

Study on the Relationship Between Breast Cancer and Female Endocrine Conditions, Hormone Therapy and Oral Contraceptive Usage among Women in Yazd, Iran During 2006-2007

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Abstract: Breast cancer is one of the most prevalent cancers among women and the prevalence of it in Yazd, Iran was reported as 2.62%. WHO mentioned postmenopausal hormone replacement and oral contraceptives as first group carcinogens. Endocrine conditions like late menopause, early menarche and nulliparity develop the risk of this cancer. This study was designed to determine the relationship between breast cancer and female endocrine conditions, hormone therapy and OCP usage among women in Yazd, Iran. In a case-control study which was done on 102 women with breast cancer and 200 healthy ones during 2006 - 2007. They were asked by a blinded interviewer about age of menarche, menopause, first full-term pregnancy, number of deliveries, history of Hormone therapy and OCP consuming. Cases selected randomly among women who was admitted in oncology department for breast cancer while controls matched with cases and did not have history of any chronic or malignant disease. Chi-square method with a confidence interval (CI) of 0.95 and two sample independent t-test was used. Results revealed that Mean \pm SD age was 48.61 \pm 10.63 for cases and 43.43 \pm 10.01 for controls. 44.4% of cases had regular monthly period while 26.3% had irregular. There was no significant difference between case and control groups for having monthly period. 61.1% of cases used contraceptives while 44.7% of healthy ones used it. Contraceptives usage was significantly different between two groups (P=0.009, CI=0.95). Mean \pm SD age of first full-term pregnancy for cases was 21.19 \pm 4.40 while in controls it was 32.75 \pm 3.25 which was significant in analysis (p=0.00, CI=0.95). There was also a significant difference between case and control groups for numbers of pregnancy (P= 0.009). It was concluded that in our society ovulatory cycles and hormone replacement therapy was not as risk factors, but using oral contraceptives recognized as a risk factor. Results also showed that younger age of first full term pregnancy and number of pregnancies were as risk factors for breast cancer in contrast with some other studies.

Key word: Breast cancer • Pregnancy • Contraceptive • Monthly period

INTRODUCTION

Breast cancer is one of the most prevalent cancers among women worldwide. Differences between high-incidence and low-incidence regions showed that environmental factors are able to influence breast cancer risk [1]. The prevalence of breast carcinoma among women in Yazd, Iran was reported as 2.62% [2].

A short duration of menopausal hormone therapy (MHT) elevated the risk of breast cancer which was disappeared 5 years after cessation [3]. The recent dramatic decline in MHT use in united states was related to decrease in the incidence of estrogen receptor positive tumors confirming a relationship between MHT and some kinds of breast cancer [4]. World Health Organization (WHO) categorized postmenopausal hormone replacement and oral contraceptives as first group

carcinogens [5]. Investigations have showed an increase risk among women who used oral contraceptives, especially in ones that used them before a first full-term pregnancy [6-8]. Some studies showed that using progesterone and estrogen in combination increased the risk of breast cancer more than estrogen alone [3, 9-14]. Endocrine conditions such as late menopause, early menarche and nulliparity develop the risk of breast cancer [15-18]. women who born their first child before 24 years old have less risk in their lifetime for developing breast cancer [16]. A meta-analysis on Asian women showed that more than three abortions, family history of breast cancer, age at first live birth more than 30 years old and age at menarche less than 12 years old increased risk of cancer in them [19].

This study was designed to determine the relationship between breast cancer and female endocrine conditions, hormone therapy and OCP usage among women in Yazd, Iran.

MATERIALS AND METHODS

In a case-control study which was done in 2006 to 2007, 102 women with breast cancer and 200 healthy ones were asked some questions about their age of menarche, age of menopause, number of deliveries and age of first full-term pregnancy. They were also asked about history of Hormone therapy and OCP consuming. Breast cancer women selected randomly among women who lived in Yazd since 10 years ago that had pathologic diagnosis for breast cancer and was admitted to Oncology Department in this city while control ones chose according to characteristics of cases and matched with them. Control women did not have history of cardiovascular disease, diabetes mellitus and any other malignancies.

All data gathered by a questionnaire designed according to the similar, previously published studies which its validity and reliability confirmed with pilot studies. Each questionnaire fulfilled by an interviewer who asked the questions and explained about them.

For more validity interviewer and analyzer were blinded and did not know about cases and controls.

All data gathered and analyzed by descriptive and analytic tests by SPSS software. For signification evaluation we used Chi-square method with a confidence interval (CI) of 0.95. Also for parametric variables two sample independent t-test used to estimate the differences between case and control groups along with logistic regression for association of variables with breast cancer.

RESULTS

The number of cases and controls were 102 and 200, respectively. All were females that their Mean \pm SD age was 48.61 \pm 10.63 for cases and 43.43 \pm 10.01 for control group.

44.4% of cases had regular monthly period while 26.3% had irregular monthly period. In control group regular and irregular monthly period was reported 55.3 and 18.1%, respectively (Table 1). Chi-square test showed that there was no significant difference between case and control groups for having monthly period.

We divided them into 2 groups: having monthly period (even irregular) and not having monthly period. Again there was no significant relationship between case and control groups.

Mean \pm SD age of menopause for cases and controls were 47.17 \pm 6.61 and 46.39 \pm 5.87. Independent Samples t-test showed that there was no significant relationship between the age of menopause and breast cancer (P=0.576, CI=0.95). Odds Ratio for age of menopause was 0.98.

61.1% of breast cancer women used contraceptives while 44.7% of healthy ones used it. Results of Pearson Chi-square test confirmed that contraceptives were as a risk factor in our society. (p=0.009, CI=0.95). Cases had 1.942 times more risk than controls for developing breast cancer by contraceptive usage (Table 1).

28.6% of women who were in menopause age used hormone replacement therapy in cases while it was 33.3% in control group. Chi-square test stated that there was no significant difference between cases and controls for taking sex hormones after menopause.

Mean \pm SD age of first full-term pregnancy for case group was 21.19 \pm 4.40 while in control group it was 32.75 \pm 3.25. Independent t-test showed a significant difference between cases and controls (p-value=0.00, CI=0.95). Age at first full-term pregnancy could be a risk factor of breast cancer in this community. Younger first full-term pregnancy could increase the risk of breast cancer in this study.

Table 1: Frequency of monthly period status and contraceptive usage in cases & controls

	Case(frequency)	Control(frequency)
Regular monthly period	44.4%	55.3%
Irregular monthly period	26.3%	18.1%
Stopped monthly period	29.3%	26.6%
Using contraceptive pills	61.1%	44.7%

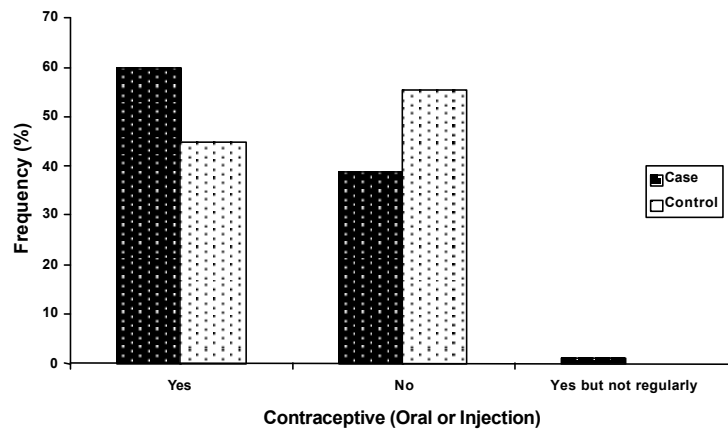


Fig. 1: Frequency percentages between case and control individuals for receiving oral contraceptives

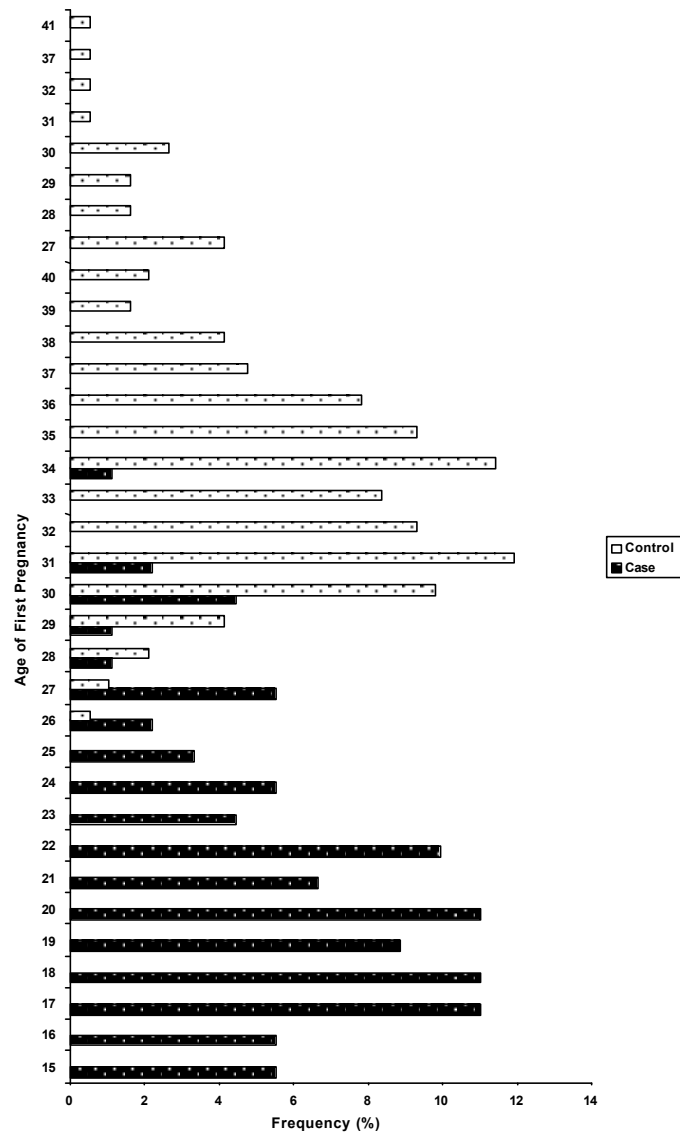


Fig. 2: Frequency percentages of the age of first pregnancy

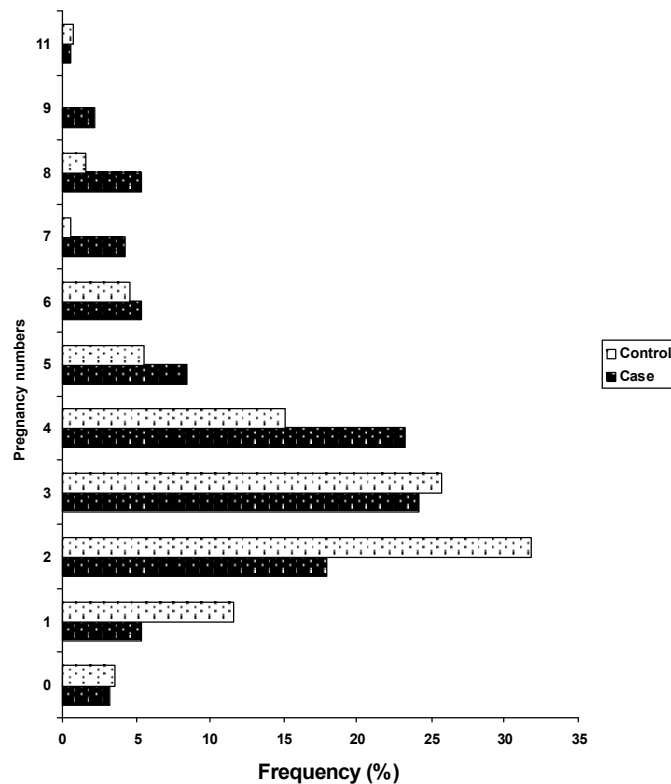


Fig. 3: Comparison of pregnancy numbers between case and control individuals

Chi-square analysis also showed a significant difference between case and control groups for numbers of pregnancy ($P=0.009$). If cases and controls divided into two categories, who had been pregnant for 3 times or lesser and who had been pregnant more than 3 times, again the difference between case and control groups become significant ($P=0.000$, $OR=0.386$ (0.23, 0.647)).

DISCUSSION

Monthly periods and age of menopause, were not significantly related to breast cancer in our population. Ovulatory and Menstrual patterns during adulthood affect the risk of chronic diseases. Age of menarche and cumulative number of ovulatory cycles are considered major risk factors of breast cancer [20].

The relationship between oral contraceptive use and breast cancer risk has been in controversy and many research was done about them and their role [21-22]. Our investigation stated that taking OCP and age of the first pregnancy were a risk factor of breast cancer (the less age of first pregnancy, the more risk of breast cancer). But some studies believed that early pregnancy is a protective factor for breast cancer [23-24].

Studies on combined estrogen and progesterone hormone therapy have generally increased risk of breast cancer [12]. But, our study showed taking estrogen therapy was not related to breast cancer. But it's not referable because of the restricted sample size. We suggested a long term cohort study by at least 1000 sample and 10 year follow up. Although, in the study have done by Andrea Eisen *et al.* showed that postmenopausal women with a *BRCA1* mutation, hormone therapy was not related with breast cancer risk, actually it was as a protective factor in this study.

Our study showed that Lower first full-term pregnancy increase the risk of breast cancer in this study. But, a study which was done in Japan on bomb-survivors and not exposed showed the different results, age at first full-term pregnancy was strongly and positively related to developing breast cancer [26].

Our data showed that increase in the number of deliveries was a risk factor for breast cancer. In addition some investigations reported number of full-term pregnancy more than one was recognized as a protective factor to reduce breast cancer risk [27-31] while some studies, such as Ana and *et al.* and Marion and *et al.* showed that number of full term pregnancy may be as risk factors for breast cancer [32-33].

CONCLUSION

According to our results, it can be concluded that ovulatory cycles and hormone replacement therapy was not as breast cancer risk factors, but using oral contraceptives recognized as a risk factor.

Our results also showed that younger age of first full term pregnancy and number of pregnancies were as risk factors for breast cancer in contrast with some other studies.

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REFERENCES

1. Terry, P.D. and T.E. Rohan, 2002. Cigarette smoking and the risk of breast cancer in women. *Cancer Epidemiology Biomarkers & Prevention*, 11(10): 953.
2. Modir, A., *et al.*, 2007. prevalence of breast cancer and positive predictive value of mammography among yazd city women. *Pakistan J. Surgery*, 23(1).
3. Beral, V., 2003. Breast cancer and hormone-replacement therapy in the Million Women Study. *Lancet*. 362(9382): 419.
4. Kerlikowske, K., *et al.*, 2007. Declines in invasive breast cancer and use of postmenopausal hormone therapy in a screening mammography population. *J. the National Cancer Institute*, 99(17): 1335.
5. Schneider, H., A. Mueck and H. Kuhl, 2005. IARC monographs program on carcinogenicity of combined hormonal contraceptives and menopausal therapy. *Climacteric*, 8(4): 311-316.
6. Romieu, I., J.A. Berlin and G. Colditz, 1990. Oral contraceptives and breast cancer review and meta analysis. *Cancer*, 66(11): 2253-2263.
7. Thomas, D.B., 1991. Oral contraceptives and breast cancer: review of the epidemiologic literature. *Contraception*, 43(6): 597-642.
8. Beral, V., *et al.*, XXXX. Collaborative group on hormonal factors in breast cancer. Breast cancer and abortion: collaborative reanalysis of data from,
9. Rosenberg, L.U., *et al.*, 2008. Menopausal hormone therapy in relation to breast cancer characteristics and prognosis: a cohort study. *Breast Cancer Res.*, 10(5): R78.
10. Stefanick, M.L., *et al.*, 2006. Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy. *JAMA: the J. the American Medical Association*, 295(14): 1647.
11. Rossouw, J.E., *et al.*, 2002. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA: the J. the American Medical Association*, 288(3): 321.
12. Anderson, G.L., *et al.*, 2004. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA: the J. the American Medical Association*, pp: 291(14).
13. Chlebowski, R.T., *et al.*, 2003. Influence of estrogen plus progestin on breast cancer and mammography in healthy postmenopausal women. *JAMA: the journal of the American Medical Association*, 289(24): 3243.
14. Anderson, G.L., *et al.*, 2006. Prior hormone therapy and breast cancer risk in the Women's Health Initiative randomized trial of estrogen plus progestin. *Maturitas*, 55(2): 103-115.
15. Lambe, M., *et al.*, 1996. Parity, age at first and last birth and risk of breast cancer: a population-based study in Sweden. *Breast cancer Research and Treatment*, 38(3): 305-311.
16. Russo, J., *et al.*, 2005. The protective role of pregnancy in breast cancer. *Breast Cancer Res.*, 7(3): 131-142.
17. Kahlenborn, C., *et al.* 2006. Oral contraceptive use as a risk factor for premenopausal breast cancer: a meta-analysis. *Mayo Clinic*.
18. Conway, K., *et al.*, 2007. Risk factors for breast cancer characterized by the estrogen receptor alpha A908G (K303R) mutation. *Breast Cancer Res.*, 9(3): R36.
19. Meta. *Chinese J. Epidemiol.*, 2011. 32(2).
20. Henderson, B.E., *et al.*, 1985. Do regular ovulatory cycles increase breast cancer risk? *Cancer*, 56(5): 1206-1208.
21. Marchbanks, P.A., *et al.*, 2002. Oral contraceptives and the risk of breast cancer. *New England J. Medicine*, 346(26): 2025-2032.

22. Dolle, J.M., *et al.*, 2009. Risk factors for triple-negative breast cancer in women under the age of 45 years. *Cancer Epidemiology Biomarkers & Prevention*, 18(4): 1157.
23. Chie, W.C., *et al.*, 2000. Age at any full-term pregnancy and breast cancer risk. *American J. Epidemiol.*, 151(7): 715.
24. Cullinane, C.A., *et al.*, 2005. Effect of pregnancy as a risk factor for breast cancer in BRCA1/BRCA2 mutation carriers. *International J. Cancer*, 117(6): 988-991.
25. Eisen, A., *et al.*, 2008. Hormone therapy and the risk of breast cancer in BRCA1 mutation carriers. *J. the National Cancer Institute*, 100(19): 1361.
26. Land, C.E., *et al.*, 1994. A case-control interview study of breast cancer among Japanese A-bomb survivors. I. Main effects. *Cancer Causes and Control*, 5(2): 157-165.
27. Ursin, G., *et al.*, 2002. Urinary 2-hydroxyestrone/16-hydroxyestrone ratio and family history of breast cancer in premenopausal women. *Breast cancer Research and Treatment*, 72(2): 139-143.
28. Sala, E., *et al.*, 2000. High-risk mammographic parenchymal patterns, hormone replacement therapy and other risk factors: a case-control study. *International J. Epidemiol.*, 29(4): 629.
29. Freedman, L.S., *et al.*, 2006. A comparison of two dietary instruments for evaluating the fat-breast cancer relationship. *International J. Epidemiol.*, 35(4): 1011.
30. Thanos, J., *et al.*, 2006. Adolescent dietary phytoestrogen intake and breast cancer risk (Canada). *Cancer Causes and Control*, 17(10): 1253-1261.
31. Dai, Q., B. Liu and Y. Du, 2009. Meta-analysis of the risk factors of breast cancer concerning reproductive factors and oral contraceptive use. *Frontiers of Medicine in China*, 3(4): 452-458.
32. Gomes, A.L.R.R., *et al.*, 2000. Risk factors for breast cancer among pre-or post-menopausal women in Belo Horizonte, Brazil. *Gynecologic and obstetric Investigation*, 52(3): 173-179.
33. Lee, M.M., *et al.*, 2005. Breast cancer and dietary factors in Taiwanese women. *Cancer Causes and Control*, 16(8): 929-937.