

A Case-Control Study of Female Breast Cancer Risk Factors in Mauritius

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Abstract

Background: Female breast cancer (FBC) is a public health issue which represents the third leading cause of deaths in Mauritius (accounting for 13.5% of all the deaths in 2017), after diabetes and cardiovascular diseases. The present research aimed to identify the potential causative factors associated with FBC in Mauritius, given the genetic polymorphisms of different ethnic groups.

Method: From January to August 2019, a questionnaire was administered to women who had consented to participate in this case-control study. Overall, there were 394 women, comprising 149 cases and 245 controls. The cases were BC patients who visited two non-governmental organizations (NGOs) involved in providing support and counselling to BC patients in Mauritius. The controls were women matched by age approached from these NGOs as well as the public at large. A logistic regression model was then applied in R statistical software to identify the potential significant factors associated with BC in Mauritius.

Results: Herein, age, family history of cancer, the prolonged use of female hormone as contraception, smoking habits, consumption of non-bio food products, and the frequent use of plastic bottles and Styrofoam containers to serve hot food were identified as the determinant factors attributing to BC incidence.

Conclusion: The extended use of female hormones for birth controls, smoking habits, consumption of non-bio food products, along with the frequent use of plastic bottles and Styrofoam containers to serve hot food were identified as modifiable factors. There is an urgent need for sensitizing people to change their lifestyle in order to minimize their risk of developing breast cancer.

Keywords: Breast neoplasms, Epidemiologic studies, Mauritius

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Introduction

Female breast cancer (FBC) is a public health issue both globally and in the Republic of Mauritius.¹ It occurs when the cells of breast change, start to divide, and spread out in an uncontrolled way. Due to their unrestrained multiplication, the cancer cells end up forming a lump or mass of tissue.² This complex disease is believed to be the result of a combination of factors interacting with each other rather than any single factor. The ability of cancer cells to breach out from their primary site and invade distant tissues with critical function can result in metastases with dreadful outcomes.³

While breast cancer (BC) rates are higher among women in more developed regions, the rates are increasing in nearly every region globally. This upsurge in the rate of BC may be partly on account of urbanisation and adoption of a modern lifestyle, as well as insufficient screening and incomplete reporting in developing countries. Mauritius, being a developing country, has not remained untouched by this global trend in BC.

Primary prevention of BC is not possible, except by undergoing prophylactic mastectomy for those who have the BRCA1 or BRCA2 gene mutation, known to cause breast cancer. Based on the available literature related to certain risk factors, ovarian and other hormones are major determinants of BC risk.⁴ The cumulative exposure of breasts to circulating levels of the ovarian hormones, oestradiol, and progesterone has an impact on BC.⁵ In fact, a number of BC risk factors can be understood in light of how they affect women's hormone profiles. Age, for instance, is related to the onset and cessation of ovarian activity. It thus serves as a chronological indicator of the onset of ovarian activity, and also as a predictor of ovulatory frequency during adolescence and hormone levels in young adults.⁶

Racial differences in hormone profiles have also been noted and found to correlate with BC incidence patterns.⁷ Pregnancy history and lactation experience are also factors that serve as hormonal markers of BC risk.⁸ Postmenopausal obesity, which is associated with higher levels of oestrogen following cessation of ovarian

activity, is thought to increase BC risk. Meanwhile, physical activity, which can limit menstrual function, is thought to reduce this risk. A relatively recent area of investigation is prenatal exposures, such as preeclampsia (the condition in pregnancy characterized by high blood pressure) and low birth weight, both of which may be associated with lower in-utero exposure to oestrogen and constitute to a lower BC risk as an adult.⁵ Recent literature has also shed light on a strong link between diet and hormone-associated cancer, such as breast cancer; for example, BC has been positively associated with increased saturated/animal fat intake,⁹ alcohol intake¹⁰ and negatively associated with intake of fruits, vegetables, and water.¹¹ Shafei et al.¹² reported that bisphenol A (BPA) found in plastic is another possible risk factor for BC. Despite the high number of studies conducted in the west on the risk factors of BC, the genetic polymorphisms among different populations and differences in dietary exposure warrants the need to shed light on factors specific to the context of Mauritius. The objective of this study was therefore to identify the potential risk factors of FBC in Mauritius.

Materials and Methods

Ethical statement

This study was approved by the National Ethics Committee of Mauritius, Ministry of Health and Quality of Life (Reference: MHC/CT/NETH/2019). A consent form was devised specifically for the data collection process. In addition, an information paper was formulated to provide the background pertaining to the purpose of the study and the use of data to be collected. Prior to their participation, each respondent gave his approval for participating in the survey through a signed consent form. The consent form also served to reassure the subjects that their participation in the survey was voluntary and that they could withdraw at any time and abstain from responding any questions which they deemed inappropriate. Medical practitioners vetted the questionnaire used in this study and trained the interviewers who conducted the interviews of the participants.

Table 1. Sociodemographic characteristics of 149 cases and 245 controls in the case-control study of breast cancer

Variables	Cases (N= 149)		Controls (N= 245)	
	N	%	N	%
Age (years)				
<45	5	3.36%	8	3.27%
45 - 54	31	20.81%	52	21.22%
55-64	70	46.98%	125	51.02%
65-74	36	24.16%	50	20.41%
>74	7	4.70%	10	4.08%
Ethnicity				
Hindu	80	53.69%	115	46.94%
Catholic	42	28.19%	80	32.65%
Muslim	26	17.45%	42	17.14%
Others	1	0.67%	8	3.27%
Marital Status				
Married	112	75.17%	155	63.27%
Divorced	26	17.45%	56	22.86%
Widowed	7	4.70%	19	7.76%
Single	4	2.68%	8	3.27%
Living with someone as if you were married	0	0.00%	7	2.86%
Education				
No formal education	19	12.75%	32	13.06%
Primary	55	36.91%	76	31.02%
Secondary	58	38.93%	80	32.65%
Vocational	10	6.71%	25	10.20%
Undergraduate	7	4.70%	20	8.16%
Postgraduate	0	0.00%	12	4.90%
Monthly Income (Rs)				
0 (unemployed)	64	42.95%	81	33.06%
< 10,000	49	32.89%	58	23.67%
10,000 - 30,000	32	21.48%	63	25.71%
30,000 - 50,000	4	2.68%	24	9.80%
> 50,000	0	0.00%	19	7.76%

Inclusion and exclusion of individuals

The inclusion criteria for the survey participants were (i) Mauritian nationality, (ii) female gender, (iii) age of 15 years and above, and (iv) willingness to take part in the survey. The exclusion criteria were (i) being pregnant or lactating or (ii) having any physical or mental disability.

Case and control definition

We also established some inclusion criteria for the cases and controls, whereby the cases were defined as “A female individual who has already been diagnosed with BC” and the controls as a “A female individual healthy without signs of BC”.

Questionnaire design and data collection method

A questionnaire was designed in English

language, in which a structured one-on-one interview was conducted. It comprised five sections, namely (i) demographics, (ii) medical history, (iii) menstrual, gynecological, and obstetrical history, (iv) biological relatives, and (v) risk factors. The demographics section mainly investigated the age, gender, marital status, ethnic group, level of education, and income of the subject. The second section was concerned with the medical history of the subject. This section pertains to any prior diagnoses with cancer and family history of non-communicable diseases, such as diabetes mellitus, high blood pressure, or cardiovascular diseases. The questions in the menstrual, gynecological, and obstetrical history section were asked in order to know the initial

Table 2. GLM output

Variables	Estimates	Std. Error	P value	Lowest Bound	Highest Bound
Intercept	-1.47787	8.45111	0.5694	-18.0420456	15.0863056
Age	0.1791	0.03426	8.58E-08	0.1119504	0.2462496
Yes to 'respondent suffering from diabetes Mellitus'	1.47468	0.68006	0.01506	0.1417624	2.8075976
Yes to 'respondent suffering from high blood pressure'	-0.44428	0.63931	0.7565	-1.6973276	0.8087676
Yes to 'respondent suffering from stroke'	-2.24366	1.53152	0.9285	-5.2454392	0.7581192
Yes to 'respondent suffering from cardiovascular disease'	0.66654	0.90336	0.2303	-1.1040456	2.4371256
Yes to 'respondent suffering from cancer'	4.06471	0.88481	2.18E-06	2.3304824	5.7989376
Yes to 'member of your family suffering from diabetes Mellitus'	-0.69009	0.63215	0.8625	-1.929104	0.548924
Yes to "member of your family suffering from high blood pressure"	-0.68843	0.63312	0.8616	-1.9293452	0.5524852
Yes to "member of your family suffering from stroke"	2.11821	0.90412	0.009569	0.3461348	3.8902852
Yes to "member of your family suffering from cardiovascular disease"	-0.57282	0.71596	0.7882	-1.9761016	0.8304616
Yes to "member of your family suffering from cancer"	0.61532	0.23112	0.00388	0.1623248	1.0683152
At what age did your menstrual periods begin?	-0.26748	0.18014	0.9312	-0.6205544	0.0855944
Have you used any female hormones for two months or more, such as Premarin or other oestrogens for hot flushes or other menopausal symptoms?	0.23521	0.11221	0.01803	0.0152784	0.4551416
How many times have you been pregnant?	-0.26087	0.15601	0.9528	-0.5666496	0.0449096
For every child, how many weeks or months in total did you breastfeed them?	0.34511	0.12031	0.002062	0.1093024	0.5809176
Duration of the use of oral contraceptives	0.33562	0.12711	0.004141	0.0864844	0.5847556
What are your smoking habits?	1.98533	0.21301	0	1.5678304	2.4028296
What is your monthly consumption of fast foods?	0.22381	0.1121	0.02294	0.004094	0.443526
How many servings of fruits do you have per day?	-0.42765	0.33268	0.9007	-1.0797028	0.2244028
How many servings of vegetables do you have per day?	-0.43889	0.41422	0.8553	-1.2507612	0.3729812
Yes to 'do you carry out any additional decontamination treatments against pesticides?'	4.29093	0.71483	9.70E-10	2.8898632	5.6919968
Do you re-use plastic water bottles?	1.05015	0.32111	0.000535	0.4207744	1.6795256
Do you eat hot food served in plastic or Styrofoam containers?	2.62271	0.7373	0.000187	1.177602	4.067818

Sig. Codes: 0 '****' 0.001 '***' 0.01 '**' 0.05 '.' 0.1 '.' 1; (Dispersion parameter for binomial family taken to be 1); Null deviance: 429.29, Residual deviance: 33.17, AIC: 103.86; Std: Standard

age of menarche, to obtain the name of any female contraceptive pills used, the age of first intercourse, age of first pregnancy, age of first breastfeeding, and use of oral contraception and its duration along with some other details. The section of biological relatives mainly consisted of questions related to the biological relatives like mother, maternal grandmother, maternal aunts, sisters, or daughters to know whether they have any types of cancer. The last section, which is the risk factor exposure assessment, gathered information on the consumption of alcohol, smoking, consumption of vegetables, the use of plastics and Styrofoam containers for hot food, exposure to pesticides and insecticides, and physical activity.

Sampling method

Prior to data collection, a pilot test was conducted using a small sample size of 10 respondents with the following objectives: (i) identification of any underlying issues which could potentially impact the obtained survey results, (ii) checking the appropriateness of the questions to the target population, (iii) checking whether the questionnaire could provide the required information, (iv) identifying if further questions had to be added or eliminated, (v) verifying if the questions were properly understood by all classes of respondents, (vi) checking if the order of the questions was appropriate and systematic, (vii) estimation of the average time required to collect data from a respondent (interview), (viii) testing the willingness of the respondents to participate in the survey. Following the pilot test, necessary amendments were made to the questionnaire considering the feedback of the respondents; the questions were revised and the flow was altered to facilitate the data collection process. To administer the questionnaire to BC patients (the cases in the study), permission was sought from two non-governmental organizations (NGOs), LinktoLife and BC Care, in order to be able to approach patients registered in their database. The questions were asked in the native language, Mauritian Creole, to ensure that the questions were properly understood and the required responses were obtained. This step was

undertaken accounting the level of literacy of the respondents. All the subjects who participated in the survey met the inclusion and exclusion criteria.

Case and control selection

The sample size was computed to be around 384, assuming the maximum variability to be equal to 50% ($P = 0.5$) and taking 95% confidence level with $\pm 5\%$ precision (Cochran, 1977). However, 400 questionnaires were administered due to the fact that the number of cancer patients in Mauritius is on the increase, which necessitated capturing reliable and detailed information so that researchers, be it academic or pharmaceutical scientists, can come up with possible solutions. Out of the 400 administered questionnaires, 26 were non-responses, resulting in a total of 384 duly filled questionnaires. Given the overarching factors in hospital environment, like noise levels, patient, and pain management, convenience sampling was preferred. Additionally, this sample size of 384 proved to be more plausible since when the case study sampling design method by Charan et al.¹³ was applied with a total proportion of 80% and a 2:1 ratio, the obtained sampling size was too minimal. Therefore, we preferred to capture 384 responses, which seemed more reliable. Table 1 illustrates the demographic statistics captured in this case-control study.

Results

Identification of the contributory effects of the factors associated with BC using the Logistic Regression

This section summarizes the results of an inferential analysis based on the logistic regression to determine the potentially significant factors explaining the attainment of BC among the Mauritian women. A multi-collinearity test was performed in R using the `olsrr` package to eliminate any confounding or redundant factors. This test consists of three diagnostics: the multi-collinearity matrix, the Variance Inflation Factor, and the eigenvalues computation. Table 2 provides the estimates of various exogenous covariates, their standard errors, and information on the changes in the odds (cases/controls) for the significant factors.

The results illustrated that certain factors, such as age, history of cancer in the family, the use of female hormones, duration of the use of oral contraception, smoking, the re-use of plastic bottles, and consumption of food served in plastic or Styrofoam containers were the most significant breast cancer-associated risk factors. That said, the aforementioned factors increase the likelihood of attaining BC by 19.6%, 85.2%, 26.5%, 39.8%, 628%, 185%, and 1277% in a woman, respectively, while breast feeding reduces the risk by 29.2%.

It is to be noted that several logistic models have been fitted, but the table above represents the optimal selection of the factors after assessing their G-statistics. The step-wise regression results can be provided to the reader upon request.

Discussion

Our results revealed that age is a potential risk factor and most women suffering from BC aged from 50 to 60 years. In a number of studies, it has been reported that those women who are in menopause were more likely to develop BC.¹⁴ However, the age of menopause is known to vary from culture to culture.¹⁵ Our research also revealed that personal cancer history of the respondent and that of her family is a highly influential risk factor associated with BC. This implies that if the subjects or their kins have had any prior diagnosis of any types of cancer, such as ovarian, vaginal, or uterine cancers amongst others, they would be at a higher risk of BC in the future. In previous studies,^{14,16,17} it has also been reported that an individual has a higher risk of developing BC, if she has some first-degree relatives who already have this disease. Based on the inferential analysis conducted in our case-control study, there is a high association ($\Pr(>|z|) = 4.35e-06$ ***) between BC and the variable of BC in the first-degree relatives. The latter includes someone's mother or maternal grandmother or maternal aunts, sisters, or daughters. The obtained findings herein demonstrated that it is important to encourage more female who have first-degree relatives with BC to undergo regular screening. The government of Mauritius is providing various

kinds of screening facilities and Mauritians are urged to undergo screening.¹⁸ Nevertheless, the findings of this study showed that decision makers need to devise more strict strategies concerning regular screening.

It has been reported in several studies that women who undergo long-term medical treatment using oral hormonal contraceptives or hormonal replacement therapy are more likely to develop BC.^{19,20} In the current work, the prolonged use of female hormones was also found to be closely related to BC. The duration of contraceptive intake was found to vary from 5 to 15 years. According to the results of our analysis, the majority of the women with BC were found to have a long history of taking female hormones-containing contraceptive pills. This is indeed a common birth control practice among the Mauritian women. The outcome regarding the consumption and duration of female hormones demonstrated that this may have been the reason behind the high incidence of BC in Mauritius. No comprehensive research has been carried out to date in Mauritius on the impact of the prolonged consumption of this oral contraception. The women who have been surveyed claimed that this contraception is readily available and free of charge. They were able to follow a family planning programme and were not advised at all on the possible side-effects. Based on the above-mentioned analysis, the women from the control group were not consuming these types of oral contraception or had just consumed them for a very short period of time ranging from 1 to 6 months only. This suggested that the prolonged use of contraception known to contain a high level of hormones is strongly associated with BC in Mauritius.

Our study revealed that high exposure to cigarettes, either by being a smoker or victim of passive smoking, leads to a higher risk of BC. In our case-control study, several women indicated that they were not smokers, but were passive smokers as their husband or close ones at home were heavy smokers. Considering smoking as a potential factor, we found that it may be hormone receptor positive (ER+) of breast cancer. Smoking was also seen to be associated with BC in an

investigation conducted in the US on a sample of 662 women.²¹ However, taking smoking into consideration as a risk factor related to BC is a debatable topic.²² On the contrary to what we found in our study, in another work,²³ smoking was found to be related to both ER- and ER+ BC in both pre- and post-menopausal women. Nevertheless, further research is needed to further explore the relationship between smoking and BC risk. Nevertheless, the results are helpful in reinforcing campaigns encouraging people to choose a healthy lifestyle since smoking is a modifiable risk factor.

Another factor revealed by this study is the consumption of non-bio products, that is, products that may have been exposed to a high dosage of pesticides. The majority of the cases were not using any techniques to remove any possible pesticides that could be present in vegetables or fruits they consumed. However, such risk factor has not yet been proven in any previous studies. This factor may be correlated with the high incidence BC in Mauritius. It is noteworthy that bio products are not easily available in Mauritius. In addition, prior to 2018, there were no standards established with regards to the use of pesticides on vegetables and fruits in Mauritius.²⁴ It is until recently, in 2018, that a pesticide bill was enforced regarding the regulation, control, and monitoring the use of pesticides in or on certain fresh fruits, plants, seeds, or vegetables.²⁵ Further investigation is required regarding the heavy use of pesticides on fruits and vegetables in order to further confirm the link between this factor and BC.

Furthermore, the re-use of plastic bottles ($\text{Pr}(> |z|) = 0.00054^{***}$) was found to be a BC-associated risk factor. However, in our study, we did not ask the participants about the type of plastic bottle they used. Since this was found to be a significant factor based on the analysis, plastic bottles probably had a certain level of bisphenol A (BPA). According to a study, BPA is a weak synthetic estrogen, known to be hormone-disruptors, which may be found in several plastic products and can interfere with the body's hormonal balance.²⁶ This finding can be used to discourage people from the re-use of plastics

bottles, which is potentially associated with an increased incidence of BC.

In addition, we observed an association between the frequent use of Styrofoam to heat food and BC ($\text{Pr}(> |z|) = 0.00018^{***}$). The use of Styrofoam to serve hot food is in fact a common practice among Mauritians. According to the literature, there is no clear evidence on the relationship between styrene and cancer.²⁷ Meanwhile, our findings shed light a strong link between styrene use and incidence of BC. Massive sensitisation campaigns regarding the negative impact of heating food or serving hot food in Styrofoam containers is thus an imperative.

On the other hand, the current paper revealed that the duration of breastfeeding had an inverse relationship with BC. This has also been confirmed in other previous research;^{28,29} the effect of this factor on breastfeeding patterns and duration has not been yet proven.²⁹ Nevertheless, it has been mentioned that breastfeeding is a protective factor against BC. These findings can definitely be conducive to encouraging people to change their lifestyle since there is a high probability that breastfeeding be associated with a decreased risk of BC.

A few limitations of this study should however be noted. Primarily, the study investigated a sample; if all cases of BC were available on a national database, it would have been preferable to conduct a census. Moreover, according to Hennessy et al.,³⁰ a case: control ratio of 1:4 has the highest statistical power, which should have been adhered to in our study. Nonetheless, due to budgetary limitations and time restrictions, only 245 controls were approached, resulting in a ~ case: control ratio of 1:2. The third limitation was trying to maintain comparability between the cases and controls, which was achieved by matching them by age; it would have been ideal to match the cases and controls in other respects as well, such as ethnic group and socio-economic status.

Conclusion

The present study contributed to the determination of the factors strongly associated

with an increased risk of FBC in Mauritius. It was found that age, family cancer history, the extended use of female hormones as contraception, smoking habits, consumption of products with a high level of pesticides, along with the re-use of plastic bottles and Styrofoam to heat food were the main possible BC-associated risk factors in Mauritius. We hope that the findings herein be disseminated to the public to assist Mauritian women to review their lifestyle and also assist policy makers in their efforts to curtail BC.

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Conflict of Interest

None declared.

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