

# Statistical Association Between Age Groups, Body Mass Index and Cancer Grade with Serological Concentrations of Immunological Biomarkers (Interleukin IL-1 $\beta$ , IL-6) among Females with Breast Cancer

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## ABSTRACT

Statistical association between age groups, body mass index and cancer grade with serological concentrations of immunological biomarkers (interleukin IL-1B, IL-6) among females with breast cancer was carried out in this study. The total number of breast cancer patients involved in this study are 80 individuals were taken from Basrah oncology center in Basrah province, the age of patients ranging from 20–80 years and 80 individuals considered as control group after they were checked and confirmed to be free from any chest or any other health problems. the lowest rate of breast cancer females was found within the age groups 20–29 years (2.5%), and highest rate in age group 50 to 59 years (32.5%). The levels of Interleukin 1 beta (IL-1 $\beta$ ) pg/mL were (5.04 pg/mL) in (>60) years and 2.87 pg/mL in age 20–29 yrs., with significant differences. The levels of IL-1 $\beta$  fluctuated between stages with high value in stage IV was (2.675 pg/mL). The levels of interleukin IL-6 were high value in (>60) years (6.65 pg/mL) with  $p = 0.01$ . The levels of IL-6 show high value in stage IIIC (18.5650 pg/mL). The mean of IL-6 pg/mL with body mass index, shown overweight recorded (6.797 pg/mL).

**Keywords:** Age group, BMI, Breast cancer, Cancer grade, IL-1B, IL-6, Statistical analysis.

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## INTRODUCTION

In Iraq, breast cancer is the most common type of malignancy in women, it accounts for one third of the registered female cancers according to the latest Iraqi Cancer Registry.<sup>1</sup> There was an increase in the incidence rates of breast cancer within the last two decades, which became one of the major threats to Iraqi female health.<sup>2</sup> Worldwide, breast cancer is the second most common type of cancer and the fifth most common cause of cancer death. Breast cancer usually originates in the cells of the lobules (lobular carcinoma) or ducts (ductal carcinoma) of the milk glands, or, much less commonly, in the stromal tissue (fatty and fibrous connective tissue of the breast).

Cancer immune surveillance is an important process by which the immune system is able to monitor, recognize, and eliminate nascent tumor cells.<sup>3,4</sup> Early proof of this was noted by pathologists who recognized that many patient tumors were densely infiltrated by innate and adaptive immune cells.<sup>5</sup> Recent studies demonstrate that these immune cells are indeed mounting an antitumor response and that tumors develop mechanisms to combat an immune response.<sup>6,7</sup>

The present study aimed to determine the Statistical association between age groups, body mass index (BMI) and cancer grade with serological concentrations of immunological biomarkers (interleukin IL-1B, IL-6) among females with breast cancer.

## MATERIALS AND METHODS

### Breast Cancer Cases

Breast cancer cases in this study (case\control study) have been collected in Basra province particularly from Basra oncology center during the period extended from January to May 2021. Medical information for patients were recorded in questionnaire paper that included name, age, residency and marital status breast cancer females who are in the early stages, the second stages, and the last stages after taking all the treatments, both patients and control samples that investigated in this study have age ranged between 20 to 80 year.

### Serological Detection of IL-1 $\beta$ , IL-6

Sandwich ELISA test was used for detection the titer of IL-1B, IL-6, Ag's in serum samples for both patients and controls by

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**Table 1:** The number and percentages of patient with breast cancer and control group according to age groups.

Age groups	Breast cancer		Control		p-value
	No.	%	No.	%	
20–29 year	2	2.5	2	2.5	0.0163
30–39 year	10	12.5	8	10.00	
40–49 year	25	31.25	23	28.75	
50–59 year	26	32.5	24	30.00	
>60 year	17	21.25	23	28.75	
Total	80	100%	80	100%	

P = 0.0163,  $\chi^2 = 20.50$ , Df = 1

**Table 2:** IL-1 $\beta$  concentration among patients with breast cancer and control groups in various age group.

Age Groups	Breast cancer patients		Mean of IL-1 $\beta$ pg/mL	Control group		Mean of IL-1 $\beta$ in control pg/mL	Standard value pg/mL
	No.	%		No.	%		
20–29 year	2	2.5	2.87	2	2.5	(0.2 – 0.57)	0.5
30–39 year	10	12.5	3.485	8	10.00		
40–49 year	25	31.25	4.168	23	28.75		
50–59 year	26	32.5	4.733	24	30.00		
>60 year	17	21.25	5.049	23	28.75		
Total	80	100%	80	100%			

p-value = 0.03669, F ratio = 0.81, DF = 1

**Table 3:** IL-1 $\beta$  levels and various stage of patients with breast cancer.

Stages of Breast Cancer	Breast Cancer No	%	Mean of IL-1 $\beta$ pg/mL
IA	2	2.5	0.4
IB	1	1.25	2.60
IIA	22	27.5	1.709
IIB	21	26.25	1.523
IIIA	19	23.75	1.405
IIIB	3	3.75	2.166
IIIC	2	2.5	1.400
IV	10	12.5	2.675

F Ratio= 0.9153, DF= 7, P-value = 0.4998

using Elabscience American ELISA kit composed of 96 well microtiter plate. The procedure of this test was done according to kit manufacture instructions.

## RESULTS

The total number of breast cancer patients involved in this study are 80 individuals from Basrah oncology center in Basrah province, the age of patients ranges from 20 to 76 yrs and (80) individuals considered as control group after they were checked and confirmed to be free from any chest or any other health problems. Microsoft Excel version 2010 and JMP Pro version 13.5.2 were used to analyzed statistical differences between variants, the data of all patients were used to build a general classification model for breast cancer. The system offer an effect summary that examine each demographic factors that have an importance across multiple responses.

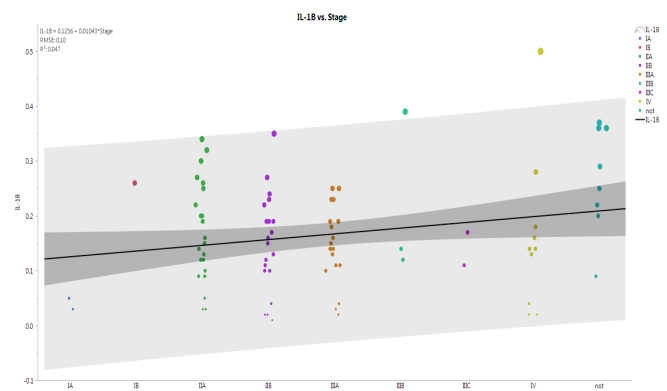
### 1- Distribution of Patients within Various Age Groups

Table 1 show the minimum number of breast cancer females was found within the age groups 20 to 29 years (2.5%), followed

**Table 4:** IL-1 $\beta$  various body mass index of patients with breast cancer

Body Mass Index	Breast Cancer No	%	Mean of IL-1 $\beta$ pg/mL
Underweight	3	3.75	0.1850
Normal	27	33.75	0.1806
Overweight	36	45.0	0.1536
Obese	14	17.5	0.1592

F Ratio = 0.0909, DF = 3, P-value = 0.9648



**Figure 1:** Show regression line of IL-1 $\beta$  levels according to various stages of patients with breast cancer

by age group 30 to 39 years (12.5%, above 40 to 49 years (31.25%), the age group 50 to 59 years (32.5%) and >60 years (21.25%) (p-value < 0.0163) (Table 1).

### IL-1 $\beta$ Concentration Among Studied Groups in Relation to Age Group

Table 2 shows the levels of interleukin IL-1 $\beta$  pg/mL among patients with breast cancer and control groups in various age group that show the age group (20–29) years (2.87 pg/

**Table 5:** IL-6 concentration among patients with breast cancer and control groups according to various age group.

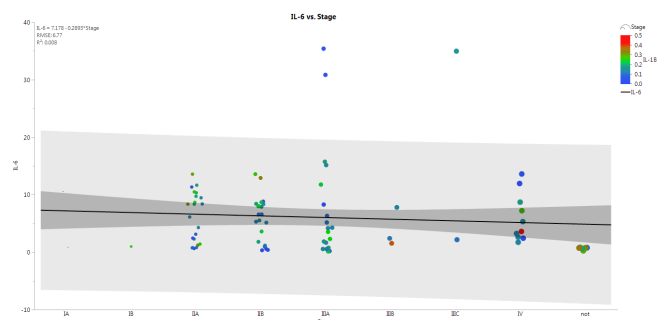
Age Groups	Breast Cancer patients		Mean of IL-6 pg/mL	Control group		Mean of IL-6 in control pg/mL	Standard value pg/mL
	No.	%		No.	%		
20–29 year	2	2.5	4.69	2	2.5		
30–39 year	10	12.5	4.97	8	10.00		
40–49 year	25	31.25	6.30	23	28.75	(0.48 – 0.82)	(0.15-0.5)
50–59 year	26	32.5	6.28	24	30.00		
>60 year	17	21.25	6.65	23	28.75		
Total	80	100%		80	100%		

p value = 0.01599, F ratio = 1.97, DF= 1

**Table 6:** Show IL6 levels in various stage of patients with breast cancer.

Stages of Breast Cancer	Breast Cancer No	%	Mean of IL-6 pg/mL
IA	2	2.5	5.6950
IB	1	1.25	0.9800
IIA	22	27.5	6.0977
IIB	21	26.25	5.8324
IIIA	19	23.75	7.8189
IIIB	3	3.75	3.9100
IIIC	2	2.5	18.5650
IV	10	12.5	6.0370

F Ratio = 1.2072, DF = 7, p –value = 0.3100



**Figure 2:** Regression line of IL-6 levels according to various stages of patients with breast cancer

mL) followed by (30-39) years (3.485 pg/mL), continued with (40–49) years (4.168 pg/mL), (50–59) years (4.733 pg/mL) and (>60) years (5.049 pg/mL) with p-value = 0.03669.

### IL-1β Various Stage of Patients with Breast Cancer

Table 3 and Figure 1 show the levels of IL-1B with stages of breast cancer in IA and IIIC 2 mean of IL-1B are (0.4) and (1.400) pg/mL respectively, IB recorded (2.60 pg/mL), followed by IIA (1.709 pg/mL), IIB (1.523 pg/mL), and IIIA (1.405 pg/mL), the IIIB (2.166 pg/mL) and the last stage IV was (2.675 pg/mL) with p-value = 0.4998.

### IL-1β various body mass index of patients with breast cancer

Table 4 shows the mean of IL-1B pg/mL various body mass index, overweight group recorded (0.1536 pg/mL), followed by underweight (0.1850 pg/mL) and normal (0.1806 pg/mL) with p-value = 0.9648.

**Table 7:** Means of IL-6 concentrations patients with breast cancer according to various body mass index

Body Mass Index	Breast C No	%	Mean of IL-6 pg/mL
Underweight	3	3.75	2.831
Normal	27	33.75	4.629
Overweight	36	45.0	6.797
Obese	14	17.5	8.719

F Ratio = 0.7924, DF= 3, p-value = 0.5018

### IL-6 Concentration among Studied Groups in Relation to Age Group

Table 5 shows the levels of interleukin IL-6 pg/mL among patients with breast cancer and control groups in various age group that show the age group (20-29) years (4.69 pg/mL) followed by (30–39) years (4.97 pg/mL), continued with (40–49) years (6.30 pg/mL), (50–59) years (6.28 pg/mL) and (>60) years (6.65 pg/mL) with p-value = 0.01599.

### IL-6 Concentration among Patients with Breast Cancer According to Cancer Stage

Table 6 and Figure 2 show the levels of IL-6 with stages of breast cancer in IA and IIIC 2 recorded concentration mean IL-6 (5.6950) and (18.5650) pg/mL respectively, IB show (0.9800 pg/mL), followed by IIA (6.0977 pg/mL), IIB (5.8324 pg/mL), and IIIA shows (7.8189 pg/mL), the IIIB (3.9100 pg/mL) and the last stage IV (6.0370 pg/mL) with p-value = 0.3100.

### IL-6 Concentration among Patients with Breast Cancer According to Various Body Mass Index:

Table 7 shows the mean of IL-6 pg/mL various body mass index, shown overweight (6.797 pg/mL), followed by underweight (2.831 pg/mL) and normal (4.629 pg/mL) with p-value = 0.5018.

## DISCUSSION

From total number of 80 patients with breast cancer, eighty women regarded as control group without any chest problems were also studies. Most of the disease was in age group 50 to 59 years (32.5%), and the lowest infection was in age 20 to 29 years (2.5%) with significant differences ( $p \leq 0.05$ ). This result was similar with other studies.<sup>8</sup> This result is due to modifiable risk factors; and non-modifiable risk factors that is increased risk of breast cancer among participants from Asia was associated

with older age. Breast cancer is the malignant tumor that forms from the uncontrolled growth of abnormal breast cells. It usually affects tissues involved in milk production (Ductal and lobular tissues). It is the most common malignancy in women, and it remains one of the greatest health threats facing women around the world as we enter the 21<sup>st</sup> century.

Interleukin IL-1 $\beta$  is a pro-inflammatory cytokine whose expression in primary tumors has been identified as a potential biomarker for predicting breast cancer patients at increased risk for developing bone metastasis. Interleukin- IL- 1 $\beta$  is the prototypical proinflammatory cytokine<sup>9</sup> and its expression in most tumors correlates with tumor invasiveness and metastasis, as well as with angiogenesis.<sup>10</sup> Several studies have shown how IL-1 $\beta$  may contribute to breast cancer development and metastasis among it multiple effects, IL-1 $\beta$  activates a hypoxia-angiogenesis.<sup>3,9</sup> The finding of IL-1 $\beta$  concentration was higher (5.049 pg/mL) in age group (>60) years comparative with (2.87 pg/mL) and (0.2–0.57) in age group (20–29) and control group respectively with significant differences. Similar study showed that the highest mean level of IL-1 $\beta$  was found in women with breast cancer comparing with healthy control women (36.92  $\pm$  11.1 and 10.1  $\pm$  3.7 pg/mL) respectively (p  $\leq$  0.05).<sup>11</sup> Cheung, *et al.*,<sup>12</sup> recorded higher level of IL-1 $\beta$  in patients with breast cancer which agreement with our study.

IL-6 in particular has been shown to play a large role in the inflammatory process following nerve injury and has been implicated in the initiation and maintenance of neuropathic pain.<sup>13,14</sup> However, IL-6 activity is dependent upon the distribution of receptors on specific cell types to which it can bind. The distribution of membrane-bound (IL-6R) receptors, to which IL-6 can bind directly, is fairly limited throughout the body, existing mainly on hepatocytes and certain subsets of leukocytes. In contrast, IL-6 can complex with soluble receptor IL-6R (sIL-6R) to activate the signal transducing receptor, gp130, which is expressed nearly ubiquitously among all cell types.<sup>15-17</sup> Our study revealed that the mean of IL-6 was (5.77 pg/mL) in patients with breast cancer women high than healthy control women (0.48–0.8) pg/mL, and the mean was elevated to (6.65 pg/mL) in age group > 60 years.

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