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REVIEW ARTICLE

INFLAMMATORY BREAST CANCER THE HIDDEN THREAT IN ONCOLOGY: A NARRATIVE REVIEW

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ABSTRACT

The understanding of inflammatory breast cancer (IBC) has advanced significantly since Dr. Haagensen established the initial diagnostic criteria in 1956 in the United States. Inflammatory breast cancer (IBC) is a rare and high destructive subtype of breast cancer, representing 1% to 6% of all breast cancer identifies, marked with rapid progression and an important tendency for metastasis, the manifesting with inflammatory symptoms in the breast that can lead to misdiagnosis as situations like mastitis. In clinically, diagnosis is based on physical signs like edema, erythema and along with histopathological evidence like dermal lymph vascular tumor emboli, and aggressive nature of IBC is evident in its poor prognosis, with survival rate five-year considerably lower than that of other breast cancer types, due to late-stage diagnosis when patients presents in advanced disease, recent progresses in the considerate of IBC have underscored the implication of its molecular characteristics in shaping treatment approaches, the embattled therapies, for HER2-positive cases, have demonstrated potential in enhancing patient outcomes when used in conjunction with neoadjuvant chemotherapy. But, the absence of standardized treatment procedures when tailored for IBC poses an important challenge, awareness of IBC increases, collaborative efforts across discipline are very important to improve early detection, and refine treatment strategies, ultimately to boost survival rates for those who are affected.

Keywords: Breast cancer, inflammatory breast cancer, diagnosis, challenges, survival

INTRODUCTION

Breast cancer continues to be a major public health issue, characterized by significant annual incidence rates. Forecasts for 2024 indicate that approximately 310,720 women will be diagnosed with invasive breast cancer. Also, about 56,500 new cases of ductal carcinoma in situ (DCIS), a non-invasive variant, were anticipated. The estimation of mortality rate for breast cancer in 2024 is 42,250 women, this disease represent about 30% of all new cancer diagnoses between women, making the most prevalent cancer in this group, excluding the skin cancers. The incidence rate is around 129.4 cases per 100,000 women yearly, showing a modest yearly increase of about 0.6% in recent years. In the overall, lifetime risk of developing breast cancer for women, estimated at 1 in 8, or roughly 13%, underscoring the critical need for awareness and early detection initiatives[1].

Breast cancer In European Union

Fuentes JDB, Morgan E et al. published a study in the European Union, breast cancer postures a considerable public health challenge, showing diverse incidence rates between its member states, in 2022, it was estimated, there were about 375,079 new cases of breast cancer in the EU-27, resulting in an age-standardized by incidence rate of 83.4 cases per 100,000 women. These accounts for approximately 29.4% of all cancer diagnoses in

women across the Europe. The incidence rates vary suggestively by region, with certain countries recording as many as 190 new cases per 100,000 women, these inconsistencies can be accredited to factors like differences in screening procedures and the prevalence of risk factors, counting maternal age at first childbirth and lifestyle habits. About mortality, it estimated that about 95,881 women submitted to breast cancer in 2022 within the Europe, leading to an age-standardized mortality rate of 14.9 per 100,000 women, the overall trends indicate a reduction in mortality rates in various areas, especially in Northern and Western Europe, which is largely due to improvements in early detection and treatment methodologies[2].

Middle East and North Africa (MENA)

Al-Shamsi HO et al. published a study, showing a significant increase in the incidence of breast cancer, as of 2022 the approximation rate was around 49 new cases per 100,000 individuals, in 2016, around 45,980 new breast cancer cases were recorded between Arab women, resulting in an incidence rate of 28 per 100,000, in 2019, the age-standardized incidence rate in female breast cancer in the MENA region rose to 37.5 per 100,000, representative a substantial rise as compared to earlier years. That increase can be accredited to various factors, with lifestyle changes and advancements in detection techniques. Although the incidence rates in this region remain lower than the worldwide average, they are trending to upward, influenced by the urbanization, shifts in lifestyle, and improved diagnostic abilities. The increase in cases is especially in more developed Arab nations with high socio-demographic pointers[3].

In Asia

Devesa SS et al. published a study, breast cancer a significant public health issue in Asia, categorized by considerable differences in incidence rates between several countries & regions, recent estimates that in 2020, about 1.04 million new breast cancer cases were identified in Asia, accounting for around 45.4% of the worldwide total for that year. That figure reflects a considerable rise as compared to last years, determined by factors such as urbanization and changes in lifestyle across many Asian nations.

"The age-standardized incidence rate" (ASIR) for breast cancer in Asia stands at about 36.8 cases per 100,000 women, that may lower than the global average, shows considerable regional difference. For instance, Singapore reports significantly high rates at about 65.7 per 100,000, while countries like Bangladesh show much less figures. Some Asian countries are experiencing a rapid increase in incidence rates. Japan, such as, had observed an annual rise of approximately 6%, whereas Singapore has seen a 3.6% increase per year over the past few decades. Breast cancer constitute about 24.5% of all cancers identified in women in Asia, constructing it the most prevalent cancer among females in the region, although the overall number of breast cancer cases is considerable and on the rise, the varying incidence rates underscore disparities shaped by socioeconomic conditions, healthcare access, and lifestyle changes in different Asian countries[4].

In Japan

Inaguma G et al. published a study about epidemiological data on inflammatory breast cancer (IBC) is limited, and estimates may derived from general breast cancer statistics. In 2020,

around 94,000 new breast cancer cases were recorded in the nation. Since IBC represents about 2.5% of all breast cancer cases, estimated there were around 2,350 new IBC cases in a year. The overall incidence rate for breast cancer in Japan is roughly 91.9 per 100,000 women; but, the specific incidence rate for IBC is expected to be lower due to its infrequency.

Table 1: Facts about breast cancer

Factors	Levels
Lifetime Probability of Developing Breast Cancer.	women = 1 in 9 approximately 11.1% [7]
Incidence Rate	The high incidence of breast cancer in Asia is observed among women aged over 50 [7].
Estimated New Cases of Breast Cancer in Women Aged Over 50 for 2022.	30,682 among females [8]
Proportion of total cancers in female patients.	About 24.1% [9]
Mortality Rate	Important reason of cancer-related mortalities in women [9]
Age group	The majority of diagnoses occur after the age of 50[10].
Provincial Distribution	The high prevalence is observed in Punjab, followed by Sindh and Khyber Pakhtunkhwa[11].
Screening and awareness	The level of awareness is low, and there is limited access to facilities for early detection and treatment[12].

About mortality, about 15,000 breast cancer-related deaths were noted in Japan in 2020, an estimated 590 of those deaths linked to IBC. The death rate for breast cancer is about 7.7 per 100,000 women, with IBC likely playing an important role in this statistic due to its aggressive characteristics, breast cancer is the most commonly diagnosed cancer amongst women in Japan, constituting roughly 21.6% of all new cancer cases, resulting, the proportion of IBC between all cancer diagnoses is suggestively less than 1%, highlighting its classification as a rare so far serious condition within the broader landscape of breast cancer statistics in the country[5].

In China

Narod SA et al published a study, inflammatory Breast Cancer (IBC) is a rare so far high aggressive variant of breast cancer, and that is an insufficiency of specific epidemiological data regarding IBC in China. However, general statistics on breast cancer can offer valuable insights, in 2020, China recorded around 4,546,400 new cancer cases, with breast cancer ranking among the most common types. The estimate number about new breast cancer cases in the country was about 367,900, accounting for approximately 18% of the worldwide total. The incidence rate for breast cancer stands at about 36 per 100,000 women, although this rate can be vary based on area and demographic variables, and estimated that around 70,400 breast cancer-related deaths happened in China in 2015, and mortality rate of about 10.50 per 100,000 women, the age-standardized mortality rate for breast cancer was about at 6.48 per 100,000 women, showing a important public health issue. Breast cancer signifies around 17.1% of all cancer diagnoses among women in China, making it the most common cancer type in females, Whereas IBC includes a smaller segment of these statistics, its aggressive features suggestively contribute in overall breast cancer death burden in the nation[6]. Limited knowledge and awareness of breast cancer, attached with financial limitations, significantly delay early diagnosis, several patients lack understanding of the meaning of self-examinations and regular screenings, although insufficient healthcare structure and ineffective strategies aggravate the difficulties in early detection, tackling these issues, it is essential to

increase health budgets, training for healthcare professionals, and implementation national awareness campaign centered on breast cancer education.

Inflammatory breast cancer in historical background

The historical background of IBC highlight key developments in its understanding and identification. The first recorded version of that now identified as inflammatory breast cancer can be traced back to 1814, when “Sir Charles Bell” acknowledged various breast diseases that included inflammatory symptoms[13]. But, until 1924 that the term "inflammatory breast cancer" was formally presented by Lee and Tannenbaum with making a specific classification for this aggressive variant of breast cancer[14]. That terms was significant in distinguishing IBC from other breast cancer types, underscoring its distinct clinical characteristics and unfavorable prognosis.

Development of Diagnostic Criteria

Inflammatory breast cancer (IBC) with clinical observations principally highlight symptoms like erythema and edema of the breast[15], regularly happening without a noticeable mass, these introductory standards were instrumental in identifying Inflammatory breast cancer as unique clinicopathological situation, over the years, organizations like the American Joint Committee on Cancer (AJCC) had included and enhanced these criteria recognizing the distinct characteristics of Inflammatory breast cancer within staging frameworks[16]. The present compromise underscores the fast emergence of symptoms, with erythema affecting at least one-third of the breast and accompanied by edema or a peau d'orange appearance[17], that can confound diagnosis due to its resemblance to other conditions like mastitis or cellulitis[18]. Despite progress in understanding Inflammatory breast cancer definitive molecular or pathological diagnostic standards remain indefinable, making clinical assessment essential[19]. Dermal lymphatic involvement is a key characteristic nevertheless is often challenging to verify without invasive techniques like skin punch biopsies that are not commonly conducted[20]. Research indicates that dermal lymphatic participation is established in fewer than 75% of cases, additional complicating accurate diagnosis[21]. The nonappearance of inclusive molecular criteria underlines the necessity for continued research to better delineate inflammatory breast cancers attribute and improve diagnostic accuracy[22], the future initiatives should objective to integrate clinical opinions with evolving molecular insights to progress the considerate and the treatment of that aggressive subtype of breast cancer.

Clinical Recognition and Treatment Evolution

Factually, the treatment method for inflammatory breast cancer (IBC) closely reflected that of locally advanced breast cancer (LABC)[23], mainly due to the destructive nature of inflammatory breast cancer and poor prognosis. In 1960s to 1970s, surgical intervention was mostly believed unproductive, like most patients accessible with unrespectable disease, resulting in a miserable five-year survival rate of about 4%[24]. So, the attention removed towards palliative care rather than curative approaches[25]. But, the introduction of chemotherapy in the late 1970 noticeable an important spinning point in treatment models[26]. Studies established that preoperative chemotherapy can shrink the tumors sufficiently to

consent some patients to experience surgery, important to improved outcomes[27]. For example, anthracycline-based regimens presented a prominent increase in five-year inclusive survival rates from less than 5% to almost 30-40% when collective with surgical involvement and radiotherapy[28].

Till the 1980s, treatment regimens started to assume a multimodal method that combined chemotherapy, surgery, and radiation therapy[29]. That tri-modality strategy had since become the standard for handling non-metastatic inflammatory breast cancer[30]. Present strategies recommend preoperative systemic therapy (PST), followed by modified radical mastectomy (MRM) and post-mastectomy radiation therapy (PMRT) for optimum products[31]. Current data show that this inclusive method has improved five-year survival rates for inflammatory breast cancer patients suggestively, with approximations reaching from 55% to 69%, depending on biological subtypes[32]. Regardless of these progressions, challenges remain, principally for triple-negative inflammatory breast cancer patients, who experience inferior survival rates and high risks of loco-regional reappearance[33].

Advancements in Research and Standardization

Research progressions in inflammatory breast cancer (IBC) had encountered important obstacles, mostly due to varying diagnostic principles and the minor scale of clinical study samples[34]. In 2007, the International Classification of Diseases for Oncology authorized that inflammatory breast cancer diagnoses would only be known when dermal lymphatic invasion is recognized with pathological assessment[35]. This situation showed the essential for accurate diagnostic principles to improve clinical outcomes and confirm patients take right treatment, in the absence of consistent standards had historically resulted in discrepancies in diagnosis and administration, very difficult efforts to conduct with clinical research and develop operative therapies for that aggressive cancer subtype[36].

To addressing these issues, an international association was established in 2008 with the objective of formulating agreement guidelines for the diagnosis and management of inflammatory breast cancer[37]. That initiative aimed to systematized practices throughout different states, so refining the quality of research and clinical care for inflammatory breast cancer patients[38]. The consensus underlined the importance of recognizing inflammatory breast cancer not only for its exclusive clinical features like the quick onset of symptoms and dermal lymphatic involvement but also for its separate biological traits associated to other breast cancer types[39], by promoting a consistent approach, that initiative aims to improve data collection, improve treatment procedures, and eventually improve patient outcomes in the management of inflammatory breast cancer[39]. The current research efforts are focused on recognizing molecular goals specific to inflammatory breast cancer[40], that may cover the way for the development of ground-breaking targeted therapies designed for that challenging subtype of breast cancer[41].

Current Understanding and Challenges

Inflammatory breast cancer (IBC) represent around 1% to 5% of all breast cancer cases[42], however it accounts for a suggestively high proportion of breast cancer related mortality due to its destructive actions and swift progression[43]. The

recognized diagnostic criteria for inflammatory breast cancer (IBC) require the opinion of symptoms like redness and swelling affecting at least one-third of the breast within a six-month timeframe[44]. The majority of inflammatory breast cancer (IBC) cases are hormone receptor-negative that obscures treatment options since these tumors do not response to conventional hormone therapies[45]. That aggressive form of breast cancer frequently postures diagnostic challenges, as it can be mistaken for mastitis or other inflammatory disorders, resulting in delays in receiving appropriate care[46], studies have uncovered unique molecular features of Inflammatory breast cancer (IBC)[47], revealing precise gene expression patterns that set it apart from additional breast cancer variants. Let's say, research has pointed to the overexpression of genes linked with inflammatory processes and cell movement[48], like RhoC GTPase, which is crucial for tumor invasion and the formation of new blood vessels[49].

These molecular findings have unlocked paths for the formation of targeted therapies that may improve survival rates for individuals diagnosed with inflammatory breast cancer (IBC)[50]. A new gene signature unique to inflammatory breast cancer (IBC) had identified[51], representative high accuracy in differentiating inflammatory breast cancer (IBC) from non- inflammatory breast cancer (IBC) cases that could lead to more effective treatment methods tailored to that aggressive subtype[52]. Furthermore, continuing research is concentrated on the therapeutic implications of these molecular insights, particularly in the development of targeted treatments that cater to the distinct biological characteristics of inflammatory breast cancer (IBC)[50], like our understanding of the genetic and molecular foundations of inflammatory breast cancer (IBC) continues to advance[53], it is important to incorporate these developments into clinical practice to improve early detection and patient outcomes.

Author's Contributions:
AA: Wrote the manuscript, and **MAD** corrected and added different paragraphs, corrected and supervised all the work.

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