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Risk Profile in a Sample of Patients with Breast Cancer from the Public Health Perspective

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Abstract

Cancer represents a major public health and economical burden in developed countries and has emerged as a major public health problem in developing countries, matching its effect in industrialized nations. Although there have been recent declines in breast cancer mortality rates in some European Union countries, breast cancer remains of key importance to public health in Europe. Now days there is increasing recognition of the causative role of lifestyle factors, as smoking, diet, alcohol consumption, or lake of physical activity. The present study aimed to appreciate the presence and magnitude of modifiable risk factors for breast cancer in a sample of patients diagnosed with the disease, and to outline a risk profile liable to be changed in the intention of reducing the global risk. Risk factors have been investigated in 65 patients diagnosed with breast cancer using a questionnaire for breast cancer risk factors evaluation. The high risk profile was identified as taking shape for urban environment, modulated by the impact of overweight-obesity, smoking, reproductive factors and environmental exposure to different chemical substances. From the public health perspective, the control of overweight and obesity comes out in the foreground of preventive activities. Public health approaches emphasize on inexpensive, practical methods and in this perspective the approach of obesity should focus on the alteration of environmental context, promoting healthy eating and increased physical activity which could have a positive, independent impact on breast cancer risk.

Keywords: Risk; Breast cancer; Obesity.

Introduction

Cancer is caused by both external factors (tobacco, chemicals, radiation, and infectious organisms) and internal factors (inherited mutations, hormones, immune conditions, and mutations that occur from metabolism). These causal factors may act together or in sequence to initiate or promote carcinogenesis. One in eight deaths worldwide is due to cancer. Worldwide, cancer causes more deaths than AIDS, tuberculosis, and malaria combined. Cancer represents the second leading cause of death in economically developed countries (following heart diseases) and the third leading cause of death in developing countries (following heart diseases and diarrhoeal diseases). Worldwide approximately 12

million of new cancers were diagnosed in 2007, of which 5.4 million will occur in economically developed countries and 6.7 million in economically developing countries. The estimated deaths for 2007 from total cancer were about 7.6 million (about 20,000 cancer deaths a day), 2.9 million in economically developed countries and 4.7 million in economically developing countries. The estimations for 2050, regarding the new cases of cancer predict 27 million new cancer cases and 17.5 million cancer deaths simply due information on survival [1]. In many countries, more than a quarter of deaths are attributable to cancer. From a global perspective, there is strong justification for focusing cancer prevention activities addressed to modifiable risk factors. In some Western countries, cancer mortality rates have recently started to decrease, as a result of reduction in smoking prevalence, improved early detection and advances in cancer therapy [2].

Although there have been recent declines in breast cancer mortality rates in some European Union countries [3], breast cancer remains of key importance to public health in Europe. Prospects for primary prevention are unclear at present and tamoxifen no longer appears to be a candidate for chemoprevention in the general population of women [4]. Population screening with mammography is effective at reducing mortality when quality control procedures are in place [5] and there are slow but continual increases taking place in treatment outcome [6]. However, there is still a clear need to accelerate prospects for preventing women getting breast cancer as well as dying from the disease.

Actual information on cancer causation has emerged from investigations of the pattern of cancer in human populations and experimental studies conducted on animal models. Now days there is increasing recognition of the causative role of lifestyle factors, as smoking, diet, alcohol consumption, or lake of physical activity. Genetic susceptibility may be significantly altering the risk from environmental exposures.

Purpose

The present study aimed to appreciate the presence and magnitude of modifiable risk factors for patients diagnosed with locally advanced breast cancer (IIB-IIIB), and to outline a risk profile liable to be changed in the intention of reducing global risk in the future.

Material and Method

The patients were enrolled in this prospective study from "Ion Chiricuţa" - Cancer Institute, Cluj-Napoca, Romania. Approval for this study was obtained from the Institutional Ethics Committee, and all study subjects provided written informed consent.

Risk factors have been investigated in 65 patients diagnosed with locally advanced breast cancer using a questionnaire for breast cancer risk factors evaluation. The diagnosis for each patient was established by evaluation of 1-2 core biopsies, using Hematoxilin & Eosin (HP) staining. The questionnaire includes 88 core questions structured in 6 category modules: socio-demographic, health status, medical and reproductive history, lifestyle, environmental exposure.

The attention was focused on modifiable risk factors. In this respect, the module of medical and reproductive history includes questions regarding exogenous hormone use (contraceptives and hormone replacement therapy). The module of lifestyle includes questions referring to lifetime history of recreational physical activity, smoking (including passive smoking), alcohol consumption, and dietary habits. Smoking questions refer to age of initiation, age when became regular smoker, number of cigarettes/day, age of quitting smoking, number of smoking years, and passive exposure to cigarette smoke. Regarding alcohol consumption subjects were asked about their average monthly, weekly, or daily consumption of beer, wine, spirits during past year. Food intake was measured by food frequency questions. Meat and dairy groups were defined using standard dietetic and nutritional guidelines. The main groups for meat consumption were red meat (pork, beef, lamb, veal) and white meat (fish, chicken, turkey). The module of environmental exposure include questions referring to household heating system, water supply, proximity to waste disposals, livestock farms, factories and plants, gas stations, airports, voltage transformers, high voltage level lines, and the utilization of pesticide and other chemical substance for combating flies, mosquitoes, ants, rodents, flees, sheep louses, trees' and different plants' insects. The data were introduced in an Excel data base for analyze.

Body Mass Index has been used in order to assess adiposity. Body Mass Index (BMI) is a simple index of weight-for-height that is commonly used to classify underweight, overweight and obesity in adults. It is defined as the weight in kilograms divided by the square of the height in meters (kg/m^2). Recommended WHO BMI cut-off points (Table 1) have been used. Additional cut-off points of 23, 27.5, 32.5 and 37.5 kg/m2 are added as points for public health action, and are for reporting purposes, with a view to facilitating international comparisons [7- 9].

Table 1. The International Classification of adult underweight, overweight and obesity according to BMI

Classification	BMI(kg/m^2)	
	Principal cut-off points	Additional cut-off points
Underweight	**<18.50**	**<18.50**
Severe thinness	<16.00	<16.00
Moderate thinness	16.00 - 16.99	16.00 - 16.99
Mild thinness	17.00 - 18.49	17.00 - 18.49
Normal range	**18.50 - 24.99**	**18.50 - 22.99**
		23.00 - 24.99
Overweight	**≥25.00**	**≥25.00**
Pre-obese	25.00 - 29.99	25.00 - 27.49
		27.50 - 29.99
Obese	**≥30.00**	**≥30.00**
Obese class I	30.00 - 34-99	30.00 - 32.49
		32.50 - 34.99
Obese class II	35.00 - 39.99	35.00 - 37.49
		37.50 - 39.99
Obese class III	≥40.00	≥40.00

Source: Adapted from WHO, 1995, WHO, 2000 and WHO 2004

Results and Discussion

Many prominent risk factors for breast cancer are not amenable to modification, especially later in life. In this category are included reproductive and menstrual factors and family breast cancer history. However, modifiable risk factors are also playing an important role. According to a recent estimate from researcher at the Harvard School of Public Health [10], nine modifiable risk factors are responsible for more than one-third of cancer death worldwide, of these, smoking and alcohol consumption being the most damaging. The other risk factors assessed include: overweight/ obesity, physical inactivity, low fruit and vegetable consumption, unsafe sex, urban air pollution, indoor smoke from household fuels and contaminated injections in health care settings.

Area of residence. 71.43% women from the investigated sample are residents in urban area. The USA Society of Radiology reported that women from urban environment tend to have a higher density of breast, and by consequence an augmented risk for cancer. It is estimated that women with higher breast density have a 4 to 5 fold higher risk to develop cancer as against those with adipose breasts [11-14].The causes of these differences remain unclear [15]. Factors from work environment, differences in lifestyle, obesity, patterns of physical activity, level of stress could all play a role. It was appreciated that some role could be played by reproductive factors, respectively pregnancies at younger ages, higher number of childbirths in rural area, as opposed to urban area where women are more career oriented. Exposure to polycyclic aromatic hydrocarbons, as polluting air particles could also be responsible for differences. These particles acts as estrogen miming and can disrupt normal hormonal functions. UK researchers [14] appreciate that traffic emission might cause estrogen-like activities at breast level.

Tobacco is a major cause of preventable death around the world, accounting for nearly 5 million each year preventable deaths [16]. Cigarette smoke contains over 4000 chemical compounds, hundreds of which are either poisonous or carcinogenic. While the link between smoking, either passively or actively and breast cancer is controversial and still being studied, it is known that inhaling the toxins in cigarette smoke is dangerous and potentially deadly. Smoking contributes to approximately 30% of all cancers in the developed world. Tobacco seems to acts on multiple stages of carcinogenesis, not only by

the carcinogens, but also causes irritation and inflammation and interferes with the body's natural protective barriers. There is direct documentation that breasts are exposed to chemicals within tobacco smoke in active smokers. Study of the fluid in the ducts of the breast of smoking women has shown the presence of tobacco chemicals at higher concentrations than were found in blood.

In our sample almost half (47.62%) of patients are smokers (Figure 1).

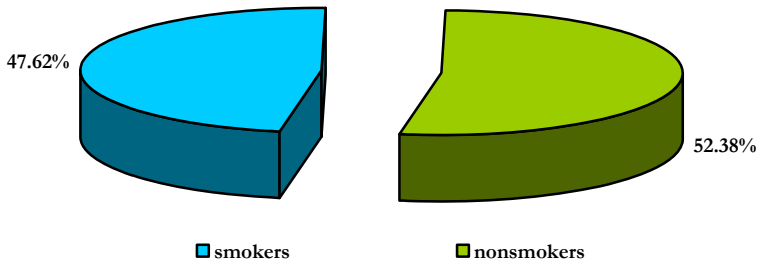

Figure 1. Percentage distribution of sample according with smoking

The analyze of the sub-group of smokers patients according with the duration of active smoking showed an average smoking duration of 20.66 years (standard deviation 11.15, Confidence Level 95.0% - 4.16441), with an average of 10 cigarettes/day (Standard Deviation 5.266354, Confidence Level-95.0%-1.966489). In addition to active smoking, 34.92% patients were exposed to other people smoke at home in childhood, and 68.25% as adults (Figure 2).

Exposure to tobacco smoke at a young age either by smoking or by being around people who smoke may be related to an increased breast cancer risk. Several studies have examined smoking at a young age. These studies compared women who smoked at a young age to women who had never smoked or who were not currently smokers. Most studies reported a small increase in breast cancer risk associated with starting smoking under age 17. Both nonsmoking and actively smoking women exposed to secondhand smoke on a regular basis appear to have an increased risk of getting breast cancer. The results of a review of 19 published studies looking at passive smoking and breast cancer risk were published in International Journal of Cancer [16]. The studies that took place between 1966 and 2004 were reviewed in an effort to understand the association between passive smoking, active smoking and breast cancer risk, and were a mixture of cohort and case-control studies including data about childhood exposure to secondhand smoke from parents, adult exposure in the home, adult occupational exposure. However, the exact risks of smoking and of exposure to secondhand smoke remain unclear [16, 17].

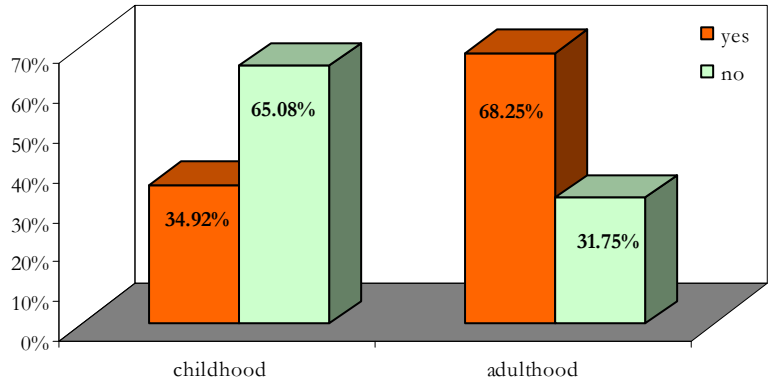

Figure 2. Passive smoking at home

Obesity, has become epidemic in many developed, as well as in some developing countries, and it appears that changes in physical activity patterns and diet in the past few decades are responsible for this

situation. In recent years, interest had grown in the relationship between ***obesity*** and cancer, which has been identified as a significant risk factor for many cancers, and after tobacco use, may be the single greatest modifiable risk factor [18, 19].

Analyzing our sample according with BMI values it appeared that more than two thirds (68.25%) of patients were overweight (34.92%) and obese (20.63% class I, and 12.70% class II) (Figure 3).

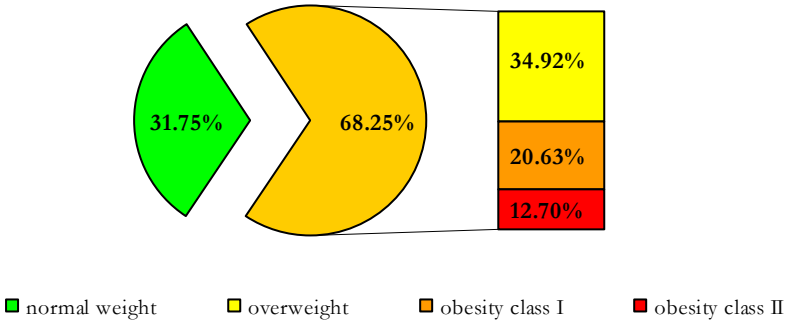

Figure 3. Percentage distribution of sample according with BMI value

It should be mentioned that obesity not only represents a risk factor for disease, but also may affect prognosis through numerous pathways, including associated adverse disease features, co morbidities that can interfere with treatment, hormonal influences, and other mechanisms.

The effect of obesity on breast cancer risk depends on a woman's menopausal status. Before menopause, obese women have a lower risk of developing breast cancer than do women of a healthy weight. However, after menopause, obese women have 1.5 times the risk of women of a healthy weight [20, 21]. Both the increased risk of developing breast cancer and dying from it after menopause are believed to be due to increased levels of estrogen in obese women. Before menopause, the ovaries are the primary source of estrogen. However, estrogen is also produced in fat tissue and, after menopause, when the ovaries stop producing hormones, fat tissue becomes the most important estrogen source [22]. Estrogen levels in postmenopausal women are 50 to 100 percent higher among heavy versus lean women [23]. Estrogen-sensitive tissues are therefore exposed to more estrogen stimulation in heavy women, leading to a more rapid growth of estrogen-responsive breast tumors.

Physical activity. Women in the majority of developed countries have mostly a sedentary lifestyle**.** Globally, inactivity causes close to 2 million deaths each year [15]. It is linked to most major chronic diseases, including type II diabetes, osteoporosis, stroke, cardiovascular disease and cancer. Inactivity increases the risk for breast cancer, among other types of cancer, according to International Agency for Research on Cancer [5]. The association of physical activity and breast cancer has been documented across levels of obesity, suggesting that physical activity acts on cancer risk independent of its effects on body weight. It has been appreciated that several mechanisms could been be involved, including the role of physical activity in the reduction of circulating levels of insulin, and hormones, modification of prostaglandin levels and the improvement of immune system functioning. Numerous studies [24-29] have investigated the relation between physical activity and the risk for breast cancer, and the majority of them noticed a reduction of risk among women with a high level of physical activity. The definition of "highly active" varied among studies according with the questions used to estimate this aspect, the studied population and the categories established by investigators. Analyzing the data from our samples we noticed that all investigated patients do not have physical activity at work place, and none of them practice regularly leisure physical activities.

Diet. The large international variations on breast risk cancer directed the interest to the possible dietary causes [30]. Numerous studies have been focused on identification of diet-cancer possible connections [31-33]. Vegetable and fruits have a high content of healthy components as vitamins, minerals, and fibers. Their consumption has been shown to decrease the risk for chronic diseases, as cardiovascular diseases and type II diabetes. Epidemiological studies suggested the role of a high intake of fruits and vegetables and the reduction of breast cancer risk. A meta-analyze of 8 cohort studies summing 351.825 women, 7.377 cases of breast cancer found no association between fruits and

vegetable consumption and breast cancer risk reduction[28]. However, higher fruits and vegetable consumption has been associated with lower BMI. An international review [34], estimated that increased fruit and vegetable consumption could prevent 5-12% of worldwide cancer burden.

The analyze of our data showed a relatively frequent intake of fruits, more than a half declaring a daily consumption of fruits, with one third of them eating fruits several timed a day. Also, we notice a quite frequent intake of vegetables and a low intake of saturated fats and fried meat meals, a relatively frequent consumption of read and white meat, and dairy products (Table 2). Numerous studies have focused on the relation between meat and dairy food consumption and breast cancer risk. A pooled analysis of more than 20 cohort studies [35] found no significant association between intake of meat and dairy products and risk for breast cancer. However, the present data in our sample represents the mirror of the actual type of diet, which in most of the cases, has been adopted after the cancer was diagnosed.

Table 2. Frequency of different food consumption

Category	More times/day %	Once/day %	2-3 times/week %	Once/week %	Less frequent %
Fruits	30.6	22.22	39.68	3.17	4.76
Vegetables	19.05	20.63	44.44	7.94	7.44
Saturated fats	1.59	9.52	26.98	19.05	42.86
Vegetable fats	10.64	27.66	38.30	21.28	2.13
White meat	7.81	32.81	45.31	7.81	6.25
Red meat	1.85	46.30	38.89	11.11	1.85
Fried meat	3.13	4.69	35.94	20.31	35.94
Diary products	11.11	14.29	44.44	17.46	12.70

Alcohol causes nearly 4% of the global cancer burden [36]. Daily alcohol consumption, even low amounts, may enhance carcinogenesis [37]. Several meta-analyses and epidemiologic data reviews confirmed a moderate association between moderate or high alcohol intake and subsequent risk for developing breast cancer [38, 98]. Alcohol consumption may be, specially, damaging for those individuals with under optimal intake of nutrients, as folate, beta-carotene, vitamin C. However, from our sample of patients more than a half (53.97%) declared they do not consume alcohol or they consume only occasionally, and 83.02% prefer low alcohol concentration beverages.

Reproductive factors. In a meta-analyze [40] nulliparity was associated with a 30% increase of risk as against women that gave birth. The more the number the childbirths was the higher was the protection. It was estimated a 5% reduction of risk for every birth after the first one, in the absence of breastfeeding [41]. The analyze of our sample showed that 11.11% patients were nullyparious, 53.57% gave birth to one child, 42.83% two children and only 3.57% to 3 children (Table 3).

Table 3. Reproductive factors

Category	YES %	NO %	1 %	2 %	3 %	WEEKS %	MONTHS %
Parity	**88.98**	**11.11**					
Number of childbirths			**53.57**	**42.86**	**3.57**		
Breast feeding	**83.43**	**16.07**					
Duration of breast feeding						**23.23**	**76.79**

Women that breastfeed have a risk reduction as against those that do not. The longer the time of breastfeeding is the higher is the protection. According to a study that compared data from 47 studies conducted in 30 countries [42] the risk of developing breast cancer decrease with approximately 4.3% for every 12 month of breastfeeding. Analyze of our data showed that 83.93% patients breastfed, but 23.21% of them breastfed only for a very short time (couple of weeks). 76.79% breastfed for more month (under 12 month), but taking into account that the majority of them gave birth and breastfed only one child, appears as obvious the fact that the protective effect of births and breastfeeding was low in the overwhelming majority of patients.

As hormonal therapy is concerned we noticed that o low percentage of patients used either oral contraceptive (6.35%) of substitution therapy (19.05%).

Environmental exposure. Many organochlorine compounds, including DDE and some PCB are considered endocrine disruptors, being low estrogenic or anti-estrogenic in experimental research [43-48]. These characteristics, along with the temporal concordance of their large scale utilization and the increase of adjusted with age incidence of breast cancer, stimulates the hypothesis that the exposure to these compounds could contribute the breast cancer etiology. Our data analyze regarding the exposure to different chemical compounds at home revealed a high percentage (61.98%) of subjects with household exposure. The chemical substances were used to combat ants, fly, cockroach, flees, rodents, ticks, garden insects.

Risk profile. Many studies have identified a number of risk factors for breast cancer, and several predictive risk profiles have been developed with the purpose of identifying women in the higher level of risk. Typical, the high risk profile includes Caucasian race, age 35-65 years, nulliparity, first childbirth after age 35, high density of breasts. Hypo-thyroidal status, high socio-economic status contributes also to the risk increase.

However, risk does not represent a cause of disease. It is the result of exposure to the hazard, according with the formula: hazard + exposure = risk.

It appears clear that if either hazard or exposure is missing, there is no risk. Theoretically, the only factors that may be influenced are those belonging to the lifestyle. Women may have control on their diet, alcohol consumption, physical activity, weight, use of hormonal therapy (contraceptives, hormonal substitution therapy). In real life these choices are modulated by a range of factors: cultural, socio-economical, psychological or pathological affecting women's life. However, individual behavior and lifestyle particularities are playing important roles.

Conclusions

The high risk profile in our sample of patients is taking shape for urban environment, modulated by the impact of overweight-obesity, physical inactivity, smoking, reproductive factors and environmental exposure to different chemical substances. As reproductive factors are concerned, majority of them can not be altered, but an important public action with multiple positive impacts is taking action to promote breastfeeding for longer period of time.

A special alarm signal requires the very high percentage of patients with overweight and obesity, which is superior to the one in the general population, that it is also high and on an alarming ascendant trend. From the public health perspective, the control of overweight and obesity comes out in the foreground of preventive activities. Public health approaches emphasize on inexpensive, practical methods and in this perspective the approach of obesity should focus on the alteration of environmental context, promoting healthy eating and increased physical activity which could have a positive, independent impact on breast cancer risk.

A special attention should be also focused on tobacco control measures in accord with WHO Mpower strategy [49] that might have a tremendous impact on global health. The alteration in lifestyle factors requires political will and efforts in health education.

Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data.

Conflict of Interest

The authors declare that they have no conflict of interest.

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