

Review Article

Implication of oestrogen in the development of breast cancer: a brief narrative review

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ABSTRACT

The presence of hormones in milk and dairy foods was discussed decades ago but more concerns were with respect to finding hormones as biomarkers in milk for diseases and pregnancy diagnosis. Considerable amount of studies demonstrated that milk is essential for infants growing and immunity, while increasing body of evidence are indicating possible negative impact on human health including the role of some estrogens in the initiation and provoking of breast cancer. In this brief narrative, we reviewed recent data on oestrogens and breast cancer risk including comparative levels of hormones in cow milk, risk of breast cancer attributable to intake of different foods and lifestyle factors. Empirical findings indicate that consumption of cow milk is probably being over-emphasized as source of exogenous oestrogen, whereas control of alcohol as well as obesity and physical activity are under-emphasized in discourses on preventive protocols.

Keywords: Anthropometric measures, Breast cancer risk, Lifestyle confounding factors

INTRODUCTION

Breast cancer is the number one cancer scourge afflicting women. It is estimated that about 12.5% of women are likely to have breast cancer in their lifetime.¹ Breast cancer is currently the most common cancer among Nigerian women (Table 1) and Nigeria is one of five countries with highest standardized mortality rate (25.9%) in the world.^{2,3} Improved diagnostics and treatment strategies have decreased breast cancer

mortality but the physical and psychological burdens of surgery radiotherapy, hormonal and chemotherapy are substantial.⁴ For this reason, breast cancer prevention represents a major focus of current research.⁵

Epidemiological and experimental evidence implicates Oestrogens in the aetiology of breast cancer. Most established risk factors for breast cancer in humans are thought to influence risk through hormone-related pathways.⁶⁻⁸

Table 1: WHO data on cancer among Nigerian women.²

	Breast	Cervix uteri	Colorectal	Liver	Others
Mortality profile (%)	34	21	4	10	31
Incidence	27304	14089	2008	4172	1778

Increased concentrations of endogenous oestrogens are strongly associated increased risk for breast cancer in postmenopausal women and trials have shown that the anti-oestrogens tamoxifen and raloxifene reduce the incidence of breast cancer.^{6,9} Experimental studies in animals have shown that oestrogens can promote mammary tumours, and a decrease in exposure to oestrogens, by performing an oophorectomy or giving an anti-oestrogenic drug, has the reverse effect.¹⁰ However, the effects of oestrogen alone between breast cancer and hormone-related risk factors. Other hormones, such as progesterone, prolactin and testosterone may also be important.^{6,11,12}

This work explores the evidence in literature that exposure to animal oestrogen is a major determinant of risk breast cancer. It is not intended to be a comprehensive review, but focuses narratively on epidemiological and experimental data relating to the implication of oestrogen in the aetiology of breast cancer and possible mechanisms that might account for the association.

NARRATIVE REVIEW

Reproductive risk factors of oestrogen-induced breast cancer

Oestrogens have an essential role, together with other hormones, in the development of the female sex organs and secondary sex characteristics, the regulation of the menstrual cycle and reproduction. Thus, it has been proposed that the effects of many established reproductive risk factors for breast cancer are mediated by hormonal mechanisms, for the most part involving oestrogens.⁶

Epidemiological studies have also firmly established associations between risk for breast cancer and other reproductive factors, including nulliparous (having no children) or low parity, late age at first birth, and breast feeding.¹³ After a transient increase in risk for breast cancer, peaking at about 5 years after giving birth having at least one child is associated with a decrease in the long-term risk of developing breast cancer compared with risk among the nulliparous, and this protective effect increases with the number of children.¹⁴ Each birth reduces the relative risk of breast cancer by an average of 7%.¹⁵ The reduction of risk per birth is greater for births at young ages than older ages, such that women who have their first birth before the age of 20 years have a 30% lower risk than women with a first birth after the age of 35 years.¹⁶

A mechanism involving oestrogens, and probably other hormones, has been proposed to explain both the transient increase in risk and the reduced risk in the long term associated with pregnancy. The very high serum

levels of oestrogen and progesterone during pregnancy stimulates the growth of the mammary epithelium and also promotes the differentiation of epithelial tissues reducing the number of epithelial structures most vulnerable to malignant transformation.¹⁷ Thus, the short-term effect of pregnancy may be to promote the growth of cancer if the malignant transformation is present in the breast, but in the longer term, the risk of breast cancer is reduced. In contrast, malignant transformations are more likely to have accumulated in the breast tissue of older women, and there might, therefore, be a high risk of cancer developing in these women when breast cells are stimulated to divide during pregnancy. Breastfeeding is associated with a modest decrease in risk for breast cancer, above and beyond that associated with multiple pregnancies (4% for every 12 months of breastfeeding).¹⁷ This effect might be due to the suppression of ovulation, reducing exposure to ovarian hormones.

Animal products risk factors, oestrogen and breast cancer

All foodstuffs of animal origin including dairy products contain oestrogens albeit with various concentrations, which depends on kind of food, species, gender, age and physiological stage of the animals. The importance of existence of the oestrogens in dairy products is considerable with respect to;

- Cow milk as the second major source of nutrients for infants and growing children after breast milk,
- Possible effect initiating or provoking tumor, and
- Growth-promoting hormones utilized in veterinary medicine results in an increase of the residues in milk and other dairy foods.¹⁸

The afore-mentioned reasons have demanded the development of sensitive analytical methods for extraction, detection and quantification of the oestrogens in animal products. For instance, advanced method of oestrogens detection in milk was provided by using hydrolysis reaction implementing before extraction which followed organic solvent and solid phase extractions and finally quantified by gas chromatography and mass spectrometry.^{19,20}

Indeed, it is known that steroid hormones occur either naturally or due to use as anabolic agents.^{21,22} Hence, virtually all foodstuff of animal origin contains 17 β -estradiol and its metabolites, although the levels of hormone and its metabolites vary with the kind of food, gender, animal species, age and physiological condition of the animals.

Yet, estrogens may be unavoidable hormones in non-vegetarian human nutrition, but 17 β -estradiol is very minimal in cow milk relative the concentration of other hormones such corticosteroids and prolactin (Figure 1).²³

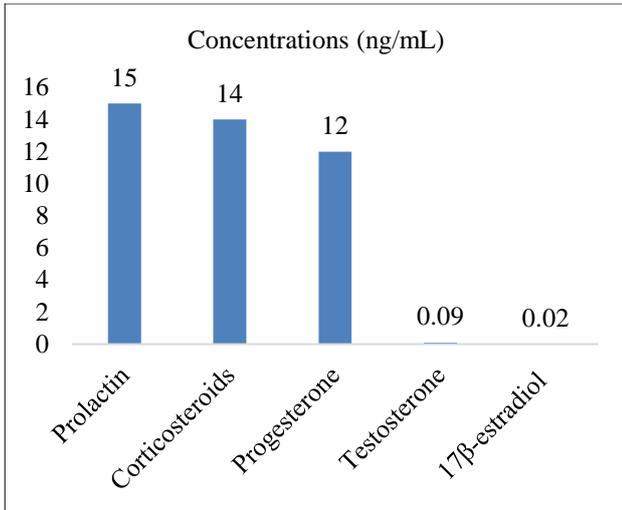


Figure 1: Comparative concentrations of hormones in cow milk.²³

That is, given the postulation that up to 80% of estrogens come from milk and dairy products in Western diets there is need to acknowledge bioactivity of oral 17β-estradiol being a bit low and oestrogen sulphate as the main conjugate in milk having a relatively high oral bioactivity.^{23,24} Further, epidemiological studies indicate a very strong relationship between milk and dairy products high consumption and high incidence of testicular and prostate cancers.²⁵ A critical review of prospective study report indicates that animal products as risk factors for breast cancer is not consistent with, highest in, or limited to milk consumption (Figure 2). In particular, the report shows an observation whereby a subpopulation that consumed zero whole milk (quintile 1) presented higher percentage of breast cancer compared to other quintile groups (Figure 3).²⁶

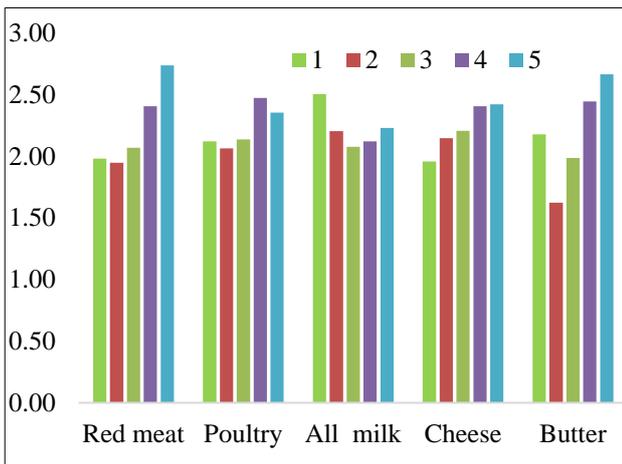


Figure 2: Comparative % breast cancer cases per quintile in EPIC report on intake of different food.²⁶

This is supported by pooled analysis of data from more than 20 studies, which found no significant association between dairy product intake and breast cancer risk and

breast cancer risk.²⁷ However, data from the Nurses' Health Study II found that adolescent total fat may be significantly associated with a higher risk of breast cancer before menopause.²⁸ Considering the observation depicted in figure 2 that both red meat and poultry diets may be equally predispose to breast cancer, it means that lifestyle is a valid confounder to be reviewed.

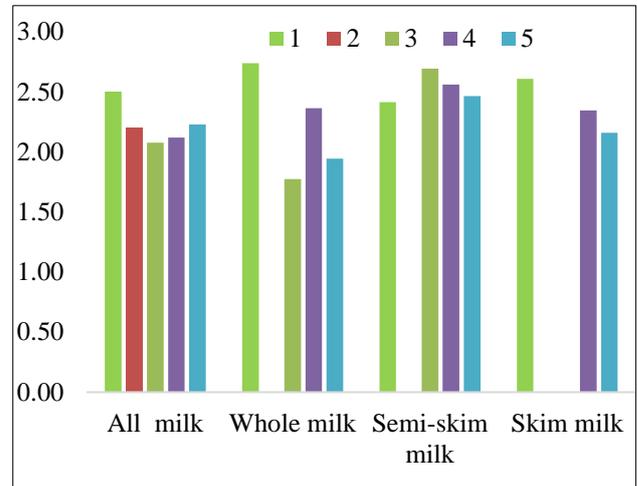


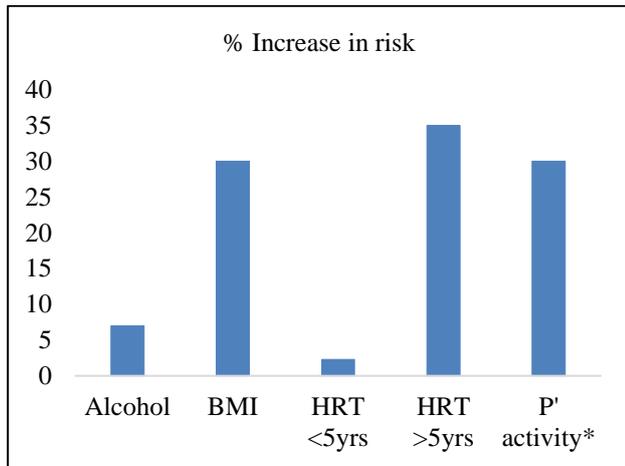
Figure 3: Comparative % breast cancer cases per quintile in EPIC report on intake of different milk.²⁶

Lifestyle confounders of breast cancer risk and screening program in Nigeria

A review on how breast cancer is related to diet and lifestyle was published in 2003 is hereby critically narrated.⁷ In the article, it is emphatic that alcohol intake and obesity have been established as breast cancer risk factors, while physical activity is suggested to modulate (Figure 4). The explanation propounded is that while the mechanism of effect of alcohol is unknown, obesity may be due to extra production of oestrogen by the excess adipose tissue in obese individual. It is also explained the physical activity reduces breast cancer risk by 20-40% (i.e. average 30%); and that this is probably due to reduced weight gain vis-à-vis less adipose tissue predisposing to less production of oestrogen. The paper went on to indicate on the disparity in effect of hormone replacement therapy (Figure 4).⁷

This idea of lifestyle confounders of breast cancer risk remains credible as it has been reported by other authors and the need for evidence-based preventive methods remains a concern.²⁹⁻³¹ In Nigeria, there is the implicit awareness that obesity need be screened as one of specific risk factors of breast cancer.³² However, whether these lifestyle confounding variables are assessed in breast cancer screening programs is yet to be articulated. For instance, in a recent report from a Nigerian study, it has been indicated that up to 19.7% of women among the study participants had breast cancer screening.³³ Interestingly, information on alcohol intake, obesity index and physical activity were reported. This calls for

research investigation into breast cancer screening and diagnostic protocols e.g. if lifestyle confounding factors are being adequately evaluated.



*Potential reduction risk level in a physically active person

Figure 4: Lifestyle factors related to breast cancer risk.⁷

To our knowledge, the existing protocols do not include assessing these lifestyle factors in breast cancer screening.³⁴ Yet, it is known that limiting alcohol intake is a potential preventive measure.¹ It is also known that there has been no operational action plan or policy statement to reduce alcohol consumption, obesity and physical inactivity in Nigeria.² Therefore, there is as yet no control of the lifestyle confounding risk factors of breast cancer among Nigerian women. Hence there is significant imperativeness to review the existing protocols for management and preventive counselling of breast cancer.

CONCLUSION

Most of the previous knowledge about oestrogen is according to their physiologic and chemical concentrations of oestrogen. Recently it has been found that this hormone even at very low doses may have significant biological effects. To this end and with respect to the considerable progress in developing of analytical methods and bioassays, it is critically needed to clarify the possible and potential impact of oestrogens in animal products on consumers' health situation. This is especially because while it is already pointed out that possible unwanted effects on human health by consumption of meat from oestrogen treated animals cannot be excluded, this narrative review indicates that breast cancer risk is neither consistent with highest intake, nor limited to milk consumption. More work is needed to clarify the effects of hormones on risk for breast cancer and the mechanisms involved as well as the implication of confounding lifestyle factors.

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