

*Original Article****The relationship between medications and estimated risk of breast cancer using Gail Model in women living in southeastern Iran***Nilofar Ghavami¹ Hossein Ansari^{2*} Malihe Gharibi³ Kouros Targarfakheri⁴ Ali Yousefzadeh⁵

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Abstract

Background and purpose: Breast cancer is one of the most common cancers in women all over the world. The death rate of this cancer is also increasing. It seems that medication is related to this cancer. The present study aimed at estimating the risk of this cancer using Gail Model and its relationship with medication in women.

Materials and Methods: In this cross-sectional study, 260 35-year-old women were selected from healthcare centers in Zahedan. The data were collected using interview and questionnaire. The risk of breast cancer was estimated by Gail Model. The medication conditions were estimated by interviewing the employees in healthcare center. The data were analyzed using independent sample t-test and linear regression.

Results: The average age of women was 49.3 ± 8.3 years old with five-year risk, and the lifetime of breast cancer were 0.37 ± 0.24 and 5.5 ± 0.79 percent, respectively. Self-medication ($P=0.043$) and medication ($p=0.035$) had a significant relationship with estimated risk of breast cancer.

Conclusion: The risk of breast cancer in women can be influenced by medication along with socioeconomic and menstrual-reproductive factors and variables, such as ethnicity, body mass index, education, age, marriage age, nursing period, and menstrual age. The final analysis showed that consuming contraceptive pills, painkillers, and anti-inflammatory pills are the most important predictive factors in 5-year risk with cancer based on Gail Model. On the other hand, consuming painkillers and contraceptive pills were found to be the most important predictive factors in lifetime risk with cancer based on Gail Model.

Keywords: Breast Cancer; Gail Model; Medication

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1. Introduction

Breast cancer is one of the most common cancers all over the world. Annually, more than 800 thousands new cases of breast cancer occur, but the death rate differs in different parts of the world up to ten times (1). The recent research shows that breast cancer comprises almost 29% of the cancers in women (2), and previous studies demonstrates that about 40000 deaths occurred in the US, in 2015 (3). In Iran, breast cancer is the first common cancer among women, and the current information demonstrates the increase of annual occurrence of breast cancer and the decrease of the age of women with this cancer (3,4). Based on recent studied, breast cancer is 24% of all cancers in Iran which has been increased since past decades (5, 6), and the occurrence rate of it in 30-year-old women and more is reported to be 25 in 100000, and the prevalence rate is reported to be 120 in 100000 (7). Different studies detecting the risk factors of breast cancers showed that this cancer is correlated with family history, early menstrual, late menopause, older people, first pregnancy over 30-years old, not having children, overweightness, and no nursing, contraceptive use and hormone therapy after menopause (8). The other issue is the relationship between over self-mediation with different cancers including breast cancer. It seems that some medicine affects this cancer specially related to hormones, such as contraceptive pills (9, 10). On the other hand, some studies showed that consuming certain complexes, such as vitamins and minerals and some medicines can prevent this cancer (11-13). However, it is highly significant to study the preventive methods of breast cancer.

It is assumed that most of risk factors of breast cancer are unmodifiable, and there are no population-based primary predictive program. Furthermore, controlling and preventing self-medication is an important factor by which the high risk of breast cancer can be prevented. Although it is reported that the age of first pregnancy, family history, mammography, and genetics have higher risks (14), it seems that the more medication a woman has, the more diseases she will experience that may lead to more medication. It is recommended to investigate whether medication is related to the risk or not. Otherwise, medication can be investigated as a risk factor in breast cancer.

To the best of the researchers' knowledge, the relationship between medication and breast cancer risk hasn't been studied, epidemiologically and comprehensively. Therefore, this research aimed at determining the role of medication in estimated risk of breast cancer with epidemiologic model in women more than 30 referring to healthcare centers in Zahedan to estimate the risk of this disease based on different variables and medication. Based on the present study, some recommendations were presented for screening and educating high risk women considering effective independent variables.

2. Materials and Methods

In this cross-sectional research, two hundred and sixty (n=260) 35-year-old women and more, referring to healthcare centers of Zahedan were studied in 2017-18. The sampling was carried out in several stages; as in the first stage, a clinic was selected randomly in each four districts of city and considered as cluster. Then, in the selected clinic, considering

the number of population in that region, a sample was selected from women referring to health centers in Zahedan, southeast of Iran. The data were collected using the results of interview and structured questionnaire after explaining the objectives of the study to the participant women and taking informed consent from them by an experienced person. In the current study, the essential data were collected based on Gail Model questionnaire including seven main questions. In this model, a score is considered for each person based on age, menstrual age, the age at first alive birth, the number of biopsies, family history regarding breast cancer, the breast biopsy history, as well as previous cancer history and race. The Gail Model computes five-year and lifetime risk of breast cancer among women older than 35 years old based on patients' conditions and their answers to the mentioned 7 questions in this model (15). In fact, according to Gail Model, each woman attains a score between 0 and 1, so that these scores are distributed normally, and higher scores indicate higher risk of breast cancer in next times. After collecting the data and information about the women, the researchers used Breast Cancer Risk Assessment Tool (BCRAT) to estimate the five-year and lifetime risk of breast cancer in each subject. It must be mentioned that this tool was suggested by Gail and is accessible in the following link: "<https://breastcancerrisk.canceraustralia.gov.au>".

After computing the risk of breast cancer, the relationship between medication (adjusting for socioeconomic and menstrual-reproductive factors) and the risk rate of this cancer (as response variable) was investigated using linear

regression. In this study, a person who was medicated (self or prescribed) for at least one year permanently during her life time, was considered in medication group. The question about medication was open-ended. After the collection of data and confirmation of healthcare employees, it was recognized that the women reported 7 types of medications including Contraceptive Pills, Hormones Modifiers, Antidepressants, Analgesic Anti-inflammatory drugs, Sedative drugs, Cardiovascular drugs, as well as Vitamins and Minerals.

The response variable in this study was the score of Gail Model. This score is a quantitative variable and represents the probability or risk of breast cancer among healthy women. As these scores are continuous and varying between 0 and 1 normally, so in order to remove the effect of potential confounders, such as socioeconomic and menstrual-reproductive factors, multiple linear regression models were used to analyze the data. The fitness of the model was then evaluated by index of R². The data were also analyzed in Sata.12 Software at significant level of 0.05. Moreover, this project was confirmed in ethical committee of Zahedan University of Medical Sciences (Ethical code 7979).

3. Results

In this study, the average age of participants was 49.3±8.3 years old in the age range of 35 to 59 years old. About 6.4% (165 people) were housewives and regarding ethnicity distribution, 55.7% (145) were Sistani and the rest were Baloch. The overall prevalence of contraceptive use was 28.8% (75 people), and the rest were either menopause or not using contraceptives devices at all. It has

to be mentioned that 22.7% (59 people) of the studied women were menopause. In this study, 65.7% (171 people) were housewives and the rest were working in public or private centers. The five-year risk and lifetime risk to breast cancer were estimated to be

0.37±0.24 and 5.5±0.79 for Zahedan women, respectively. The frequency distribution or mean risk of breast cancer and socioeconomic and menstrual-reproductive variables in women more than 35 years old are listed in Table 1.

Table 1. Frequency distribution characteristic variable and mean risk of breast cancer in women more than 35 years old in Zahedan, southeastern Iran

	Maximum	Minimum	Mean±SD
Age	59	35	49.3±8.3
Age at Marriage	33	12	15.1±6.9
Menstrual Age	13	10	13.1±2.8
Age at first pregnancy	33	12	17.5±6.9
Number of children	12	1	5.9±4.8
BMI (Body Mass Index)	36.6	17.9	24.5±5.2
5-year risk of breast cancer	2.2	0.11	0.37±0.24
Life time risk of breast cancer	6.5	0.22	5.5±0.79
History of Cancer Family (not breast cancer) n (%)	12(4.6)		
History of breast cancer in family n (%)	13(5)		
Sistani ethnicity (Persian) n (%)	145(55.7)		
Academic Education n (%)	51(19.6)		
Working in public and private places n (%)	89(34.2)		
Contraceptive pills use n (%)	75(28.8)		
Menopause n (%)	59(22.7)		

Regarding medication, it was identified that only 3.3% were self-medicated, and the rest were medicated by doctor. In this study, the lifetime prevalence medication was about 49.4% based on presented definition in methods section (permanent medication at least for one year in lifetime). This study showed that the medication rate of Contraceptive Pills, Hormones Modifiers, Antidepressants, Analgesic Anti-inflammatory drugs, Sedative drugs, Cardiovascular drugs, Vitamins and Minerals were 28.8%, 11.1%, 7.3%, 21.1%, 19.1%, 7.7% and 29%, respectively.

Based on the results of Kolmogorov-Smirnov, the distribution of scores related to risk of breast cancer was normal in this study. Therefore, multiple linear regression was used to analyze and control the

potential confounders. The final model showed that using contraceptive pills, painkillers, and anti-inflammatory pills were the most important predictive factors in five-year risk, based on Gail Model. On the other hand, using contraceptive pills, painkillers and anti-inflammatory pills were found to be the most important predictive factors in lifetime risk based on Gail Model (Table 2).

Table 2. Confidence intervals and coefficients for independent variable related to estimated risk of breast cancer using Gail Model in final multiple linear regression model among women referring to healthcare centers in Zahedan*

Drugs use status	5-Year Risk (Based on Gail Model) (%)		Lifetime Risk (Based on Gail Model) (%)	
	Regression Coefficient (95% CI)	P	Regression Coefficient (95% CI)	P
Contraceptive Pills				0.001
Yes	0.47 (0.201-0.927)	0.001	2.21 (1.19-3.61)	
No	1		1	
Analgesic Anti-inflammatory drugs				0.1
Yes	0.23 (0.091-1.22)	0.001	0.21 (-0.071-1.01)	
No	1		1	
Antidepressants		0.21		0.11
Yes	0.09 (-0.001-0.89)		1.06 (-0.95-4.02)	
No	1		1	
Sedative drugs		0.17		0.001
Yes	0.16 (-.09-3.08)		1.91 (0.81-3.99)	
NO	1		1	
Cardiovascular drugs				0.18
Yes	0.14 (-0.38-2.81)	0.086	1.16 (-0.73-4.92)	
No	1		1	
Vitamins and Minerals				0.09
Yes	0.16 (-0.19-4.10)	0.21	1.06 (-0.65-4.22)	
No	1		1	
Hormones Modifiers				0.11
Yes	0.18 (-0.77-3.99)	0.29	1.43 (-0.73-3.84)	
No	1		1	

*Adjusted for Family history of cancer, Family history of breast cancer, Body Mass Index, Age at First Pregnancy, Age, Number of children, Age at Menarche, Age of Marriage, Ethnicity, Educational Level, Job, and number of live births.

4. Discussion

The results of the present study demonstrated that the annual risk of breast cancer in women more than 35 years old in southeastern Iran was 74 in 100000. On the other hand, according to the results of this study, the lifetime risk of cancer in this region was found to be 5.5% or 55 in 1000 for the women in the same age range. In certain previous reports (16, 17), the rate of breast cancer was estimated to be about 22 in 100000 people, and the prevalence in this population was calculated to be 120 in 100000 people, hence, it can be said that the probability of breast cancer according to Gail Model was higher than the national reports. However, the present study was in concordance with certain previous similar studies in Iran (18). In a study conducted about African-American women, the five-year risk of breast cancer was reported to be

14.5% (15). The other explanation about low cancer reports, as compared with the estimated values in Gail Model, may be due to low sensitivity of care system in reporting this cancer.

The final regression model in this study showed that the family history, age at first pregnancy, ethnicity and age were the most important predictive factors in five-year risk of breast cancer based on Gail Model. On the other hand, family history with breast cancer, family history with cancer, the age of first pregnancy, body mass index, and divorce were found to be the most important predictive factors in lifetime risk of breast cancer based on Gail Model. Therefore, the family history of cancer in family, divorce, older women, being Persian, the first pregnancy in older ages, and overweightness were documented to increase the average risk of breast cancer in

women. These results were parallel with the results of certain previous studies in Iran (18). According to the results of this study and previous studies, adding some effective variables on the risk of breast cancer in Gail Model can help the accuracy of model, and increase its capability to be applied on different ethnics, races and regions (19). In all cancers, family history is effective, but in the current study, the estimated risk of breast cancer had a significant relationship with family history with any cancer. As the correlation between risk factors in traditional families (e.g. southeast Iran) is similar, therefore, it seems that life conditions and risk factor distributions are almost similar in the same families.

This study showed that using contraceptive pills, painkillers and anti-inflammatory pills were the most important predictive factors in five-year risk based on Gail Model. On the other hand, using contraceptive pills, painkillers and anti-inflammatory pills were the most important predictive factors in lifetime risk based on Gail Model. This result was similar to the results of previous studies (9-13). However, some previous studies had different results. Some of them mentioned that using contraceptive pills increased breast cancer risk (9, 10, 20) while others didn't confirm it (21). However, it is clear that medication for a long time can influence the function of the body. This effect can be direct or indirect (e.g. fatness). The doctors should consider these reasons in prescription, and essential education should be presented to different classes of women about the side effects.

The study and improvement of early detection is very important regarding breast cancer, which is increasing among women all over the world. In order to determine the effective and important variables in the

estimated risk by Gail Model, it would be better to evaluate some women with breast cancer through this model so as to be compared with healthy women.

This study showed that a modified Gail Model can be designed for Iranian women based on variables, such as medication pattern. This paper confirmed that Gail Model could be considered as a screening tool in any region by removing or adding other variables, to refer the high risk people to higher levels in surveillance system. The risk of breast cancer in women can be related to medication along with controlling socioeconomic and menstrual-reproductive factors and variables, such as ethnicity, body mass index, education, age, marriage age, nursing period, and menstrual age. The final analysis showed that using contraceptive pills, painkillers and anti-inflammatory pills were the most important predictive factors in five-year risk based on Gail Model. On the other hand, using contraceptive pills, painkillers and anti-inflammatory pills were found to be the most important predictive factors in lifetime risk based on Gail Model. The medication can be considered as a factor to evaluation of breast cancer by Gail Model.

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Conflict of interest

The authors declare no conflict of interests with respect to the research, authorship and publication of this article.

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