

## HEPATITIS C. VIRAL INFECTION IN PATIENTS WITH NON-HODGKIN LYMPHOMA

\*Khldoun Salah Aslan

MD, Department of Laboratory, Tishreen University Hospital, Lattakia, Syria.



\*Corresponding Author: Khldoun Salah Aslan

MD, Department of Laboratory, Tishreen University Hospital, Lattakia, Syria.

Article Received on 07/04/2024

Article Revised on 28/04/2024

Article Accepted on 19/05/2024

## ABSTRACT

**Background:** Lymphoma is considered a serious disease with an increased prevalence, so it was necessary to research all its possible causes, including HCV infection, to search for new treatments and prevention methods. This study is the first of its kind in Syria to investigate the relationship between HCV infection and the occurrence of lymphoma. Numerous studies have proven that the correct treatment of HCV infection in patients with some types of lymphoma significantly improves the prognosis and therefore the detection and treatment of HCV is extremely important. **The aim of the study:** Measurement of the level of HCV antibodies in patients with non-Hodgkin Lymphoma and comparison with two groups (healthy people, patients with solid tumors) in order to study the possible relationship between Hepatitis C and lymphoma. **Materials and Methods:** This study was conducted at Tishreen University Hospital, Syria between 2023-2024. Serological samples were collected for three groups: the first group consists of 58 patients with all types of non-Hodgkin lymphoma, the second group consists of patients with solid tumors (64 patients), and the third healthy group (61 people). After separating the hematogram using a micropipette and transferring it to the Eppendorf tubes, Direct ELISA technique was used to detect anti HCV IgG. **Results:** The study sample included 58 patients, 50 patients were negative in hepatitis C Virus Antibodies (86.2%), while the number of positive patients were 8 patients by (13.8%). We can say that there is an association between Hepatitis C infection and non-Hodgkin lymphoma, but we cannot say for sure that HCV infection will inevitably lead to non-Hodgkin Lymphoma.

**KEYWORDS:** Non-Hodgkin Lymphoma, Hepatitis HCV, ELISA, Antibodies.

## INTRODUCTION

Lymphomas are a group of heterogeneous malignancies that originate from lymphoid tissue, and constitute more than 3% of all cancers around the world. The origin of most lymphomas is B cells with a small percentage of T cells. These malignancies are mainly divided into Hodgkin Lymphoma (HL) and non-Hodgkin's non-Hodgkin Lymphoma (NHL).<sup>[1]</sup>

**☒ Non-Hodgkin Lymphoma**

There are 3 main types of Hodgkin lymphoma: B-cell lymphoma (about 90% of all cases) of non-Hodgkin lymphoma globally, while the second type, T-cell lymphoma (10% of all cases), and the third type, NK-cell lymphoma (about 1% of all cases).<sup>[2],[3]</sup>

**☒ Risk factors for non-Hodgkin Lymphoma**

Risk factors of developing non-Hodgkin lymphoma have been widely studied. These factors include autoimmune diseases, medications, infections, lifestyle, genetic factors, race, family history and occupational factors.<sup>[4,5]</sup> Obesity has been shown to be a risk factor for Diffuse Large B-cell lymphoma (DLBCL).<sup>[6]</sup>

The risk of developing non-Hodgkin lymphoma in patients with autoimmune diseases-including Rheumatoid Arthritis, Sjogren Syndrome, systemic Lupus continued to increase.<sup>[7]</sup>

**☒ Viral infections and non-Hodgkin Lymphoma**

Both viral and bacterial infections have been shown to be closely related to the development of non-Hodgkin lymphoma, with Helicobacter Pylori causing the majority of muco-infectious associated lymphomas (MALT).<sup>[8]</sup>

Epstein-Barr virus is related to both Burkitt Lymphoma, T-cell and nasal NK lymphoma.<sup>[9,10]</sup> Hepatitis C virus is associated with splenic marginal zone lymphoma and DLBCL.<sup>[11]</sup>

**Study design:** observational cross-sectional study.**Sample collection**

This study was conducted at Tishreen University Hospital Lattakia, Syria between 2023-2024. Serological samples were collected for three groups: the first group of 58 patients with all types of non-Hodgkin lymphoma,

the second group consists patients with solid tumors (64 patients), and the third healthy group (61 people).

The blood samples were collected by drawing 3 mL of venous blood on tubes containing EDTA anticoagulant in the hematology Laboratory of the hospital. We separated the hematogram using a Micropipette and transferred it to the Eppendorf tubes and the samples were kept in the Freezer at Tishreen Hospital at a temperature of (-60 degrees Celsius). In this study, *Direct ELISA* technique was used to detect anti HCV IgG.

### Reading and Interpretation of Results

To determine the valence of human HCV antibodies we compare the sample well with the controls.

### Limit value = mean negative witness with standard deviation $\pm 0.2$

When the standard deviation (SD) of the sample is less than the limit value means the result is negative . When the standard deviation of the sample is greater or equal to the limit value means the result is positive.

### Statistical analysis

Using the Mann-Whitney Test to compare averages. Use The Chi-square test to compare the percentages of categorical variables between the studied groups. The differences at the  $p$ -value  $\leq 0.05$  were considered statistically significant. The statistical analysis was carried out with SPSS to determine the results.

**Table 1: Distribution of sample groups by gender.**

Gender	Non- Hodgkin Lymphoma group	58 patients (35:23 M:F)
M:male	Solid tumors group	64 patients ( 36: 28 M:F)
F:Female	Healthy people	61 patients (34:27 M:F)

### HCV Antibodies In Our Study

#### 1. Non-Hodgkin Lymphoma Patients

The study sample included 58 patients, 50 patients were negative in hepatitis C Virus Antibodies (86.2%), while the number of positive patients were 8 patients by (13.8%).

#### 2. Distribution of HCV antibodies by Type of non-Hodgkin Lymphoma

We performed cross-table analysis of the distribution of HCV antibodies in patients with Non-Hodgkin

### RESULTS

#### 1. Characterization Of The Sample For Non-Hodgkin Lymphoma (58 patients)

**According to Gender:** The study sample included 58 people consisted of 35 males (60.3%) and 23 females (39.7%)

**According to Non- Hodgkin Lymphoma types:** The study sample included 58 patients consisted of 35 patients with B-cell lymphoma (93.1%), 3 patients with T-cell lymphoma (5.2%). And one undiagnosed patient only.

**According to the date of diagnosis:** The study sample included 58 patients, 15 patients have been treated (25.9%), while the number of newly-diagnosed was 43 patients (74.1%).

#### 2. Characterization of healthy sample (61 patients)

**According to Gender:** The study sample included 61 people consisted of 34 males (55.7%) and 27 females (44.3%).

#### 3. Characterization of the sample of patients with solid tumors

**According to Gender:** The study sample included 64 people consisted of 36 male (56.3%) and 28 females (43.7%).

lymphoma according to the types and subtypes of Lymphoma. The results showed that the  $P$ -value = 0.709, which is higher than the threshold value . So there are no significant differences between the distribution of antibodies in the types of non- Hodgkin's lymphoma. As for the sub - types of lymphoma, the following table shows the distribution of HCV antibodies in patients with percentages for each group so as to ensure the negative and positive ratios for the antibodies:

**Table 2: HCV antibodies in patients with lymphoma according to types and sub-types.**

Total	Antibodies HCV		Non-Hodgkin Lymphoma sub-types
	Positive	Negative	
29	5	24	N
50.0%	62.5%	48.0%	%
4	0	4	N
6.9%	0.0%	8.0%	%
9	3	6	N
15.5%	37.5%	12.0%	%
1	0	1	N
1.7%	0.0%	2.0%	%

2	0	2	N	<b>Hairy B-cell Lymphoma</b>
3.4%	0.0%	4.0%	%	
2	0	2	N	<b>Cutaneous B-cell Lymphoma</b>
3.4%	0.0%	4.0%	%	
2	0	2	N	<b>MCL</b>
3.4%	0.0%	4.0%	%	
1	0	1	N	<b>CTCL Mycosis Fungoides</b>
1.7%	0.0%	2.0%	%	
2	0	2	N	<b>Burkitt Lymphoma</b>
3.4%	0.0%	4.0%	%	
1	0	1	N	<b>Peripheral T-cell Lymphoma</b>
1.7%	0.0%	2.0%	%	
1	0	1	N	<b>B PBLL</b>
1.7%	0.0%	2.0%	%	
1	0	1	N	<b>ALCL</b>
1.7%	0.0%	2.0%	%	
2	0	2	N	<b>Marginal Lymphoma B-cell</b>
3.4%	0.0%	4.0%	%	
1	0	1	N	<b>Other</b>
1.7%	0.0%	2.0%	%	
58	8	50		<b>Total</b>
100.0%	100.0%	100.0%		

## DISCUSSION

In this study, we measured Hepatitis C virus antibodies in three groups, the first is a group of patients with all types of non- Hodgkin lymphoma, consisting of 58 patients, the second for solid tumor patients, consisting of 64 patients, and the third for a group of healthy people, consisting of 61 people. The results showed that there was a significant difference between the distribution of antibodies in both the non-Hodgkin lymphoma group and the other groups, but there was no significant difference between the tumor group and the group of non-Hodgkin lymphoma patients.

When Analyzing the results, we found that there is a clear relationship between the incidence of non- Hodgkin lymphoma and Hepatitis C antibody positivity, and there is also a clear relationship between the incidence of tumors and hepatitis C antibody positivity, even though it could not be definitely assured that the incidence of Hepatitis C is a specific risk factor to non- Hodgkin lymphoma, due to the absence of a statistically significant difference between the distribution of antibodies in both the lymphoma group and the other tumor group.

## CONCLUSION

We can say that there is an association between Hepatitis C infection and non- Hodgkin lymphoma, but we cannot say for sure that HCV infection will inevitably lead to non- Hodgkin lymphoma

## ACKNOWLEDGMENT

The authors have no financial interests to disclose. This research didn't receive any specific grant from funding agencies in public, commercial or non-profit sectors.

We wish to thank all medical staff for their hard work even with great difficulties.

## REFERENCES

1. Robert Marcus, J.W.S., Michael E. Williams, *LYMPHOMA Pathology, Diagnosis and Treatment*, 2007: New York.
2. Armitage, J.O., et al., *Non-Hodgkin lymphoma*. *Lancet*, 2017; 390(10019): 298-310.
3. Singh, R., et al., *Non-Hodgkin's lymphoma: A review*. *Journal of family medicine and primary care*, 2020; 9(4): 1834-1840.
4. Morton, L.M., et al., Etiologic heterogeneity among non-Hodgkin lymphoma subtypes: the InterLymph Non-Hodgkin Lymphoma Subtypes Project. *J Natl Cancer Inst Monogr*, 2014; 2014(48): 130-44.
5. Cerhan, J.R. and S.L. Slager, Familial predisposition and genetic risk factors for lymphoma. *Blood*, 2015; 126(20): 2265-73.
6. Castillo, J.J., et al., Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. *Clin Lymphoma Myeloma Leuk*, 2014; 14(2): 122-30.
7. Zintzaras, E., M. Voulgarelis, and H.M. Moutsopoulos, The risk of lymphoma development in autoimmune diseases: a meta-analysis. *Arch Intern Med.*, 2005; 165(20): 2337-44.
8. Bayerdörffer, E., et al., Regression of primary gastric lymphoma of mucosa-associated lymphoid tissue type after cure of *Helicobacter pylori* infection. *MALT Lymphoma Study Group*. *Lancet*, 1995; 345(8965): 1591-4.
9. Kwong, Y.L., Natural killer-cell malignancies: diagnosis and treatment. *Leukemia*, 2005; 19(12): 2186-94.

10. Saha, A. and E.S. Robertson, Epstein-Barr virus-associated B-cell lymphomas: pathogenesis and clinical outcomes. *Clin Cancer Res.*, 2011; 17(10): 3056-63.
11. Giordano, T.P., et al., Risk of non-Hodgkin lymphoma and lymphoproliferative precursor diseases in US veterans with hepatitis C virus. *Jama*, 2007; 297(18): 2010-7.