RESEARCH ARTICLE

Relationship Between Locus of Control Belief and IL-6 in Breast Cancer Patients

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ABSTRACT

Recent studies indicated to the immune disturbances in cancer patients in comparison with healthy individuals. Several studies suggested that individuals with external locus of control (E-LOC) have more symptoms of depression. Other studies indicated to the effective role of psychological status on the immune system. The association between E-LOC and immunity in cancer patients it is not clear. Study the relation between Rotter internal-external locus of control (I-E LOC) and God health locus of control (GHLC) and interleukin-6 (IL-6) in breast cancer patients. The study included hundred breast cancer patients and fifty healthy controls. Patients and participators responded to I-E LOC and GHLC questionnaires. Peripheral blood samples were collected to measure gene expression of IL-6 by using real time PCR. Breast cancer patients showed higher GHLC which was associated with higher level of IL-6 as compared to control subjects. By contrast, a significant inverse correlation between GHLC and IL-6 was found. However, there was no relationship between I-E LOC and IL-6. The results suggest no significant effect of LOC belief according to life on immune response against cancer, but high GHLC belief correlate with decreased IL-6. Further studies on the relations between other types of LOC and immune response in breast cancer is recommended.

Keywords: locus of control, breast cancer, IL-6.

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INTRODUCTION

Cancer is one of the major leading cause of death all over the world (Jemal *et al.,* 2008). It has a negative effect on immune system as it causes loss of T cell specific, non-specific recognition and altered natural killer (NK) cells. It also associates with functional inhibition of macrophages and dendritic cells as well as increases in the recruitment of T regulatory (T_{reg}) cells, myeloid-derived suppressor cells (MDSC) and monocytes (Jewett and Tseng, 2011).

Cancer is not affected only by biological factors but also by psychological factors which are known to have significant impact on the immune responses to cancer (Saxton *et al.,* 2014). With this regard, one study on breast cancer suggested that women with depression symptoms showed suppressed immunity (Turner-cobb *et al.,* 2000). High inflammatory cytokines are characteristic of both depression and cachexia. The effects of cachexia can be more deleterious than the tumor growth itself, where thirty % of all patients with cancer die as a result of cachexia (Pirisi, 2000).

Previous studies have suggested a relationship between locus of control and depression. For instance, one -study indicated to an overall inverse

relationship between spiritual well-being and depression has been reported (Holt *et al.,* 2003). Another study also suggested that, awareness of God is associated with a better health (Ryan and Francis, 2012). Specifically, external locus of control (E. LOC) belief is often related to more symptoms of depression than internal locus of control (I-LOC) (Gibson *et al.,* 2013). Accordingly, it can be suggested that there is a relation between LOC belief and immune status in cancer patients.

This study was aimed to investigate the relationship between I-E LOC and GHLC belief with IL-6 in breast cancer patients as compared to control subjects.

MATERIALS AND METHODS

Participants included 100 females (40-60 years old) with breast tumor at different stages. Participants were recruited from Damanhur Cancer Center and Tanta University Hospital, Egypt. Exclusion criteria included neurological disorders, ill conditions that affect immune status, diagnoses with another type of cancer, any anti-cancer treatment (chemotherapy, radiation, surgery) or any drugs that affect the immune system. Control subjects included 50 healthy females (40 to 60 years old), who were not diagnosed for any illness condition that affects the immune status or any psychological disorders. The research was approved by the ethical committee at Cairo University, Egypt.

Rotter internal-external locus of control (I-E LOC) scale

Rotter I-E LOC scale was used to measure LOC belief according to general life. It differentiates participants on one axis (internality-externality). High degree in I-E LOC means high E-LOC and low degree means high I-LOC (Rotter, 1966).

Questionnaire of God health locus of control (GHLC)

GHLC consists of 6 questions, which measures to what extent individual believes that God controls health. It is considered as a type of E-LOC. Each question ranged from 1= strong disagree to 6= strong agree. The total score ranges from 6 to 36 (Wallston *et al.,* 1999).

Gene expression assay

RNA extraction was done by the Gene JETTM whole blood RNA purification mini kit. RNA was quantified in a single step assay by thermo scientific verso SYBER Green 1-step QRT-PCR kit plus ROX vial. Briefly, 500 µl of blood samples was centrifuged, the supernatant was discarded, and the pellet was lysed in 600µl lysis buffer. The lysate cells were washed by washing buffers. Then RNA was dissolved in RNA free water and stored at -80^{o}C until use. Master mix was prepared by adding enzyme mix, 1-step QPCR SYBER `mix, RT enhancer, forward primer and reverse primer of IL-6 (Table 1). The cycling conditions were cDNA synthesis at 50^{o}C for 15 min, thermo-start activation at 95^{o}C for 15 min, denaturation at 95^{o}C for 15 min, annealing at 95^{o}C for 15 min and extension at 72^{o}C for 30 sec. The relative level of mRNA expression of IL-6 was calculated based on ΔΔCT method and normalized to mRNA level of the house keeping gene β2 macroglobulin.

Table (1): Primer used in measuring gene expression

Gene	Sequence
B2 macroglobulin (Forward)	CCCCCACTGAA
B2-Microglobulin (Reverse)	TCATCCAATCCA
IL-6 (Forward)	GCCAGAGCTGT
IL-6 (Reverse)	AGGAACTCCT

Statistical analysis

Statistical presentation and analysis of the present study was analyzed by one-way ANOVA and bivariate co-relation by SPSS V.20

Table (4): Correlation between locus of control and IL-6 in breast cancer patients group

Locus type	Correlation coefficient	IL-6
I-E LOC	r	-0.38
GHLC	r	-0.67*

*: Significant at p ≤ 0.05. GHLC: God health locus of control, I-E LOC: internal–external locus of control.

Table (2): Locus of control belief in healthy control and cancer breast patient's groups

Group	GHLC	I-E LOC
Controls	26.69 ± 0.92	8.44 ± 0.58
Patients	32.13 ± 1.15*	9.63 ± 0.38

*, Significantly different as compared to other group (p < 0.05).

RESULTS

Locus of control belief in healthy and cancer breast patients.

This research studied Rotter I-E LOC and GHLC in healthy control and cancer breast patients. The results showed that patients had significantly higher GHLC than control subjects

Table (3): Pro-inflammatory cytokines in healthy control and cancer breast patients

Group	IL-6
Controls	1.00
Patients	2.19 ± 0.26*

*, Significantly different as compared to control (p < 0.05).

(Table 2), while they did not significantly different with regard to I-E LOC.

IL-6 in healthy control and cancer breast patients.

We then analyzed IL-6 expression in patients with breast cancer and control subjects. The results showed that patients had significant higher level of IL-6 than controls (Table 3).

2. Correlation between locus of control and pro-inflammatory cytokines in breast cancer.

We then analyzed the correlation between locus of control belief and **IL-6** in breast cancer patients. The results showed that significant inverse correlation between GHLC and IL-6 (Table 4).

DISSCUSSION

In the present study the LOC of breast cancer patients was correlated to the level of IL-6. LOC belief was assessed by I-E LOC and GHLC scales. The gene expression of IL-6 was assessed by real time PCR. Both I-E LOC and GHLC belief and IL-6 were studied in breast cancer patients and compared to control subjects.

When healthy controls and breast cancer patients were compared, no significant difference was found with regard to I-E LOC between patients and controls. However, it was observed that patients showed higher GHLC than healthy controls. Similar finding was concluded in a previous study which suggested that women with breast cancer are higher GHLC belief than healthy women (Iskandarsyah *et al.,* 2014). These data suggest that facing serious diseases such as cancer call for increasing needs for external support.

Regarding to IL-6, it was found that patients express higher serum levels of IL-6 than healthy controls. These results are consistent with a previous study, which suggested that IL-6 is dramatically up-regulated in breast cancer patients in comparison with healthy controls (Nariţa *et al.,* 2011). In addition, another study on breast cancer patients indicated that high levels of IL-6 is associated with poor overall survival (ShuChen *et al.,* 2015).

By correlating the relationship between IL-6 and LOC, it was found that there is no significant correlation between I-E LOC and IL-6. By contrast, there was a significant inverse correlation between GHLC and IL-6. These data would suggest the external support to cancer patients may require adjuvant therapy to correct the balance in immune system. It also suggests that GHLC belief itself is important for

a healthy immune response in breast cancer since IL-6 was found to be associated with poor clinical outcomes in breast cancer patients (Ravishankaran and Karunanithi, 2011). To the best of our knowledge, the present study is the first to investigate the relationship between GHLC belief and IL-6.

In conclusion, although there was no significant difference in LOC belief according to general life between healthy control and patients, cancer patients expressed higher belief in God belief as a controller of their health than healthy controls. Also patients had higher IL-6 expression than healthy controls. As such, both IL-6 and GHLC belief might be important factors in response of cancer patients to combat this disease.

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