

# Stress and Cortisol Levels among Breast Cancer Survivors

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## ABSTRACT

**Objective:** This cross sectional study was conducted in Selangor. The main objective of the study was to determine the association between stress and cortisol levels among breast cancer survivors.

**Method:** Forty seven respondents with a history of breast cancer were selected as the survivor group and 37 respondents without the history of breast cancer were selected as the comparative group. Stress levels were determined by using the O'Donnell Stress Questionnaire (Personal Stress Inventory). Respondents with total score of more than 40 were classified as stressed. Saliva samples were collected from each respondent and cortisol level was determined using the Elisa-kit (Salivary Cortisol Enzyme Immunoassay-Kit).

**Result:** Findings showed that the mean and standard deviation for the cortisol level among the survivor group in the morning was 3.392 µg/dL and 0.873µg/dL respectively, while in the evening the mean was 4.89 µg/dL with a standard deviation of 0.852µg/dL. There was a significant difference ( $p < 0.001$ ) between the mean of the early morning cortisol level with the late evening cortisol level. However, statistics showed no significant difference between the morning and evening cortisol levels of the survivor group with that of the comparative group. The mean stress scores of the survivor group was significantly higher than the comparative group ( $z = -0.861$ ,  $p = 0.389$ ).

**Conclusion:** The stress level in terms of nutritional status, physical problem, depression and the need for attention were significantly related with the cortisol hormone level. However, no significant difference in the salivary cortisol level between the survivor and comparative groups were found.

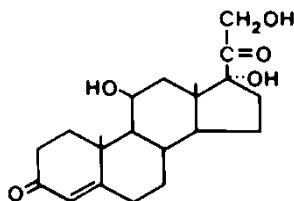
**Keywords:** *Salivary cortisol, stress and breast cancer survivors*

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## 1. Introduction

The Malaysian National Cancer Registry (NCR) was only launched in June 2003 and there was a lack of incidence data on cancers before this time in Malaysia. In 2003, 3738 new cases of breast cancer were reported to the NCR, giving an age-standardized incidence rate (ASR) of 46.2 per 100,000 women. This means that 1 in 20 women in Malaysia will develop breast cancer in her lifetime (Vital Statistics Malaysia, 2005).

Cortisol is a steroid hormone made in the adrenal glands, which are small glands adjacent to the kidneys (McEwen, 1987). The hormone is released in the body during stress and is hence called the "stress hormone". However, cortisol is more than a simple marker of stress levels. It is necessary for the proper functioning of almost every part of the body. Cortisol is synthesized from cholesterol and acts through specific intracellular receptors to affect numerous physiologic systems, including immune function, glucose counter regulation, vascular tone, and bone metabolism (Aeron Biotechnology Inc., 2007). It is one of the many hormones that help regulate the immune system, including the activity of cells that help the body to fight against cancer. The physical and medical implications of cumulative exposure to increased cortisol levels are substantial, since cortisol binds to glucocorticoid receptors, which are present in almost every tissue and organ in the body. Cortisol mediates many metabolic processes, ranging from the induction of liver enzymes involved in energy metabolism to the regulation on the trafficking of immune cells and cytokine production. Without cortisol, body can not react properly to the stress (Aardal & Holm, 1995). The high cortisol level in the body could increase risks of infection, increase blood stress levels, diabetes, osteoporosis and depression. Meanwhile, low cortisol level could lead to pain and tiredness (National Institute of Diabetes and Digestive and Kidney Disease, 2004).



**Figure 1.** Structural formula of cortisol (National Health Research Center (NHRC), 2006)

Studies done by Swedish researchers showed that woman under stress may double her risk of developing breast cancer. This was based on their findings from surveys of more than 1,400 Swedish women in the late

1960s, who formed part of a long-term health-care study. The women, who were reported to be a representative sample of the Swedish population, were asked to fill out a health survey, which included a question about stress. They were asked whether at any time in the last five years they had experienced a feeling of stress for a month or more (Osterweil, 2003). Examples of stressful situations the women might have encountered were tension, fear, anxiety, or sleep disturbances related to family or work problems. The question about stress was only one of many different questions asked at the time, and the researchers felt that their answers would probably have accurately reflected the way they felt at that time (Osterweil, 2003).

A new preliminary study on breast cancer patients with high levels of stress concerning their diagnosis and treatment evidence shows a weakened immune system when compared to patients experiencing less stress. Researchers found that the highly stressed women had lower levels of natural killer cells than women who reported less stress. Natural killer cells are one vital weapon which makes up the immune system (Grabmeier, 1995).

## 2. Materials and Method

This research was carried out in Selangor and involved women whose ages range between 30 to 60 years old, and who reside in the Klang Valley. The survivor groups were made up of those who had once been diagnosed of having breast cancer. Meanwhile, those without breast cancer participated as the comparative group. Another criteria for the selection was that the body mass index (BMI) should be less than 30.

Stress level of respondents was determined by using the standardized O'Donnell Stress Questionnaire (Personal Stress Inventory). It consists of 11 sections and has a total of 52 questions which include health problems such as musculoskeletal, gastrointestinal system, depression, anxiousness, sleep pattern, attention span, eating habit, daily activities and personal relationship. The total scores indicate the stress level and those with more than 40 total score were classified as having a stress problem.

The cortisol levels in saliva were determined using the ELISA Kit (Salivary Cortisol Enzyme Immunoassay-Kit) and ELISA Reader at wavelength of 405 nm. Saliva samples were collected at 7:00 am and 5:00 pm to compare the cortisol levels between the two groups. Cortisol levels of respondents were compared with the normal cortisol level, which is 8 µg/dL in the morning and will be reduced to 5 µg/dL in the evening (Knowlden, 2004). A cortisol concentration not equal to or higher than the normal level

will indicate showed that the respondent is experiencing a disturbance of cortisol secretion.

Elisa Reader – It was used to read the absorbance of the saliva sample after adding all the reagents. The plate has to be read at 450nm wavelength within 10 min. after adding the stop solution. It is important to make sure that there is no error while doing the analysis because each sample will represent each respondent.

Elisa Kit – It contains reagents that were used to analyze saliva samples. Each kit has a plate, cortisol standard, wash buffer, enzyme conjugate, stop solution and tetramethylbenzidine (TMB)

### 3. Results

Eighty four respondents were selected in this study. Forty seven respondents made up the survivor group, while 37 respondents made up the comparative group. Table 1 showed the socio-demographic background of the respondents.

**Table 1.** Socio-demographic background of respondents

| Variables             | Survivor Group<br>(n=47)<br>Frequency(%) | Comparative Group<br>(n=37)<br>Frequency(%) |
|-----------------------|--|---|
| <b>Race</b>           |  |   |
| Malay                 | 36(76.6)                                 | 37(100)                                     |
| Chinese               | 5(10.6)                                  |   |
| Indian                | 4(8.5)                                   |   |
| Others                | 2(4.3)                                   |   |
| <b>Marital Status</b> |  |   |
| Married               | 42(89.4)                                 | 18(48.6)                                    |
| Single                | 1(2.0)                                   | 17(46.0)                                    |
| Divorce               | 2(4.3)                                   | 2(5.4)                                      |
| Widow                 |  |   |
| <b>Religion</b>       |  |   |
| Islam                 | 38(80.9)                                 | 37(100)                                     |
| Hinduism              | 5(10.6)                                  |   |
| Christianity          | 1(2.1)                                   |   |
| Buddhism              | 3(6.4)                                   |   |

#### 3.1. Home factor

Results in Table 2, showed that from the various family factors, financial problem was the main factor causing stress among survivors. The next factors were the house work and the child care.

**Table 2.** Percentage of respondents experiencing stress from various home factors

| Factors                            | % Survivor Group<br>(n=47) | % Comparative Group<br>(n=37) |
|------------------------------------|----------------------------|-------------------------------|
| Financial problem                  | 18.83                      | 18.65                         |
| House work                         | 17.53                      | 13.49                         |
| Conflict with children             | 11.04                      | 6.35                          |
| Inadequate time spent with family  | 8.12                       | 11.11                         |
| Uncomfortable home environment     | 6.49                       | 11.11                         |
| House work                         | 7.79                       | 10.32                         |
| Conflict with husband              | 6.17                       | 5.16                          |
| Depression due to personal problem | 5.52                       | 4.37                          |
| Child care                         | 5.19                       | 3.97                          |
| Sexual conflict                    | 4.87                       | 1.19                          |
| Conflict with relatives            | 4.55                       | 7.14                          |
| Conflict with friends /neighbours  | 3.90                       | 7.14                          |

N = 84

#### 3.2. Workplace factor

Results from Table 3, showed that excessive work load which need to be completed in a short period of time was the main problem among respondents. Compared to the other factors, which were causal factors of stress at work place, this factor contributed to about 43.59 % for the survivor group and 31.15 % for the comparative group.

**Table 3.** Percentage of respondents experiencing stress from various workplace factors

| Factor                              | %<br>Survivor<br>group<br>(n=47)         | %<br>Comparative<br>group<br>(n=37) |
|-------------------------------------|--|-------------------------------------|
|                                     | Excessive work load with short datelines | 43.59                               |
| Working overtime                    | 23.08                                    | 22.13                               |
| Uncomfortable with job              | 17.95                                    | 13.93                               |
| Conflict with co-workers            | 8.97                                     | 10.66                               |
| Lack of facilities to complete task | 6.41                                     | 22.13                               |

N = 84

### 3.3 Disease factor

The comparative group were free from breast cancer disease as compared to the survivor group who felt stress due to the breast cancer disease and showed difficulty in sleep pattern. These two factors contributed 22.95 % each of the other disease factors. It showed that this stress maybe due to the breast cancer diagnosis. From the interview session, some of the survivors revealed that they always wake up in the middle of night because of the worries and the pain they felt around their breasts.

**Table 4.** Percentage of survivors experiencing stress from various disease factors

| Factor                                   | % Survivors<br>(n=47) |
|--|-----------------------|
| Feeling depressed with the disease       | 22.95                 |
| Sleeping disorder due to the disease     | 22.95                 |
| Long duration of treatment process       | 21.23                 |
| Difficulty in traveling to get treatment | 13.36                 |
| Too many procedures to get treatment     | 12.33                 |
| High cost of medication                  | 7.19                  |

N = 47

### 3.4 Respondents factor

There was no significance difference for the stress level between the survivor and the comparative group ( $z = -0.861$  and  $p = 0.389$ ). The stress factors include family, workplace, breast cancer disease factor and lifestyle event factor that can cause depression. For the life event factor, it can be divided into death, divorce and others, such as frustrations in relationships and difficulties in taking care of sick family members.

Each individual was exposed to a different stress factor. Table 5 shows the frequency and percentage of respondents who experience the factors which contribute to stress.

**Table 5.** Stress factors experienced by respondents factors

| Variable                 | Survivor<br>(n=47) |       | Comparative<br>(n=37) |       |
|--------------------------|--------------------|-------|-----------------------|-------|
|                          | Frequency          | %     | Frequency             | %     |
| <b>Family Factor</b>     |                    | 28.27 |                       | 46.98 |
| <b>Work Place Factor</b> |                    | 17.24 |                       | 53.02 |
| <b>Disease Factor</b>    |                    | 54.49 |                       |       |
| <b>Life Event</b>        |                    |       |                       |       |
| None                     | 25                 | 53.2  | 26                    | 70.3  |
| Death                    | 14                 | 29.8  | 11                    | 29.7  |
| Divorce                  | 1                  | 2.1   |                       |       |
| Others                   | 7                  | 14.9  |                       |       |

### 3.5 Comparison of cortisol levels among respondents

Results showed that the mean and standard deviation for cortisol levels among survivor group in the morning was 3.392 µg/dL and 0.873 µg/dL respectively, while in the evening the mean was 4.89 µg/dL with a standard deviation of 0.852 µg/dL. The t-test showed no a significant difference between the two groups for either the morning cortisol or the evening cortisol level (Table 6). The secretion of cortisol hormone was significantly higher in the morning than in the evening ( $t = -10.814$ ,  $p = 0.001$ ).

**Table 6.** Comparison of cortisol levels among respondents

| Variable                       | Survivors<br>(n=47)       | Comparative<br>(n=37) | t      | p     |
|--------------------------------|---------------------------|-----------------------|--------|-------|
|                                | Mean (Standard deviation) |                       |        |       |
| Morning<br>Cortisol<br>(µg/dL) | 3.392<br>(0.873)          | 3.55 (1.208)          | -0.709 | 0.480 |
| Evening<br>Cortisol<br>(µg/dL) | 4.89<br>(0.852)           | 4.80 (0.717)          | 0.524  | 0.601 |

### 3.6 Stress factor that effect the cortisol level

Results showed that the mean and standard deviation for cortisol levels among survivor group in the morning was 3.392 µg/dL and 0.873 µg/dL respectively, while in the evening the mean was 4.89 µg/dL with a standard deviation of 0.852 µg/dL. The t-test showed no a significant difference between the two groups for either the morning cortisol or the evening cortisol level (Table 6). The secretion of cortisol hormone was significantly higher in the morning than in the evening (t = -10.814, p = 0.001).

**Table 7.** Stress factors that influence cortisol levels

| Variable                 | Cortisol level |        |       |
|--------------------------|----------------|--------|-------|
|                          | Beta           | t      | P     |
| <b>Stress factors</b>    |                |        |       |
| Eating habit             | -0.372         | -2.311 | 0.024 |
| Depression               | 0.410          | 2.295  | 0.025 |
| Physical system disorder | -0.352         | -2.252 | 0.027 |
| Attention                | -0.358         | -2.053 | 0.044 |

N=84

The result will be formed as absorbance data. The linear equation that will be formed using the standard cortisol

curve can be used to convert the absorbance data into saliva cortisol concentration in µg/dL unit.

## 6. Discussion

Results from the study showed that about 54.49 % of the breast cancer survivor group experienced stress due to the breast cancer disease itself. While for the comparative group, the majority experienced stress due to activities in the workplace.

The cortisol levels for both groups were normal and were not significantly different from each other. However, studies showed that women with breast cancer had higher cortisol level compared to those from the comparative group (Abercrombie et al., 2004). The different stages of breast cancer among respondents also influenced the study results, since treatment and medicine used also influenced the cortisol secretion (Vendhara et al., 2006).

This study also showed that the stress scores for survivor group was not significantly different from the comparative group. This probably was because the survivors tend to appreciate life and slowly develop positive thinking, especially after they have succeeded in undergoing cancer treatment, such as surgery, chemotherapy, radiation and therapy. However, for the comparative group, who experienced stress as much as the survivors are actually susceptible to the risk of lowering their immunity due to the stressful life. They may, in the future be inflicted with the metabolic and cardiovascular diseases or other health problems. In a study by McEwen & Stellar (1993), it was stated that the activation of hormone cortisol by high stress level that occur repeatedly along with an individual’s life had significant relationships with the increased rate of cardiovascular and metabolic diseases. When stress was detected by the brain, the hypothalamus would secrete the corticotrophin-releasing hormone (CRH) which then stimulates the adrenal gland to secrete the cortisol hormone. This showed that the stress level was influenced by the secretion of cortisol hormone (Detterbern et al., 2005 and Lucia et al., 2004).

On the contrary, the results of this study found no association between stress scores and cortisol levels. This is probably due to the limitation of this study, in which the saliva were collected for only one day. The accuracy of the collection time depended on the respondents (Lucia et al., 2004). The best time to collect is at 6.00 am, whereby the respondents just woke up in the morning. Thus, the respondents were requested to collect their own saliva in labelled containers. For the evening cortisol, the different activities among the respondents would also increase the evening level. Therefore, the number of sampling days

should be increased and the consistency in the time of saliva collection would give better results.

Results showed that bad eating habits, bad diets, physical problems and increased attention would influence the cortisol level. The increased levels of cortisol hormone would not usually result in negative effects because it is needed in controlling the body functions. Problems of high depression would increase cortisol levels. Other factors which include energy level, skeletal muscle system, gastrointestinal system, risk factor of breast cancer and the body mass index (BMI) did not influence the cortisol hormone secretion.

Perhaps alternative indicator could be used as Yong et al. (2013) found that relationship between the psychological stresses using salivary  $\alpha$ -amylase with physical symptoms as reported by the breast cancer survivors. On contrary, in another paper, Yong et al. found that workplace stressors and job strain influenced the psychological stress.

## 5. Conclusion

The results showed that there was no significant difference for either cortisol levels in the morning and in the evening, or for the stress scores between the survivors and the comparative group. The morning cortisol levels were significantly lower than the evening cortisol levels. The survivors experienced stress in relation to their health condition, while the comparative group experience stress due to their workplace.

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