

Comprehensive Study of Breast Cancer Risk Factors in Young Adults

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Abstract- Purpose—Risk factors for occurrence of breast cancer can be broadly divided into two categories non-modifiable and modifiable factors. Non-modifiable factors include age, gender, geographical conditions and modifiable factors include but are not limited to age at menarche, teenage adiposity, physical activity, mammography screening, dietary exposures to nutrients, number of pregnancies etc. Contrary to popular belief, cancer is in reality a result of accumulated factors over a lifetime and not just a few years. Understanding the factors observed from an early age in a young adult is therefore essential for the risk assessment of breast cancer occurrence. In this article we aim at understanding the risk factors observed from an early age and present a comprehensive study of research work and case studies concluded so far on various modifiable factors identifiable in young adults.

Methods— Review Article

Results— The factors that are directly linked to breast cancer accumulate much earlier in life contrary to popular belief. Different factors such as early onset of menarche, higher childhood adiposity, peak height growth velocity, mammography screening, lesser physical activity, genetic factors and family history of cancer greatly affect a woman's risk of acquiring breast cancer later on in life.

Implications and Contribution— Breast cancer prevention must begin at an early age, especially where the women is known to have certain factors on the higher side. This paper aims to compare and comprehensively present the findings from research work concluded so far on the risk of breast cancer in young adults. This study will prove to be beneficial as it provides a concise and proper review in one place of various reputed studies conducted so far.

Index Terms- Breast Cancer, Cancer Risk Factors, Mammography, Menarche, Women's Health, Young Females

I. INTRODUCTION

About 1 in 8 U.S. women (around 12%) develop invasive breast cancer over the course of her lifetime. In 2015, an estimated 231,00 new cases of invasive breast cancer are expected to be diagnosed in women in the U.S., along with 60,000 new cases of non-invasive (in situ) breast cancer [1]. Risk factors for breast cancer may be divided into modifiable and non-modifiable.

Their study belongs in the field of epidemiology¹. Despite a number of epidemiological factors being identified, the cause of an individual case of breast cancer is often not knowable. Also, some of the epidemiological factors are non-modifiable, such as age, gender and genetic factors.

However, there are other risk factors as well such as age at menarche, adiposity in teenage, physical activity, mammography screening, alcohol consumption, coffee & tea consumption, dietary exposures to nutrients, number of pregnancies etc. Risk factors are accumulated from a very young age as opposed to the common notion that there is a sudden onset of breast cancer.

In the recent years, there has been an upward trend in the number of breast cancer survivors, mainly owing to research pertinent to avoid recurrence, new instances of breast cancer and mortality rates etc.; is therefore necessary. The assessment of risk accumulation from a very young age must be taken into consideration, as more cases of breast cancer occurrence have been observed in young females. Also, it is worth noting that breast cancer in a young female is much more aggressive as compared to older females; women above the age of 50 years. [2] Hence the risk factor assessment and prevention is essential for young adults.

In this comprehensive study we do an in depth analysis of research work and case studies concluded so far on various risk factors which are identifiable in young adults and take into account the statistics and calculations based on already performed academic research. The objective of this article is to present a review of the published epidemiologic research on lifestyle and risk factors involved in a young adult being diagnosed with breast cancer. This review focused on modifiable factors—menarche, teenage adiposity, physical activity and exercise, mammography screening.

II. FACTORS

A. Menarche

One of the ways in which a women's reproductive system is understood is by way of the starting and ending of the ovarian and endocrine functions, the terms used for which are menarche (start) and menopause (end), consequently, an early menarche and subsequently a late menopause are known to increase the overall period during which reproductive system is active, this overall increase in the duration is known to increase risk of breast cancer. Breast tissue undergoes the most number of

¹Epidemiology is the study of the patterns, causes, and effects of health and disease conditions in defined populations.

changes from the time a female hits puberty, i.e. menarche and till the first full term pregnancy, it is during these initial years most of the risk accumulates in a woman as the breast is developing rapidly. [3] First pregnancy is an important detrimental factor for accumulation of risk, the later the first pregnancy occurs, the longer is the interval between first reproductive activity i.e. menarche and first pregnancy, therefore higher is a woman's breast cancer risk later on in life. [4]

According to an article by Lancet Oncology, a research reported findings which evaluated the risk associated with onset of menarche and breast cancer, also aiming to determine if there is an association at all and how does it affect the type cancer or tumor. [5]. The meta-analysis included individual data from 117 epidemiologic studies involving 118,964 women diagnosed with invasive breast cancer and 306,091 women without cancer. The median year of birth of women having breast cancer was 1939, and the median age at the time of cancer diagnosis was 54 years. [5][6] The mean age at menarche was reported as 13.1 years, with 65% reporting menarche between 12 to 14 years and onset of menarche for almost 16% at 11 years or less. Risk of breast cancer seemed to increase by 5% for each younger year for when the menarche began as cited in the research article. [6]

Having a comparatively young age at menarche is known to be associated with many factors affecting breast cancer risk. According to the same article of Lancet Oncology [5], the effect on breast cancer risk was higher if menarche happened earlier than the late occurrence of menopause, these findings suggest that longer is the total duration of reproductive years in a woman, higher are the chances of her acquiring cancer. In most cases women's average age at menarche has been declining each consecutive generation, resulting in increased number of breast cancer occurrence worldwide.

There are a large number of factors contributing to earlier onset of menarche, the most widespread being the changing climatic conditions, poor health during infancy, inaccessible health resources for both the mother and child, fluctuating hormonal changes etc. Being a modifiable risk factor for breast cancer cases, it is therefore important that all young girls and females are made aware of the risk factors they are exposing themselves to by not having an adequate diet at the time of pregnancy and also lack of proper nutrients in the diet of a girl from the time of birth.

B. Teenage Adiposity²

According to various studies concluded so far, it has been observed that a higher adiposity during childhood has a negative impact in association with the risk of breast cancer in women, independent of current Body Mass Index. [7–9]. Body fatness at a young age has a directly proportional effect on risk of acquiring breast cancer as this indicates higher breast density, which in itself is a seriously established risk factor for breast cancer risk [10]. Although it is worth noting that adult BMI is inversely related to breast density, there however have been few researches focusing on the role of body fatness at younger ages [11–16]. Most breast development occurs during puberty, body fatness during this time period appears to have an important role on breast density later in life. Results from recent studies [11, 12,

14, 15, 18] also support the notion that a higher body weight at a young ages may directly have an impact on breast density later in life, which in turn increases the risk of breast cancer in case higher density.

As mentioned in the research article by Breast Cancer Research [17], in the Dietary Intervention Study in Children 2006 (DISC06) Follow-up Study, an observational study took place among women in order to ascertain whether the fatness in body during teenage is in anyway linked to breast density and consequent risk of breast cancer. [17]

The conclusive finding from observational studies was that childhood adiposity was linked with a 30% increased risk of breast cancer. It is however interesting to note the parallel findings indicate an inverse relation between body fatness during childhood/adolescence and premenopausal breast density with subsequent detection of premenopausal breast cancer, independent of current adult BMI. [19][20]

In further studies, the findings of a higher weight during childhood and adolescent show a direct correlation with breast cancer into the later years at the time of menopause or post-menopause, wherein higher adiposity during childhood is directly linked with a higher risk of breast cancer in adult years, despite controlling weight in adult life. [21]. Evidence points to this relation persisting across most subtypes of breast cancer — estrogen and progesterone receptor status and those of the type ERBB2 (also known as HER2) [22]. So far strong evidence suggest a direct relation of childhood adiposity in a female and the possibility of acquiring breast cancer later in life, further research is needed to evaluate these associations with premenopausal breast density and how changes in breast density over the life course may relate to future breast cancer risk. However, to ascertain and be on the safer side in order to avoid breast cancer as well as other diseases emanating from high adiposity, it is advisable that young girls and females inculcate a proper diet and a healthy lifestyle to maintain an adequate weight as per their body mass index.

C. Physical Activity and Exercise

Physical activity has been inversely related to the associated risk of breast cancer. According to a review by Lynch et al, the reduction in the risk of having breast cancer depending on the level and amount of physical activity was found as 17% for women aged 50+, 16% during adolescence, 15% for middle aged women and 8% for adulthood respectively. [23].

As seen in a review by Monnikopf et al, an inverse relation was observed between early physical activity in females and a reduced risk of breast cancer in them, where about half the studies assessed physical activity that took place before the women turned 20. [24]. Some studies have reported that physical activity in the recent years tends to have a stronger effect as compared to activity in say childhood, however this could also be due to a more accurate recollection of physical activity in recent past leading to more direct reporting of recent physical activity. [25].

It has been ascertained for both premenopausal and postmenopausal women that huge benefits of physical activity during pre-teen and teenage years exist, but it is also very essential that the level of physical activity be maintained from younger years well in to the later year of adulthood to retain the

² Adiposity is the quality or state of being fat: obesity.

benefits. In the Nurses' Health Study II, women engaging in high levels of physical activity during teenage and as adults, displayed a highly reduced risk of breast cancer, almost 30% reduction as compared to women with lower levels of physical activity. [26] As strengthened by the Shanghai Breast Cancer Study, which clearly depicts that women who had done more physical activity during both their adolescence as well as adulthood had highest reduction in risk of occurrence of breast cancer before menopause and after menopause in comparison to women with lower levels of physical activity or exercise. [27].

The benefits associated with physical activity during youth vary from the type of activity, its duration and most importantly the intensity of physical activity. Despite the variation in the studies that collect a wide variety of information regarding physical activity, the conclusive finding remains that an intense physical active workout incorporated in the lifestyle for a longer duration proves to be beneficial. [23]. An individual's physical activity and frequency of the same has a direct effect on sex hormones, endocrine activity, insulin related issues, weight fluctuations and immune system. [28].

It has been observed that higher levels of physical activity decreases the risk of breast cancer, more so due to a mechanism which also results in reduced mammographic density. In the prevention of breast cancer a number of major challenges need to be dealt with, since most of the non-modifiable risk factors are established in childhood itself, pertaining to family history, number of pregnancies, age of menarche etc. and are difficult to influence. However, physical activity remains to be one of the few modifiable factors that have been linked to show observable results in reduction of breast cancer. [29-32].

Mammographic density or in other words breast tissue density, is another extremely strong risk factors of breast cancer, it is observed that women with a higher mammographic density have a four to six times increased risk of breast cancer. [34-36]. consequently studies conducted on how mammographic density can be reduced have shown that women who have inculcated physically active schedules have a lower mammographic density compared with less active women. [37-39].

All in all results suggest that women at high risk of breast cancer may have to engage in more intense physical workouts in order to achieve a reduction in their mammographic density compared with women at lower risk and the overall positive effects of a physical activity will strengthen the women's immunity and disease fighting capabilities.

D. Mammography Screening

Mammography screening is a kind of test that helps in detecting breast cancer in women with no directly identifiable symptoms of the disease, it helps in diagnosing the cancer at an early curable stage. The x-ray images obtained during the screening process make the detection possible for detect tumor that cannot be felt on the surface, therefore for early detection to be beneficial, a growth pattern of tumor is expected, along with the anticipation that the cancer also has not spread at the time when tumor are detectable at mammography.

Mammography screening for breast cancer is a widely available medical test in many countries for women. Initially it was touted as a universal achievement in order to improve women's health by virtue of early detection in breast cancer, the

benefits and harms of mammography screening however have largely been debated in the past years. One of the primary benefit of mammography screening is early detection, leading to a quicker response time in order to successfully cure the cancer, thereby resulting in reduction of breast-cancer related death.

However in despite the benefits provided by regular mammography screening, a number of risks are also associated to it. Primarily being that of false positive and false negative result or in other words over diagnosis and under diagnosis of breast cancer. Based on recent estimates from the United States, the relative amount of over diagnosis (including ductal carcinoma in situ and invasive cancer) is 31%. This means that in the results of mammography, there are about 15 women who are over diagnosed for every 1,000 women invited for regular mammography screening for 20 years starting from the age of 50.

It is essential that Women be informed about the benefits and harms of mammography screening, biopsies being relatively simple surgeries, pose no direct harm to the women undergoing the test, however it can induce stress, scarring and disfigurement, also add to health care costs.

If the assumptions made regarding growth of tumor are not correct or if tumor is heterogenic, meaning thereby, it is a result of some other form of cancer & not originating in the breast, in such scenarios mammographic screening might not be an adequate tool [40].

In order to have relative insight about benefits and harms of a screening: it is found that among 1,000 women who begin regular mammographic screening at age 50 and continue being tested for 20 years, among these about 2 to 3 will benefit from the screening and evade serious consequence or death from breast cancer and 200 women will have at least one false positive test where cancer will be diagnosed in the patient wrongly, however in actual it will not be present, such a woman then might be undergoing treatment for breast cancer which was never actually present in her body, 30 will undergo a biopsy to confirm the findings resulting from screening, 3 will be diagnosed with an interval cancer, and subsequently breast cancer will be over diagnosed.

Apart from the over diagnosis, mammography can sometimes lead to false negative results as well, indicating that cancer is no longer present in the breast tissue but in reality however the traces of cancer remain in the body and go undetected.

III. CONCLUSION

The factors that are directly linked to breast cancer accumulate much earlier in life contrary to popular belief. Different factors such as early onset of menarche, higher childhood adiposity, mammography screening, lesser physical activity, genetic factors and family history of cancer greatly affect a woman's risk of acquiring breast cancer later on in life. It is therefore of utmost importance that all young girls and females follow a healthy lifestyle along with adequate dietary supplements, especially at the times when the body of the girl changes, for example at the time attaining maturity in teens, during pregnancy and menopause to name a few. It is essential that the females understand the risks they are exposing their

bodies to in the present scenario, wherein the environmental changes are at an all-time high.

Also, females with a higher risk of having breast cancer—those above the age of 65, inherited gene mutations such as BRCA1/BRCA2, family history of cancer, or personal history of cancer— must especially take extra care of their health and immunity. Such females might largely benefit from engaging in more intense physical workouts in order to achieve a reduction in their mammographic density thereby also reducing slight chances of acquiring breast cancer.

Apart from this, the females that undergo regular mammography screening must be made aware of the plethora of options available with them to get their regular check-up done. They should be informed about the positives and the negatives of undergoing a mammography screening test, as this particular method of diagnosing a case of breast cancer in preliminary stage, has been debated quite a lot in the recent past. For one, this screening results in cases of over diagnosis, wherein cancer is not present in the body but the test falsely suggests that it might be, post which the patient may be misguided and need more tests or even might start getting treated for cancer. Another, problem posed by screening is that of under diagnosis where mammography lead to false negative results as well, indicating that cancer is no longer present in the breast tissue but in reality however the traces of cancer remain in the body and go undetected.

With the ever evolving technology and advancements in the field of medical science, it is important the females are well aware and well informed on how their bodies work and the risk factors they might be having. Advancement in technology is meant to bring down the cases of breast cancer, and improve the overall mortality rate in those who have been diagnosed with it.

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Authors' contributions— Both the listed authors collaborated and came up with the research topic. AS provided essential research work concluded previously which was then studied and analysed in detail by KR. KR picked out few factors linked directly to breast cancer i.e. *Age at Menarche, Childhood Adiposity, Peak Height Growth Velocity, Physical Activity, Mammography* and drew out conclusions on how these affect the risk of a young female being detected with breast cancer later in life and explored more research articles from various journals. After the conclusion phase, KR began the drafting process. AS actively participated in the revision and conception process of the final draft. Both authors give their final consent for publication of the manuscript.

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