THE STRESS OF WAR AND BREAST CANCER INCIDENCE

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SUMMARY
Approximately 94,000 persons were killed or disappeared and about 1.8 million people were forced to flee from their homes during the war in Bosnia and Herzegovina, from April 1992 to December 1995. The Dayton Peace Agreement, signed on November 21, 1995, ended the war. Life and health conditions of the population in B&H characterized with severe disorders caused by severe war and post-war traumatic events. The aim of this work is to establish the connection between breast cancer in women and stress caused by traumatic experiences during the war in B&H. We performed this study of pairs at the Clinic for Oncology, University Clinical Hospital Mostar, from November 2008 to March 2009. Two hundred women from Herzegovina region participated in this research. The study group consisted of 100 women with diagnosed breast cancer. The control group consisted of 100 women without breast cancer diagnosis, of the same age and living in the same area. We have found that women with breast cancer had statistically considerably more war traumatic experiences and thus more stress than the women in control group (p=0.000). The following conclusions are also noteworthy: 39% of women in the study group were under the ages of 50, when diagnosed breast cancer. Only one woman got psychosocially care within breast cancer treatment. High middle age of physiological loss of period (fertile period, as well as the smoking habit are breast cancer risk factors statistically more present. Related stress considered a risk factor. Women with breast cancer have experienced more stress due to significantly more war traumatic experiences, so that war-related stress considered a risk factor.

Key words: war in Bosnia and Herzegovina – stress - breast cancer - women

INTRODUCTION
Breast cancer is the most commonly diagnosed malignancy in women in the Federation of B&H with a proportion of about 25%, which means that nearly one in four women with cancer had breast cancer (Annual Health Statistics FB&H 2008).

We have found following data in the Population-Based Cancer Registry F B&H: in the last 10 years, proportion of malignant breast cancer neoplasms ranged from 24.21 to 27.51%. Breast cancer in men is rare, with a proportion of 1.39 to 2.49% of the registered breast cancer. The illness rate based on age groups of 100,000, is the highest in the age group of 60-64 (153.82), followed by the groups of 65-69 years (143.38), 70-74 years (127.39), 55-59 years (115.04), 50-54 years (103.35).

In the Federation of B&H, breast cancer has been, for many years, the most common cause of death in women with malignant disease. According to data of the Institute for Public Health (IPH) F B&H for 2011, most women died from breast cancer, C50 (14.2%), followed by malignant neoplasm of bronchus and lungs C34 (12.6%), liver and intrahepatic bile ducts C22 (8.0%), stomach C16 (7.1%), malignant neoplasm of the brain C71 (5.5%). Other malignant neoplasms in women account for 52.7%. There has been a decreasing trend in mortality of breast cancer in developed countries due to improvements in early detection and treatment, but we are not even remotely satisfied with the situation in the F B&H. There is still no comprehensive screening for breast cancer, neither is women's health education satisfactory.

Stress, as a risk factor for breast cancer, has not been clarified completely. Whether or not we experience a situation as stressful depends on our assessment – on our own capacity to deal with the situation, or on the support, we get from our surrounding.

Stressor, stress stimulus that leads to a state of stress in an organism can be physical (e.g., exposure to cold or heat), psychological (e.g., exposure to frustrations at work), social (e.g., exposure to war).

Reactions to stress can be physiological-the ones that prepare an organism to respond with "fight or flight" reaction, psychological-emotional and cognitive, behavioural changes-when an organism fights with the cause of stress or flees from it (Havelka 1998).

When a certain stress stimuli disturbs homeostasis-the internal balance of the organism, the organism includes physiological defence mechanisms. Then they begin to secrete the stress hormone cortisol and launch the hypothalamic-pituitary-adrenal system, activating direct physiological connections between the central nervous and immune system and lead to increased activation of specific organ systems.

The impact of stress on the entire cardiovascular system is undisputed, as well as its impact on the immune system. Secretion of cortisol and epinephrine is associated with decreased activity of T and B-lymphocytes, which affect the development and progress of
various diseases, such as cancer (Sarafino 1994, Šamija at al. 2007, Fajdić at al. 1998).

Nervous, endocrine and immune system communicate with each other via neurotransmitters that synthesized in nerve cells, through hormones that synthesized by endocrine cells and through lymphocytes that produced by immune system cells.

Emotions associated with stress, such as anxiety and depression, are crucial for the balance of the immune system. Studies have shown that pessimism, depression and stress are connected to a weakened immune system functioning. It is believed that chronic stress has immunosuppressive effects, leading to a decline in the number of T and B-lymphocytes in the circulation, and weakening the innate and cellular immunity, which may increase morbidity and mortality. Psychological instability and depression are often found in women with breast cancer (Havelka 1998, Sarafino 1994, Fajdić at al. 1998).

Studies on the psychological effect of catastrophic events on the survivors have shown prolonged and sometimes devastating consequences of traumatic experiences on the individual. After the Vietnam War, the concept of post-traumatic stress disorder was formally introduced. Posttraumatic stress disorder is by definition associated with a traumatic experience, and trauma is by most people recognized as something extremely disturbing.

More severe traumas and prolonged exposure to traumas increase the risk of developing PTSD symptoms. Different people react differently to a traumatic event. Younger people, more single traumatic events, longer duration of traumatic events, possible presence of a mental disorder tendency, loss of a loved one, poor socioeconomic status and poor family relationships are predisposing factors for PTSD (Fajdić at al. 1998, Havelka 1998, Krizmanić at al. 1991).

The feeling of control or a sense of helplessness in stressful situations depends on social support that an individual gets from his or her environment (Fajdić at al. 1998). If an individual feels in control over the source of stress, it reduces the intensity of the stress response in a particular situation. In contrast, the sense of helplessness occurs when an individual assesses not to have control over the source of stress (Sarafino 1994).

The aim of the research was to determine the effect of stress experienced in the war on breast cancer incidence, as well as the presence of certain risk factors. We have also wanted to confirm the hypothesis that women with breast cancer experienced more stress during the war because of experiencing significantly more traumatic experiences.

**PARTICIPANTS AND PROCEDURE**

The study group consisted of 100 women living in Herzegovina and diagnosed with breast cancer. All the women are from three cantons in F B&H: Herzegovina- Neretva, West Herzegovina and Hercegbosnian Canton. The majority of women were treated or being treated in the Department of Oncology, University Clinical Hospital Mostar. Many of them are active in associations for women treated for malignant diseases: "New Look" from Mostar and Siroki Brijeg and "Bistrica" from Livno. In collaboration with these associations, we held public discussions in all three cantons, using audiovisual methods to present the Early Detection of Breast Cancer Project, F BiH Ministry of Health, breast cancer risk factors, diagnosis and the latest advances in the treatment of breast cancer, as well as this study. We informed women about this study at the associations, and gave the form of informed consent to participate in the research.

All women diagnosed with breast cancer admitted to the Clinic for Oncology, UCH Mostar during November and December 2008, and in January, February and March 2009, were included in the study. We excluded twenty-six women from the research, who did not want or were not able to participate in the study because of ill health. Respondents were happy to participate in the study because they felt they could help other women (to behave more cautiously and detect the disease earlier) and learn something new while talking to the doctor. The average age of the patients was 57.5±12.6 years.

Comparative, control group consisted of women not suffering from breast cancer, who are the same age as the diseased women and belong to the same socio-cultural and geographical surroundings (those were matching criteria). These women also informed about breast cancer at our lectures, through diseased women in the family and immediate surroundings. They showed great interest in our study and were happy to participate in it.

The Ethics Committee of the University Clinic Hospital Mostar approved the study, and we conducted the study in accordance with the ethical principles of the profession and the Helsinki Declaration of Human Rights. It was a case control study, conducted in November and December 2008 and January, February and March 2009 in the Clinic for Oncology, University Clinic Hospital Mostar. In this study we used Harvard Trauma Questionnaire (HTQ), Bosnia-Herzegovina Version, Part I: Traumatic Events and a Questionnaire for examining socio-demographic data and breast cancer risk factors (self-created).

Women gave YES or NO answers to 46 questions about traumatic events that could have been the result of the war in Bosnia and Herzegovina, in the questionnaire for examining traumatic events. In the second questionnaire, we requested general information on the year of birth, weight and height, education, year of diagnosis, menstrual cycle, giving births, smoking etc.

**Statistical Analysis**

We stored the data in the MS Excel 2003 database and used the statistical program SPSS (SPSS for Windows 13.0, SPSS Chicago IL, USA) for statistical
analysis. We also used methods of descriptive and inferential statistics for data processing. We presented the results with absolute and relative frequencies, and with tables and graphs. In order to assess the differences between the study and control group, we used the $\chi^2$ test. In order to determine differences in the representation, we used Fisher's exact test and the Student's t-test for differences in average values. We took $P<0.05$ value as statistically significant difference.

RESULTS

Two hundred women were included in the study: 100 women with breast cancer (study group) and 100 women not suffering from breast cancer (control group). We presented the results as answers to questions from the Harvard Trauma Questionnaire and the Questionnaire on risk factors for breast cancer. We presented the results with tables and figures (graphs).

Harvard Trauma Questionnaire

From forty-six questions about traumatic experiences from HTQ, a big number of women in both groups had 10 traumatic experiences, while a smaller number of women had 12 traumatic experiences, mainly from the study group, and none of the women had 24 traumatic experiences.

As shown in Table 1, women in the study group had higher number of traumatic experiences (471) than the women in the control group (361), with a statistically significant difference ($p<0.05$).

Table 1. Distribution of the total number of traumatic experiences

<table>
<thead>
<tr>
<th>Groups</th>
<th>Number of traumatic experiences</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>471</td>
<td>$\chi^2=14,543; df=1; p=0.000$ (p&lt;0.050)</td>
</tr>
<tr>
<td>Control</td>
<td>361</td>
<td></td>
</tr>
</tbody>
</table>

Of the 10 most common experiences (Table 2), women in the study group more often had nine experiences, while women in the control group more often had only one experience; being forced to abandon their home, but statistically not significantly higher ($p=0.662$).

Women in the study group had significantly more of the following three experiences: being forced to hide, finding out about a murder or violent death of a family member or friend, and the experience of extortion or robbery ($p<0.05$).

A small number of women experienced the following traumatic events: having nowhere to hide, being hungry or thirsty, lacking treatment, experiencing abuse or sexual humiliation, arrest and detention, abduction, being separated from others by force, being forced to stay at home because it was too dangerous to go outside, finding out about disappearance or kidnapping of a family member or friend, having a family member or friend severely injured in battle, being an eyewitness of others being hit on the head and body, being an eyewitness of others being tortured (Table 3).

Table 2. Distribution of traumatic experiences experienced by a big number of women

<table>
<thead>
<tr>
<th>Question</th>
<th>Number of participants (%)</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Study group</td>
<td>Control Group</td>
</tr>
<tr>
<td>Experience property being taken away or destroyed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>39 (39%)</td>
<td>28 (28%)</td>
</tr>
<tr>
<td>Surviving shelling or taking part in fighting</td>
<td>81 (81%)</td>
<td>76 (76%)</td>
</tr>
<tr>
<td>Being forced to abandon one’s home</td>
<td>60 (60%)</td>
<td>64 (64%)</td>
</tr>
<tr>
<td>Being tortured (intentional infliction of physical or psychological suffering)</td>
<td>11 (11%)</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Extorted or robbed</td>
<td>22 (22%)</td>
<td>9 (9%)</td>
</tr>
<tr>
<td>Forced to hide</td>
<td>73 (73%)</td>
<td>51 (51%)</td>
</tr>
<tr>
<td>Separated from family members by force</td>
<td>50 (50%)</td>
<td>37 (37%)</td>
</tr>
<tr>
<td>Have one’s home inspected</td>
<td>28 (28%)</td>
<td>19 (19%)</td>
</tr>
<tr>
<td>Finding out about a murder or violent death of a family member or friend</td>
<td>60 (60%)</td>
<td>42 (42%)</td>
</tr>
<tr>
<td>Experiencing a frightening situation (torture, rape, murder)</td>
<td>42 (42%)</td>
<td>30 (30%)</td>
</tr>
</tbody>
</table>
Risk factors for breast cancer

The average age was 57.5±12.6 years. There was no statistically significant difference between the women in the study and control group in terms of age, since we used age of women with breast cancer to specify the age of women selected for the control group (Figure 1).

Age groups were set up so that the first group consisted of women younger than 40, with each subsequent age group increased by 5 years. The last age group consisted of women older than 70. Most respondents, 42 (42%), were in the group of 50-54 years, and the least, four (4%) in the group of up to the age of 40.

The highest number of women with diagnosis was 17 (17%) in the age group of 45-49 years, while the least women, eight (8%), were in the group of 65-69 years. There was statistically no significant difference between the numbers of women by age groups at the time of diagnosis (p=0.704). It is important to note that 39 (39%) women with diagnosis were younger than 50, and 61 (61%) were older than 50 years.

We didn’t find statistically significant difference between the study group and the control group in the following risk factors: nutrition level (p=0.778), marital status (p=0.111), positive family history (p=0.275), the first menstruation age (p=0.572), middle age of women with physiological loss of menstruation, giving and not giving birth (p=0.447), age of first birth (p=0.594), number of births (p=0.628).

We found statistically significant difference:
- Middle-aged women who lost their menstrual periods (p<0.05): women in the study group were older when they experienced cessation of menstrual period (51±3.2 years) than the women in the control group (50±2.3 years);
- Average duration of women’s fertile period (p<0.05); average fertile period in the study group was 38 ± 3.3 years, and 36±2.4 years in the control group;
- Smoking habits (p<0.05), 44 (44%) women in the study group smoked at the time of research, at times before that, and 28 (28%) in the control group (Table 4).

Table 4. Distribution of women according to their smoking habits

<table>
<thead>
<tr>
<th>Smoking habit</th>
<th>Study group (%)</th>
<th>Control group (%)</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Now</td>
<td>16 (16%)</td>
<td>17 (17%)</td>
<td>χ²=0.030; df=1; p=0.862</td>
</tr>
<tr>
<td>Earlier</td>
<td>28 (28%)</td>
<td>11 (11%)</td>
<td>χ²=7.410; df=1; p=0.006</td>
</tr>
<tr>
<td>Never</td>
<td>56 (56%)</td>
<td>72 (72%)</td>
<td>χ²=2.000; df=1; p=0.157</td>
</tr>
<tr>
<td>Total</td>
<td>100 (100%)</td>
<td>100 (100%)</td>
<td></td>
</tr>
</tbody>
</table>
DISCUSSION

Life threatening situations, endangered lives of close ones, destruction of home and property, as well as the overall negative psychophysical surrounding makes some of the negative traumatic experiences of the war in Bosnia and Herzegovina.

**Harvard Trauma Questionnaire: Bosnia-Herzegovina Version, Part I**

From 46 traumatic experiences listed in HTQ, a big number of women have endured 10 traumatic experiences, while a small number of women have endured 12 traumatic experiences, and none of the woman who participated in this study endured 24 traumatic experiences.

War-related traumatic experiences, such as life under siege, every-day shelling, inspection of homes, extortion, arrests, torture, involuntary separation from family members, hiding, murders and violent deaths of family members, as well as experiencing other frightening situations are the elements that can be observed and associated with psychiatric, cardiovascular, and cerebrovascular morbidity and breast cancer (Speirs at al. 2008, Annual Health Statistics F B&H 2008, Ferlay at al. 2006).

War related stress that the population of B&H wear exposed to affected the health: the studies confirmed the affiliation of experienced stress due to the war with increased morbidity from acute coronary syndrome and cerebrovascular disease (Annual Health Statistics F B&H 2008, Ferlay at al. 2006).

Studies on the psychological impact of catastrophic events on the survivors have shown prolonged and sometimes devastating consequences of traumatic experiences on the individual. The concept of post-traumatic stress disorder was formally introduced after the Vietnam War. Posttraumatic stress disorder is by definition associated with a traumatic experience, and most people experience trauma as extremely disturbing. Residents of Bosnia and Herzegovina, especially women, were not able to control the source of stress - the war and had to endure its most traumatic events.

For example, life under the German occupation in Guernsey (1940-1945) resulted in a menstrual period delay for 12 months, and instead of it being protective (as usual), it proved to be associated with an increased risk of breast cancer (Fentiman IS 2007).

In our study, women in the study group had 471 traumatic experiences, which are significantly higher than 361 in the control group. The difference was statistically significant (p <0.05). Of the 46 traumatic events, which are listed in the HTQ, most women in the study group and in the control group experienced 10 of the following traumatic experiences: experiencing fighting or shelling at 81:76 (81%:76%), hiding 73:51 (73%:51%), abandoning their homes at 60:64 (60%:64%), finding out about a murder or violent death of a family member 50:37 (50%:37%), experiencing a frightening situation 42:30 (42%:30%), seizure and destruction of property 39:28 (39%:28%), inspection of homes 28:19 (28%:19%), extortion or robbery 22:9 (22%:9%), and infliction of physical or mental suffering, 11:4 (11%:4%).

There is a statistically significant difference (p=0.05) in women’s answers in the study and control group to the following three questions: being compelled to hide (p=0.002), finding out about a murder or violent death of a family member or friend (p=0.018) and being extorted or robbed (p=0.018).

Women from the study group had more positive answers to other questions, except the question about being compelled to leave their homes, where women in the control group had more positive answers than women in the study group (64%:60%). That can be associated with consequently greater exposure to more severe stress experiences in women who remained at the place where they lived.

In addition, women in the study group witnessed more of those traumatic events (30:4 (30%:4%) also experienced by a small number of women.

Those are the following traumatic experiences (the ratio of positive answers in the study and control group): not being able to hide 6:1 (6%:1%), feeling hunger or thirst 5:1 (5%:1%), sexual abuse or humiliation 4:0 (4%:0%), finding out about the disappearance or kidnapping of a family member or friend 3:0 (3%:0%), lack of treatment 2:0 (2%:0%), involuntary separation from others 2:1 (2%:1%), finding out about family members or friends being hurt 2:0 (2%:0%), witnessing others being tortured 2:0 (2%:0%), being arrested or imprisoned 1:1 (1%:1%), being kidnapped or taken away 1:0 (1%:0%), witnessing others being hit on the head and body 1:0 (1%:0%) and being forced to stay at home because of the possible danger 1:0 (1%:0%).

All of these traumatic experiences and stress that accompanies them, undoubtedly, leave their mark on all women including the ones who participated in this study. We can conclude that the women in the study group experienced more stress considering significantly higher number of traumatic events and the nature of those events.

When we look at traumatic events experienced by a small number of women (34 or 17% of women in both groups), we should emphasize their brutality and direct endangering of women’s mental and physical health. Traumatic experiences, such as sexual abuse and humiliation and witnessing others being tortured, have long-term effects on women’s mental health.

If an individual assesses to have control over the source of stress, that reduces the intensity of the stress response in a particular situation. In contrast, the sense of helplessness occurs when an individual assesses not
to have control over the source of stress (Havelka 1998, Krizmanić et al. 1991, Medix 2001).

Residents of Bosnia and Herzegovina, especially women, were not able to control the source of the stress-the war and they had to endure its most traumatic experiences.

Two factors, the diagnosis of breast cancer and the second generation of the Holocaust survivors, had a synergistic effect on a stronger presence of symptoms of depression and psychosis (Baider at al. 2008). Baider in his study examined affiliation psychological distress and breast cancer in four groups of women. The first group consisted of women suffering from breast cancer, whose mothers experienced the Holocaust, and the second group consisted of women suffering from breast cancer, whose mothers didn’t experience the Holocaust, healthy women whose mothers experienced the Holocaust were in the third group and healthy women whose mothers had not lived through the Holocaust – the fourth group. The conclusion was that severity of symptoms of distress in mothers and daughters in the first group are significantly higher than in other groups. The intensity of distress in daughters in all four groups is in correlation with the intensity of symptoms of distress in mothers, and significantly higher in daughters with breast cancer.

Are our women in the study group, who experienced significantly more traumatic events and diagnosed breast cancer, in psychological distress or depression?

The health care system in the Federation of B&H has not recognized and adequately responded the need for psychological assistance to women in war and post-war period, as well as the need for a comprehensive treatment of women suffering from breast cancer, as shown in the statement of only one psychosocially treated woman.

**Risk factors for breast cancer**

The average age of women who participated in this study was 57.5±12.6 years. There were 78% of women over 50 in the study group and 77% of women in the control.

In this study, 39% of women in the study group were younger than 50 years of age at diagnosis (10 women were diagnosed with breast cancer until the age of 40, and 29 women at the age of 40 to 49), which indicates the need for health education and program for early detection of breast cancer for women younger than 50 years. This is particularly important since in our study, the biggest number of women were between the age of 45 and 49 (17%), followed by the age group of 60-64 years (15%), aged 55-59 years (14%), aged 50-54 years (13%), aged 40-44 years (12%) and aged 70 or over (11%).

According to data of the Cancer Registry of F B&H for 2009 and 2010, 28.04% of women under the age of 50 were registered with breast cancer, which is significantly less than in our study. Also, the number of women aged 45-54 in the study group accounted for 30%, which is also more than 24.7%, registered in the F B&H for 2008 and 17% in Croatia in 2011 (Croatian National Institute of Public Health – Cancer Registry 2013).

The work of S. Lambaša et al., during an 11-year long period (2007-2011) at CH “Dubrava”, Zagreb, analyzed the age of women and the stage of breast cancer at the time of surgery, with most women in the age group of 50-59, except in 1999, when 42.8% of women were under 50. Women’s age at diagnosis ranged from 54.6 in 1999 up to 58.7 in 2004 year (Lambaša 2011). Ministry of Health in F B&H supported the Early Detection of Breast Cancer Project in 2008 with the recommendation for screening mammography for all women aged 50-70 years (B&H, Government of F B&H 2008) but unfortunately, the project was not realize yet.

**CONCLUSIONS**

By studying war related stress as a risk factor for breast cancer incidence, we concluded the following:

- Women suffering from breast cancer experienced more stress due to significantly more traumatic events, than the women in the control group (471:371), (p<0.05).
- Out of 46 traumatic experiences listed in HTQ, none of the women who participated in this study experienced 24 traumatic events, a big number of women experienced 10 traumatic events, while a small number of women experienced 12 traumatic events.
- Traumatic events that were experienced by significantly more women in the study group (p<0.05): being forced to hide (p=0.002), finding out about a murder or violent death of a family member or friend (p=0.011) and extortion or robbery (p=0.018).
- Traumatic events that were experienced by a small number of women were mostly women in the study group 30:4 (30%:4%) with a statistically significant difference (p<0.05).
- Average age of women who participated in the study was 57.5±12.6 years, while 39% of women in the study group were younger than 50 years at diagnosis (higher percentage of diseased women up to the age of 50 than in the F BiH and Croatia). This only indicates the need for health education, promotion and implementation of program for early detection of breast cancer for women under 50.
- Breast cancer risk factors, which have been confirmed in this study: higher middle age at the time of physiological loss of menstruation (p=0.004), loss of the menstrual cycle with ≥50 years of age (p=0.038),
longer fertile period (p=0.004) and smoking habits (p=0.018).

- Breast cancer risk factors which have not been confirmed: BMI, positive family history, age of getting the first period (p=0.572), giving and not giving birth (p=0.447), the age of giving the first birth (p=0.594), number of births (p=0.628).

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**Conflict of interest:** None to declare.

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