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Evaluation the levels of Lactate dehydrogenase (LDH), Alkaline phosphatase (ALP), Calcium and Phosphorus in Iraqi non-Hodgkin lymphoma patients treated and untreated

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Abstract: Non-Hodgkin lymphoma (NHL) is a disorder caused by malignant change of lymphocytes that affect the lymph nodes or extra-node areas. Lactate dehydrogenase (LDH) and alkaline phosphatase (ALP) play an important role in non-Hodgkin lymphoma.Our current study aims at estimating levels of lactate dehydrogenase, alkaline phosphatase, calcium and phosphorus in Iraqi non-Hodgkin lymphoma patients treated and untreated.Patients and Methods: Our study included 120 people, including 80 people with non-Hodgkin (34 females, 46 males, ages 25-70 years) were visiting the Oncology Hospital in Mosul, Iraq. And 40 uninfected people were considered as a control group, identical in age (19 females, 21 males). In addition, the patients were divided into two groups, one under treatment and the other newly diagnosed (untreated). Serum lactate dehydrogenase, alkaline phosphatase, calcium and phosphorus were measured.The results of our study showed that the average age of patients was 56.1±11.1 years, and the average age of healthy persons is 52.2±13.8 years. The results indicated that non-Hodgkin lymphoma patients have a significant increase (P<0.0001) in levels of lactate dehydrogenase (529±164.5 U/L, NHL patients versus 299.1±34.5U/L controls) and alkaline phosphatase (298±115.7 U/L NHL patients versus 98.8±39.4U/L controls) compared to healthy people. Also, the results indicated that untreated NHL patients have a significant increase (P< 0.0001) in levels of LDH (697.6±292.3 untreated NHL patients versus 317.6±92.3 treated NHL patients) and ALP (336.3±122.4 untreated NHL patients vs. 112.3±42.3 treated NHL patients) compared to treated NHL patients.While no significant difference was shown in the levels of LDH, ALP, calcium and phosphorus between the groups of treated and healthy people.It is possible to use lactate dehydrogenase and alkaline phosphatase as an indicator to diagnose and to know the severity of the disease as well as to monitor the effect of treatment for patients.

Key words: Non-Hodgkin lymphoma, Lactate dehydrogenase, Alkaline phosphatase

Introduction

Lymphoma is a type of slag disease, characterized by the proliferation of malignant cells of the lymphatic system. Lymphoma is classified into two distinct types: Non-Hodgkin's Lymphoma (NHL) and Hodgkin's Lymphoma (HL), (Galleze et al., 2017; Yildirim, Gundogdu, & Erdem, 2009; Zinzani, 2005).

non-Hodgkin lymphoma is a disorder caused by malignant change of lymphocytes that affect the lymph nodes or extra-node areas (Purnamasidhi, Suega, & Bakta, 2019). The incidence of the contract outside the lymph nodes is 24-48%. The incidence has increased since the previous decade, and areas outside the lymph nodes may occur in any organ, and the most commonly occurring areas are the digestive system, skin and bones. (Lu et al., 2013; Yadav et al., 2016). Non-Hodgkin lymphoma affects males more than females (50-75%), and it affects between 60 and 70 years of age. (Yadav et al., 2016).

Lactate dehydrogenase (LDH) is a cytoplasmic enzyme that stimulates the reverse reaction of pyruvate to lactate, which is the last step in the glycolytic (Galleze et al., 2017; Long et al., 2019; Purnamasidhi, Suega, &

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Bakta, 2019) (Galleze et al., 2017). It is a widespread enzyme in various tissues such as liver cells and muscles such as the heart muscle. (Galleze et al., 2017; Purnamasidhi et al., 2019; Yadav et al., 2016). Also, the activity of lactate dehydrogenase increased in heart patients and types of cancer such as pancreatic and colon cancer(Galleze et al., 2017; Lu et al., 2013). Galleze et al., 2017 which has showed a significant rise of lactate dehydrogenase in non-Hodgkin's lymphoma patients, but the activity of lactate dehydrogenase in non-Hodgkin Lymphoma (NHL) is higher than Hodgkin lymphoma (HL) (Galleze et al., 2017).

Alkaline phosphatase (ALP) belongs to the enzyme group that activates the decomposition of mono-aster phosphate. It is capable of interacting with various foundation materials, ALP is found in all tissues of the body, especially in the membrane, found at a high level in the bone renal tubes, the liver Intestinal epithelium and placenta(Tahannejad, Dayer, & Samie, 2012; Taher, Hummadi, AL-Bashir, & AL-Araji, 2016). Calcium is a major structural component of the skeleton(Kalita & Choudhury, 2017; Kumar & Bhaskar, 2012).

Our current study aims at estimating levels of lactate dehydrogenase, alkaline phosphatase, calcium and phosphorus in Iraqi non-Hodgkin lymphoma patients treated and untreated.

Materials and Methods:

Our study was conducted in Mosul city through the period from the 1st of May of 2018 to the 1st march in 2019. Our current study included 120 people, including 80 people with non-Hodgkin (34 females, 46 males, ages 25-70 years) were visiting the Oncology Hospital in Mosul, Iraq. In addition, the patients were divided into two groups, one under treatment and the other newly diagnosed (untreated). All patients have written information included: medical history, physical examination related to history of non-Hodgkin lymphoma, age, gender, and family history of non-Hodgkin lymphoma. Cases were excluded from the study such as: Hodgkin lymphoma (HL) and other disease.

Also, forty healthy people aged- 25-70 years (19 females, 21 males) were considered as a control group. 5 milliliters (5ml) were pulled from the vein and placed in a clean tube and centrifugeated at 3000xg and then separated the fine part of the serum samples were kept under freezing -20 until the tests were performed.Serum lactate dehydrogenase, alkaline phosphatase, calcium and phosphorus were measured.

Estimation the level of lactate dehydrogenase (LDH) activity: The activity of lactate dehydrogenase (LDH) was measured using a factory kit by Bay Labo (French). The principle of measurement includes that LDH stimulate the internal transformation of the pyruvate converted to lactate and the presence of NADH as coenzyme, Optical absorption measured at 340 nm(Burtis, Ashwood, & Bruns, 2012).

Estimation the level of Alkaline phosphates (ALP)activity: Alkaline phosphate activity (ALP) was measured according kind and king method(Kind & King, 1954) by using a factory kit by Biomerex (French). The principle of measurement includes the measurement of phenol released from the interaction of potassium ferricyanide and 4- aminoantipyrine.

Estimation the level of calcium: calcium was measured in the spectrophotometric method and using a factory kit by Bay Labo (French). The principle of measurement involves the interaction of calcium with O-Cresolphthalein (CPC) at alkaline medium. Formation a pink color complex, which measured at 570 nm (Burtis et al., 2012).

Estimation the level of phosphorus: Phosphorus was measured in the spectrophotometric method and using a factory kit by Bay Labo (French). The principle of measurement involves the interaction of interaction of ammonium molybdate with phosphomolybdic complex, in acid medium, releasing phosphorus ion. The absorbance was measured at λ= 340 nm (Burtis et al., 2012).

Statistical Analysis: The statistical analysis was carried out using statistical programe (SPSS). The results expressed a mean± SD (standard deviation). Consider significant when P values are less than 0.05 (Beddo & Kreuter, 2004).

Results and Discussion

The results of our study showed that the average age of non-Hodgkin lymphoma patients (NHL) was 56.1±11.1 years, and the average age of healthy persons (controls) was 52.2±13.8 years as shown in Table 1.

Table 1. Clinical Distribution of Patients (A)

	Controls	Patients (NHL)
Total number (Sex (F/M))	(19/21)	80 (34/46)
Treated patients (Sex (F/M))	-	40 (18/22)
Untreated patients(Sex (F/M))	-	40 (16/24)
F: Females; M: males; NHL: non-Hodgkin lymphoma.		

The results as shown in Table 2. indicated that non-Hodgkin lymphoma patients have a significant increase (P<0.0001) in levels of lactate dehydrogenase (529±164.5 U/L, NHL patients versus 299.1±34.5U/L controls) and alkaline phosphatase (298±115.7 U/L NHL patients versus 98.8±39.4U/L controls) compared to healthy people.

The results showed the high lactate dehydrogenase for patients and this is consistent with (Gandhi, Pophali, & Witzig, 2019)Galleze et al., 2017; Lu et al., 2013; Tahannejad, Dayer, & Samie, 2012(Gandhi et al., 2019))This is probably due to the fact that in non-hodgkin's lymphoma patients gets in an increase in the rate of sugar decomposition (GLYCOLUYSIS) and thus increases the effectiveness of lactate dehydrogenase, thus it is possible to consider LDH as a tumor index for lymphatic non-Hodgkin's patients. (Galleze et al., 2017; Shamoon & Polus, 2010).

Also, the results indicated that untreated NHL patients have a significant increase (P< 0.0001) in levels of LDH (697.6±292.3 untreated NHL patients versus 317.6±92.3 treated NHL patients) and ALP (336.3±122.4 untreated NHL patients vs. 112.3±42.3 treated NHL patients) compared to treated NHL patients as shown in Table 3. Increase in LDH activity possibly due to the use of too much glucose in metastatic tissues and increased glucose conversion to pyrophosphate(Tahannejad et al., 2012; Taher, Hummadi, AL-Bashir, & AL-Araji, 2016).

While no significant difference was shown in the levels of LDH, ALP, calcium and phosphorus between the groups of treated and healthy people as shown in Table 4.Also, increased significant (P<0.0001) level of alkaline phosphatase in NHL patients compared with the controls were agreement with (Tahannejad, Dayer, & Samie, 2012). The high level of activity of ALP may probably be attributed to the high use of too much energy by cancer cells. The results of the study also showed that there is non-significant difference in the level of calcium and phosphorus between patients and healthy people.

Table 2. Comparing the variables studied between the patients of the non-Hodgkin lymphoma and the healthy subjects (B)

Variables	Controls	Patients (NHL)	p-value
Age (no.)	52.2±13.8 (40)	56.1±11.1 (80)	0.122
LDH (U/L)	299.1±34.5	***529±164.5	0.0001
ALP (U/L)	98.8±39.4	***298±115.7	0.0001
Calcium (mg/ml)	8.1±1.3	8.3±1.6	0.09
Phosphorus (mg/ml)	3.6±0.6	3.7±0.73	0.13
NHL: non-Hodgkin lymphoma; LDH: lactate dehydrogenase; ALP: alkaline phosphatase; mg: milligram; ml: milliliter; U: unit no.: number. ***significant at (p≤ 0.0001) when p value be at (0.0001).			

Moreover, the results indicated that untreated NHL patients have a significant increase (P< 0.0001) in levels of lactate dehydrogenase (697.6±292.3 versus 317.6±92.3) and alkaline phosphatase (336.3±122.4 vs. 112.3±42.3) compared to treated patients, as shown in Table 3.

Moreover, the results also showed a significant increase of lactate dehydrogenase in untreated non-Hodgkin lymphoma compared to therapists, while there is no significant difference to the activity of lactate dehydrogenase among patients treated with healthy people and this is consistent with (Galleze et al., 2017; Purnamasidhi et al., 2019) which means LDH can be used as an indicator of the response to chemotherapy and the improvement of patients' health. The increased activity of lactate dehydrogenase reflects the prevalence of

the tumor, as the increased activity of LDH (Purnamasidhi et al., 2019). Also in the advanced stages of the disease the shattered tissues increase and as a result gets more liberalization of ALP and LDH enzymes that explain the results we have obtained in untreated patients. While no significant difference was shown in the levels of calcium and phosphorus as shown in Table 3

Table 3. Comparing the variables studied between treated and untreated non-Hodgkin lymphoma (D)

Variables	Patients (NHL) (treated)	Patients (NHL) (untreated)	p-value
Age (no.)	52.4±10.5 (40)	6.1±10.4 (40)	0.913
LDH (U/L)	317.6±92.3	***697.6±292.3	0.0001
ALP (U/L)	112.3±42.3	***336.3±122.4	0.0001
Calcium (mg/ml)	8.2±1.1	8.3±1.35	0.075
Phosphorus (mg/ml)	3.65±0.53	3.75±0.73	0.85
NHL: non-Hodgkin lymphoma; LDH: lactate dehydrogenase; ALP: alkaline phosphatase; mg: milligram; ml: milliliter; U: unit no.: number. ***significant at (p≤ 0.0001) when p value be at (0.0001).			

While no significant difference was shown in the levels of lactate dehydrogenase, alkaline phosphatase, calcium and phosphorus between the groups of treated and healthy patients as shown in Table 3.

Table 4. Comparing the variables studied between treated non-Hodgkin lymphoma and healthy (C)

Variables	Controls	Patients (treated)	p-value
Age (no.)	52.2±13.8 (40)	54.4±10.5 (40)	0.913
LDH (U/L)	299.1±34.5	317.6±92.3	0.289
ALP (U/L)	98.8±39.4	112.3±42.3	0.155
Calcium (mg/ml)	8.1±1.3	8.2±1.1	0.075
Phosphorus (mg/ml)	3.6±0.6	3.65±0.53	0.85
NHL: non-Hodgkin lymphoma; LDH: lactate dehydrogenase; ALP: alkaline phosphatase; mg: milligram; ml: milliliter; U: unit no.: number. ***significant at (p≤ 0.0001) when p value be at (0.0001).			

The results showed that untreated patients get a significant increase (P<0.0001) for ALP and LDH enzymes compared to treated patients, while the results indicated that there was non-significant increase in ALP and LDH for treated patients compared to healthy patients.

The activity of lactate enzyme increases when lymphatic proliferation disorder occurs, in non-Hodgkin's lymphoma patients the level of activity of lactate dehydrogenase increases, so it can be an important predictive indicator and can therefore be used as an indicator to respond to treatment. (Yadav et al., 2016).

Conclusion

The results of our study showed significant increase in the activity of ALP LDH for NHL patients compared to healthy people. Moreover, a significant increase in the activity of ALP LDH for untreated NHL patients compared to treated NHL patients and a non-significant difference of levels of LDH, ALP, calcium and phosphorus between treated NHL patients when compared with healthy patients. It is possible to use lactate dehydrogenase and alkaline phosphatase as an indicator to diagnose and to know the severity of the disease as well as to monitor the effect of treatment for patients.

Acknowledgements or Notes

Please provide acknowledgements or notes in a separate section at the end of the article before the references.

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