

Oral Contraceptives and Breast Cancer Risk: A Study among the Bengalee Females of West Bengal, India

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Abstract

Breast Cancer is the one of the diseases affecting the world wide women population. In Indian perspective, breast cancer is one of the leading cancers, being the most common carcinoma among the females in West Bengal. The present study attempts to understand the association of oral contraceptives use and breast cancer in Bengalee Hindu Caste Females of West Bengal. To best of the knowledge oral contraceptive use and breast cancer risk among the females is yet to be taken in consideration in Bengalee Hindu caste females. To achieve the purpose 108 diagnosed breast cancer patients were considered along with 120 age matched controls without the history of breast cancer in the family. Result indicated use of oral contraceptives have significant ($p < 0.001$) association with breast cancer. Therefore, the present study vindicated other than genetic predisposition modification of reproductive and lifestyle factors might be taken into consideration in early prognosis of breast cancer among the studied population.

Keywords: Oral Contraceptives; Breast Cancer; Bengalee Hindu Females; West Bengal; India

Abbreviations: OC: Oral Contraceptive.

Introduction

Breast cancer is represented as the most common form of cancer and the leading cause of Cancer death among women worldwide [1]. Reproductive history and exogenous hormonal exposures are acknowledged risk factors for Breast Cancer in general population [2]. Cancer is the leading cause of death worldwide including India and second leading cause of death in developing countries [3]. According to Siddhartha Mukherjee, Cancer is the "emperor of all Maladies" [4]. Cancer can be reduced and controlled by implementing evidence based strategies for cancer prevention, early detection and management. One

third of cancers could be cured if detected early and treated adequately, based on the observation that treatment is more effective at early stages. In addition, more than 30% of cancers could be prevented simply by behavioral changes that include abstinence from using tobacco, use of healthy diet, maintaining a healthy weight, being physically active and preventing infections that may cause cancer death [5].

According to the epidemiological studies, 80 to 90% of all cancers are due to environmental factors of which, lifestyle related factors are the most important and preventable. The major risk factors for cancer are tobacco, alcohol consumption, infections, dietary habits and behavioral factors. Dietary practices, reproductive

and sexual practices account for 20 to 30% of cancers. Studies have shown that appropriate changes in lifestyle will reduce the mortality and morbidity caused due to cancer. This offers the prospect for initiating primary and secondary prevention measures for control and prevention [6]. Thus, nowadays it is believed that breast cancer is a complex multi-factorial, polygenic and multi-step process [7,8].

Some studies have reported an increased risk of breast cancer among women who have had induced abortions [9,10]. In incomplete pregnancy, the breast is exposed only to the high estrogen levels of early pregnancy and thus may be responsible for the increased risk seen in these women. However, some other studies have found no association between abortions and increased risk of breast cancer [11].

To best of the knowledge oral contraceptive use and breast cancer risk among the females is yet to be taken in consideration in Bengalee Hindu caste females. The present study attempts to understand the association of oral contraceptives use and breast cancer in Bengalee Hindu Caste Females of West Bengal.

Methodology

Study participants included cases and controls ranging in age from 30-72 years. The cases included subjects visiting the main cancer referral centers of West Bengal; Cancer Center Welfare Home and Research Institute, Kolkata, National Medical College and Hospital, Kolkata. The controls were such selected that none of them had any personal or family history of breast cancer.

Data on reproductive performances included parity, age at first child, menarche, menopause, duration of breast feeding, physical activity and diet with detailed information regarding OCP use and abortion incidents. History of breast cancer and oncologic data was retrieved from the medical records after consent from the patients. Demographic data were also collected for all participants.

Data collected were analyzed using SPSS 20.0. Binary logistic regression was used to assess the correlation of any other possible risk factors and the degree of their contribution to breast cancer.

Oral contraceptive use has been defined as use of Oral Contraceptive pills for a total or more than 6 months. Women who never used oral contraceptives or who never

used them for less than 6 months were classified as non-users.

Results

The use of oral contraceptives slightly increases the risk of breast cancer in current and recent users, cancers diagnosed in women who have used OC tend to be less clinically advanced than those detected in never users. OC users are generally younger women whose breast cancer risk is comparatively low. The risk seems to go back to normal over time since the pills are stopped. Women who stopped using oral contraceptives more than 10 years ago do not appear to have any increased breast cancer risk. Over the past 30 years, the levels of the female hormone estrogen in the combined pill have decreased. It is not yet clear whether the modern, low doses in the combined pill are associated with the same breast cancer risk as the older, higher dose pills. While the combined pill is the most commonly used contraceptive pill, some women use the progesterone only pill (or "mini pill"). There is currently not enough evidence to determine whether or not there is a link between other forms of hormone-based contraception and breast cancer.

An important criterion for evaluating causality is the biological plausibility of the relationship. Estrogen causes proliferation of breast tissue and would be expected to increase breast cancer risk by stimulating growth of stem cells and intermediate cells. Progestin causes alveolar cell growth in the estrogen-primed breast, but it also causes differentiation. The influence of estrogen and progestin on breast epithelium proliferation and differentiation appears to differ.

	Patients		Controls		ODDS Ratio
	No.	%	No.	%	
No	37	34.3	75	58.6	2.7677***
Yes	71	65.9	52	40.6	95% CI = 1.63 - 4.71
Total	108	100	128	100	

Table 1: Distribution of Oral Contraceptives use among the cases and controls.

There is a marked difference in users and non-users of oral contraceptives among the patients and controls. 65.7% of the patients and 40.6% of the controls are users of the oral contraceptives, whereas 34.3% of the patients and 58.6% of the controls are non-users of the same. Ever use of oral contraceptives increases the risk of having

breast cancer by 2.77 times than non-users (OR-2.77; 95% CI= 1.63 to 4.71, $p < 0.0001^{***}$).

Discussion

Age and family history are commonly considered to have effect on prognosis and survival of breast cancer. The present study revealed substantial variation in breast cancer risk among the mutation carriers, particularly in terms of age variation and cancer type which basically envisaged that the concomitant effect of genetic variability and environmental factors which eventually modify the expression of the status.

The implication of natural hormones specially the sex hormones on developing cancers such as endometrial cancer [12], breast and prostate cancer [13] (among sex organ related neoplasm) or colon cancer [14], gall bladder cancer [15], kidney cancer [16] etc (non sex organ related neoplasm) have been reported globally. Furthermore, breast cancer risk is enhanced by increasing the duration of exposure to endogenous hormones (Endogenous Hormones and Breast Cancer Collaborative Group, 2011). It has also been reported that age at menarche, parity and age at first full-term pregnancy are risk factors for breast cancer [17,18]. In addition to that breast cancer risk is associated with several reproductive factors. It is well established that breast cancer risk increases with early age at menarche [19].

Cancer risk is thought to be a function of the number of cells at risk, which varies with age. It is possible to posit that any carcinogenic risk of oral contraceptives may be strongly mediated by age of exposure or by the timing of exposure in relation to other events that are thought to affect epithelial proliferation or differentiation (e.g., menarche, full-term pregnancy). The etiology of breast cancer has strong hormonal themes.

Furthermore, long-term users of Oral Contraceptives (OCs) were at a higher risk of breast cancer than never users. Association studies regarding current/recent use of OCs with breast cancer risk demonstrated heterogeneous results to the extent of increased risk to no or weak association of OCs use among BRCA1 mutation carrier in Breast Cancer [20]. In this context, the present study revealed significant association ($p < 0.0019$) of prolong use (more than six months) of OCs and breast cancer in comparison (Table 1) to the controls and the use of OCs increased the risk of breast cancer by 2.77 times than those of non-users (OR- 2.77; 95% CI= 1.63 – 4.71; $p < 0.0001$). The controversial effects of OCs on breast

cancer have been studied extensively. But currently there is conflicting epidemiological evidence regarding the role of oral pills in causation of breast cancer, so it is difficult to make a blanket statement [21]. For instance, several studies have found no significant association between history of oral contraceptive uses and breast cancer but other studies have shown diametrically opposite results [22-24]. The present study also could not measure the relationship of breast cancer with duration, type, dosage, and pattern of OCs usage because most of the subjects were not able to recall the details. For the females those have mutated tumor suppressor genes like BRCA1, the gene already fails to perform its tumor suppressing activity; elevated estrogen and progesterone stimulate breast cell proliferation, finally uncontrolled growth leads to carcinoma. Studies have found association between the OCs usage and BRCA1 mutation carriers. However, paucity of literature has been found from Indian context [25,26]. The present study reports significant association ($p < 0.0019$) between OCs and breast cancer from eastern India for the first time. Since, hormones are considered to play a role in the etiology of breast cancer therefore, it is likely that BRCA1 might have important regulation of growth and differentiation in hormonally responsive epithelial cells. In addition to that, breast and ovary being the main estrogen receptor sites, the increased levels of the estrogen due to prolonged consumption of oral contraceptives gets accumulated in these sites. Such finding is similar to the present study mentioned earlier, which has significant association with use of OCs and increased breast cancer risk, while many studies have represented that exogenous hormonal factors such as estrogen replacement therapy and combined oral contraceptive use might cause to some extent increase in the risk for breast cancer [12].

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