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Psychosocial Suffering as a Risk Factor of Breast Cancer: A Study Conducted at NTHC-HKM of Cotonou in 2020

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Abstract: Breast cancer is the leading cause of cancer death among women worldwide. In addition to the known risk factors, many studies have looked at the possible influence of psychosocial suffering factors on the occurrence of this cancer. In Benin, no study has been conducted in this regard. The objective of our research was therefore to study the exposure to psychosocial suffering factors influence on the occurrence of breast cancer. This study is a case-control study, conducted at the CNHU-HKM over a period of five months, involving patients with breast cancer (cases) and women without breast cancer (controls). Two controls were recruited for every one case. Thus, 180 people were recruited including 60 cases and 120 controls. The mean age was 48.28 (±10.52) years old for the cases and 48.6 (±10.67) years old for the controls. Death of the spouse and divorce were the major events more reported in the cases than in the controls. The risk of developing breast cancer was significantly 03 times higher in subjects who reported the death of their spouse (adjusted OR=3; 95% CI=1.10-8.55; p=0.033). There were no other significant associations for other major life events. There is no significant association between psychosocial distress factors in general and the occurrence of breast cancer. Only the death of the spouse was significantly associated with the occurrence of breast cancer.

Keywords: Benin, Breast Cancer, Psychosocial Suffering, Risk Factor

1. Introduction

A study conducted in 185 countries covered by Globocan [1] revealed that breast cancer is the most common and the most lethal cancer in women. In 2018, there were an estimated 2.1 million new cases worldwide and 627,000 deaths from breast cancer worldwide, with an 11.6% mortality rate [1].

In Africa, incidence and mortality data remain limited [2]. In 2018, breast cancer incidence in Africa was 15.3% of cancers, with an estimated mortality of 10.5% [3]. In Benin, breast cancer is the leading cancer in women, with an incidence of 19% and a mortality of 13.3%. According to Globocan data 2018 [4], it is a real public health problem.

Psychological factors, including stress and psychological

trauma, have been described in the literature as associated or triggering factors in breast cancer situations [5]. Thus, many epidemiological studies over the past decades have focused on the possible influence of these factors.

One of the earliest reports on the interaction between psychosocial factors and the problem of breast cancer comes from the medical literature of ancient Greece. The ideas of Hippocrates were adopted by Galen, who wrote that cancer was much more common in "melancholic" (depressed) women than in "sanguine" (happy, spirited) women [6]. However, until the 19th century, the only evidence provided of a possible link between psychological factors and cancer was still anecdotal.

The first scientific work was available in 1893, with the publication by Snow of a report. It is described in this report that 156 of the 250 cancer patients were influenced by the death of a family member and that 32 were confronted with a significant professional problem. Only 19 of the 250 patients did not mention any psychological or social factors as the cause of their illness [7].

The analyst Evans in 1926, after having given a post-diagnostic psychological evaluation to 100 cancer patients, concluded that the loss of an important emotional relationship was a major factor contributing to the development of malignant disease [7]. Subsequently, Dalton and al. in 2002 [8], reviewed the scientific literature published between 1967 and 2001 on the association between major life events (death, family illness, divorce, job loss) and the risk of cancer occurrence. These studies showed weak associations and inconsistent results. In a meta-analysis, Lin and al. [8] concluded that adverse life events do not affect the risk of developing breast cancer.

Some authors have stated that only a few psychosocial variables effect on tumor growth and development [9-11]. The idea that psychological stress may promote breast cancer has been supported by the results of some cohort and case-control studies [12-15]. These researchers inferred from their studies that controlling for confounding variables, cumulative life event analysis, and sample size were sufficient to assess the relationship. Psychological stressors would be associated with anthropometric, behavioral, and lifestyle factors to contribute to breast cancer [16, 17].

As presented above, the epidemiological data from the last three decades on stressful life events in relation to the occurrence of breast cancer remain limited and the results of different studies are often inconsistent, making the scientific evidence inconclusive.

In Benin and in the sub-region, the available data mainly concern the risk factors classically found for breast cancer. The psychosocial component has been underestimated or not evaluated. Psychosocial distress could be a risk factor for breast cancer in Benin, which motivated the conduct of the present study. The objective is to study the influence of exposure to psychosocial distress factors on the occurrence of breast cancer. To have an illustration a breast cancer case in CNHU-HKM of Cotonou we can look at Figure 1.

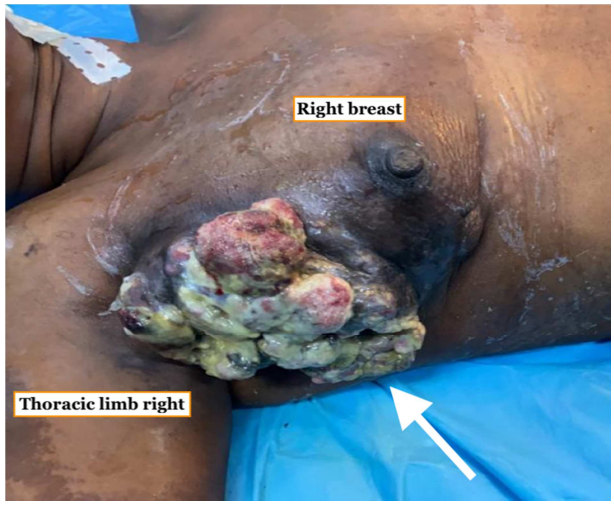

Figure 1. *Locally advanced cancer of the right breast with necrotic and ulcerating aspect in a patient in dorsal decubitus position. (image by Dr Gnangnon Freddy, M.D., Visceral Surgery Departement of CNHU-HKM, Cotonou, Benin).*

2. Materials and Methods

2.1. Place of Study

The city of Cotonou alone represents the Littoral department of Benin. It is bordered to the south by the Atlantic Ocean, to the north by Lake Nokoué, to the west by the city of Abomey-Calavi (in the Atlantic department), and to the east by the city of Sèmè-Kpodji (in the Ouémé department). Cotonou is home to Benin's only national referral hospital center, the National University Hospital Center (CNHU-HKM), which is the focus of our study. Actually, the study occurred at the CNHU-HKM of Cotonou and more precisely in the three departments that treat patients with breast cancer: Internal Medicine and Medical Oncology Department, Visceral Surgery Department and Gynecology and Obstetrics Department.

2.2. Methods

This is a case-control study conducted over a period of five (05) months from May 4, 2020 to October 1, 2020. It involved two groups of patients recruited in the same period: the case group and the control group. The subjects of the case group were patients with breast cancer, seen in consultation or hospitalization and whose diagnosis was histologically confirmed. The control group were women who came to the gynecology-obstetrics clinic for various reasons.

The case group did not include patients with a very altered general state or state of consciousness. Relatives of patients already included in the case group were not included in the control group.

For convenience, the option of a comparative study of sixty (60) subjects in the case group matched in age to one hundred and twenty (120) subjects in the control group was

made. For each case, two controls were recruited whose ages did not differ by more than 2 years. All patients encountered during the study period were successively recruited as cases. The controls were recruited randomly.

The study participants were interviewed individually on the basis of a self-directed questionnaire including sociodemographic, clinical, risk factor, and Holmes and Rahe stress scale 1967 [18]. The questionnaire was completed with data from the medical records of the cases.

The dependent variable is the presence or not of breast cancer. The independent variables were sociodemographic and clinical data, risk factors, and psychosocial suffering factors. The Holmes and Rahe score was calculated for each respondent. A score of over 300 was classified as high; a score of between 150 and 299 as moderate; and a score of less than 150 as mild.

Data processing was done with the statistical software R version 3.5.1. This made it possible to obtain the number and proportions for the categorical variables; the minimum, mean, median, standard deviation, and maximum for the quantitative variables. The different frequencies were compared using the Chi-square test. The significance level, α was set at 0.05 throughout the work. When p is less than 0.05, a statistically significant association is concluded. Then, the logistic regression parameters were estimated with each of the explanatory variables. The parameters of the final model were estimated with the variables previously retained. A deviance analysis and verification of the accuracy of the model were used to interpret the results.

From an ethical point of view, a favorable opinion was requested and obtained from the CNHU-HKM authorities before the start of the study. Likewise, to access the subjects of study, the authorization of the heads of the departments concerned has been obtained. Each patient was given an explanation of the study and informed consent was obtained. For the controls, explanations were also provided and informed consent was obtained. Anonymity and confidentiality of the data were guaranteed. And the favorable opinion of the Local Ethics Committee for Biomedical Research of the University of Parakou (REF: 0342/CLERB-UP/P/SP/R/SA) has been obtained.

Note that the difficulties encountered during this study were mostly related to the health crisis due to COVID 19.

During the study period, the flow of patients to the CNHU-HKM was limited.

3. Results

3.1. Preliminary Analyses

At the end of the survey, 180 subjects was recruited such as 60 patients with breast cancer and 120 women without any breast cancer at the time of the survey.

3.1.1. Age

The average age of the subjects in the case group was 48.28 years old with a standard deviation of 10.52, a minimum of 19, and a maximum of 68 years. The maximum frequency was observed in the 39 to 49 years old age group. In the control group, the average age of the subjects was 48.60 years with a standard deviation of 10.67, a minimum of 22, and a maximum of 69 years. The maximum frequency was also observed between the age group of 39 to 49 years old. The difference between the two groups was not statistically significant (p=0.99). Actually, the age group distributions of the patients are in table 1.

Table 1. *Distribution of case and control subjects by age group.*

	Case (%)	Control (%)	Total (%)	p
[19; 29]	2 (3.3)	4 (3.3)	6 (3.3)	
[29; 39]	11 (18.3)	22 (18.3)	33 (18.3)	
[39; 49]	19 (31.7)	38 (31.7)	57 (31.7)	0.99
[49; 59]	18 (30.0)	33 (27.5)	51 (28.3)	
[59; 69]	10 (16.7)	23 (19.2)	33 (18.4)	

3.1.2. Education

In the case group, about 1 over 2 patients got a secondary education level (55%). In contrast, in the control group, 1 over 2 patients had a higher level of education (50%). This difference between the two groups was statistically significant (p=0.001). It can be checked in table 2.

Table 2. *Distribution of case and control subjects by education level.*

	Case (%)	Controls (%)	Total (%)	P
Not educated	6 (10.0)	7 (5.8)	13 (7.2)	
Primary	9 (15.0)	16 (13.4)	5 (13.9)	0.001
Secondary	33 (55.0)	37 (30.8)	70 (38.9)	
Higher education	12 (20.0)	60 (50.0)	72 (40.0)	

3.1.3. Occupation

In the case group, the most represented socio-professional category was shopkeepers (28.3%), followed by civil servants (23.3%). In the control group, on the other hand, the most represented socio-professional category was the latter (24.2%), followed by shopkeepers (22.5%). However, in table 3, the difference between the two groups was not statistically significant (p=0.343).

Table 3. *Distribution of cases and controls' occupation.*

	Case (%)	Control (%)	Total (%)	p
Health worker	6 (10)	19 (15.8)	25 (13.9)	
Craftswoman	7 (11.7)	17 (14.2)	24 (13,3)	
Shopkeeper	17 (28.3)	27 (22.5)	44 (24.4)	
Pupil/student	1 (1.7)	2 (1.7)	3 (01.7)	0.343
Civil servant	14 (23.3)	29 (24.2)	43 (23.9)	
Housewife	11 (18.3)	10 (8.3)	21 (11.7)	
Retired	4 (6.7)	16 (13.3)	20 (11.1)	

3.1.4. Marital Status

In the case group, 1 over 2 subjects were married (50%). In the control group, more than one subject out of two was married (60.8%). In table 4, the difference between the two groups was not statistically significant (p=0.295).

Table 4. *Distribution of case and control subjects by marital status.*

	Case (%)	Control (%)	Total (%)	P
Divorcée	1 (1.7)	1 (00.8)	2 (01.1)	
Célibataire	8 (13.3)	17 (14.2)	25 (13.9)	
Mariée	30 (50.0)	73 (60.9)	103 (57.2)	0.295
Concubinage	12 (20.0)	22 (18.3)	34 (18.9)	
Veuve	9 (15.0)	7 (5.8)	16 (08.9)	

In this series, 16.7% of the subjects in the case group had a family history of breast cancer compared with 12.5% in the control group. This difference was not statistically significant (p=0.446).

3.1.5. TNM Classification of Cases' Cancer

The average age of diagnosis for the case group was 25.30 months with a standard deviation of 18.34 months, a minimum of 1 month, and a maximum of 168 months (14 years). There were three (3) cases out of sixty (60) who were not yet on treatment at the time of recruitment. The majority of cases recruited had advanced stages. Figure 2 details the distribution of the case group by TNM stage.

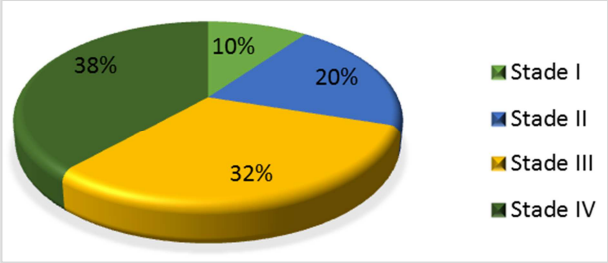

Figure 2. *Distribution of case group by TNM Stage.*

3.2. Psychosocial Suffering Factors

Among the 43 events in the Holmes and Rahe score, 36 events were reported at least once by subjects in both case and control groups. Some subjects reported events in addition to the 43 items considered, such as: polygamy of the spouse, the spouse's inability to provide for the household, desire for motherhood, family disagreement, sexual assault, physical aggression, lack of parental affection, preoccupation with the realization of life projects.

The mean score of the subjects in the case group was 125.56 with a standard deviation of 81.76, a minimum of 0, and a maximum of 341. In the control group, the mean score of the subjects was 132.32 with a standard deviation of 91.59 and a range of 0 and 422. Besides, the comparison of the categorized severity of Holmes and Rahe scores between cases and controls did not give any significant difference (p=0.748). The maximum frequency was observed in the case group with a mild score (65%). This trend was similar in the control group with a proportion of 61.7%. Table 5 details the comparison.

Table 5. *Severity of Holmes and Rahe scores in case and control groups.*

	Case (%)	Control (%)	Total (%)	p
Light	39 (65.0)	74 (61.7)	113 (62.8)	
Moderate	19 (31.7)	39 (32.5)	58 (32.2)	0.748
High	2 (03.3)	7 (05.8)	9 (05.0)	

Some items were never reported by the subjects in this study such as: imprisonment, minor law violations, mortgage or loan foreclosure, changes in social activities, change in school. Events such as death of spouse and divorce were more frequently reported in the case group than in the control group. The difference was statistically significant only for divorce (p=0.014). In the case group, the most frequent events were those related to family life (73.3%), followed by those related to marital life (55%). In the control group, this pattern appeared similar with proportions of 78.3% and 42.5% for family life and marital life events, respectively. However, the difference was not statistically significant (p=0.455). The events with the highest scores on the scale were considered as major events. The most reported major event in the case group was the death of a family member (56.7%), followed by the death of a spouse (18.3%). In the control group, the most reported major event was also the death of a family member, followed by marital separation, with proportions of 66.7% and 18.3%, respectively.

3.3. Modeling

By adjusting the major events constituting factors of psychosocial suffering between them, the odds ratio expressing the risk was calculated. Thus, it is found that the risk of developing breast cancer was three times higher in subjects who reported the death of their spouse (adjusted OR=3; 95% CI=1.10-8.55; p=0.033). Retirement tended to be a protective factor (adjusted OR=0.31; 95% CI=0.08-0.96; p=0.06).

There were no other significant associations for the other major events: marital separation (adjusted OR=1.23; 95%CI=0.5-2.91; p=0.634); death of a close family member (adjusted OR=0.68; 95%IC=0.35-1.33; p=0.262); personal injury or illness (adjusted OR=0.69; 95%CI=0.21-1.95; p=0.502); and job termination (adjusted OR=0.14; 95%CI=0.01-0.93; p=0.087).

4. Discussion

In this study, the average age of the subjects in the case group was 48.28 years, with the maximum frequency observed in the 39 to 49 years old age group. In the control group, the average age of the subjects was 48.6 years. The difference between the two groups was not statistically significant. Lin and al in China [19], in a series of 265 cases and 265 age-matched controls, had also found a higher incidence of breast cancer in women aged 40 to 49 years (44.5%) in the case group. In contrast, Kruk and al. in Poland [20], had found a slightly higher mean age of 55.3 years (±9.7) for cases and 54.8 years (±9.5) for controls in a series of 858 cases and 1085 controls. Peled and al in Israel [15], noted a slightly lower average age than ours (40 years±4.8 for the cases; 34.7 years±6.3 for controls) in a population of 255 cases and 367 controls. The first two authors, unlike the last, did not find a statistically significant difference between the ages of cases and controls. Moreover, these variations according to geographical areas could be due to genetic

factors, or to the relative youth of the population and the lower life expectancy in African countries compared to Western countries.

In the case group of this study, about 1 subject out of 2 had a secondary education (55%). In contrast, in the control group, 1 subject out of 2 had a higher level of education (50%). This difference between the two groups was statistically significant. This finding is similar to that of Kruk, 2012 in Poland [20]. In contrast, Peled and al. [15], found that cases were significantly more educated than controls in a series of 255 cases and 367 controls. It may have been their level of education that helped them to seek the diagnosis. Lambe and al. [21] and Butow and al. in Australia [22], in each of their series, had matched cases and controls on this socio-demographic data. This explains why cases and controls had the same level of education in each of their study populations. This pattern likely reflects the overall status of the population in this country.

The case group in our study had more family history of breast cancer than the control group. However, this difference was not statistically significant (p=0.446). A similar trend was reported in Finland by Aro and al. [23] in a prospective cohort of 10892 subjects. The same was reported in Poland by Kruk, and al. in a series 858 cases and 1085 controls [20]. The fact that the difference was not statistically significant in these series could perhaps be explained by the smaller size of the sample. Indeed, first- and second-degree family history are risk factors classically described in the literature [24, 25].

The subjects this study had reported 36 events out of the 43 that made up the Holmes and Rahe [18] score, as well as other events not included in it. Similarly, some items were never reported by the subjects in this study. The events not reported in these series had been mentioned in several Western series including Kruk [20]; Aro and al in Finland [23]; Surtees and al. in the UK [26]. In the absence of initiating a score that can better respond to the African realities, it would be important to adapt the Holmes and Rahe score to the social context.

The most frequent events in the cases were those related to family life, followed by those related to marital life. In the control group, this pattern appeared similar. Work life events were most commonly reported in cases and controls in the series by Kruk, and al., [14] (66.9% in cases and 64.6% in controls), followed by family life events in lesser proportions (10.9% in cases and 11.1% in controls). Lin and al. [19], as well as Peled and al. [15] instead reported events related to illness and bereavement as the most frequently reported by the survey subjects. In Benin, the extended family occupies a primordial place in the life of the individual. This difference in culture with the West, where people are more focused on their own people, their personal and professional achievements, and their nuclear family, could explain the above findings.

The most reported major event in general in both groups in the study was the death of a family member. Bereavement, when it concerns a close family member, is a major event in the African culture. This is especially important because in rural Africa, the majority of people live in families. However, elsewhere in Poland, this finding has also been made by Kruk and al [20]. On the other hand [27], the most reported major event was emotional and marital instability. The latter had recruited much younger women as survey subjects, who were likely not to have experienced a significant death, which may explain this difference.

Events such as spousal death and divorce were more common in the cases than in the controls in the series. Kruk and al. [20] had also made the same finding regarding spousal death (14.1% vs. 12.3%) and divorce (11.9% vs. 9.1%). Bereavement is both a personal and social trauma. When it concerns the spouse, the widow feels a void in relation to the disappearance of the object of love (the husband), but also of the emotional attachment to the deceased. In the mourning process, the widow may "let herself die". Under these conditions, her immunity drops and could facilitate the occurrence of cancer. The dissolution of marital ties, either through divorce or death, weakens mental and social balance and, in turn, disrupts physical health. Butow and al. [22] and Peled and al. [15], in studies carried out in Australia and Israel, found a contrary trend. The death of the spouse and divorce were more frequent among the controls in their respective series. It should be noted that these two authors had studied younger populations, with respective mean ages of 43 (±14.5) and 40 (±4.8) years.

The risk of developing breast cancer was significantly 03 times higher in subjects who reported the death of their spouse. The death of a spouse in the social context of this study is often a source of conflict between the in-laws and the widow. This could explain the fact that African women experience the mourning of their spouses in a particular way. The suffering they feel is more pronounced. Regarding this event, these results are consistent with those of Ozkan, and al., (2017) [28] in Turkey (OR=3.66; 95% CI=2.23-5.98). However, Kvikstad [29] in Norway, Liand and al. [27] in China, Kruk in Poland [20] as well as Schoemaker, and al., [30] in the UK reported a slightly lower risk of 1.13 (95%IC=0.94-1.36), 1.16 (95%IC=1.06-1.26; p=0.001); 1.30 (95%IC=0.63-2.35) and 1.13 (95%IC=0.88-1.46) respectively.

This study did not find a significant association between psychosocial distress factors in general and the risk of breast cancer in particular. Schoemaker and al. [30], and Surtees, and al [26], had made the same finding. This state of affairs could be explained in this context by the individual management made of the milestone event. Indeed, this study did not take into account the psychological differences and the individual response of each subject to stress.

5. Conclusion

Breast cancer is the most common cancer in women and the leading cause of cancer death worldwide. It is a real public health problem in our country. The population of this study was 180 subjects, including 60 breast cancer patients and 120 unaffected control women. The comparison of the

two groups allowed to study the influence of psychosocial suffering factors on the occurrence of breast cancer. At the end of the study, in the univariate analysis, there was no significant association between psychosocial distress factors in general and the risk of developing breast cancer. The only major event in multivariate analysis, significantly associated with breast cancer was the death of the spouse, with a 3-fold increase in risk. The reduction of mortality due to breast cancer requires early detection and treatment, but also the control of modifiable risk factors. It is also important to adapt the Holmes and Rahe score to the African socio-cultural realities to improve research on the psychosocial suffering factors associated with breast cancer.

Future Directions

It would be interesting to complete this study on a larger sample, taking into account the individual aspects of each patient with breast cancer and using a psychosocial suffering assessment score adapted to the African context.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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