

## Psychological traumatic events in the recent past and association with diagnosis of cancer

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### ABSTRACT

Emotional stress due to psychological trauma causes immune system dysfunction resulting in high risk of development of cancer. The study aimed to correlate psychological trauma in the past five years of cancer diagnosis. This study was a community based survey including cancer patients diagnosed with different cancers undergoing treatment or follow-up by using snowball sampling and questionnaire based technique. The study was conducted during a period of one year from December 2019 till December 2020. All recruited patients were requested for an interview. The results of the study showed a high rate of major psychological trauma among cancer patients. Sudden death of a close relative with and without trauma of natural disaster were most commonly reported events. The study concluded that the risk of cancer development rises with major emotional trauma specially death of a close relative.

**Key Words:** Emotional stress, psychological trauma, cancer

## INTRODUCTION

Cancer is one of the oldest known diseases and currently leading cause of mortality around the globe. The rate of cancer is at rise and further increase is predicted by World Health Organization in its Gobocan project(1). Cancer has demonstrated multifactorial causation and risk factors including endogenous factors such as chronic inflammation, environmental factors (ie exposure to carcinogens), drugs, compromised immunity and genetic mutations(2). Emotional stress is known to affect intracellular mechanisms thereby disturbing immunity(3). It has also been suggested that inflammation results in depression and vice versa. The immune disruption has been associated with stressful events resulting in emotional disturbances(4). Stress immune response relationship has been studied previously and a whole new science of psychoneuroimmunology has been established. The stress or emotional events trigger immune response by releasing cytokines including Interleukins which activate vagus nerve response and to a lesser extent trigeminal nerve response causing feelings of sickness(5). Acute stress response physiologically activates adrenal medulla which releases epinephrine and norepinephrine, which in turn activates Hypothalamic- pituitary axis thereby rising basal metabolic rate, resulting in rise in heart rate, respiratory rate and blood pressure. However, if the response remains there for a longer period, or if it becomes severe the autonomic nervous system become dysfunctional. Autonomic nervous system also controls immune system causing chronic inflammatory response(6) as a result of continuous stress. Chronic inflammation causes glucocorticoid resistance thus inflammatory response

progresses further. Chronic inflammation is also known to be linked with cancer development and also poor clinical outcome(7,8).

Recently (ie 2019) a systematic review of cohort studies was reported suggesting a rise in cancer incidence after depression and chronic emotional stress levels and also there was a link of poor prognosis in stressed patients(9). However, there is limited literature available suggesting association of stress induced chronic inflammation and cancer. Also there is limited research available exploring association of acute severe psychological trauma and later development of cancer. Thus this study was designed to explore cancer patients and correlate severe stressful event in the recent past and the diagnosis of cancer.

## METHODOLOGY

The study was a community based survey conducted at Hyderabad. Patients with confirmed diagnosis of cancer were identified from NIMRA hospital and informed consent was taken followed by questionnaire based interview. Further samples were identified through snowball sampling. The patients identified through the patients treated at NIMRA were also included. Those patients who refused to share information were excluded. There were 16 close ended questions (Table 1) and responses were categorized into five categories

- A- it happened to you personally,
- B- you witnessed it happen to someone else,
- C- you learned about it happening to someone close to you,
- D- you're not sure if it fits,
- E- it doesn't apply to you.

All the patients who consented to be part of the study were asked these questions or in case of English literate patients were requested to go through questions and respond accordingly.

### Statistical methods

The data was analyzed by using Statistical Package for Social Sciences (SPSS) Version 21 IBM. Frequency distribution was reported for the events and mean time for the events was calculated along with standard deviation (SD).

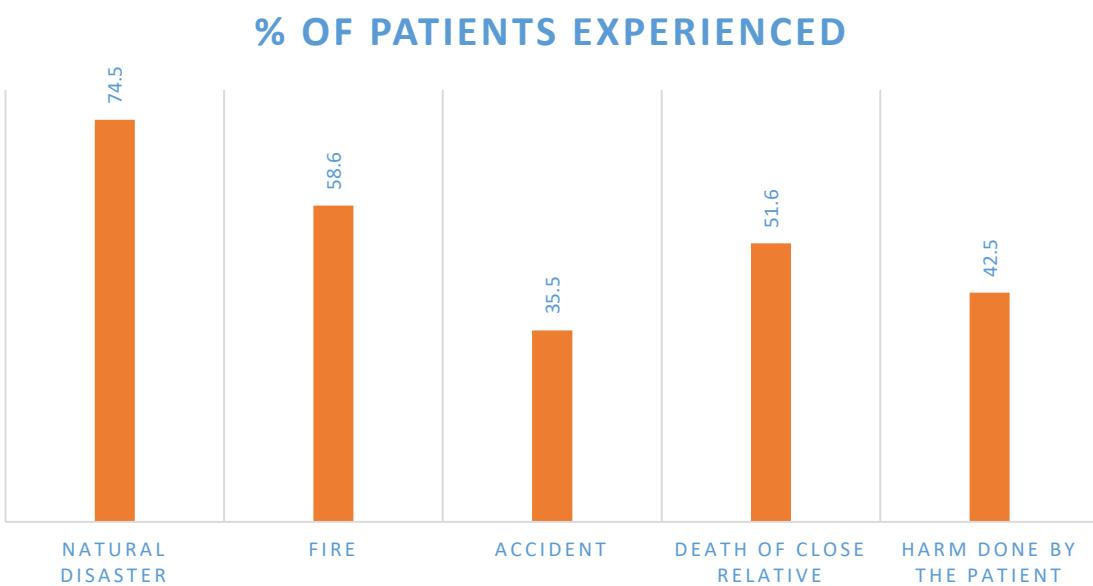
## RESULTS

A total of 428 patients were interviewed including 168 males (ie 39.3%) and 260 females (ie 60.7%). A total of 380 patients disclosed their site of cancer and 48 declined to inform about the site of the cancer. Breast cancer patients were 151 (39.7%) followed by head and neck including oral cancers (n=94, 24.7%). Gastrointestinal and reproductive cancers were 34 (7.9%) in each while 22 patients with lung cancer (5.8%) and remaining were diagnosed with liver, blood, bone and neuroendocrine cancers. Natural disaster, death of the close relative and fire/ explosion were major psychological trauma they faced. Natural disaster with death of the close relative was even higher. A summary of the responses is given Table 1. Mean time of event happened and diagnosis of cancer 3.49 (SD±3.726) years.

**Table 1. List of the questions asked for Life events from patients undergoing treatment/ follow-up of cancer and summary of their responses**

No	Event	A	B	C	D	E
1	Natural disaster (for example, flood, hurricane, tornado, earthquake)	316 (74.5)	0	0	0	108(25.5)

<b>2</b>	Fire or explosion	251 (58.6)	4(0.9)	0	0	173 (40.4)
<b>3</b>	Transportation accident (for example, car accident, boat accident, train wreck, plane crash)	152(35.5)	13(3.0)	0	0	259(60.5)
<b>4</b>	Serious accident at work, home, or during recreational activity	57(13.3)	12(2.8)	0	0	347(81.1)
<b>5</b>	Exposure to toxic substance (for example, dangerous chemicals, radiation)	53(12.4)	17(4.0)	0	0	357(83.4)
<b>6</b>	Physical assault (for example, being attacked, hit, slapped, kicked, beaten up)	35(8.2)	8(1.9)	0	0	384(89.7)
<b>7</b>	Assault with a weapon (for example, being shot, stabbed, threatened with a knife, gun, bomb)	24(5.6)	8(1.9)	0	0	396(92.5)
<b>8</b>	Sexual assault (rape, attempted rape, made to perform any type of sexual act through force or threat of harm)	14(3.3)	5(1.2)	0	0	409(95.6)
<b>9</b>	Combat or exposure to a war-zone (in the military or as a civilian)	17(4.0)	4(0.9)	0	0	406(94.9)
<b>10</b>	Captivity (for example, being kidnapped, abducted, held hostage, prisoner of war)	32(7.5)	8(1.9)	0	0	388(90.7)
<b>11</b>	Life-threatening illness or injury	115(26.9)	4(0.9)	0	0	305(71.3)
<b>12</b>	Severe human suffering	108(25.2)	4(0.9)	0	0	316(73.8)
<b>13</b>	Sudden, violent death (for example, homicide, suicide)	132(30.8)	0	0	0	296(69.2)
<b>14</b>	Sudden, unexpected death of someone close to you	221(51.6)	0	0	0	207(51.6)
<b>15</b>	Serious injury, harm, or death you caused to someone else	182(42.5)	1(0.2)	0	0	245(57.2)
<b>16</b>	Any other very stressful event or experience	149(34.8)	1(0.2)	0	0	278(65.0)



**Figure 1. Most commonly reported traumatic events experienced by patients undergoing treatment or follow-up of cancer**

## DISCUSSION

Psychological stress is one of the major causes associated with chronic illness including metabolic syndrome, hypertension, diabetes and even cardiac disease and stroke. Wear and tear of cells is an ongoing process thus the dividing cells have strong system of DNA repair mainly governed by p53 gene pathway while those cells which cross the boundaries of being repaired go through a clearance system of apoptosis (ie cell suicide) governed by Bcl2 pathway(10). Mitochondria is an important organelle for cell energy metabolism and normal cellular functions. Stress response has been associated with mitochondrial dysfunction and at the same time mitochondrial dysfunction has been significantly linked with cancer(11). Cancer cells tend to develop at all times in human body but the immune system has a mechanism to remove them. Continuously dividing cells such as Gastroenterological lining epithelium, oral mucosa, bone marrow cells and breast cells have a higher chance of being masked by immune system and escape destruction and develop into cancer.

There is literature available suggesting freezing of immune system in response to acute psychological trauma. In our study natural disaster, fire, accident, death of a close relative and harm done by the patient to someone else were identified as the key events happened in the past. The mean time for the past event was three and half years in our study. Further elaboration stated that this natural disaster, fire and accidents also resulted in death of family members. Previously reported studies have suggested that natural disasters and death of close relatives have been associated with higher rate of cancer development. War situations raise the reported cases of cancer however it cannot be directly linked with stress but the environmental factors such radiations from ammunition may also play a role. A large study was conducted including 485864 adults from United States of America showed that psychological stress was associated with higher mortality. The study also demonstrated associated with the degree of

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stress categorizing in mild moderate and severe, where higher the level of stress and more the relative risk of cancer mortality(12).

A previously reported study was conducted through telephonic survey of newly diagnosed breast cancer patients to evaluate association of major life stressors within two years. A total of 222 patients were included and 51.3% reported stressors in the recent past. Great majority had family related stressor while considerable number (ie 21%) had financial worries. This was an interesting study in a way supporting our study results where death of a close relative came up as one of the major trauma while financial stress was not included in our study(13).

Following Houston hurricane a survey was conducted which explored allergy and stress in the affected population. Results suggested that the affected population showed higher rate of allergies and high stress score(14). However association with cancer or longer follow-up of the population was not done as part of the study.

A large number of studies have been conducted looking at the psychological stress among cancer survivors and those undergoing treatment of cancer (ie chemotherapy, radiotherapy). However, there is limited literature available looking at the association of major psychological trauma as a risk factor for development of cancer. On the other hand, Post-traumatic Stress disorder(PTSD) is one of the known psychological trauma response seen. Even early life stresses have been linked with immunological and metabolic abnormalities later in life(15).

Meta-analysis and systematic review of 11 studies showed a moderate rise in breast cancer risk after going through a stressful life event(16). Work stress is a form of chronic stress where colorectal cancer, lung cancer, esophageal cancer have been reported to be significantly associated. These results were concluded in a meta-analysis of observational studies with pooled analysis of 281,290 participants(17). Another study not only confirmed association of stress with risk of breast cancer but also suggested a dose response fashion(18), higher the stress level higher the risk of breast cancer. However, work stress was not explored in our study but its seems like chronic stressful environment has strong association with development of cancer. Another nested case- control study was conducted exploring association of post-traumatic stress disorder in different cancer groups but the results were not significant in correlating PTSD and cancers(19). The duration of the PTSD and coping strategies were not focused, which might have influenced these results.

## CONCLUSION

Emotionally traumatic events specially death of a close relative appears to be associated with high risk of cancer development. It is therefore required to provide appropriate psychological support to high risk population. Further studies with long term follow-up and interventional studies to minimize the risk and understanding of pathogenesis of the association of stress and psychological stress will be required.

**Ethical Consideration:** Informed consent was taken from all the patients, the codes were used for data collection. Names of the patients or any kind of identity was not mentioned in questionnaire or any other form of data.

**Conflict of Interest:** There is no conflict of interest.

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