International Journal of Psychosocial Rehabilitation, Vol. 24, Issue 04, 2020
ISSN: 1475-7192

# Relationship between ABO Blood group and Chronic Myeloid Leukemia with the Role of the Oxidative Stress as Risk Factor

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***Abstract***- *Chronic myeloid leukemia characterized by the expansion of a clone of hematopoietic cells that carries the Philadelphia chromosome (Ph). The Ph chromosome results from a reciprocal translocation between the long arms of chromosomes 9 and 22, t (9;22). The aim of study are to find if there is an association between blood groups and chronic myeloid leukemia and to study some of the causes that may be lead to this association .Also , it aim to determine the role of the oxidative stress as risk factor. Ninety persons include in the study (45 as patient and 45 as control group). Where the patient suffering from CML, the control are free from this disease. There are ranged from (21-60) years old where they are divided in to four group according to blood group (A, B, AB, and O). This study is based in case control study done in the middle Euphrates center for cancer in Al-Najaf city from December 2018 to April 2019. The sera were collected from the 90 persons and analyzed by using enzyme linked immunosorbent assay (ELISA) for MDA and GSH. The results of the study show that blood group O (44%) predominates in CML patients group followed by blood group A (22%), B (18 %) and AB (16%). The mean serum level MDA value shows highly significance at (P<0.001) change in the patients group in comparison with control. Also show that the level of MDA in male (900. 99 ± 603.89) is significantly higher than in female (582.28 ± 562.29). The mean serum level of GSH show that significant decrease at (P<0.05) in patients group (40. 12 ± 27.33) than in control groups (55.20 ± 28.79). As a conclusion from this study, the importance of MDA and GSH in CML patients can be used to detect the complications related to the among these patients.*

***Index Terms***- *ABO, CML, Oxidative stress.*

## I. INTRODUCTION

Chronic myeloid leukemia is a clonal myeloproliferative disorder of primitive hematopoietic progenitor cells. The BCR-ABL tyrosine kinase produced by the t(9;22)(q34;q11) translocation fuses the parts of the q arm of chromosome 9 to the q arm of chromosome 22, creating a hybrid BCR-ABL gene, also known as the Philadelphia

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**Received: 15 Jan 2020 | Revised: 5 Feb 2020| Accepted: 30 Mar 2020** 

chromosome and initiates the event of CML (Hochhaus *et al.*,2017). The mechanism whereby the (9:22) translocation occurs is unknown, although some studies suggest that oxidative stress may be involved in the genesis of CML. Moreover, BCR-ABL positive cells are a source of reactive oxygen species (ROS), which cause oxidative DNA damage and may contribute to the formation of additional abnormalities leading to disease progression to the more advanced stages (accelerated and blast crisis phases) (Shu *et al.,* 2018). Chronic myeloid leukemia occurs very rarely in children. In the Western world, the median age of onset is 50–60 years, which reflects the average age of the population. Although symptoms at presentation may include lethargy, weight loss, unusual bleeding, sweats, anemia, and splenomegaly, in more developed countries, 50% of patients are asymptomatic and are diagnosed as a consequence of blood tests performed for unrelated reasons. The incidence of CML is approximately 1-2 per 100,000 population per year. Males are affected more than females in CML, with a 2:1 ratio (Perrotti *et al.,* 2010). Oxidative stress is often described as a self-propagating phenomenon on the basis of observations that when oxidative stress–induced excessive ROS release triggers cellular damage, damaged macromolecules themselves may behave as and/or become ROS. Oxidative phosphorylation occurring in the mitochondria is a major source of ATP. As a by-product, this process produces free radicals or reactive oxygen species (ROS), reactive nitrogen species (RNS), and carbon- and sulfur-centered radicals (Salim, 2017). The ABO blood group system consists of four basic groups, namely A, B, AB, and O, depending on the presence of the A and B antigens. These antigens are controlled by three allelic A, B, and O genes located on the long arm of chromosome 9The blood groups in the Rhesus system are classified as Rh− and Rh+, depending on the presence of the Rhesus D antigen located on the red blood cell surface (Mitra *et al.,* 2014). The ABO blood group has been associated with a number of diseases or hemostatic complications. For example, meta-analyses have detected associations between increased risk of coronary heart disease, and venous thromboembolism and the non-type O blood types (Zhou & Welsby, 2014). The first report describing a link between the A antigen and increased risk of stomach cancer was published in 1953(Rummel & Ellsworth, 2016). Other recent studies have reported the association between blood groups O and A individuals with increased incidence of duodenal ulcers and gastric carcinoma as well as, the association of B group type and pancreatic cancer, Hodgkin's lymphomas and cardiac cancer. Therefore, blood group antigens on the surface of cancer cells can be used as useful prognostic and diagnostic markers in different types of human cancers (Rummel & Ellsworth, 2016).

## II. Materials and Methods

**Patients :**

A case control study conducted at Middle AL-Furat Center for cancers in Al-Najaf Al-Ashraf city-Iraq, from the period of November (2018) to April (2019). This study include (45) patients (Male 30 and female 15), who were selectively collected and were suffering from chronic myeloid leukemia that sample taken. Their ages ranged from (20 to 60) year old. Patient are divided into four groups according to blood type (group A, group B, group AB, group O) and divided according age groups into two groups (20-40 and 41-60).

**Control :**

Forty-five apparently healthy were selected as the control, the patient and controls (N: 90) were age and sex matched. All control group was had no family history of disease.

**Sample collection:**

5 ml of blood samples were collected from CML patients and healthy control. A tourniquet was applied directly on the skin around the arm, the skin over the vein was sterilized with ethyl alcohol 70%, and then blood was collected by syringe. The sample divided into two part the first (2ml) transfer to EDTA tube for determination of ABO blood group and second part transfer to gel tube then left for 30 min at room temperature to clot, centrifuged at 3000 rpm for 10 min to get the serum for (MDA&GSH) estimation. The serum was separated and stored at -80 C until use for ELISA.

**Immunological Assays :**

The study parameters estimated by ELISA kit ,the biochemical kits used in the study for MDA and GSH performed by **Elabscience company (USA)**.

**Statistical Analysis :**

The data was collected and transfer to statistical analysis using SPSS program (V. 23) in including the test of two independent -t- test to find the variances between study group. The results expressed as (Mean ± SD). P value at <0.05 was considered statistically significant and highly significant at P<0.001.

## III. Results and Discussion

The mean serum level MDA value shows highly significance (P<0.001) change in the studied groups in comparison with control. Table (1) show that the level of MDA in male (900. 99 ± 603.89) is higher than in female (582.28 ± 562.29). In the table the mean serum level of GSH show that significant decrease (P <0.05) in patients group (40. 12 ± 27.33) than in control groups (55.20 ± 28.79). In addition, the table show that the level of GSH in male is high (42.30 ± 29.04) in comparison with female (35.77 ± 24.94). Table (2) show that blood group B of patients has a significant increasing in the level of serum MDA (1387.07±520.89) in comparison with other blood groups in patients and blood group O(447.27±260.58) of controls also has a significant increase in the level of serum MDA in comparison with the other blood groups of controls. In addition, the table show the level of GSH in different blood groups for patient and controls, which refers to that blood group A (53.23±12.76) has high level of serum GSH in comparison with other blood groups of patients. In addition, the table show that blood group AB (81.87±5.50) of controls has high level of serum GSH in comparison with other blood group of controls. The results show that blood group O predominates in the study groups (patients and controls), (44%) followed by blood group A (22%), B (18) %) and AB (16%) (Table 4.1). These result agree with study done in Kurdistan by Mohammed (2010) who found that blood group O has highest percentage (37.1%) ,followed by A (32.4%) , B (32.8%) and AB (6.5%). Another study done by

Abdullahi (2009) in Iran found that blood group O also predominates (32.1%), then A (30.1%), B (23.3%) and AB (13.7%). ABO blood groups have also association with other diseases like hepatitis and gastric carcinoma (Waseem *et al.,* 2012). A study conducted in republic of Bosnia revealed that O blood group have 40.9%, A have 37% and B have 16 % leukemia patients (Sakić, 2012). Another study was conducted in Iraq during 2008-10 and it was found that 41.8% of CML patients have blood group O while 28.8% have B (Shahzad *et al.,* 2013). In this study, the result of table (1) show that there is significant increase in the level of serum MDA is differ in each blood group in CML patients this agree with the study done by Rizwan Ahmed (2008) that found there is significant increase in the level of MDA n CML patients as compared to healthy volunteers. In addition, the study agree with study done by Zelen (2010) that found the level of MDA is higher in compared with controls. In patient blood group B has high level of MDA followed by blood group O has high level of MDA. Some previous studies shows increased MDA levels in different types of leukemia. Oxidative stress occurring in patients with leukemia may be due to the elevated number of mature and immature myeloid or lymphoid series cells. This can also due to increased formation or reduced clearance of free radicals by the cellular antioxidant system (Pujari *et al.,* 2018). Table (1) show the result of the level of serum glutathione in patients and controls groups. The level of GSH in CML patients is lower than control group in different blood groups this agree with study done by Rizwan (2008) that found Antioxidant status was found to be significantly decreased ($p<0.05$) in Chronic myeloid leukemia patients and its phases as compared to healthy participants. It could be concluded that oxidative stress may be associated with the pathophysiology of chronic myeloid leukemia. The actions of different antioxidants show different patterns during neoplastic transformation, and tumor, cancer or leukaemic cells, which exhibit abnormal activities of the antioxidant enzymes as well as the concentrations of non-enzymatic antioxidants, when compared with their appropriate normal cells. GR is a glutathione regenerating enzyme that permits the conversion of oxidized glutathione (GSSG) to reduced glutathione (GSH) by the oxidation of NADH to NAD+ (Giftson *et al.,* 2010). Glutathione reductase is a secondary antioxidant enzyme that helps in the detoxification of reactive oxygen species by decreasing peroxide levels or by maintaining a steady state supply of metabolic intermediates like GSH (Rajeshwari *et al.,* 2013).

**Table (1): Concentration of MDA & GSH in Patients and Control**

| Parameters | Sex | Patient<br>Mean± SD | Control<br>Mean± SD | P-value |
|---|---|---|---|---|
| **MDA**<br>**ng/mL** | Male<br>(N=30) | 900.99±603.89 | 396.89±215.12 | **<0.001** |
| | Female | 582.28±562.29 | 367.76±328.40 | **<0.001** |

**Received: 15 Jan 2020 | Revised: 5 Feb 2020| Accepted: 30 Mar 2020** 

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| | (N=15) | | | |
| **Total Mean** | | **794.75±596.62** | **387.18±252.12** | **<0.001** |
| **GSH µg/mL** | Male (N=30) | 42.30±29.04 | 51.61±30.25 | **<0.05** |
| | Female (N=15) | 35.77±24.94 | 62.37±26.19 | **<0.05** |
| **Total Mean** | | **40.12±27.33** | **55.20±28.79** | **<0.05** |

**Table (2): Concentration of MDA& GSH for total.**

| Parameter | ABO | Patients Mean ± SD | Control Mean ± SD | P-value |
|---|---|---|---|---|
| MDA ng/mL | A (N=10) | 480.70±411.21 | 324.44 ±256.62 | <0.001 |
| | B (N=8) | 1387.07±520.89 | 447.27±260.58 | <0.001 |
| | AB (N=7) | 671.66±560.75 | 330.77±329.76 | <0.001 |
| | O (N=20) | 757.94±559.78 | 414.25 ±231.10 | <0.001 |
| GSH µg/mL | A (N=10) | 53.23±12.76 | 49.92±8.95 | <0.05 |
| | B (N=8) | 30.75±22.28 | 52±40.6 | <0.05 |
| | AB (N=7) | 17±4.30 | 81.87±5.50 | <0.001 |
| | O (N=20) | 45.42 ±33.90 | 49.78 ±31.56 | <0.05 |

**Received: 15 Jan 2020 | Revised: 5 Feb 2020| Accepted: 30 Mar 2020**

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