Comparison of some risk factors between non-familial and familial breast cancer females in Jordan

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ABSTRACT

Objective: To compare the risk factors such as age, menopause, menarche, age at the first pregnancy, number of pregnancies and breast feeding period between the familial and non-familial breast cancer females in Jordan.

Methods: This study was carried out in Al-Basheer Hospital, Amman, Jordan during the period 2000 and 2002. A questionnaire was used to collect information from 99 females who were histologically and pathologically diagnosed with breast cancer. Data of the questionnaire were entered and analyzed using statistical package for social sciences.

Results: The highest percentage of non-familial and familial breast cancer occurrence was among age group 51-60 years. The age of the first pregnancy is another risk factor of which the highest percentage of breast cancer was reported for both familial (57.1%) and non-familial (65.4) breast cancer females who have their first pregnancy while they were 20-years-old and above. More than 4 pregnancies also represents a risk factor for both non-familial (67.9%) and familial (68.6%) breast cancer patients. In this study, there are no statistical differences between menopause and menarche age among the breast cancer females. Finally, an inverse relationship was shown between breast feeding period (equal or more than 24 months) and the occurrence of breast cancer in both non-familial (2%) and familial (0%) breast cancer.

Conclusion: This study found that age 51-60 years and the increase number of pregnancies (more than 4) in the age of 20 years or more are risk factors for both types of breast cancer. On the other hand, longer period of breast feeding (more than 24 months) decreases the risk of breast cancer in both types.

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Breast cancer is the most common invasive cancer in women worldwide, with approximately 5 fold higher incidence in women of Western countries as compared with Asian countries.[1] Deaths in year 2001 makes it the second leading cause of cancer deaths.[2] Its incidence has been rising in both developed and developing countries.[3] An important feature of breast cancer is heterogeneity on the molecular level, mammary carcinogenesis is a multistep process, involving the accumulation of genetic and epigenetic changes that result from the interaction between genetics and environment.[4] Genetics of breast cancer linked to breast cancer susceptibility gene (BRCA1) and BRCA2 genes.[5] Mutation in these genes are responsible for 5-15% of overall breast cancers.[6] Environmental factors are believed to be responsible for approximately 85% of the cases.[7] Epigenetic of breast cancer is linked to predisposing risk factors such as gender, obesity, early menarche, no pregnancy, age at birth of the first child and late menopausal.[8-11] Post-menopausal estrogen therapy and oral contraceptives (estrogen and progestin oral therapy) may also be considered as possible breast

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Table 1 - Age at breast cancer diagnosis as a risk factor among familial and non-familial breast cancer females.

Age group	Non-familial cancer	Familial cancer	Total
≤30	-	2 (4.7%)	**2**
31-40	10 (17.9%)	7 (16.3%)	**17**
41-50	16 (28.6%)	12 (27.9%)	**28**
51-60	19 (33.9%)	17 (39.5%)	**36**
≥ 61	11 (19.6%)	5 (11.6%)	**16**
Total	**56**	**43**	**99**

Table 2 - Risk factor statistics among familial and non-familial breast cancer females.

Risk factor	Cancer origin	Mean	Significant (2-tailed)
Menarche	Non-familial	13.39 ± 1.28	0.313
	Familial	13.14 ± 1.03	
Menopause age	Non-familial	46.30 ± 4.86	0.197
	Familial	48.15 ± 5.56	

Table 3 - Age at the first delivery, number of pregnancies and breast feeding period as risk factors among non-familial and familial breast cancer females.

Risk factors	Non-familial cancer	Familial	Total
Age at the first delivery (years)			
15-19	18 (34.6)	15 (42.9)	**33**
≥ 20	34 (65.4)	20 (57.1)	**54**
Number of pregnancies			
1-4	17 (32.1)	11 (31.4)	**28**
5-12	36 (67.9)	24 (68.6)	**60**
Breast feeding period (months)			
Few days to 12	31 (60.8)	17 (54)	**48**
13-24	19 (37.3)	14 (45.2)	**33**
> 24	1 (2.0)	0	**1**

cancer risk factors.[12,13] In Jordan, cancer registry[14] identified cancer as a second leading cause of death, and breast cancer was the most common in that year, representing 28% of all cancers. Genetic predisposition of breast cancer cases in Jordan may be due to the fact that over 50% of marriages are consanguineous;[15] however, there is a limited literature on hereditary of breast cancer. Few studies in Jordan analyzed age, gender, environmental, lifestyle, behavioral, and nutritional risk factors.[15,16-18] The aim of this study was to compare the genetic and environmental risk factors among familial and non-familial breast cancer in Jordanian females.

Methods. To determine the risk factors among breast cancer Jordanian females, 99 breast cancer females were investigated during the period 2000 to 2002. A signed permission was obtained from every female enrolled in this study. A questionnaire was used to collect information in Al-Basheer Hospital, Amman, Jordan (a major center for the diagnosis and treatment of breast cancer) for all breast cancer females who were histologically and pathologically diagnosed with breast cancer. The questionnaire includes information on age, marital status, age at the first pregnancy, number of pregnancies, menarche, menopause, breastfeeding period and familial history of breast cancer. Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS 9.0.0; SPSS Inc, Chicago, IL, USA, 1998). The means and standard deviations (SD) along with percentages were calculated. The independent sample t-test and chi-square were also performed to analyze the differences between the 2 groups. Statistical significance was set at $p<0.05$. In this study, breast cancer were classified into either familial or non-familial. Criteria for classification for familial breast cancers were based on at least one first or second-degree relative (from any of both parents sides) of the same lineage who was affected with invasive cancer at any age.

Results. The comparison risk factors among familial and non-familial breast cancer females is shown in **Tables 1-3.**

Breast cancer classification. Forty-two females out of 99 (42.4%) had familial breast cancer, while 57 females (57.6%) had non-familial breast cancer.

Risk factors. The overall participant's age was between 22-73 years. The age of the familial breast cancer participants ranged between 22-73 years and the age of non-familial breast cancer females ranged between 35-69 years. Among the age group 51-60 years, the occurrence of breast cancer for familial was 39.5% and for non-familial was 33.9% (**Table 1**). For the age group 41-50, showed a percentage of 27.9% in familial breast cancer females and 28.6% for non-familial breast cancer females and (**Table 1)**.

All cancerous women enrolled in this study were married (including divorced and widowed) except for 5 subjects. The menarche (mean ± SD) for non-familial breast cancer females was 13.39 ± 1.28 compared with 13.1 ± 1.03 for familial breast cancer females. The menopause age for non-familial was 46.30 ± 4.86 compared with 48.15 ± 5.56 for familial breast cancer females (**Table 2**). An inverse relationship was found between the age at the first delivery and breast cancer incidence. Approximately 65% of non-familial breast cancer females had their first baby while they are 20 years or more. On the other hand, approximately 35% had their first delivery while they were between 15 and 19 years. An inverse relation was also noticed among familial breast cancer females, approximately 57% had their first baby by age of 20 or more, while approximately 43% had their first delivery when they were between 15 and 19 years (**Table 3**). This study showed increased breast cancer risk with the increased number of pregnancies above 4. Approximately 68% of the non-familial breast cancer females had 5-12 pregnancies, while approximately 32% of the same group had 1-4 pregnancies. At the same time, 69% of familial breast cancer females had 5-12 pregnancies, while approximately 31% had 1-4 pregnancies (**Table 3**). **Table 3** shows a lower incidence in non-familial breast cancer females with longer breast feeding period. Approximately 61% of non-familial females' breast feeding period was equal or lesser than 12 months, while approximately 37% of the same group breast feed between 13 and 24 months. Approximately 54% of familial breast cancer females' breast feeding period was equal or less than 12 months while approximately 45% of the same group breast feed between 13-24 months. Only one familial and non-familial breast cancer females fed equal or more than 2 years.

Discussion. Previous studies reported that breast cancer genetic inheritance (such as BRCA1 and BRCA2 genes) account for approximately 5% of breast cancer cases, although some authors reported a higher rate up to 10%.[3] Literature on breast cancer is limited in Arab women, and genetics on breast cancer are even rare. Among Arab women, a comparison study was made between Arab and American breast cancer females.[19] It showed a difference in age distribution, marital status and parity among these 2 groups and these differences reflect the population characteristics, socio-cultural practices and local attitude toward disease among these females. Another comparison study was made between Arab and Jewish breast cancer females,[16] evaluated the nutritional risk factors among these populations and explain the lower reported incidence of breast cancer among Arab (compared to Jewish) by the different food consumption patterns, in addition to the level of calories, protein, fat, and fiber intake.

In Jordan, most breast cancer studies before the establishment of Jordan cancer registry[14] was confined to pathological and histological studies and relates these results to risk factors such as gender and age.[17, 20-21] Other studies analyzed the lifestyle patterns and risk factors among Jordanian breast cancer females and showed that stressful events, use of hair dye, use of oral contraceptive and trauma to the breast were the major significant risk factors among breast cancer females.[15,18] Jordan cancer registry[14] showed that 62% of Jordanian breast cancer women were less than 53 years. Similar percentages were reported in Jordan.[18] In this study the highest percentage of non-familial and familial breast cancer was among the age group 51-60 years. Approximately 47% of non-familial breast cancer and approximately 49% of familial breast cancer were less than 50 years of age, while approximately 80% of non-familial and 88.4% of familial were less than 60 years (**Table 1**). This study also showed that higher percentage of breast cancer incidence was among familial breast cancer females compared to non-familial breast cancer. This is an expected finding since hereditary breast cancer occurs at an early age, the mean age of diagnosis among BRCA1 carriers is approximately 40 years and among BRCA2 carriers is approximately 45 years.[22] Worldwide cancer statistics shows inflection of cancer incidence rate around the age 50, the time of menopause reflecting ovarian hormone production.[23] Occurrence of breast cancer among women in Jordan is a major public concern, therefore breast self examination should be encouraged at early ages especially among families who have a hereditary history of breast cancer. At the same time, educational programs should be encouraged to increase knowledge and awareness of risk factors and early signs of breast cancer such as hormonal therapy, increase breast size, irregular menstruation, and nipple changes.[18,24-25] Breast cancer females showed early mean menarche and late mean menopause age. In this study, no statistical difference was found between familial and non-familial regarding these risk factors. Other risk factors such as weight, height and body mass index may interact and increase the risk of postmenopausal breast cancer.[26] The average menarche and menopause age were similar to the previous study in Jordan.[18] The physiology of female breast cancer is dependent on the mammary proliferation effect of the ovarian hormones, estrogen and progesterone. Estrogen is responsible for elongation and branching of breast ducts whereas progesterone is important for breast development.[27] During pregnancy, circulating hormones results in differentiation of terminal duct lobular unit, which is the major site of malignant transformation. This process of differentiation is a

major permanent protective mechanism against breast carcinoma.[28] Therefore, the inverse association was expected between first full-term pregnancy at young ages and breast cancer, owing to early breast cell differentiation.[29] Our finding showed an increase risk of age at first birth for either familial or non-familial breast cancer females.

In epidemiological studies of breast cancer, the association between breastfeeding and the subsequent risk of breast cancer was controversial.[30-32] In this study, longer breast-feeding period in months decreases breast cancer percentage (**Table 3**), because breast feeding may cause involution and lowered gonadotropin level as well as it causes elimination of carcinogens via breast milk.[23,33-34] Oxytocin which causes contraction of myoepithelial cells as a response to suction has been reported to inhibit cell proliferation and tumor growth in animal models.[35] It showed that breast feeding decrease the risk of breast cancer in BRCA1 but not in BRCA2 carriers without known biological basis for these differences.[36]

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