

STRESS IN BREAST CANCER PATIENT AND MINDFULNESS THERAPY OF BHAGWAN MAHAVEER CANCER HOSPITAL AND RESEARCH CENTER

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Abstract:

Depression is a leading cause of disability and disease worldwide, stress and depression is of public health concern and specially for the breast cancer patient cause short & long term detrimental effects to the women and her family. This article describe a conceptual framework about the complex relationship between stress, depression & health outcomes in breast patient and mindfulness therapy for depression, stress control of these cancer patient may be helpful for adding depth to the body of knowledge about the use of mind-body therapies. Mindfulness questionnaire used as a reliable and valid comprehensive for assessing different aspects of mindfulness in breast cancer patient.

KEYWORDS: Stress, depression, mindfulness, questionnaire self-consciousness.

INTRODUCTION:

Stress have a bidirectional relationship with depression and health outcomes is represented in the conceptual frame work in womens specifically. The cyclic interplay of stress vulnerability, depression & health outcome is represented in the conceptual frame work. Women with advanced breast cancer who have abnormal daytime levels of cortisol, a hormone released in response to stress, this studied found that women with these abnormal cortisol level had fewer immune system cells and this reduced immunity. The cortisol system is one of two primary systems of responding to stress Patients with a flatter cortisol pattern also had fewer natural killer cells, immune system cells that spontaneously kills abnormal cells in their vicinity, including tumour cells and infected cells, previous studies have shown that the absence of natural killer cells is related to the progression of breast cancer (Acc. to spiegel). He also states that cortisol might have an impact on the progression of the disease, for instance, cortisol causes normal cells to release glucose into the blood, but tumour cells ignore this signal and thus cortisol levels tend to favour the nourishment of tumor cells over normal ones. And also it was studied that cortisol level can be controlled by the Mindfulness technique including meditation yoga. As we seen stress vulnerabilities are based upon numerous factors associated with acute and chronic stress including individual chronic/acute burdens, the biological environmental and the psychosocial environment, it is studied by the researcher that individual with stressful life situations, because of environmental factors outside of the individual's control have higher stress-related psychoneuro immunologic changes (Haven Stein 1996 Geronimuesetal 2006/Clark etal 2007, Johansson et al 2007). Stress is a common belief among breast concern patients and the public to explain variation in breast cancer incidence in this paper breast cancer patient. Who were suffering of chronic stress they faced before the disease detection and after & during the treatment effects health states.

Stress is not a discrete value but rather a continuous interplay between an individual & their environment. If we distinguish between the stress process i.e. stressors, stress & distress, then we can define stressors as precursors in the environment both internal & external that create "Conditions of threat challenge, demands or structural constraints, these conditions of threat can manifest in the form of idiosyncratic events, but it is important to note that not every individual experience/induce stress in the same way, stress described as a biological state of the body - a generalized physiological alert in response to threatening agents often referred as the "fight or flight response. That is a stressor is as much a physical response to an individuals environment as it is psychological. It may cause hormonal neurological or cardiovascular changes. In the mathematical field, to apply stress on an object means to apply "an external force acting against a resisting body, however the object applying force is not characterized as stress until the force of the object exceeds the "elastic limit" of the object being stressed upon It is at this point that stress occurs ; i.e. when the integrity of the body being acted upon cannot be maintained : Acc. to perlin theories that psychosocial stress

on the human body acts in a similar fashion. People with general anxiety disorders. (Roemier et al 2008) small effects on depression and anxiety have been formed for people with chronic disease. A systematic review examination of 50 breast cancer patient during corona period in Bhagwan Mahaveer Cancer Research Hospital, Jaipur, Rajasthan. When we interviewed with the patient with the questioner. We get to know the women, before the prediction of cancer sign appear was suffering from increased emotional suppression, dissatisfaction, anxiety as they shared their personal experiences and some condition they are facing during the treatment also. A well validated study intervention in cancer patient that is offered, mindfulness based stress reduction.

Mindfulness practice called "the wheel of Amareners" it is being aware of the aspects of the mind itself Mindfulness in its most general sense is about waking up from a life in which we are set in "automatic", to becoming more aware of and sensitive to the novelty of our everyday. Experiences, when we develop focused attention, open awareness & kind intention, research reveals that we will be better equipped to weather life's storms with a stronger sense of overall calm & happiness. Research also reveals that we can impact the health of our bodies in very real & immeasurable ways including (g) improving of immune function to help fight infection (b) optimizing the level of the enzyme telomerase. Which repair and maintains the end of your chromosomes, keeping your cells and you youthful, functioning well & healthy, enhancing epigenetic "Regulation of genes/to help prevent life threatening inflammation. Reduce, stress and improve cardiovascular functions, help the brain grow more linkages among separate regions - Something called "integration", which is the neural basis for restriction and well being. Mindfulness practice has been incorporated in several treatment programs well known programs are mindfulness based stress reduction (MBSR, Kabat-Zinn, 1990) mindfulness - based cognitive therapy. There is empirical support for the efficiency of mindfulness based cognitive therapy in people with recurrent depression (e.g. MO and Teasdale 2004, mindfulness based intervention in people). Our life is made up of light and dark. One of the biggest challenges that we face in our negative minds is the tendency to judge the harsh self-criticism that is happening in mind, every multiple times per day is not only painful but also increases. Our cortisol levels and as we know cortisol is a stress hormone produced first by our own mind and then it express itself through body, increase stress always weaken our immune defence one should much judge his/herself before judging or any type of situation and ask oneself if these allegations are actually all true? Or are they simply a construction of one's own assumption when focusing in one's body, a certain part of our brain is activated that guides to more self-awareness and self-reflection in the long run and mindfulness also make us change. Our perspective, helps us balance situations and situations and also helps to see things holistically. If our open eyes embraced the uncertainty that is all around us and recognize that you have the power to design, your own thoughts, then the next couple of month will have a more positive outlook. Mindfulness & meditation can help it allows to stop negative feeling by changing perspective onto the positive. In positive psychology, the concept of gratitude refers to the feeling of appreciation of the beautiful things in life. Gratitude is also a part of mindfulness therapy, it make the person more hope and more optimism, it has been proven that people who keep a gratitude journal are happier than those who just look at what they lack sessions consisted of 5 steps combined with concrete exercises to pause and reflect (a) awareness (b) acceptance (c) recognition (d) routine (e) resistance

The meditations sessions and videos were followed through app or the website. Participant were invited to practice at home for 45 min each day, and also psycho-education about grief was added we also take help to conduct the training by onychopsychologist, yoga trainer with meditation and the practices are a way to reconnect to ourselves in moments of particular stress, numerous studies have successfully proven the positive effects that mindfulness can have on our body and mind, as our muscles also our brain can be changed throughout our entire life, this phenomenon is called neuroplasticity, that's why meditation and mindfulness exercises can help us be more resistant to stress anxiety burnout attention, deficits and hyper activity sleep disorders, addictions, disease and pain, high blood pressure, social anxiety, difficult emotion during the training, mind take different path to change our routine in order to stop nurturing our negative emotion, and remaining anchored to our breath, even when our mind really seem to be in the middle of a storm or we perceive slight discomfort. Our goal for the breast cancer patient was to plant a seed inside the patients, a seed that will continue to cultivate so that it will become a strong and resistance, that will be the centre of stability in the most difficult moment and in the positive ones finding balance accepting all situations with a certain level of kindness to become resistant means to have firm, stable like the tree, that despite winds, storms and scorching sun, remain rooted in the ground. As mindfulness results in a reduction of identification with emotions thoughts and body sensation as it has been related to improved well being through mechanism such as better self-regulation 2003 / experimental acceptances (S.C. Hayes, Loomna Bond, Masuda and billis 2006, Ostafun and Marlatt 2008) comparison & self acceptance (Corson & Langer 2006, Gilbert & Proctor 2006) and interpersonal behaviour (Dekeyes, Raes, Liejssers, Leysen and Dewulf 2008). We have seen the stress level, anxiety, depression level become reduced, the ability to accept aversive internal experience, such as negative emotions thought & memories and to pursue goals in the presence of the experiences, such as negative emotions thought and memories and to pursue goals in the presence of these experiences. Participants were asked to rate from 0 to 3 point as per PHQ 9 type scale the

degree to which each statement is true for them before the mindfulness programme and after i.e. acceptance & action questionnaire. Onwards was computed by summing the scores on the individual items higher scores indicate high level of general acceptance and less experimental avoidance.

Data Analysis : As we compare significant difference between stress in (low- average), (average - high) & (low - high) mindfulness we get the following graph and table groups has been divided according to questionnaire.

Ho1 -There is no significant difference between stress in below 65 years old and 65 years old breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur.

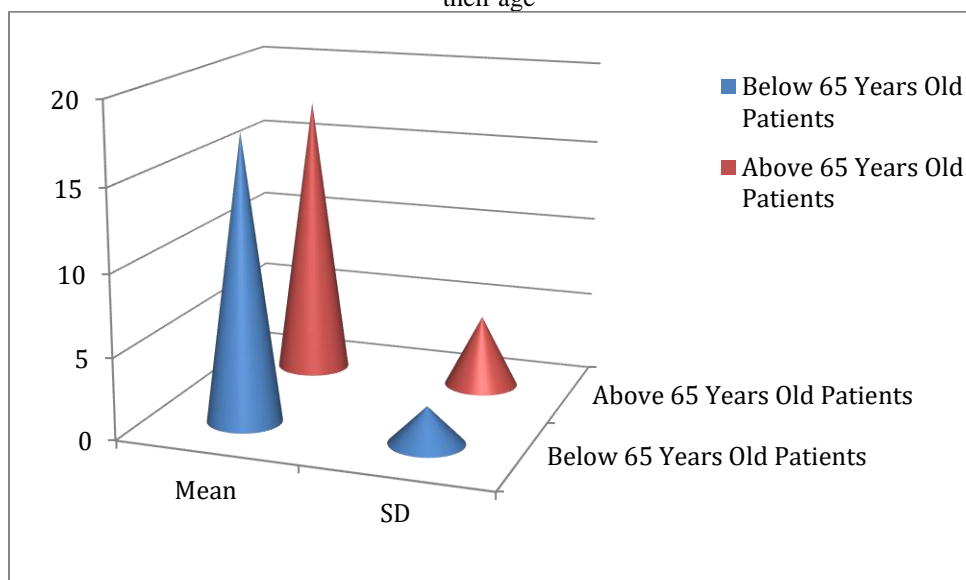
Table : 1 Significant difference between Stress in Breast Cancer Patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur in reference to their age

Group	N	Mean	SD	t-value	P-Value $\alpha=0.05$
Below 65 Years Old Patients	21	17.57	2.29	0.15	0.89
Above 65 Years Old Patients	28	17.43	4.45		

As per usual of above table makes it clear that mean value of stress of below 65 years old patients and above 65 years old patients were found 17.57 and 12.07 respectively and the standard deviation of the same were found 2.29 and 4.45 respectively. The significance difference in the stress has been calculated by the t-test. Due to this, the value of t- test was obtained as 0.15. The t-value in terms of the stress of breast cancer patients was found 0.15. The P-Value for the same was found at 0.89. The p-value is the analysis was greater than α ($P>0.05$), which shows that the difference between the stress in below 65 years old patients and above 65 years old patients is insignificant.

As a result, the null hypothesis is accepted and it is concluded there is no significant difference between stress in below 65 years old and above 65 years old breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur.

Figure : 1 Stress in Breast Cancer Patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur in reference to their age



Ho2 -There is no significant difference between mindfulness in below 65 years old and above 65 years old breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur.

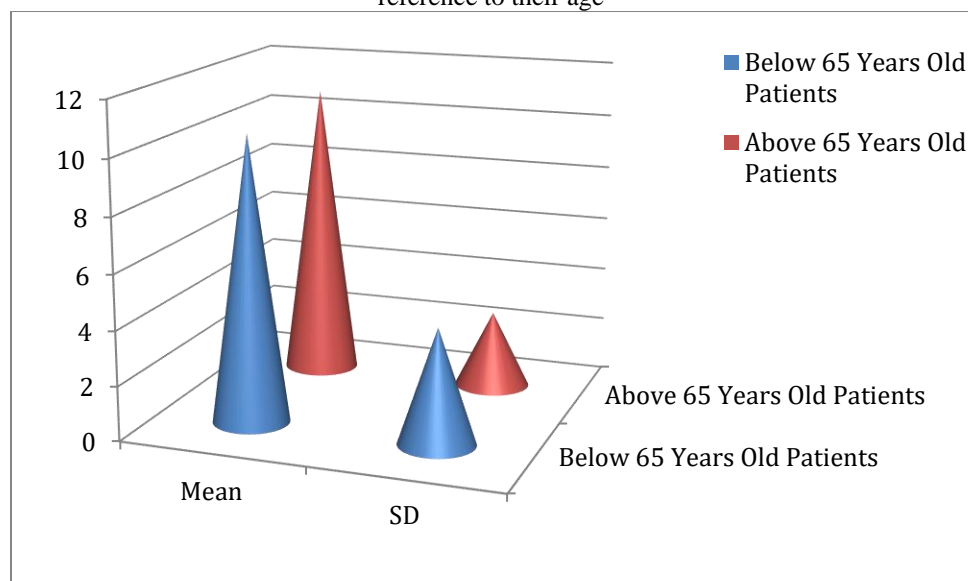
Table : 2 Significant difference between mindfulness in Breast Cancer Patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur in reference to their age

Group	N	Mean	SD	t-value	P-Value $\alpha=0.05$
Below 65 Years Old Patients	21	10.48	4.23	0.39	0.68
Above 65 Years Old Patients	28	10.89	2.82		

As per usual of above table makes it clear that mean value of mindfulness of below 65 years old patients and above 65 years old patients were found 10.48 and 10.89 respectively and the standard deviation of the same were found 4.23 and 2.82 respectively. The significance difference in the mindfulness has been calculated by the t-test. Due to this, the value of t- test was obtained as 0.39. The t-value in terms of the mindfulness of breast cancer patients was found 0.39. The P-Value for the same was found at 0.68. The p-value is the analysis was greater than α ($P>0.05$), which shows that the difference between the mindfulness in below 65 years old patients and above 65 years old patients is insignificant.

As a result, the null hypothesis is accepted and it is concluded there is no significant difference between mindfulness in below 65 years old and above 65 years old breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur.

Figure : 2 Mindfulness in Breast Cancer Patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur in reference to their age



Ho3 -There is no significant difference between stress in low and average mindfulness breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur.

Table : 3 Significant difference between stress in low and average mindfulness breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur

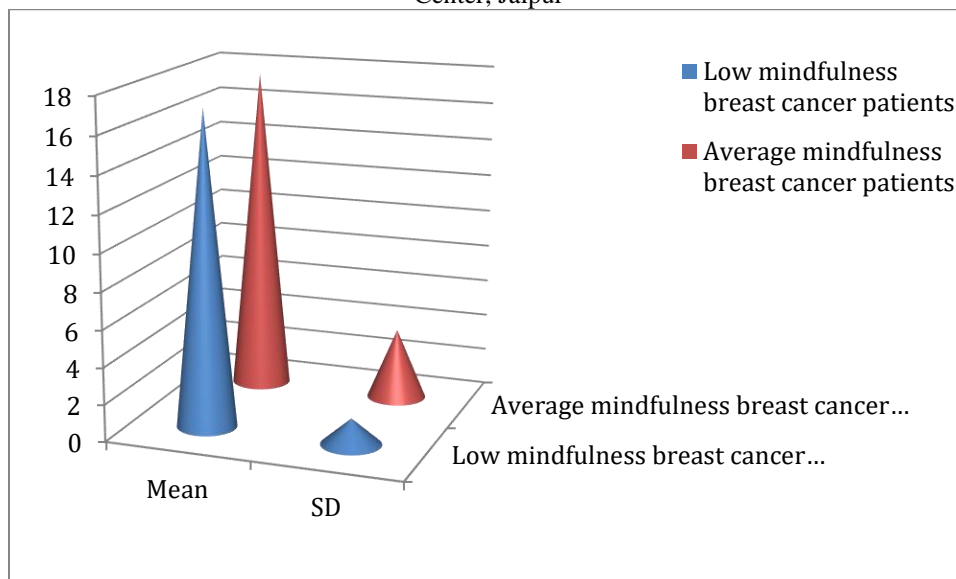
Group	N	Mean	SD	t-value	P-Value $\alpha=0.05$
Low mindfulness breast cancer patients	5	17.00	1.41	0.64	0.91

Average mindfulness breast cancer patients	37	17.57	3.83		
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As per usual of above table makes it clear that mean value of stress in low and average mindfulness breast cancer patients were found 17.00 and 17.57 respectively and the standard deviation of the same were found 1.41 and 3.83 respectively. The significance difference in the mindfulness has been calculated by the t-test. Due to this, the value of t- test was obtained as 0.64. The t-value in terms of the stress in low and average mindfulness breast cancer patients was found 0.64. The P-Value for the same was found at 0.91. The p-value is the analysis was greater than ∞ ($P>0.05$), which shows that the difference between the stress in low and average mindfulness breast cancer patients is insignificant.

As a result, the null hypothesis is accepted and it is concluded there is no significant difference between stress in low and average mindfulness breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur.

Figure : 3 Stress in low and average mindfulness breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur



Ho4 -There is no significant difference between stress in average and high mindfulness breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur.

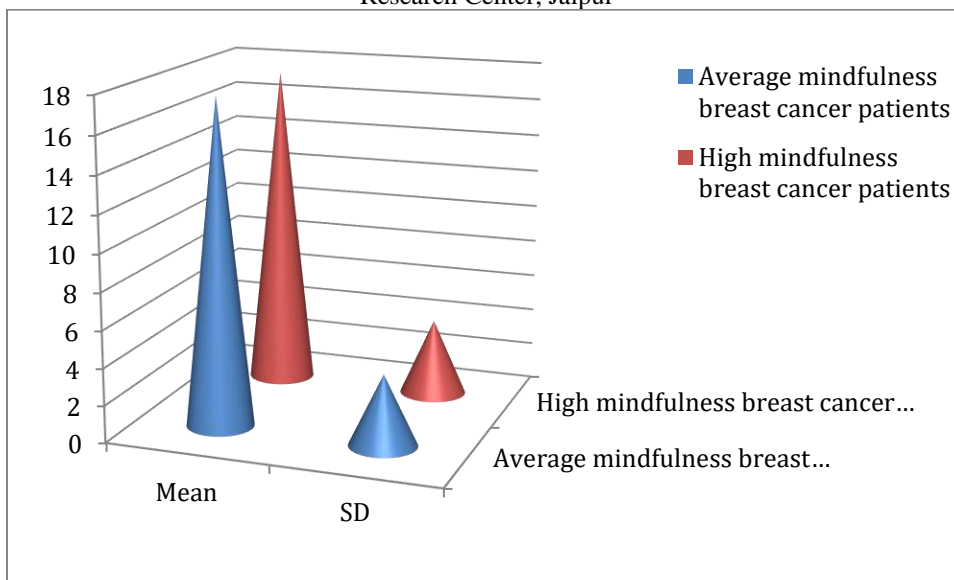
Table : 4 Significant difference between stress in average and high mindfulness breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur

Group	N	Mean	SD	t-value	P-Value $\infty=0.05$
Average mindfulness breast cancer patients	37	17.57	3.83	0.08	0.77
High mindfulness breast cancer patients	7	17.43	4.12		

As per usual of above table makes it clear that mean value of stress in average and high mindfulness breast cancer patients were found 17.57 and 17.43 respectively and the standard deviation of the same were found 3.83 and 4.12 respectively. The significance difference in the mindfulness has been calculated by the t-test. Due to this, the value of t- test was obtained as 0.08. The t-value in terms of the stress in average and high mindfulness breast cancer patients was found 0.08. The P-Value for the same was found at 0.77. The p-value is the analysis was greater than ∞ ($P>0.05$), which shows that the difference between the stress in average and high mindfulness breast cancer patients is insignificant.

As a result, the null hypothesis is accepted and it is concluded there is no significant difference between stress in average and high mindfulness breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur.

Figure : 4 Stresses in average and high mindfulness breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur



Ho5 -There is no significant difference between stress in low and high mindfulness breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur.

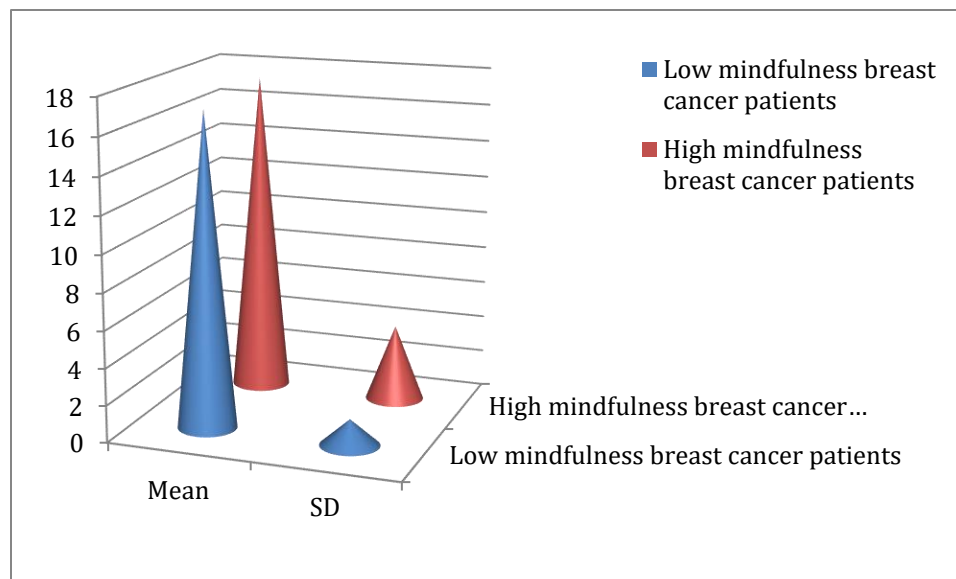
Table : 5 Significant difference between stress in low and high mindfulness breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur

Group	N	Mean	SD	t-value	P-Value $\alpha=0.05$
Low mindfulness breast cancer patients	5	17.00	1.41	0.26	0.82
High mindfulness breast cancer patients	7	17.43	4.12		

As per usual of above table makes it clear that mean value of stress in low and high mindfulness breast cancer patients were found 17.00 and 17.43 respectively and the standard deviation of the same were found 1.41 and 4.12 respectively. The significance difference in the mindfulness has been calculated by the t-test. Due to this, the value of t- test was obtained as 0.26. The t-value in terms of the stress in low and high mindfulness breast cancer patients was found 0.26. The P-Value for the same was found at 0.82. The p-value is the analysis was greater than α ($P>0.05$), which shows that the difference between the stress in low and high mindfulness breast cancer patients is insignificant.

As a result, the null hypothesis is accepted and it is concluded there is no significant difference between stress in low and high mindfulness breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur.

Figure : 5 Stress in low and high mindfulness breast cancer patients of Bhagwan Mahaveer Cancer and Research Center, Jaipur



CONCLUSION :

As we want to find that mindfulness therapy is validated to control the stress factor in cancer patients of breast cancer, whether there is any difference in the handling of the stress factor before the Origin during the treatment and after the treatment but as some limitation factors were also include, sample in the study consisted of people were concluded according to questionnaire & interview method but they are not detected clinically as that was corona time and patients also don't have time & concern to go for clinical test so that we are not able to measure the effect of stress, anxiety and depression part it was just seem that when the word "Cancer" word came it's swipe away the positivity, it is only increase the anxiety & fear related to this disease. Patient's statement that whatever they do fear of death is always there, but still there is an open option for more research required clinically, we are not able to relate any significance relation in our research. Cancer with a big picture of pain of death without knowing how much time they will survive whether they can able to survive without the cancer, the acceptance of these thought are so big that they always give them anxiety, depression, stress during the medication of chemotherapy, radiation. Proper clinically based research in future, will be able to find that what actually scenerio of inter relation of stress of breast cancer patient signifies with mindfulness therapy. May be mindfulness therapy will be helpful for patients of Chronic Stress not with the patients who were already facing the Cancer and its treatment, which build fear in there emotion, physical, social and life threatening part.

REFERENCES:

1. Antoni, M.H.; Lutgendorf, S.K.; Cole, S.W.; Dhabhar, F.S.; Sephton, S.E.; McDonald, P.C.; Stefanek, M.; Sood, A.K. The influence of bio-behavioural factors on tumour biology: Pathways and mechanisms. *Nat. Rev. Cancer* 2006, 6,240-248. [CrossRef]
2. Antonova, L.K.; Aronson, C.R. Mueller, Stress and breast cancer: From epidemiology to molecular biology. *Breast Cancer Res.* 2011, 13, 208. [CrossRef] [PubMed]
3. Bahri, N.; Fathi Najafi, T.; Homaei Shandiz, F.H.; Tohidinik, H.R.; Khajavi, A. The Relation Between Stressful Life Events and Breast Cancer: A Systematic Review and Meta-Analysis of Cohort Studies. *Breast Cancer Res, Treat.* 2019, 176, 53-61. [CrossRef] [PubMed]
4. Bleiker, E.M.A.; van der Ploeg, H.M. Psychosocial factors in the etiology of breast cancer: Review of a popular link. *Patient Educ. Couns.* 1999, 37, 201-214. [CrossRef]
5. Bostock, S.; Crosswell, A.D.; Prather, A.A.; Steptoe, A. Mindfulness On-The-Go: Effects of a Mindfulness Meditation App on Work Stress and Well-Being. *J. Occup. Health Psychol.* 2019, 24, 127-138. [CrossRef]
6. Bryla, C.M. The relationship between stress and the development of breast cancer: A literature review. *Oncol. Nurs. Forum* 1996, 23, 441-448. [PubMed.]
7. Butow, P.; Price, M.; Coll, J.; Tucker, K.; Meiser, B.; Milne, R.; Phillips, K.-A. Does stress increase risk of breast cancer? A 15-year prospective study. *Psycho-Oncology* 2018, 27, 1908-1914. [CrossRef]
8. Chiriac, V.-F.; Baban, A.; Dumitrascu, D.L. Psychological Stress and Breast Cancer Incidence: A Systematic Review. *Clujul Med.* 2018, 91, 18-26. [CrossRef]

9. Conklin, Q.A.; Crosswell, A.D.; Saron, C.D.; Epel, E.S. Meditation, stress processes, and telomere biology. *Curr. Opin. Psychol.* 2019, 28, 92-101. [CrossRef]
10. Dohrenwend, B.P., Inventorying stressful life events as risk factors for psychopathology: Toward resolution of the problem of intracategory variability. *Psychol. Bull.* 2006, 132, 477. [CrossRef] [PubMed]
11. Fischer, A.; Ziogas, A.; Anton-Culver, H. Perception matters: Stressful life events increase breast cancer risk. *J. Psychosom. Res.* 2018, 110, 46-53. [CrossRef]
12. Guo, L.; Liu, S.; Zhang, S.; Chen, Q.; Zhang, M.; Quan, P.; Lu, J.; Sun, X. C-reactive protein and risk of breast cancer: A systematic review and meta-analysis. *Sci. Rep.* 2015, 5, 10508. [CrossRef]
13. Kocic, B.; Filipovic, S.; Vrbic, S.; Pejic, I.; Rancic, N.; Cvetanovic, A.; Milenkovic, D. Stressful life events and breast cancer risk: A hospital-based case-control study. *Age Years* 2015, 20, 487-491.
14. Krieger, N.; J.L.; Waterman, P.D. Jim Crow and estrogen-receptor-negative breast cancer : US-born black and white non-Hispanic women, 1992-2012. *Cancer Causes Control* 2017, 28, 49-59. [CrossRef] [PubMed]
15. Kroenke, C.H.; Hankinson, S.E.; Schernhammer, E.S.; Colditz, G.A.; Kawachi, I.; Holmes, M.D. Caregiving stress, endogenous sex steroid hormone levels, and breast cancer incidence. *Am. J. Epidemiol.* 2004, 159, 1019-1027. [CrossRef]
16. Kruk, J. Self-reported psychological stress and the risk of breast cancer: A case-control study. *Stress* 2012, /5, 162-171. [CrossRef]
17. Lillberg, K.; Verkasalo, P.K.; Kaprio, J.; Teppo, L.; Helenius, H.; Koskenvuo, M. Stressful Life Events and Risk of Breast Cancer in 10,808 Women: A Cohort Study. *Am. J. Epidemiol.* 2003, 157, 415-423. [CrossRef]
18. McEwen, B.S.; Gianaros, P.J. Central role of the brain in stress and adaptation: Links to socioeconomic status, health, and disease. *Ann. N. Y. Acad. Sci.* 2010, 1186, 190-222. [CrossRef]
19. Nielsen, N. R.; Gronbaek, M. Stress and brease cancer : A systematic update on the current knowledge. *Nat. Clin. Pract. Oncol.* 2006, 3, 612-620. [CrossRef] [PubMed]
20. Nielsen, N.R.; Stahlberg, C.; Strandberg-Larsen, K.; Kristensen, T.S.; Zhang, Z.F.; Hundrup, Y.A.; Gronbaek, M. Are work-related stressors associated with diagnosis of more advanced stages of incident breast cancers? *Cancer Causes Control* 2008, 19, 297-303. [CrossRef] [PubMed]
21. Protheroe, D.; Turvey, K.; Horgan, K.; Benson, E.; Bowers, D.; House, A. Stressful life events and difficulties and onset of breast cancer : Case-control study. *BMJ* 1999, 319, 1027-1030. [CrossRef]
22. Sanada, K.; Montero-Marin, J.; Aida Diez, M.; Salas-Valero, M.; Perez-Yus, M.C.; Morillo, H.; Demarzo, M.M.; Garcia-Toro, M.; Garcia-Campayo, J. Effects of Mindfulness-based interventions on salivary cortisol in healthy adults: A meta-analytical review. *Front. Physiol.* 2016, 7, 471.
23. Schernhammer, E.S.; Hankinson, S.E.; Rosner, B.; Kroenke, C.H.; Willett, W.C.; Colditz, G.A.; Kawachi, I. Job Stress Breast Cancer Risk: Nurses' Health Study. *Am. J. Epidemiol.* 2004, 160,1079-4086. [CrossRef]
24. Schoemaker, M.J.; Jones, M.E.; Wright, L.B.; Griffin, J.; McFadden, E.; AshWorth, A.; Swerdlow, A.J. Psychological stress, adverse life events and breast cancer incidence: A cohort investigation in 106,000 women in the United Kingdom. *Breast Cancer Res.* 2016, 18, 1-8. [CrossRef] [PubMed]
25. Tas, F.; Karalar, U.; Aliustaoglu, M.; Keskin, S.; Can, G.; Cinar, F.E. The major stressful life events and cancer: Stress history and cancer. *Med. Oncol.* 2012, 29, 1371-1377. [CrossRef] [PubMed]
26. Vesterlund, G.K.; Hoeg, B.L.; Johansen, C.; Heitmann, B.L.; Bidstrup, P.E. Prolonged job strain and subsequent risk of cancer in women-A longitudinal study, based on the Danish Nurse Cohort. *Acta Oncol.* 2007, 56, 301-306. [CrossRef]
27. Williams, D.R.; Neighbors, H.W.; Jackson, J.S. Racial/ethnic discrimination and health: Findings from community studies. *Am. J. Public Health* 2008, 98 (Suppl. 9), S29-S37. [CrossRef]
28. Zhang, Q.; Zhao, H.; Zheng, Y. Effectiveness of mindfulness-based stress reduction (MBSR) on symptom variables and health-related quality of life in breast cancer patients-a systematic review and meta-analysis. *Supportive Care Cancer* 2019, 27, 771-781. [CorssRef] [PubMed]
29. Zinzi, B.; Williams, R. Stress, Health, and Disparities. In *Neurobiology of Brain Disorders: Biological Basis of Neurological and Psychiatric Disorders*; Zigmond, M., Rowland, L., Coyle, J., Eds.; Academic Press: Cambridge, UK, 2005; pp. 765-779. [CrossRef]