IJBC 2021; 13(3): 72-77

Iranian Journal of Blood & Cancer

Journal Home Page: www.ijbc.ir

ORIGINAL ARTICLE

The Frequency of Breast Cancer Risk Factors and the Correlation of the Results of the Risk Assessment Models in The Iranian Population

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ARTICLE INFO

Article History:
Received: 20.05.2021
Accepted: 18.08.2021

Keywords:
Breast cancer
Risk factors
Risk assessment
Risk management
Prevention

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ABSTRACT

Background: Breast cancer is an important preventable health problem, worldwide. In this study, the frequency of breast cancer risk factors and the level of individuals risk using different risk assessment instruments were assessed.
Methods: This cross-sectional study was conducted in Kerman, Iran, 2018. Seven hundred women referred to the comprehensive health care centers were participated in the study using a cluster sampling method. The International Breast Cancer Intervention Study (IBIS) and Breast Cancer Screening (BCS) risk assessment models were used. The frequency of different breast cancer risk factors was asked using the self-administered questionnaire. Data were entered into the SPSS software. The descriptive analysis and Pearson correlation test were used.
Results: The frequency of being overweight/obesity, having a sedentary lifestyle, second-hand exposure to tobacco, and having anxiety was 54.1%, 54.7%, 21.3%, 26%, respectively. Considering the lifetime risk ≥20% according to the IBIS and BCS models, 2.8% and 0.1% of participants were high risks. There was a significant positive correlation between the IBIS 5-year risk of breast cancer and the BCS chart risk (r=0.716, P≤0.001). There was not any significant correlation between the IBIS lifetime risk of breast cancer and the BCS chart risk (r=0.035, P=0.358).
Conclusion: The prevalence of modifiable risk factors of breast cancer is considerable in Iranian women. Community-based, primordial and primary prevention intervention should design. There are some national and international breast cancer risk assessment models, but their accuracy in the Iranian population and the perfect threshold score to determine high-risk individuals is not clear.

Please cite this article as: Danaei M, Hoseini Z, Momeni M. The Frequency of Breast Cancer Risk Factors and the Correlation of the Results of the Risk Assessment Models in The Iranian Population. IJBC 2021; 13(3): 72-77.

Introduction

Breast cancer is the most common malignancy of women worldwide, with about 30% of all cancers in women.[1] According to the World Health Organization, in the year 2018, around 627,000 people have died because of breast cancer, accounting for about 15% of all cancer deaths among women.[2] Although the incidence of breast cancer in developing countries is much lower than in developed countries, the high population of these countries and the lack of timely diagnosis and treatment are the main causes of cancer deaths in these countries.[3] In Iran, breast cancer accounts for 21.4% of all reported cases of cancer. The incidence of breast cancer in Iran is estimated at 4 per 100,000 women, and the available data indicate that the disease in Iran is rising.[4]

Breast cancer is a multifactorial disease and aging, oral contraceptives consumption, obesity, high fat diet, alcohol consumption, tobacco smoking, personal or

family history of breast or ovarian cancer and history of chest radiation can increase the chance of developing this disease.[5] Identifying breast cancer risk factors and primary prevention interventions are very important for breast cancer but, secondary prevention interventions and down staging efforts are more important. There are age-based recommendations for breast cancer screening with mammography, but mammography screening is not enough acceptable and practical and many women do not follow the recommendations in practice. Therefore, risk-based screening methods using mathematical models to identify high-risk women are more practical and cost-effective methods for secondary prevention of breast cancer.[6, 7]

Various models are used to check the risk of breast cancer. The International Breast Cancer Intervention Study (IBIS) or Tyrer-Cuzick is one of these models that could estimate the 5years or lifetime risk of developing breast cancer with respect to family history and various risk factors including age, age at menarche, age at first childbirth, age at menopause, history of hyperplasia or Lobular carcinoma in situ, history of breast or ovarian cancer in first or second degree relatives, weight, Height, and the history of using alternative hormones. This model has been used and approved in different countries.[8] In Iran, Ghoncheh et al., in 2017, reviewed the validity of this model and found that this model is a reliable and valid model to assess the risk of breast cancer.[9]

Another model is used to assess the risk of breast cancer in Iranian population is Breast Cancer Screening (BCS). The model determines the risk of breast cancer by using information such as age, body mass index, age of the last menopause, history of benign and malignant tumors, and history of breast cancer in first-degree relatives and second-degree relatives. This model categorizes the risk level into 4 categories (low risk, medium risk, high risk, and very high risk).[10]

Primary prevention is the effective strategy to reduce the burden of breast cancer in community. For primary screening of breast cancer, the prevalence of its risk factors should identify. On the other hand, identifying high-risk individuals and performing screening care can prevent the development of advanced breast cancer. Valid and reliable risk assessment models are needed for secondary prevention and down-staging. Therefore, in this study, the prevalence of breast cancer risk factors in women in Kerman was measured. Also, the population risk was estimated by IBIS and BSC models. The correlation between these two models was estimated to determine the practical application of them.

Material and Methods

This cross-sectional study was conducted in Kerman, Iran, 2018. Kerman province is one of the vast provinces of Iran that is located in the southeast of Iran with nearly 2 million residents. Participants included 700 women with 30 -75 year old referring to the comprehensive health care centers. The cluster sampling method was used. Considering 4 Municipality district in Kerman, 2 comprehensive health care centers were selected in each Municipality district (1 was located in the center of the city and 1 was located in the marginal of the city) by randomization method. In each health care center, 30-75-year-old women who have not any history of breast cancer and had oral consent to contribute to the study were included in the study.

The IBIS and BCS risk assessment models were used. The questionnaire was designed considering the demographic characteristics (marital status, education level, employment status, and self-reported socioeconomic status) and risk factors of breast cancer that were used in these two models including age, age at menarche, age at menopause, age at first childbirth, weight, height, using hormone replacement therapy, existing benign breast disease, and family history of breast cancer (First degree, second /third-degree relatives). Also, some questions were asked about the consumption of fruit and vegetables, consumption of fried foods and seafood, exposure to tobacco products, Regular use of toothbrushes, consumption of alcohol exposure to industrial chemicals or pesticides, exposure of breast cancer with cell phone, history of shift working and history of diabetes mellitus. The frequency of anxiety and depression were assessed using the Hospital Anxiety and Depression Scale questionnaire (HADS). The frequency of happiness was assessed using one question about the self-reported of the level of happiness.

The IBIS model is used in different countries for distinguishing high-risk persons. Guidelines recommended that high-risk persons (Lifetime risk ≥20%) should receive more conservative screening interventions. one study in Iran evaluated the IBIS model in Iranian population and estimated that this model nearly 49.36% could accurately identify healthy peoples from breast cancer patients.[8, 9]

The BCS model is a regression model that was designed to provide the risk probability of breast cancer. This chart is stratified and colored the probability of breast cancer as green (<5%), yellow (5–9%), orange (10–14%), red (15–19%), brown (20–24%) and black (≥25%). Also, in this model, the participants' risk could be categorized as low (green), moderate (yellow and orange), high (red and brown), and very high (black). The results of a study showed that this model could truly discriminate 71.53% of patients from healthy peoples in Iranian population.[10]

The Hospital Anxiety and Depression Scale questionnaire (HADS) was used as a valid and reliable instrument (Cronbach's alpha: 0.83 for anxiety and 0.82 for depression subscales) to assess the severity of anxiety and depression through last week. This questionnaire includes 14 items, 7 items for depression and 7 items for anxiety subscales. The answers were coded as a Likert scale (0-3). Each subscale was classified into 4 classifications including normal (0-7), mild disorder (8-10), moderate disorder (11-14), and severe disorder (15-21) scores.[11, 12]

The level of happiness was assessed in participants by asking one self-reported question "How happy do you feel?", and Participants mention their level of happiness as never, rarely, sometimes, and always.[13]

After obtaining the ethical code (IR.KMU.AH.REC.1396.2210), researchers were referred to the selected health care centers and asked participants to answer the self-administered questionnaire. Data were entered into the SPSS software, version 20. The descriptive analysis and Pearson correlation test were used. The significant level was set at 0.05.

Results

The mean±SD of participants' age was 39.76±9.1. The majority of participants were married (79.1%), university-educated (50.7%), employed (54.5%), with a moderate level of socio-economic status (65.8%) (Table 1).

Table 1: The socio-demographic characteristics of participants

Variable	Frequency	Percent
Marital status		
Single	144	20.9
Married	546	79.1
Education level		
Less than high school	146	21.2
High school diploma	194	28.2
University	349	50.6
Employment status		
Employed	366	53.5
Unemployed	305	44.5
Socio-economic status		
Week	65	9.5
Moderate	383	56.2
Good	211	31.0
Very good	22	3.2

As the aspect of the risk factors of breast cancer, nearly half of the participants were ≥40 years old. Approximately, 55% of participants were overweight or obese. Nineteen percent of participants experienced the menarche at age less than 12 and 11.7% of them delivered their first child at age ≥30 years. The frequency of having Benign Breast diseases (BBD), first degree relative with breast cancer and second degree relative with breast cancer were 2%, and 5.7%, respectively. Nearly, 84.1% of participants did not consume adequate vegetables per day, and 36.7% did not consume adequate fruits. The frequency of consuming fried foods more than 2 times per week was 50.6%. Approximately 21.3% of participants were exposed to the second-hand smoke and 2.5% and 8.5% of them experienced cigarette smoking and waterpipe smoking, respectively. Only 1.9% of participants reported experimental alcohol consumption. About 24.5% of the population did not have good oral health, and 9.8% and 3.1% of them reported exposure to industrial chemicals and pesticides, respectively. Nearly 19.4 % of participants put their cell phone in their breast pocket and 11.9% of them had shift work. The frequency of sedentary lifestyle and diabetes mellitus was 54.7% and 11.2%, respectively. The frequencies of anxiety and depression disorders were 26% and 12.2%, respectively. Nearly 46.2% of participants reported that they feel happiness rarely in their life (Table 2).

Table 2: The frequency of breast cancer risk factors in participants

Variables	Frequency	Percent
Age group (year)		
30-39	405	58.7
40-49	183	26.5
50-59	66	9.6
60-75	36	5.2
BMI (Kg/M^2)		
<24.9	313	46.0
25-29.9	266	39.1
≥30	102	15.0
Age at menarche		
<12	129	19.1
12-13	192	28.4
≥14	356	52.6
Age at first childbirth		
<20	107	19.6
20-24	196	35.9
25-29	179	32.8
≥30	64	11.7
Late menopause (≥55 year)		
No	683	99.0
Yes	7	1.0
Having BBD		
No	669	97.0
Yes	21	3.0
Family history with breast cancer		
No	637	92.3
First-degree relative	14	2.0
Second-degree relative	39	5.7
Inadequate consumption of vegetable		
No	85	15.9
Yes	451	84.1
Inadequate consumption of fruit		
No	359	63.3
Yes	208	36.7
Consumption fried foods more than 2 times per week		
No	326	49.4
Yes	334	50.6
Consumption seafoods less than 2 times per week		
No	298	45.2
Yes	362	54.8
Second-hand exposure to tobacco		
No	515	78.7
Yes	139	21.3
Experimental use of cigarette		
No	668	97.5
Yes	17	2.5
Experimental use of water pipe		
No	627	91.5
Yes	58	8.5
Alcohol consumption		
No	562	98.1
Yes	11	1.9
Regular use of toothbrushes		
No	164	24.5
Yes	506	75.5

Exposure to industrial chemicals		
No	583	90.2
Yes	63	9.8
Exposure to pesticides		
No	595	96.9
Yes	19	3.1
Put the cell phone in the breast pocket		
No	516	80.6
Yes	124	19.4
Shift working		
No	575	88.1
Yes	78	11.9
Sedentary lifestyle		
No	291	45.3
Yes	351	54.7
History of diabetes mellitus		
No	580	88.8
Yes	73	11.2
Anxiety disorders		
Normal	179	27.3
Borderline	306	46.7
Abnormal	170	26
Depression disorders		
Normal	344	52.3
Borderline	234	35.6
Abnormal	80	12.2
Feeling happiness		
Never	50	7.3
Rarely	316	46.2
Sometimes	274	40.1
Always	44	6.4

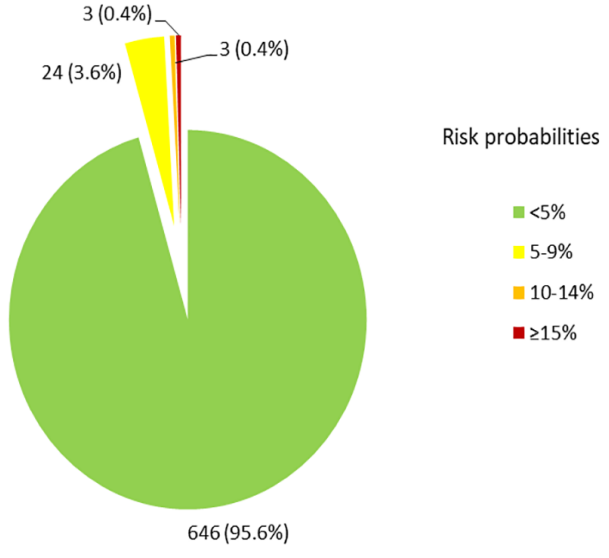

Figure 1: The frequency of different risk categories according to the BCS model

According to the BCS chart, the 95.6% of participants (N=646) has less than 5% risk for developing breast cancer. Approximately 3.6% of participants (N=24) has 5-9% risk and 0.4% (N=3), 0.3% (N=2), and 0.1% (N=1) of participants have 10-14%, 15-19%, and 20-24% risk for developing breast cancer respectively (Figure 1).

Considering the lifetime risk ≥20% for IBIS lifetime risk, 2.8% of participants (N=19) were high risk for developing breast cancer. Considering the BCS risk≥5% or BCS risk ≥10%, 5.1% of participants (N=35) or 1% of participants (N=7) were high risks for developing breast cancer, respectively. There was a significant positive correlation between the IBIS 5 year risk of breast cancer and the BCS chart risk (r=0.716, P≤0.001). There was not any significant correlation between the IBIS lifetime risk of breast cancer and the BCS chart risk (r=0.035, P=0.358) (Table 3).

Discussion

According to the results of this study, about 19.1% of the participants reported that they experience their first menstruation period when they have less than 12 years old. About 11.7% of them reported that their first childbirth was at age ≥30. Nearly 7.7% of the participants mentioned the history of breast cancer in their first or second-degree relatives. About 54.1% of the participants in this study were overweight or obese. Only 0.3% of the participants had a history of breast biopsy. The results of different studies differ with regard to the studied populations. The results of the study in Zanjan on women ≥35 years old showed that 3.5% of participants reported a positive family history and 0.3% had a history of breast biopsy.[14] The case-control study in Shiraz, about the prevalence of breast cancer risk factors in healthy women aged less than 50 years estimated that about 7% of controls reported that they experience their first menstruation period when they have less than 12 years old. About 11.1% of controls did not have children. In 10.9% of controls, the age of the first birth was over 25 years. About 66.5% of the controls had abnormal BMI, and 10% of the healthy participants had reported breast cancer in their relatives.[15] In the research of Nouri et al in 2008 in Rasht, 16.1% of the participants mentioned their first menstruation period at the age of ≤12 years old. Approximately 7.9% of the subjects completed their first delivery at the age of ≥30. About 4.5% of the population reported having at least one cancer in their first-degree relatives and about 4.6% of them had breast biopsy.[16]

In this study, 84.1% and 36.7% of participants did not consume enough vegetables and fruits, respectively. The prevalence of sedentary lifestyle was 54.7%. Also, the

Table 3: The participants' indicators of central tendency and dispersion of breast cancer risk according to the IBIS and BCS models (in percent)

Type of Risk	Mean	SD	Median	IQR	Minimum	Maximum
IBIS 5 year risk (in this study)	0.61	0.55	0.40	0.60	0.10	5.10
IBIS 5 year risk (Standard of IBIS model)	0.65	0.48	0.50	0.60	0.20	2.00
IBIS lifetime risk (in this study)	11.90	3.79	11.40	4.70	3.50	44.00
IBIS lifetime risk (Standard of IBIS model)	12.47	1.51	13.10	0.80	4.00	13.3
Risk according to the BCS chart	2.13	1.94	1.41	1.08	1.13	20.42

prevalence of cigarette smoking, water pipe and second-hand exposure to tobacco was 2.5%, 8.5%, and 21.3%, respectively. Nearly 61.3% of women in Kerman were inactive or have low physical activity in 2016.[17] The result of a study showed the frequency of cigarette smoking among Iranian women was varied from 0.04% to 10.5% in different studies.[18] The results of a population-based study in Kerman estimated the frequency of passive smoking as 30.1% in Iranian women.[19] Another population-based study in Kerman estimated the frequency of ever, current and daily waterpipe smoking among Iranian women as 30.4%, 20.6%, and 3.7%, respectively.[20] Diversity of prevalence of different risk factors in different studies could be due to the diversity of the understudy populations. However, these frequencies of risk factors in this study raise concern. To reduce the incidence of breast cancer in the population, we should pay particular attention to its risk factors and policy-makers should design and implement effective interventions to reduce the risk factors at the individual and community level with special attention to the primary and secondary prevention.

Considering mood disorders, the prevalence of anxiety was 26% in this study. The results of a Meta-analysis study estimated the prevalence of anxiety in Iranian women as 36%.[21] Also, the prevalence of mood/anxiety disorder was 34.8% in Australian women.[22] In this study, only 6.4% of participants reported that they feel always happiness, but in a national study in 2012, only 3% of Iranian population feels they were very happy in their life.[13] Iranian population, especially Iranian women do not feel enough level of happiness. The dominant culture, gender discrimination, and other social factors could affect the level of happiness in Iranian women. Policymakers should design effective strategies to improve life satisfaction and the level of happiness in Iranian women.

The mean±standard deviation of the 5-year risk and lifetime risk of breast cancer based on the IBIS model was 0.464±0.6%, and 11.99±3.8%, respectively. Also, the mean±standard deviation of breast cancer risk based on the BSC model was 2.13±1.9%. In the study of Goncheh et al in Tehran, similar to this study, the 5-year risk and lifetime risk of breast cancer based on the IBIS model in healthy individuals selected from the general population was 1.96 and 13.6% respectively.[9]

Comparing the prevalence of high-risk individuals according to the 20% risk level for IBIs and BCS models showed that the risk level of 20% is not a good threshold for the BCS model. Due to limited resources in Iran and the impossibility of providing age-based screening services, the importance of risk assessment and risk-based screening services is evident. Different models of risk assessment have been investigated in developed countries, but in our country, only limited studies have been conducted based on the Gail model. It seems that more studies are needed to determine the appropriate tool for assessing the risk of breast cancer in Iranian population, as well as further studies to determine the appropriate threshold for dividing people into high-risk groups according to different models.

The results of this study showed the significant positive correlation between the 5-year risks of breast cancer calculated based on the IBIS and BCS models. On the other hand, there was no significant relationship between the risks of life-threatening breast cancer based on these two models. The results of the study by Ghonche and colleagues show that the IBIS model is somewhat successful in differentiating between cancer patients and healthy people, and it is better than BOADICEA model, but the BCS model is the best model.[9] The present study did not have control and patient group, therefore we could not conclude that the results of which model is closer to reality, but it seems that it is unlikely that the BCS model can be used to estimate the lifetime risk of breast cancer.

The present study compared the results of the BCS and IBIS model for the first time in Iran. The sample size above this study is the strength of the study. In this study, the majority of participants were 30-40 years old. Women who referred to health care centers were not a good representative for the whole of the community, therefore it is expected that the risk level in the present study was underestimated. The case-control studies and population-based studies are suggested for future evaluation.

Conclusion

The prevalence of modifiable risk factors of breast cancer is considerable in Iranian women. Community-based, primordial, primal, and primary prevention intervention should design to modify these risk factors. Secondary prevention and down-staging are also two cost-effective methods for reducing the burden of breast cancer in the community. There are some national and international breast cancer risk assessment models to determine the individual risk level of breast cancer, but their accuracy in the Iranian population and the perfect threshold score to determine high-risk individuals is not clear. Producing and implementing the native risk assessment tool in the Iranian population is essential. It could help policy-makers to identify high-risk individuals and to allocate resources to this high-risk group.

Acknowledgement

The authors would like to appreciate all health care workers for their kind cooperation. The present article is based on the thesis by Zahra Hoseini and was financially supported by Kerman University of Medical Sciences (Grant No. 96000620).

Conflict of Interest: None declared.

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