Oxidative stress-Antioxidant status in Egyptian Lymphoma patients.

Hossam Darwish [1]; El-Shahat A. Toson[2]; Hatem A. El-mezayen [3]; Ghada T. El Zanaty [4] and Camelia A. Abdel Malak[2]

[1]Medical Oncology Department, Damietta Cancer institute, Egypt
[2]Chemistry Department, Mansoura University (Damietta), Egypt
[3]Chemistry Department, Helwan University, Egypt
[4]Clinical pathology Department, Damietta Cancer institute, Egypt
hatem_mezayen@yahoo.com

Abstract: There are two major types of lymphoma: Hodgkin's lymphoma and non- Hodgkin's lymphoma. Hodgkin's lymphoma (HL) tends to affect younger patients and be relatively curable, whereas non- Hodgkin's lymphoma (NHL) tends to affect older patients and carry a worse long-term prognosis as a group. Antioxidants are molecules that can neutralize free radicals by accepting or donating an electron to eliminate the unpaired condition. One of these antioxidant molecules was reduced glutathione (GSH) that can reduce free radicals by hydrogen donation. Also, superoxide dismutase (SOD) is one of the most important natural antioxidant enzymes manufactured in the body provide an important defense against free radicals, that converts two superoxide radicals into one hydrogen peroxide and one oxygen. Malondialdehyde (MDA), the end product of lipid peroxidation (LPO), arising from the free radical degradation of polyunsaturated fatty acids, can cause cross-linking in lipids, proteins and nucleic acids. Our study aimed to detection of GSH, SOD and MDA as prognostic biomarkers associated with lymphoma patients in a population from Damietta, Egypt. This hospital-based case-control study was conducted during (2007-2010); 50 lymphoma cases and 14 controls were enrolled. Information was collected and blood samples were obtained and parameters were determined by standard techniques. Associations between variables of interest and non-Hodgkin, Hodgkin Lymphoma(NHL, HL) were assessed using conditional logistic regression. We found that at initial diagnosis of NHL patients, GSH was negative for all patients (100%) and remain negative after treatment applied with cut-off value (2.09 $X10^3$ m Mol/L cells). Also, SOD was negative for all patients (97.1%) before treatment applied except one case (2.9%) was positive. It still negative (100%) after treatment applied with cut-off value (33.95%). On the other hand, MDA was positive for patients (94.3%) and negative for patients (5.71%). Then, it was positive for patients (73.7%) and negative for patients (26.3%) after treatment applied with cut-off value (0.53 $X10^{-5}$ Mole / mL packed cells). On the other side, at initial diagnosis of HL, GSH was negative for all patients (100%) and remain negative after treatment applied with cut-off value (2.09 $X10^3$ m Mole/L cells). Also, SOD was negative for patients (93.3%) before treatment applied except one case (6.7%) It still negative (100%) after treatment applied with cut-off value (33.95%). On the other hand, MDA was positive for patients (100%). Then, it became positive for patients (83.3%) and negative for patients (16.7%) after treatment applied with cut-off value (0.53 X 10^{-5} Mole / mL packed cells). These findings suggest that MDA level was elevated in NHL and HL patients, before and after treatment on comparison to that of controls. But SOD, GSH levels were decreased before and after treatment at all.

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1. Introduction

There are two major types of lymphoma: Hodgkin's lymphoma and non-Hodgkin's lymphoma. Hodgkin's lymphoma (HL) tends to affect younger patients and be relatively curable, whereas non-Hodgkin's lymphoma(NHL) tends to affect older patients and carry a worse long-term prognosis as a group. Hodgkin's disease (HD) is a malignancy of lymphoid tissue. In contrast to non- Hodgkin's lymphoma (NHL), it tends to spread in an orderly, predictable fashion to adjacent sites of lymph tissue. Hodgkin's diseases comparatively rare with approximately 7.500 new cases diagnosed each year in the United States. On the other hand, there are approximately 60.000 new cases of NHL per year **[1].**

In Egypt, non- Hodgkin's lymphoma is the fifth most common cancer in both the sexes. The general incidence rate was 5.9 in 1995 and reached 8.99 in 2004, with a peak (9.4) in the year 2002. The male incidence of non- Hodgkin´s lymphoma demonstrated an obvious rise from 1995 to 1998, with a slowing from 1999 to 2002, followed by another evident rise from 2003. Women showed an increase in non-

Hodgkin´s lymphoma incidence rates from 1995 to 2000, then a decline afterwards till 2004 **[2].** Hodgkin´s disease represents 20-25 percent of all lymphomas. In developing countries the overall incidence of Hodgkin´s disease is lower than that in developed countries but the incidence before the age of 15 years is rising, with a modest increase throughout adolescence and young adulthood (15-35years). The disease is more common in male than females. There is a bimodal age distribution with the first peak seen in the twenties and a second rise after the age of 50**[3].** Antioxidants are molecules that can neutralize free radicals by accepting or donating an electron to eliminate the unpaired condition. Typically this means that the antioxidant molecule becomes a free radical in the process of neutralizing a free radical molecule to a non-free-radical molecule. But the antioxidant molecule will usually be a much less reactive free radical than the free radical neutralized. The antioxidant molecule may be very large (allowing it to "dilute" the unpaired electron), it may be readily neutralized by another antioxidant and/or it may have another mechanism for terminating its free radical condition. Molecules with loosely-held hydrogen atoms can use those hydrogen atoms like electrons to neutralize free radicals. The hydrogen atoms are called reducing equivalents, and the molecules having such hydrogen atoms are said to be in a reduced state **[4].** Thiols (molecules with -SH groups) such as thioredoxins (small disulphide-containing proteins), cysteine and reduced glutathione (GSH) are also examples of molecules that can reduce free radicals by hydrogen donation. Metallothioneins are small cysteine-rich proteins that can reduce oxidative stress by metal-binding as well as by hydrogen donation **[5].** Glutathione reductase then adds hydrogens to the oxidized glutathione (GSSG) to regenerate reduced glutathione (GSH). A high GSH/GSSG ratio indicates a high level of reduced glutathione available for antioxidant activity. Normal mouse liver GSH/GSSG ratios typically range from 50 to 200. Glutathione peroxidase contains selenium. Selenium in the diet can increase glutathione peroxidase levels, which is why a Recommended Dietary Allowance (RDA) for selenium was established in the United States in **1989**. Selenium deficiencies result in glutathione peroxidase depletion. Epidemiological studies strongly indicate a protective effect of selenium against many cancers. Selenium can also reduce mercury toxicity, but in excess selenium is a toxic poison itself. There are many similar biochemical processes that oxidize reduced antioxidant molecules to neutralize free radicals and then restore the antioxidant molecules to a reduced state. In mitochondrial membranes, Vitamin E that has donated a hydrogen to neutralize a free radical can be regenerated (reduced) by CoEnzyme Q, which has two hydrogens to donate, and can avoid becoming a free radical by donating both hydrogens**[6].** Organisms possess natural defenses against free radicals in the form of antioxidant enzymes, such as superoxide dismutase (which neutralizes superoxide) and catalase (which neutralizes hydrogen peroxide). Organisms also synthesize non-enzymatic antioxidant molecules such as glutathione and CoEnzyme Q. Animals can also obtain antioxidants through diet, such as Vitamin E and the phytochemical carotenoid substances. The element selenium has antioxidant properties because it is an essential component of the enzyme glutathione peroxidase which uses glutathione to neutralize hydrogen peroxide. Metal chelating substances can be antioxidant by preventing metal ions from producing free radical reactions**[6].** The enzyme superoxide dismutase converts two superoxide radicals into one hydrogen peroxide and one oxygen. To eliminate hydrogen peroxide before the Fenton Reaction can create a hydroxyl radical, organisms use catalase and/or glutathione peroxidase. The brain, which is very vulnerable to free radical damage (due to high metabolic rate, high unsaturated fat in neurons, and the fact that neurons are post-mitotic) has seven times more glutathione peroxidase activity than catalase activity**[7].** Superoxide dismutase (SOD) activity has been estimated in serum and leucocytes isolated from adults and children with acute lymphoblastic leukemia (ALL), non-Hodgkin's lymphoma (NHL), Hodgkin's lymphoma (HD) and neuroblastoma. Superoxide dismutase levels in leukocytes isolated from adult patients with HD, ALL and NHL were significantly higher than the corresponding control values. Serum SOD activity of adult patients with ALL and NHL was significantly decreased compared to the normal value, while its activity was not significantly changed in patients with HD. There were no apparent differences in serum SOD activity in children suffering from ALL, NHL, HD and neuroblastoma. It is concluded that the assay of leukocyte SOD can be used to differentiate between HD and NHL in both adults and children **[8].** Malondialdehyde (MDA), the end product of lipid peroxidation (LPO), arising from the free radical degradation of polyunsaturated fatty acids, can cause cross-linking in lipids, proteins and nucleic acids**[9,10].** Superoxide dismutase(SOD) activity (antioxidant enzyme) was not changed in NHL patients before or after chemotherapy. Malondialdehyde (MDA) level and osmotic fragility of red blood cells of patients with lymphomas were increased before and after treatment in comparison to the control group **[11].** So that, in our study we are interested to determine GSH, SOD and MDA levels in non-Hodgkin and Hodgkin lymphoma patients.

The aim of this work is to detection of GSH, SOD and MDA as prognostic biomarkers associated with lymphoma patients in a population from Damietta, Egypt.

Experimental

The study was performed on total 50 lymphoma patients aged between 7 to 76 years with a median age of 49 years and the Mean ± SD is 44.8 ± 17.9. Seven of them accounting to (14%) are less than 18 years (children), on the other hand, 30 of them accounting to (60%) are between 18 and 57 years, the last 13 patients accounting to (26%) are more than 57 years old. As regard to their histopathological type, 35 of them showed non-Hodgkin's lymphoma (NHL) that accounting to (70%) and 15 are diagnosed as Hodgkin's lymphoma (HL) accounting to(30%), 29(58%) of them are males and 21(42%) of them are females with male to female ratio (1.4 : 1). The 15 patients diagnosed as Hodgkin's lymphoma (HL)were divided into 6 females and 9 males accounting to(40%), (60%) respectively. The 35 patients diagnosed as non-Hodgkin's lymphoma (NHL) were divided into 15 females and 20 males accounting to(42.85%), (57.14%) respectively. All cases were treated at Damietta Cancer Institute, Egypt. In addition, 14 apparently normal healthy control individuals with ages ranged from 24 to 64 years old were included in our study.

Venous blood samples were collected from patients and cotrols into sterile glass tubes. The blood samples were permitted to coagulate at room temperature for 30 min and centrifuged at 2.000 rpm for 10 min. Serum was separated, aliquoted for detection of SOD level. Also, blood samples with EDTA were collected for detection of GSH and MDA levels. The samples were collected from patients at two time intervals, as follows :

(i)Before Treatment

The first serum samples was obtained from 50 patients at the time of diagnosis before any treatment applied, from non-Hodgkin's lymphoma (NHL) and Hodgkin lymphoma (HL) patients, for detection of SOD level. Also, blood samples with EDTA were collected for detection of GSH and MDA levels, starting from October/2007 until january /2009.

(ii) After Treatment

The second serum sample was obtained from only 25 patients (the only available) after 24 months from the first sample collection, (the rest of 50 patients samples were not available), for detection of SOD level. Also, blood samples with EDTA were collected for detection of GSH and MDA levels, starting from March /2010 until November /2010.

Measurement of GSH

Reduced glutathione in blood was determined by the standard method **[12].** Virtually all of the nonprotein sulfhydryl of red cells is in the form of reduced glutathione GSH 5.5-Dithiobis(2-Nitrobenzoic acid) (DTNB) is a disulfide compound which is reduced by sulfhydryl compounds, forming a highly colored yellow anion. The optical density of this yellow substance was measured at 412nm, using colorimeter (Jenway6051).

Measurement of SOD

Superoxide dismutase activity in serum was determined by the standard method **[13].** The method depends on the ability of the enzyme to inhibit the phenazine methosulphate –mediated reaction of nitroblue tetrazolium dye. The optical density of this dye was measured at 560nm, using colorimeter (Jenway6051).

Measurement of MDA

Malondialdehyde (MDA) was determined by the standard method **[14].** The reaction of malondialdehyde (MDA) with thiobarbituric acid (TBA) forming a MDA-TBA_2 adduct that can be measured colorimetrically, absorbs strongly at 532 nm, using colorimeter (Jenway6051).

Statistical analysis

Data were analyzed by using the statistical analysis program package, instate software, version 2.03(Graph pad, USA) and an IBM PC/At compatible computer. The different clinical and pathological variables were examined by chi-square test as described on results. Linear regression analysis was used for correlation's statistical analysis. Statistical significance was defined as $P \leq 0.05$.

Results and Discussion

The results obtained in the present study were illustrated as follows :-

The clinical features of 50 lymphoma patients that were selected for this study with ages ranging from 7 to 76 years with a median age of 49 years and the Mean ± SD is 44.8 ± 17.9. Seven of them accounting to (14%) were less than 18years (children), on the other hand, 30 of them accounting to (60%) were between 18 and 57 years, the last 13 patients accounting to (26%) were more than 57 years old. As regard to their histopathological type, 35 of them showed non-Hodgkin's lymphoma(NHL) that accounting to (70%) and 15 were diagnosed as Hodgkin's lymphoma (HL) accounting to(30%), 29(58%) of them were males and 21(42%) of them were females with male to female ratio (1.4 : 1). The 15 patients diagnosed as Hodgkin's lymphoma (HL) were divided into 6 females and 9 males accounting to(40%), (60%) respectively. The 35 patients diagnosed as non-Hodgkin's lymphoma (NHL) were

divided into 15 females and 20 males accounting to (42.85%), (57.14%) respectively. According to family history of cancer, there are 6/50(12%) patients are positive (4males,2 females) accounting to(8%), (4%) respectively classified as 2 children, 4 adults. The rest of patients are negative family history accounting to 44(88%). Regarding to survival rate 48/50 (96%) still live with 3 years survival rate, Hodgkin lymphoma showed (100%) survival rate and non-Hodgkin's lymphoma showed (94.28%) survival rate. These results are presented by (Table1). The biomarkers which were performed to the 50 lymphoma patients (35 non-Hodgkin lymphoma patients and 15 Hodgkin lymphoma patients) at initial diagnosis, first one Superoxide dismutase (SOD), the mean ± SD is 14.7±9, the minimum value is 2.29, the maximum value 40.8. Compared with control value, the p-value is 0.176 (not significant) with Cut-off value of 33.95%. The second parameter MDA (Malondialdehyde), the mean ± SD is 0.86±0.29, the minimum value is 0.46, the maximum value 1.5. Compared with control value, the p-value is < 0.0001(extremely significant) with Cut-off value of (0.53X10 Mole/ml packed cells).The third parameter GSH (reduced glutathione) was performed on 19 patients, the mean ± SD is 0.776±0.0.532, the minimum value is 0.091, the maximum value 1.95. Compared with control value, the p-value is 0.4039(not significant) with Cut-off value of (2.09 X10 m Moles per litre cells) and there were 25 lymphoma patients under follow up (19 non-Hodgkin lymphoma patients and 6 Hodgkin lymphoma patients) before receiving any treatment, first one SOD(Superoxide dismutase), the mean ± SD is 15±9.5, the minimum vale is 2.29, the maximum value 40.8. Compared with control value, the p1-value is 0.235(not significant). After receiving treatment, the mean ± SD is 13±4.7, the minimum value is 2.1, the maximum value 15.4. Compared with control value, the p2-value is 0.0532 (not significant). On comparison between before and after treatment values, the p3-value is 0.176 (not significant). The second parameter MDA (Malondialdehyde) was performed to the 25 lymphoma patients (19 non-Hodgkin lymphoma patients and 6 Hodgkin lymphoma patients) the mean ± SD is 0.84±0.29, the minimum value is 0.46, the maximum value 1.5. Compared with control value, the p1-value is < 0.0001 (extremely significant). After receiving treatment, the mean ± SD is 0.68±0.23, the minimum value is 0.23, the maximum value 1.26. Compared with control value, the p2-value is < 0.0001 (extremely significant). On comparison between before and after treatment values, the p3-value is 0.018(considered significant). The third parameter GSH(reduced glutathione) was performed on 19 patients including (NHL, HL), the mean ± SD is 0.776±0.0.532, the minimum value is 0.091, the maximum value 1.95. Compared with control value, the p1-value is 0.4039(not significant). After receiving treatment , the mean ± SD is 0.43±0.18, the minimum value is 0.11 the maximum value 0.83. Compared with control value, the p2-value is 0.027 (considered significant). On comparison between before and after treatment values , the p3-value is 0.0064 (very significant). These results are given in (Table 2), at initial diagnosis, 33 (94.3%) NHL patients had positive MDA values, all of them had negative SOD values 32 (97%) except one case (3%) had positive SOD value. The others 2 (5.7%) patients had negative values for MDA and SOD were illustrated by (Table 3). 15 (100%) HL patients had positive MDA values, all of them had negative SOD values 14 (93.3%) except one case (6.7%) had positive SOD value were illustrated by (Table4). After treatment applied, 14 (73.7%) NHL patients had positive MDA values, all of them had negative SOD values 14 (100%). The others 5 (26.3%) patients had negative values for MDA and SOD were illustrated by (Table5). 5 (83.3%) HL patients had positive MDA values, all of them had negative SOD values 5(100%). The other one (16.7%) patients had negative values for MDA and SOD presented by (Table 6).

In this study, there were 3 biomarkers GSH, MDA and SOD which have been determined in blood samples and serum respectively of lymphoma patients. Our study is divided into two parts: **Part one** consists of 50 lymphoma patients under investigation, 35 (70%) of them diagnosed as non-Hodgkin's lymphoma (NHL) and the others 15(30%) diagnosed as Hodgkin's lymphoma (HL). **Part two** consists of 25 patients under follow up, 19 of them are diagnosed as non-Hodgkin's lymphoma (NHL) and the others 6 diagnosed as Hodgkin's lymphoma (HL). Two samples are taken before and after treatment from these patients as a predictive samples for evaluation of disease during treatment. As regard to part one, there are 50 lymphoma patients with median age 49 years and ranging from 7 to 76 years , 60% of them are of range 18-57years. According to family history of cancer , 6/50(12%) patients are positive (4males, 2 females)(2 children, 4 adults), the rest of patients 44/50(88%)are negative. Only 2/50 (4%)were dead, 48/50 (96%) still live with 3 years survival rate.

Table 1 : Clinical features of Lymphoma Patients

Parameter	Total Patients No (%)	NHL	HL
Age ≤18 18-57 ≥57	 7 (14%) 30 (60%) 13 (26%)	 2 (5.71%) 23 (65.7%) 10 (28.57%)	 5 (33.33%) 7 (46.66%) 3 (20%)
Sex Male Female	 29 (58%) 21 (42%)	 20 (57.14%) 15 (42.85%)	 9 (60%) 6 (40%)
Family history Positive (+) Negative (-)	 6 (12%) 44 (88%)	 4 (11.42%) 31 (88.57%)	 2 (13.33%) 13 (86.6%)
Lymphoma	50 (100%)	35 (70%)	15 (30%)
Survival Rate of Lymphoma	48/50 (96%) still live with 3 years survival rate	33/35 (94.28%) live 14females, 19males	15/15(100%)live 6females, 9 males

* NHL : Non-Hodgkin's lymphoma
HL: Hodgkin's lymphoma

Table 2 : Superoxide dismutase (SOD), reduced glutathione (GSH) and malondialdehyde (MDA) associated with NHL and HL Patients at initial diagnosis and under follow up

Parameter	SOD %	MDA $\bar{X}10^{-5}$ Mole/mLpacked cells	GSH $X^{3}10$ mMoles/ L cells
Control Mean±SD (N) Range	 17.15±8.4 14 (7.6-33%)	 0.29±0.12 11 (0.14-0.46)	 0.83±0.63 12 (0.26-2.38)
Patients At initial diagnosis Mean±SD (N) Range	 14.7±9 50 (2.29-40.8)	 0.86±0.29 50 (0.46-1.5)	 0.776±0.532 19 (0.091-1.95)
Patients under follow up Before treatment Mean±SD (N) Range	 15±9.5 25 (2.29-40.8)	 0.84±0.29 25 (0.46-1.5)	 0.77±0.53 19 (0.09-1.95)
Patients under follow up After treatment Mean±SD (N) Range	 13±4.7 25 (2.1-15.4)	 0.68±0.23 25 (0.23-1.26)	 0.43±0.18 25 (0.11-0.83)
P–values	0.176, Not sig.	<0.0001***	0.4039, Not sig.
P1 –values	0.235, Not sig.	<0.0001***	0.403, Not sig.
P2 –values	0.053, Not sig.	<0.0001***	0.027*, Considered sig.
P3 –values	0.176, Not sig.	0.018*	0.0064**

* SOD :Superoxide dismutase.
MDA :Malondialdehyde.
GSH :Reduced glutathione.
P-value :Compared with control.
P1 –value : Comparing before with control.
P2-value : Comparing after with control.
P3-value : Comparing after with before.
*means : Considered significant.
**means : Very significant.
***means : Extremely significant.

Table 3: Concordance and unconcordance between SOD and MDA in NHL patients at initial diagnosis

Parameter	SOD +ve	SOD -ve	Total
MDA +ve	1 (3%)	32 (97%)	33 (94.3%)
MDA -ve	-	2 (100%)	2 (5.7%)
Total	1 (2.9%)	34 (97.1%)	35 (100%)

***-ve = negative and +ve = positive**

Table 4: Concordance and unconcordance between SOD and MDA in HL patients at initial diagnosis.

Parameter	SOD +ve	SOD -ve	Total
MDA +ve	1 (6.7%)	14 (93.3%)	15 (100%)
MDA -ve	-	-	-
Total	1 (6.7%)	14 (93.3%)	15 (100%)

***-ve = negative and +ve = positive**

Table 5: Concordance and unconcordance between SOD and MDA in NHL patients after treatment.

Parameter	SOD +ve	SOD -ve	Total
MDA +ve	-	14 (100%)	14 (73.7%)
MDA -ve	-	5 (100%)	5 (26.3%)
Total	-	19 (100%)	19 (100%)

***-ve = negative and +ve = positive**

Table 6: Concordance and unconcordance between SOD and MDA in HL patients after treatment .

Parameter	SOD +ve	SOD -ve	Total
MDA +ve	-	5 (100%)	5 (83.3%)
MDA -ve	-	1 (100%)	1 (16.7%)
Total	-	6 (100%)	6 (100%)

***-ve = negative and +ve = positive**

Regarding biomarkers which were performed to the 50 lymphoma patients (35 non-Hodgkin lymphoma patients and 15 Hodgkin lymphoma patients) before receiving any treatment , first one SOD(Superoxide dismutase), the mean ± SD is 14.7±9, the minimum value is 2.29, the maximum value 40.8. Compared with control value, the p-value is 0.176(not significant). The second parameter MDA (Malondialdehyde), the mean ± SD is 0.86±0.29, the minimum value is 0.46, the maximum value 1.5. Compared with control value, the p-value is < 0.0001(extremely significant). The third parameter GSH(reduced glutathione) was performed on 19 patients , the mean ± SD is 0.776±0.0.532, the minimum value is 0.091, the maximum value 1.95. Compared with control value, the p-value is 0.4039(not significant). These three parameters MDA, SOD, GSH were concerning to lipid peroxidation and antioxidant status respectively. There were also significant differences in the activities of the antioxidant enzymes, concentrations of antioxidants, MDA and osmotic fragility in the most of the malignant lymphoma patients. These data suggest that hematological complications and autoimmune hemolytic anemia might be attributed to the oxidative stress produced by malignant lymphomas **[11].** As regard to part two, after treatment, these biomarkers which were performed to the 25 lymphoma patients under follow up (19 non-Hodgkin lymphoma patients and 6 Hodgkin lymphoma patients) before receiving any treatment, first one SOD(Superoxide dismutase), the mean ± SD is 15±9.5, the minimum value is 2.29, the maximum value 40.8. Compared with control value, the p1-value is 0.235 (not significant). After receiving treatment , the mean ± SD is 13±4.7, the minimum value is 2.1, the maximum value 15.4. Compared with control value, the p2-value is 0.0532 (not quite significant).

On comparison between before and after treatment values, the p3-value is 0.176(not significant). The MDA (Malondialdehyde) was performed to the 25 lymphoma patients (19 non-Hodgkin lymphoma patients and 6 Hodgkin lymphoma patients) the mean ± SD is 0.84±0.29, the minimum value is 0.46, the maximum value 1.5. Compared with control value, the p1-valueis < 0.0001 (extremely significant). After receiving treatment , the mean ± SD is 0.68±0.23, the minimum value is 0.23, the maximum value 1.26 . Compared with control value, the p2-value is < 0.0001 (extremely significant). On comparison

between before and after treatment values, the p3-value is 0.018 (considered significant). The GSH (reduced glutathione) was performed on 19 patients including (NHL, HL), the mean ± SD is 0.776±0.0.532, the minimum value is 0.091, the maximum value 1.95. Compared with control value, the p1-value is 0.4039(not significant). After receiving treatment , the mean ± SD is 0.43±0.18, the minimum value is 0.11 the maximum value 0.83. Compared with control value, the p2-value is 0.027 (considered significant). On comparison between before and after treatment values , the p3-value is 0.0064 (very significant). In other study, changing levels of serum oxidant / antioxidant with chemotherapy were investigated and their relation to treatment in 34 Hodgkin's lymphoma patients. The patient population consisted of 19 males and 15 females. Mean age was 30.41 +/- 12.08 years. All patients received the adriamycin, bleomycin, vincristine and dexamethasone (ABVD) treatment protocol. Blood samples were taken before treatment, and on days 1 and 7 during treatment for measurement of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), catalase (CAT), malondialdehyde (MDA), nitric oxide (NO) and enzyme activities. After ABVD treatment, mean free radical levels were increased and antioxidant levels were significantly decreased in the serum. ABVD treatment results in an increase of free radical levels and a decrease of antioxidant levels in the serum of patients with Hodgkin's lymphoma **[15].**

Conclusions:

Our findings indicate that MDA level was elevated in NHL and HL patients, before and after treatment on comparison to those of controls. But SOD, GSH levels were decreased before and after treatment at all.

Corresponding Author:
Dr: Hatem A. El-mezayen
Chemistry department, Helwan University
Cairo - Egypt
E-mail: hatem_mezayen@yahoo.com

References

1. Giancarlo Pillot, Marcia L.chantler, Holly M. Magiera, Shachar peles, Geoffrey L.Uy, Judah D. Friedman, Matthew A. Ciorba, Tammy L. Lin (2004): The Washington Manual hematology and Oncology Subspecialty consult Book, Chapter (31) lymphoma.
2. Abdel-fattah MM and Yassine OG, (2007): Non-Hodgkin's lymphomas in Alexandria, Egypt; incidence rates and trend study (1995-2004). Eur J Cancer prev. oct; 16(5):479-85.
3. Robert de W. Marsh, J. Samuel, George Jacob, Jame Abraham, K. Pavithran and Shirley George (2007): Essentials of Clinical Oncology Book.
4. Hossain MA, Asada K, (1985): Monodehydroascorbate reductase from cucumber is a flavin adenine dinucleotide enzyme. J Biol Chem. 1985 Oct 25;260(24):12920-6.
5. Zhang, B (2003): Molecular And Cellular Biology; 23 (23): 8471-8485 (2003).
6. Sies H, Stahl W, (1995): Vitamins E and C, beta-carotene, and other carotenoids as antioxidants. Am J Clin Nutr. 1995;62(6 Suppl):1315S-1321S.
7. Marklund SL, (1982): Human copper-containing superoxide dismutase of high molecular weight. Proc Natl Acad Sci USA. 1982 Dec; 79(24):7634-8.
8. Abdel-Aziz AF, and El-Naggar MM, (1997): Superoxide dismutase activities in serum and white blood cells of patients with some malignancies. Cancer Lett Feb 26;113(1-2):61-4.
9. Freeman BA, Crapo JD, (1982): Biology of disease: Free radicals and tissue injury. Lab Invest 1982;47:412-26.
10. Flohe L, Beckmann R, Giertz H, Loschen G, (1985): Oxygen-centered free radicals a mediators of inflammation.*In* : Sies H, editor. Oxidative stress. New York: Academic Press; 1985. p. 405-37.
11. Abou-Seif MA, Rabia A, Nasr M,(2000): Antioxidant status, erythrocyte membrane lipid peroxidation and osmotic fragility in malignant lymphoma patients. Clin Chem Lab Med. Aug;38(8):737-42.
12. Beutler, E; Duron, O. and Kelly, B.(1963): Improved method for the determination of blood glutathione. J. Lab . Clin. Med., 61:882-890.
13. Dechatelet LR, Mc Call CE, Mc Phial LC, Johnston RB, (1974): Superoxide dismutase activity in leukocytes J. Clin. Invest. 53:1197-1201.
14. Stocks J, and Donnandy T,(1971): The autoxidation of human red cell lipids induced by hydrogen peroxide . Br. J. Haematol , 20:95-111.
15. Kaya E, Keskin L, Aydogdu I, Kuku I, Bayraktar N, Erkut MA, (2005): Oxidant / antioxidant parameters and their relationship with chemotherapy in Hodgkin's lymphoma. J Int Med Res. Nov-Dec; 33(6) : 687-92.

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