Gail Model Score in Women With Breast Cancer

Rabiya Khan,[1*] Rufina Soomro,[2] Salim A. Soomro,[1] Zahid Mehmood [1]

ABSTRACT

Objective — *To determine the frequency of raised score of the Gail model (GM) in women diagnosed with breast cancer in Karachi.*

Study design — *Cross sectional study.*

Place & Duration of study — *Department of General Surgery, Jinnah Post Graduate Medical Centre and Liaquat National Hospital Karachi, from September 2016 to March 2017.*

Methodology — *All female patients with breast cancer were included. Patients with the complaint of a breast lump underwent either a mammogram (aged 35 years and above) or an ultrasound breasts (<35 years of age) with or without a concomitant mammogram (depending on the results of the ultrasound). In patients with findings suspicious of malignancy, a core biopsy was carried out. Data was entered on the online Gail model calculator and the score was obtained. A score of 1.7 and above was considered significant (high risk for breast cancer) and less than 1.7 was taken as insignificant (low risk for breast cancer).*

Frequencies and percentages were computed for categorical variables. Values were presented as mean ± standard deviation for continuous variables. Effect modifiers like age, duration of symptoms, etc was also controlled through stratification. P value less than 0.05 was considered as significant.

Results — *The study included 184 breast cancer patients with the mean age of 47.17 years. Nine (4.89%) patients had Gail model score on higher side, while in 175 (95.11%) GM score was low. High risk prediction by GM was found to be for women who were 60 years old, those in whom age of menarche was 12-13 years, the ones who had no previous benign biopsy, without having any history of a first-degree relative previously with breast cancer and whose age at their first live birth was 24 to 30 years. GM estimated five year higher predicted risk of having breast cancer in 9 out of 184 patients (4.89%).*

Conclusion — *The GM prediction for our study population was only 4.89%. This discrepancy may be multifactorial which needs to be studied further.*

Key words — *Gail model, Breast Cancer, Risk Prediction.*

INTRODUCTION:

Breast Cancer is a major global public health issue with over 1 million new cases diagnosed each year; resulting in over 400,000 deaths and about 4.4 million women continuing to live with the disease.[1] Variation in incidence of breast cancer occurs over geographical and international boundaries as well as rural versus urban areas. There is growing interest in trying to stratify women into groups of different levels of risk for the development of breast cancer. Several models and tools for the prediction of breast cancer development risk have been described, incorporating major risk factors. The purpose of the model is to identify and place women into risk categories.[2]

[1] Department of General Surgery JPMC Karachi.

[2] Department of General Surgery Liaquat National Hospital Karachi.

Correspondence:
Dr. Rabiya Khan [1*]
Department of General Surgery
Jinnah Post Graduate Medical Centre
Karachi
E mail: maekani@hotmail.com

Tools for breast cancer risk assessment are helpful in determining the risk group the patient is in. These tools, especially the Gail model, expresses risk in clinically meaningful ways, giving percentages for risk over a 5-year period as well as risk over a lifetime.[3] However, for individual cases, the accuracy is considered only moderate, in part because not all important risk factors are identified and also because accurate risk stratification requires strong risk factors.[4]

Gail developed a tool for the estimation of risk of developing breast cancer from the case-control data of the Breast Cancer Detection Demonstration Project (BCDDP). This was called Gail model 1 (GM 1). Statisticians of the National Surgical Adjuvant Breast and Bowel Project (NSABP) further modified it to project the risk of developing invasive breast cancer merely for the determination of eligibility for the breast cancer prevention trial. This was called the Gail model 2, which is available on the National Cancer Institute (NCI) website. [2]

One major drawback of the GM tool is that it includes only first-degree relatives, which leads to underestimation of the risk in 50% of families who have cancer in the paternal lineage.[4] Many other models were used in different studies such as the Claus model a case-control study, the BRCAPRO

model by Parmigiani and his associates which used hereditary factors in assessing risk of BRCA 1 and BRCA 2 mutations in a family and the Tyrer–Cuzick model which is the only model that incorporates multiple epigenetic factors and uses detailed family history for assessing risk. This was used as an alternative for the GM for eligibility for the International Breast Intervention Study (IBIS-1).[3]

In a study of Turkish women Gail model had sensitivity of 13.3% and specificity of 92% in estimating the risk of breast cancer development.[5] The Gail model can be refined by using national race-specific invasive breast cancer rates and mortality rates for causes other than breast cancer. A revised model was formed which contained only three variables to provide a simpler approach for projecting absolute risk of invasive breast cancer in South-East Asian women (S-GAIL-SBSP).[6] Several studies have validated the Gail model, but there are few validation studies outside the western population. The modified Gail model and Asian American Gail model have been validated for the 5-year risk of breast cancer in a study of 28,104 Singaporean women.[7] The aim of this study was to determine the frequency of raised score of the Gail model in women diagnosed with breast cancer attending tertiary care centers in Karachi.

METHODOLOGY:

This cross sectional study was conducted in the Breast division, Department of General Surgery, Jinnah Post Graduate Medical Centre, and Liaquat National Hospital Karachi, from September 2016 to March 2017. By consecutive non-probability sampling women of 30-60 years of age attending breast OPD with diagnosis of breast carcinoma (assessed by history, clinical examination, presence of breast lump, mammography (BIRADS IV, V, VI) and histopathology (ductal carcinoma in-situ - DCIS, lobular carcinoma in-situ - LCIS, invasive ductal carcinoma, invasive lobular carcinoma) were included. Males with the diagnosis of breast cancer and non-cancer female patients (assessed by history, clinical examination and mammography - BIRADS I, II,III, and histopathology ie. benign pathology), were excluded.

After obtaining informed consent, data was entered on Gail model calculator and the score was calculated. A score of 1.7 and above was considered significant (high risk for breast cancer) and less than 1.7 was taken as insignificant (low risk for breast cancer). Data was entered on SPSS 17.

RESULTS:

This study included 184 breast cancer patients with the mean age of 47.17±8.76 year. Of the total, 175 patients (95.1%) were of the non-specified race and 9 (4.9%) were Asians. Duration of the symptoms of 6 months to 1 year was reported by the 29 (16%) patients, 1-1.5 year duration by 3 (2%), 1.5 to 2 years and 2 years and above by 3 (2%) and 4 (2%) patients respectively. Oral contraceptive pill (OCP) usage was reported in 21 (11.41%) patients. History of smoking was noted in 4 (2.17%) and passive smoking in 70(38%) patients.

Patients were also asked about history of breast cancer in their first degree family members i.e. sisters, daughters and mother. Breast cancer was seen in one of the family members in 14 (7.61%) patients and was seen in 2 or more members from the family in 1 (0.54%) patient. Only 1 (0.54%) patient had 2 or more benign breast biopsies.

In 9 (4.9%) patients menstrual cycle started at the age of 11 years or earlier, in 116 (63%) at the age of 12-13 years and in 59 (32.1%) at the age of 14 years or later. Twenty-one (11.3%) patients had never given birth, 68 (37%) gave birth to their first live child at the age of 20-24 years, 36 (19.6%) at the age of 19 years or even earlier, 41 (22.3%)

at the age of 25-29 years, 18 (9.8%) at the age of 30 years or earlier. Nine (4.89%) patients had Gail model score on higher side, while in 175 (95.11%) GM score was low. GM overestimated five year higher predicted risk of breast cancer in 9 out of 184 patients (4.89%) in our study population.

DISCUSSION:

Gail model was developed more than two decades ago. It is still used to predict the 5-year risk of invasive breast cancer. It is still endorsed in some recent studies.[8] GM is an important tool used in predicting the absolute risk of invasive breast carcinoma in Western population.[9-11] Few research publications are found on use of GM outside United States and Europe. These studies are based upon case-control data which is more appropriate for relative risk prediction rather than estimating absolute risk.[12]

In Singapore Breast Cancer Screening Project (SBCSP) study it has been reported that more breast cancer cases were associated with early menarche, previous breast biopsy, a late age at first childbirth, and at least one first-degree relative with breast cancer than the controls. There was a similar influence of various breast cancer risk factors on the incidence of both DCIS and invasive breast cancers when compared to the corresponding estimated impact on risks calculated by the GM. Also the relative risk for each risk factor was larger on the basis of SBCSP data.[13]

The GM provides the greatest overestimation of risk in women who had late menarche, with no affected first-degree relative, with those more than 50 years of age and no prior breast biopsy at screening. A meta-analysis and systematic review with trial sequential analysis done recently by Wang et al showed that the Gail model was more accurate in predicting the incidence of breast cancer in American and European women, but not so much for the prediction of individual-level risk. Also, the Gail model was noted to overestimate the risk in Asian women and the results were further proved accurate by trial sequential analysis.[14]

A recent study in Saudi women included the type of diet along with the GM1 model.[15] A Nigerian study conducted by Wang and Ogundiran also included alcohol consumption and BMI in their study model.[16] A study on Qatari women further added other socio-demographic factors into their study such as breast-feeding duration, consanguinity of marriage among parents, lifestyle and BMI.[17]

In our study the mean age was 47.7 year. Over-prediction by GM was higher for women who were 58-60 years old than for those who were 50-58 years of age which is almost similar to Chay et al study.[7] In this study, the GM overestimates higher risk of breast cancer for women in whom the age of menarche was 12-13 years, and who had no previous benign biopsy, or women not having a first-degree relative with breast cancer and age at first live birth of 24 to 30 years, which was almost similar to Chay et al study.[7]

Models have been refined as the application of these models to non-Caucasian women has limitations. It can not be that useful for women of other ethnic groups. In our study GM overestimated five year higher risk of breast cancer in only 9 out of 184 patients. The use of simpler but more targeted models such as by predictions of estrogen receptor-positive breast cancer in postmenopausal women in USA has been highly suggested based on analytical evidence. [18] It has also been suggested that there should be addition of mammographic breast density and the incorporation of polygenic risk scores in order to further improve the Gail model for Caucasian women as the density is noted to be associated with an increased risk of breast cancer.[19-21] For our population a modified Gail model needs to be used based upon age of the patient, age-at-menarche, age-at-birth of first live child, number of benign breast biopsies, history of smoking and number of first-degree-relatives with breast cancer. This is a simple approach for projecting absolute risk of invasive breast cancer in Pakistani women.

CONCLUSIONS:

Gail model over–predicted breast cancer in only 4.89% of our study population, thus the Gail model needs to be further revised and refined for the projection of risk of invasive breast cancer in our population.

REFERENCES:

1. Veronesi U, Boyle P, Goldhirsch A, Orecchia R, Viale G. Breast cancer comment. Review 160 refs. Lancet. 2005;365(9472):1727-41.

2. Joy JE, Penhoet EE, Petitti DB. Saving women's lives, Strategies for improving breast cancer detection and diagnosis. Washington (DC): National Academies Press (US); 2005.

3. Mealiffe ME, Stokowski RP, Rhees BK, Prentice RL, Pettinger M. Assessment of

clinical validity of a breast cancer risk model combining genetic and clinical information. J Natl Cancer Inst. 2010;102:1618-27. doi: 10.1093/jnci/djq388.

4. Wald NJ, Hackshaw AK, Frost CD. When can a risk factor be used as a worthwhile screening test. BMJ. 1999;319(7224):1562-5.

5. Ulusoy C, Kepenekci I, Kose K, Aydintug S, Cam R. Applicability of the Gail model for breast cancer risk assessment in Turkish female population and evaluation of breastfeeding as a risk factor. Breast Cancer Res. 2010;120:419-24.

6. Min JW, Chang MC, Lee HK, Min MH, Noh DY. Validation of risk assessment models for predicting the incidence of breast cancer in Korean Women. J Breast Cancer. 2014;17;3:226-35.

7. Chay WY, Ong WS, Tan PH, Jie Leo NQ, Ho GH, Wong CS. Validation of the Gail model for predicting individual breast cancer risk in a prospective nationwide study of 28,104 Singapore women. Breast Cancer Res. 2012;14-19.

8. Schonfeld SJ, Pee D, Greenlee RT, Hartge P, Lacey JV Jr, Park Y, et al. Effect of changing breast cancer incidence rates on the calibration of the Gail model. J Clin Oncol. 2010; 28:2411–7.

9. Ng EH, Ng FC, Tan PH, Low SC, Chiang G, Tan KP, et al. Results of intermediate measures from a population based randomized trial of mammographic screening prevalence and detection of breast cancer among Asian women: the Singapore Breast Screening Project. Cancer 1998;82:1521-8.

10. Shapiro S, Strax P, Venet L. Evaluation of periodic breast cancer screening with mammography: methodology and early observations. Cancer J Clin. 1990; 40:111-25.

11. Alexander FE, Anderson TJ, Brown HK, Forrest AP, Hepburn W, Kirkpatrick AE, et al. 14 years of follow-up from the Edinburgh randomised trial of breast-cancer screening. Lancet. 1999, 353:1903-08.

12. Boyle P, Mezzetti M, La Vecchia C, Franceschi S, Decarli A, Robertson C: Contribution of three components to individual cancer risk predicting breast cancer risk in Italy. Eur J Cancer Prev 2004, 13:183-191.

13. Yew CK, Aizhen J, Yun LE, Ho W. Singapore Cancer Registry, interim report, trends in cancer incidence in singapore, 2004-2008 Singapore: National Registry of Diseases Office, Health Promotion Board; 2010.

14. Wang X, Huang Y, Li L, Dai H, Song F, Chen K. Assessment of performance of the Gail model for predicting breast cancer risk: a systematic review and meta-analysis with trial sequential analysis. Breast Cancer Res. 2018;20:18. doi: 10.1186/s13058-018-0947-5.

15. Al Otaibi HH. Breast cancer risk assessment using the Gail model and Its predictors in Saudi women. Asian Pac J Cancer Prev. 2017;18 :2971-5.

16. Wang S, Ogundiran T, Ademola A, Olayiwola OA, Adeoye A, Sofoluwe A, et al. Development of a breast cancer risk prediction model for women in Nigeria. Cancer Epidemiol Biomarkers Prev. 2018;27:636-43. doi: 10.1158/1055-9965

17. Bener A, Çatan F, El Ayoubi HR, Acar A, Ibrahim WH. Assessing breast cancer risk estimates based on the Gail Model and its predictors in Qatari women. J Prim Care Community Health. 2017;8:180-7.

18. Bjurstam N, Bjorneld L, Duffy SW, Smith TC, Cahlin E, Eriksson O, et al. The Gothenburg breast screening trial: first results on mortality, incidence, and mode of detection for women ages 39-49 years at randomization. Cancer. 1997; 80:2091-9.

19. Gail MH, Pfeiffer RM. Breast cancer risk model requirements for counseling, prevention, and screening. J Natl Cancer Inst. 2018;110:994-1002.doi: 10.1093/jnci/djy013.

20. Decarli A, Calza S, Masala G, Specchia C, Palli D, Gail MH. Gail model for prediction of absolute risk of invasive breast cancer:

independent evaluation in the Florence-European Prospective Investigation Into Cancer and Nutrition cohort. J Natl Cancer Inst. 2006; 98:1686-93.

21. Trends in cancer incidence in Singapore 1968-2007. Singapore Cancer Registry Report Number 7 Singapore: National Registry of Diseases Office, Health Promotion Board; 2010.[Internet] Available from URL:https://www.nrdo.gov.sg/-docs/librariesprovider3/Publications-Cancer/inc_report_v745ce06a5c9d76bafab5aff000014cdee.pdf?sfvrsn=0 accesses on June 2018.

Received for publication: 16-08-2018

Accepted after revision: 28-12-2018

Author's Contributions:
Rabiya Khan: Design of the work, acquisition, interpretation, & analysis of the data, drafting the work.
Rufina Soomro: Conception of the work, design of the work.
Salim A. Soomro: Critical Revision of the work for important intellectual content. Final approval of the version to be published.
Zahid Mehmood: Drafting the work, critical revision of the work for important intellectual content.

Conflict of Interest:
The authors declare that they have no conflict of interest.

Source of Funding:
None

How to cite this article:
Khan R, Soomro R, Soomro SA, Mehmood Z. Gail model score in women with breast cancer. J Surg Pakistan. 2018;23 (4):127-31. Doi:10.21699/jsp.23.4.3.