

## Inflammatory Breast Cancer: Challenges and Opportunities in the Management

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### Abstract

**Background:** Inflammatory Breast Cancer (IBC) is a rare and highly aggressive form of breast cancer characterized by rapid onset, inflammatory changes in the breast, and a poor prognosis. Its management requires a multidisciplinary approach due to its aggressive nature and diagnostic challenges. **Objective:** The objective of this study is to comprehensively evaluate the management of Inflammatory Breast Cancer at the Cancer Centre, CMH Dhaka, and Border Guard Bangladesh (BGB) Hospital in Dhaka, focusing on clinical presentation, diagnostic methods, treatment strategies, and patient outcomes. **Methods:** This prospective study included patients who presented with Inflammatory Breast Cancer at CMH, Dhaka and BGB Hospital Dhaka Cancer Centre over a specified period from June 2021 to June 2023. **Results:** The study revealed that IBC continues to pose significant diagnostic challenges, often leading to delayed treatment initiation. Among the studies, a total of N=13 patients were managed within the past two years, and the prognosis remained unfavorable. Even after receiving neoadjuvant chemotherapy, a patient passed away from the illness within half a year of being diagnosed. Physical examinations consistently identified signs of inflammation, with skin changes in 54% of cases and palpable masses in 85%. Hormone receptor status revealed 23% of patients with triple-negative breast cancer (TNBC), while 31% were HER2 positive. Molecular classification showed that 31% belonged to the Luminal type-A category, and 31% were HER2 positive. **Conclusion:** Inflammatory Breast Cancer management at CMH, Dhaka and BGB Hospital, Dhaka, underscores the critical need for early detection and a multidisciplinary approach. The aggressive nature of IBC, coupled with diagnostic uncertainties, highlights the importance of a high clinical suspicion. To improve patient outcomes, timely and comprehensive management by a multidisciplinary team is imperative. This study highlights the complexity of IBC and underscores the importance of early intervention and holistic patient care despite the challenges faced.

**Keywords:** Inflammatory breast cancer (IBC), Neo-adjuvant chemotherapy (NACT).

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## INTRODUCTION

Inflammatory Breast Cancer (IBC), often referred to as the most aggressive form of breast cancer, has long captivated the attention of researchers and oncologists due to its unique and devastating characteristics. First documented by Cho, Chang Geun in 1998 as a malignancy characterized by "a purple color on the skin over the tumor, accompanied by shooting pain," [1]. IBC has since been a subject of intense study and clinical exploration. Its distinct clinical features and poor prognosis have made it a formidable adversary in the realm of oncology.

The term "Inflammatory Breast Cancer" itself was formally introduced by Lee and Tannenbaum, marking a pivotal moment in the understanding and classification of this aggressive subtype [2]. IBC

represents a relatively small fraction of all breast cancer cases but stands out due to its rapid progression, distinctive clinical presentation, and formidable challenges in diagnosis and management.

One of the defining characteristics of IBC is its aggressive nature. Unlike other forms of breast cancer, IBC often presents with sudden and dramatic changes in the breast, such as redness, swelling, warmth, and an orange-peel-like appearance of the skin, a phenomenon known as "peau d'orange." These clinical manifestations can occur within a matter of weeks, and the rapid onset of symptoms can lead to delays in diagnosis and treatment initiation. The urgency of diagnosis cannot be overstated as IBC progresses swiftly, and its aggressiveness can result in a poorer prognosis.

Compounding the challenges of IBC is its association with poorer survival outcomes compared to non-IBC breast cancers. The aggressive behavior of IBC is not only limited to its clinical presentation but also extends to its impact on patient outcomes. Studies have consistently shown that women diagnosed with IBC experience shorter survival times and higher rates of metastasis compared to those with non-IBC tumors [3]. This grim reality underscores the urgency and critical importance of effectively managing IBC from diagnosis to treatment and beyond.

The management of IBC requires a multidisciplinary approach to comprehensively address its complex and aggressive nature. Typically, the treatment regimen involves a combination of neoadjuvant chemotherapy (NACT), ablative surgery, and locoregional radiotherapy. Neoadjuvant chemotherapy is administered to reduce the size of the tumor before surgery, and this approach has been shown to be effective in many cases [4, 5]. Ablative surgery aims to remove the tumor and affected breast tissue, while locoregional radiotherapy targets residual cancer cells in the breast and nearby lymph nodes.

In the study, Inflammatory Breast Cancer (IBC) stands as a formidable challenge in the field of oncology, characterized by its rapid onset, distinctive clinical presentation, and dismal prognosis. Its historical roots date back to the early 19th century when Sir Charles Bell first documented its unique features. The introduction of the term "Inflammatory Breast Cancer" by Lee and Tannenbaum marked a milestone in our understanding of this aggressive entity. Women diagnosed with IBC face a daunting battle, with poorer survival outcomes compared to their non-IBC counterparts. Given the gravity of the disease, ongoing research and clinical advancements are crucial in improving the prognosis and quality of life for individuals affected by IBC.

## OBJECTIVE

### General Objective

- This study will comprehensively investigate and enhance our understanding of Inflammatory Breast Cancer (IBC) and its management at the Cancer Centre, CMH Dhaka, and Border Guard Bangladesh (BGB) Hospital in Dhaka.

### Specific Objectives

- To evaluate the clinical presentation of IBC patients.
- To assess the diagnostic challenges associated with IBC.
- To analyze the pathological characteristics and hormone receptor status of IBC cases.
- To determine the outcomes of multidisciplinary treatment for IBC.

- To establish standardized protocols for the diagnosis and management of IBC.

## MATERIALS AND METHODS

### Study Design

This study employed a prospective observational approach conducted at the Cancer Centre, CMH Dhaka, and Border Guard Bangladesh (BGB) Hospital in Dhaka. The primary objective was to comprehensively assess the clinical presentation, diagnostic methods, and treatment modalities for Inflammatory Breast Cancer (IBC) within two years. A review of existing literature and publications on IBC was also conducted to draw comparisons and inform the study's findings.

### Patient Selection

The study enrolled patients diagnosed with IBC who received treatment at CMH, Dhaka and BGB Hospital Dhaka's Cancer Centre over the preceding two years. A total of 13 cases of IBC were included in the study cohort. Patient data was sourced from various records, including medical charts, clinical notes, radiological and pathology reports, and surgical records. Detailed information was extracted about the clinical presentation of IBC, diagnostic procedures employed, and the specifics of treatment regimens.

### Inclusion Criteria

- Patients diagnosed with Inflammatory Breast Cancer (IBC) at the Cancer Centre, CMH Dhaka, and Border Guard Bangladesh (BGB) Hospital in Dhaka in the last two years.
- Evidence of invasive carcinoma from a breast core biopsy.
- Rapid onset of breast erythema, edema, or peau d'orange appearance.

### Exclusion Criteria

- History of other breast cancer types.
- Previous breast cancer treatment.
- Incomplete medical records.
- Contraindications to standard IBC treatments.

The literature review encompassed a thorough examination of published research, peer-reviewed studies, clinical guidelines, and relevant Inflammatory Breast Cancer (IBC) articles. This comprehensive analysis provided a contextual backdrop for the study's findings. The primary study objectives included elucidating the unique clinical presentation of IBC, evaluating diagnostic approaches, assessing multifaceted management strategies, comparing study data with existing literature, and proposing a standardized protocol for IBC diagnosis and treatment based on study outcomes and insights from the literature review.

### Epidemiological Review

The initial phase of the study included a review of epidemiological data related to IBC, underscoring the prominence of breast cancer as the second leading cause of cancer-related death among women, with IBC constituting 2.5% of breast cancer cases. Furthermore, the study acknowledged the suboptimal median survival rate of less than four years for individuals diagnosed with IBC, even when subjected to multimodal therapeutic interventions [10].

### Risk Factors Assessment

An exploration of risk factors associated with IBC was undertaken, encompassing variables such as age at menarche, age at first live birth, menopausal status, ethnicity, socioeconomic status, and body mass index (BMI). The relevance of these factors within the local context was assessed.

### Clinical Characteristics

The study distinguished between primary and secondary IBC, with primary IBC signifying the development of breast carcinoma in previously

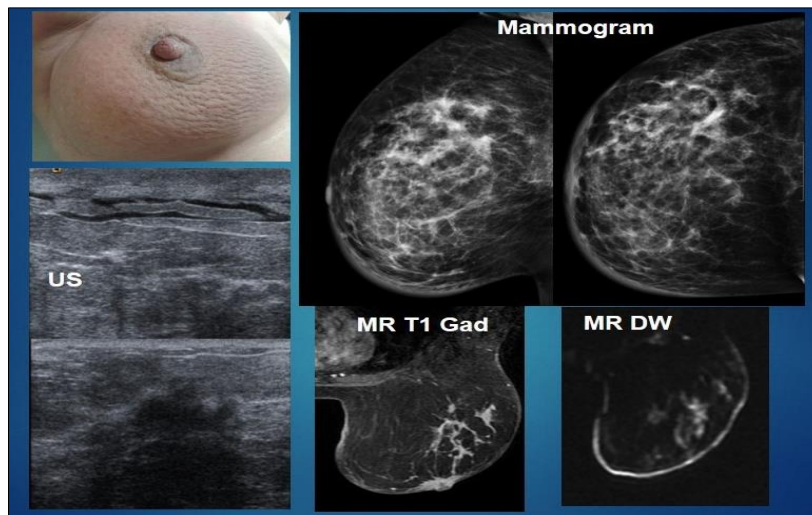
unaffected breast tissue and secondary IBC denoting inflammatory skin changes in conjunction with invasive breast carcinoma in a breast with a pre-existing malignancy or in the chest wall post-mastectomy for non-inflammatory breast carcinoma.

### Diagnostic Criteria

The study established the fundamental diagnostic criteria for IBC, including a history of rapid-onset symptoms, clinical examination findings, and histopathological confirmation of invasive carcinoma through core biopsy. The importance of full-thickness skin biopsy to confirm dermal lymphovascular tumor emboli was underscored.

### Diagnosis and Staging

The diagnostic process for IBC was delineated, encompassing history and physical examination, mammography, and advanced imaging modalities such as ultrasonography, magnetic resonance imaging (MRI), and positron emission tomography/computed tomography (PET/CT). The staging was performed according to the AJCC TNM classification system.



**Figure 1: Inflammatory Breast Cancer**

The diagnosis can be made by core biopsy if a breast mass is present. A full-thickness skin biopsy should also be obtained if IBC is suspected since a hallmark of this disease is dermal lymphatic invasion by tumor cells.

- The AJCC tumor–node–metastasis (TNM) system for the staging of IBC [10] designates IBC as follows:
- IBC is defined as T4d
- N staging will depend on the presence of involvement of nodes
- So, patients with non-metastatic disease are designated as stage II IB, and those with metastatic disease are designated as stage IV

### Management Strategies

The multifaceted approach to IBC management was elucidated, featuring primary systemic chemotherapy, surgery, and radiation therapy. The significance of primary systemic chemotherapy in downsizing the tumor before mastectomy was highlighted. The role of mastectomy, timing concerning chemotherapy, and the predictive value of initial chemotherapy response were emphasized.

The materials and methods adopted for this study encompassed a comprehensive data collection process from a study cohort of IBC patients, a thorough literature review, risk factor assessment, diagnostic and staging criteria, and an analysis of management strategies. These methodologies facilitated a holistic examination of IBC, informed by both patient data and

existing research, with the ultimate aim of contributing to developing a standardized diagnostic and treatment protocol.

**Data Collection**

We gathered data from 13 Inflammatory Breast Cancer (IBC) cases treated at the Cancer Centre, CMH Dhaka, and Border Guard Bangladesh (BGB) Hospital in Dhaka within the last two years. Patient records, clinical charts, and radiological and pathology reports were scrutinized for clinical presentations, diagnostic tests, and treatment history.

**Data Analysis**

Descriptive analysis was applied to summarize patient data, while a literature review compared findings with established knowledge. We assessed risk factors, diagnostic criteria, staging, and management strategies. We proposed a standardized protocol for IBC diagnosis and treatment based on these findings.

**Ethical Considerations**

Ethical clearances for this study were rigorously observed. Institutional Review Board (IRB) approval was obtained from Border Guard Bangladesh (BGB)

Hospital Dhaka, ensuring ethical compliance. All patients provided informed consent after being fully informed about the study's purpose and procedures. Patient privacy and data confidentiality were diligently maintained. The study adhered to regulations governing research conduct and patient rights. In literature reviews, proper citations and references were employed to acknowledge original authors. These ethical measures ensured the study's integrity, protected patient rights, and upheld research standards.

**RESULTS**

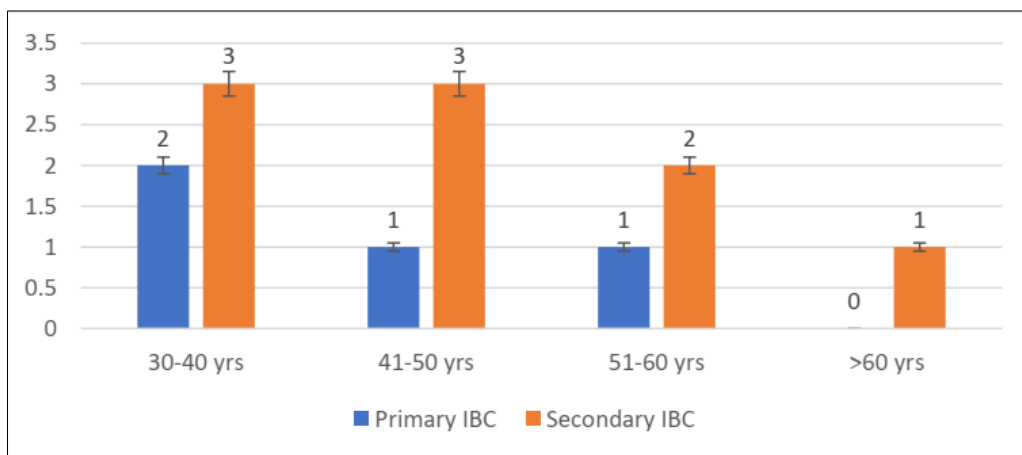
The results highlight the challenges and complexities associated with IBC, including its diagnostic dilemma and poor prognosis. Out of the 13 IBC cases managed in the past two years, one patient succumbed to the disease six months after diagnosis, showing no response to NACT. Another challenging case involved a pregnant patient diagnosed with secondary IBC. These findings emphasize the critical need for improved diagnostic approaches and effective treatment strategies for IBC, as well as the importance of regular follow-up and patient compliance in managing this aggressive form of breast cancer.

**Table 1: Demographic Data**

Age Group	Primary IBC	Secondary IBC
30-40 yrs	2	3
41-50 yrs	1	3
51-60 yrs	1	2
>60 yrs	0	1

Table 1 presents the distribution of patients based on age. The mean age of patients with Primary IBC

is approximately 43 years, while for secondary IBC, it is about 46 years.



**Figure 2: Demographic data in this study encompassed various factors**

Various factors related to the participants, providing insights into their backgrounds and characteristics. These data included age groups, with distinctions between patients aged 30-40, 41-50, 51-60, and those over 60. Additionally, the data distinguished

between primary IBC and secondary IBC cases within each age group. This demographic information is crucial for understanding the composition of the study cohort and how IBC may manifest in different age brackets.

**Table 2: Presenting Complaints of IBC**

Condition	Number	Percentage
Breast lump	11	85%
Skin change (puckering, dimpling, ulcer)	7	54%
Nipple change (discharge, retraction)	0	0%
Sign of inflammation (Redness, Edema, Warmth)	13	100%
Breast abscess-like features	1	2%

Table 2 reveals that the majority of IBC patients presented with a breast lump (85%), while all patients

exhibited signs of skin inflammation such as erythema, edema, and warmth.

**Table 3: Distribution of Patients According to Hormone Status**

Hormone Status	Number	Percentage
ER, PR Positive	4	31%
ER, PR Negative	6	46%
TNBC	3	23%
HER2 Positive	4	31%
HER2 Negative	6	46%

Table 3 illustrates the distribution of patients based on hormone receptor status. In the series, 3 patients (23%) were diagnosed with Triple Negative Breast

Cancer (TNBC), and 4 patients (31%) were HER2 positive.

**Table 4: Distribution of Patients According to Luminal Type**

Luminal Type	Number	Percentage
Luminal type – A	4	31%
Luminal type - B	2	15%
Basal-like/TNBC	3	23%
HER-2 Enrich	4	31%

Table-4 presents the distribution of patients according to luminal type. In the series, 4 patients (31%)

were classified as Luminal type - A, and 4 patients (31%) were HER2 positive.

**CLINICAL CASES**



**Figure 3: A 35-year-old patient presented as a case of secondary IBC (T4B N3 M0). After Neoadjuvant Chemotherapy (NACT), a simple mastectomy with axillary dissection was performed, and the patient is currently on regular follow-up.**



**Figure 4:** A 32-year-old presented as a case of primary IBC during her 16th week of pregnancy. After four cycles of NACT, the tumor showed a positive response, but the patient dropped out and did not undergo surgery. Later, after a normal vaginal delivery (NVD) at home, she presented with a large ulcer with maggots.

The outcome of IBC is very poor. It also has a diagnostic dilemma at presentation. We have managed 13(Thirteen) IBCs within the last two years. Among them, one died after 06 months of diagnosis, and the patient did not respond to NACT. It was a progressive disease. Another patient presented as 16 weeks pregnant with Ca-Breast and was diagnosed with secondary IBC.

## DISCUSSION

Inflammatory Breast Cancer (IBC) is characterized by its aggressive clinical features, including rapid onset, erythema, breast edema, and the characteristic "peau d'orange" appearance of the skin, often accompanied by positive metastatic lymph node involvement and, in some cases, distant metastasis at the time of diagnosis [6]. Our series reflects the aggressiveness of IBC, with one of three patients diagnosed with primary IBC succumbing to the disease within six months despite neoadjuvant chemotherapy (NACT) treatment.

The diagnostic criteria for IBC, initially proposed by Krone & Bernd in 2014, remain in use today. Haagensen's criteria stipulate that at least one-third of the breast must exhibit redness or edema for an IBC diagnosis. In his study, 85% of patients had tumors, 54% exhibited skin changes other than inflammation, and all patients displayed signs of inflammation, such as edema and warmth of the skin [7]. The lack of specificity in these criteria, coupled with frequent misdiagnoses as mastitis, contributes to delayed diagnosis and management of IBC. Additionally, women with neglected locally advanced breast cancer are often later diagnosed with IBC, highlighting the need for improved diagnostic precision [8]. The variability in diagnostic criteria across studies has also been recognized as a

significant factor contributing to differences in treatment outcomes.

Pathologically, the presence of dermal and stromal tumor emboli is a hallmark of IBC, leading to lymphatic obstruction and the characteristic inflammatory nature of the disease [9]. Dermal Lymphatic Invasion (DLI) contributes to lymphatic obstruction and is a key factor behind the high metastatic potential of IBC [10]. Some researchers advocate for skin punch biopsies as a standard requirement for diagnosing clinically suspected IBC [11]. However, studies have shown that despite adequate skin sampling, including examination of multiple tissue sections, DLI is identified in less than 75% of IBC patients, suggesting it is not an absolute diagnostic requirement [12].

Hormone receptor status plays a significant role in IBC, with a higher frequency of negative estrogen receptor (ER) and progesterone receptor (PR) status compared to non-IBC tumors [13]. Lack of hormone receptor expression is associated with a more aggressive clinical course and decreased overall survival among women with IBC tumors [14]. Moreover, IBC tumors exhibit a higher incidence of HER2 overexpression, though its prognostic significance remains uncertain compared to non-IBC tumors [15].

In our study, we observed a significant proportion of patients with triple-negative breast cancer (TNBC), HER2-positive, and HER2-negative disease, emphasizing the molecular heterogeneity of IBC and the need for personalized treatment approaches. Primary systemic chemotherapy is the standard treatment for all patients diagnosed with IBC, aimed at shrinking the tumor before surgical intervention [16]. Despite clinical

responses to treatment, residual disease may persist in the breast skin. Sentinel lymph node biopsy is not reliable for assessing axillary lymph nodes in IBC, necessitating a modified radical mastectomy as the definitive surgical approach following preoperative systemic treatment. Skin-sparing mastectomy is contraindicated, and breast-conserving approaches are typically explored within clinical trials. Radiation therapy following mastectomy is recommended, especially for women with HER2-positive disease, where trastuzumab may be administered concurrently with radiation therapy.

Post-treatment follow-up adheres to established guidelines, including regular physical examinations and mammograms. Extensive radiological imaging and laboratory work-up with tumor markers for early systemic recurrence detection are not recommended. Genetic screening is advisable for women with a strong family history of breast and ovarian cancer, in line with published guidelines [17-21].

In the study, IBC presents unique clinical and pathological challenges, underscoring the importance of a multidimensional approach to diagnosis and treatment. Early recognition, standardized diagnostic criteria, and tailored treatment strategies based on hormone receptor and HER2 status are crucial to improving outcomes for patients with this aggressive form of breast cancer. Ongoing research and collaborative efforts are essential to furthering our understanding of IBC and refining its management [18].

## CONCLUSION

Inflammatory Breast Cancer (IBC) is an exceptionally aggressive form of the disease, predominantly affecting young women. Its rapid progression, complex clinical presentation, and limited treatment options contribute to a poor prognosis. Despite advancements in therapy, IBC remains challenging to diagnose and manage effectively. Innovative treatments and a deeper understanding of their molecular characteristics are essential to improving outcomes for IBC patients. Collaborative research efforts are critical to addressing this urgent medical need and offering hope to those affected by this devastating cancer.

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