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## DETECTION OF CIRCULATING NK CELLS IN BREAST CANCER PATIENTS UNDER CHEMOTHERAPY IN AL HILLAH CITY, IRAQ

Mustafa Jawad Abed Al-Imari\*, Fuad Ghazi Hassan, Laith A.I.K. Al-Kaif, Saif Anwar Jaafar, and Haider Abdulameer Al-Asady

Department of Medical Laboratory Technique, Al-Mustaqbal University College, Babylon, Hilla, Iraq

\*Corresponding E-mail: [mustafaalammary85@gmail.com](mailto:mustafaalammary85@gmail.com)

### ABSTRACT

The natural killer (NK) cells role has been investigated in the therapy of many cancer types and in breast cancer but little information is known about the effect of chemotherapy on circulating CD56 marker of NK cells in plasma of chemotherapy patients. A total of 24 plasma sample of breast cancer patients were compared with 24 plasma sample of apparently healthy control, the CD56 concentration was detected by Elabscience ELISA kit from Elabscience. The demographic data revealed the mean±SD age of breast cancer cases was 51.16±8.91. The mean±SD of CD56 concentration for breast cancer patients and apparently healthy control was 72.76±30.5, 53.19±12.66 respectively. There were significant differences between patients and control at probability P = 0.0057. The level of NK cells was elevated in breast cancer patients compared to the control group due to chemotherapy which increase the proliferation of these cells to overcome cancer.

**Keywords:** CD56, NK cells, Breast cancer, cancer chemotherapy.

### Introduction

Cancer is the second leading cause of death globally and classified as a single leading cause of death in many countries in the 21st century. The report of (WHO) in 2015 reported the cancer is primary or second leading cause of premature death 70 years in 91 of 172 countries, and ranked third or fourth in 22 additional countries (Bary *et al.*, 2018). The morbidity and mortality of cancer in Iraq show a horrible results in increased incidence of breast cancer (4,542) cases in female annually, The mortality 9,000 deaths in female annually 1 in 6 women worldwide develop cancer during their lifetime, 1 in 11 women die from the disease (WHO, 2018).

Natural killer (NK) is a lymphoid cells play an important role in innate immunity as effectors against virus-infected cells and tumor cells (Wulff *et al.*, 2009). In human NK cells can be divided into two functional subgroups, CD56<sup>bright</sup> immune cells and cytotoxic CD56<sup>dim</sup> NK cells and representing 10–20% of peripheral blood mononuclear cell and localized in peripheral blood, lymph nodes, spleen, and bone marrow. It can be induced to migrate toward inflammation sites by different chemoattractant (Rebuli *et al.*, 2018).

CD56 was considered biomarker for NK cells (Oboshi *et al.*, 2016). NK cells can express a lytic action able to kill target cells independently from any previous activation (Krzewski and Coligan, 2012). A decrease in NK cell infiltration into tumor tissue might be a predictive marker for failure of chemotherapeutic treatment in breast cancer (Garcia-Chagollan *et al.*, 2018). In squamous cell carcinoma patients it was reported a very weak NK antibody defense against cancer cells (Sotille *et al.*, 2019). So the study of

circulating NK cells roll in cancer is very important and promising to introduce immunotherapy for most cancer types (Hu *et al.*, 2019). The present study aimed to evaluate the plasma level of NK cells in breast cancer patients under chemotherapy compared to apparently healthy control groups.

### Material and Methods

**Study design:** case control study was conducted throughout the period of January 2019 to March 2019 to assess NK cells among breast cancer patients in Babylon city.

**Study samples:** A total of 24 plasma sample of breast cancer patients subjected to chemotherapy were compared with 24 plasma sample of apparently healthy control, the plasma samples was collected from cases referred to Babylon tumor center in Marjan medical city in Babylon province. The direct contact with patients were avoided because the Iraqi patients with cancer suffering depression (Alkediry and Drub, 2016).

**Study instrument:** the CD56 concentration was detected by Elabscience ELISA sandwich kit from Elabscience<sup>®</sup>, China. The optic density on 450 nm of reactants was obtained by BioTek<sup>®</sup> Instruments, USA.

**Statistical analysis:** Data are analyzed through using the Statistical Package of Social Sciences (SPSS, Version 16.0). The mean, standard deviation, t test and confidence intervals was performed through SPSS. The comparison of two means to calculate significance probability value (P-value) was analyzed in the present study.

**Ethical approval:** the ethical statement of all study cases were approved by ethical committee in Al Mustaqbal

University College and In accordance with the instructions of the Ethics Committee in the Health presidency of Babylon.

**Results**

**Demographic data:** a total of 24 cases suffering breast cancer were enrolled in the present study, all cases sex were female and compared also with female as control. The mean±SD age of patients were 51.16±8.91 years at 95% confidence interval from 47.4 to 54.9. The age range of cases from were 37 to 63 year.

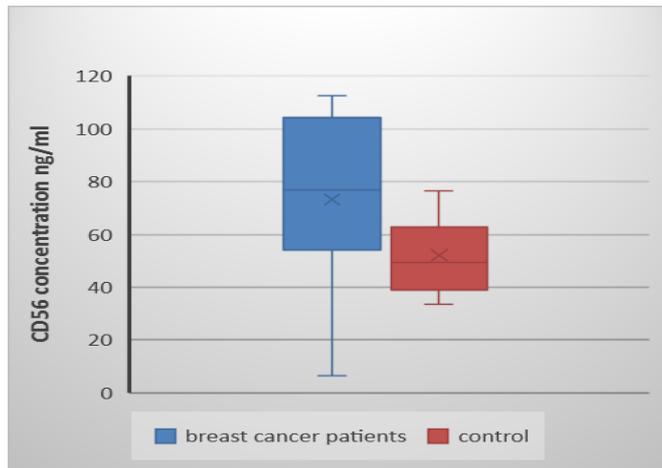
**Concentration of CD56:** the plasma level concentration of CD56 was detected in all study groups; patients and control. The mean±SD of CD56 concentration for breast cancer patients and apparently healthy control was 72.76±30.5, 53.19±12.66 respectively. There were significant differences between patients and control at probability P = 0.0057. (Table 1)

**Table 1:** Distribution of Human CD56 among study population; breast cancer cases and apparently healthy control

Study groups	Mean CD56 ng/ml	SD	P-value
Breast cancer cases n=24	72.76	31.19	0.0057**
Healthy Control n=24	53.19	13.52	

\*\* (P<0.01), SD: standard deviation, ml: milliliter, P-value probability value

The present finding revealed clearly high level distribution of CD56 in breast cancer patients subjected to chemotherapy compared with apparently healthy control error bar graphic (figure 1).



**Fig. 1 :** Graphic of error bar distribution of CD56 concentration for breast cancer patients and healthy control

**Discussion**

Breast cancer is the most common malignancy in women and the principal cause of death from cancer among women globally (Torre *et al.*, 2017). Previous studies and the recently studies have reported that functional activity of NK cells is decreased and apoptosis in patients with cancer (Taouk *et al.*, 2019). In contrast, increased NK-cell numbers and NK activity have also been reported in breast cancer and colon cancer before neo-adjuvant immunotherapy and

correlated to time to treatment failure (Mozaffari *et al.*, 2007; Qin *et al.*, 2017).

No all chemotherapies can induce the CD56 in breast cancer, the study of Mitsis *et al.* (2018) was concluded the treatment of breast cancer cells with serotonin may represent a novel therapeutic but cannot increase the expression of CD56 and CD15.

The study of Itoi *et al.* (2019) explain the infiltration of a small number of CD56-positive natural killer cells and accumulated at the tumor site after dosing with chemotherapy Trastuzumab Tz and suggest that Tz therapy induces adaptive cellular immunity into the breast carcinoma lesion.

It was concluded that the immunotherapy with dendritic cells and cytokine-induced killer cells combined with chemotherapy administration resulted in advanced therapy for non-small cell lung cancer (Zhao *et al.*, 2019). The study of NK cell role in many cancer types have being promising, Further studies are required to improve the expression of CD56 before and after chemotherapy for breast cancer.

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