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Impact of Breast Cancer and Its Treatment on Female Reproductive Health: A comprehensive Review

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Abstract: *Breast cancer ranks among the most prevalent cancers affecting women worldwide and remains a significant contributor to cancer-related illness and death in females. In light of the increasing incidence of breast cancer in women of reproductive age, emphasis is transitioning from mere survival to the preservation of reproductive health and endocrine functionality. The progress in multimodal treatment for breast cancer, encompassing surgical procedures, chemotherapy, radiotherapy, endocrine therapy, targeted therapy, and immunotherapy, has enhanced survival rates for patients; however, numerous therapies may adversely impact reproductive health. In this review, impact of breast cancer and its therapies on the reproductive physiology of women, particularly focusing on ovarian reserve, endocrine functionality, and the underlying pathophysiology of the resultant reproductive toxicity has been observed. A thorough literature review was performed using various search engines that includes PubMed, Scopus, Web of Science, and Science Direct. According to the present research, the primary factor contributing to ovarian follicular depletion from DNA damage, oxidative stress, apoptosis, vascular injury, and stromal fibrosis is cytotoxic chemotherapy, which may result in diminished ovarian reserve, chemotherapy-induced amenorrhea, primary ovarian insufficiency, and infertility. On the other hand, endocrine therapy may cause more harm to ovarian function through disruption of hormonal balance and delayed pregnancy, while the long-term impact on fertility from treatments like targeted therapies and immunotherapy is yet to be clarified. Anti-Müllerian hormone, follicle-stimulating hormone, antral follicles, and estradiol are some of the biomarkers used to assess ovarian reserve and reproductive prognosis in women with breast cancer. Mechanisms of treatment-induced reproductive dysfunction need to be elucidated in order to improve therapeutic choices and reduce reproductive side effects.*

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1. Introduction

Breast cancer is the most commonly diagnosed cancer and one of the leading causes of cancer-related mortality among women worldwide. According to the Global Cancer Observatory (GLOBOCAN), approximately 2.3 million new breast cancer cases and over 665,000 deaths were reported globally in 2022, accounting for nearly one in four cancers diagnosed in women. Although the disease predominantly affects postmenopausal women, its incid ence among women of reproductive age has steadily increased over the past two decades, raising important concerns regarding fertility, endocrine function, and long-term quality of life [1, 2].

In India, breast cancer has surpassed cervical cancer to become the most frequently diagnosed malignancy among women. The increasing burden has been attributed to rapid urbanization, delayed childbearing, reduced breastfeeding duration, obesity, sedentary lifestyle, dietary transitions, alcohol consumption, and environmental exposures. In addition, improved awareness and screening programs have contributed to earlier detection. Despite advances in diagnosis and treatment, younger women continue to experience unique reproductive and psychosocial challenges because they are diagnosed during their peak reproductive years [3, 4].

The remarkable progress in breast cancer management through surgery, chemotherapy, radiotherapy, endocrine therapy, targeted therapy, and immunotherapy has significantly improved patient survival. Consequently, increasing attention has shifted from survival alone to survivorship issues, particularly the preservation of reproductive function and quality of life. Several anticancer therapies exert gonadotoxic effects that compromise ovarian function, leading to diminished ovarian reserve, menstrual irregularities, infertility, premature ovarian insufficiency (POI), and early menopause. The severity of reproductive impairment depends on several factors, including the patient's age, baseline ovarian reserve, cumulative treatment dose, treatment duration, and specific therapeutic agents employed [5, 6].

Chemotherapy remains one of the principal causes of treatment-induced reproductive dysfunction. Alkylating agents such as cyclophosphamide are particularly gonadotoxic because they induce DNA double-strand breaks, oxidative stress, apoptosis of primordial follicles, stromal fibrosis, and vascular injury within the ovary, resulting in accelerated depletion of the ovarian follicular pool. Endocrine therapies, including tamoxifen and aromatase inhibitors, although highly effective for hormone receptor-positive breast cancer, frequently delay pregnancy because of prolonged treatment duration and may contribute to menstrual disturbances and menopausal symptoms. Radiotherapy involving the pelvic region can further impair ovarian reserve and uterine function through radiation-induced tissue damage, whereas breast-directed radiotherapy

generally has minimal direct effects on fertility [5, 7].

Loss of reproductive potential has profound consequences extending beyond biological infertility. Women undergoing breast cancer treatment frequently experience premature menopause, sexual dysfunction, reduced libido, vaginal dryness, dyspareunia, body image concerns, anxiety, depression, and fear regarding future parenthood. These physical and emotional consequences substantially affect interpersonal relationships, psychological well-being, and overall quality of life, particularly among adolescents and young adults diagnosed before completion of family planning [8, 9, 10].Recognition of these challenges has led to significant advances in fertility preservation. Current international guidelines recommend that reproductive-age women diagnosed with breast cancer should receive fertility counselling before initiation of systemic therapy. Established fertility preservation options include embryo cryopreservation, mature oocyte cryopreservation, ovarian tissue cryopreservation, and temporary ovarian suppression with gonadotropin-releasing hormone agonists during chemotherapy in selected patients. Early multidisciplinary collaboration among oncologists, reproductive specialists, and mental health professionals is increasingly recognized as essential for optimizing both oncological outcomes and future reproductive potential [11, 12, 13].

This review aims to comprehensively examine the effects of breast cancer and its treatment on female reproductive health by integrating current evidence on the mechanisms of treatment-induced gonadotoxicity, clinical consequences for fertility and ovarian function, available fertility preservation strategies, and the psychological impact experienced by survivors. Understanding these aspects is crucial for developing patient-centered treatment approaches that balance effective cancer management with the preservation of reproductive health and long-term quality of life.

2. Global Epidemiology of Breast Cancer

Breast cancer represents the most prevalent neoplasm in females and poses a considerable public health challenge worldwide. Over the past thirty years, the incidence of breast cancer has risen owing to demographic shifts, urban development, modifications in reproductive patterns, lifestyle changes, and advancements in diagnostic techniques. Despite advancements in screening and treatment leading to a decline in breast cancer mortality in industrialized nations, it remains a significant cause of cancer-related deaths among women, particularly in impoverished countries. The occurrence of breast cancer in young women has highlighted the importance of preventive strategies and the preservation of fertility[2, 14].

2.1 Global Burden of Breast Cancer

Breast cancer is the most commonly diagnosed cancer among women and remains a major contributor to global cancer morbidity and mortality. According to the Global Cancer Observatory (Figure 1)(GLOBOCAN 2022), breast cancer accounted for approximately 2.3 million new cases (24.5% of all cancers) and 666,103 deaths worldwide, making it the most frequently diagnosed malignancy in women across the majority of countries. The incidence of breast cancer exhibits marked geographical variation,

with the highest age-standardized incidence rates observed in Australia/New Zealand, Western Europe, and North America, whereas the highest mortality rates occur predominantly in low- and middle-income countries (LMICs). These disparities largely reflect differences in healthcare infrastructure, participation in population-based screening programmes, stage at diagnosis, access to effective treatment, and socioeconomic conditions [15].

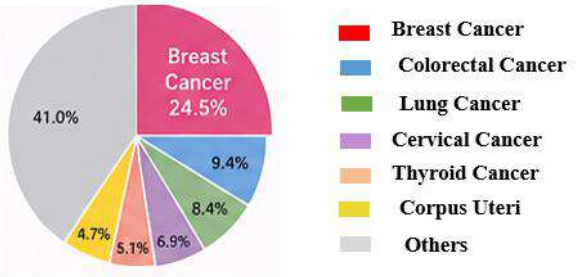

Figure 1: Epidemiology of Cancer Cases in Female (GLOBOCAN 2022)

The global burden of breast cancer has increased steadily over the past three decades owing to population growth, increased life expectancy, urbanization, and changes in reproductive and lifestyle behaviours, including delayed childbearing, lower parity, obesity, physical inactivity, alcohol consumption, and reduced breastfeeding. Although survival rates exceed 85–90% in many high-income countries because of advances in early detection and multimodal therapy, mortality remains disproportionately high in resource-limited settings where late-stage presentation and inadequate access to diagnostic and treatment facilities are common. Recent projections suggest that, if current trends continue, annual breast cancer cases may exceed 3 million, with more than one million deaths annually by 2050, underscoring the urgent need for strengthened prevention strategies, equitable healthcare delivery, timely diagnosis, and improved access to evidence-based treatment worldwide [14, 16].

2.2 Breast Cancer Among Young Women

Breast cancer in women younger than 40 years represents a distinct clinical and biological entity with unique epidemiological, pathological, and survivorship challenges. Although young women account for only 5–7% of all breast cancer cases worldwide, the incidence of early-onset breast cancer has increased steadily over the past two decades in several regions, including North America, Europe, and Asia. This rising trend has been attributed to changes in reproductive behaviour, increasing obesity, sedentary lifestyles, environmental exposures, improved diagnostic awareness, and genetic susceptibility [4, 17].

Compared with breast cancer diagnosed in older women, tumors in younger patients are generally more aggressive and are characterized by larger tumor size at diagnosis, higher histological grade, increased lymph node involvement, elevated proliferative activity, and a greater prevalence of triple-negative breast cancer (TNBC) and HER2-positive molecular subtypes. Furthermore, hereditary breast cancer associated with pathogenic variants in BRCA1, BRCA2, TP53, and PALB2 occurs more frequently in this population, contributing to poorer clinical outcomes and an increased lifetime risk of second primary malignancies [18].

The diagnosis of breast cancer during the reproductive years presents complex therapeutic and psychosocial challenges. Systemic treatments, particularly chemotherapy and prolonged endocrine therapy, may impair ovarian function by accelerating follicular depletion, resulting in diminished ovarian reserve, premature ovarian insufficiency, infertility, and delayed childbearing. These reproductive consequences are accompanied by significant psychological distress, including anxiety, depression, concerns regarding future fertility, altered body image, sexual dysfunction, and reduced quality of life. Consequently, current international guidelines recommend that fertility risk assessment, timely reproductive counselling, and discussion of fertility preservation options should be integrated into the multidisciplinary management of all reproductive-age women before initiation of systemic cancer therapy [11, 13, 19].

2.3 Breast Cancer Epidemiology in India

Breast cancer has emerged as the most frequently diagnosed cancer among Indian women, surpassing cervical cancer, and now constitutes a major public health challenge. According to the Indian Council of Medical Research–National Centre for Disease Informatics and Research (ICMR–NCDIR), breast cancer accounts for nearly one-third of all female cancers in several urban cancer registries, with incidence rates continuing to rise across both metropolitan and semi-urban populations. This increasing burden is attributed to demographic transitions, rapid urbanization, changing reproductive behaviour, adoption of westernized lifestyles, delayed childbearing, reduced parity, shorter duration of breastfeeding, obesity, physical inactivity, and increasing life expectancy. Improvements in cancer awareness and diagnostic facilities have also contributed to higher detection rates [20].

A distinctive epidemiological feature of breast cancer in India is its occurrence at a younger age compared with Western countries. Approximately 45–50% of Indian patients are diagnosed before the age of 50 years, nearly a decade earlier than women in high-income countries. Younger women frequently present with biologically aggressive tumours, larger tumour size, lymph node involvement, and advanced clinical stage at diagnosis, which adversely affect treatment outcomes and survival. Delayed diagnosis remains common due to limited awareness, sociocultural barriers, absence of organized nationwide screening programmes, and unequal access to specialized oncology services, particularly in rural and resource-constrained regions [21, 22].

Considerable geographical disparities are observed across India, with higher incidence rates reported in urban centres such as Delhi, Bengaluru, Chennai, Mumbai, and Thiruvananthapuram than in rural populations. Nevertheless, the incidence in rural areas has also increased steadily over the past decade, reflecting ongoing epidemiological and lifestyle transitions. Strengthening population-based cancer registries, promoting breast health awareness, implementing risk-based screening strategies, improving timely referral systems, and ensuring equitable access to multidisciplinary cancer care are essential to reduce the growing burden of breast cancer in India and improve patient outcomes [20, 23].

2.4 Risk Factors Associated with Breast Cancer

Breast cancer is a heterogeneous and multifactorial disease arising from the complex interplay of genetic predisposition, hormonal and reproductive factors, lifestyle behaviours, metabolic disturbances, and environmental exposures. While female sex and increasing age remain the principal non-modifiable determinants, inherited pathogenic variants in high-penetrance genes such as BRCA1, BRCA2, PALB2, TP53, and CHEK2 markedly increase susceptibility by impairing DNA repair mechanisms and genomic stability. A positive family history further elevates the lifetime risk, particularly among women carrying germline mutations [24].

Hormonal and reproductive factors that prolong cumulative lifetime exposure to estrogen are strongly associated with breast carcinogenesis. Early menarche, late menopause, nulliparity, delayed first full-term pregnancy, shorter duration of breastfeeding, and prolonged use of combined menopausal hormone therapy increase the risk by stimulating mammary epithelial cell proliferation and enhancing the accumulation of genetic alterations. Conversely, multiparity and prolonged breastfeeding have been consistently associated with a protective effect, particularly against hormone receptor-positive breast cancer [2, 24].

Lifestyle-related factors play a substantial role in breast cancer development and account for a significant proportion of preventable cases. Obesity, especially after menopause, physical inactivity, excessive alcohol consumption, tobacco smoking, unhealthy dietary patterns, and metabolic syndrome promote chronic inflammation, insulin resistance, oxidative stress, and increased peripheral estrogen synthesis, thereby facilitating tumour initiation and progression. In addition, growing evidence suggests that exposure to endocrine-disrupting chemicals, environmental pollutants, and ionizing radiation may contribute to breast carcinogenesis through hormonal dysregulation, epigenetic modifications, and DNA damage. Given that many of these risk factors are modifiable, promoting healthy lifestyle practices, improving breast cancer awareness, implementing risk-stratified screening, and providing genetic counselling for high-risk individuals are essential components of comprehensive breast cancer prevention strategies [24, 25].

3. Female Reproductive Physiology and Ovarian Reserve

The female reproductive system is regulated by a highly coordinated interaction between the hypothalamus, pituitary gland, ovaries, and uterus, collectively referred to as the hypothalamic–pituitary–ovarian (HPO) axis. Normal reproductive function depends on the maintenance of ovarian reserve, endocrine homeostasis, and synchronized follicular development throughout the reproductive lifespan. Unlike males, females are born with a finite number of primordial follicles that gradually decline because of continuous follicular recruitment and atresia. Consequently, both the quantity and quality of oocytes decrease with advancing age, resulting in diminished fertility and eventual menopause. Ovarian reserve therefore represents an important indicator of female reproductive potential and has become a key parameter in reproductive medicine and oncofertility. Accurate assessment of ovarian reserve is particularly important in women diagnosed

with breast cancer, as systemic anticancer therapies may accelerate follicular depletion and precipitate premature ovarian insufficiency (POI), thereby compromising future fertility [26, 27]

3.1 Ovarian Follicular Development

Folliculogenesis is a dynamic biological process through which dormant primordial follicles mature into ovulatory follicles capable of releasing a fertilizable oocyte. Human females possess approximately 1–2 million primordial follicles at birth, which decline to 300,000–500,000 by puberty, with fewer than 400–500 follicles ultimately reaching ovulation during the reproductive lifespan. The majority undergo apoptosis through physiological follicular atresia.

Follicular development proceeds through sequential stages comprising primordial, primary, secondary, pre-antral, antral, and preovulatory (Graafian) follicles. Initial follicle recruitment occurs independently of gonadotropins and is regulated by intra-ovarian signalling pathways involving phosphatidylinositol-3 kinase (PI3K)/Akt, mammalian target of rapamycin (mTOR), forkhead box O3 (FOXO3), and growth differentiation factor-9 (GDF-9). As follicles progress to the antral stage, their growth becomes increasingly dependent on follicle-stimulating hormone (FSH), which stimulates granulosa cell proliferation, aromatase activity, and estradiol synthesis. A mid-cycle luteinizing hormone (LH) surge subsequently triggers oocyte maturation, ovulation, and corpus luteum formation. Disturbance of any stage of folliculogenesis by ageing, disease, or gonadotoxic treatments may accelerate depletion of the primordial follicle pool, ultimately impairing reproductive capacity [28].

3.2 Hormonal Regulation of Female Reproduction

Female reproductive function is governed by the hypothalamic–pituitary–ovarian (HPO) axis, which maintains hormonal balance through tightly regulated endocrine feedback mechanisms. Pulsatile secretion of gonadotropin-releasing hormone (GnRH) from the hypothalamus stimulates the anterior pituitary to release FSH and LH. During the early follicular phase, FSH promotes recruitment and maturation of ovarian follicles, while LH stimulates theca cells to produce androgens that are subsequently converted into estradiol by granulosa cells through aromatase activity.

Increasing estradiol concentrations promote proliferation of the endometrium and exert negative feedback on gonadotropin secretion during most of the menstrual cycle. Sustained elevation of estradiol during the late follicular phase switches to positive feedback, inducing the preovulatory LH surge responsible for ovulation. Following ovulation, the corpus luteum secretes progesterone together with estradiol, preparing the endometrium for implantation and maintaining early pregnancy. Anti-Müllerian hormone (AMH), secreted by granulosa cells of pre-antral and small antral follicles, functions as an important regulator of follicular recruitment by preventing excessive activation of dormant primordial follicles. Disruption of this endocrine network by chemotherapy or endocrine therapy frequently results in menstrual dysfunction, diminished ovarian reserve, premature ovarian insufficiency, and infertility [26, 27].

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3.3 Biomarkers of Ovarian Reserve

Assessment of ovarian reserve is essential for estimating reproductive potential and identifying women at increased risk of treatment-induced infertility, particularly before initiating gonadotoxic therapies. Because no single biomarker accurately reflects the entire ovarian follicle pool, a combination of biochemical and ultrasonographic markers is recommended.

Anti-Müllerian Hormone (AMH): AMH is secreted by granulosa cells of pre-antral and small antral follicles and is considered the most reliable marker of ovarian reserve. Its concentration remains relatively stable throughout the menstrual cycle and closely correlates with the size of the primordial follicle pool. Reduced AMH levels indicate diminished ovarian reserve and are widely used to predict ovarian response and assess the impact of chemotherapy on ovarian function [29, 30].

Follicle-Stimulating Hormone (FSH): Basal serum FSH, measured during the early follicular phase, has traditionally been used to evaluate ovarian function. Elevated FSH levels reflect reduced ovarian reserve due to decreased ovarian feedback; however, considerable inter-cycle variability limits its sensitivity. Therefore, FSH is most informative when interpreted alongside AMH and other ovarian reserve markers [31].

Antral Follicle Count (AFC): AFC is determined by transvaginal ultrasonography and represents the number of small antral follicles (2–10 mm) present in both ovaries. It is a reliable predictor of ovarian reserve and ovarian responsiveness during assisted reproductive treatments and complements serum AMH assessment [32].

Estradiol: Serum estradiol reflects ovarian steroidogenic activity and follicular development. Although its cyclical variation limits its utility as an independent marker of ovarian reserve, early follicular-phase estradiol measurement assists in interpreting basal FSH values and identifying subtle ovarian dysfunction when used in combination with other biomarkers [33].

4. Breast Cancer Treatment Modalities and Their Mechanisms

Breast cancer treatment is tailored according to tumour stage, molecular subtype, hormone receptor status, menopausal status, and patient characteristics. Current management involves surgery, chemotherapy, radiotherapy, endocrine therapy, targeted therapy, and immunotherapy. Although these therapeutic approaches have substantially improved survival, several treatments exert gonadotoxic effects that may impair ovarian function and fertility, particularly in women of reproductive age [34, 35].

4.1 Surgical Management

Surgery remains the primary treatment for localized breast cancer and includes breast-conserving surgery or mastectomy, with or without axillary lymph node dissection. Surgical procedures generally do not directly affect ovarian reserve or fertility. However, prophylactic bilateral salpingo-oophorectomy performed in selected high-risk **BRCA1/BRCA2** mutation carriers induces permanent loss of ovarian function and premature menopause [35].

4.2 Chemotherapy

Chemotherapy is widely used in early-stage and metastatic breast cancer. Common agents include anthracyclines, alkylating agents, taxanes, and platinum compounds, which inhibit tumour growth through DNA damage, oxidative stress, and mitotic arrest. These agents can also damage ovarian follicles by inducing apoptosis, vascular injury, mitochondrial dysfunction, and stromal fibrosis, leading to diminished ovarian reserve, premature ovarian insufficiency, and infertility. Among these, cyclophosphamide is considered the most gonadotoxic [36].

4.3 Radiotherapy

Radiotherapy reduces local recurrence by inducing DNA damage and reactive oxygen species-mediated tumour cell death. Breast irradiation has minimal direct effects on ovarian function, whereas pelvic or total-body irradiation may cause irreversible follicular depletion, vascular injury, and uterine damage, increasing the risk of premature ovarian failure[37].

4.4 Endocrine Therapy

Hormone receptor-positive breast cancers are treated with tamoxifen, aromatase inhibitors, and ovarian suppression using GnRH agonists. Tamoxifen blocks estrogen receptors, whereas aromatase inhibitors suppress estrogen synthesis. Although these therapies are less directly gonadotoxic than chemotherapy, prolonged treatment may suppress ovarian function, delay pregnancy, and induce menopausal symptoms that affect reproductive health [38].

4.5 Targeted Therapy

Targeted agents, including HER2 inhibitors (trastuzumab, pertuzumab), CDK4/6 inhibitors, PARP inhibitors, and PI3K inhibitors, selectively inhibit signalling pathways involved in tumour proliferation and survival. Their direct impact on ovarian reserve appears limited; however, long-term reproductive safety remains insufficiently characterized because these therapies are commonly administered in combination with chemotherapy [36].

4.6 Immunotherapy

Immune checkpoint inhibitors, particularly pembrolizumab, enhance antitumour immunity by blocking the PD-1/PD-L1 pathway. Although their reproductive effects are not fully understood, immune-related endocrine disorders, including hypophysitis and autoimmune ovarian dysfunction, may indirectly impair fertility. Additional long-term studies are needed to establish their reproductive safety profile [39].

5. Effects of Breast Cancer Treatment on Female Reproductive Health

5.1 Ovarian Dysfunction and Fertility Impairment Following Breast Cancer Treatment

Breast cancer treatment has significantly improved survival rates among women, however, its impact on reproductive health has emerged as a major survivorship concern, particularly for adolescents and women of reproductive age. The extent of reproductive impairment depends on several factors, including the patient's age, baseline ovarian reserve, cumulative treatment dose, treatment duration, and

the specific therapeutic modality employed. Among the available treatment options, chemotherapy is considered the principal cause of gonadal toxicity because it directly damages ovarian follicles, whereas radiotherapy, endocrine therapy, targeted therapy, and immunotherapy may also adversely influence reproductive function through endocrine disruption or indirect ovarian injury [19].

A major consequence of systemic therapy is the accelerated depletion of ovarian reserve, which represents both the quantity and quality of the remaining primordial follicles. Cytotoxic agents, particularly alkylating drugs such as cyclophosphamide, induce DNA double-strand breaks, oxidative stress, mitochondrial dysfunction, granulosa cell apoptosis, stromal fibrosis, and vascular injury within the ovary. These pathological changes result in irreversible follicular loss, leading to diminished ovarian reserve and reduced endocrine function. Biomarkers such as anti-Müllerian hormone (AMH), antral follicle count (AFC), follicle-stimulating hormone (FSH), and estradiol are routinely used to monitor ovarian function before and after cancer treatment. Among these, AMH has emerged as the most sensitive indicator of chemotherapy-induced ovarian damage, often declining rapidly during treatment and remaining persistently low in women who develop premature ovarian insufficiency [19, 40].

Chemotherapy-induced amenorrhea (CIA) is one of the most common manifestations of ovarian toxicity and is characterized by the temporary or permanent cessation of menstruation following systemic treatment. The incidence of CIA varies widely depending on patient age, baseline ovarian reserve, and chemotherapy regimen, with older premenopausal women and those receiving alkylating agents exhibiting the highest risk. While menstruation resumes in some younger patients after completion of therapy, restoration of menstrual cycles does not necessarily indicate preservation of fertility because ovarian reserve may remain significantly compromised. Consequently, menstrual recovery should not be considered a reliable surrogate marker of reproductive potential [40].

Persistent ovarian damage may ultimately progress to premature ovarian insufficiency (POI), a condition characterized by loss of ovarian activity before the age of 40 years. POI is associated with persistent amenorrhea, hypoestrogenism, elevated gonadotropin concentrations, infertility, vasomotor symptoms, osteoporosis, cardiovascular complications, and long-term metabolic disturbances. The likelihood of developing POI increases with advancing age at treatment, cumulative chemotherapy exposure, and combined treatment modalities. Although ovarian function may partially recover in selected younger women, many survivors experience irreversible endocrine failure with substantial implications for reproductive and overall health [27].

Infertility and reduced fecundity are among the most distressing long-term consequences of breast cancer therapy. Depletion of the primordial follicle pool reduces the probability of spontaneous conception, shortens the reproductive lifespan, and accelerates reproductive ageing. Endocrine therapy further contributes to reduced fecundity by delaying pregnancy attempts for five to ten years, during which natural age-related decline in fertility

continues. Although advances in assisted reproductive technologies have improved pregnancy prospects for many survivors, fertility outcomes remain highly dependent on pretreatment ovarian reserve, patient age, and treatment-related ovarian injury [42].

5.2 Reproductive and Sexual Health Outcomes in Breast Cancer Survivors

Current evidence indicates that pregnancy after successful breast cancer treatment is generally safe for appropriately selected patients and does not adversely affect disease-free or overall survival, including many women with hormone receptor-positive disease. Several studies have demonstrated that pregnancy does not increase the risk of cancer recurrence when conception occurs after adequate completion or temporary interruption of therapy under careful clinical supervision. Nevertheless, survivors exhibit slightly increased risks of adverse obstetric outcomes, including preterm birth, low birth weight, and cesarean delivery, particularly among women exposed to intensive chemotherapy or radiotherapy. Therefore, pregnancy planning should be individualized through multidisciplinary consultation involving oncologists, reproductive specialists, and obstetricians [13].

Menstrual disturbances are frequently observed throughout and following breast cancer treatment and include oligomenorrhea, irregular menstrual cycles, secondary amenorrhea, and premature menopause. These alterations result primarily from disruption of the hypothalamic–pituitary–ovarian axis, follicular depletion, and endocrine dysfunction. Hormonal therapies, particularly aromatase inhibitors and ovarian suppression with gonadotropin-releasing hormone agonists, may further induce reversible hypoestrogenic states associated with vasomotor symptoms, menstrual irregularity, and temporary suppression of ovarian activity [43].

Beyond fertility impairment, breast cancer treatment substantially affects sexual and reproductive wellbeing. Hypoestrogenism resulting from ovarian dysfunction commonly leads to vaginal dryness, dyspareunia, reduced libido, impaired sexual arousal, and decreased sexual satisfaction. These physical symptoms are frequently accompanied by psychological distress, altered body image following breast surgery, anxiety regarding recurrence, concerns about future childbearing, and relationship difficulties, all of which contribute to reduced quality of life. Emerging evidence highlights that sexual dysfunction is highly prevalent among breast cancer survivors but remains under-recognized in routine oncology practice, emphasizing the importance of comprehensive survivorship care that addresses both physical and psychosexual health [44].

Overall, the reproductive consequences of breast cancer treatment extend well beyond temporary menstrual disruption and encompass long-term endocrine dysfunction, infertility, impaired sexual health, and compromised quality of life. Early identification of women at increased risk of gonadotoxicity, careful assessment of ovarian reserve, and individualized reproductive counselling before treatment initiation are essential for optimizing long-term reproductive outcomes and improving survivorship care.

6. Challenges and Future Directions

Despite significant advances in breast cancer management, preserving reproductive health remains a major challenge, particularly for young women undergoing gonadotoxic therapies. Predicting individual reproductive outcomes is difficult because ovarian toxicity varies with age, baseline ovarian reserve, genetic factors, treatment type, and cumulative drug exposure. Although biomarkers such as anti-Müllerian hormone (AMH), follicle-stimulating hormone (FSH), and antral follicle count (AFC) are widely used to assess ovarian reserve, their ability to accurately predict long-term fertility and pregnancy outcomes remains limited. Furthermore, evidence regarding the reproductive safety of emerging therapies, including CDK4/6 inhibitors, PARP inhibitors, antibody–drug conjugates, and immune checkpoint inhibitors, is still evolving. In many low- and middle-income countries, limited access to fertility assessment, specialized oncofertility services, and financial constraints further hinder comprehensive reproductive care [19, 41].

Future research should focus on developing personalized risk prediction models integrating clinical characteristics, ovarian reserve biomarkers, and genomic profiling to better identify women at high risk of treatment-induced infertility. Long-term prospective studies are needed to evaluate the reproductive effects of newer systemic therapies and establish standardized reporting of ovarian function, fertility, and pregnancy outcomes. Advances in ovarian-protective therapies, regenerative medicine, and fertility restoration techniques may provide new opportunities to preserve reproductive function without compromising cancer treatment efficacy. Strengthening multidisciplinary oncofertility care, incorporating routine fertility counselling into clinical practice, and improving equitable access to reproductive healthcare services should remain priorities for optimizing the long-term quality of life of breast cancer survivors.

7. Conclusion

Breast cancer remains the most frequently diagnosed malignancy among women and, owing to improvements in early detection and multimodal treatment, survivorship has increased substantially. Consequently, preservation of reproductive health has become an important component of comprehensive cancer care, particularly for adolescents and women of reproductive age. Although treatment modalities such as chemotherapy, endocrine therapy, radiotherapy, targeted therapy, and immunotherapy have significantly improved clinical outcomes, they may adversely affect ovarian reserve, endocrine function, menstrual cyclicity, fertility, pregnancy outcomes, and sexual health. Chemotherapy, especially alkylating agents, remains the principal cause of treatment-induced gonadotoxicity through mechanisms involving DNA damage, oxidative stress, apoptosis, and accelerated follicular depletion.

Assessment of ovarian reserve using biomarkers such as anti-Müllerian hormone, follicle-stimulating hormone, antral follicle count, and estradiol provides valuable information for evaluating reproductive potential before and after treatment. However, predicting long-term fertility remains challenging because reproductive outcomes vary according to age, baseline ovarian reserve, treatment regimen, and

individual susceptibility. Therefore, routine reproductive risk assessment, timely counselling, and multidisciplinary collaboration between oncologists, reproductive specialists, and gynecologists are essential to optimize patient care.

Future advances in molecular biomarkers, precision oncology, ovarian-protective therapies, and reproductive medicine are expected to improve prediction, prevention, and management of treatment-related reproductive toxicity. Integrating reproductive health into standard breast cancer care will not only enhance fertility preservation and endocrine outcomes but also improve the long-term quality of life and overall well-being of breast cancer survivors.

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