Effectiveness of Gail Model in Assessing the Risk of Developing Breast Cancer in Baghdad, Iraq

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Abstract

Background: The Gail Model is a statistical breast cancer risk assessment algorithm that was developed in 1989 by Dr. Mitchell Gail and colleagues with the Biostatistics Branch of the National Cancer Institute's Division of Cancer Epidemiology and Genetics. The Gail Model looked at a woman's personal medical history, familial history, and reproductive history. The Gail model has been widely used and validated with conflicting results.

Method: A Gail model were assessed for 200 convenient patients, 100 patients with history of breast cancer diagnosed during the last year (case) and other 100 patients with benign breast disease (control) and who attended the oncology hospital in medical city and Imamin Al-kadhimin medical city during 2019. The relative risk was measure for each patients and calculated 5 year risk >1.7% was regard as high risk, chi-square and student T test was used to find association between two groups.

Results: Calculated 5 year risk >1.7% found in 21% of case and in 11% of control and no association was found between two groups in the relative risk of breast cancer ($\chi^2 = 3.7$, df = 1, p = 0.054).

Conclusions: The Gail model is not useful in identifying risk of breast cancer in women and should not be used for that purpose.

Keywords: *Gail model, breast cancer, relative risk, Baghdad, Iraq.*

Introduction

Breast cancer is the most frequent cancer among women, impacting 2.1 million women each year, and also causes the greatest number of cancer-related deaths among women. In 2018, it is estimated that 627,000 women died from breast cancer – that is approximately 15% of all cancer deaths among women [(1)]. And in Iraq it regard as second cause of cancer-related deaths [(2).]

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Thus the increasing in breast cancer rate has enhanced global breast health initiatives, and attention towards breast cancer risk assessment and awareness [(3,4)]. Breast cancer causes serious concerns even in healthy women, both because of its incidence and mortality. The steps that should be taken in order to decrease this threat can be arranged as following: assessment of breast cancer risk of women, determination of risk groups, careful monitoring of such high-risk groups, informing individuals with risk factors, and extending screening and reachable treatment programs in every society[(5,6)]. Breast cancer risk factors have been defined by previous studies. Age and female sex are important risk factors for breast cancer. Other factors can be increase breast cancer risk including personal and family history of breast, ovarian, and endometrium cancer; history of lobular carcinoma in situ-matched biopsy of atypical

hyperplasia; positive BRCA 1 and BRCA 2 genes; early menarche (<12 yr), late labor (>30 yr); induced abortion; late menopause (>55 yr); hormonal replacement treatment (HRT); alcohol over-consumption; smoking; lack of physical activity; diet rich in fat; body mass index (BMI); and high socio-economic level [7-9].

Over the past two decades, a number of statistical models that predict the risk of breast cancer have been designed to select high risk women for risk reduction strategies based on some risk factors that are associated with increased risk. There are two main types of models. The first type assesses the probability of BRCA mutations such as Claus model in which all predictions are only based on family history [10] .The second type used risk factors of breast cancer includes Gail model (GM) and its modified one (GM2) which calculates 5-year and lifetime invasive breast cancer risk [11] .The GM is the most commonly used risk prediction model and has been well studied, validated and applied in various studies worldwide[12]

Objective: To evaluate the performance of model in estimating the risk of breast cancer in the clinical setting.

Material and Method

A total of 200 patients equal or above 40 years, 100 patients with history of breast cancer diagnosed during the last year (case) and other 100 patients with benign breast disease (control) and who attended the oncology hospital in medical city and Imamin Al kadhimin medical city between June and December 2019. The required information was age, age at menarche, age at first live birth, first degree relative numbers with breast cancer, previous breast biopsies with or without atypical hyperplasia, BRCA mutations and woman race. Unknown BRCA mutations and the white race/ethnicity variables were used for all the women in this study in estimating their risks[14]. The relative risk was measure for each patient which available at (http://www.cancer.gov/bcrisktool/) and calculated 5 year risk >1.7% was regard as high risk [15], chi-square and student T test was used to find association between two groups. p≤0.05 was considered significant.

Results

The mean age of breast cancer patients was 51.3±9 years which was higher than the mean age of control benign patients (49±6.5 years) and it was statistically significant (p=0.02).Distribution of participants in different categories of age at menarche, age at first lived baby and family history was almost similar in both groups and no association were observed between the two groups(P= 0.62, 0.717, 0.27 respectively). Higher frequencies of previous breast biopsy were recorded in control patients compared to breast cancer patients (P<0.001), Gail model scores, that predict 5-year risk of invasive breast cancer, in breast cancer patients and control patients were 1.25±0.7 and 1.26±0.7, respectively and no statistically difference existed between them (P = 0.9) table 1.

Table 1: Difference in Risk factor used in Gail model among studied groups.

Variable		Participants (No)		P value
		Breast cancer patients	Control patients	
Age	40-49 years	53	55	0.02*S
	50-59 years	25	36	
	≥60 years	22	9	
	mean±SD	51.3±9	49±6.5	
Age at menarche	≤11 years	10	13	0.62*
	12-13 years	73	74	
	≥14 years	17	13	
Age at first live birth	Nil parity	17	12	0.717*
	<20 years	20	17	
	20-24 years	26	25	
	25-29 years	21	26	
	≥ 30 years	16	20	

Variable			Participants (No)		P value
			Breast cancer patients	Control patients	
Family history of breast cancer	Negative		78	84	0.27*
	Positive	One	21	14	
		≥ Two	1	2	
Previous breast biopsies	Negative		94	77	0.001*[s]
	Positive		6	23	
Gail score			1.25±0.7	1.26±0.7	0.9**

*Chi-square test, ** Student T test, [S] significant ≤0.05.

Using the cut-off value of 1.7 in Gail score, patients were categorized into high and low risk groups .The model was able to correctly characterize 21 patients in the breast cancer group as having high risk of breast cancer (sensitivity = 21%) and the model was correctly characterize 89 patients in control group as having low risk of breast cancer (Specificity =89%) and no association was found between two groups in the relative risk of breast cancer (χ^2=3.7, df=1, p= 0.054).

Discussion

As the incidence of breast cancer is rising in Iraq, it is important to detect women with a high risk for early detection, timely treatment and prevention. Mitchell Gail, a biostatistician, developed a mathematical model in 1989 to assess the risk of breast cancer risk based on the results from the BCDDP–a large screening study that included 284,780 women who had been undergoing annual mammographic examination [(16).] Later, it was modified by involving atypical hyperplasia in breast biopsy, race, and ethnicity [(17)].Most Western countries use the Gail model to assess the risk of breast cancer. The drawbacks of the Gail model were that it does not consider lobular neoplasia, family history of breast cancer in second-degree relatives and family history of ovarian cancer. This led to the development of various other models considering the factors that were neglected in the GM such as history of breast cancer in second-degree relatives, which was included in the Tyrer–Cuzick model. To many countries and cities around the world validated the GM apart from the United States like Canada [(18),] Italy [(19)] and England [(20)]. Several reports focused on the performance of the Gail model in Asian population and the results of these reports were in agreement with the finding of the current study, there are no studies in Iraq to date assessed predictive breast cancer risk models. In this study, Gail model was assessed by case control study to validated in risk prediction for breast cancer and different components of the Gail model were compared between patients with confirmed breast cancer and control patient, In this study, the two groups differed significantly in terms of age, number of previous breast biopsies, sensitivity of model was 21%, specificity was 89% and it failed to differentiated between breast cancer patient and control patients, this resembled to A study of Gail model in Turkish women compared 650 breast cancer patients with 640 healthy women as control group. In this study, age and first live birth (≥30) were statistically significant between case and control groups but other risk factors used in Gail model were not different between two groups, sensitivity of model 13.3% and specificity was 92%. They concluded that Gail model is not appropriate for risk estimation in Turkish population [(21)], Iranian study on 560 women that showed a significant association of patients age , age at first baby and history of previous biopsy, no association was found between age at menarche, first degree family history and Gail model also showed very low sensitivity(13.9%) and high specificity (91.4%) of the Gail model in Iranian population and Indian study [(22)] that showed Gail model is not useful in identifying the risk of breast cancer in Indian women. Several points noted regarding the limitations of the current study. Most importantly, that a sample of patients selected from a referral center in Bagdad might not be representative of Iraqi female population. Larger studies including women from different parts of country should be conducted in order to obtain an accurate assessment of the Gail model performance in Iraqi women, the relatively small number of patients that were included in current study, may hinder detection of significant association between the variables and risk of breast cancer and limit proper interpretation of results, Case-control nature of the study and lack of patients follow-up, do not allow researchers

to assess absolute risk of cancer development among study population. Based on the results of the current study, it could be suggested that current version of Gail model should be modified to make it applicable for breast cancer risk estimation in Iraqi women.

Conclusions

The Gail model underestimate risk of breast cancer in Iraqi women and should not be used for that purpose.

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Conflict of Interest: No conflict of interest.

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