

SPECIAL ARTICLE

Changes in the incidence of breast cancer due to the use of radioactive materials for warfare or nuclear and environmental accidents over the last 60 years in Europe and Asia

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Summary

This article investigates the possibility and the extent of breast cancer rates being higher in European and Asian countries that have been damaged by warfare or nuclear accidents and the use of chemical weapons in relation to the rest of the countries in those two continents. After a literature review, although there are gaps in the local reports of the responsible bodies as well as many economic, geopolitical, cultural and time constraints, the rates of breast cancer

incidence and mortality of the citizens of those areas are significant and have been increasing over time, especially in people of older ages, who were exposed to various disease factors at each specific period of time.

Key words: breast cancer, gene mutations, warfare and nuclear accidents

Introduction

This article is based upon the discovery that there is a research gap, as there are specific researches that focus each time on a certain region (see Chernobyl, etc.) but it has not been easy to find centralized and comparative research that clearly highlights breast cancer rates in the female population before and after local disasters. Thus, the present study focuses on the effort to gather as much data and information as possible in order to help addressing this research gap.

Breast cancer is the most common form of cancer in women and this is evidenced by the enormous number of diseased women worldwide: more than 1.6 million. In the wider region of Europe, the number of women diagnosed with breast cancer exceeds 450,000 while about 140,000 per year lose their battle with the disease. There are several types of breast cancer, which are classified according to a) the depth at which the disease progresses, b) the cells from which the disease originates, c)

the grade of malignancy, d) the differentiation of its cells, e) whether the cells have positive or negative hormone receptors; and f) whether they have HER2 receptors or not. According to the latter category, the analysis goes as follows:

- a. HER2 - Positive Breast Cancer: This type of cancer accounts for about 1/5 of the women diagnosed with the disease, meaning the 18 to 20% of the cases diagnosed with breast cancer. This form is considered extremely aggressive.
- b. HER2 - Negative Breast Cancer: There is a percentage (circa 80%) that when diagnosed with cancer does not show increased HER2 receptor and therefore belongs to HER2-negative breast cancers.

It should, also, be noted that the most studied genes are BRCA1 and BRCA2. Women with BRCA mutations are at risk of developing breast cancer in 45-75% [1-7].

Incidence

Serbia and Bosnia & Herzegovina

The war in Serbia in March 1999 can be described as warfare, environmental, but also as a chemical disaster as a result of Depleted Uranium (DU) ammunition use. This chemical is used in impact missiles and other types of reinforcement. Upon impact it breaks into tiny particles, which can easily be swallowed and/or inhaled. There are data concerning the 1999-2009 decade which indicate that breast cancer incidence and new cases in Serbia increased significantly over the years. In detail, in 1999 cancer cases were 3,193 while in 2004 went up to 3,625 and in 2009 soared to 4,518. This also means an increase in percentages: from 51.5% in 1999 to 70.8% in 2009 [8].

It is noted that breast cancer is at a very high level in both Serbia and other parts of Europe (Central-Eastern Europe, Bosnia and Herzegovina / B&E and so on), which have been affected in the past by many military, chemical, environmental and nuclear disasters. In comparison with the rest of Europe, Serbia, due to the use of DU, comes last among European countries regarding 5-year survival rates of lung, breast, rectal, prostate, testicular, ovarian, gastric and cervical cancer [9].

In addition, it is worth mentioning that the efforts made in recent years to prevent and correct breast cancer treatment in Serbia involve the participation of both gynaecologists and radiotherapists in order to fully inform patients and to have a correct follow-up. Even though surgery is the main treatment for operable breast cancer in this country, it has been known that post-operative

or pre-operative neoadjuvant chemotherapy (NAT) administration is extremely important. In fact, emphasis is given on the significance of chemotherapy, which aims at avoiding the risk of metastases and limiting tumors. Evidence for administration of NAT has been extended over the years, and today this type of treatment is an inevitable choice in the treatment of early breast cancer, mainly with the aim of avoiding mastectomy [10].

A report on cancer incidence and mortality rates in Serbia, carried out in 1999 and published in 2002 by the country's Cancer Centre, revealed once again that the dominant type of malignancy is breast cancer (24.7%) [9]. Moreover, other researchers, who also relied on the aforementioned research (CRCS 2002), claimed that in 2008 Serbia held a negative mortality record for women with breast cancer (22.7/100,000) in relation to each other European country. Furthermore, the same research (CRCS 2002) suggested that by 2014 the percentage of women with breast cancer would increase, as no modern methods of treating the disease have been adopted by Serbia, women's history is aggravated and there are many financial problems in both the State and the patients [8].

It should be noted that the Cancer Registry of Central Serbia, about a decade ago, warned that the radiotherapy equipment often does not have all the necessary spare parts, and that chemotherapy drugs are not readily available. For this reason, the number of cancer cases detected on time fell from 35% in 1990 to 13% just a year later, coinciding with the end of the conflict [9]. However, according to Eurostat, breast cancer is the number one cancer that threatens both Serbs and other women in the Balkans [11] (death rates from breast cancer among women in Serbia per 100,000 41.5%) [8], and as a consequence, the state has established the National Cancer Diagnostic Office since 2012. The main objective of breast cancer screening is to reduce mortality. Target population comprises women between the ages of 50 and 69 and an attempt is made to include at least 75% of this population, through a 2-year mammography control program.

In B&H, because of the three-year war (1992-1995), breast cancer has been, for many years, the most common cause of death amongst women with malignant diseases. According to data from the Institute of Public Health (IPH) for 2011, most women (14.2%) died of breast cancer, followed by other types of cancer. In an extensive study conducted by Korda-Vidić et al. an attempt was made to link post-traumatic stress as a result of war with the rise in the incidence of native women's cancer [12]. The conclusion of this was that distress has many psychological and physical consequences, but there

are also social factors that create it (e.g. warfare) and women who suffered of breast cancer had much higher levels of anxiety than women who had not experienced something as intense and extreme as the war.

The truth is, however, that the effects of DU on human health have not yet been studied with precision, not only regarding those involved in warfare operations but also for people living in security zones due to the absence of epidemiological studies. On the other hand, breast cancer has been shown to be the most commonly diagnosed malignancy amongst women in B&H, according to the Annual Health Statistics of B&H (2008), of about 25%, which means that almost one out of four women with cancer had breast cancer [12]. The war in B&H left thousands of people dead and wounded, driving about 1.8 million people out of their homes. This tragic situation led to a strong post-war shock. In fact, the same study by Korda-Vidić et al. showed that women with breast cancer from the study group had suffered on average 9 traumatic shock experiences from warfare compared to women in the control group without breast cancer who had only 1 traumatic experience.

Regarding Serbia and other southeast countries such as B&H and Ukraine, all affected directly or indirectly by DU (due to distance proximity), the following applies: breast cancer cases in Serbia rose from 3,193 in 1999 to 4,518 in 2009 while in another survey conducted in 2017 for the rest of the South-Eastern countries, the effects of breast cancer soared to 2-4% (in ages 15-39), 2-5% (in ages 40-49), 1-4% (in ages 50-69) and 1-6% (in ages 70+) (Figure 1).

In addition, mortality rates increased in Serbia (and Ukraine) by 5% for those aged 55 and

over (while in the remaining age groups they decreased). This means that the citizens belonging to this age group were about 18 years during the war in Serbia [13].

Iraq - Chernobyl - Hiroshima & Nagasaki

Iraq

The “Mother of Battles” or more commonly known as “Gulf War”, the Iraq-Kuwait War took place in 1990-91 (followed by a second one in the same area in March/April 2003). In their study, Alim Yaqoub et al., for the years 1990-1997, stress that the relationship between the use of DU and the increase in cancer incidence is immediate and obvious. In Basra, in particular, an increase in breast cancer (102%) was recorded in 1997 compared to 1990. How could that possibly be avoided since the contamination of the area was evident in the air, soil and water? The author and analyst, Dr. Al-Azzawi, argues that the catastrophic magnitude of the complications and the damage caused by the use of such radioactive and toxic weapons, such as the DU in the environment and on human population, was intensified as a result of the deliberate concealment and the misleading information released by the Pentagon regarding the amount, characteristics and regions of Iraq in which these weapons were used [14]. The extended use of the DU after the Gulf War in 1991, as well as during and after the military operations and the invasion in Iraq in 2003, increased the total DU contamination. As a consequence, hundreds of thousands of Iraqis have received higher doses of radioactivity. As a result, since 1995 there has been a manifold increase in disease among Iraqis, including the increase of breast cancer in women [14].

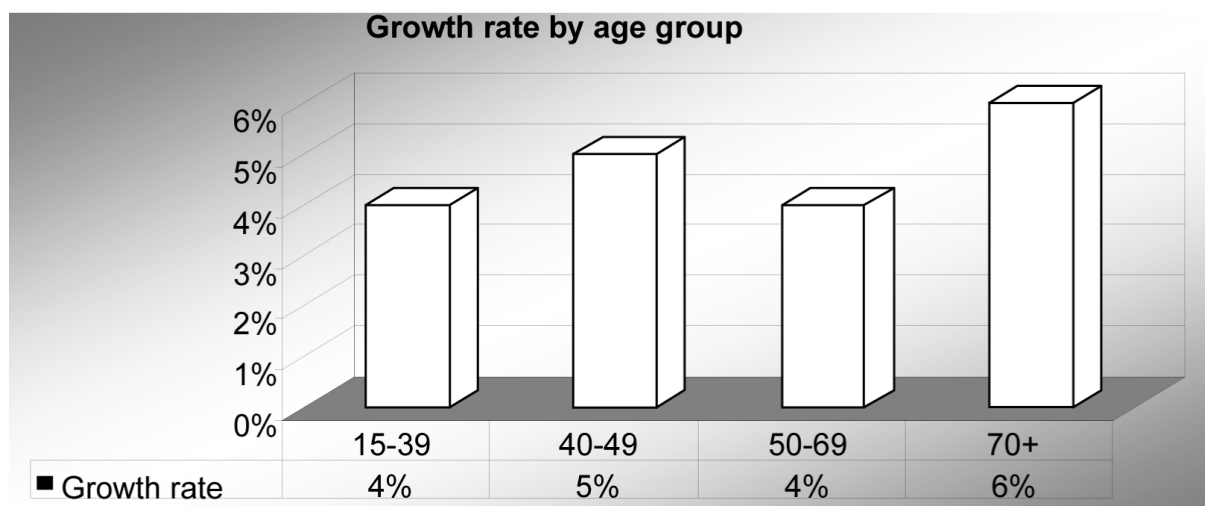


Figure 1. Breast cancer rates per age group.

Breast cancer has become a major threat to Iraqi women's health, as it is the leading cause of death after cardiovascular diseases, with a mortality rate of 23%. In a survey in 2010 [15] 1/3 of Iraqi women was diagnosed with breast cancer (between the ages of 40-49), while almost 72% were urban residents. The overwhelming 90.6% of women discovered the tumor by themselves via palpation but only 32% of them started treatment within the first month, with 47% seeking treatment when already in stages III and IV [15,16]. In general, breast cancer has been the most common malignancy among the Iraqi women since 1986 [17].

Gulf Wars A&B (1991/2003), oil leakage and the use of DU had extremely negative effects on both the environment and people. During the oil spill, gas pollutants released into the atmosphere (sulfur dioxide, carbon monoxide, soot and carcinogenic combustion products such as benzopyrene, polyaromatic hydrocarbons (PAHs) and dioxins) were estimated at 500 metric tons per day. The oil spill in the Persian Gulf was the largest in history with incalculable damages in fauna and coasts. Both radioactive ash and DU have remained in the atmosphere for a long time [18]. It is noted that it will be difficult to identify a relationship between exposure to an environmental disaster and breast cancer (and other disease forms).

Chernobyl, April 1986

Explosions at the 4th reactor of the Chernobyl nuclear power plant in Ukraine led to massive releases of radioactive materials into the atmosphere. These materials settled mainly in European countries, but especially in large areas of Belarus, the Russian Federation and Ukraine.

As a result of the nuclear accident in the spring and summer of 1986, 116,000 people were evacuated from the area around the reactor and installed in uninfected areas. Another 230,000 people were transferred elsewhere in the following years. The World Health Organization (WHO) held a series of expert meetings from 2003 to 2005 to examine all scientific evidence on accident-related health consequences [19]. According to them and in relation to breast cancer, in the most polluted areas of Ukraine the incidence of this type of cancer remained fairly stable and rather lower than in the surrounding areas throughout the period 1980-1992. However, from 1992 onwards, the effects of breast cancer on the infected areas began to increase. More specifically, they highlight that some areas of Belarus, the Russian Federation and, of course, Ukraine have shown and continue to show high rates of various cancers, including breast cancer. Long periods of delay that cancer takes to grow (in some cases over

40 years) inevitably mean that new cases are likely to appear in the future. Unfortunately, the same survey itself notes that the full assessment of the consequences of the Chernobyl accident on human health is likely to remain virtually impossible so that the real extent of the incidence and mortality cannot be fully appreciated.

Hiroshima & Nagasaki, August 1945

August 1945, World War II is underway, and the United States is dropping two atomic bombs in Japan, with the excuse of overthrowing it and forcing it to withdraw its troops and end the war. The bomb in Hiroshima was of Uranium-type -235 while the second one in Nagasaki was of Plutonium type [20].

One of the major diseases present in Hiroshima and Nagasaki is breast cancer. There are numerous and long-term researches [21-24] which confirm that breast cancer is one of the five most basic cancer types caused by the dropping of atomic bombs, with the rest being gastric, lung, intestinal and liver cancer. Li et al. carried out a survey on the effects of radiation on the Nagasaki and Hiroshima bombings' survivors, which monitored them from 1950 to 2002 (when the whole process completed) [25]. This particular study monitored 10,031 primary cancer survivors, including 1,088 survivors developing secondary cancers. Radiation is a potent carcinogen and those with significant exposure to it, who are diagnosed with primary cancer, should also be carefully examined for secondary cancers, especially for those who are sensitive to radiation such as lung, bowel, breast, thyroid and bladder. In fact, the study indicated that youngsters at the time of the bombings and women are more prone to those cancer types.

In harmony with the findings of the aforementioned surveys was Land's surveys which monitored circa 51,000 Japanese women, the results of which showed that there is a direct link between Hiroshima and Nagasaki bombings and breast cancer [22]. Once again, the age of women when bombings occurred, was highlighted. Hereditary mutations were observed in specific breast cancer genes, such as BRCA1 gene.

There are various surveys with regard to Hiroshima and Nagasaki bombings and their aftermath, but there is one that is considered the most important of all: the Life Span Study (LSS). LSS is a research program that investigates long-term health effects based on epidemiological studies (group studies and case-control studies). Its main objective is to investigate the long-term effects of atomic bomb radiation on causes of cancer deaths and incidence in Hiroshima and Nagasaki. The

survey monitored 120,321 participants, 86,611 of whom were bombing survivors in the two aforementioned Japanese cities, while the rest were permanent residents who were out of town on the day of the bombings and publish their findings on reports. The first report concerned the years 1950-1958, while the 14th concerned the whole period (cumulatively) from 1950 to 2003. It should be noted that there was a supplementary survey that followed up the survivors for another 6 years, i.e. until 2009 [26]. This research concludes that 58% of the participants, out of the sample of 86,611, died, while another 17% died during the additional 6 years of the follow-up due to cancer, with emphasis on gastric, liver, colon, breast, gallbladder, oesophageal, bladder and ovarian cancers, while cancers of the rectum, pancreas, uterus, prostate and renal parenchyma did not display any significant risks [27]. Thus, Hiroshima and Nagasaki cases indicate that breast cancer can be caused by large doses of radioactivity/radiation, as evidenced by the diseases that affected the victims of the Uranium-235 and Plutonium bombs that hit Hiroshima and Nagasaki.

It is worth mentioning one of Busby's articles in which the author argues that the Fukushima, Hiroshima and Nagasaki nuclear disaster was indeed a brutality that has caused irreversible problems and is a continuous source of cancers (breast, thyroid, stomach, intestine, lungs etc) and of teratogenesis [20]. Even though the true numbers and actual effects of these disasters are concealed by governments and scientific circles, the implications and reality show that even so many years after the disaster (as stands for the case of Chernobyl's radioactivity) they still greatly affect the population of Europe and Asia and of other adjacent areas.

Chernobyl (1986) was the consequence of an accident due to human error, while Hiroshima and Nagasaki (1945) underwent grave bombings with nuclear weapons but the release of radioactivity in all cases and its devastating effects are their common denominator. Thirty-two and seventy-three years later, respectively, the impact dichotomises scientists' opinion, and most of all, whether radioactivity has led to an increase in cancer rates among residents in those areas. The International

Atomic Energy Commission notes, though, that cancer incidence rates and cancer death rates (only 9 deaths) in Chernobyl, Hiroshima and Nagasaki are not so high.

Conclusions

Breast cancer was and unfortunately still appears to be one of the three most grave and most prevalent types of cancer in the world for the female population, both in incidence and mortality.

Breast cancer is caused by various factors, i.e. smoking, obesity, premature menstruation or delayed menopause, heredity, intense anxiety and distress that can be experienced during somebody's life and - as indicated in the present article - large-scale warfare, chemical, nuclear and environmental disasters. The latter, in fact, has a direct negative impact but also long-lasting effects on the offspring of the citizens who have experienced them.

There are several limitations in this study and consequently in the drawing of the final conclusions. The most pivotal ones are related to the following: a) the health and welfare infrastructure of each country; b) each country's health systems and their Medical Record and Follow-up Bodies (note: according to WHO only 34 out of 194 member countries have qualitative reports on cancer deaths and 68 out of 194 on cancer consequences [28] c) the political situation and the regime of each of the analyzed countries; (d) the cultural infrastructure and women's social situation and status; (e) the records and statistics on the economics of each country; and (f) the duration and nature of the warfare and the disasters taken place in each country.

To sum up, Europe and Asia regions investigated in this article are of great scientific interest as their population (and the adjacent ones as well) suffered severe disasters and both women's incidence and mortality rates are high enough. What is yet to be investigated is the degree that nuclear and chemical weapons are responsible for such severities.

Conflict of interests

The authors declare no conflict of interests.

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