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Dietary Patterns and Oxidative Stress in a Population of Women with Breast Cancer in the North-Western Regions of Algeria (Saida and El-Bayadh)

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ABSTRACT

Objective: The aim of this work is the study of risk factors for breast cancer in a population of women in the north-western regions of Algeria (Saida and El-Bayadh)

Methodology: A case-control study was carried out on 40 women including 20 cancerous women and 20 control women, in order to determine the dietary patterns and general characteristics of the population studied and to compare the hematological and biochemical parameters, and markers of oxidative/antioxidant status between control women and breast cancer women.

Results: The results obtained show that there is no significant difference in the average age however the body mass index was significantly increased in cancer women, revealing overweight ($p < 0.05$), compared to control women. The marital status of the target population is predominantly a married woman status and the level of education shows a relatively low level in breast cancer cases compared to women controls. The illiteracy rate is exceptionally high in cancer women compared to controls (35% versus 20%). In addition, the levels of glucose, creatinine, HDL and ALAT are similar between the two groups of women. The contents of urea, cholesterol, triglyceride, LDL, ASAT, malondialdehyde and uric acid are significantly increased in women with breast cancer compared to women controls. But the vitamin C content is significantly reduced in cancer women compared to control women.

Conclusion: We conclude from this study that there is an association between breast cancer and lipid alteration, oxidative stress, age, increase in BMI, socio-demographic data, professional situation, age, means of menstruation and menopause, and ultimately the lifestyle. All these factors are risk factors for breast cancer in the region of Saida and El-Bayadh.

Keywords: Breast Cancer, Risk Factors, Dietary Patterns, Oxidative Stress.

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INTRODUCTION

Each year, nearly 1.38 million new cases are recorded worldwide and 458,000 deaths from breast cancer. This type of cancer is by far the first in women. In Algeria, its incidence is increasing steadily and currently. More than 12,000 new cases are recorded each year, particularly the young age and often very advanced stage of the patients. According to Algerian statistics, the annual increase in breast cancer is 8%, of which nearly 8,000 cases were recorded in western Algeria in 2017 [1].

Several risk factors have been clearly identified. The reproductive factors associated with prolonged exposure to endogenous oestrogen, precocious puberty, menopause, late first pregnancy, are among the most important factors. The use of oral contraceptives or hormonal treatment increases the risk, breastfeeding would have a protective effect [2]. The link between cancer and nutrition is very apparent. In our

country and others, breastfeeding can prevent cancer because regular consumption of fruits and vegetables lowers the carcinogenic risk, so a high fat ratio is associated with an increased risk [3]. Oxidative stress is another etiologic factor in breast cancer. It can be broadly defined as an imbalance between oxidants and antioxidants in favor of oxidants, potentially leading to damage. The increase in reactive oxygen species (ROS) and the resulting high oxidative stress are key features of malignant tumours [4].

To better understand the evolution of breast cancer in Algerian women in the region of Saida and El-Bayadh (north-western of Algeria), we carried out a study on the nutritional profile and oxidative stress in women with breast cancer of this region. The objective is to determine the risk factors for breast cancer and to measure its frequency in hospitalized women.

MATERIAL AND METHODS

Studied population, clinical data and the dietary patterns assessment

This is a non-randomized clinical conducted at the oncology department of the public hospitals in Saida and El-Bayadh regions, from November 2018 to April 2019. The case study includes women who present the risk factors in developing breast cancer in the population of Saida and El Bayadh (north-western regions of Algeria). The recruitment of diagnosed cases of breast cancer was based on a diagnosis confirmed by mammography, biopsy and/or surgery. The inclusion criteria for breast cancer patients were confirmed breast cancer women of all ages and from the same region of habitat with the exclusion of pregnant and breastfeeding patients. However, the control patients were women in good health, who had not had any type of cancer, were free from any pathology and were from the same region and of all ages. The information were collected through a basic questionnaire of which includes the identification of the patient, body parameters (height, weight), socio-demographic data (residence, level of education), marital status (single, married, divorced, etc.), professional situation, fertility history (age of first menstruation, marriage age, breastfeeding period ...), contraceptive using (age and period of taking contraceptives), drug consumption (type of drug and year of taking, etc.), diet and lifestyle (favorite meals, consumption of meat, vegetables, fruits, practice of sport ...) and history of breast cancer diagnosis (stage and location of breast cancer). The questionnaire takes into account physical activity as a whole, including daily activities and participation in sports activities (walking, jogging or running, the way to work, the way to the nursery, shopping at the market, cleaning, washing clothes, manual crafts, crafts and gardening) before the diagnosis or interview [5].

Biochemical analysis

Blood samples were taken in the morning on an empty stomach, from the vein at the bend of the elbow, on dry tubes and on tubes with anticoagulant (EDTA or heparin). All of these tubes are precisely labelled and listed. After coagulation, the blood taken from dry tubes is centrifuged at 3000 rotations/min for 10 minutes at room temperature. The recovered serum is used for biochemical analysis (glucose, creatinine, urea, cholesterol and triglyceride contents; and the enzymatic activity of transaminases 'ALAT and ASAT'). The blood collected in tubes with anticoagulant is used for hematological assays (blood smears and complete blood count), and it is centrifuged in order to recover the plasma for the determination of markers of oxidative stress in plasma (uric acid, plasma vitamin C and malondialdehyde contents). The concentration of uric acid was assessed by the use of the test kits (Spinreact Inc., Spain). However, the concentration of plasma vitamin C and malondialdehyde was determined by the method of Jagota and Dani [6] and Beauvieux *et al.* [7], respectively.

Statistical analysis

The data were expressed as mean ± SD. Statistical analysis was carried out using Sigmaplot 11 (Systat Software, Inc.). The significance of the differences between control group and patient group was determined by Student's t-test. Univariate associations between variables were analyzed using Pearson's correlation coefficients. $P<0.05$ was considered as significant.

RESULTS AND DISCUSSION

Our work contributes to the advancement of scientific knowledge on the early diagnosis, screening and treatment of cancer and the improvement of prevention and care measures in the health services offered. to women with breast cancer. The main goal is to reduce the number of new cases, increase the number of recoveries, improve the quality of life of patients and the quality of support given to all those concerned. This work is geared towards researching environmental risk factors that could predispose women to breast cancer. Indeed, there is sufficient evidence to suggest that exposure to environmental and lifestyle factors play an important role in the etiology of this disease. Breast cancer is a clinically heterogeneous and complex pathology [8]. Constant identification of risk factors, which can be acted upon, should facilitate the implementation of effective prevention strategies.

The characteristics of the population studied are shown in Table 01. The women volunteers for this study are recruited in a hospital environment. The recruitment of breast cancer cases is based on the diagnosis of breast cancer confirmed by mammography, biopsy and/or surgery by physicians specializing in oncology. After consent of the women to participate in the study, the selected population reached 20 control women and 20 breast cancer women.

The results obtained show that there is no significant difference in the average age. Age is one of the most important risk factors for breast cancer. The risk increases between 41 and 50 years, with almost half of cancer population studied. Indeed, several studies suggest that breast cancer is more aggressive in women aged 40 to 49 [5].

On the other hand, the body mass index was significantly increased in cancer women, revealing overweight ($p<0.05$), compared to control women. Overweight is defined as excess body fat (BMI 25-29.9 kg/m^2), which from a certain threshold is referred to as obesity [9]. Weight gain from the age of 30 and from the age of 40 plays an important role in the etiology of breast cancer, increasing the risk of this cancer by 1.96 times and 2.5 times, respectively [10]. Excess fatty tissue causes increased production and increased exposure time to steroid hormones. Indeed, obesity has an impact on hormone regulation because it advances puberty in girls, by exposing them more to breast cancer [11].

Table 1: Population characteristics

	Control (n = 20)	Breast cancer (n = 20)
Age (years)	40.16 ± 11.08	46.85 ±11.59
≤30 (N°)	5	2
31-40 (N°)	8	3
41-50 (N°)	3	9
51-60 (N°)	3	4
≥60 (N°)	1	2
BMI (Kg/m2)	24.11 ± 1.14	28.66 ± 2.36
18-25 (N°)	14	04
25-30 (N°)	05	13
30-35 (N°)	01	03
Average age of menstruation onset (%)		
Before 12 years	30	60
After 12 years	70	40
Contraceptive use before the age of 20 (%)	0	25
Physical activity (%)		
Low	20	30
Medium	25	55
High	55	15
Average age at 1st pregnancy (years)	23.45 ± 2.52	26.18 ± 3.29
Breast feeding (%)	45%	55 %
Residence (%)		
Urban	35	40
Rural	65	60
Marital status (%)		
Single	30	25
Married	45	40
Divorced	10	25
Widow	15	10
Educational level (%)		
Illiterate	20	35
Primary	15	15
Fundamental	20	30
Secondary	35	15
University	10	05
Professional situation (%)		
Employer	55	20
Housewife	45	80

The marital status of the target population is predominantly a married woman status, dominant for women with cancer (40%) and controls (45%). Overall, the level of education shows a relatively low level in breast cancer cases compared to women controls. The illiteracy rate is exceptionally high in cancer women compared to controls (35% versus 20%). The vast majority of cancerous women are unemployed vis-à-vis the controls (80% versus 45%). The low level of education of women with cancer, expressed as a risk factor, indicates a very high rate of illiteracy. This result is consistent with those from other studies. Indeed, one study detected the existence of a positive association between educational level and breast cancer in postmenopausal women [12]. Kaffashian *et al.* [13] found a high rate of death from breast cancer among women belonging to a disadvantaged social class. In contrast, Robert *et al.* [14] found the risk to be higher in women with high socioeconomic status (SES) living in urban areas. Similar research results are found regarding weak SES, considered as a predictive factor in our study.

Socio-economic factors such as unemployment, lack of education, and poverty are among the most important social determinants of health. It is well established that people with low incomes are at increased risk for a range of health problems and are more likely to die prematurely [15]. People who are food insecure often consume a diet low in nutrients, which can contribute to breast cancer risk factors such as obesity and diabetes [16, 17]. To purchase food or due to budget constraints, low-income families may postpone medical care and under-use drugs [18]. Food insecurity is associated with stress, anxiety, depression and psychological distress [19]. It is well established that socio-economic factors influence the risk of breast cancer [20]. Socio-economic position is an aggregate construction which includes both measures based on resources (income, wealth, consumer credit) and measures based on prestige (education, social status) which represent both position individual social welfare and access to material goods [21]. Poverty is associated with other factors related to the late stage of breast cancer diagnosis and poorer survival, such as inadequate health insurance, lack of primary care physicians, and limited access to health care. Many studies have examined breast cancer outcomes based on measures of socioeconomic status such as income and education [22, 23].

Of the above factors, some are associated with an increased risk of breast cancer, others are associated with a reduced risk. Thus, to determine the predictive or protective factors for breast cancer in the Saida and El-Bayadh region, a logistic analysis is performed, including the various etiological factors as exposure variables. The values of the odds – ratio (OR) for each factor show that menstruation before the age of 12 is a significant risk factor for breast cancer (OR = 3.5). Consumption of contraceptives before the age of 20 is also a very significant predictor of breast cancer (OR = infinity).

Age at first pregnancy is also an important factor in breast cancer risk [24]. In women whose first pregnancy was at age 35, the risk of breast cancer is 1.5 times higher than in those who became pregnant at age 20. It is 1.2 times higher compared to a nulliparous. Also, pregnancy before the age of 20 reduces the risk of breast cancer by 50% compared to a nulliparous one [25]. Pregnancy causes accelerated differentiation of breast tissue and rapid proliferation of the epithelium. The changes initiated during the first pregnancy, especially if it occurred early, are accentuated by each of the subsequent pregnancies, and the development of breast cancer is related to the rate of proliferation of mammary epithelial cells and conversely to the degree of differentiation [26].

The absence of high physical activity appears to be the most important factor in breast cancer in our study population (OR = 6.93). Physical activity is a component of nutrition along with food. Indeed, the latter is understood as the balance between the contributions related to food and the expenses caused by physical activity. Physical activity in the broad sense includes all movements performed in daily life and is not reduced to the sole practice of sport, whether for leisure or competition. It also integrates the physical activity practiced in the context of professional and everyday life (household activities, gardening, transport, etc.). Physical activity is defined as any bodily movement produced by the contraction of skeletal muscles resulting in an increase in energy expenditure greater than that in rest expenditure [27].

Physical activity is one of the few modifiable risk factors known to have a role in the development of breast cancer. Numerous epidemiological studies have observed a decrease in breast cancer risk with increasing levels of physical activity. Indeed, some studies report that patients who had the highest total physical activity had a 22% reduction in breast cancer risk compared to sedentary patients; Similarly, women who walked regularly for 30 minutes per day had a significant risk reduction of 18% compared to sedentary [28]. According to Lagerros *et al.* [29], the relationship between physical activity and breast cancer registers a 20% reduction in risk associated with exercise, especially in adolescence and adulthood. For every increase of one hour of physical activity per week during adolescence, a 3% decrease in breast cancer risk was observed. The biological mechanisms by which physical activity is associated with decreased risk involve reduced estrogen production and maintenance of energy balance [5].

Mohseny *et al.* [30] found that education level and municipal district of residence were associated with breast cancer survival. Reduced obesity, healthy diets, increased physical activity, and use of health services can improve health and reduce the risk of disease recurrence, and these factors are influenced by social determinants such as income, employment and education [31, 32].

The second part of this study concerns the exploration of nutritional status in cancer cases and controls (Table 2). In the etiology of breast cancer, and with reference to the risk factors cited in the literature, several epidemiological and experimental studies conducted around the world have resulted in the involvement of nutritional factors [33].

Table 2: Dietary patterns in the study population

Dietary, N° (%)	**Control (n = 20)**	**Breast cancer (n = 20)**
Meals on a regular basis during the day	8 (40)	4 (20)
Fat in the diet		
Low	5 (25)	4 (20)
Medium	12 (60)	7 (35)
High	3 (15)	9 (45)
Consumption of meat on a regular basis	7 (35)	11 (55)
Fish consumption	10 (50)	11 (55)
Consuming tea on a regular basis	14 (70)	10 (50)
Consumption of soft drinks	7 (35)	14 (70)
Smoking on a regular basis	0	0
Consumption of alcoholic beverages	0	0
Consumption of canned food	3 (15)	6 (30)
Consumption of FAST FOOD	7 (35)	8 (40)
Milk consumption	20 (100)	20 (100)
Consuming fruits and vegetables on a regular basis	13 (65)	9 (45)

Low tea consumption is observed to be an important factor in women with cancer. The consumption of soft drinks as well as canned food is other factors in breast cancer with ORs of 4.33 and 2.43, respectively. A percentage of 45% of women with cancer have a high intake of fat. Particular interest has been focused on dietary fats. Indeed, it has been pointed out that a high fat intake would be associated with an increased risk of carcinogenesis risk. Fatty acids are involved in many biological reactions and exert numerous effects in terms of initiation, promotion and suppression of tumor development [34]. The majority of studies show a positive association between fatty diet and breast cancer [35]. 55% of women with cancer consume meats on a regular basis. Meat has estrogenic properties, such as heterocyclic amines, iron, and hormone residues. An effect via hormone receptors is possible [36].

Moreover, our results indicate that the early age at the first maternity and the duration of breastfeeding are not considered as predictive factors of breast cancer in our population since the OR values obtained are not significant. On the other hand, studies have suggested that breastfeeding reduces the risk of breast cancer in women which may differ between subtypes so that breastfeeding may be more protective against certain types of invasive breast cancer [37].

The average values of red blood cells, haemoglobin, haematocrit, is similar in both groups, but there is an increase in white blood cells, decrease in the average value of platelets in women with cancer (Table 3).

Table 3: Complete blood count in the study population

Biochemical parameters	**Control (n = 20)**	**Breast cancer (n = 20)**
Red blood cells (10^6/mm^3)	4.31 ± 0.99	3.88 ± 0.75
White blood cells (10^9/mm^3)	4.34 ± 1.25	6.89 ± 1.5
Platelets (10^3/mm^3)	359.1 ± 83.32	220.35 ± 70.38
Hemoglobin (g/dl)	13.02 ± 1.17	10.49 ± 1.05
Hematocrit (%)	40.76 ± 5.33	32.5 ± 3.62

The serum glucose and creatinine contents are similar between the two groups, on the other hand a significant increase in the urea content in cancerous women, it therefore appears that renal function is affected in cancerous women (P^*<0.050). A significant increase in cholesterol, LDL (figure 1). There is a link between cholesterol levels and breast cancer, women with breast cancer have high cholesterol in their blood. Also the serum triglyceride contents are significantly increased in cancerous women (P^* <0.050). In the majority of cases, the increase in triglycerides is secondary to several situations or pathologies. Alterations in the lipid profile are significantly correlated with breast cancer risk and clinical status [38]. The excess of plasma triglyceride in cancerous women can be interpreted on the one hand by an increase in the synthesis of VLDL and on the other hand by a reduction in the catabolism of VLDL due to the decrease in the stimulation of the tissue lipoprotein lipase. HDL comes in part from the catabolism of VLDL. So, a decrease in this catabolism will be responsible for the breakdown of HDL [39].

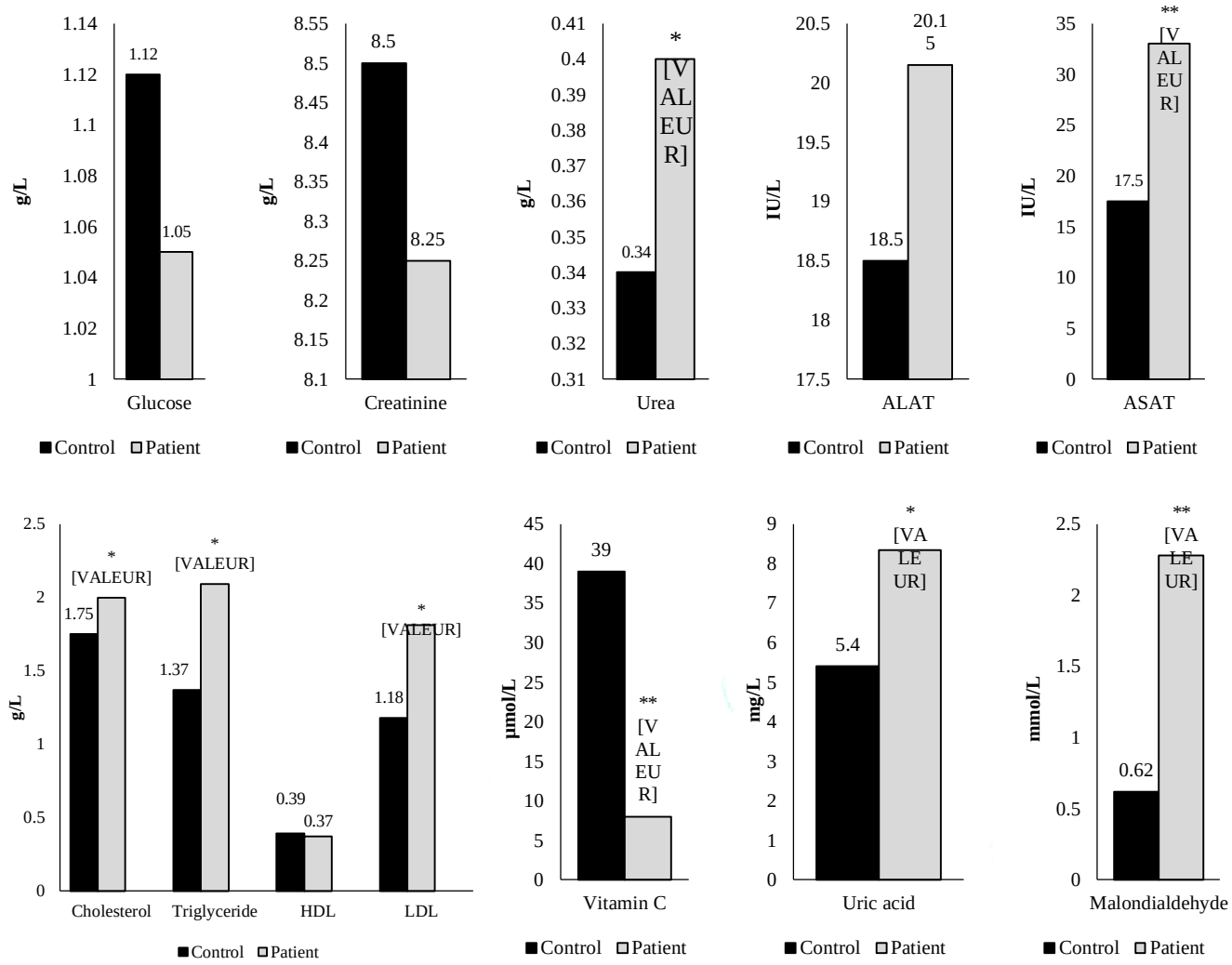

Figure 1: Serum and plasma levels of glucose, creatinine, urea, cholesterol, triglyceride, HDL, LDL, ALAT, ASAT, uric acid, plasma vitamin C and malondialdehyde in control and breast cancer women (p^* < 0,050 and p^{**}= <0,01)

The level of alanine aminotrasferase is similar between the two groups of women. Serum aspartate aminotransferase activities are significantly increased (p ** = <0.01) in women with cancer, transaminases increase in the blood during destruction of liver cells, it may also be linked to autoimmune diseases, obesity and overweight (figure 1).

A final part in our study is concerned with oxidative stress, potentially aggressive and discreet, that recognized today as the source of all pathologies. In this part, we try to research the part of oxidative stress in breast cancer. A state of oxidative stress is triggered following an imbalance in the balance between the anti-oxidant defense systems and the production of ROS, in favor of the latter. ROS are important factors for the development and angiogenesis of tumors [40]. The main parameters that were investigated in our study in erythrocyte plasma are: Malondialdehyde, vitamin C and uric acid. A very significant decrease in vitamin C in women with cancer, most often linked to a diet low in animal products and devoid of plant products. Uric acid and malondialdehyde are very significantly increased in women with cancer (p^{**} = <0.01) (figure 1). The high level of uric acid can be explained by: an inherited disease, enzyme abnormalities, taking certain medications such as diuretics. Plasma malondialdehyde is a marker for lipid oxidation. It is considered to be one of the end products of the oxidation of polyunsaturated fatty acids [4]. The high levels of malondialdehyde therefore signify oxidative stress, particularly on the oxidation of lipids. Due to the presence in large quantities and the essential role of lipids in the body and the richness of our cell membranes in lipids particularly sensitive to oxidative stress: polyunsaturated fatty acids, the oxidation of lipids, more than that of others products, is an essential sign of oxidative stress [41].

CONCLUSION

Breast cancer is a serious pathology that has posed a real public health problem because of its physical and psychological complications. This pathology presents a costly overload for the individual, state and society. The main objectives of this work are to research the relative details of this problem in the region of Saida and El-Bayadh. The data collected has shed light on some risk factors relating to this pathology. We can conclude that the main producing factors of breast carcinogenesis are late menopause, BMI greater than 25, low economic status, low level of education, sedentary lifestyle and weight gain. A balanced diet can reduce the risk of breast cancer because the presence of vitamins and trace elements is important to fight against this pathology. In addition, our results have shown that oxidative stress is a major factor in the metabolic complications associated with this disease, the increase in malondialdehyde, uric acid and decrease in vitamin C, interpret the imbalance between antioxidants and pro - oxidants. At the end, we will be able to suggest that a healthy

balanced diet rich in vitamin, a moderate consumption of red meat and an orientation towards fish and white meat, a regular moderate physical activity and an annual screening (mammogram) may decrease the risk of breast cancer.

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CONFLICT OF INTEREST

No

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