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Editorial

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Artificial Intelligence: Reshaping the Future of Cancer Care

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The landscape of oncology is undergoing a profound transformation, driven by rapid advances in Artificial Intelligence. AI is no longer a futuristic concept but a powerful tool actively reshaping how we detect, diagnose, treat, and monitor patients with cancer, promising a future of more precise, efficient, and personalized care[1].

One of AI's most immediate and impactful contributions is in enhancing diagnostic accuracy and early detection. Deep learning algorithms are proving invaluable in interpreting complex radiological images. For instance, AI systems have demonstrated the ability to detect breast cancer on mammograms with accuracy comparable to that of expert radiologists, while also reducing false-positive rates[2]. This capability not only streamlines the diagnostic process but also enables earlier intervention, which is critical for improving patient outcomes[3].

The impact of AI extends significantly into pathology, particularly through digital histopathology[4]. By analyzing vast amounts of whole-slide images, AI-driven tools are revolutionizing the identification of tumor subtypes, the quantification of biomarkers, and even the prediction of genetic mutations directly from routine tissue samples[5]. These capabilities lead to more objective and consistent diagnoses, fostering a deeper understanding of cancer biology. AI also contributes to improving the quality of these images, for example, through efficient autoencoders designed for denoising histopathological images and enhancing hybrid feature extraction[6].

In precision oncology, AI is indispensable for tailoring treatments to individual patient profiles. Machine learning models integrate diverse data—genomic sequencing, imaging, and treatment history—to predict which therapies will be most effective[7]. This enables optimized treatment selection, exemplified by AI algorithms that predict immunotherapy responsiveness by analyzing tumor mutational burden and radiomic signatures[8]. Such personalization reduces the use of ineffective treatments and minimizes patient suffering[9].

Furthermore, AI significantly improves radiation oncology workflows. Automated contouring tools precisely delineate tumors and critical organs at risk on patient imaging scans. AI-guided adaptive radiotherapy enables daily adjustments to treatment plans based on subtle anatomical changes, ensuring precise dose delivery and minimizing harm to healthy tissues[10].

Beyond treatment, AI enhances prognostic modeling and patient monitoring. Predictive models estimate

recurrence risk and survival outcomes, while AI-powered remote monitoring tools detect early signs of complications or disease progression[11]. These capabilities allow for proactive management and can significantly improve the quality of life for cancer patients.

However, the integration of AI in oncology is not without its challenges. Concerns around data privacy, potential algorithmic biases, and the critical need for rigorous clinical validation remain paramount. Human oversight is and will continue to be essential to ensure the ethical, equitable, and safe deployment of AI technologies[12].

In conclusion, AI is fundamentally reshaping oncology, moving us closer to a future where cancer care is not only more precise and practical but also more accessible and responsive to individual needs. As research continues to advance, AI will undoubtedly play an increasingly vital role in our global fight against cancer.

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Original Article

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Role of Preoperative MRI for the Assessment of Surgicopathological Factors in Early Cervical Cancer

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Abstract

Background: *Accurate preoperative assessment of surgicopathological factors in early-stage cervical cancer is essential for optimal surgical planning and prognosis. MRI is a valuable non-invasive tool to assess tumor size, stromal, parametrial, and nodal status. This study aimed to assess the role of preoperative MRI in detecting surgicopathological factors in early cervical cancer.* ***Methods:*** *This cross-sectional study was conducted at the Gynecological Oncology Unit, Dhaka Medical College Hospital, Dhaka, Bangladesh from June 2021 to May 2022. Fifty women with biopsy-confirmed early-stage cervical cancer (stage IA2, IB, IIA1) undergoing radical hysterectomy with bilateral pelvic lymph node dissection were enrolled.* ***Results:*** *Clinically, 100% of tumors were <4 cm, with no parametrial involvement and vaginal involvement in 14.0% of cases. MRI detected tumors <4 cm in 92%, with parametrial and lymph node involvement absent in all cases, vaginal involvement in 10%, and deep stromal invasion in 18%. Histopathology confirmed tumors <4 cm in 94%, parametrial involvement in 6%, vaginal involvement in 14%, lymph node metastasis in 14%, and deep stromal invasion in 32%. MRI demonstrated high diagnostic accuracy for tumor size, correctly identifying 46 true positives and 3 true negatives. Discrepancies between clinical, MRI, and histopathological staging were observed, with 7 patients having higher-stage disease on histopathology not detected clinically or on MRI.* ***Conclusion:*** *Preoperative MRI is a reliable, non-invasive tool for assessing tumor size and local spread in early-stage cervical cancer, aiding surgical planning and improving staging accuracy.*

Keywords: *Cervical cancer, Early-stage, MRI, Tumor size, Parametrial invasion, Histopathology.*

Introduction

Cervical cancer remains one of the most common gynecological malignancies worldwide, particularly affecting women in low- and middle-income countries. Early detection and accurate staging are critical for guiding optimal treatment and improving patient outcomes.[1,2] Radical hysterectomy with bilateral pelvic lymph node dissection is the standard treatment for early-stage cervical cancer (FIGO stage IA–IIA), and surgical planning relies heavily on precise assessment of tumor characteristics and local spread.[3] Accurate evaluation of tumor size, depth of stromal invasion,

parametrial extension, vaginal involvement, and lymph node metastasis is essential to determine the extent of surgery and predict prognosis.[4]

Traditionally, clinical examination, including bimanual pelvic assessment and examination under anesthesia, has been the cornerstone of preoperative evaluation.[5] However, clinical staging alone has limitations, often underestimating tumor size and local invasion.[6] Histopathological examination of surgical specimens remains the gold standard for definitive diagnosis and staging, but it is inherently postoperative and cannot guide preoperative surgical planning.[7] Therefore, imaging modalities that can reliably predict surgicopathological factors before surgery are of significant clinical value.[8]

Magnetic resonance imaging (MRI) has emerged as a superior modality for preoperative assessment due to its high soft-tissue contrast, multiplanar capability, and non-invasive nature.[9] MRI accurately delineates tumor margins, measures tumor dimensions, and evaluates local invasion into adjacent structures, including the parametrium, vagina, and lymph nodes.[10] Reported accuracy of MRI in determining tumor size ranges from 70% to 93%, while its accuracy for assessing stromal invasion, parametrial involvement, vaginal extension, and lymph node metastasis ranges from 78% to 97%.[101,12] These capabilities allow surgeons to tailor the extent of radical surgery, potentially sparing patients from overtreatment and minimizing morbidity.[1]

Several studies have demonstrated that preoperative MRI improves staging accuracy compared with clinical examination alone and correlates well with histopathological findings.[3,7] Moreover, MRI aids in identifying high-risk features that may influence the need for adjuvant therapy, such as deep stromal invasion or lymph node metastasis. Despite its advantages, the accuracy of MRI may vary depending on tumor size, radiologist expertise, and imaging protocols, necessitating continued evaluation of its predictive value in diverse clinical settings.[13]

This study aimed to assess the role of preoperative MRI in evaluating surgicopathological factors in patients with early-stage cervical cancer and to compare MRI findings with final histopathology. By determining the accuracy of MRI in identifying tumor size, stromal invasion, parametrial and vaginal involvement, and lymph node metastasis, this study seeks to clarify its utility in preoperative surgical planning and risk stratification, ultimately contributing to improved patient management and outcomes.

Methodology & Materials

This cross-sectional study was conducted at the Gynecological Oncology Unit, Dhaka Medical College Hospital, Dhaka, Bangladesh from June 2021 to May 2022. Women with biopsy-confirmed early-stage cervical cancer (stage IA2, IB, IIA1) attending the hospital for surgery were enrolled. Due to time constraints, the sample size was limited to 50 patients. Inclusion criteria were biopsy-confirmed early-stage cervical cancer, no medical or surgical contraindications for radical hysterectomy with bilateral pelvic lymph node dissection (BPLND), and informed consent for surgery as primary treatment. Exclusion criteria included advanced-stage cervical cancer, contraindications to MRI, other cancers, or concomitant pregnancy.

Dependent variables are MRI and surgicopathological findings that included tumor size, deep stromal invasion, parametrial extension, vaginal extension, and lymph node involvement. Early-stage cervical cancer was defined as disease limited to the cervix and upper vagina (stage IA–IIA), with detailed definitions provided for each sub-stage (IA1, IA2, IB1, IB2, IB3, IIA1, IIA2).

Preoperative MRI was performed in all patients by an expert radiologist to assess tumor size, depth of stromal invasion, parametrial invasion, vaginal involvement, and lymph node metastasis. Reported MRI accuracy for these parameters ranges from 70% to 97%. All patients underwent radical hysterectomy with BPLND, and histopathological examination of surgical specimens was performed to evaluate surgicopathological factors. MRI findings were compared with histopathology, and FIGO staging was determined postoperatively. Surgicopatho-logical factors considered included tumor size, depth of stromal invasion, vaginal extension, parametrial invasion, and lymph node metastases, which have prognostic significance.

Results

Table 1: *Comparison of Clinical Examination, Preoperative MRI, and Surgicopathological Findings (N = 50)*

Findings	Categories	Clinical Examination (%)	Preoperative MRI (%)	Surgicopathology (%)
Tumor Size	<4 cm	100	92	94
	≥4 cm	0	8	6
Parametrium	Involved	0	0	6
	Not involved	100	100	94
Vagina	Involved	14	10	14
	Not involved	86	90	86
Lymph Node	Involved	0	0	14
	Not involved	100	100	86
Deep Stromal Invasion	Present	0	18	32
	Absent	100	82	68

Table 1 compares the findings of clinical examination, preoperative MRI, and surgicopathology among 50 patients with early-stage cervical cancer. Clinical assessment identified all tumors as <4 cm with no parametrial or lymph node involvement. Preoperative MRI closely correlated with histopathology in assessing tumor size, vaginal involvement, and parametrial status, while also detecting deep stromal invasion in 18% of cases. Surgicopathology revealed higher rates of deep stromal invasion (32%) and lymph node metastasis (14%) than detected clinically or by MRI, highlighting its role as the gold standard for final staging.

Table 2: *Per operative findings of the cervical growth (N= 50)*

Local examination		Frequency(n=50)	Percentage
Mobilization of the uterine cervix	Yes	50	100.0
	No	0	0.0
Mobilization of the urinary bladder	Yes	50	100.0
	No	0	0.0
Growth	Exophytic	30	60.0
	Endophytic	4	8.0
	Ulcerative	11	22.0
	Normal looking cervix	5	10.0
Size	< 4 cm	47	94.0
	e" 4 cm	3	6.0
Vaginal extension	Present	7	14.0
	Absent	43	86.0
Corpus extension	Present	18	36.0
	Absent	32	64.0

Data were expressed as Frequency and percentage

Findings of cervical cancer growth during operation are presented in table 2. Mobilization of the uterine cervix and bladder was found in 100% of cases which indicate parametrium not involved. 94% of cervical growth were <4cm in size. On per operative examination, the vaginal extension was found present in 7 (14%) cases and corpus extension was found present in 18 (36%) cases.

Table III: *Comparison of Clinical, MRI, and Histopathological Staging (N = 50)*

Staging	Clinical taging	MRI Staging	Histopathology
Stage Ia2	5	5	5
Stage Ib1	18	17	15
Stage Ib2	20	19	13
Stage Ib3	0	4	3
Stage IIa1	7	5	7
Stage IIIc1	0	0	7

Table IV compares clinical, MRI, and histopathological staging of 50 early cervical cancer patients. Clinical staging identified most tumors as Stage Ib2 (40.0%), while MRI slightly underestimated or overestimated some stages. Histopathology revealed additional higher-stage disease, including 7 patients with Stage IIIc1 not detected clinically or on MRI. This highlights discrepancies between preoperative assessment and final pathological staging, emphasizing the importance of MRI and histopathology for accurate staging.

Table V: *Diagnostic Performance of MRI for Detecting Tumor Size <4 cm (N = 50)*

MRI Findings	Histopathology: <4 cm (Yes)	Histopathology: ≥4 cm (No)	Total
Tumor size <4cm	46 (TP)	0 (FP)	46
>4cm	1 (FN)	3 (TN)	4
Total	47	3	50

Table V shows the diagnostic performance of MRI for detecting tumors <4 cm in 50 cervical cancer patients. MRI correctly identified 46 tumors <4 cm (true positives) and 3 tumors ≥4 cm (true negatives), with 1 false negative and no false positives. These results indicate that MRI is highly accurate (98%) for preoperative tumor size assessment, demonstrating excellent sensitivity (97.87%) and specificity (100%) in detecting small cervical tumors.

Table VI: *Diagnostic Performance of MRI for Detecting Parametrium Involvement (N = 50)*

MRI Findings	Histopathology: Involved (Yes)	Histopathology: Not Involved (No)	Total
Parametrium involed	0 (TP)	0 (FP)	0
Not involved	3 (FN)	47 (TN)	50
Total	3	47	50

Table VI shows the diagnostic performance of MRI for detecting parametrial involvement in 50 early cervical cancer patients. MRI correctly identified 47 patients without parametrial involvement (true negatives) but missed all 3 cases with histopathologically confirmed parametrial invasion (false negatives). No false positives were observed, indicating that while MRI is highly specific (100%) for ruling out parametrial involvement, it may underestimate rare cases of microscopic invasion.

Table VII : *Diagnostic Performance of MRI for Detecting Lymph Node Involvement (N = 50)*

MRI Findings	Histopathology: Yes	Histopathology: No	Total
MRI Positive lymph node	0 (TP)	0 (FP)	0
MRI Negative lymph node	7 (FN)	43 (TN)	50
Total	7	43	50

Table VII shows the diagnostic accuracy of MRI for identifying lymph node involvement in cervical cancer patients. Histopathology served as the gold standard. MRI failed to detect any of the 7 histopathologically positive lymph node metastases (0 true positives), resulting in 7 false negatives. All 43 lymph node–negative cases were correctly identified by MRI (43 true negatives). No false positives were recorded which indicate MRI has 86% accuracy 100% specificity for determination of lymph node involvement

Table VIII : *Diagnostic performance of MRI for detecting deep stromal invasion*

Deep Stromal Penetration		Histopathology		Total
		Yes	No	
MRI	Yes	9 (TP)	0 (FP)	9
	No	7 (FN)	34 (TN)	41
Total	16	34	50	

Table VIII Comparison of deep Stromal involvement determined by preoperative MRI and histopathology .On preoperative MRI there were 9 cases with deep stromal invasion , whereas on histopathology 16 cases were found with deep stromal invasion

Discussion

Accurate preoperative assessment of surgicopathological factors in early-stage cervical cancer is essential for optimal surgical planning and prognostication.Clinical examination revealed that most tumors were 2–4 cm (54.0%), with no parametrial involvement and vaginal involvement in 14.0% of cases, indicating predominantly early-stage disease. Preoperative MRI detected tumors <4 cm in 92% of patients, with 100% of parametrium and lymph nodes negative, vaginal involvement in 10%, and deep stromal invasion in 18%. Histopathology confirmed tumors <4 cm in 94%, parametrial involvement in 6%, vaginal involvement in 14%, lymph node metastasis in 14%, and deep stromal invasion in 32%. These results demonstrate that MRI provides reliable preoperative assessment of tumor size and local extension, although some pathological risk factors, such as deep stromal invasion and lymph node metastasis, were underestimated by MRI. Similar findings have been reported by Xiao et al., and Ren et al., emphasizing that MRI has high sensitivity for tumor size but may miss microscopic stromal invasion or lymphatic involvement.[7,8]

Comparison of staging showed discrepancies between clinical, MRI, and histopathological assessments. While clinical staging identified most tumors as Stage Ib2 (40.0%), MRI slightly overestimated or underestimated certain stages, and histopathology revealed higher-stage disease in seven patients (Stage IIIc1) not detected preoperatively. In this study accuracy of MRI for detection of lymph node involvement was 86%.Kim et al reported the accuracy of MRI in detecting lymph node metastases was also 86% (10). These findings align with previous reports by Woo et al., and Sala et al., highlighting that MRI complements but does not fully replace histopathological staging.[19,20]

The diagnostic performance of MRI for tumor size <4 cm was excellent, with 46 true positives, 3 true negatives, 1 false negative, and no false positives, yielding high sensitivity (97.87%) and specificity (100%). This corroborates findings by Vetter et al., and Bourgioti et al., supporting MRI as a valuable tool in surgical planning.[16,21] However, deeper stromal invasion was present in 32% of cases on histopathology versus 18% on MRI, suggesting that while MRI is effective for gross tumor assessment, microscopic infiltration (Deep stromal invasion) may remain undetected in most cases.[18, 22] This study shows 72% accuracy in determining deep stromal invasion. Berek et al observed accuracy of MRI was 78% for determining deep stromal invasion. Which is near similar.[25]

This study underscores the importance of integrating MRI findings with clinical assessment and histopathology to guide individualized surgical approaches, minimize overtreatment, and predict prognosis. Identifying patients with parametrial or nodal involvement preoperatively remains critical, especially in the context of minimally invasive or fertility-sparing procedures.[15, 23] Overall, our results demonstrate that preoperative MRI is highly accurate for assessing tumor size and local spread in early cervical cancer, with some limitations in detecting microscopic factors e.g., stromal invasion, consistent with current literature.[17, 18, 24]

Conclusion:

This study revealed that preoperative MRI demonstrated significant similarity with definitive histo-pathological diagnosis. It can be concluded that preoperative MRI is a valuable, noninvasive, accurate diagnostic procedure for detecting tumor size, parametrial extension, vaginal extension, lymph node metastasis in early cervical cancer. Its definite value in diagnosis of tumor size, vaginal extension, lymph node metastases emphasizes its role as a sensitive and specific diagnostic procedure before surgery and aids treatment planning.

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Original Article

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Clinico-pathological Spectrum of Paediatric Brain Tumours: A Hospital-Based Study

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Abstract

Background: Brain tumors are the most common solid tumors in children and are the leading cause of morbidity and mortality worldwide. Previous studies have demonstrated considerable variation in the incidence and histological distribution of primary brain tumors (PBTs) among different global populations. Nevertheless, epidemiological data on PBTs in Bangladesh are scarce Objective: This study aimed to summarise the epidemiology of paediatric brain tumours managed at the National Institute of Neurosciences and Hospital, a tertiary referral centre in Bangladesh. An ethics-approved retrospective review was conducted including all patients younger than 18 years diagnosed with paediatric brain tumours between January 2022 and January 2024. Demographic and clinical data were collected and analysed, including age, sex, tumour characteristics, presenting symptoms, and anatomical location. Results: Among the 100 patients diagnosed with primary brain tumors (PBTs), the 11–18 years age group constituted the largest proportion of cases (43%). A male predominance was observed, with males accounting for 55% of cases and females 45%, yielding a male-to-female ratio of 1.22:1. The cerebral hemispheres were the most frequently involved anatomical site (64%), followed by the cerebellum (25%). Astrocytic tumors (50%) were the most common histological subtype, followed by medulloblastomas (20%), together accounting for three-quarters of all tumors. Ependymomas (10%) and craniopharyngiomas (10%) were the third most common tumors. Histopathological grading showed that 47% of tumors were of low-grade histology (WHO Grade I and II) and 41.5% were of high-grade histology (WHO Grade III and IV). Conclusion: This hospital-based study at a tertiary referral hospital revealed that medulloblastomas and astrocytomas were the predominant histologic subtypes in pediatric patients, require special attention and highlight the need for a national registry and population-based studies to define their actual burden.

Introduction:

Brain tumors are a significant cause of mortality and morbidity, and their diagnosis and treatment require substantial resource allocation and sophisticated diagnostic and therapeutic technologies. Marked geographical and regional differences in the incidence of CNS cancer may be attributed to variations in diagnostic procedures and reporting practices. CNS cancer exerts a disproportionate burden on healthcare systems relative to its incidence, largely due to high mortality rates and its inherently disabling impact on patients that often compromises independent

functioning.[1] Primary brain tumours (PBTs) comprise a heterogeneous group of benign and malignant neoplasms that originate from various cell types within the brain parenchyma. In children, brain tumours represent the most common solid tumours and are the second most prevalent cancer after leukemia comprising up to 20% of all childhood cancers.[2,3] Although substantial data exist on the epidemiology of pediatric brain tumours in Western populations, reports from developing countries such as India remain limited. According to the National Cancer Registry data from the Indian Council of Medical Research, the incidence of pediatric brain tumours ranges from 0% to 2.11%.[4] In the United States, the incidence of pediatric brain tumors (PBTs) and central nervous system (CNS) tumors among children and adolescents was 6.06 cases per 100,000 population during 2016–2020, of which 27.9% were malignant and 72.1% were non-malignant.[5] Over the past several decades, cure rates for certain pediatric brain tumors—particularly medulloblastoma—have improved substantially, largely reflecting advances in multiparametric neuroimaging, neurosurgical techniques, radiation therapy, multiagent chemotherapy, and supportive care.[6]. Therefore, this hospital-based study was conducted as an initial step to characterize the demographic profile and histopathological spectrum of brain cancers among pediatric patients presenting to our institution.

Methodology:

Data regarding age, gender, anatomical site, and histopathological findings (according to the World Health Organization classification prevalent at the time of diagnosis) were collected from 100 patients aged 0–18 years with brain tumors who were admitted to the National Institute of Neurosciences and Hospital. The data were retrospectively reviewed and analyzed over a two-year period from January 2022 to January 2024. Patients with metastatic brain tumors, benign cystic lesions (including arachnoid cysts, epidermoid cysts, and colloid cysts), space-occupying lesions of infectious etiology, and vascular malformations were excluded from the study.

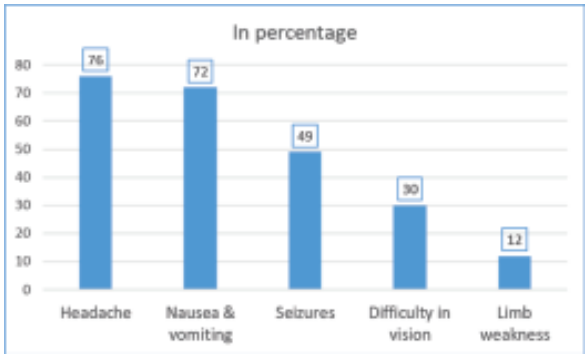
Results:

It was found that, the 11-18 years age group was the commonest age group in our study (43%). Regarding gender, 55% were male children (Table 1).

Table I: *Socio-demographic characteristics and history of the respondents (n=100)*

Characteristics	Frequency	Percentage
Age group (in years)		
0-5	22	22.0
6-10	35	35.0
11-18	43	43.0
Mean (±SD)	9.6 (4.7) yrs.	
Gender		
Male	55	55.0
Female	45	45.0

The bar chart below depicts the symptoms commonly present in the patients of childhood brain tumours. It needs to be mentioned that, in some cases, more than one symptom was found. It is evident that, headache and nausea along with vomiting were found in 76% and 72% cases respectively. In addition, 12% patients reported about weakness in limbs (Figure 1).



*Multiple responses were found.

Figure 1: Clinical presentation of the respondents (n=100)

Table II: *Anatomical site of the tumours (n=100)*

Location	Frequency	Percentage
Cerebrum	64	64.0
Cerebellum	25	25.0
Ventricles	7	7.0
Sellar region	3	3.0
Cranial nerve	1	1.0

Table II reveals the distribution of the patients on the basis of site of the brain tumours. It was evident that, majority of the tumours (64%) were found to be located in the cerebrum. The next common site was cerebellum (25%). One of the patients had a tumor located in the cranial nerves (1%).

Table III: *Histological types of the tumor (n=100)*

Tumor variety	Frequency	Percentage
Astrocytoma	50	50.0
Medulloblastoma	20	20.0
Ependymoma	10	10.0
Craniopharyngioma	10	10.0
Meningioma	4	4.0
PNET	3	3.0
Glioblastoma	2	2.0
Ganglioglioma	1	1.0

*PNET: Primitive Neuro-Ectodermal Tumor

The table above illustrates the different histological types of tumours we found in this study. It was clear that, astrocytoma, which is a diffuse astrocytic tumor, was the most common tumor variety (52%) followed by medulloblastoma (21%). Ganglioglioma (1%) occur in cranial nerves.

The bar chart below reports about the distribution of tumor grading in the patients. We can see that; majority of the tumours were either Grade IV (38%) or Grade II (31%) (Figure 2).

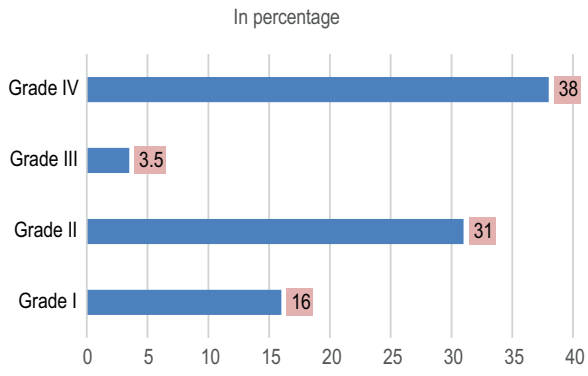


Figure 2: *Bar chart showing the grading of the tumours (n=100)*

Discussion:

Pediatric brain tumors (PBTs) represent the most common solid malignancy in children and account for approximately 25% of all pediatric cancers worldwide.[1] Despite their clinical importance, the true burden of these tumors in developing countries such as Bangladesh is likely underestimated due to incomplete cancer registries and limited nationwide reporting systems. In such circumstances, hospital-based studies remain an important source of epidemiological data, helping to describe regional disease patterns and guide the development of neuro-oncological healthcare infrastructure.

The present study analyzed 100 pediatric brain tumor cases over a two-year period. Considering the large population of Bangladesh, the number of cases observed is comparatively low. This finding may reflect underreporting, limited access to specialized healthcare services, or weaknesses in referral systems that are commonly encountered in low- and middle-income countries (LMICs). Similar concerns were raised in a study conducted at the National Institute of Cancer Research and Hospital, which reported 368 pediatric brain tumor cases over a ten-year period. The authors suggested that the relatively small number of treated patients likely reflected underrepresentation of the actual disease burden. Furthermore, the study documented a substantial increase in referrals over time, rising from only five patients in 2009 to 95 patients in 2018, suggesting growing awareness and improved access to tertiary care facilities.[7]

Demographically, pediatric brain tumors often demonstrate a male predominance. The current study observed a male-to-female ratio of 1.22:1, which is relatively balanced compared with findings from other regional studies. Research from India reported a ratio of 1.78:1, while studies from Pakistan and Saudi Arabia reported ratios of 1.4:1 and 1.5:1 respectively.[2,4] These variations may reflect both biological differences and socio-cultural factors influencing access to tertiary healthcare for female children in some regions.

Tumor location patterns also demonstrate regional variation. Classical descriptions of pediatric neuro-oncology suggest that most tumors arise in the infratentorial compartment, particularly within the cerebellum. Studies from India and Saudi Arabia have

reported cerebellar or infratentorial predominance in approximately 46–55% of cases.[2,4] However, the present study identified the cerebral hemispheres as the most frequent tumor location (64%), with only 25% of tumors occurring in the cerebellum. Similar variations in tumor distribution have been reported in studies from Bangladesh, where nearly equal proportions of supratentorial and infratentorial tumors have been observed.[8]

Histopathologically, pediatric brain tumors comprise a heterogeneous group of neoplasms with diverse biological behaviors and clinical outcomes. The classification of these tumors is periodically updated by the World Health Organization to incorporate advances in neuropathology and molecular genetics.[3] In the present study, astrocytic tumors accounted for approximately 50% of cases, followed by medulloblastomas (20%), together representing the majority of tumors. These findings are broadly consistent with reports from regional studies in India, where astrocytic tumors and embryonal tumors constitute the predominant histological types.[2] Earlier studies conducted in Bangladesh also reported medulloblastoma as one of the most common pediatric brain tumors, followed by astrocytoma and ependymoma.[9]

Globally, pediatric neuro-oncology is undergoing a paradigm shift toward molecular classification of tumors. Recent advances have identified multiple molecular subtypes of major tumor entities such as medulloblastoma and pediatric high-grade gliomas, allowing improved risk stratification and the development of targeted therapeutic strategies[5,6] However, many centers in South Asia, including Bangladesh, still rely primarily on conventional histopathological grading systems because molecular diagnostic testing remains expensive and limited in availability. Strengthening diagnostic infrastructure and expanding access to molecular testing will therefore be essential for LMICs to participate in modern risk-adapted treatment protocols and international clinical trials.

Overall, the findings of the present study contribute valuable clinicopathological data on pediatric brain tumors in Bangladesh and highlight regional variations in demographic characteristics, tumor location, and histological patterns. These observations underscore the need for improved cancer registry systems, better referral networks, and expanded diagnostic capabilities to ensure more accurate estimation of disease burden and improved management of pediatric brain tumors in the country.

Conclusion

This study outlines the clinico-pathological profile of pediatric brain tumors in Bangladesh, with astrocytomas and medulloblastomas being the most common, and a predominance of supratentorial and high-grade lesions. The findings highlight the need for earlier recognition and timely referral to specialized centers. Strengthening diagnostic facilities and improving access to pediatric neuro-oncology care could significantly enhance outcomes and survival for children with brain tumors in Bangladesh.

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Original Article

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Determinants of Surgical Treatment Delays in Breast Cancer Patients: Identifying Solutions for Improved Care

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Abstract:

Background: *Breast cancer remains the most common cancer among women in Bangladesh and a major cause of cancer-related deaths. Despite advancements in diagnosis and treatment, delays in initiating surgery remain a critical challenge, especially in low-resource settings. This study explores the factors contributing to such delays at the National Institute of Cancer Research and Hospital (NICRH), Bangladesh.* ***Aim:*** *The primary objective was to identify demographic, clinical, and healthcare-related factors responsible for surgical treatment delays in breast cancer patients and assess their impact on quality of life.* ***Methods:*** *A prospective observational study was conducted at NICRH from January to May 2025. Adult female patients newly diagnosed with breast cancer were enrolled. Data were collected using structured questionnaires & medical records. Surgical treatment delay was defined as a gap of more than 30 days between diagnosis and surgery. Statistical analyses were performed using SPSS for Windows (version 25) to determine significant predictors.* ***Results:*** *Most patients were middle-aged (30–49 years), with significant representation from both urban and rural regions. Nearly half of the participants had no formal education, and the majority belonged to lower socioeconomic groups. Invasive Ductal Carcinoma (IDC) was the predominant histological type, and most patients presented at Stage II. Surgery was not performed in 37.2% of cases, often due to late diagnosis or systemic barriers. Significant predictors of surgical delay included older age, rural residence, low socioeconomic status, larger tumour size, and presenting symptoms such as discharge or bleeding. No association was found with marital status, occupation, or histological subtype.* ***Conclusion:*** *This study found that delays in breast cancer treatment (surgery) were mostly caused by poverty, living in rural areas, larger tumors, and certain symptoms. Occupation or marital status did not affect delays. To improve this, cancer services should be made easier to reach, the referral system should be introduced, and people should be more aware of early treatment.*

Key words: *surgical treatment delay, breast cancer, improved care, Bangladesh*

Introduction

Breast cancer is the most common cancer among women in Bangladesh. According to the World Health Organization (WHO) and the International Agency for Research on Cancer (IARC), the incidence of breast cancer has been steadily increasing, and it is now a leading cause of cancer-related deaths among women in the country. The incidence rate of breast cancer in Bangladesh is estimated to be around 9.1 per 100,000 women, which is much lower than in Western countries but reflects the growing impact of the disease on women's health in the country.[1]

Breast cancer mortality rates in Bangladesh are notably high, due to factors such as late-stage diagnosis, lack of awareness, and limited access to treatment options. According to recent estimates, the mortality rate for breast cancer in Bangladesh is much higher than in developed countries, where advanced screening and treatment are more accessible. In Bangladesh, many women are diagnosed at an advanced stage of the disease, which makes treatment more challenging and outcomes less favorable.[2]

In Bangladesh, the healthcare system for cancer care is still developing. Many women face challenges in accessing timely and affordable treatment. They often encounter long waiting times for diagnosis and surgery, which can delay treatment and worsen the prognosis. The lack of widespread breast cancer screening programs means that many women do not receive early detection, which is crucial for improving survival rates.[3]

A significant concern in Bangladesh is the delayed diagnosis and treatment of breast cancer. Patients often present with advanced disease, and treatment options may be limited in rural areas. Social stigma, lack of awareness, and the high cost of treatment contribute to delays in seeking medical help. In many cases, patients do not seek care until symptoms become severe.[4]

Moreover, women in Bangladesh with comorbidities such as diabetes, hypertension, and chronic respiratory conditions may face worse outcomes due to the added complexity of managing these conditions alongside cancer treatment. These comorbidities can negatively affect the patient's overall health, making it more difficult to tolerate cancer treatment.[5]

Effective coordination between healthcare professionals in both primary care and specialized hospital settings is crucial to ensure that breast cancer patients receive consistent care throughout their treatment journey. Healthcare providers must work together to manage the complexities of treatment, from diagnosis to follow-up care. Improved infrastructure and better coordination can help reduce delays in treatment and enhance the quality of care.[6]

Delays in surgical treatment (surgical treatment delay or STD) are a significant concern in Bangladesh. Such delays can occur due to a variety of factors, including a lack of medical resources, long waiting times for surgery, and a shortage of trained surgeons. The delay in treatment can lead to psychological distress for patients and may even impact survival, although other factors such as the stage of the cancer, the patient's age, and overall health also play important roles in treatment outcomes.[7]

Addressing these challenges requires greater awareness, more accessible screening programs, and improvements in the healthcare system to ensure timely and effective treatment for all women with breast cancer in Bangladesh.[8]

Breast cancer is rising in Bangladesh, and many patients face harmful delays that lead to late diagnoses and poorer outcomes. Limited resources, long waiting times, and unequal access to care worsen these delays and affect patients' well-being. This study helps identify the key causes of treatment delay and provides evidence to improve early diagnosis, timely care, and overall outcomes for Bangladeshi women.

Materials and Methods

This prospective observational study was conducted at the National Institute of Cancer Research and Hospital (NICRH), Dhaka, from January to May 2025. A total of 218 adult female breast cancer patients were selected using purposive and convenient sampling. Data were collected through structured questionnaires and medical record reviews. Demographic, clinical, and healthcare-related variables were recorded, and treatment delay (STD) was defined as more than 30 days between biopsy and surgery.

Primary data included patient interviews on demographic and healthcare access information, while secondary data were obtained from hospital records detailing tumor characteristics, type of surgery, biopsy

and surgery dates, and comorbidities. Patient, doctor, treatment, system, and total delays were defined using standardized operational definitions. All data were anonymized and stored securely.

Descriptive statistics summarized patient characteristics, and bivariate and multivariate analyses identified factors associated with significant treatment delays. A *p*-value <0.05 was considered statistically significant. Ethical approval was obtained from the NICRH Institutional Review Board (IRB), and patient confidentiality was strictly maintained.

Results

A total of 218 breast cancer patients were included in the study.

Socio-Demographic Characteristics

Socio-demographic variables are summarized in Table I. Most participants were aged 40–49 years (30.3%), followed by 30–39 years (29.4%). Nearly half had no formal education (46.8%), and most lived in rural (49.5%) or semi-urban (35.3%) areas. Almost all were married (98.6%), and two-thirds lived with their spouse.

Table I: *Socio-Demographic Characteristics of Study Participants (n = 218)*

Variable	Category	Frequency	Percent
Age (yrs.)	<30	14	6.4
	30–39	64	29.4
	40–49	66	30.3
	50–59	47	21.6
	≥60	27	12.4
Division	Dhaka	114	52.3
	Chattogram	44	20.2
	Khulna	19	8.7
	Rajshahi	16	7.3
	Barishal	12	5.5
	Mymensingh	11	5.0
	Rangpur	2	0.9
Education	No formal	102	46.8
	Primary	55	25.2
	Secondary	43	19.7
	College/University	13	6.0
	Graduate+	5	2.3
Area	Rural	108	49.5
	Semi-urban	77	35.3
	Urban	33	15.1
Marital Status	Married	215	98.6
	Divorced	2	0.9
	Unmarried	1	0.5
Living Status	With spouse	145	66.5
	With family	66	30.3
	Alone	7	3.2

Clinical and Surgical Characteristics

Most patients underwent modified radical mastectomy (49.1%), while 37.2% did not have surgery. Stage II was most common (56.9%), and IDC predominated (90.8%) (Table II).

Table II: Clinical and Surgical Characteristics (n = 218)

Variable	Category	Frequency	Percent
Type of Surgery	Modified radical mastectomy	107	49.1
	Lumpectomy	18	8.3
	Oncoplastic breast surgery	12	5.5
	No operation	81	37.2
Side Operated	Left	69	31.7
	Right	61	28.0
	Both	7	3.2
	Not applicable	81	37.2
Tumor Stage	I	31	14.2
	II	187	85.8
Histopathology	IDC	198	90.8
	ILC	3	1.4
	DCIS	13	6.0
	Others	4	1.8

IDC= Invasive Ductal Carcinoma; ILC= Invasive Lobular Carcinoma; DCIS= Ductal Carcinoma in Situ

Treatment Delays

Mean patient delay was 210 days, diagnostic delay 27 days, surgical treatment delay 28 days, system delay 29 days, and total delay 294 days (Table III).

Table III: Summary of Treatment Delays (n = 218)

Delay Type	Mean (days)	Median (days)	SD	Min.	Max.
Patient Delay	210.03	210	40.44	112	348
Diagnostic Delay	26.81	27	10.49	2	55
Surgical Treatment Delay	27.71	27	7.68	4	51
System Delay	29.10	29	12.12	2	59
Total Delay	293.64	298	43.40	177	430

Patient Delay: The time interval between first recognition of symptoms by the patient and the first contact with a qualified healthcare provider. Diagnostic Delay: The time interval between the first healthcare consultation and the establishment of a definitive diagnosis, typically confirmed by histopathology or biopsy. Surgical Treatment Delay: The time interval between biopsy confirmation and the initiation of surgery. System Delay: The time interval attributable to the healthcare system, encompassing delays from first healthcare contact to initiation of treatment, excluding pure patient-related delays. Total Delay: The cumulative time interval from initial symptom recognition to the start of definitive treatment.

Surgical Treatment Delay (>30 days)

Table IV shows all comparisons of surgical delay with demographic, clinical, and socioeconomic factors, along with logistic regression predictors. Older age, larger tumor size, alarming initial symptoms, rural residence, and lower socioeconomic status were associated with significant surgical delay.

Table IV: Factors Associated with Surgical Treatment Delay and Predictors (n = 218)

Variable	Category	≤30 days n (%)	>30 days n (%)	*p*-value	OR (95% CI)
Age (yrs.)	<30	10 (6.8)	4 (5.6)	<0.001	7.48 (1.12–49.73)
	30–39	53 (36.3)	11 (15.3)		
	40–49	47 (32.2)	19 (26.4)		
	50–59	24 (16.4)	23 (31.9)		
	≥60	12 (8.2)	15 (20.8)		
Area of Residence	Rural	63 (43.2)	45 (62.5)	0.025	0.376 (0.15–0.94)
	Semi-urban	59 (40.4)	18 (25.0)		
	Urban	24 (16.4)	9 (12.5)		
Tumor Size	<2 cm	73 (50.0)	14 (19.4)	<0.001	8.44 (2.98–23.92)
	2–4 cm	46 (31.5)	18 (25.0)		
	>4 cm	27 (18.5)	40 (55.6)		
Education	No formal	64 (43.8)	38 (52.8)	0.144	–
Socioeconomic Status	Lower	98 (67.1)	62 (86.1)	0.011	–
Initial Symptoms	Discharge /bleeding	34 (24.3)	57 (81.4)	<0.001	28.48 (7.95–102.08)

Discussion:

This study explores the key factors contributing to delays in surgical treatment among breast cancer patients at NICRH. Most of the women in the study were between 30 and 49 years old, which matches what regional data already show—breast cancer tends to occur earlier in South Asian women than in Western countries.[1,2] Nearly half of the participants had no formal education, and many came from rural or semi-urban areas. These patterns reflect the well-known gaps in cancer awareness, limited access to diagnostic services, and slow referral processes seen across the region.[3-5]

From a clinical standpoint, the high number of Stage II cases and the dominance of invasive ductal carcinoma are consistent with trends reported in South Asia.[6,7] Even though timely surgery is crucial, more than one-third of the patients did not receive their operation during the study period. This mirrors findings from other low- and middle-income countries, where limited surgical capacity, financial barriers, and late presentation often delay treatment.[8,9] The overall delay approached 300 days, with the longest waiting period occurring before patients sought medical care. This type of patient-related delay is widely documented and often linked to low awareness, stigma, and difficulty identifying early symptoms.[10, 11]

Several factors—older age, living in rural areas, larger tumors, more alarming early symptoms, and lower socioeconomic status—were strongly associated with surgical delay. Similar associations have been reported in other Asian and African settings, where long travel distances, complex disease presentations, and financial hardship slow down access to surgery.[12–18] Although lower education levels showed some relationship with longer delays, the association was not statistically significant, possibly because it overlaps with socioeconomic and geographic disadvantages. Overall, the findings point to the need for stronger early detection programs, better community awareness, and wider availability of oncology services outside major cities. Improving referral systems, coordinating preoperative steps more efficiently, and offering financial support may also help shorten delays. These recommendations are consistent with the WHO Global Breast Cancer Initiative, which highlights timely diagnosis and treatment as crucial for improving survival in LMICs.[19]

In sum, surgical delays at NICRH were substantial and were driven mainly by late presentation and barriers within the health system. Efforts to promote earlier help-seeking, streamline referrals, and widen access—especially for rural and low-income patients—are essential for ensuring that women receive surgery without unnecessary delay.

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Original Article

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Initial Experience of Open Radical Retropubic Prostatectomy at the National Institute of Cancer Research & Hospital: Analysis of 15 Cases

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Abstract

Background: *Prostate cancer is a leading malignancy in men. Open radical prostatectomy (ORP) remains a fundamental treatment for localized disease, especially in settings with limited robotic access. This study reports our initial experience with ORP.* ***Objective :*** *To evaluate the perioperative, oncological, and functional outcomes of open radical retropubic prostatectomy.* ***Methods:*** *This prospective study involved 15 patients at the National Institute of Cancer Research & Hospital, Dhaka, from January 2022 to December 2023. We collected perioperative and oncological data. Functional outcomes (continence assessed by pad count and erectile function assessed by International Index of Erectile Function [IIEF-5]) were evaluated preoperatively and at 1, 3, 6, and 12 months postoperatively.* ***Results:*** *The median age was 64 years, the Gleason score was 7, and PSA was 9.4 ng/dl. There was no major morbidity or mortality. Two patients had transient urinary leakage, and one (6.66%) developed an anastomotic stricture. Continence recovery rates were 53%, 73%, and 93% at 3, 6, and 12 months, respectively. Potency recovery was 60% for bilateral and 42.9% for unilateral nerve-sparing procedures. Positive surgical margins were found in two patients (13.33%) with pT3a disease.* ***Conclusion:*** *Open radical prostatectomy is a safe and effective procedure, demonstrating excellent continence recovery and acceptable potency rates with minimal major complications. It remains a crucial surgical option in resource-conscious healthcare systems.*

Keywords: *Functional results, Oncological results, Open radical prostatectomy, ORP, Prostate cancer, Retropubic radical prostatectomy.*

Introduction

Prostate cancer (PCa) represents a significant global health burden, consistently ranking as the second most common cancer diagnosed in men and a leading cause of cancer-related mortality worldwide.[1] The incidence of PCa exhibits considerable geographical variation, with higher rates typically observed in developed regions; however, the burden is rapidly increasing in developing

nations due to aging populations, the adoption of Western lifestyles, and improved diagnostic capabilities.[2] A substantial majority of newly diagnosed cases—approximately 77%—are classified as localized or locally advanced disease, for which curative-intent treatment remains a primary objective.[3] The management landscape for localized prostate cancer includes active surveillance for low-risk disease, radiotherapy, and radical prostatectomy (RP).[4] Since its first description in the early 1980s, radical prostatectomy has evolved into the gold-standard surgical intervention, with robust level-one evidence from randomized controlled trials demonstrating its superiority over watchful waiting in reducing disease-specific mortality, the risk of metastasis, and local progression.[5,6] The primary oncological goals of RP are complete tumor excision with negative surgical margins, eradication of the disease, and accurate pathological staging, all of which are critical for long-term cancer control.[7] The surgical approach to RP has undergone a significant transformation over the past two decades with the widespread adoption of robot-assisted radical prostatectomy (RARP). RARP offers technical advantages such as magnified 3D visualization, wristed instrumentation, and improved ergonomics, which have contributed to its dominance in many high-income countries.[8,9] Proponents highlight studies associating RARP with reduced blood loss, shorter hospital stays, and potentially faster recovery of continence in the early postoperative period compared to open retropubic radical prostatectomy (ORP).[10] Despite this technological shift, ORP remains a highly relevant, well-established, and commonly performed procedure across the globe, particularly in regions with financial constraints or limited access to robotic platforms.[11] Furthermore, contemporary comparative effectiveness research indicates that when performed by experienced surgeons, ORP achieves equivalent long-term oncological outcomes and functional results to its robotic counterpart.[12,13] The key surgical principles of ORP—meticulous apical dissection, precise neurovascular bundle preservation, and a tension-free vesicourethral anastomosis—are universally recognized as the cornerstones of achieving the trifecta of cancer control, urinary continence, and erectile function preservation. In Bangladesh, the rising incidence of prostate cancer necessitates the establishment of robust, high-quality surgical programs. Therefore, ORP continues to be the primary surgical modality. This study aims to detail the initial experience and evaluate the perioperative, oncological, and functional outcomes of the first 15 cases of open radical retropubic prostatectomy performed at the National Institute of Cancer Research & Hospital (NICRH) in Dhaka, thereby contributing to the local and global understanding of this essential surgical technique.

Methodology

Study population

This prospective study was conducted in the Department of Uro-Oncology at the National Institute of Cancer Research & Hospital (NICRH), Dhaka, between January 2022 and December 2023. A total of 15 consecutive patients with clinically localized prostate cancer underwent open radical retropubic prostatectomy (ORP) performed by a single surgical team. The study was approved by the institutional ethical review board.

Inclusion criteria

Patients with biopsy-proven, clinically localized prostate cancer (cT1-T2c) who were deemed suitable for radical prostatectomy were included. Eligibility was based on a comprehensive assessment, including life expectancy greater than 10 years, satisfactory performance status, and patient consent for open surgical intervention after a detailed discussion of all treatment options.

Exclusion criteria

Patients with evidence of distant metastasis (M1 disease) or fixed, locally advanced tumors (cT4) on imaging were excluded. Additional exclusion criteria included a history of prior pelvic radiotherapy or radical pelvic surgery, and the presence of severe cardiopulmonary comorbidities that contraindicated major abdominal surgery.

Study procedure

All patients underwent ORP via the standard retropubic approach. A detailed history, perioperative data, and oncological outcomes (including pathological stage and margin status) were recorded. Functional outcomes were assessed using a daily pad count for continence and the 5-item International Index of Erectile Function (IIEF-5) questionnaire. These were evaluated preoperatively and at 1, 3, 6, and 12 months postoperatively. Other postoperative complications were also documented.

Data analysis

Data were analyzed using descriptive statistics. Continuous variables were presented as medians with ranges, while categorical variables were expressed as frequencies and percentages. Functional recovery rates for continence and potency were calculated at the specified postoperative intervals. Statistical analysis was performed using SPSS software (Version 26.0).

Result

The study analyzed 15 patients who underwent open radical retropubic prostatectomy (ORP). The median age of the cohort was 64 years (range: 52-73). The median preoperative PSA was 9.4 ng/dl, and the median biopsy Gleason score was 7, with scores ranging from 6 to 9. The distribution of clinical staging showed that the majority of patients (86.7%) had cT1 or cT2a disease. Intraoperatively, the median blood loss was 450 ml, and the median operative time was 135 minutes. There were no major intraoperative complications or perioperative mortality. Postoperative complications were classified using the Clavien-Dindo system. Grade I complications were most common, observed in 26.7% of patients, primarily self-limiting hematuria. Two patients (13.3%) experienced Grade II complications in the form of postoperative urinary leakage, which were managed successfully with prolonged drain placement for two weeks. One patient (6.7%) developed an anastomotic stricture, a known late complication with reported rates ranging from 0.48% to 32%, which required a urethral dilation (Grade IIIa complication). Oncological outcomes revealed positive surgical margins (PSMs) in two patients (13.3%), both of whom had pT3a disease. This finding is consistent with larger series, such as a SEER registry study, which reported PSMs in 21.2% of cases, noting they were significantly more common in pT3a than in pT2 tumors (44% vs. 18%, P<0.001). Functional outcomes were promising. The continence recovery rates, defined as using 0-1 safety pad per day, were 53.3%, 73.3%, and 93.3% at 3, 6, and 12 months, respectively. These figures align with established benchmarks, such as those reported by Stolzenburg et al., who noted continence rates of 84% at 6 months and 92% at one year. Potency, defined as the ability to achieve intercourse with or without the aid of sildenafil, was strongly associated with the extent of nerve-sparing. The recovery rate was 60.0% for patients who underwent a bilateral nerve-sparing procedure compared to 42,9% for those with a unilateral approach. This difference, while notable, was not statistically significant in our small cohort (p=0.651), though it mirrors the trend reported by William et al., who found a significant association (68% vs. 47%, p=0.001).

Table I: *Baseline patient demographics and clinical characteristics (N=15)*

Characteristic	Value
Age (years), Median (Range)	64 (52 - 73)
Preoperative PSA (ng/dl), Median (Range)	9.4 (5.8 - 25.0)
Biopsy Gleason score, Median (Range)	7 (6 - 9)
Clinical stage	n (%)
cT1	7 (46.7)
cT2a	6 (40.0)
cT2b	1 (6.7)
cT2c	1 (6.7)

Table II: Intraoperative parameters (N=15)

Parameter	Value
Operative time (minutes), Median (Range)	135 (110 - 175)
Estimated blood loss (ml), Median (Range)	450 (300 - 700)
Nerve-sparing procedure	n (%)
Bilateral	5 (33.3)
Unilateral	7 (46.7)
Non-nerve-sparing	3 (20.0)

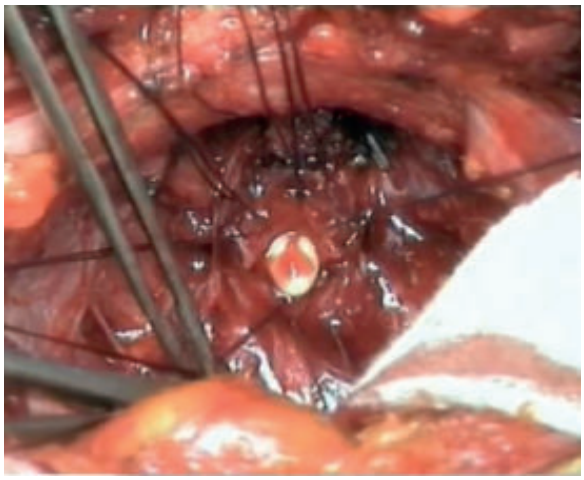

Figure 1: After taking stay sutures from the urethral margin

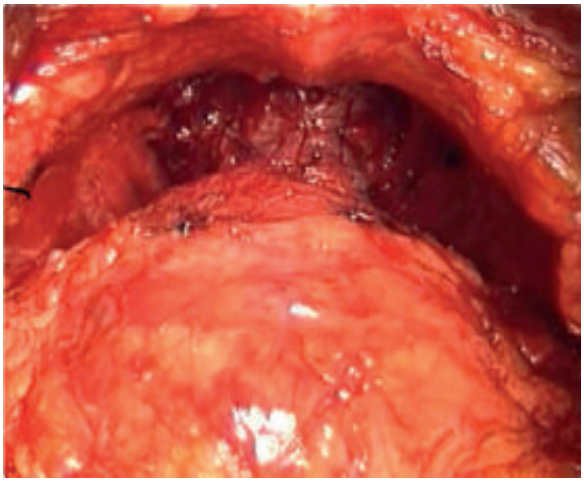

Figure 2: After complete anastomosis between the urethra and UB neck

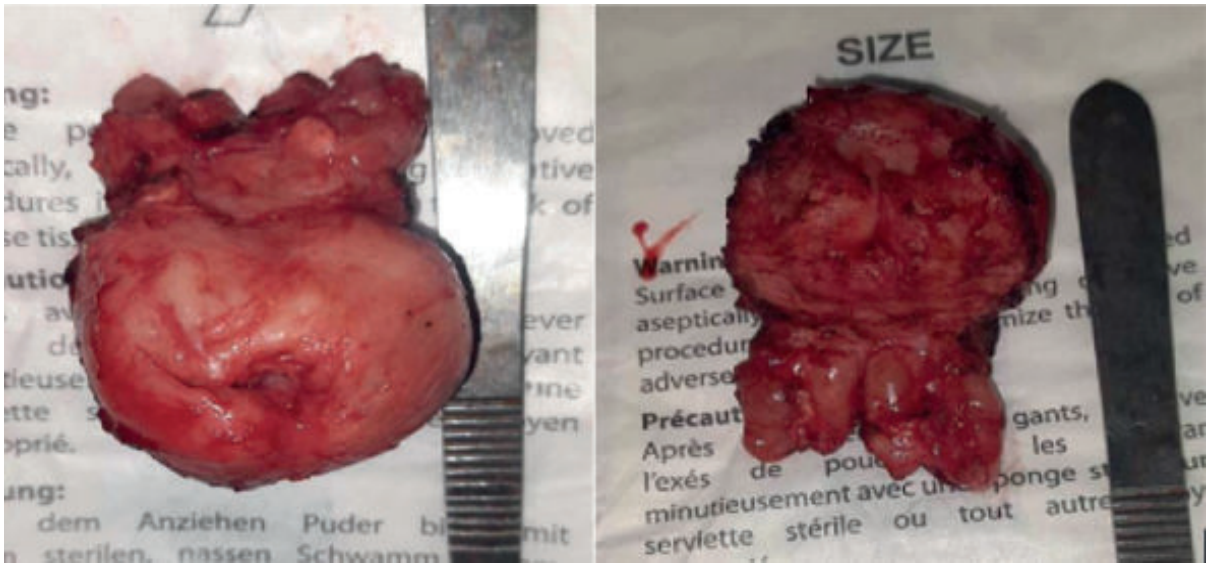

Figure 3: *After removal of the specimen*

Table III: Postoperative complications (Clavien-Dindo classification)

Complication grade	Type of complication	n (%)
Grade I	Self-limiting hematuria, Fever	4 (26.7)
Grade II	Urinary leakage (prolonged drainage)	2 (13.3)
Grade IIIa	Anastomotic stricture (requiring dilation)	1 (6.7)
Grade IIIb/IV/V	None	0 (0.0)

Table IV: Pathological outcomes and margin status

Pathological parameter	n (%)
Pathological T stage (pT)	
pT2	11 (73.3)
pT3a	4 (26.7)
Positive surgical margins (Overall):	2 (13.3)
pT2	0 (0.0)
pT3a	2 (50.0)

Statistical test: Fisher's Exact Test for PSM in pT2 vs. pT3a, p=0.033

Table V: Continence recovery following ORP (N=15)

Time point	Continent (0-1 pad/day), n (%)
3 Months	8 (53.3)
6 Months	11 (73.3)
12 Months	14 (93.3)

Table 6: *Potency recovery stratified by Nerve-Sparing technique*

Nerve-Sparing status	Potent at 12 months n (%)	*p*-value
Bilateral (n=5)	3 (60.0)	0.651
Unilateral (n=7)	3 (42.9) *	
Non-Nerve-Sparing (n=3)	0 (0.0%)	

*One patient in the unilateral group was lost to follow-up for potency assessment. Analysis is for patients with available data (n=14). Statistical test: Fisher's Exact Test (Bilateral vs. Unilateral). *

Discussion

This prospective analysis of our initial 15 cases of open radical retropubic prostatectomy (ORP) demonstrates that this established technique remains a safe and effective modality for managing localized prostate cancer, yielding outcomes comparable to contemporary series in terms of oncological safety, continence recovery, and potency preservation. In an era dominated by robotic technology, our findings reinforce the continued relevance of the open approach, particularly in healthcare systems with resource constraints. The demographic and clinical profile of our patient cohort, with a median age of 64 years and a median PSA of 9.4 ng/ml, is consistent with populations described in other studies from the region.[14] The perioperative safety of ORP was a key finding, with no major complications or mortality recorded. Our median blood loss of 450 ml and low transfusion rate are acceptable and align with modern open surgical series that have refined their techniques.[15] The observed complication profile, including transient urinary leakage in 13.3% of cases and a 6.7% rate of anastomotic stricture, falls within the widely reported range for this procedure and was managed effectively with conservative or minimally invasive measures.[16] Oncologically, the positive surgical margin (PSM) rate of 13.3% overall is favorable. It is noteworthy that both PSMs occurred in patients with pT3a disease, resulting in a 50% PSM rate in this pathological subgroup, while margins were negative in all pT2 cases. This pattern is well-documented, as extracapsular extension presents a greater surgical challenge. Our findings are, in fact, more favorable than the 21.2% overall PSM rate reported in the large SEER registry, which highlighted a significant disparity between pT3a (44%) and pT2 (18%) diseases.[17] This suggests that meticulous surgical technique in ORP can achieve excellent cancer control, especially for organ-confined disease. Functional outcomes are a critical measure of success in modern prostatectomy. Our continence recovery rates of 73.3% at 6 months and 93.3% at 12 months are excellent and mirror the outcomes reported by high-volume centers. For instance, Stolzenburg et al. reported a 92% continence rate at one year, a benchmark our initial experience closely meets.[18] This indicates that the fundamental principles of apical dissection and urethral length preservation in ORP are highly effective for achieving urinary control. Regarding erectile function, we observed a clear trend favoring more extensive nerve-sparing. The potency recovery rate was 60.0% for bilateral and 42.9% for unilateral nerve-sparing procedures. While this difference was not statistically significant in our small cohort (p=0.651), the direction and magnitude of the effect are consistent with larger studies. William et al. demonstrated a significant 21% absolute improvement in potency with bilateral nerve-sparing (68% vs. 47%, p=0.001), underscoring the importance of this technique where oncologically feasible.[19] Our results confirm that

nerve-sparing ORP can successfully preserve sexual function. The primary limitation of this study is its small sample size and relatively short-term follow-up from a single institution, which limits the generalizability and power for statistical comparisons. Future studies with larger cohorts and longer follow-up are necessary to validate these findings and assess long-term cancer-specific survival. In conclusion, this initial experience confirms that open radical retropubic prostatectomy is a viable and robust surgical option. It provides excellent oncological and functional outcomes with minimal major morbidity. In settings like ours, where financial limitations and limited access to robotics are a reality, ORP is not merely a historical procedure but a necessary and highly competent mainstay of surgical treatment for prostate cancer.[20] With continued refinement in technique and patient selection, ORP will continue to play a crucial role in global cancer care.

Limitations:

The primary limitations of this study are its small sample size, single-center design, and short-term follow-up, which limit the generalizability of the findings and the statistical power for more detailed comparative analyses.

Conclusion

This initial experience demonstrates that open radical retropubic prostatectomy provides safe and effective management for localized prostate cancer. The procedure achieved favorable oncological outcomes, with low overall positive margin rates, and excellent functional recovery of continence and potency. These results affirm that ORP remains a vital surgical option, particularly in resource-limited settings where robotic platforms are inaccessible, ensuring high-quality prostate cancer care can be delivered.

Recommendation:

We recommend open radical retropubic prostatectomy as a standard of care in institutions with financial or technological constraints. Future multi-center studies with larger cohorts and longer follow-up are encouraged to further validate and refine its surgical outcomes.

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Case Report

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Vulvovaginal Tuberculosis- Mimicking Vulvar Carcinoma- A Case Report

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Abstract:

Though tuberculosis is common in TB endemic region like Bangladesh, vulvovaginal tuberculosis is a rare condition that frequently mimics carcinoma of the vulva. This misdiagnosis can lead to delayed and inappropriate treatment. Here we report a case of primary vulvo vaginal tuberculosis that clinically mimicked malignant lesion of vulva. Histopathological report confirmed the diagnosis of vulvar tuberculosis. The patient had good response to standard antitubercular therapy and had a successful pregnancy after treatment .This case high lights the importance of suspecting tuberculosis in chronic non healing vulvar lesions in endemic area.

***Key words**: Vulvovaginal tuberculosis, vulvar carcinoma, Bangladesh*

Introduction

Primary tuberculosis of vulva and vagina is a rare event. Tuberculosis in female most frequently affects the upper genital tract. The prevalence varies from 1-19% depending on the countries [1] and occurs in 10% of the patient with pulmonary tuberculosis[2].Vulval TB accounts for 0.2% of the cases of genital TB[3]. There are only 10 reported cases in the literature mainly in developing countries[4]. Tuberculosis of vulva occurs at any age. The diagnosis is very challenging due to the unusual presentations[5]. Tuberculous lesions are either hypertrophic, ulcerative or present with multiple sinuses with discharge. Due to its vegetative appearance, this lesion often mimics vulver cancer. Due to bizarre clinical presentations clinical diagnosis of vulval TB is a challenging task to the clinicians[5]. Generally vulval tubercular lesion responds very well to medical therapy with significant reduction or total resolution of the mass within a few months.

Case report

A 26 years old women was referred to our institute NICRH with the complaints of in vulva having foul smelling vaginal discharge for last 3 years, difficulty in micturition, dysparonea and inability to perform coital function for last 3 months. She was treated by various antiviral, antifungal and antibiotics regimen but did not respond. She denied any history of fever, weight loss, anorexia, cough, menstrual irregularity or abdominal pain. There was no history of contact with tuberculosis patient. On general examination she was of average body built, afebrile and there was no lymphadenopathy. On local examination, whole clitoris was involved by a 3x3 cm growth with surface ulceration and purulent discharge (Fig. 1). The mass was free from underlying structures. There was pinpoint narrowing of vaginal orifice due to disease process. This made unable to introduce vaginal speculum speculum, even a tip of finger couldn't be introduced in introitus. Vaginal canal was obliterated, bimanual vaginal examination was not possible. Per rectal examination revealed no mass in pelvis. Biopsy taken from clitorial growth and histopathology showed chronic caseating granulomatous inflammation (Fig. 2) most likely due to tuberculosis. No malignant cells were seen on biopsy specimen. Complete blood picture showed raised lymphocyte count and high erythrocyte sedimentation rate (ESR). Montoux test and chest X-ray, ultrasonography of whole abdomen were unremarkable. Smear test and culture and advanced imaging were not performed. Antitubercular drugs (CAT-1) was started with regular monthly follow up. There was rapid relief of symptoms with good response. After 1 month of anti-tubercular treatment (Fig. 3) size of the clitoral growth reduced, associated redness, swelling and discharged were subsided. Vaginal orifice resumed in normal appearance. After 6 months, the mass was totally disappear (Fig. 4). Clitoris was normal in size, shaped and appearance. Speculum examination showed whole vaginal wall smooth and cervix healthy. Two years after patient gave birth of another child.

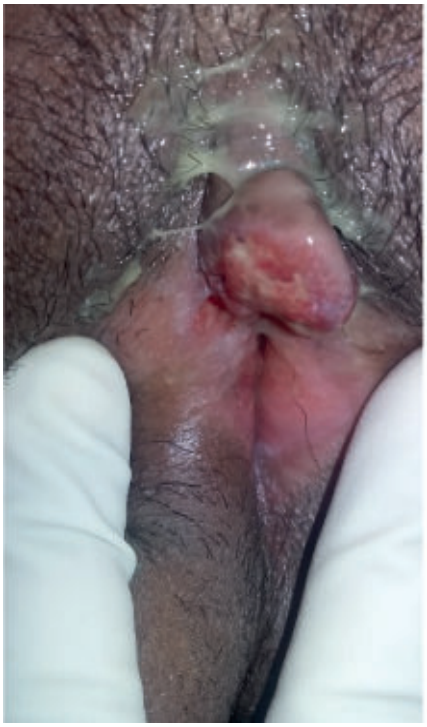

Figure 1: At first presentation

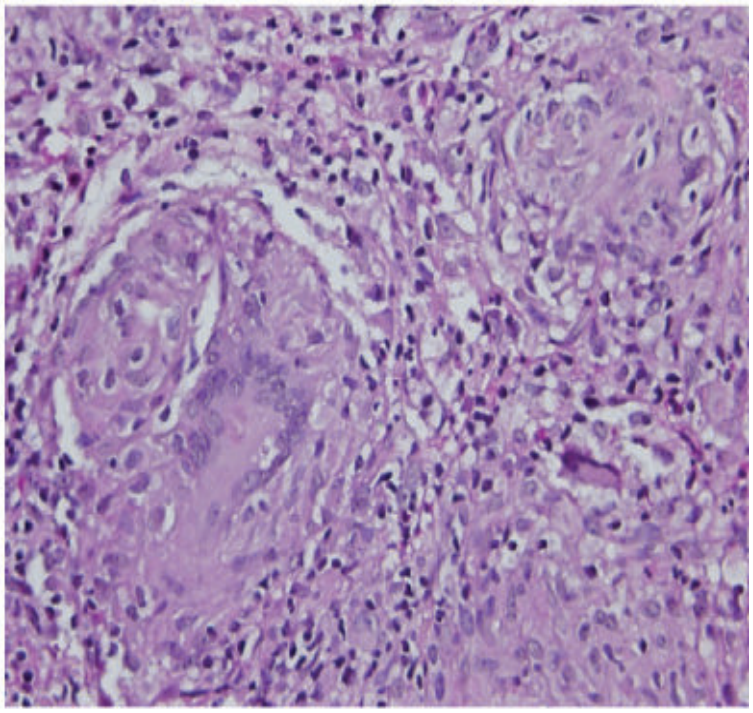

Figure 2: Caseating granulomatous inflammation

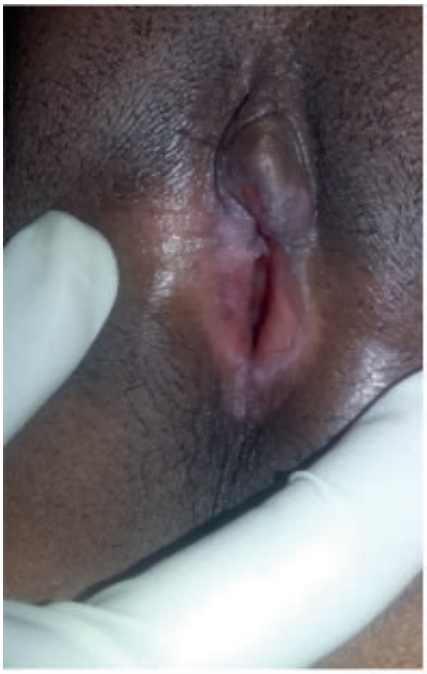

Fig. 1: At first presentation

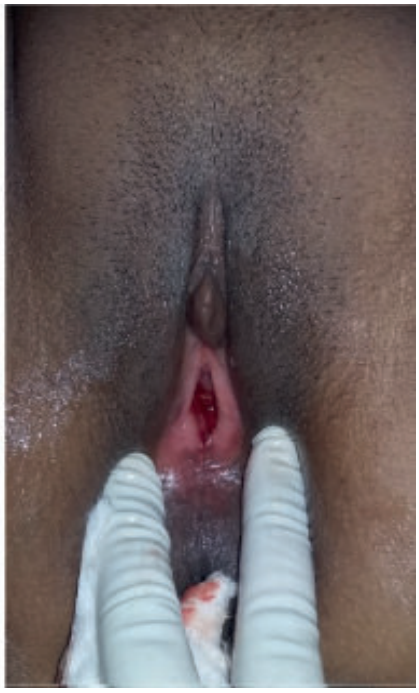

Fig. 2: Caseating granulomatous inflammation

Discussion

Female genital tuberculosis is rare and usually is secondary to the haematogenous spreading from pulmonary or other non-genital tract foci.[4] In majority cases genital TB spreads haematogenously and in a minority, direct extension from the lesion in the upper genital tract or exogenously from excretion of tubercle bacilli in stool, urine, sputum or sexual contact[4,5].The highest incidence is seen in young women of childbearing age in rural area. Except for very few cases, tuberculosis of the vulva is usually associated with tuberculosis elsewhere in the body.[6] Our case is one of them.

The presentation of vulvovaginal TB is very variable. It can present with shallow small ulcers with multiple sinuses or rarely with elephantiasis of the vulva. In the case reported by Tiwari et al[4] there was a hypertrophic lesion of the vulva and good outcome. In our case there was clitoral growth with ulceration and purulent discharge which respond well to antitubercular therapy. The diagnosis of vulvovaginal tuberculosis is usually made by histological examination of vulvovaginal biopsy specimen. Isolation of mycobacterium bacilli is the gold standard for diagnosis of tuberculosis. How ever bacilli are very rarely found in female genital tract tuberculosis even with fluorescent techniques. Most authors agree that histopathological examination is one of the most useful means of establishing diagnosis of genital tract tuberculosis and presence of typical granulomas is sufficient for confirming the diagnosis. The differential diagnosis for granulomatous disease includes amoebiasis, schistosomiasis, brucellosis, tularemia, sarcoidosis and foreign body granuloma. However, the disease is so uncommon that it is seldom encountered in the gynaecologist's usual practice, therefore the clinical index of suspicion is generally low. In many cases, the clinical presentation is obscure and the diagnosis delayed.[5] Tiwari and coworkers[3] suggested that re-emphasis of tuberculosis should be kept in mind when a particular symptom fails to respond to empirical treatment. Chakrabarti and coworkers[8] reported that the clinicopathological aspect of female genital tuberculosis showed typical (classical) tuberculosis granuloma of 77.6%, atypical tuberculosis lesions of 22.4% and AFB positive in smear of 81.9% whereas AFB negative was of 18.1% with a positive culture. In other reports[6,7] the frequency of female genital tuberculosis was low because demonstration of AFB (the most important criteria for diagnosis) was difficult.

In this case the patient had been treated with various antibiotics such as doxycycline, ciprofloxacin, antifungal and antiviral but the ulcer persist. Tissue biopsy confirmed the diagnosis. The other internal genital structures were not evaluated thoroughly especially via laparoscope or endometrial biopsy. Bimanual pelvic examination was not done as vaginal canal was obliterated by growth. Tuberculosis of the vulva and vaginal orifice is very rare, as in this case. Based on clinical findings and histopathological reports treatment with antitubercular drugs was planned for 9 months regimen including four drugs in the initial phase (Isoniazide, rifampicin, ethambutol and pyrazinamide) and two drugs in the continuation phase (rifampicin and isoniazide). It is not known that what should be the optimal duration of treatment. The total duration of treatment should be six months to a year.[7] In our case patient received 9 months treatment. Excellent cure rate was reported.

Conclusion

Given the rarity and potential for mis diagnosis as malignancy, a high index of suspicion for tuberculosis is required, particularly in patients from endemic areas. So we suggest that TB should be kept in mind in differential diagnosis of unresponsive chronic vulval lesions. Presence of granulomatous lesion in microscopic examination can act as reliable diagnostic tools in detecting and managing vulval tuberculosis and help in prevention of unnecessary surgical intervention.

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Case Report

Cancer J Bangladesh 2025;6(2): 87-91
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The Untold Story of the Neuroendocrine Cancer of the Cervix: A Case Report

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Abstract

Neuroendocrine carcinoma of the cervix (NECC) is a rare and highly aggressive subtype of cervical cancer, accounting for less than 5% of cases. It is frequently associated with high-risk human papillomavirus (HPV), particularly HPV-18, and is characterized by rapid progression, early metastasis, and poor prognosis. Diagnosis is often delayed due to nonspecific clinical features and inconclusive initial biopsies. Most importantly, no consensus for early-stage treatment, management guideline is available.

We report the case of a 37-year-old multiparous woman who initially presented with lower abdominal pain and was managed conservatively due to non-specific findings. Over a two-year period, she developed recurrent symptoms, including post-coital bleeding and menorrhagia. Initial cervical biopsy was inadequate. On referral to a gynaecologic oncologist, examination revealed a friable, barrel-shaped cervix with a 5 × 4 cm lesion. HPV DNA testing was positive for HPV-18. Cone biopsy demonstrated a poorly differentiated carcinoma with neuroendocrine features. Immunohistochemistry showed positivity for synaptophysin and pan-cytokeratin, confirming the diagnosis of neuroendocrine carcinoma of the cervix. Imaging revealed localized disease without distant metastasis. The patient underwent radical hysterectomy, and final histopathology confirmed the diagnosis.

Neuroendocrine carcinoma of the cervix poses significant diagnostic challenges and may be missed on initial evaluation. Persistent cervical symptoms, inconclusive biopsies, and HPV-18 positivity should prompt repeat biopsy and immunohistochemical analysis. Early recognition and appropriate multimodal management are crucial to improving outcomes in this aggressive malignancy.

Keywords: *Neuroendocrine carcinoma of cervix; HPV-18; Small cell carcinoma; Immunohistochemistry; Case report*

Introduction

Neuroendocrine carcinoma of the cervix (NECC) is a rare and highly aggressive subtype of cervical cancer, accounting for less than 5% of all cervical malignancies.[1-3] Despite its low incidence, NECC contributes disproportionately to cervical cancer–related mortality due to rapid tumor progression, early lymphovascular invasion, and a high propensity for distant metastasis.[1,2]

The classification and terminology of cervical neuroendocrine tumors have evolved over time. According to the current World Health Organization (WHO) classification, cervical neuroendocrine neoplasms are divided into well-differentiated

neuroendocrine tumors and poorly differentiated neuroendocrine carcinomas, including small cell and large cell subtypes. According to the Grades of Neuroendocrine Neoplasms, WHO 2022, poorly differentiated neuroendocrine carcinomas is characterised by >20 mitoses/10 HPF; >20% Ki- 67% index.[4,5] Among these, small cell neuroendocrine carcinoma is the most common and the most aggressive histologic variant.[6]

High-risk human papillomavirus (HPV) infection plays a pivotal role in the pathogenesis of cervical neuroendocrine carcinoma. Approximately 85% cases are associated with HPV infection, with HPV-18 being the predominant genotype, accounting for more than half of reported cases.[7] HPV-18 is significantly more prevalent in neuroendocrine tumors than in squamous cell carcinoma of the cervix and is believed to exhibit a greater affinity for glandular and neuroendocrine cervical cells, contributing to early nodal involvement and aggressive tumor behavior.[7]

Clinically, NECC often presents with nonspecific symptoms such as abnormal vaginal bleeding, post-coital bleeding, pelvic pain, or may be incidentally detected during routine cervical screening.[2,3] Cytological screening alone may fail to detect these tumors, as neuroendocrine cells are often sparse and easily overlooked.[8] Consequently, diagnosis frequently requires deep cervical biopsy and immunohistochemical confirmation using neuroendocrine markers such as synaptophysin, chromogranin A, neuron-specific enolase, and CD56.[6]

Due to the rarity of NECC, prospective randomized clinical trials are lacking, and current management strategies are largely guided by retrospective studies and expert consensus.[9,10] Early-stage disease is generally treated with radical surgery followed by platinum-based chemotherapy, whereas advanced disease requires multimodal treatment including chemoradiation.[9,10] Despite aggressive therapy, prognosis remains poor, underscoring the need for heightened clinical awareness and early diagnosis.

This case report highlights the diagnostic challenges and clinical course of neuroendocrine carcinoma of the cervix and emphasizes the importance of repeat biopsy, HPV testing, and immunohistochemistry in patients with persistent or recurrent cervical symptoms.

Case Presentation

Patient Information

A 37-year-old multiparous woman (para 3) with an Eastern Cooperative Oncology Group (ECOG) performance status of 0 presented to a private hospital on 31 December 2022 with complaints of lower abdominal pain. She had no significant past medical or surgical history.

Clinical Findings

On per abdominal examination: No abnormality detected; per speculum examination Acetowhite areas were found at the 1, 6, and 11 o'clock positions on the cervix and biopsy was taken. Bimanual examination revealed bulky anteverted uterus. Colposcopic findings were suggestive but non-specific. Colposcopy was suggestive of CIN-I and biopsy was taken.

Histopathology report was Chronic Cervicitis and she was treated conservatively.

Diagnostic Timeline

December 2022: Initial presentation; managed conservatively

Nine months later: Recurrent symptoms; treated symptomatically without definitive diagnosis.

November 2024: She complained of post-coital bleeding (2 episodes) and menorrhagia.

At that time, examination under anesthesia (EUA), dilatation and curettage (D&C), and cervical biopsy were performed.

TVS report suggestive of endometrial pathology.

Then fractional curettage and cervical biopsy done, unfortunately reports were inconclusive, inadequate for diagnosis, while endometrial sampling revealed an endometrial polyp.

Referral and Re-evaluation

The patient was subsequently referred to a gynecological oncologist for further evaluation.

Cervix was broad, friable, bleeding on touch on **per speculum examination**; **per vaginally h**ard, barrel-shaped cervix and **per rectally p**arametrium found soft bilaterally; **tumor size was a**pproximately 5 × 4 cm.

Based on clinical findings, the provisional diagnosis was carcinoma cervix, FIGO stage IB_3.

Investigations Report

HPV DNA testing was conducted and result was positive for HPV-18.

Cone biopsy of cervical tissue reported poorly differentiated carcinoma with neuroendocrine features, then immunohistochemistry was suggested.

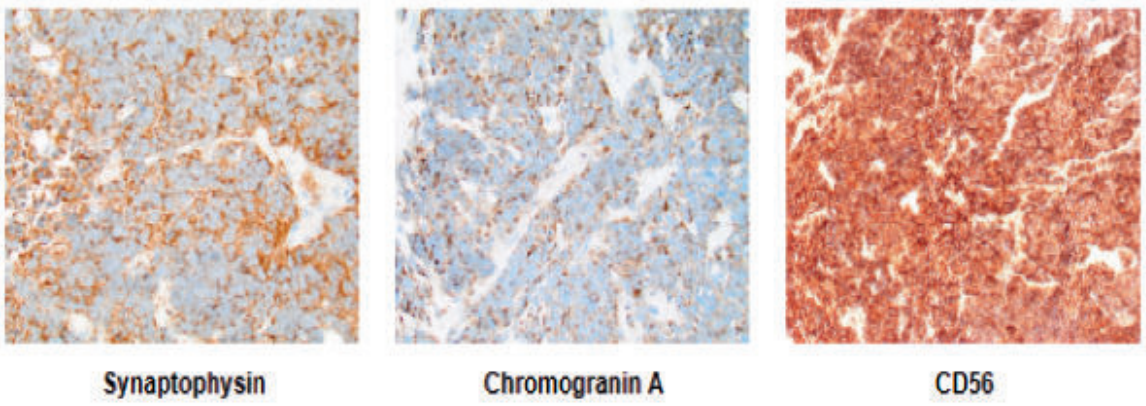

Figure 1. *Immunohistochemistry results*

Immunohistochemistry results showed Synaptophysin and Pan-cytokeratin Positive.
Immunohistochemistry report confirmed small cell neuroendocrine carcinoma of the cervix, stage $1B_3$ (clinical).

Imaging
Radiological findings-
MRI pelvis shown localized cervical lesion without parametrial invasion and staging was IB_2 r .

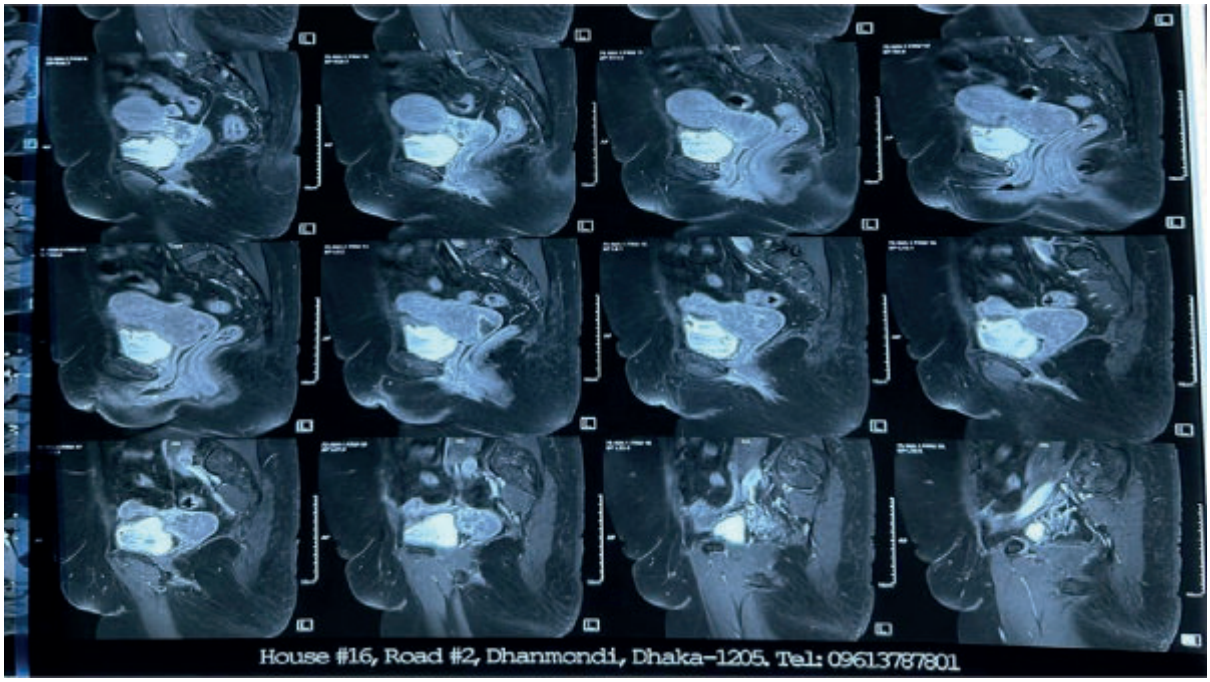

Figure 1. *MRI Findings*

MRI findings were-
Cervical carcinoma (48 x 47 x 50) mm without extension into uterus or vagina. No extension into parametrium. Multiple left common iliac, right external iliac, internal iliac and inguinal lymphadenopathy. No focal lesion in liver. No ascites. Radiological staging: T1b2 N1 M0

CECT chest was normal with no evidence of distant metastasis.

As 18F-FDG PET-CT is crucial for staging of cervical NEC. Because hematogenous spread can occur early. It can detect lymph node involvement or early hematogenous dissemination that might change FIGO - staging.

Thus, before surgery, her PET-CT scan done on June, 2025 and report revealed staging lllC_1 r.

PET-CT scan reported in Abdomen & Pelvis area:
FDG avid ill-defined residual soft tissue lesion was seen at utero-cervical junction with no obvious evidence of extrauterine junction (3.2 × 2.5 × 2.2 cm, SUV max 9.8).

Rest of the uterus & bilateral adnexae appeared unremarkable with no evidence of abnormal FDG uptake.

FDG avid few subcentimetric and enlarged lymph nodes were seen in left common iliac and right obturator regions (largest – right obturator – 3.4 × 1.9 cm, SUV max 23.9).

Finally, the diagnosis was small cell neuroendocrine carcinoma of the cervix stage IB_3 (clinical).

Therapeutic Intervention (Treatment)

After confirmation of diagnosis, patient was placed to multidisciplinary tumour board (TB) on 26.01.2025.

The decision of the Tumor Board was to administer NACT – 4/6 cycles (Cisplatin + Etop)'! Radical surgery or CCRT (EBRT weekly CT + ICRT) '! Adj. Radiation therapy ±

According to TB board decision, patient received 4cycles NACT with Cisplatin+Etoposide and underwent Radical Hysterectomy on 21.5.2025.

Then she completed adjuvent radiotherapy (CCRT+Brachytherapy) on October, 2025.

Final, histopathological examination of the surgical specimen confirmed small cell neuroendocrine carcinoma of the cervix.

Here, **EBRT** – External Beam Radiation Therapy, **ICRT** – Intracavitary Radiation Therapy, **CCRT** – Concurrent Chemoradiotherapy

Follow up
Patient is now complaining of severe low back pain.

Discussion
Neuroendocrine carcinoma of the cervix is an exceptionally rare entity that exhibits highly aggressive biological behavior, including early lymphovascular invasion and distant metastasis.[2,3] Due to its rarity and histological overlap with other cervical malignancies, diagnosis is often delayed, as demonstrated in the present case.

A major diagnostic challenge in Neuroendocrine Carcinoma of the Cervix (NECC) is the focal and patchy distribution of neuroendocrine cells, which may be present only in small nests and easily missed on superficial cervical biopsies[6,8] In this patient, initial colposcopic evaluation and biopsy were inconclusive, leading to prolonged conservative management. Similar diagnostic delays have been reported in the literature, emphasizing the importance of repeat biopsy and adequate tissue sampling in symptomatic patients with persistent cervical abnormalities.[6]

The strong association between high-risk HPV infection and cervical neuroendocrine carcinoma is well established. Approximately 85% of cases are HPV positive, with HPV-18 accounting for nearly 51% of reported cases.[11] HPV-18 is four times more frequently associated with neuroendocrine tumors than with other histological variants of cervical cancer and demonstrates a predilection for glandular and neuroendocrine cells, which may explain the aggressive disease course.[11] HPV-18 positivity in the present case further supports this etiological link.

Immunohistochemistry is indispensable for confirming the diagnosis of NECC. Classic neuroendocrine markers include synaptophysin, chromogranin A, neuron-specific enolase, and CD56.[7] In this case, positivity for synaptophysin and pan-cytokeratin confirmed neuroendocrine differentiation and helped distinguish the tumor from poorly differentiated squamous cell carcinoma or adenocarcinoma of the cervix.

Molecular studies have identified frequent alterations in genes such as *PIK3CA*, *KRAS*, *PTEN*, *TP53*, and amplification of *c-MYC* in small cell neuroendocrine carcinoma of the cervix, highlighting its molecular heterogeneity and aggressive nature.[11] Although no single mutation predominates, the presence of potentially targetable alterations suggests future opportunities for personalized therapy.

Prognosis in NECC depends on pathological stage, lymph node involvement, depth of stromal invasion, and lymphovascular space invasion.[5] Even in early-stage disease, recurrence rates remain high, with approximately 67% of patients experiencing relapse within a median of 8 months.[12] Five-year survival rates range from 30–50% in limited-stage disease, while outcomes in advanced-stage disease remain poor.[13]

Given the absence of randomized prospective trials, treatment recommendations are based on retrospective data and expert consensus. The Society of gynaecologic Oncology (SGO) and the gynaecologic Cancer InterGroup (GCIG) advocate a multimodality treatment approach, including radical surgery followed by platinum-based chemotherapy for early-stage disease and chemoradiation for advanced disease.[9,10] In the present case, radical hysterectomy was performed following definitive diagnosis, in line with current recommendations.

Therapeutic Challenge

There are no randomized prospective trial data but only limited retrospective data regarding Small Cell Neuroendocrine Carcinoma (SCNEC) treatment.

The gynaecologic Cancer Inter Group (GCIG) published a consensus review on the treatment of SCNEC and recommended radical surgery with or followed by chemotherapy for early-stage disease.

For patients with advanced - stage disease, chemoradiation or systemic chemotherapy consisting of etoposide and cisplatin was recommended.[10]

Regarding surgery or radiation therapy, a conclusion has not been reached concerning which treatment should be recommended for early-stage SCNEC.

Conclusion

Neuroendocrine carcinoma of the cervix is a rare but highly aggressive malignancy that may be missed on initial evaluation. It is strongly associated with HPV infection. Persistent cervical symptoms, TCT (thin prep cytology test) and HPV testing significantly enhance the detection rate before biopsy. Thus, HPV-18 positive case should prompt repeat biopsy and immunohistochemical analysis. Increased clinical awareness is essential to facilitate early diagnosis and timely multimodal management, which may improve outcomes in this challenging disease.~~c.~~ No Consensus for early-stage treatment, management guideline is available. In this case, the best available treatment was given.

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Review Article

Cancer J Bangladesh 2025;6(2): 92-107
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Serum Tumour Markers in Cancer Management: Literature Review

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Abstract

Serum tumour markers are molecules whose elevated levels in serum indicate the presence of cancer. These cost-effective and minimally invasive cancer-detection tools have been used in clinical practice for many decades. They are mainly used to monitor the effectiveness of cancer treatment and to detect cancer recurrence after remission. They are also used to predict the prognosis of tumours. Even though they are generally unsuitable for screening and diagnosis because of their low sensitivity and specificity, some tumour markers are used for these purposes in some circumstances. Serum tumour marker concentrations may increase in many cancers, many benign tumours, some non-tumourous diseases, and even in some physiological conditions. Thus, an increased serum tumour marker concentration does not always mean the presence of a particular cancer or even the presence of a cancer. On the other hand, serum tumour marker concentration may not be increased in the early-stage cancers and may not be expressed at all by some individuals. As a result, a normal concentration of serum tumour marker cannot exclude the presence of a cancer. These make the correct application of serum tumour markers and the correct interpretation of test results difficult. Therefore, ordering an appropriate serum tumour marker for the appropriate purpose and correct interpretation of test results needs understanding of their properties and relevant cancers and noncancerous conditions in which their concentration increases. This review aims to facilitate a better understanding of serum tumour markers to ensure their optimal and justified application and accurate interpretation of test results.

Introduction:

Serum tumour markers are soluble molecules produced by tumour cells or by nontumourous cells under the influence of a tumour and are released into the blood or body fluids. Under the physiological conditions, a trace amount is produced by various tissues. Large amounts are produced in individuals suffering from malignant and some nonmalignant tumours. Hence, a high concentration of these molecules in the blood indicates the presence of a tumour[1–4]. Generally, their concentration in the blood rises with the increase of the tumour burden and tumour progression, drops with the decrease of the tumour burden and returns to a normal physiological level when the tumour regresses completely. Therefore, measurement of their concentration in blood can be utilised to monitor the clinical course of cancers and to assess the effectiveness of cancer treatment[1,2,5]. Serum tumour markers are effective in detecting tiny masses of cancerous tissue before they become detectable by imaging techniques. Thus, they are useful in monitoring cancer recurrence during follow-up after remission. In addition, serum tumour marker tests are cost-effective and minimally invasive. For these reasons, they have been used in clinical practice for many decades[6–9].

An ideal serum tumour marker is expected to be highly sensitive so that its concentration rises in the early stages of cancer. It is also expected to be highly specific so that its concentration rises only in the presence of a specific cancer, and does not rise in other cancers, benign tumours or non-tumorous diseases[10,11]. In reality, serum tumour markers are not sensitive enough to detect early cancers, e.g., CEA is usually normal in early colorectal cancer, CA 125 is usually normal in early ovarian cancer, and CA 15-3 is usually normal in early breast cancer. They may not be expressed by some individuals, e.g., CA 19-9 is not expressed in Lewis a/b negative individuals, which constitute 3-7% of the population[12–16]. Hence, the normal concentration of serum tumour markers cannot exclude the presence of cancer. None of the serum tumour markers is specific for a particular cancer. A serum tumour marker concentration may rise in many cancers, many benign tumours, some non-tumourous diseases, and even in some physiological conditions[2,4,17–20]. Thus, a raised serum tumour marker concentration does not always mean the presence of a particular cancer or even the presence of a cancer. Serum tumour marker concentration and/or change in the concentration may also be affected by the blood supply of the tumour, necrosis or lysis of tumour cells, and excretion by the kidneys[2]. The rise of serum tumour marker concentration in some tumours may be very high, while in other tumours the rise is mild[19]. So, all the conditions in which a particular serum tumour marker may rise and how much it has increased should be considered for the correct ordering of a tumour marker test and the correct interpretation of the test result. Therefore, understanding the properties of individual serum tumour markers, conditions in which the concentration of a serum tumour marker rises, and relevant cancers is necessary to ensure their optimal use and accurate interpretation of test results. This review will address these issues on some commonly used serum tumour markers to facilitate a better understanding.

Purposes of Application of Serum Tumour Markers in Cancer Management

In cancer management, serum tumour markers are primarily used to monitor treatment response and detect recurrence. They are also used to predict the prognosis and are rarely used for screening, making diagnosis and staging of cancers[20–23].

Screening: Serum tumour markers are generally not suitable for cancer screening because of their low sensitivity and low positive predictive value, particularly in early-stage cancers. However, they can be used for screening in the following circumstances: (i) PSA in the screening of prostate cancer in men over 50 years of age, (ii) AFP in individuals at increased risk of hepatocellular carcinoma (HCC) e.g., liver cirrhosis or chronic hepatitis due to hepatitis B virus (HBV) or hepatitis C virus (HCV) infection[2,19,24,25].

Diagnosis: Diagnosis of cancers is made from clinical findings, imaging studies and peroperative findings and is confirmed by histological (for solid tumours) or cytological (for leukaemias) findings. Serum tumour markers often aid in the diagnosis of some cancers. In a few instances they are used to make a diagnosis e.g., (i) in patients with cirrhosis of the liver and a focal lesion >2 cm in diameter with arterial hypervascularisation, serum AFP level >200 ng/mL is considered suggestive of HCC and biopsy is not necessary, (ii) highly raised serum AFP &/ beta subunit of hCG (b-hCG) in individuals at increased risk of germ cell tumours (e.g. patients with undescended testis) suggests diagnosis of germ cell tumours, (iii) b-hCG is used for diagnosis of choriocarcinoma and other gestational trophoblastic diseases (GTD) without need of histological evidence, and (iv) CA 19-9 can complement diagnosis of pancreatic cancer[14,19–23,25–27].

Prognosis: A relationship exists between the prognosis of some tumours and pre-treatment concentration of serum tumour markers, e.g., germ cell tumours and AFP + b-hCG, colorectal cancer and CEA, breast cancer and CA 15-3, ovarian cancer and CA 125. Very high levels are generally associated with an advanced stage and poor prognosis. Normal or slightly elevated levels are more likely to have prolonged recurrence-free intervals. Half-life of serum marker after treatment may indicate prognosis in some tumours, e.g., longer half-life of AFP + -hCG in germ cell tumours may indicate poor prognosis[13,15,19,21,22].

Monitoring treatment response: Serum tumour markers are most commonly used to assess the effectiveness of the cancer treatment and to monitor the clinical course of the cancer after treatment. Almost all serum tumour markers can be used for this purpose. To monitor the treatment response, it is necessary to measure the serum

tumour marker concentration before starting treatment and serial measurements after treatment to see whether it is decreasing or increasing. The post-treatment decline of a pre-treatment elevated serum tumour marker indicates that the treatment was effective. If it decreases, the serum half-life of the marker and the time required to decline to a reference level should be noted. It may provide a clue to the clinical course and prognosis. Too little or no decline suggests incomplete resection, the presence of multiple tumours, or non-response. Sometimes, serum tumour markers may rise transiently after chemo or radiotherapy due to tumour cell lysis[2,11,12,17,18].

Detecting recurrence: Serum tumour markers are valuable noninvasive tools for detecting cancer recurrence after remission, e.g., CEA is used for detecting recurrence of colorectal cancer, CA 19-9 for pancreatic cancer, CA 15-3 for breast cancer, and PSA for prostate cancer. They can detect recurrence before it becomes detectable by imaging[2,11,17,18].

Staging: Serum tumour markers are not generally used for staging of cancers. However, PSA is included in the staging of prostate cancer with clinical (TNM) staging and histological grading[21,24].

Properties of Serum Tumour Markers and Application in Cancer Management

Alpha-fetoprotein (AFP)

AFP is a glycoprotein produced at high concentration by the foetal liver and yolk sac. It acts as a carrier protein until an adequate amount of albumin is synthesised in the foetus. Its synthesis during the G1 and S phase of the cell cycle indicates its role in cell growth regulation. It crosses the placenta to enter maternal circulation, possibly to protect the foetus from rejection by the mother's immune system[28–30]. At birth, its serum concentration is about 70 ng/mL. It drops markedly immediately after birth and becomes 10-20 ng/mL by the age of one year[21,22]. It drops further with age. In healthy adults, serum AFP concentration is <10 ng/mL[19]. Its serum half-life is 4-6 days[2,7]. Serum AFP level rises primarily in HCC and non-seminomatous germ cell tumours (NSGCT). It also increases in some other malignant tumours, benign diseases and physiological conditions[19,21,22,31–34]. These are listed in Table 1.

In HCC and NSGCT, serum AFP levels rise to very high levels, often exceeding 1000 ng/mL. Its concentration increases in other cancers like gastric, biliary, pancreatic or colon cancer, but usually remains <1000 ng/mL. In cirrhosis of the liver, the rise usually does not exceed 500 ng/mL. In acute viral hepatitis, the rise is mild and transient. In hereditary increase and ataxia-telangiectasia, the AFP rise is mild but persistent[19,21,22,32,35,36].

AFP is used for monitoring treatment response, predicting prognosis and detecting recurrence of HCC. Along with imaging, it may be used for screening and diagnosis of HCC in high-risk individuals. Along with b-hCG, it is used for monitoring treatment response, detecting recurrence and predicting prognosis of NSGCT. AFP and b-hCG may also be used for early diagnosis of NSGCT in individuals at risk of germ cell tumours. AFP increases in other cancers, but is rarely used for them[19,21,31,34,37].

Carcinoembryonic antigen (CEA)

CEA is a glycoprotein produced at high concentration by the endodermal epithelium of foetal gastrointestinal tissue, particularly colorectal mucosa, gastric mucous

Table 1: Conditions in which increased serum AFP concentration is found

Primary tumour(s)	Other associated tumour(s)	Non-tumourous diseases(s)	Physiological condition(s)
Hepatocellular carcinoma	Gastric cancer	Cirrhosis of the liver	Pregnancy
	Biliary cancer	Viral hepatitis	Age <1 year
Germ cell tumours*	Pancreatic cancer	Ataxia-telangiectasia	Age >40 years
	Colorectal cancer	Hereditary increase	
	Hepatoblastoma		

*Serum AFP concentration increases in histologically yolk sac tumours or embryonal cell carcinoma (NSGCT) and remains normal in choriocarcinoma, teratoma, seminoma, and dysgerminoma.

Table II : *Conditions in which increased serum CEA concentration is found*

Primary tumour(s)	Other associated tumour(s)	Non-tumourous diseases(s)	Other condition(s)
Colorectal cancer	Pancreatic cancer	Peptic ulcer	Smoking
Secondary liver cancer	Breast cancer	Cirrhosis of the liver	
	Ovarian cancer*	Pancreatitis	
	Gastric cancer	Biliary obstruction	
	Oesophageal cancer	Inflammatory bowel disease	
	Lung cancer	Hypothyroidism	
	Medullary thyroid carcinoma		
	Bladder cancer		
	Head & Neck cancers		
	Lymphoma		
	Cervical cancer		

*Mainly in mucinous-type epithelial ovarian cancer

cells, sweat glands and vaginal epithelium. It is involved in cell adhesion, proliferation and migration[21,38]. After birth, only a trace amount is produced by the colonic epithelial cells and therefore its concentration drops[38–41]. In healthy adults, its serum concentration is <5 ng/mL. Its serum half-life is 2-8 days[2,21]. Its serum concentration increases primarily in colorectal cancer and secondary liver cancer. Its concentration may rise in many other cancers and some benign conditions[21,38,42–44]. These are listed in Table 2.

CEA elevation is more commonly found in late-stage and metastatic cancers than in early-stage. It increases steadily with the progressive increase of tumour burden. Therefore, serial measurement of CEA over time is more important than a single measurement. In malignant diseases, it frequently increases to greater than 8-10-fold of the upper limit of baseline. In benign diseases, elevation is usually mild[38].

It is mainly used for detecting recurrence of colorectal cancer after curative treatment. It is also used for monitoring treatment response and predicting the prognosis of colorectal cancers[21,45–47]. Along with imaging, it is used for the diagnosis of secondary (metastatic) liver cancer. It is found highly elevated in secondary liver cancer from the colorectal and pancreatic primary[38,48]. Along with CA 15-3, it can be used for monitoring treatment response and predicting the prognosis of breast cancer[49,50]. Along with CA 19-9, it can be used for making diagnoses, predicting prognosis, and monitoring treatment response of pancreatic cancer[51].

Human Chorionic Gonadotrophin (hCG)

Human chorionic gonadotrophin is a glycoprotein hormone mainly produced by syncytiotrophoblast and, to some extent, by cytotrophoblast cells of the placenta to support pregnancy. A trace amount is also produced by the pituitary gland, which mimics luteinizing hormone functions[20,52,53]. An intact hCG molecule is composed of two subunits, an a-subunit and a b-subunit held together by non-covalent bonds. These subunits are antigenically distinct. During pregnancy, this hormone is found in serum mainly as intact hCG, and a small amount as free a-subunit and free b-subunit[54,55]. Its a-subunit shares epitopes with follicle-stimulating hormone, luteinizing hormone and thyroid-stimulating hormone, but the b-subunit does not. Therefore, to avoid cross-reactivity and false-positive test results, available immunoassays usually measure b-subunit either as a total b-hCG test (b-subunit in intact hCG plus free b-hCG) or a free b-hCG test. Free b-hCG is mainly produced by nontrophoblastic malignant cells, which support the growth of the tumour. Total b-hCG test is preferred for gestational trophoblastic diseases (GTD), whereas the free b-hCG test is preferred for nontrophoblastic tumours like germ cell tumours of testis, ovary or extragonadal site[55–59]. In men and non-pregnant premenopausal women, serum concentration of hCG is usually <5 mIU/mL. In postmenopausal women, its serum level is slightly higher but usually <10 mIU/mL[37]. Its serum half-life is 1-2 days[7]. As it is produced mainly by placental cells, its concentration increases during pregnancy. If pregnancy is excluded, an increased serum hCG level generally indicates the presence of a tumour[37].

Table III: Conditions in which increased serum b-hCG concentration is found

Primary tumour(s)	Other associated tumour(s)	Non-tumourous condition(s)	Physiological condition(s)
Gestational trophoblastic neoplasms (GTN)	Hydatidiform mole and other benign GTDs	Hypogonadism	Pregnancy
	Gastric cancer	Renal insufficiency	Menopause
Germ cell tumours*	Colorectal cancer	Marijuana use	
	Pancreatic cancer		
	Lung cancer		
	Epithelial ovarian cancer		
	Breast cancer		
	Renal cell carcinoma		
	Epithelial ovarian cancer		
	Cervical cancer		

*Serum b-hCG concentration increases in certain histological types, e.g., embryonal cell carcinoma and choriocarcinoma. Occasional minimal increase may occur in seminoma and dysgerminoma. Concentration remains normal in the yolk sac tumour and teratoma.

Primary tumours in which its concentration increases are gestational trophoblastic neoplasms (GTN), benign GTDs, and germ cell tumours[21,37,60]. Its concentration increases in other malignant and non-malignant tumours, some benign nontumorous diseases and physiological conditions[21,37,69,61–68]. These are listed in Table III.

In clinical oncology practice, b-hCG is commonly used for pre-evacuation diagnosis, monitoring treatment response and clinical course, and detecting recurrence of GTN and GTD. Along with AFP, it is used for monitoring treatment response, assessing prognosis, detecting recurrence, and diagnosing of germ cell tumours in high-risk individuals. It is rarely used for other cancers[7,21,23,37,59]. In GTD and GTN, its concentration increases to a very high level. It may exceed 100,000 mIU/mL and may reach up to 1,000,000 mIU/mL. In germ cell tumours, it rarely exceeds 1000 mIU/mL. In other conditions, usually, there is a mild increase[7,21,37]. These should be considered while ordering the b-hCG test and interpreting the test result.

Cancer Antigen 125 (CA 125)

It was first captured and detected with the monoclonal antibody OC 125; therefore, it was named. It is a mucin expressed by the coelomic epithelium during foetal life. After birth, a trace amount is expressed by the epithelium of the ovary, fallopian tube, endometrium, endocervix, colon, stomach and mesothelial cells of serous membranes[13,70,71]. In healthy adults, serum concentration is usually <35 U/mL in females and <20 U/mL in males. Its serum half-life is 5 days[2,13,72]. Its serum concentration rises primarily in ovarian cancer. Its concentration also increases in other cancers, benign diseases and some physiological conditions[13,21,73–78]. These are listed in Table IV.

Table 4: Conditions in which increased serum CA 125 concentration is found

Primary tumour(s)	Other associated tumour(s)	Benign disease(s)	Physiological condition(s)
Ovarian cancer	Pancreatic cancer	Ovarian cysts	Pregnancy
	Endometrial cancer	Uterine fibroid	Menstruation
	Fallopian tube cancer	Endometriosis	
	Cervical cancer	Pelvic inflammatory disease	
	Oesophageal cancer		
	Gastric cancer	Cirrhosis of the liver	
	Colorectal cancer	Pleural effusion	
	Lung cancer	Peritonitis	
	Breast cancer	Acute pancreatitis	
	Hepatocellular carcinoma		

Among the histological types of epithelial ovarian cancer, it is frequently elevated in the serous type. It is also found elevated in undifferentiated and endometrioid types of ovarian cancer, but rarely in the mucinous type. It is elevated more commonly in advanced stages than in early stages of ovarian cancer[13,76]. It is used as a marker to assist in diagnosis, assessing prognosis, and monitoring treatment response and the clinical course of ovarian cancer. Along with transvaginal ultrasonography (TVS), it is often used for ovarian cancer screening in women with a strong family history. As it is not usually elevated in mucinous ovarian cancers, it is used along with CEA and CA 19-9 to increase sensitivity for ovarian cancer. It may be used as a marker for the diagnosis of pancreatic cancer along with CA 19-9[13,76,79].

Cancer Antigen 19-9 (CA 19-9)

It is a chemically glycolipid, a hapten of Lewis-a blood group antigen. It was first detected with monoclonal antibody 1116NS-19-9, hence the name[14]. Under physiological conditions, a trace amount is produced by the ductal cells of the pancreas, and epithelial cells of the biliary system, stomach, colon, uterus, and salivary glands during the synthesis of sialyl Lewis a[80,81]. In healthy individuals, its serum concentration is usually <37 U/mL, and serum half-life is 4-8 days[2,14]. Its concentration primarily increases in pancreatic cancer. Its concentration increases in other cancers, benign diseases and physiological conditions[7,14,21,44,82]. These are listed in Table 5. As its concentration increases in many gastrointestinal cancers, it is also called gastrointestinal cancer antigen (GICA)[14].

In pancreatic cancer, its rise is gradual and persistent and frequently exceeds 1000 U/mL and may reach 100000 U/mL. In other cancers, its concentration rises but usually remains <1000 U/mL. In benign disease with elevated CA 19-9, its concentration is usually <100 U/mL. In physiological conditions, its rise is mild and often transient[14,21].

CA 19-9 is primarily used as a marker for early diagnosis, assessment of prognosis, monitoring treatment response, and detecting recurrence of pancreatic cancer[14,80,81]. It is also used to aid in diagnosis and to monitor treatment responses in biliary tract and gastric cancers. Along with CEA, it may be used for aiding diagnosis, assessing prognosis, and monitoring treatment response in colorectal cancer and along with CA 125 in epithelial ovarian cancer[14,83–85].

Cancer Antigen 15-3 (CA 15-3)

It was first detected by two monoclonal antibodies, 115D8 and DF3, which bind to its two epitopes, hence the name. It is mucin, produced by the alveolar and ductal cells of the breast and endometrial epithelial cells. Its physiological role is protection and lubrication. Its serum concentration in healthy adults is <30 U/mL, and serum half-life is 5-7 days[2,15,86]. Its concentration increases primarily in breast cancer. Its concentration increases in many other cancers and benign conditions[15,87–89]. These are listed in Table VI.

Table V: Conditions in which increased serum CA 19-9 concentration is found

Primary tumour(s)	Other associated tumour(s)	Non-tumourous disease(s)	Physiological condition(s)
Pancreatic cancer	Colorectal cancer	Pancreatitis	Pregnancy
	Oesophageal cancer	Biliary diseases	Menstruation
	Gastric cancer		
	Biliary tract cancer		
	Ovarian cancer*Lung cancer		
	Breast cancer	Cirrhosis of the liver	
	Hepatocellular carcinoma	Diabetes mellitus	

*Mainly in mucinous-type epithelial ovarian cancer

Table 6: *Conditions in which increased serum CA 15-3 concentration is found*

Primary tumour(s)	Other associated tumour(s)	Benign disease(s)
Breast cancer	Ovarian cancer	Mastopathy
	Endometrial cancer	Fibroadenoma of the breast
	Gastric cancer	Renal insufficiency
	Pancreatic cancer	Chronic liver disease
	Biliary tract cancer	HIV infection
	Lung cancer	Tuberculosis
	Prostate cancer	Rheumatic diseases
	Hepatocellular carcinoma	

CA 15-3 concentration rises mainly in advanced breast cancer and rarely in early-stage breast cancer. Therefore, it is not suitable for screening. As it increases in many other cancers. It is not suitable for diagnosis or screening. It is primarily used for assessing prognosis, monitoring treatment response and clinical course, and detecting recurrence of breast cancer[15,90,91]. The use of CA 15-3, along with CEA, increases sensitivity in detecting the presence of localised breast cancer and its recurrence and metastasis after treatment[15].

Cancer Antigen 72-4 (CA 72-4)

It is a mucin-like glycoprotein initially identified by monoclonal antibodies B72.3 and CC49 on the cell surfaces of certain cancer cells. It was initially named tumour-associated glycoprotein 72 (TAG-72) and later CA 72-4. Under physiological conditions, a trace amount is released from the endometrial and colonic mucosa. Consequently, its high expression indicates the presence of a tumour[92,93]. In healthy adults, its serum concentration is <6 U/mL[93]. Its serum half-life is 3-7 days[2].

It is mainly elevated in gastric and ovarian cancers. It is found elevated in some other cancers. It may be elevated in a very low percentage of some benign diseases, which makes it a good choice as a tumour marker[92–94]. These are listed in Table VII.

It is mainly used as the first-line marker for monitoring treatment response and clinical course of gastric cancer, along with the second-line markers CEA or CA 19-9. It may aid in the diagnosis and prognosis of gastric cancer[93–96]. It is used as the second-line marker of ovarian cancer, along with the first-line marker CA 125, because of its high sensitivity for mucinous-type epithelial ovarian cancer[93,94,97]. It is also used as an aid in diagnosis and monitoring response for colorectal cancer, along with CEA[98–100].

Table 7: Conditions in which increased serum CA 72-4 concentration is found

Primary tumour(s)	Other associated tumour(s)	Non-tumourous disease(s)
Gastric cancer	Ovarian cancer	Pancreatitis
	Colorectal cancer	Cirrhosis of the liver
	Pancreatic cancer	Ovarian cysts
	Oesophageal cancer	Benign breast diseases
	Lung cancer	Rheumatic diseases
	Breast cancer	Pulmonary diseases

Prostate Specific Antigen (PSA)

It is a glycoprotein primarily synthesised by the acinar and ductal cells of the prostate. It is mainly released into the prostatic ductal system as a component of semen. Its function is to prevent semen coagulation. A small amount is released into the circulation. It is released in large amounts into the prostatic stroma. Therefore, it reaches the circulation when there is disruption of the prostatic structure by tumours, trauma, or inflammation. In blood, it remains mainly as complex PSA (cPSA) bound to a1-antichymotrypsin and a2-macroglobulin. A small amount remains as unbound free PSA (fPSA). Complex and free PSA together constitute total PSA. Serum concentration of total PSA in healthy adult males is <4 ng/mL. Its serum half-life is 2-3 days[2,24]. A small amount of PSA is also synthesised by male and female periurethral and perianal glands and female breast cells(101). Its concentration increases primarily in prostate cancer. In prostate cancer, its concentration rises >10 ng/mL. Its concentration increases in breast cancer and many noncancerous conditions. In breast cancer, PSA is mainly found as fPSA[7,21,24,102]. These are listed in Table 8. In benign diseases, its concentration is usually 4- 10 ng/mL[24].

PSA is mainly used for monitoring treatment response, clinical course, and recurrence of prostate cancer. It is also used for screening and supplementing the staging of prostate cancer[21,24,103].

Human Epididymis Protein 4 (HE4)

It is a glycoprotein first identified in the epithelial cells of the epididymis, where it helps in spermatogenesis. Later, it was found to be expressed in the tissues of the lung, breast, salivary gland, prostate and endometrium[104]. It is over-expressed and secreted into the circulation in ovarian cancer, some other cancers and some benign diseases[105,106]. These are listed in Table 9.

It is used for monitoring treatment response and assessing the prognosis of ovarian cancer. It may also be used for screening of ovarian cancer[105,107]. HE4 is used along with CA 125 in the Risk of Ovarian Malignancy Algorithm (ROMA), which helps to distinguish malignant from benign pelvic masses. The clinical utility of ROMA has been demonstrated in both pre- and postmenopausal women[108–111]. It may also be used for detecting recurrence of endometrial cancer[104].

Pepsinogen I and Pepsinogen II

Pepsinogen I (PG I) and pepsinogen II (PG II) are two immunologically distinct precursors of pepsin[112]. PG I is synthesised predominantly by the chief cells of the stomach fundus, while PG II is by the mucous cells of the cardiac and pyloric part of the stomach and duodenum. Most PG I and PG II are secreted into the stomach, and a small portion enters the bloodstream[113,114]. The serum concentration of PG I is 28- 100 ng/mL, and PG II is 3-50 ng/mL, and the PG I/PG II ratio is >3 in healthy adults[112,115]. Changes in the

Table 8: Conditions in which increased serum PSA concentration is found

Primary tumour(s)	Other tumour(s)	Other disease conditions(s)	Physiological condition(s)
Prostate cancer	Breast cancer	Prostatitis	After ejaculation
		Benign prostatic hyperplasia	
		Prostatic trauma	

Table 9: Conditions in which increased serum HE4 concentration is found

Primary tumour(s)	Other associated tumour(s)	Nontumourous disease(s)
Ovarian cancer	Endometrial cancer	Endometriosis
	Cervical cancer	Renal failure
	Vulvar cancer	
	Lung cancer	
	Colorectal cancer	

serum concentration of PG I and PG II provide an idea about the integrity and function of gastric glands. The serum concentration of both PG I and PG II increases with *Helicobacter pylori* infection, gastric erosion, and peptic ulcer. PG I drops if this infection progresses to chronic gastritis, gastric atrophy or gastric cancer while PG II concentration remains high. As a result, the PG I/ PG II ratio decreases in atrophic gastritis, gastric epithelial dysplasia, metaplasia and gastric cancer[113,114,116]. Therefore, the measurement of serum PG I and PG II and calculating the PG I/PG II ratio is valuable for screening and diagnosis of gastric cancer[117–120].

Thyroglobulin (TG)

Thyroglobulin is a glycoprotein produced by the follicular cells of the thyroid gland. It is the precursor of the hormones triiodothyronine (T3) and thyroxine (T4). A small amount of TG is released into the blood. Under physiological conditions, its serum concentration may be up to 50 ng/mL[121]. Its serum half-life is about 65 hours. Serum TG is used as a marker for monitoring the success of treatment and detecting recurrence of papillary and follicular thyroid carcinomas[122].

Calcitonin (CT)

Calcitonin is a polypeptide hormone synthesised by the parafollicular (C) cells of the thyroid gland. Its serum concentration in healthy adult males is 2-48 ng/L, and in females is 2-10 ng/L[123]. Its serum half-life in healthy individuals is about 10 minutes[124]. It is used for diagnosis, monitoring treatment response, and detecting the recurrence of medullary thyroid carcinoma (C-cell carcinoma). In medullary thyroid carcinoma, serum concentration of CT may increase 10-10,000 fold. Postoperatively CT level returns to the baseline within hours. Postoperative persistence of elevated CT indicates incomplete resection or the presence of metastasis[123].

Cancers and Application of Serum Tumour Markers

In clinical oncological practice, patients present with a cancer and oncologists have to decide whether a serum tumour marker will help in its management or not. A decision is needed regarding which serum tumour marker or combination of markers to order and for what purpose. Some common cancers, and the names of serum tumour markers that can be used in their management and the purposes of their application are listed in Table 11.

Table X: Conditions in which a raised serum TG concentration is found

Primary tumour(s)	Other associated tumour(s)	Non-tumourous disease(s)
Papillary thyroid carcinoma	Benign thyroid nodules	Graves' disease
Follicular thyroid carcinoma		Hushimoto thyroiditis
		Iodine deficiency
		Physical trauma to the thyroid gland

Table XI: *Cancers and application of serum tumour markers*

Cancer	Serum Tumour Marker	Purpose of application
Primary liver cancer (HCC)	AFP	Monitoring treatment responsePredicting prognosis Detecting recurrenceScreening (along with imaging)Diagnosis (along with imaging)
Secondary liver cancer	CEA	Diagnosis (along with imaging)Monitoring treatment response
Germ cell tumours	AFP + b-hCG	Monitoring treatment responseDetecting recurrencePredicting prognosisDiagnosis in high-risk individuals
GTN and GTD	b-hCG	Pre-evacuation diagnosisMonitoring treatment responseMonitoring clinical courseDetecting recurrence
Colorectal cancer	CEA	Detecting recurrence Monitoring treatment responsePredicting prognosis
	CA 19-9 (along with CEA)	Monitoring treatment response and predicting prognosis

Table XI: *Cancers and application of serum tumour markers (Cont'd)*

Cancer	Serum Tumour Marker	Purpose of application
Pancreatic cancer	CA 19-9	Making a diagnosisPredicting prognosisMonitoring treatment response Detecting recurrence
	CEA (along with CA 19-9)	An aid in making diagnosis, predicting prognosis and monitoring treatment response along with CA 19-9
	CA 125 (along with CA 19-9)	An aid in making a diagnosis
Ovarian cancer	CA 125	Monitoring treatment responsePredicting prognosis ScreeningAn aid in making a diagnosis (along with TVS)ROMA (along with HE4) to differentiate benign from malignant pelvic mass
	CEA (mucinous type)	Monitoring treatment responseDetecting recurrence
	CA 19-9 (along with CA 125)	Monitoring treatment response As an aid in the diagnosis
	HE4	Monitoring treatment responsePredicting prognosisROMA (along with CA 125) to differentiate benign from malignant pelvic mass
Breast cancer	CA 15-3	Monitoring treatment responsePredicting prognosisDetecting recurrence
	CEA	Monitoring treatment responsePredicting the prognosis along with CA 15-3
Prostate cancer	PSA	Monitoring treatment responsePredicting prognosisDetecting recurrenceScreening in men over 50 yearsAs a component in staging
Gastric cancer	CA 72-4	Monitoring treatment response and clinical course
	CEA (along with CA72-4)	Monitoring treatment response
	PG I and PG II	ScreeningDiagnosis
Papillary thyroid carcinoma	Thyroglobulin	Detecting recurrence and Monitoring treatment response
Follicular thyroid carcinoma	Thyroglobulin	Detecting recurrence and Monitoring treatment response
Medullary thyroid carcinoma	Calcitonin	Monitoring treatment responseDetecting recurrence
	CEA (along with calcitonin)	Monitoring treatment response along with calcitonin

Conclusion

Serum tumour markers are less expensive and noninvasive tools for the detection of the presence of cancers. They can detect the presence of a tiny mass of cancerous tissue that may not be detectable by imaging or other techniques. But they have low sensitivity in the early-stage cancers and low specificity. Therefore, they should be applied, and their results should be interpreted cautiously and purposefully to ensure the best utilisation of these cancer management tools.

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