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REVIEW ARTICLE

Risk-Based Approach to Breast Cancer Prevention Among Adolescents and Young Adult Females

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Abstract

Introduction: Breast cancer, although predominantly a disease of older women, is increasingly being diagnosed in adolescents and young adult (AYA) females, aged 15–39 years. This emerging trend necessitates a shift from traditional prevention strategies to a more nuanced, risk-based approach tailored for this younger population. The aim of this review is to explore the epidemiology, risk factors, and prevention strategies specifically designed for AYA females. Despite increasing awareness, a significant gap exists in understanding how risk stratification can guide prevention in this age group, which is often excluded from routine screening programs and underrepresented in breast cancer research.

Methodology: A systematic search of peer-reviewed articles was conducted using Google Scholar, PubMed, Hinari, Scopus, and Web of Science, covering publications from 2000 to 2025. Keywords included "breast cancer," "adolescents," "young adults," "risk-based prevention," and "epidemiology." Inclusion criteria focused on studies addressing breast cancer epidemiology, risk assessment models, and preventive interventions applicable to the AYA population. Narrative synthesis was employed to integrate findings across diverse study designs.

Results: The review highlights an increasing incidence of breast cancer in AYAs, with risk factors such as genetic predisposition (e.g., BRCA1/2 mutations), lifestyle behaviors, environmental exposures, and reproductive history playing a significant role. Risk-based approaches, including personalized risk assessment tools, genetic counseling, and lifestyle modification programs, were found to be promising yet underutilized in this age group.

Conclusion: There is a critical need for targeted, evidence-based prevention strategies that consider the unique biological, psychosocial, and behavioral characteristics of AYA females. Implementing a risk-based framework may enhance early detection and reduce long-term breast cancer burden in this vulnerable population.

Keywords: Breast cancer, adolescents, young adults, risk-based prevention, epidemiology

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Introduction

Breast cancer remains a significant public health challenge, with a rising incidence and more aggressive disease among young females[1]. While it is commoner in older women, addressing modifiable risk factors and implementing early preventive strategies among adolescents and young adults (AYAs) can significantly reduce long-term morbidity and mortality in line with the planned 2.5% reduction in the annual mortality rate from breast cancer by the World Health Organization[2]. Current trends show that new cases occur at an annual rate of 1-5% and by 2050, new cases and death rates will increase by 38% and 68% respectively[2]. These figures are alarming and deserve a risk-based preventive approach to forestall this trend aside early diagnosis and improved access to treatment. A risk-based approach to the prevention of breast cancer involves identifying high-risk individuals, educating them about preventive measures, and integrating early screening where necessary to improve early diagnosis. This paper explores the epidemiology, risk factors, and prevention strategies tailored for AYAs.

Epidemiology of Breast Cancer in Young Females

Although breast cancer is predominantly diagnosed in postmenopausal women, an increasing number of cases are seen in younger populations. According to the Global Cancer Observatory (GLOBOCAN) 2022, breast cancer is the second most commonly diagnosed cancer worldwide, with a considerable percentage affecting women under 40 years of age[3]. While rare, breast cancer in young women tends to be more aggressive and is associated with poorer prognoses compared to cases in older women due to cancer biology differences in AYA females resulting in advanced stages of breast cancer at presentation in this age group[1,4–6].

Incidence and Demographic patterns

Globally, the incidence of breast cancer among AYA females varies widely, with rates ranging from 4 to 31.6% of BC cases annually, depending on geographical region, ethnicity, and socioeconomic factors[6–8]. Data from the Surveillance, Epidemiology, and End Results (SEER) program in the United States indicate a gradual increase in incidence rates in females under 40 over the past few decades, albeit at a slower pace compared to older age groups[9,10]. AYA females with breast cancer tend to have lower estrogen receptor (ER) positivity, higher rates of Her2/neu overexpression, and more lymph node positivity[7].

In sub-Saharan Africa, the burden of breast cancer in AYA females appears disproportionately high, often representing a larger fraction of total breast cancer cases compared to high-income settings, likely due to the younger population structure and delayed age of peak incidence[11]. Additionally, young women of African and Hispanic descent have been shown to have higher rates of aggressive breast cancer subtypes and lower survival rates compared to their Caucasian counterparts and are more likely to die from the disease than any other race[9,11,12].

Breast Cancer Risk Factors in AYAs

Several risk factors have been linked with breast cancer in the AYA population. Genetic predisposition, particularly BRCA1 and BRCA2 mutations, plays a significant role in this age group, with up to 12% of breast cancers in women under 40 linked to hereditary syndromes[13]. Other potential risk factors include early menarche, late first pregnancy or nulliparity, oral contraceptive use, obesity, alcohol consumption, and ionizing radiation exposure, especially during childhood or adolescence[14].

Broadly, breast cancer risk factors in AYAs are categorized into genetic, hormonal, lifestyle, and environmental factors.

Genetic and Familial Factors

BRCA1 and BRCA2 are tumor suppressor genes that play a crucial role in DNA repair, specifically in homologous recombination repair (HRR) [15–20]. Mutations in these genes lead to genomic instability, increasing the risk of breast cancer, particularly in adolescents and young adults (AYA) (Fig. 1). BRCA1 is involved in sensing DNA damage and signaling repair through interaction with ATM, ATR, and CHK2 kinases. BRCA2 facilitates RAD51 loading onto single-stranded DNA, a critical step in homologous recombination. In normal cells, HR accurately repairs DSBs using the sister chromatid as a template. In BRCA-deficient cells, HR is impaired, leading to the activation of error-prone repair mechanisms like non-homologous end joining (NHEJ), which increases genomic instability. Individuals with pathogenic variants in BRCA1 or BRCA2 have over 60% lifetime risk of having breast cancer compared with the general population[10,16,21–23]. BRCA1 and BRCA2 breast cancer survivors have 30-40% and 25% risk of developing contralateral breast cancer compared with 8% of the general population[16].

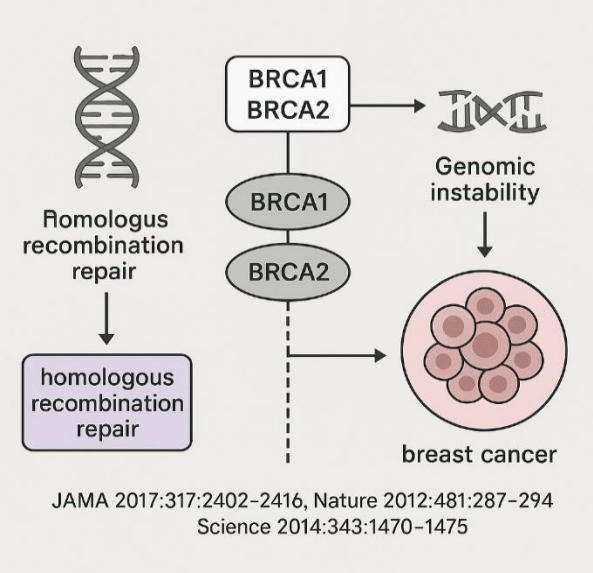

Figure 1: A schematic diagram showing the role of BRCA1 and BRCA2 in homologous recombination repair and the consequences of their loss leading to breast cancer.

BRCA1-associated breast cancers are more frequently triple-negative (ER-/PR-/HER2-), aggressive, and high-grade while BRCA2-associated breast cancer is often estrogen receptor-positive (ER+), resembling sporadic breast cancers but with an earlier onset[24–26]. The consequences of BRCA mutations in breast cancer development include increased genomic instability, defective cell cycle checkpoints and apoptosis enhanced susceptibility to hormonal and environmental carcinogens and increased lifetime breast cancer risk (up to 72% in BRCA1 and 69% in BRCA2 mutation carriers)[27–29]. Figure 1 shows a schematic diagram illustrating the role of BRCA1 and BRCA2 in homologous recombination repair and the consequences of their loss leading to breast cancer.

Family history is a well-established breast cancer risk factor, particularly among adolescents and young adults (AYA) and the risk is 10%[23]. A positive family history of breast cancer significantly increases an individual's lifetime risk due to the potential inheritance of pathogenic gene mutations, shared environmental exposures, and epigenetic modifications. In the genetic basis of family history and breast cancer risk, aside BRCA 1 and BRCA2 related mutations, other high-penetrance gene mutations identified in familial breast cancer syndromes include TP53 mutations (Li-Fraumeni Syndrome), PTEN mutations (Cowden Syndrome),CHEK2 mutations and PALB2 gene, ATM gene, STK11 gene mutations[30]. TP53 encodes the p53 protein, which regulates cell cycle arrest and apoptosis. Germline mutations in TP53 significantly increase the risk of early-onset breast cancer[31,32]. PTEN regulates cell proliferation and apoptosis. Individuals with PTEN mutations have an increased risk of breast cancer[33,34]. CHEK2 encodes a checkpoint kinase involved in DNA repair, and mutations in this gene moderately

increase breast cancer risk[35]. CHEK2 genetic mutation is linked with hormone resistance in premenopausal Her-2 negative, hormone receptor positive breast cancer patients[35–37].

Breast cancer risk follows an autosomal dominant inheritance pattern when associated with BRCA1, BRCA2, TP53, and other high-risk genes. The presence of a first-degree relative (mother, sister) with breast cancer significantly increases an individual's risk. If multiple first-degree relatives are affected, particularly at an early age (<40 years), the risk is even higher[30,38]. Figure 2 shows how family history influences breast cancer risk while figure 3 shows the mechanism of BRCA1/2 leading to breast cancer.

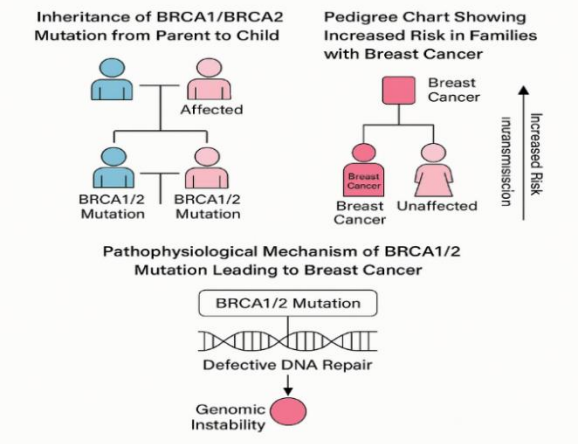

Fig. 2: A schematic representations of how family history Influences breast cancer risk

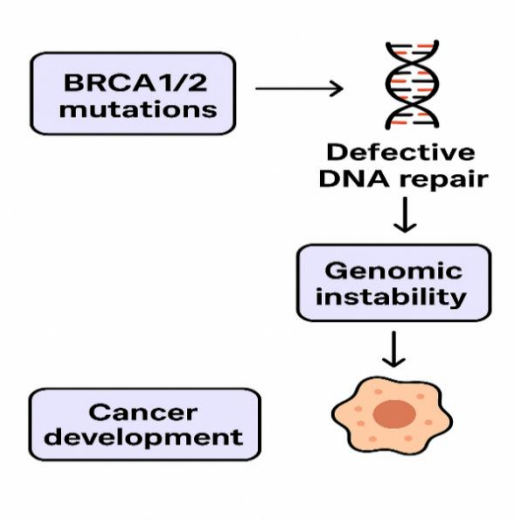

Fig. 3: Pathophysiologic mechanism of BRCA1/2 mutation leading to breast cancer.

Environmental and epigenetic interactions

Apart from genetic predisposition, family history may reflect shared environmental exposures, such as diet, lifestyle, and hormonal influences, which can further modulate cancer risk (Fig. 4). Additionally, epigenetic changes, such as DNA methylation and histone modifications, can be inherited and contribute to breast cancer risk[23].

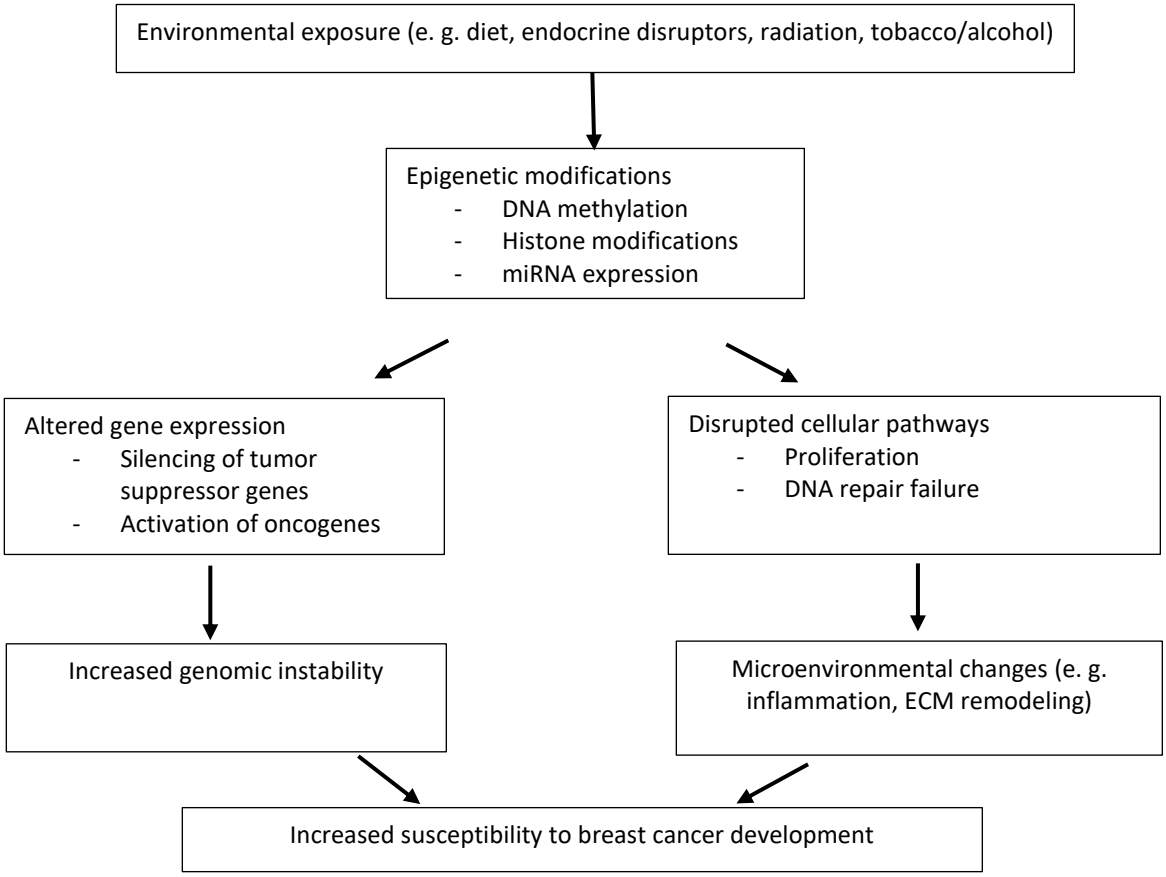

Figure 4: Environmental exposures during adolescence and young adulthood are critical due to the rapid development of breast tissue. Epigenetic changes are reversible and influenced by modifiable factors, making them crucial for preventive interventions. This model can guide risk stratification and personalized prevention strategies.

Hormonal Factors

Hormonal factors play a significant role in the development of breast cancer, particularly in adolescents and young adults (AYA). Estrogen and progesterone, the primary female sex hormones, influence breast tissue growth and differentiation. Prolonged exposure to endogenous or exogenous hormones can lead to dysregulated cellular proliferation, increasing the risk of carcinogenesis in breast tissue.

Mechanisms of hormone-induced breast carcinogenesis

1. Estrogen-mediated DNA damage. Estrogens, particularly 17β-estradiol, can be metabolized into genotoxic metabolites, such as catechol, estrogen, quinones, which form DNA adducts leading to mutations in key tumor suppressor genes like TP53 and BRCA1[39,40].
2. Increased cellular proliferation. Estrogen and progesterone stimulate cell proliferation by binding to estrogen receptors (ER) and progesterone receptors (PR), activating downstream signaling pathways like PI3K/AKT and MAPK. This can result in uncontrolled cell division, a hallmark of cancer[41,42].
3. Disruption of apoptotic pathways. Estrogen has anti-apoptotic effects by upregulating BCL-2, an oncogene that inhibits programmed cell death. This

promotes the survival of abnormal cells, increasing the likelihood of malignant transformation[43].

4. Impact of early menarche and late menopause. A longer lifetime exposure to estrogen due to early menarche and late menopause increases the risk of breast cancer. The cumulative exposure leads to sustained stimulation of mammary epithelial cells, predisposing them to oncogenic mutations. The risk is 30% higher than the general population[44,45].
5. Oral contraceptive use and hormone replacement therapy (HRT). Exogenous hormones from oral contraceptives and hormone replacement therapy (HRT) have been linked to an increased risk of breast cancer due to their prolonged stimulation of breast epithelial cells. Studies indicate that long-term use of combined estrogen-progestin contraceptives elevates breast cancer risk, particularly in younger women. The risk is 24%[46–48].

The role of estrogen and progesterone in breast cancer development is shown in Figure 3.

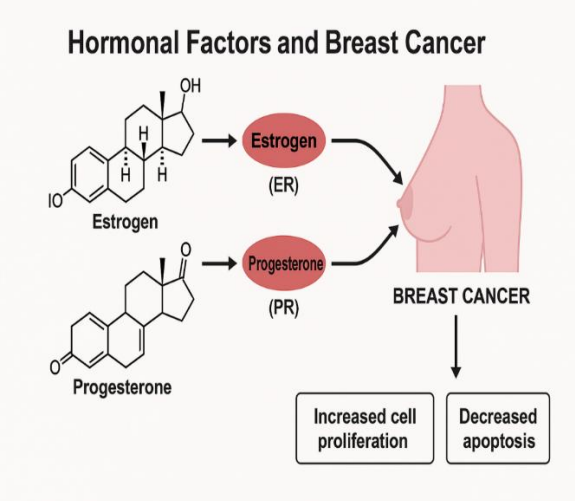

Figure 5: A schematic representation showing estrogen and progesterone interactions with their receptors, leading to increased cell proliferation and decreased apoptosis.

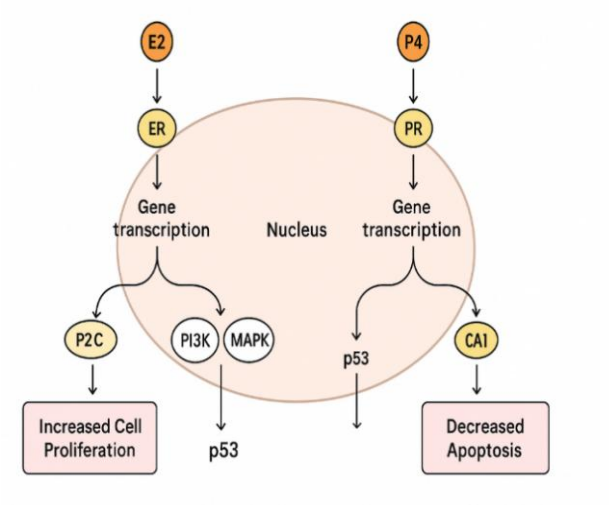

Figure 6: A schematic diagram illustrating how estrogen and progesterone interact with their receptors to promote cell proliferation and inhibit apoptosis.

Lifestyle and Behavioral Factors

High-fat diets and obesity, especially in post-pubertal adolescence, have been linked to increased risk. Regular physical activity reduces lifetime breast cancer risk. Alcohol consumption and smoking: Early initiation of alcohol use and smoking has been linked to increased risk[49].

Environmental Factors

Chemicals such as bisphenol A (BPA) found in plastics may influence estrogen activity while radiation exposure, particularly during adolescence, can elevate risk[7,50].

Risk-Based Prevention Strategies

A risk-based approach to breast cancer prevention in adolescents and young adults (AYAs) integrates individual risk profiles—genetic, behavioral, and environmental—into targeted preventive strategies. This tailored approach enhances effectiveness, improves adherence, and minimizes over- or under-treatment. A tiered approach involving primary, secondary, and tertiary prevention measures is crucial for effective breast cancer risk reduction (Fig. 5).

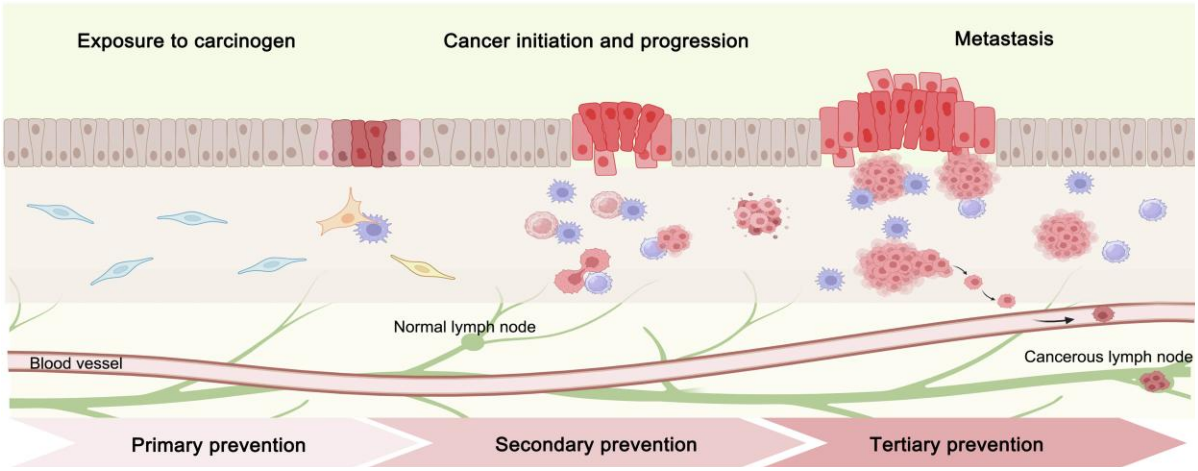

Figure 7: Cancer prevention can be effective throughout the entire process of cancer initiation, progression, and metastasis. (Courtesy: Ren et. al.[59]).

Primary prevention

Primary prevention focuses on minimizing risk factors before disease onset. This is achieved through health education, lifestyle modification interventions, hormonal and reproductive health awareness, vaccination and chemoprevention and community-based and school-based interventions.

Awareness campaigns in schools and universities about breast cancer risk factors and prevention. Health education targeting AYAs should emphasize:

- Physical activity: At least 150 - 300 minutes of moderate activity weekly has been linked to reduced breast cancer risk[51–53].
- Dietary habits: A diet rich in fruits, vegetables, and fiber while low in saturated fats and red meat has a protective effect[54].
- Alcohol avoidance: Alcohol consumption, even at low levels, increases breast cancer risk in young women[55].
- Smoking avoidance: Smoking is a confirmed risk of breast cancer accounting for 10% higher risk compared to women who have never smoked[56].
- Obesity and weight management: Obesity during adolescence and young adulthood is associated with elevated lifetime breast cancer risk, particularly postmenopausal cancers[57]. Risk-based strategies should include BMI monitoring and structured interventions for weight control[57].
- Hormonal and reproductive health awareness: Understanding the role of hormonal exposure in breast cancer development is critical. AYAs should be informed of the potential risks associated with early menarche, late first pregnancy, and prolonged use of hormonal contraceptives. Counseling should be personalized based on individual risk assessments[58].

The role of HPV vaccines in reducing breast cancer risk is still under study. For those high-risk AYAs with strong familial predisposition or confirmed genetic mutations, chemoprevention with selective estrogen receptor modulators (SERMs) like tamoxifen may be considered. This strategy has been shown to reduce the incidence of estrogen receptor-positive breast cancer in high-risk women[59].

Prevention strategies should also leverage peer education, digital platforms, and school-based programs to reach a broader AYA population. These initiatives can improve knowledge, reshape attitudes, and encourage proactive health behaviors[60–62].

Secondary prevention

Secondary prevention involves early detection and risk stratification. This involves breast self-examination, clinical breast examination, and genetic risk stratification, counseling and testing. Rather than routine breast self-exams, which are not recommended for general populations, breast awareness — knowing what is normal and reporting changes—should be promoted among AYAs. This empowers young women to seek timely medical attention[63]. Clinical breast examination (CBE) is recommended for high-risk young females. For AYAs with a family history of breast, particularly those with BRCA1 or BRCA2 mutations, genetic counseling and testing are recommended. Early identification of high-risk individuals facilitates timely initiation of enhanced surveillance and prophylactic strategies[63].

AYAs with personal or family history of breast cancer, triple-negative breast cancer, bilateral breast cancer and known familial mutation in a cancer susceptibility gene should be referred for genetic counselling. Preventive strategies guided by counseling include earlier and more frequent screening (e.g., MRI starting at age 25), prophylactic mastectomy and/or salpingo-oophorectomy in high-risk individuals, use of medications like tamoxifen to reduce breast cancer risk, promoting physical activity, healthy diet, and avoiding alcohol/smoking.

Tertiary prevention

For those diagnosed with high-risk lesions or breast cancer, early interventions using surveillance programs, prophylactic surgery in individuals with BRCA mutations and psychosocial support addressing the psychological impact of being at high risk for breast cancer form the basis for tertiary prevention[10,50].

Challenges in implementing a risk-based approach

Several barriers exist in executing a risk-based approach among AYAs. These include:

1. Limited Awareness. Many young females do not perceive themselves at risk.
2. Cost and Accessibility of Screening. Mammography is not recommended for young women, and alternative screening tools may be expensive.
3. Genetic Testing Barriers. There are limited availability and ethical concerns surrounding genetic testing.
4. Psychosocial Impact. The anxiety associated with being labeled high-risk may deter participation in preventive programs.

Future Directions and Research

The development of non-invasive biomarkers and targeted prevention strategies can further optimize early intervention efforts. Additionally, integrating digital health interventions such as mobile applications for risk assessment and awareness can improve outreach among this population.

Conclusion

Breast cancers in AYA females tend to present with more aggressive histological and molecular characteristics. They are more likely to be high-grade, hormone receptor-negative, HER2-positive, or triple-negative breast cancers (TNBC), all of which are associated with poorer prognosis and limited therapeutic options. Additionally, AYA patients often present with more advanced-stage disease at diagnosis, likely due to a combination of biological aggressiveness and diagnostic delays.

A positive family history remains a significant risk factor for breast cancer in adolescents and young adults. Early genetic screening, lifestyle modifications, and surveillance strategies are crucial for individuals with a strong family history of breast cancer.

Hormonal factors significantly influence breast cancer risk in adolescents and young adults. Estrogen and progesterone contribute to breast carcinogenesis through mechanisms such as increased cellular proliferation, DNA damage, and inhibition of apoptosis. Understanding these hormonal pathways is crucial for developing targeted preventive and therapeutic strategies for AYA breast cancer patients

A risk-based approach to breast cancer prevention among adolescents and young adult females is crucial in reducing the burden of the disease. Identifying high-risk individuals and implementing tailored preventive strategies can lead to early intervention and improved outcomes. A multidisciplinary effort involving healthcare providers, educators, policymakers, and community stakeholders is essential in promoting breast health awareness and risk reduction among young females.

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