria: Secondary breast malignancy and non-carcinoma tumors.

Clinical staging was performed using TNM classification. FNAC was used for initial diagnosis and confirmed by histopathology. Neoadjuvant chemotherapy was administered in selected advanced cases. Surgical management mainly involved modified radical mastectomy. Follow-up was conducted up to 18 months to evaluate recurrence and metastasis.

Results:

Table I: *Stage Distribution of Patients*

Stage	Frequency	Percentage
Stage II (a & b)	5	7.70
Stage IIIa	7	10.77
Stage IIIb	46	70.77
Stage IV	7	10.77

Maximum patients 46 (70.8%) were in stage IIIb, and no patient were in stage I. Seven patients (10.77%) were in stage IV. This reveals that large percentage of patients presented in advanced stage of disease (Table I).

Table II: Comparison between FNAC and Histopathology report

FNAC	Histopathology		Sn	Sp	PPV	NPV	DA
	Malignant	Benign					
Malignant	62	0	95.38%	Not defined	100%	0%	95.38%
Benign	3	0					
Total	65	0					

Sensitivity (Sn) = TP / (TP + FN) = 62 / (62 + 3) = 62 / 65 = 95.38%
Specificity (Sp) = TN / (TN + FP) = 0 / (0 + 0) → Not defined (no benign cases in histopathology)
Positive Predictive Value (PPV) = TP / (TP + FP) = 62 / (62 + 0) = 100%
Negative Predictive Value (NPV) = TN / (TN + FN) = 0 / (0 + 3) = 0%
Diagnostic Accuracy (DA) = (TP + TN) / Total = (62 + 0) / 65 = 62 / 65 = 95.38%

Fine-needle aspiration cytology (FNAC) demonstrated high sensitivity (95.38%) in detecting malignant cases when compared with histopathology, correctly identifying 62 out of 65 malignancies. The positive predictive value (PPV) was 100%, indicating that all FNAC-diagnosed malignant cases were confirmed by histopathology. However, specificity could not be determined due to the absence of histopathologically confirmed benign cases, and the negative predictive value (NPV) was 0% as all FNAC benign results were false negatives. The overall diagnostic accuracy (DA) was 95.38%, reflecting strong performance in identifying malignancy but limited ability to assess true benign conditions (Table II).

Table III: *Response to Neoadjuvant Therapy*

Response	Frequency	Percentage
Responders	13	50
Non-responders	13	50

Among patients who received neoadjuvant therapy, 50% showed a clinical response while the remaining 50% did not demonstrate significant improvement. This suggests that neoadjuvant therapy is beneficial in a substantial proportion of advanced cases, although response is variable (Table III).

Table IV: *Recurrence and Metastasis*

Outcome	Frequency	Percentage
Local recurrence	11	33.33
Distant metastasis	10	23.26

Outcome analysis reveals that local recurrence occurred in 33.33% of patients and distant metastasis in 23.26% during follow-up. These relatively high rates highlight the aggressive nature of advanced-stage disease and emphasize the importance of adequate adjuvant therapy and regular follow-up to improve long-term outcomes (Table IV).

Discussion:

This study demonstrates that most patients presented with advanced-stage carcinoma breast, consistent with findings in developing countries.[2,3] Late presentation significantly limits treatment options and worsens prognosis.

FNAC showed high diagnostic accuracy, supporting its use as a cost-effective tool in resource-limited settings. Similar findings have been reported in previous studies.[6]

Neoadjuvant therapy showed significant benefit in tumor downstaging and improving operability, consistent with studies by Newman et al.[3] and Cance et al.[4] However, response rates were lower than some international data, possibly due to incomplete therapy and limited resources.

Local recurrence and metastasis rates were relatively high, particularly among patients with incomplete chemotherapy. Adequate adjuvant therapy significantly reduces recurrence and improves survival.[5,7]

Conclusion

Carcinoma breast commonly presents at an advanced stage in Bangladesh. FNAC is a reliable diagnostic tool, and neoadjuvant therapy plays an important role in downstaging tumors. Early detection, improved awareness, and adherence to treatment protocols are essential to improve outcomes.

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Original Article

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Prescribing Pattern of Osimertinib among Non-small Cell Lung Cancer Patients

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Abstract

Background: *Non-small cell lung cancer (NSCLC), accounting for 80–85% of lung cancers according to the American Cancer Society, has unfavorable results in advanced stages. Osimertinib, a third-generation EGFR-TKI, has demonstrated efficacy, particularly in CNS metastases. This survey assessed physicians' prescribing behaviors, covering decision-making, the frequency of EGFR mutation-positive cases, treatment methods, management of adverse effects, progression-free survival (PFS) and tactics for addressing resistance or treatment failure.* ***Materials and methods:*** *This research involved 112 oncologists throughout Bangladesh from cancer treatment facilities and private practices who have experienced in administering Osimertinib for lung cancer. Data were gathered through the KoBoToolbox using smartphone-based surveys that matched study aims and the aggregated data were examined with SPSS.* ***Results:*** *NSCLC was the most commonly treated lung cancer type, with 77.68% of physicians reporting osimertinib use in both adjuvant and metastatic settings. Over half (52.68%) reported using EGFR testing or empirical prescribing according to patients' financial circumstances, reflecting variation in real-world practice. Combination therapy with chemotherapy was most common (58.93%). Most physicians (94.64%) reported no serious adverse events. Physician-reported PFS was mainly 6–18 months, while 25.89% reported resistance or treatment failure, most commonly managed with repeat EGFR testing.* ***Conclusion:*** *Osimertinib was widely reported to be used in both adjuvant and metastatic settings, with combination therapy with chemotherapy being commonly reported for EGFR-positive patients. Most physicians did not report encountering serious adverse events; however, this finding reflects physician-level clinical experience and cannot be interpreted as a measure of the incidence or overall safety of osimertinib. Similarly, the reported PFS and resistance findings should not be interpreted as patient-level treatment outcomes because the survey did not collect individual patient data or treatment denominators.*

Keywords: *Osimertinib, Non-small Cell Lung Cancer, KoBoToolbox*

Introduction

Non-small cell lung cancer (NSCLC) accounts for roughly 85% of all lung malignancies, with small-cell lung cancer accounting for approximately 13% with a poor prognosis, especially in advanced cases.[1] Over the last two decades, identifying biomarkers or genetic drivers has improved the prognosis for metastatic non-small cell lung cancer.[2] Osimertinib is an oral, third-generation, CNS-penetrant EGFR-TKI that can potentially and selectively suppress both sensitizing EGFR mutations and Thr790Met (T790M) resistant mutations.[3] Because the therapeutic results of Osimertinib, such as disease progression, development of resistance and adverse events, differ depending on the patient's clinical characteristics, physicians consider them when prescribing this medication. Wu et al., evaluated the impact of age on EGFR-TKI treatment, with conflicting results indicating that EGFR-TKI treatment demonstrated low efficacy in relatively young patients with EGFR mutation-positive lung cancer. However, the underlying reason is unknown.[4]

In another retrospective research, it was found that individuals with advanced NSCLC who progressed during treatment with Osimertinib had a greater survival rate when receiving chemotherapy regimens than non-chemotherapy regimens.[5]

According to growing literature supporting consideration of dose escalation of Osimertinib to 160 mg in patients with EGFR-mutant NSCLC suffering CNS progression as a viable clinical strategy.[6]

Again, clinical characteristics such as metastasis, disease stage, and mutation type can influence the efficacy of EGFR-TKIs in treating patients with advanced EGFR-mutant NSCLC; therefore, it is vital to consider the treatment regimen.[7] Sites of metastasis were identified as prognostic factors that determine treatment efficacy according to multiple studies.[8,9] A comprehensive prognostic analysis of Osimertinib treatment of NSCLC showed that progression-free survival (PFS) of the prior EGFR-TKI treatment, performance status score and bone metastasis were independent prognostic indicators of the Osimertinib treatment that can aid decision-making while prescribing the drug [10]. Again, Osimertinib combined with platinum-based chemotherapy demonstrates superior efficacy in patients with brain metastases.[11] Another real-world data from a study on first-generation EGFR-TKI-resistant advanced NSCLC patients showed that heart disease and thrombosis before treatment influence the patient's overall survival.[12] Resistance to osimertinib remains an important clinical challenge, and the underlying mechanisms may vary according to the treatment line and molecular characteristics of the tumor. Although acquired EGFR T790M is a well-established mechanism of resistance to earlier-generation EGFR-TKIs and an important biomarker for selecting osimertinib therapy, resistance following osimertinib treatment can involve diverse mechanisms, including secondary EGFR alterations such as C797S, MET amplification, and histologic transformation. Therefore, molecular reassessment at disease progression may help identify potentially actionable resistance mechanisms and guide subsequent treatment decisions.[13] The pattern of empirical prescribing of Osimertinib based on patient characteristics and clinical condition, development of adverse reactions and resistance and disease progression following therapy is still unclear in our country due to a lack of documented evidence. It thus warrants further research considering the drastic rise in the number of lung cancer patients in Bangladesh. Since there is insufficient data or literature in Bangladesh to support the evidence, the insights of clinicians who have prescribed Osimertinib as a therapeutic approach to treat non-small cell lung cancer (NSCLC) can be a valuable source of data from which documentation can be obtained in our country.

Materials and Methods:

A cross-sectional survey was conducted among 112 oncologists from different metropolitan areas of Bangladesh who manage lung cancer patients and have experience prescribing Osimertinib. Participants were selected and provided informed consent.

Data was collected using a digital questionnaire developed on KoBoCollect/Toolbox, allowing for efficient smartphone-based data entry and secure electronic submission. The platform enabled easy integration with statistical software for analysis. This software is designed to be compatible with statistical software (Excel and SPSS version 27).

Key outcomes assessed included reported prescribing rationale and treatment settings, approaches to EGFR mutation testing, physician-reported PFS duration, treatment resistance or failure, and management of adverse reactions. Data was cleaned and analyzed descriptively using SPSS software.

Results

The total number of Practitioners have experience with NSCLC Patients

Table I shows that for all the practitioners, non-small Cell Lung Cancer (NSCLC) was the most common type of lung cancer encountered.

Table I: *Total Number of Practitioners who have experience with NSCLC patients*

Total number of Practitioners	Frequency (n)	Percentage (%)
Number of Practitioners	112	100

Settings for prescribing Osimertinib

Figure 1 presents patients with non-small cell lung cancer, Osimertinib was recommended at 8.04% in the adjuvant setting, 14.29% in the metastatic setting and 77.68% in both adjuvant and metastatic situations.

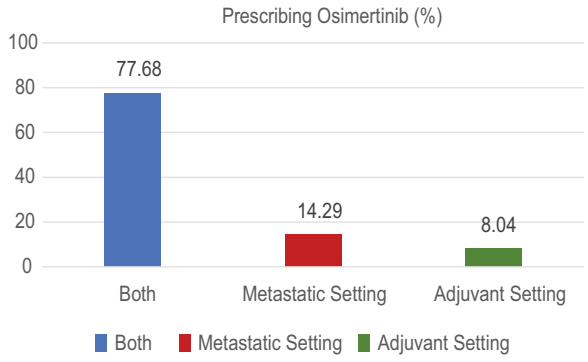


Figure 1: *Distribution of Osimertinib Prescribing Settings in NSCLC (Adjuvant, Metastatic, and Both)*

Decision-making for prescribing Osimertinib

Table II shows that 41.96% of physicians reported prescribing osimertinib based on EGFR mutation testing, 5.36% reported empirical prescribing, and 52.68% reported using either approach depending on patients' financial circumstances.

Table II: *Decision-Making Approaches for Prescribing Osimertinib Among Practitioners*

Approaches for Prescribing Osimertinib	Frequency	Percentage
Both empirically and by doing EGFR Mutation Analysis	59	52.68
By doing EGFR Mutation Analysis	47	41.96
Empirically	6	5.36

EGFR-positive cases in the last 6 months

Table III presents the proportion of EGFR-positive cases reported by physicians during the previous 6 months. Of the 112 physicians, 106 responded to this question. Among these respondents, 45.28% reported that 0–20% of their NSCLC patients were EGFR-positive, 46.23% reported 20–40%, 7.55% reported 40–60%, and 0.94% reported 60–80%.

Table III: *Distribution of EGFR-Positive Cases Among NSCLC Patients Reported by Physicians in the Previous 6 Months (n=106)*

Distribution of EGFR-positive cases	Frequency	Percentage
0–20%	48	45.28
20–40%	49	46.23
40–60%	8	7.55
60–80%	1	0.94
Total	106	100.00

Note: Percentages are calculated using the 106 physicians who responded to this question as the denominator.

Choice of treatment regimen for EGFR-positive patients

Figure 2 shows the treatment regimens reported by physicians for EGFR-positive patients. Osimertinib combined with chemotherapy was the most commonly reported regimen (58.93%), followed by osimertinib monotherapy (23.21%). Erlotinib/gefitinib, chemotherapy alone, and immunotherapy were reported by 8.93%, 6.25%, and 2.68% of physicians, respectively. The survey did not separately determine whether osimertinib–chemotherapy combinations were used in the adjuvant, locally advanced, metastatic, first-line, or later-line settings.

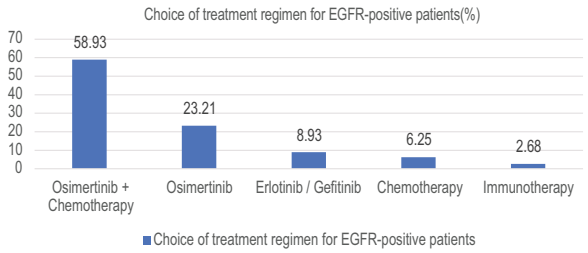


Figure 2: *Choice of treatment regimen for EGFR-positive patients*

Serious adverse events following Osimertinib therapy

Table IV shows that 6 of 112 physicians (5.36%) reported serious adverse events following osimertinib therapy, while 106 (94.64%) reported none. The specific adverse events reported are presented in Table V. Because the survey assessed physicians reported clinical experience rather than individual patient-level events, these findings represent physician-reported adverse-event experience.

Table IV: *Occurrence of Serious Adverse Events Following Osimertinib Therapy*

Serious Adverse Event	Frequency	Percentage
No	106	94.64
Yes	6	5.36
Total	112	100.00

Types of Serious Adverse Events

Table V shows among the 6 physicians who reported encountering serious adverse events, gastrointestinal issues and hand-foot syndrome were each reported by 2 physicians, while new-onset hypertension and pneumonitis were each reported by 1 physician. These frequencies describe physician-reported clinical experience and do not represent the incidence of these events among patients receiving osimertinib.

Table V: Types of Adverse Events Reported by Practitioners Following Osimertinib Treatment

Types of Adverse Events	Frequency	Percentage
Gastrointestinal issues	2	1.79
New onset of hypertension,	1	0.89
Pneumonitis	1	0.89
Hand-foot syndrome	2	1.79

Note: Percentages are based on all 112 participating physicians. The frequencies represent physician-reported experiences and should not be interpreted as patient-level adverse-event rates.

Duration of PFS (Progression-free survival)

Table VI shows the PFS durations reported by physicians based on their clinical experience with patients receiving osimertinib. Among the respondents, 42.86% reported observing PFS durations of 6–12 months, 38.39% reported 12–18 months, 10.71% reported more than 18 months, and 8.04% reported 2–6 months. These findings represent physicians' reported experience and should not be interpreted as patient-level PFS estimates.

Table VI: *Duration of Progression-Free Survival (PFS) Observed by Practitioners Following Osimertinib Treatment*

Duration of PFS	Frequency	Percentage
2-6 months	9	8.04
6-12 months	48	42.86
12-18 months	43	38.39
More Than 18 Months	12	10.71

Resistance against Osimertinib

Table VII presents physician-reported experience of resistance or treatment failure following osimertinib therapy. Among the 112 participating physicians, 29 (25.89%) reported encountering resistance or treatment failure, whereas 83 (74.11%) reported that they had not encountered such cases. These percentages represent the proportion of physicians reporting such clinical experiences and should not be interpreted as a patient-level resistance or treatment-failure rate. The survey did not collect the total number of patients treated with osimertinib or the number of patients who developed resistance or treatment failure.

Table VII: *Incidence of Resistance or Treatment Failure Against Osimertinib Reported by Practitioners*

Resistance or Treatment Failure	Frequency	Percentage
No	83	74.11
Yes	29	25.89
Total	100	100

Management approaches for Osimertinib resistance/failure cases

Figure 3 among the 29 physicians who reported encountering resistance or treatment failure following osimertinib therapy, 28 provided information regarding subsequent management. Repeat EGFR mutation testing was the most commonly reported approach, reported by 14 physicians (50.00%), followed by platinum-doublet chemotherapy with monoclonal antibodies (5, 17.86%). One physician (3.57%) reported platinum-doublet chemotherapy with a tyrosine kinase inhibitor, and one (3.57%) reported increasing the osimertinib dose. The remaining 7 physicians (25.00%) reported other management strategies. These findings represent physician-reported clinical practice among respondents who encountered resistance or treatment failure and should not be interpreted as patient-level treatment proportions.

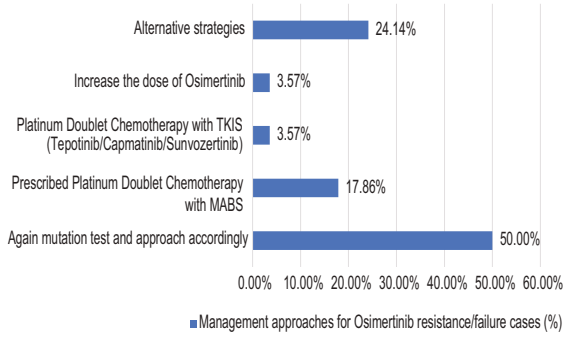


Figure 3: *Management approaches for Osimertinib resistance/failure cases other specific methods to manage Osimertinib resistance/failure*

Discussion

This study provides descriptive insights into prescribing patterns and physicians' clinical experiences regarding osimertinib use for non-small cell lung cancer (NSCLC) in Bangladesh. The majority of participating physicians reported using osimertinib in both adjuvant and metastatic settings. Combination therapy with chemotherapy was also commonly reported for EGFR-positive patients, although the survey did not determine the specific clinical setting or treatment line in which these combinations were used. These findings therefore describe real-world prescribing practices rather than comparative treatment effectiveness.[3]

In this survey, 58.93% of physicians reported using osimertinib in combination with chemotherapy for EGFR-positive patients. However, the questionnaire did not specify the clinical setting in which these combinations were used. Therefore, this finding should be interpreted as a reported prescribing pattern rather than evidence that osimertinib plus chemotherapy was preferentially used in the adjuvant or metastatic setting. The reported use of combination therapy may reflect differences in disease stage, treatment line, patient characteristics, and physician practice [11]. Further studies should assess treatment regimens according to clearly defined clinical settings.

Interestingly, the survey highlights a considerable reliance on empirical prescribing (5.36%) and mixed approaches based on EGFR mutation analysis and patient affordability (52.68%). This suggests that, despite advances in molecular diagnostics, access to EGFR mutation testing remains a significant barrier in Bangladesh. Economic constraints likely influence these decisions, consistent with findings from other low-resource settings.[2] Improving access to affordable molecular testing could reduce empirical prescribing and enable more precise, personalized treatment.

The reported serious adverse-event experience was generally low, with 5.36% of physicians reporting such events. Reported events included gastrointestinal toxicity, new-onset hypertension, pneumonitis, and hand-foot syndrome. These findings should be interpreted as physician-reported clinical experience rather than patient-level adverse-event rates. The relatively low frequency of reported serious events is broadly consistent with the established tolerability profile of osimertinib [3]. However, because the survey did not collect individual patient-level safety data, the findings cannot be used to estimate the incidence of specific adverse events.

Regarding PFS, most physicians reported observing durations between 6 and 18 months among patients treated with osimertinib. Specifically, 42.86% reported 6–12 months and 38.39% reported 12–18 months, while 10.71% reported durations exceeding 18 months. These findings are broadly consistent with clinical trial and real-world evidence demonstrating prolonged disease control with osimertinib in EGFR-mutated NSCLC.[10] However, because this study collected physician-reported experience rather than

patient-level follow-up data, these findings should not be interpreted as estimates of median PFS or patient-level survival outcomes. Prospective studies using individual patient data are required to determine the actual PFS associated with osimertinib treatment in Bangladesh.

Despite the clinical activity of osimertinib, acquired resistance remains a challenge in the management of EGFR-mutated NSCLC. In this survey, 29 of 112 physicians (25.89%) reported encountering resistance or treatment failure following osimertinib therapy. This represents the proportion of participating physicians reporting such clinical experience and should not be interpreted as a patient-level resistance or treatment-failure rate. Among the 28 physicians who provided information on subsequent management, repeat EGFR mutation testing was the most commonly reported approach. Molecular reassessment at disease progression may help identify actionable resistance mechanisms; however, resistance after osimertinib is heterogeneous and may involve secondary EGFR alterations, including C797S, MET amplification, HER2 or other pathway alterations, as well as histologic transformation [13]. Therefore, resistance management should be guided by the clinical context and, where feasible, appropriate molecular and histopathological reassessment rather than relying specifically on T790M testing. The variation in reported management strategies in this survey reflects differences in physician practice and available treatment options in the local setting. The survey revealed that 50% of practitioners managed resistance by repeating EGFR mutation testing to guide subsequent therapy, which aligns with global recommendations emphasizing the importance of rebiopsy or liquid biopsy at progression.

Additional strategies included chemotherapy, immunotherapy, alternative TKIs (such as Tepotinib, Capmatinib, or Lazertinib), radiotherapy, and individualized approaches. The diversity of these management plans indicates a lack of standardized protocols and highlights the need for local treatment guidelines tailored to the Bangladeshi context.

The study underscores the importance of integrating molecular profiling into routine clinical practice to optimize treatment outcomes and reduce empirical prescribing. Moreover, it reveals an urgent need for educational initiatives and policy support to improve accessibility to targeted therapies and diagnostic tests.

While this survey offers valuable real-world data, it is important to acknowledge its limitations. The sample size was relatively small and restricted to a specific group of oncologists. Additionally, the reliance on self-reported data may introduce recall bias. Nevertheless, the findings provide a foundational understanding of current practice patterns and pave the way for further multicenter, large-scale studies to validate and expand these observations.

Conclusion

This physician-level survey provides descriptive information on real-world prescribing patterns and clinical experiences with osimertinib among oncologists treating NSCLC in Bangladesh. Osimertinib was commonly reported to be used in both adjuvant and metastatic settings, and combination therapy with chemotherapy was frequently reported for EGFR-positive patients. Physicians commonly reported PFS durations of 6–18 months, and most did not report encountering serious adverse events during their clinical experience with patients receiving osimertinib. However, these findings do not represent patient-level estimates of treatment efficacy, survival, or toxicity because individual patient data and treatment denominators were not collected. Resistance or treatment failure was reported by 25.89% of physicians, representing physician-level clinical experience rather than a patient-level resistance rate. Management approaches varied among physicians who encountered such cases. Overall, the findings describe current prescribing practices and clinical experiences with osimertinib in Bangladesh and highlight the need for larger prospective studies using patient-level data to evaluate its safety and effectiveness.

Limitations

This study has several limitations. The sample size was relatively small and included oncologists predominantly from metropolitan areas, which may limit generalizability. Purposive sampling and self-reported responses may have introduced selection and recall bias. Importantly, the survey collected physician-level clinical experience rather than individual patient-level data. Therefore, the reported

adverse events, PFS durations, and resistance or treatment-failure findings cannot be interpreted as patient-level incidence or treatment outcome estimates. The study did not record the total number of patients treated with osimertinib, treatment exposure duration, or the number of adverse events per patient. In addition, the absence of patient-level clinical details and the use of descriptive analysis limited assessment of factors associated with treatment outcomes. As a cross-sectional survey, the study also does not capture changes in prescribing practices or outcomes over time. Finally, the study was industry-sponsored and involved authors affiliated with the sponsor; therefore, the possibility of sponsorship-related bias cannot be completely excluded.

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Original Article

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Utility of Risk of Malignancy Index (RMI) in Predicting Malignancy in Patients with Adnexal Mass Experience in A Tertiary Hospital

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Abstract

Background: *Ovarian malignancy is one of the silent killers as most of the cases present in advanced stages. Pre-operative assessment regarding the nature of adnexal mass is necessary in order to make a standard management plan. Risk of malignancy index (RMI) is a simple scoring system based on three factors - serum CA -125, USG score and menopausal status. The objective of the study was to evaluate risk malignancy index (RMI) in pre-operative prediction of malignancy in women with adnexal mass.* ***Materials and Methods:*** *This was a cross-sectional study. Study population was patients with clinical or radiological diagnosis of adnexal mass who were admitted under gynecological oncology department of NICRH for surgery between July 2022 and June 2023. Information on demographic characteristics, ultrasound findings, menopausal status, preoperative CA125 level, and post-operative histopathology was collected. Sensitivity and specificity of each parameter of RMI (menopausal status, USG score and CA 125 level) was measured. RMI score for each patient was calculated. ROC curve was constructed to find predictive power of RMI level in detecting malignant adnexal mass and also to find best cut-off value.* ***Results:*** *Total 57 patients were enrolled for the study. Thirty-eight (66.7%) cases were found to be malignant in postoperative histopathological report. Analysis of the individual parameters of RMI revealed that menopausal status, raised CA 125 level (>35 IU/ml) and ultrasound score were not good predictors of malignancy individually (sensitivity and specificity 47.4%, 63.2%; 84.2%, 47.4%; and 65.8%, 78.9%, respectively). RMI level >200 had sensitivity and specificity of 78.9% and 78.9%, respectively, with an AUC of 0.839 in predicting malignancy in adnexal mass.* ***Conclusion:*** *RMI is highly reliable tool in differentiating benign and malignant ovarian lesions. A cut-off of 200 may be suitable for triaging patients with adnexal mass and early referral to tertiary care centers.*

Keywords: *Adnexal mass, Malignancy, RMI*

Introduction

Internationally, ovarian cancer is among the most common cancers affecting women. According to GLOBOCAN 2024 estimates, Bangladesh had approximately 2,808 new ovarian cancer cases and 1,831 deaths from ovarian cancer in 2024. Ovarian cancer is often called a "silent killer" because many cases are detected at an advanced stage, partly because of the anatomical location of the ovaries and the absence of an effective population-based screening test.[1]

An adnexal mass is one of the most frequent indications for referral to specialist gynecologists.

Management of malignant masses are different than that of beni

gn and require referral to special center. Up to 24% of ovarian tumors in premenopausal women are malignant and up to 60% are malignant in postmenopausal women.[2] Preoperative evaluation and discrimination of adnexal masses as benign and malignant is of utmost importance and play central role in decision making regarding - clinical management and proper surgical planning of patients. There should be a standardized and available method specially for rural areas for this purpose. This will allow optimization of first-line treatment for women with ovarian cancer.

Patients with suspected ovarian malignancy should be referred to gynecological oncologist, for treatment planning, proper preoperative evaluation, choosing proper surgical procedure and improving the quality of cytoreductive surgery. Accurate per operative surgical staging and optimal cytoreduction are important prognostic factors in ovarian malignancy. Oncological outcome of ovarian cancer is largely dependent on its surgical management.[2] On the other hand, unnecessary referral of benign cases to tertiary oncology center increases burden to these centers. So timely and appropriate evaluation of adnexal masses and referral of the suspected patients to a gynecological oncologist is important and has been proven to improve outcome of patients with ovarian cancer.[3]

Currently standard workup for evaluation of adnexal mass includes clinical examination, imaging assessment, tumor markers assay. In most cases, however, the history and physical examination alone are insufficient to make a diagnosis, and ultrasound imaging, with or without laboratory studies, is necessary. The ultimate diagnostic tool is histological examination.

Various diagnostic tests for evaluation of adnexal mass are available to date, but they are not very dependable due to low diagnostic performances. The commonly available tests are tumor markers and radiological imaging methods. Serum CA125 level is often used for distinguishing malignant tumors in case of adnexal pathology. But CA -125 level has limited value as individual parameter as it is elevated mostly in advanced stage (92%) ovarian malignancy and only 50% cases in early-stage tumors[4]. Though IOTA simple rule has emerged as promising tool for predicting malignancy, but it is inconclusive in about 25% cases.[5] MRI has excellent soft tissue resolution with high accuracy[6] for evaluation of adnexal mass. But it is expensive and unavailable in many peripheral areas-that makes it unsuitable for routine use. Risk of malignancy algorithm (ROMA) is a recent test, which combines the serum CA 125 and HE4 with menopausal status into a numerical score. But HE4 is currently not available in all peripheral areas of Bangladesh and it requires a complicated calculation.[7]

To reduce the diagnostic dilemma between benign and malignant ovarian masses, a formula-based scoring system - risk of malignancy index (RMI) was introduced in 199[8-11]. Jacobs et al. originally developed the RMI, which is now termed RMI 1. Tingulstad et al. developed RMI 2 in 1996 and subsequently modified it in 1999 to produce RMI 3.[12] Risk of malignancy index (RMI) is a diagnostic model with combined parameter. RMI is calculated with a simplified regression equation obtained from the product of menopausal status score (M), ultrasonographic score (U), and absolute value of serum CA-125.[9-10]The main advantage of RMI is that it is a simple and objective scoring system that can be applied directly into clinical practice with simple set up, without the necessity of expensive or complicated methods (such as computed tomography scan, magnetic resonance imaging and whole-body emission tomography). As all parameters (menopausal status, CA 125, USG) are available in all areas, this is a suitable method of evaluation of adnexal masses in peripheral areas where it is much needed. A systematic review in 2009 concluded that the risk of malignancy index is the best available test to triage patients with ovarian tumors for the referral to the gynecologic oncologist.[12] The aim of this observational study was to evaluate the role of Risk of Malignancy Index (RMI) in differentiating benign and malignant ovarian masses preoperatively.

Methodology

This study was observational cross- sectional study which was conducted in gynecological oncology department of National Institute of Cancer Research and Hospital, Dhaka. A total of 57 patients within a period of 12 months from July 2022 to June 2023, who

attended the outpatient department with radiological or clinical evidence of an adnexal mass and for whom surgical treatment was planned, were included in the study. Patients below 18 years or who had evidence of obvious malignancy (ie-extensive metastases in imaging or biopsy proven malignancy or prior history of taking chemotherapy) were excluded from study. Detailed history was taken and for each patient trans abdominal and transvaginal USG with color doppler was performed. Obtained data included: age, menopausal status, clinical features at presentation, ultrasound findings and CA125 levels. RMI 3 was calculated for all patients. The RMI-3 was calculated using the formula RMI=M x U x serum CA- 125 where (M) refers to the patient's menopausal status, (U) refers to the ultrasound score and serum (CA -125) was the assayed level expressed in U/ml.

Postmenopausal status is defined as more than 1 year of amenorrhea. A score of M = 3 is given to postmenopausal women and M=1 for premenopausal status.

5 ml of venous blood was collected for serum CA-125 estimation. Abnormal CA 125 level is defined as serum level ≥ 35 U/mL.CA 125 level was entered directly into the equation. For USG score calculation-patients were evaluated by trans abdominal or transvaginal ultrasonography in the radiology and imaging department of this institute. Adnexal masses were evaluated for five sonographic morphological criteria – presence of solid structure, bilaterality, presence of ascites, presence of metastasis and multilocularity. If there is presence of 1 or no feature- USG score will be 1 and in presence of two or more feature- USG score will be 3.

Total score was calculated for each patient.

After surgery specimen was sent for histopathological examination.

Postoperative histopathology of all the cases was collected and patients were classified as benign and malignant group. Borderline tumors were included in malignant group. Histopathological finding was correlated with RMI score. The diagnostic performances of three parameters of RMI and RMI score, were evaluated in sensitivity, specificity, NPV, and PPV. Histopathology report was considered as gold standard.

Result

The study included a total of 57 patients. Distribution of cases by age and histopathological category (benign and malignant) is shown in Table 1. The age of the patients varied from 18 to 79 years (mean, 43.16 years). Thirty-three (58%) patients were aged >40 years and 24 (42%) were aged ≤40 years. Among patients aged ≤30 years, 10 of 16 (62.5%) had malignant disease. In the 31–40-year age group, 6 of 8 (75.0%) had malignant disease; in the 41–50-year group, 4 of 8 (50.0%) were malignant; in the 51–60-year group, 13 of 18 (72.2%) were malignant; and among those aged >60 years, 5 of 7 (71.4%) were malignant.

Table 1: *Age group distribution of the patients(n=57)*

Age group (yrs.)	Malignant n (%)	Benign n (%)	Total n (%)
≤30	10 (62.5)	6 (37.5)	16 (100.0)
31-40	6 (75.0)	2 (25.0)	8 (100.0)
41-50	4 (50.0)	4 (50.0)	8 (100.0)
51-60	13 (72.2)	5 (27.8)	18 (100.0)
>60	5 (71.4)	2 (28.6)	7 (100.0)

Based on postoperative histopathological examination reports, 38 patients (66.7%) had malignant tumors and 19 patients (33.3%) were diagnosed as benign (Table-2). Serous cystadenoma and endometriotic cyst were commonest benign tumor. Each of these types were found in 6 cases. Dermoid cyst and mucinous cystadenoma were next common benign types. Serous cystadenocarcinoma was commonest malignant tumor. Out of 38 malignant cases 23 patients (63%) were serous cystadenocarcinoma. Next common type was mucinous cystadenocarcinoma. Malignant germ cell tumor and low-grade serous tumor were found in 3 and 2 cases respectively.

Among 57 patients, 25 patients are postmenopausal and 32 patients are premenopausal. Benign cases are more frequent in premenopausal (21.05% vs 35.09%) than postmenopausal (12.2% vs 31.58%).

RMI scores of patients varied from 12 to 20700 (mean, 1874±3196.3). Figure 1 shows distribution of patients according to RMI status. Total 34(59.65%) patients had RMI score ≥200. Among them (within 59.65%) 52.63% were malignant and 7.02% were benign. On the other hand,23(40%) patients had RMI level<200. Majority of patients (26.32% vs 14.04%) were benign when RMI score <200.

Table II: *Distribution of patients according to histopathological finding*

Histopathologic diagnosis	Total no.
Benign cases (19)	
Serous cystadenoma	6
Endometriotic cyst	6
Dermoid cyst	4
Mucinous cystadenoma	3
Malignant cases (38)	
Serous cystadenocarcinoma high grade	23
Serous cystadeno carcinoma low grade	2
Mucinous cystadenocarcinoma	7
Malignant germ cell tumour	3
Malignant brenner tumour	1
Clear cell adenocarcinoma	1
Borderline tumor	1

The serum CA125 levels in the patients varied from 4 to 7500 U/mL (mean, 491.88 U/ml).

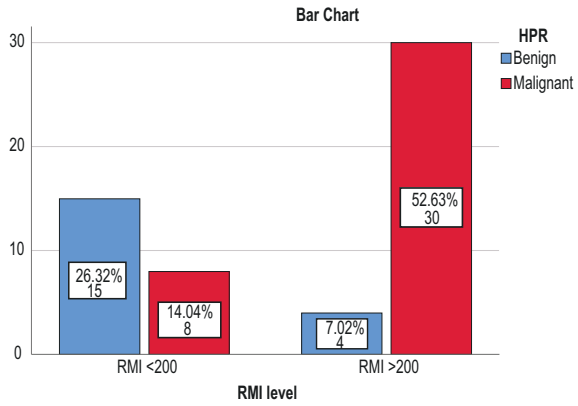


Figure 1: *Distribution of histopathological nature according to RMI value(n=57)*

Table 3 shows individual performances of three parameters of RMI (CA-125, menopausal statis, USG scoring) in prediction of malignancy. Out of 57, 42 patients had their preoperative serum CA 125 level >35 U/ml (Table 3). Among them 32 (76.19%) patients were found to have malignant disease and 10 (23.8%) had benign disease in postoperative histopathology. 9 out of 15 patients (60%) patients with CA125 levels less than 35U/mL had benign lesions. Sensitivity, specificity, PPV and NPV of raised CA 125 (>35 u/ml) in detecting malignancy is 84.2%, 47.4%, 76.2% and 60%.

Table 3: *Predictive values of USG score, CA 125 and RMI scores and menopausal status of malignant and benign lesions(n=57)*

Variables	Malignant	Benign	Sn (%)	Sp (%)	PPV (%)	NPV (%)
Premenopausal	20	12	47.4	63.32	72.0	37.5
Postmenopausal	18	07				
USG score 1	13	15	65.8	78.9	86.2	53.6
USG score 3	25	04				
CA 125 ≤ 35	06	09	84.2	47.4	76.2	60.0
CA 125 > 35	32	10				
RMI ≤ 200	08	15	78.9	78.9	88.2	65.2
RMI >200	30	04				

Note: For each binary predictor, sensitivity, specificity, PPV and NPV refer to the stated positive-test category (postmenopausal status, USG score 3, CA-125 >35 U/mL, and RMI >200).

The performance of USG score 3 as an individual factor in predicting malignancy was analyzed. USG score 1 and 3 were found in 28 and 29 cases respectively. Among 29 cases who have USG score 3, 25 were found malignant postoperatively and 4 are benign. Sensitivity of USG score was 65.8% and specificity 78.9% (table-3) as predictor of malignancy. The positive predictive value was 86.2% and negative predictive value was 53.6 % for this parameter in the present study.

In present study sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of menopausal status in predicting adnexal malignancy are calculated which are 47.4%, 63.32%, 72% and 37.5% respectively.

Comparing as individual predictive performances of the three criteria, an ultrasound score of 3 had the highest specificity in detecting adnexal malignancy (78.9%), while a raised CA 125>35 had the highest sensitivity (84.2%).

Total 34 (59.65%) patients had RMI score ≥200, where 52.63% were malignant and 7.02% were benign. On the other hand, majority of patients (26.32% vs 14.04%) were benign when RMI score <200 (table-3).

To find out the RMI value that could most effectively classify the disease, we calculated the sensitivity, specificity of RMI cut-off levels of 100, 150, 200, and 250. A comparison of the diagnostic indices with these cutoffs is shown in Table 4. As shown in this table, an RMI score of 200 had the ideal combination of sensitivity (81%), specificity (79%). Lower cut-off value of 100 and 150 showed higher sensitivity (86% & 84% respectively) in detecting malignant disease. But these values had lower specificity (58% and 74% respectively) compared to cut-off 200. RMI value 250 showed higher specificity (85%) but lower sensitivity (78%).

Table-IV: *Diagnostic performance of the different RMI cut-offs*

RMI cut off	Sensitivity (%)	Specificity (%)
100	87	58
150	84	74
200	78.9	78.9
250	76	84

A receiver operating curve was plotted (figure-2) to find sensitivity and specificity of different RMI point and to identify best RMI cut-off value in predicting adnexal malignancy. Area under curve (AUC) was .89. So, RMI as a diagnostic test has high discriminatory power to differentiate benign and malignant ovarian masses. RMI level 200 was found to be best cut-off point with sensitivity 81% and specificity 79%.

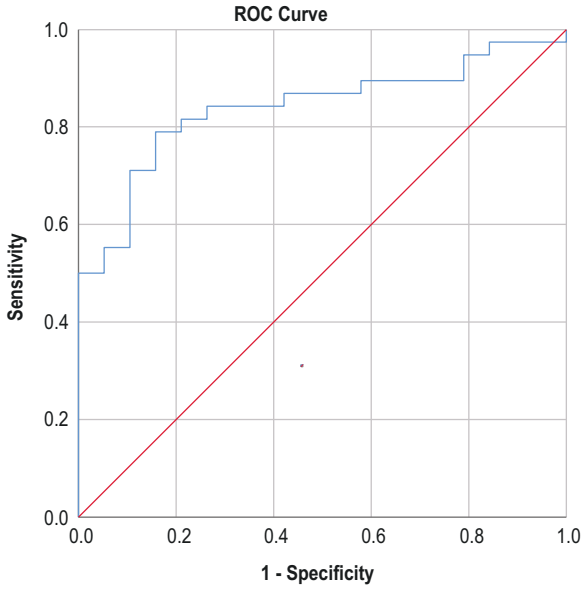


Figure-2: *The ROC curve for RMI level*

To see the predictive power of RMI in detecting malignancy in adnexal mass a ROC curve was constructed.

Discussion

Ovarian cancer has aggressive clinical course, mainly due to late diagnosis and lack of effective diagnostic tool for early-stage detection of the disease.

This was a cross-sectional study conducted in gynecological oncology department of National Institute of Cancer Research and Hospital. The objective of this observational study was to evaluate utility of Risk of Malignancy Index (RMI) in differentiating benign and malignant ovarian masses preoperatively. Fifty-seven patients with adnexal masses who were planned for surgery between July 2022 to June 2023, were enrolled in the study. Among them based on postoperative histopathological examination reports, 38 patients (66.7%) had malignant tumors and 19

patients (33.3%) were diagnosed as benign. Some other studies like Yamamoto et al[13] study and Jenitha et al study[14] showed majority patients were benign (84.2%). Majority of patients were malignant in this study as our center is a tertiary oncology referral center. Serous cystadenocarcinoma was most common malignant tumor in this study (23 out of 38 malignant cases). Next was mucinous adenocarcinoma. Serous cystadenoma and endometriotic cyst (both 6 in number) were commonest benign tumor type. Dermoid cyst was next common type. This result is compatible with Jenitha et al[14] study. Serous cystadenoma (28%) was the most frequent benign tumor and serous cystadenocarcinoma was 2nd commonest malignant tumor in their study after mucinous adenocarcinoma.

Chance of ovarian mass to be malignant is more common in postmenopausal women in comparison to premenopausal group. In our study premenopausal women had more chance of benign lesion (12% vs 7%) in comparison to postmenopausal women. These data seem to agree with earlier Aziz et al study[15]. Jenitha et al.[14] study also showed more frequency of malignancy among postmenopausal women (16% vs 42.4%)

Higher age is one of the risk factors for ovarian malignancy. In this study mean age of malignancy was 56 years and mean age for benign disease was 38 years. Incidence of malignancy peaked in the age group 41-50, while most frequent for benign group was 31-40 years which had least chance of malignancy (25%). Aziz et al.[15] study had also shown highest occurrence of malignancy in this age group. Rate of malignancy was highest (7.4%) in this group in her study. Another recent study[16] also showed 40-51 to be pick age group for malignancy.

Serum CA125 level is widely appreciated as a useful biomarker for estimating the risk of ovarian cancer, though other gynecological pathology can also increase its levels. It is more significant in postmenopausal females as compared to premenopausal females as it can be raised in various benign conditions in before menopause.

Myers et al.[17] have earlier reported sensitivity and specificity of less than 80%, for this marker, in the prediction of ovarian cancers. Simsek et al.[18] reported a sensitivity of 78.6% and specificity of 63.5% for a CA125 cut-off of 35 U/ml.

In this study CA125 >35 IU/L was found to be highly sensitive (84.2%) in detecting adnexal malignancy, though specificity was low 47.4%. Reason for low specificity in different studies is due to rising of CA 125 in different benign adnexal lesion. In Amarjeet Kaur et al study, they have got almost similar result. In that study, sensitivity of CA 125 in diagnosing malignancy was 90.91% and specificity was 57.89%. The positive predictive value was 55.56% and negative predictive value was 91.67%[19].

In RMI scoring there are five ultrasonographic features. Scoring 3(presence of 2 or more out of 5 sonographic feature) has found to have low sensitivity 65.8% and moderate specificity 78.9% with PPV 86.2, NPV 53.6 as independent factor in detecting malignancy. In another study[20] USG score had a sensitivity of 76.4 % (52.74–90.44), a specificity of 75.6 % (60.66–86.17), a positive predictive value of 56.5 %, and a negative predictive value of 88.5 %. In Aziz et al. study[15] sensitivity and specificity were 78.3% and 81.5% respectively. Specificity of RMI USG score 3 of these studies are almost similar to our study specificity. Less sensitivity of this feature in this study may be due to small sample size.

Diagnostic accuracy of RMI value>200 in predicting adnexal malignancy was calculated (table-4). This parameter was found to have high sensitivity and specificity which was 81% sensitive and 79% specific with high PPV (88.2%) and NPV (65.2%) in detecting malignant adnexal mass. A receiver operating curve was plotted (figure-3) to find sensitivity and specificity of different RMI point and to identify best RMI cut-off value in predicting adnexal malignancy. Area under curve (AUC) was .89. So, RMI is a good test to differentiate benign and malignant ovarian masses. RMI value 200 was found to be best cut-off point with sensitivity 81% and specificity 79%.

In Malla V G study[21] sensitivity 87.5, specificity 91.3, PPP 73.6 and NPV 96.5 for RMI score >200 (value = 0.0001), while in another study by Kaur et al[19], the sensitivity of RMI 3 to detect malignancy in adnexal pathology – 100, specificity was 91.89%, positive predictive value was 78.57%, negative predictive value was 100%.

Predictive performances of different RMI cut-off were compared (table-5). To find out the RMI score

that could most effectively classify the disease, we calculated the sensitivity, specificity of RMI cut-off levels of 100, 150, 200, and 250. As shown in this table, an RMI score of 200 had the ideal combination of sensitivity (78.9%) and specificity (78.9%). Lower cut-off value of 100 and 150 showed higher sensitivity (86% & 84% respectively) in detecting malignant disease. But these values had lower specificity (58% and 74% respectively) compared to cut-off 200. RMI value 250 showed higher specificity (84%) but lower sensitivity (76%). In Aliya B et al study15 RMI cut-off 250 was found to have best predictive performance (54.05% sensitivity 93.4% specificity).

A receiver operating curve was plotted(figure-3) to find sensitivity and specificity of different RMI value and to identify best RMI cut-off value in predicting adnexal malignancy. Area under curve (AUC) was .89. So, RMI is a good test to differentiate benign and malignant ovarian masses. RMI level 200 was found to be best cut-off point with sensitivity 81% and specificity 79%.) In another study by Karimunnisha et al.s[22] the best performance obtained for RMI-3 was at the cut-off point 236 with a sensitivity of 72.5%, a specificity of 98.2%, a PPV of 98.1%.

In this study, among the parameters of RMI, CA125 as an individual parameter had good sensitivity. On the other hand, USG score 3 was found to have good specificity. Postmenopausal status as individual feature had both low sensitivity and specificity. As a predictor of malignancy of adnexal mass, RMI with cut-off >200 was found to be a sensitive tool with high specificity, PPV and NPV.

Conclusion:

It is concluded from the study that RMI with a cut-off >200 has useful sensitivity and specificity for differentiating benign from malignant adnexal masses preoperatively. RMI is a simple, feasible and objective diagnostic tool for preoperative prediction of malignancy in patients with an adnexal mass and may assist appropriate triage and referral to tertiary care centers.

It is concluded from the study that RMI with cut-off >200 has high sensitivity and specificity for differentiating benign from malignant adnexal masses preoperatively. RMI is a simple, feasible, objective diagnostic tool for preoperative prediction of malignancy in patients with adnexal mass thus providing the patients a chance for early referral, treatment, and better survival rate.

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Original Article

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KRAS mRNA Expression in Ovarian Cancer Patients of a Tertiary Level Cancer Hospital of Bangladesh

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Abstract

Background: *Ovarian cancer is the most lethal gynaecological cancer. Genetic, environmental, and hormonal factors contribute to its pathogenesis. Among the genetic factors, BRCA1 and BRCA2 have been extensively studied, leading to the development of Poly(ADP-ribose) polymerase inhibitors (PARPi) for targeted therapy of breast and ovarian cancer. The KRAS oncogene is associated with many cancers, including ovarian cancer. There are studies on KRAS mutations in ovarian cancer, but studies on its mRNA expression are scant and have not been explored in the population of Bangladesh. This study aimed to examine the status of KRAS mRNA expression in ovarian cancer tissue and analyse its association with cancer-related characteristics.* **Methods:** *Total RNA was extracted from formalin-fixed paraffin-embedded (FFPE) ovarian cancer tissues and FFPE non-cancerous ovarian tissues. The extracted mRNA was amplified by two-step RT- PCR using a commercial cDNA synthesis kit and gene expression assay kits for KRAS and GAPDH. Samples in which both the KRAS and GAPDH gene amplification curves were detected were included for KRAS mRNA expression calculation using the formula* $2^{-\Delta\Delta Ct}$. *The expression of KRAS mRNA was then analysed for association with cancer-related characteristics using IBM SPSS Statistics 25.0 software.* **Results:** *KRAS mRNA expression was significantly higher in ovarian cancer tissues compared to non-cancerous ovarian tissues. Increased KRAS mRNA expression was associated with histologically high-grade ovarian cancers. KRAS mRNA expression was not associated with the histological type or stage of cancer.* **Conclusion:** *Increased KRAS mRNA expression and its association with high-grade ovarian cancer is the first evidence of KRAS gene expression in ovarian cancer patients of Bangladesh.*

Keywords: *KRAS mRNA expression, real-time RT-PCR, FFPE ovarian tissue, ovarian cancer patients of Bangladesh*

Introduction

Ovarian cancer is the most lethal gynaecological neoplasm[1]. Even though newly diagnosed patients respond well to debulking surgery and adjuvant chemotherapy, relapse is frequent, and recurrent ovarian cancer is usually incurable.[2-4] A high case fatality rate is due to diagnosis at a late stage and limited therapeutic options.[2,5] There is no effective biomarker for molecular targeted therapy, predicting prognosis, or monitoring response to treatments of ovarian cancer.[6] This is because its pathogenesis is complex and not fully understood. Genetic changes in combination with environmental and hormonal factors contribute to its pathogenesis[7-10]. Among the genetic factors, the contributions of the tumour suppressor genes BRCA1 and BRCA2 have been extensively studied. This resulted in the development of molecular targeted therapy for BRCA1/BRCA2 mutation-positive breast and ovarian cancers by PARPi drugs.[11-13]

KRAS is a proto-oncogene of the RAS gene family. RAS genes (KRAS, HRAS, NRAS) regulate cell proliferation by acting through the Mitogen-activated protein kinase (MAPK) signalling pathway.[14] Mutations of KRAS are frequently found in ovarian cancer.[15,16] Activating mutations of proto-oncogenes to oncogenes result in increased gene expression and signalling, which causes increased cell proliferation and malignant transformation[17]. However, epigenetic changes may cause upregulation or downregulation of proto-oncogenes, resulting in increased or decreased expression.[18,19] Therefore, gene expression studies of proto-oncogenes, such as KRAS, may provide valuable insights into understanding the pathogenesis of cancers.

The contribution of the KRAS in ovarian cancer is less well studied. Though there are some studies on KRAS mutations, few studies have examined KRAS expression. Among the available studies, some show increased KRAS expression in ovarian cancer tissue compared to non-cancerous tissues and its association with early stages of ovarian cancer in some populations.[20-22] Conversely, a study found variable KRAS and decreased HRAS expression in a diverse population with recurrent ovarian cancer.[23]Among the studies on expression of other genes in ovarian cancer, increased expression of p53 and PTEN tumour suppressor genes was found to be associated with longer overall survival.[24,25] On the other hand, increased expression of HSPA1A, CD99, RAB3A, and POM121L9P was found to be associated with shorter overall survival.[26] These findings suggest that KRAS expression in ovarian cancer may have potential as a diagnostic and prognostic marker and therapeutic target, which calls for extensive studies on various populations. KRAS expression in ovarian cancer patients of Bangladesh has not been studied yet. This study aimed to assess the KRAS mRNA expression level in FFPE ovarian cancer tissue compared to FFPE non-cancerous ovarian tissue and to explore whether the KRAS mRNA expression level is associated with ovarian cancer and cancer-related characteristics of ovarian cancer patients of Bangladesh.

Materials and Methods

This cross-sectional study was conducted in the Department of Immunology and Molecular Biology of the National Institute of Cancer Research and Hospital (NICRH) during December 2024 to May 2025.

FFPE tissue sample collection and sectioning

In this study, 61 FFPE ovarian cancer tissue blocks and 40 FFPE non-cancerous ovarian tissue blocks archived from January 2023 to December 2024 were collected from the Department of Histopathology of NICRH. Cancer tissue blocks were from patients with histologically diagnosed ovarian cancer, irrespective of the histological type of cancer. Non-cancerous tissue blocks are of patients who had undergone oophorectomy for gynaecological diseases other than ovarian cancer and did not have malignant cells in their ovaries. Patients' cancer-related characteristic data were collected from the records in the Department of Histopathology and the Department of Gynaecological Oncology of NICRH. From each FFPE block, four tissue sections, each 10 µm-thick, were taken in an RNase-free micro-centrifuge tube.

RNA extraction

Total RNA was extracted from tissue samples using PureLink FFPE Total RNA extraction kit (Invitrogen by Thermo Fisher Scientific, USA) according to the manufacturer's instructions. The quality and quantity of RNA were measured with an Eppendorf Biophotometer D30 (Eppendorf AG, Germany).

The 260/280 nm absorbance ratio of extracted RNA samples was from 1.80 to 2.04, and RNA concentration was from 5.7 to 272.8 ng/µl. Extracted RNA was stored at -80°C until used as a template for amplification by two-step real-time PCR.

Reverse Transcription of RNA and the First-strand cDNA Synthesis

In the first step, reverse transcription (RT) of mRNA was done to synthesise the first-strand cDNA using Verso cDNA synthesis Kit (Applied Biosystems by Thermo Fisher Scientific, USA) according to the manufacturer's protocol. The blend of primers was prepared as a ratio of 3:1 of random hexamer and oligo(dT) primer, respectively. A ProFlex PCR system (Thermo Fisher Scientific, USA) thermal cycler was used. The reaction volume was 20 mL, in which the RNA template volume was 4 mL (RNA concentration 22.8 to 1091.2 ng). The temperature profile was one cycle at 42ºC for 60 min for reverse transcription, and 95ºC for 2 min for enzyme inactivation. The newly synthesised cDNA was stored at -80ºC until used as the template for real-time PCR amplification in the second step.

Amplification of cDNA by Real-Time PCR

Commercially available TaqMan gene expression (GE) assay kits containing primer-probe mixtures for KRAS (KRAS GE Assay, Assay ID Hs00364284_g1, Catalogue no. 4331182, Thermo Fisher Scientific, USA) and GAPDH (GAPDH GE Assay, Assay ID Hs02786624_g1, Catalogue no. 4448489, Thermo Fisher Scientific, USA) gene were used for PCR amplification. Each GE assay mix consisted of a pair of unlabeled PCR primers, a TaqMan probe with a dye (FAM for KRAS and VIC for GAPDH) label on the 5′ end, a minor groove binder (MGB), and a non-fluorescent quencher (NFQ) on the 3′end. The template cDNA was amplified using the 7500 Fast Dx Real-Time PCR System (Applied Biosystems by Thermo Fisher Scientific, USA) with a relative quantification multiplex PCR protocol. PCR reaction mix was prepared with 5 µL TaqMan Fast Advanced Master Mix (Applied Biosystem by Thermo Fisher Scientific, USA), 0.5 µL KRAS GE Assay mix, 0.5 µL GAPDH GE Assay mix, 2 µL cDNA template, and 2 µL nuclease-free water to make a total reaction volume of 10 µL. The PCR temperature profile consisted of one cycle at 95ºC for 20 seconds to activate the DNA polymerase enzyme, followed by 45 cycles at 95ºC for 3 seconds to denature the DNA and 60ºC for 30 seconds for primer annealing, extension, and fluorescence detection. Samples in which amplification failed to occur for KRAS or GAPDH, or both, were repeated following the same PCR protocol, and the results of the second PCR were considered as the final result.

Analysis of KRAS mRNA Expression

The cycle threshold (Ct) value of fluorescence of KRAS (target gene) and GAPDH (reference gene) was noted from the multiplex PCR amplification curves of each sample. Samples in which the amplification of both genes occurred were used for the calculation of the expression of KRAS mRNA. If the amplification curve of any of the genes was missing in any sample, PCR was repeated from the cDNA of that sample. Samples with no amplification curve of either of the genes in the repeat PCR were excluded from expression calculation. The expression of the KRAS gene was calculated from the Ct values, using Microsoft Excel 2007. At first, the ΔCt of KRAS was calculated by the formula ΔCt = Ct of KRAS - Ct of GAPDH of the sample. Then, the average of ΔCt of KRAS in non-cancerous ovarian tissue samples (control) was calculated. The ΔΔCt of KRAS was calculated as ΔΔCt of KRAS = ΔCt of KRAS of a sample – average ΔCt of KRAS of the control samples. The gene expression level in a given sample was represented as $2^{-\Delta\Delta Ct}$, because the PCR product doubles with each cycle, in the linear amplification range.

Data analysis

The collected data were checked manually for any technical discrepancies. In the histopathology reports, histological diagnosis and classification of the tumour were according to the WHO classification system[27]. Epithelial ovarian cancers were graded using a two-tier histological grading system of Mastuno et al.,.[28] Cancer staging was according to the International Federation of Gynaecology and Obstetrics (FIGO) staging system.[29]

Statistical analysis was done using IBM SPSS Statistics, version 25.0. The Shapiro-Wilk test was used to determine whether the KRAS mRNA expression data were normally distributed for the variables. Means were compared using an independent

t-test for normally distributed data, and the median was compared with the Mann-Whitney U test or the Kruskal-Wallis test for the data with a skewed distribution. All statistical tests were considered significant if the *p*-value was <0.05.

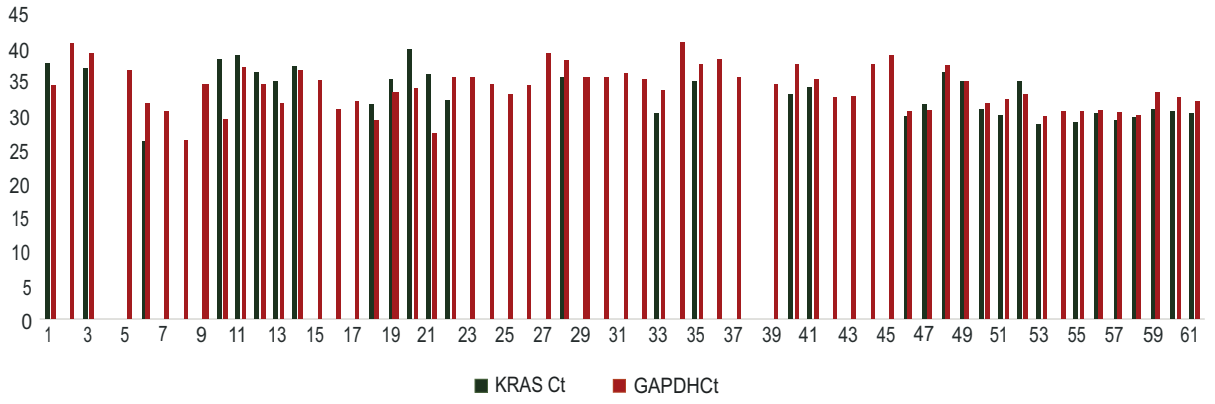
Ethical issues

The research was conducted after getting approval from the Institutional Review Board (IRB) of NICRH (Memo no: NICRH/IRB/2024/403, Date: 23/12/2024). Safeguards were followed to ensure the confidentiality and security of all information. As the samples were archived FFPE ovarian tissue and data were collected from hospital records, there was no physical, psychological, social, or legal risk for the patients. Each selected patient was coded with a unique code number to maintain confidentiality and anonymity.

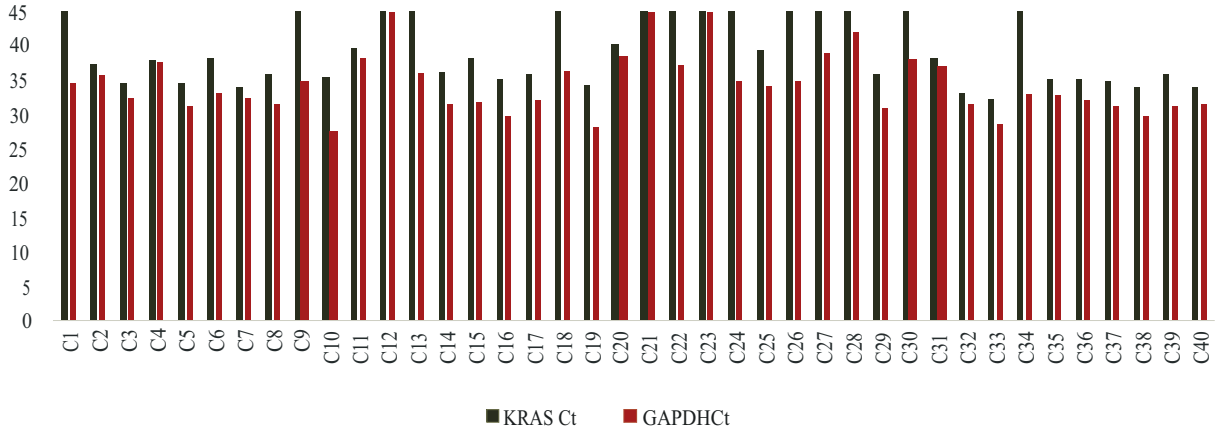
Results

RT-PCR amplification and Ct values of KRAS and GAPDH

Out of 61 ovarian cancer tissues and 40 non-cancerous ovarian tissues, both the KRAS and GAPDH genes were amplified by RT-PCR in 33 (54.09%) ovarian cancer tissues and 27 (67.50%) non-cancerous ovarian tissue samples. They were included for expression calculation and association analysis. The Ct values of KRAS and GAPDH of individual ovarian cancer and non-cancerous ovarian tissue samples are shown in Figure 1A and Figure 1B, respectively.



(A)



(B)

Figure 1: *Ct value of KRAS and GAPDH in ovarian cancer tissue (A) and non-cancerous ovarian tissue (B) samples. Bars 1 through 61 indicate the sample numbers of ovarian cancer tissues, and C1 through C40 indicate the sample numbers of non-cancerous ovarian tissues.*

Age distribution of patients

Ovarian cancer patients were aged between 21 and 86 years, with a mean and standard deviation of 48.88±13.12, and patients with non-cancerous ovarian tissue were aged between 26 and 68 years, with a mean and standard deviation of 49.44±9.38. Age was normally distributed in both groups. An independent sample t-test was used to compare the means, and there was no significant difference in age between the groups ($p = 0.85$).

Comparison of KRAS mRNA expression in cancerous and non-cancerous ovarian tissue

KRAS mRNA expression level varied in both cancerous and non-cancerous ovarian tissue samples. We categorised mRNA expression level <1 as low expression and >1 as high expression according to Zhang et al.[30]. According to these criteria, low expression of KRAS mRNA was observed in 4 ovarian cancer and 13 non-cancerous ovarian tissue samples, and high expression was observed in 29 ovarian cancer and 12 non-cancerous ovarian tissue samples. KRAS mRNA expression in neither cancerous nor non-cancerous ovarian tissue samples had a normal distribution; therefore, the medians and interquartile ranges (IQRs) were used for analysis. The median of KRAS mRNA expression in ovarian cancer tissue was statistically higher ($p < 0.001$) than that of non-cancerous ovarian tissue (Figure 2).

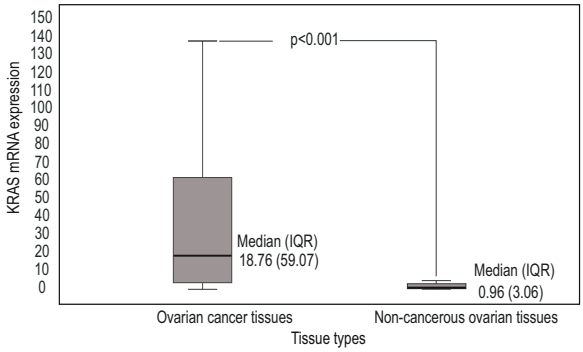


Figure 2: *Distribution of KRAS mRNA expression in ovarian cancer tissue and non-cancerous ovarian tissue. The Mann-Whitney U test was used to compare the medians of KRAS mRNA expression between two groups, and a p-value <0.05 was considered statistically significant.*

When the KRAS mRNA expression of ovarian cancer tissues was compared with the median of KRAS mRNA expression of non-cancerous ovarian tissues, KRAS mRNA expression was found to be higher in all of the ovarian cancer tissue samples than the median of KRAS mRNA in non-cancerous tissue samples, except for three. KRAS mRNA expression was 10-fold higher in 21 ovarian cancer samples than the median of non-cancerous tissue samples (Figure 3).

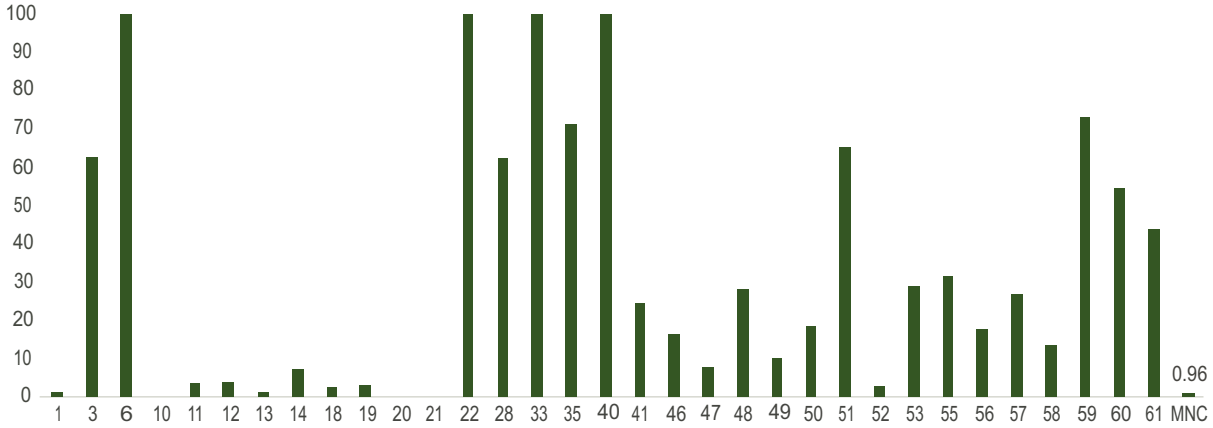


Figure 3: *KRAS mRNA expression in ovarian cancer tissues compared to the median of KRAS mRNA expression in non-cancerous ovarian tissues. Bars 1 through 61 represent the sample numbers in which the KRAS mRNA expression level was quantified, and bar MNC represents the median value (0.96) of the KRAS mRNA expression level in non-cancerous ovarian tissues. KRAS mRNA expression levels of samples 6, 22, 33, and 40 were 580.04, 121.09, 138.14, and 237.21, respectively, which exceeded the limit of this graph.*

Table I: *Association of KRAS mRNA expression with cancer-related characteristics of ovarian cancer patients (n = 33)*

Cancer-related characteristics	Number (percentage)	KRAS mRNA expression Median (IQR)	p-value
Histological types			
Serous carcinoma	26 (78.8)	22.93 (57.14)	0.301
Mucinous carcinoma	3 (9.1)	3.75	
Endometrioid carcinoma	1 (3.0)	580.04	
Teratoma	2 (6.1)	3.39	
Dysgerminoma	1 (3.0)	24.42	
Histological grades			
High grade	27 (81.8)	28.24 (57.56)	**0.049**
Low grade	3 (9.1)	2.41	
Not graded	3 (9.1)	3.63	
Cancer stages			
Stage I	13 (39.4)	10.33 (23.71)	0.223
Stage III	11 (33.3)	62.24 (119.77)	
Stage IV	9 (27.3)	28.24 (55.43)	

A Kruskal-Wallis test was used to compare the medians of KRAS mRNA expression of the groups, and a *p*-value <0.05 was considered statistically significant.

Association of KRAS mRNA expression with cancer-related characteristics

Most of the ovarian cancers were of epithelial cell cancers (90.9%). The majority were serous carcinoma (78.8%), followed by mucinous carcinoma (9.1%), and endometrioid carcinoma (3.0%). The rest, 9.1% were germ cell tumours. Most of the epithelial ovarian cancers were histologically high-grade cancers (81.8%), and only a few were of low-grade (9.1%). Germ cell tumours (9.1%) were not graded. The majority of ovarian cancer patients were in FIGO Stage I (39.4%), followed by Stage III (33.3%) and Stage IV (27.3%). There was no Stage II patient. The distribution of KRAS mRNA expression with all these cancer-related characteristics was skewed, and nonparametric tests were used to analyse the association with them. KRAS mRNA expression was significantly higher in high-grade ovarian cancers (p = 0.049). Association of cancer-related characteristics and KRAS mRNA expression are shown in Table I.

Discussion

This study found that KRAS mRNA expression was significantly higher in ovarian cancer tissue compared to non-cancerous ovarian tissue. It also found an association of high KRAS mRNA expression with high-grade ovarian cancers. These results demonstrate new insights into the molecular features of ovarian cancer in the Bangladeshi population and are consistent with earlier reports from other regions, highlighting the relevance of KRAS expression in ovarian carcinogenesis.

Previous studies have reported frequent mutations and altered expression of KRAS in ovarian cancer. Jumaa et al. observed increased KRAS mRNA expression in Iraqi women with ovarian carcinoma, similar to our findings[20]. Likewise, a study in Poland found increased KRAS protein expression in ovarian cancer tissues.[21] These findings suggest that KRAS gene activation, either by mutation or transcriptional upregulation, plays a role in ovarian tumour development. Conversely, A study in the USA on a diverse population found variable KRAS and decreased HRAS expression depending on tumour subtype and endometriosis association in ovarian cancer, suggesting that the role of RAS family genes may differ according to tumour subtypes.[22]

Among the cancer-related characteristics, KRAS mRNA expression was found to be significantly

higher in high-grade ovarian cancer. Most of our patients had high-grade epithelial ovarian cancer. That may be the reason behind this finding.

In this study, with relative-quantification multiplex real-time RT-PCR, we found KRAS amplification in 55% of ovarian cancer tissue and 67.5% of noncancerous ovarian tissue. Extraction of RNA from FFPE tissue and amplification of recovered mRNA by RT-PCR is challenging because formalin fixation and paraffin embedding cause degradation of RNA by fragmentation and chemical modifications[31-34]. In a study on BRCA1 mRNA expression in FFPE breast tissue conducted by Al-Mulla et al., using real-time RT-PCR, they found amplification of BRCA1 mRNA in 21% of breast cancer tissues, while Kim et al. found BRCA1 and BRCA2 mRNA amplification by real-time RT-PCR in 65.45% of FFPE gastric tissue samples[35,36]. Thus, although FFPE specimens provide valuable archived material, the extraction and amplification are still challenging for gene expression studies.

To our knowledge, this is the first study of KRAS mRNA expression in ovarian cancer patients of Bangladesh. It created evidence of KRAS mRNA expression in a small population of Bangladeshi ovarian cancer patients. Its findings may add value in the understanding of the role of KRAS in the pathogenesis of ovarian cancer, advance knowledge of KRAS biology in ovarian cancer worldwide, and provide a foundation for future studies in South Asian populations.

However, this study has several limitations. These include inability to triplicate samples for RT-PCR that may have resulted in no amplification in many samples. Its sample size was small and we could not follow-up the patients. Therefore, we could not analyse findings in relation to the clinical and survival characteristics of the patients and cannot comment on whether this finding has any prognostic significance. Future studies with a larger sample size, integrated with genomic mutation and longitudinal follow-up, are required to clarify whether KRAS expression can function as a diagnostic biomarker, a prognostic indicator, or possibly a therapeutic target in ovarian cancer.

Overall, our findings support growing evidence that KRAS dysregulation plays a role in the pathogenesis of ovarian cancer. In particular, the strong association with high-grade tumours underscores its potential role in aggressive disease biology.

Conclusion

KRAS mRNA expression is significantly higher in FFPE tissue of Bangladeshi ovarian cancer patients. It formed evidence of KRAS expression in the Bangladeshi population. Along with similar studies in other populations, it will add value to the understanding of the role of KRAS in the pathogenesis of ovarian cancer.

Recommendation

Further studies with a larger sample size and longitudinal follow-up are required for a better understanding of its clinical significance in predicting prognosis and its utility as a marker for selecting or monitoring the treatment of ovarian cancer.

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Author contributions

Conception or design of the work, the acquisition, analysis, and interpretation of data for the work: SHZR, FA, LN, KH, MA and SMI. Laboratory work: SHZR and KH. Data analysis: SHZR and LN. Drafting the work or critically reviewing it for important intellectual content: SHZR, FA, LN, KH, MA and SMI. Final approval of the version to be published: SHZR, FA, LN, KH, MA and SMI. Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: SHZR, FA, KH and MA.

Conflict of interest:

The authors declare no conflict of interest.

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Case Report

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Solitary Iliac Bone Metastasis as a Presentation of Papillary Thyroid Carcinoma: A Case Report

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Abstract:

Background: Papillary thyroid carcinoma (PTC) typically metastasizes via lymphatics to cervical nodes. Distant hematogenous spread to bone is rare, occurring in only 1.4%–7% of cases, and is even more unusual as the initial clinical presentation. Case Presentation: A 52-year-old male presented with a four-month history of localized left hip pain. Magnetic resonance imaging (MRI) revealed a 7.4 cm expansile lytic lesion in the left iliac bone. Subsequent CT-guided core biopsy suggested metastatic adenocarcinoma. A systematic search for the primary malignancy identified a 4 cm firm thyroid nodule. Fine-needle aspiration cytology (FNAC) and subsequent histopathology confirmed a follicular variant of papillary thyroid carcinoma (FVPTC). Management involved palliative radiotherapy to the ilium, total thyroidectomy with central neck clearance, and adjuvant radioactive iodine (RAI) therapy. Conclusion: This case highlights the necessity of considering thyroid malignancy in the differential diagnosis of solitary lytic bone lesions. Despite the aggressive presentation, the differentiated nature of FVPTC allows for targeted multimodal therapy, including RAI, which can significantly improve morbidity.

Key words: *Papillary thyroid carcinoma (PTC), Follicular variant of papillary thyroid carcinoma (FVPTC).*

Introduction

Papillary thyroid carcinoma (PTC) is the most prevalent form of differentiated thyroid malignancy, generally characterized by an indolent course and a high affinity for regional lymph node metastasis. While the prognosis for localized PTC is excellent, distant metastasis significantly alters the clinical trajectory. Bone metastases (BM) are infrequent in PTC compared to follicular thyroid carcinoma (FTC), with reported incidences ranging from 1% to 7%.[1,2]

The axial skeleton and proximal long bones are the most common sites for osseous involvement, usually occurring in the setting of known advanced disease. However, it is exceedingly rare for a patient to present with symptomatic bone pain as the first indication of an underlying thyroid malignancy [3]. We report a rare case of a 52-year-old male whose journey toward a diagnosis of follicular variant PTC (FVPTC) began with chronic hip pain and an expansile lytic lesion of the ilium.

Case Presentation:

Patient Information and Clinical Presentation

A 52-year-old male presented with a four-month history of continuous, localized left hip pain. The pain

was aggravated by movement and partially relieved by analgesics. He had no significant comorbidities. Physical examination revealed a tender swelling around the left hip joint with mild overlying erythema. Notably, the patient also had a firm, bosselated, non-tender 4 x 4 cm swelling in the right lobe of the thyroid that moved with deglutition. There were no clinical signs of lateral or retrosternal extension and thyroid dysfunction.

Diagnostic Assessment

Initial MRI of the pelvis identified a large, well-defined expansile lytic lesion (7.4 x 6.6 cm) in the iliac part of the left hip bone, showing hyperintensity on T2WI/STIR and vivid contrast enhancement. A CT-guided core biopsy of the lesion confirmed metastatic carcinoma with cells arranged in clusters and glandular patterns.

The search for the primary source was intensive. While prostate-specific antigen (PSA), CEA, CA-19-9, and gastrointestinal endoscopies were all normal, attention turned to the neck. Neck USG showed a 43 x 40 mm hypoechoic nodule in the right thyroid lobe and bilateral cervical lymphadenopathy. FNAC of the thyroid nodule (Bethesda VI) and a right-sided neck node both confirmed papillary carcinoma with classic features: nuclear grooves, intranuclear inclusions, and gummy colloid.

Therapeutic Intervention and Surgical Philosophy

The management strategy focused on a multimodal approach:

1. Radiotherapy: The patient received a single fraction of 800cGy radiotherapy to the left ilium to halt bone erosion and provide pain relief 1 month before surgery.
2. Surgical Management: A total thyroidectomy with central clearance and bilateral neck exploration was performed one month after radiotherapy.
3. Histopathology: The resected specimen confirmed a Follicular Variant of Papillary Thyroid Carcinoma (FVPTC) involving the isthmus (4 cm necrotic growth), staged as pT2Nx. 4. Immunohistochemistry (IHC): IHC of the iliac bone biopsy (1.3.26) was definitive, showing positivity for TTF-1, Thyroglobulin (focal), and CK7, confirming the thyroid origin.

Follow-up and Outcomes

Following surgery, the patient underwent Radioactive Iodine Ablation (RAI) 2 month after surgery. The philosophy behind avoiding immediate orthopaedic resection of the iliac mass was the highly differentiated nature of the tumor; utilizing RAI allows for targeted destruction of metastatic tissue, thereby reducing surgical morbidity and preserving mobility.

Discussion

The occurrence of bone metastases in PTC varies widely, typically occurring in 1.4%–7% of cases.[1,2] While FTC is traditionally associated with hematogenous spread (7%–20%), PTC remains the largest single histologic group in some bone metastasis cohorts (28%–37.8%) simply due to its overwhelming prevalence among all thyroid cancers.[2,3,4]

In our patient, the metastasis was located in the ilium. While the vertebrae are the most common site for osseous thyroid spread, the pelvis is a recognized secondary site.[5,6] Literature highlights that solitary bone metastasis as the sentinel sign of PTC is an 'extremely rare occurrence'.[7] Similar cases have been reported where hip pain or pathological fractures led to the discovery of occult PTC, often involving the femoral neck or iliac crest.[8,9,10,11]

The diagnosis in this case was particularly challenging as the bone biopsy initially suggested a generic metastatic adenocarcinoma. The breakthrough moment arrived through the integration of the thyroid FNAC and the IHC profile of the core biopsy specimen. The follicular variant of PTC often mimics follicular neoplasms both grossly and microscopically, which explains why the iliac lesion demonstrated a follicular architecture.[12]

Our surgical philosophy prioritized systemic control. Total thyroidectomy was essential to remove the primary foci and prepare the patient for RAI. Central neck clearance was performed to address the most common site of regional spread in PTC. The decision to use RAI as the primary modality for the hip lesion aimed to exploit the tumor's iodine avidity to induce regression without the need for high-morbidity pelvic exenteration.[9]

Conclusion

This case underscores that while PTC is generally associated with lymphatic spread to the neck, it can

present aggressively with hematogenous distant metastasis. Clinicians should maintain a high index of suspicion for thyroid carcinoma when encountering lytic bone lesions. The combination of total thyroidectomy and RAI remains the cornerstone of management, offering the potential for disease stabilization and improved quality of life.

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Case Report

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Co-Incidental Peritoneal Tuberculosis During Laparotomy for Carcinoma Endometrium: A Case Report and Review of Literature

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Abstract

Endometrial carcinoma is a prevalent malignancy in women, while peritoneal tuberculosis is a common form of extrapulmonary tuberculosis (EPTB). Reports of the coexistence of endometrial carcinoma and tuberculosis are scarce in the literature. The presence of peritoneal tuberculosis complicates the diagnosis, staging, and management of endometrial cancer due to overlapping clinical and biochemical features and the presence of multiple incidental tubercular deposits in the abdomen and pelvis, which may simulate extensive metastasis.

We describe a recent case of a 60-year-old woman with postmenopausal bleeding who underwent elective laparotomy with comprehensive surgical staging for pre-operatively confirmed endometrial carcinoma. Histopathologic and immunohistochemical examination of samples from a type 2 modified radical hysterectomy (RH) with bilateral salpingo-oophorectomy (BSO), systematic bilateral pelvic and para-aortic lymphadenectomy, and total omentectomy revealed endometrial endometrioid carcinoma, grade 1, FIGO stage IA2. Additionally, omental and peritoneal tissues showed granulomatous inflammation consistent with tuberculosis. The patient received anti-tubercular therapy alongside protocol-supported malignancy management.

Several similar cases in the literature were reviewed to explore the symptoms, laboratory results, and surgical findings of co-existing female genital malignancy and EPTB. These cases highlight the importance of surgical staging for the diagnostic accuracy of endometrial cancer and emphasize the need for thorough peri-operative optimization by a multidisciplinary approach to enhance treatment outcomes.

Keywords: *Tuberculosis, Peritoneal tuberculosis, Endometrial cancer*

Introduction

Tuberculosis (TB) remains a major global public health challenge and is the world's leading cause of death from a single infectious agent. In 2024, an estimated 10.7 million people developed TB worldwide, while approximately 1.23 million people died from TB.[1,2] In 2024, an estimated 3.6% of the world's tuberculosis (TB) cases occurred in Bangladesh, making it one of the countries with the highest TB burden globally. The estimated TB incidence rate in Bangladesh was approximately 201 cases per 100,000 population in 2024.[3] Pulmonary tuberculosis remains the most prevalent form of the disease; however, the incidence of extrapulmonary tuberculosis (EPTB) has risen in

recent years, largely due to the increasing number of cases co-infected with human immunodeficiency virus (HIV).[4] Peritoneal tuberculosis is a common class of extra-pulmonary tuberculosis (EPTB). The ingestion of Mycobacterium bovis via unpasteurized milk and dairy products, as well as a history of or current pulmonary tuberculosis, contributes to the development of abdominal as well as peritoneal tuberculosis by reactivating dormant infections and spreading via lympho-hematologic system, particularly in immunocompromised individuals. This includes those with concurrent HIV infection, comorbidities such as diabetes and chronic renal failure, or those receiving immunosuppressive therapy.[5] Diagnosing abdominal tuberculosis (TB) presents significant challenges due to its clinical manifestations closely resembling those of other chronic diseases, such as malignancies, Crohn's disease and irritable bowel syndrome (IBS). As a subacute condition, TB peritonitis progresses slowly, with symptoms including fever, night sweats, weight loss, abdominal pain, and ascites. Additionally, the presence of an abdominal mass and markedly elevated CA-125 levels can obscure the underlying diagnosis.[6] The symptom overlaps with other disease conditions and the limited accuracy of diagnostic tests necessitate increased awareness of abdominal tuberculosis to facilitate early diagnosis and timely treatment.

Endometrial cancer complicated by abdominal and/or peritoneal tuberculosis may infrequently be observed in geographic regions with elevated tuberculosis prevalence like Bangladesh. In this writing, we presented a rare case of endometrial cancer with co-existing peritoneal tuberculosis.

Case Report

Our patient is a 60-year-old para-2 post-menopausal, dyslipidaemic and hypertensive female with a history of post-menopausal bleeding for 6 months. Magnetic Resonant Imaging (MRI) of pelvis showed regional thickening of endometrium at anterior wall with abnormal signal intensities & enhancement, may be endometrial hyperplasia and apparently without infiltration of surrounding pelvic organs with mild hepatomegaly and left renal cyst. CA-125 was elevated to 90.8 U/ml. Fractional curettage was performed. Histopathological report (HPR) showed endometrial endometrioid carcinoma grade-1 with extension to endocervix, raising suspicion of endocervical involvement. Preoperative staging was therefore considered as apparent stage-II according to FIGO[1] staging 2023.

The patient subsequently underwent therapeutic laparotomy with comprehensive surgical staging. Following standard aseptic preparation and draping, the abdomen was opened through a Maylard incision. Upon entry into the peritoneal cavity, a small amount of straw-coloured ascitic fluid was noted. Systematic exploration of the abdominal and pelvic cavities revealed multiple small peritoneal deposits, approximately 1–2 cm in size, diffusely distributed over the pelvic and abdominal peritoneum, the undersurface of the diaphragm, mesentery, and omentum. Bilateral external iliac and para-aortic lymph nodes were enlarged. Approximately 100 mL of peritoneal washings were collected and sent for cytological examination. Following exploration, a Type II modified radical hysterectomy with bilateral salpingo-oophorectomy, systematic complete bilateral pelvic and para-aortic lymphadenectomy, and total omentectomy was performed using successive clamping, division, and ligation techniques. The pelvic peritoneal deposits were also excised. The operative field was thoroughly irrigated with warm normal saline, and meticulous haemostasis was achieved. A drain was placed in situ, and the abdomen was closed in layers, with skin closure performed using staples. All resected specimens were submitted for histopathological examination.

HPR showed- Endometrial endometrioid carcinoma grade 1, Tumor size (1.5x1) cm, Myometrial invasion less than half. LVSI not involved, cervical stromal involvement and other tissue involvement- not identified, confirming that the endocervical extension noted on preoperative curettage reflected glandular sampling rather than true stromal invasion. Right and left pelvic lymph node and paraaortic lymph nodes not involved. Peritoneal fluid– no malignancy. Omentum and peritoneal tissue showed epithelioid granulomas with central caseation; Ziehl–Neelsen staining was negative. Immunohistochemistry shows- ER & PR-positive, P53- patchy and weak expression. Diagnosis was made as endometrial endometrioid Carcinoma, grade-1, FIGO (2023) stage- 1A2 with clinically diagnosed peritoneal tuberculosis.

According to a Multi-disciplinary Tumor Board (MDTB), anti-TB drug regimen was commenced; and the patient was discharged with advice to follow-up visits routinely for close observation. On subsequent 2 three-monthly follow-up visits, patient's history, physical and pelvic examinations were normal; and CA-125 levels were 28 U/ml & 20 U/ml respectively.

Discussion

Abdominal and peritoneal tuberculosis most commonly present with abdominal pain (95%), weight loss (88%), fever (84.6%), and abdominal mass (46.1%). Other symptoms may include constipation, vomiting/nausea, abdominal pain, and possible signs of ascites and peritonitis.[7] These clinical features can simulate advanced gynecological cancers, complicating the diagnosis of either condition.

The potential role of tuberculosis, a chronic inflammatory condition, in facilitating carcinogenesis remains undetermined. There is controversy over whether the coexistence of genital malignancy and tuberculosis is incidental, if cancerous cachexia provides a favorable environment for dormant tuberculosis bacilli to survive, or if carcinoma develops on a background of chronic progressive tuberculosis. Typically, patients present with cachexia as both malignancy and tuberculosis cause significant weight loss.

Several authors have documented cases where abdomino-pelvic tuberculosis mimicked advanced female genital carcinoma. Among these, the coexistence of tuberculosis and cervical cancer has been rarely reported. Yamabe et al. documented such a case diagnosed via histopathology in 1972 (8). Similarly, Hsu et al. reported two cases from China in 1985, both presenting with postmenopausal bleeding.[9] Rajaram et al. described a case of cervical cancer with coexisting endometrial tuberculosis in 2004.[10] Cervical cancer has been included in the list of AIDS-defining illnesses in HIV-infected patients, and tuberculosis has resurged with the HIV pandemic. The immunosuppression caused by HIV is a risk factor for developing both cervical cancer and tuberculosis, suggesting an increased incidence of concurrent cases in the HIV era.[11]

To date, numerous authors have reported cases of ovarian cancer concurrent with tuberculosis. (11–20). CA-125, which usually increases in ovarian carcinoma, has been reported to also rise in pelvic and peritoneal tuberculosis, returning to normal after anti-tuberculous therapy, thus serving as a follow-up marker.[21–23] Additionally, CA-125 levels can rise in endometrial adenocarcinoma in line with disease stage[24] and in benign genital lesions such as myoma.[25] In our case, high initial CA-125 levels normalized after three months of anti-tubercular drug treatment.

Reports of endometrial adenocarcinoma coinciding with tuberculosis of the abdominal or genital tracts are rare in literature. In 1995, Castelo-Branco et al. reported a primary endometrial adenocarcinoma associated with genital tuberculosis.[26] Saygili et al. (2002) and Onal et al. (2017) described similar cases, with the latter involving tubercular lymphadenitis (27,28). Ashraf et al. (2021) reported a series of three cases.[29] These cases highlight the importance of accurate staging for the proper diagnosis, treatment, and prognostication of endometrial cancer.

The FIGO 2023 classification staged endometrial cancer based on surgico-pathological findings. According to local institutional practice following NCCN (National Comprehensive Cancer Network) guidelines, a Total Hysterectomy (TH) or Radical Hysterectomy (RH) and Bilateral Salpingo-Ophorectomy (BSO) and surgical staging is performed depending on pre-operative histopathological guidance. In our case, radical hysterectomy and bilateral salpingo-oophorectomy with systematic bilateral pelvic and para-aortic lymphadenectomy and total omentectomy was performed in view of the intraoperative findings of multiple peritoneal deposits and enlarged pelvic and para-aortic lymph nodes raising suspicion of advanced disease, together with the preoperative concern for possible stage II disease based on the suspected endocervical extension noted on curettage; and later, surgical staging yielded FIGO stage IA2 with endometrial endometrioid carcinoma grade-1 on histopathological report. Observation with regular follow-up was chosen.[30] Although not bacteriologically confirmed by positive Ziehl–Neelsen staining, underlying peritoneal tuberculosis was clinically diagnosed through histopathological evaluation of laparotomy specimens and treated accordingly by commencing anti-mycobacterial regimen.[31]

Conclusion

Co-existence of peritoneal tuberculosis with endometrial carcinoma is a rare entity. Data regarding outcome of such patients, the influence of one condition over the other as well as survival are unavailable due to the rarity of the association. However, its possibility should be strongly considered in TB-endemic regions and, if found, cases should be reported and follow-up routinely for future research to find out any epidemiological, etiological and clinico-pathological relations. A missed diagnosis of co-existent TB may result in vastly different post-surgical therapeutic regimens, leading to poor quality of life for patients. Moving forward, there is scope for further research to better distinguish between peritoneal or other extrapulmonary TB and metastatic gynaecological cancer and further elucidate the immunosuppressive relationship between those conditions.

Declaration Of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Authors' Contributions

Performed data acquisition and writing of report:
Dr. Rahima Khatun, Dr. Md. Sayem Shahriar
Made contributions to conception of the study, editing and review of the report:
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Role of Intraoperative Frozen Section in Surgical Pathology – A Comprehensive Review

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Abstract

Intra-operative frozen section plays an important role in the management of surgical patients and yet it must be used prudently to avoid the indiscriminate usage of this important technique. As it is subjected to many limitations in comparison to the paraffin embedded tissue sections, this review aims to highlight the important concepts and principle of intra-operative frozen section consultation as well as discussing the limitations of this technique. This will then allow the end-users of this technique to be more informed and more selective in their decisions when requesting for a frozen section report.

Keywords: *Frozen section, concepts, applications and limitations*

Introduction & Historical Context

The history of the intraoperative frozen section dates back to 1891, when William H. Welch performed the first documented consultation at Johns Hopkins Hospital.[1] The technique was further refined by Thomas S. Cullen and Louis B. Wilson in the early 1900s, but it was the commercial and clinical development of the refrigerated cryostat microtome in 1959 that completely transformed the practice.1,2 By allowing thin, high-quality tissue sections to be cut at sub-zero temperatures, the cryostat elevated frozen section analysis from an experimental procedure to an indispensable, daily intraoperative tool used worldwide.[2]

Now a days, frozen section analysis serves as a rapid, definitive pathway to alter or guide a surgical plan while a patient is still under anesthesia.

Clinical Indications

Frozen sections are not intended to replace formal, formalin-fixed paraffin-embedded (FFPE) permanent processing. Instead, they are strictly reserved for situations where immediate pathological feedback will directly dictate the next steps of a surgical intervention.[2]

The primary clinical indications include:
Determination of Margin Status:
Assessing whether surgical resection margins are clear of tumor cells (e.g., in breast-conserving surgeries, head and neck carcinomas, or skin cancer excisions) to ensure complete local control.[2,3]

Establishment of a Primary Diagnosis:
Differentiating between benign and malignant neoplasms when preoperative imaging, fine-needle

aspiration cytology (FNAC), or core needle biopsies are inconclusive or unavailable.[1,4,5]

Identification of Unknown Extra-organ Extension or Metastasis:

Evaluating unexpected intraoperative findings, such as suspicious peritoneal or hepatic nodules, or confirming metastatic involvement via sentinel lymph node biopsies.[2,3]

Assessment of Tissue Adequacy:

Ensuring that an open biopsy has successfully captured viable, representative diagnostic material prior to closing the patient, especially critical in deep-seated lesions or central nervous system (CNS) tumors.[6]

Technical Methodology & Workflow

Achieving a high-quality frozen section requires a highly coordinated, rapid sequence of steps executed by a pathologist and an advanced histotechnologist. Unlike the routine process that takes days, the frozen section workflow is designed to yield a stained slide within 15 to 20 minutes.

The Standard Intraoperative Sequence

1. Specimen Reception & Grossing: 1–3 minutes.

The biopsy tissue is dispatched from the operating room completely fresh, without any fixatives or saline fluids.[1] The pathologist performs immediate gross examination, takes measurements, and trims a highly representative sample block (typically less than 5 mm in thickness).[7]

2. Embedding & Rapid Freezing: 2–4 minutes.

The tissue is placed on a metal chuck and encapsulated using a water-soluble glyco-alcohol embedding medium (e.g., OCT compound). The specimen is rapidly frozen inside the cryostat chamber, typically held at -20°C to -30°C, or accelerated using liquid nitrogen or carbon dioxide freezing sprays.[1,2]

3. Microtomy (Sectioning): 2–3 minutes.

Using the microtome housed inside the refrigerated cryostat, the frozen block is faced and cut into ultra-thin sections, usually calibrated between 4 to 5 micrometers.[1] The fragile sections are gently transferred and mounted onto warm glass slides.

4. Rapid Staining & Cover-slipping: 2–3 minutes.

The mounted section is immediately fixed (usually in 95% alcohol or formalin) to prevent air-drying artifacts and then passed through an accelerated Hematoxylin and Eosin (H&E) staining sequence.[1] It is then dehydrated, cleared, and cover-slipped for microscopic analysis.

Diagnostic Accuracy & Concordance Rates

Extensive global literature demonstrates that the diagnostic accuracy of frozen section analysis is remarkably high, with concordance rates with the final FFPE permanent diagnosis consistently exceeding 95%.[2,3,8]



Cryostat Machine

Sensitivity 89.5% – 96.7% Impacted by minimal focal involvement or micro-metastases.[2,8]

Specificity 98.5% – 98.9% Driven down by rare interpretive or morphological look-alikes.[2,8]

Deferral Rate ~2.1% Cases deferred to permanent sections due to severe technical or diagnostic ambiguity.[8]

Diagnostic reliability varies according to the architectural patterns of different tissue types:
Gastrointestinal & Hepatic: Excellent concordance (>97%) for verifying adenocarcinoma metastasis or margin clearance.[3] However, distinguishing benign bile duct hamartomas or adenomas from well-differentiated metastatic adenocarcinoma remains a prominent pitfall due to freezing distortions.[3]

Central Nervous System (CNS): Widely utilized to confirm tissue adequacy and classify pediatric and adult brain tumors.[6] Minor discordances are typically attributed to dense calcifications, extensive necrosis, or distinguishing low-grade gliomas from reactive astrocytosis.[2,6]

Endocrine (Thyroid & Pancreas): The thyroid gland is a known classic challenge. While frozen section is excellent at identifying overt papillary thyroid carcinoma, definitively ruling out follicular thyroid carcinoma is structurally impossible on FS because finding capsular or vascular invasion requires comprehensive, exhaustive sampling of the entire tumor capsule.[2,5]

Technical Artifacts & Diagnostic Pitfalls

Due to the absence of the slow, protective overnight tissue processing and infiltration steps utilized in permanent sections, frozen sections are prone to distinct microscopic distortions.

Ice Crystal Artifacts

If tissue is frozen too slowly, water inside and around the cells coalesces into large ice crystals. Upon thawing or sectioning, these crystals leave behind optical vacuoles, creating a "Swiss-cheese" effect that can distort nuclear architecture and mask subtle cellular atypia.

Chatter and Compression

Sections cut inside a cryostat that is too cold, or tissue blocks containing dense collagen, calcifications, or adipose tissue, often produce parallel fractures or severe compression lines across the tissue section. Fatty structures (like breast margins) are notoriously difficult to freeze and slice smoothly at standard cryostat temperatures.[2]

The Three Operational Pillars of Discrepancy

When a discrepancy arises between an intraoperative frozen section and the final permanent pathology report, it is universally classified into one of three distinct error types:

1. Sampling Error: The diagnostic lesion or micro-metastasis was entirely missed during intraoperative sectioning but captured later during thorough, deeper sectioning of the remaining permanent block.[8,9]
2. Interpretation Error: The critical tissue features were present on the frozen section slide, but the pathologist mischaracterized the lesion (e.g., misinterpreting a highly reactive xanthogranulomatous lesion or an inflammatory process as a malignant neoplasm).[8,9]
3. Technical Error: Suboptimal staining, excessive thickness, or severe freezing distortions rendered the nuclear and cytoplasmic details completely uninterpretable.[8]

The Intersect of Frozen Sections and Biobanking

Beyond its primary role in intraoperative guidance, the collection of fresh-frozen tissue (FFT) has become foundational for advanced genomic, transcriptomic, and proteomic research.[7] Formalin-fixed paraffin-embedded tissue often suffers from cross-linked proteins and fragmented nucleic acids. In contrast, biobanked fresh-frozen human tissue preserves the structural integrity of both DNA and RNA.[7]

Recent quality management assessments demonstrate that nucleic acid integrity indices (such as the RNA Integrity Number, or RIN) remain completely stable over long-term deep storage in liquid nitrogen.[7] The frozen section workflow acts as the ultimate quality-control checkpoint for modern biobanks; cutting a brief frozen section immediately prior to cryovial banking confirms the actual presence of viable tumor cells, filtering out tissue fragments that consist entirely of necrotic debris or non-diagnostic normal stroma.[7]

Conclusion

Intraoperative frozen section analysis remains an irreplaceable pillar of surgical oncology and surgical pathology.[2] Despite technical challenges, including ice crystal distortions and inherent sampling limitations, it maintains an outstanding safety profile and a concordance rate approaching 98%.[8] Mitigating errors relies heavily on a two-pronged approach: maximizing the technical expertise of the pathology team and fostering open, bidirectional communication between the operating surgeon and the reporting pathologist.[3,9] By sharing precise clinical history, radiologic data, and immediate gross impressions, the clinical team ensures that this rapid intraoperative diagnostic modality continues to maximize patient safety and optimize oncological outcomes.

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