Mediterranean Journal of Hematology and Infectious Diseases

Original Article

High Prevalence of Hepatitis C Virus among B-Cell Non Hodgkin Lymphoma Patients in Mansoura Region (Egypt), ANRS 12263 Study

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Competing interests: The authors have declared that no competing interests exist.

Abstract. ***Background:*** **The prevalence of Hepatitis C virus in Egypt reaches 15%, which is considered the highest in the world. Genotype 4 represents 93 % of Egyptian HCV infections. Non-Hodgkin lymphoma (NHL) is the 5th most common cancer in Egypt. The association between HCV infection and occurrence of B-cell NHL is well known while data are scarce in Eastern countries.**
Objectives: **We aimed to evaluate the prevalence of HCV infection among patients with B-cell NHL and the clinical characteristics of HCV associated B-cell NHL in the Delta region (Mansoura-Egypt).**
Methods: **Between March 2012 and March 2013, 110 adult patients newly diagnosed with B-cell NHL were enrolled in the current study. This study was carried out at Oncology Center, Mansoura University. Study subjects provided serum for HCV testing.**
Results: **The prevalence of HCV infection among these patients was 61% (67/110 patients). Among them, 80% (32/40 tested patients) presented with viremia. In contrast with the histological distribution previously described in Northern regions, the majority of HCV associated lymphomas were DLBCLs (72%) followed by SLL/CLL (13%), follicular lymphomas (7.5%) and marginal zone lymphomas (7.5%).**
Conclusions: **B-cell lymphomas are highly associated with HCV infection in Egypt. Further developments are needed to give access to antiviral treatment for these patients.**

Keywords: HCV, Non-Hodgkin lymphoma, Viremia, Egypt.

Citation: Saleh L.M., Canioni D., Shamaa S., El-Zaafarany M., Emarah Z., Abdel-Aziz S., Eladle E., Abdelaziz A., Hermine O., Besson C., Abdel-Ghaffar H. High prevalence of hepatitis C virus among B-cell lymphoma patients in Mansoura region (Egypt), ANRS 12263 study. Mediterr J Hematol Infect Dis 2019, 11(1): e2019011, DOI: http://dx.doi.org/10.4084/MJHID.2019.011

Published: January 1, 2019 **Received: June 2 , 2018** **Accepted:November 25 , 2018**

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Introduction. In the 2008 publication of WHO (World Health Organization) classification of hematological malignancies, infectious agents including HCV (Hepatitis C Virus) have been implicated in several types of non-Hodgkin's lymphoma (NHL).[1] WHO estimates that about 3% of the world's population has been infected with HCV and that there are more than 170 million chronic carriers.[2] HCV is an RNA hepatotropic and lymphotrophic virus, replicating within the B cells and triggering lymphomagenesis.[3] Despite etiologic heterogeneity among NHL subtypes,[4] several studies have shown a higher prevalence rate of HCV in B-NHL cases in comparison to controls.[5,6] Globally, approximately 8% of NHL may be attributable to HCV.[8] The EPILYMPH consortium documented an almost two-fold increased risk of NHL in patients with chronic HCV infection compared to HCV negative control.[9,10] This increased risk may be more dramatically evident in populations with high HCV prevalence.[10,7] Egypt has a very high prevalence of HCV: according to Egypt Demographic and Health Survey 2008 (EDHS, 2008), HCV prevalence reaches 14.7 % in 15-59 years age group.[11] This percentage is even higher in rural areas.[12] Approximately 8–10 million Egyptians have serological evidence of HCV infection.[13,14] Interestingly, the WHO Glocobocan Project for cancer incidence and mortality, reported that NHL, is the 5th malignancy in Egypt in both genders compared to the 12th place in Northern countries.[11] Therefore, Egypt provides a rationale for investigating the association between HCV and NHL. We performed a study in Mansoura region (Egypt) aimed to estimate the prevalence of HCV infection among B-cell NHL patients and to determine the clinical characteristics of HCV associated B-cell NHL patients in comparison to their non HCV counterpart.

Patients and Methods.

Study participants. Between March 2012 and March 2013, 110 patients were diagnosed with B-NHL in Mansoura Oncology Center – Delta region, Egypt. Patients with a new NHL diagnosis were included prospectively in the present study. The inclusion and exclusion criteria were similar as for ANRS HC-13 Lympho-C study,[15] which is a large French series of patients with HCV-associated B-NHL.[15] Lymphoma staging was determined using the Ann Arbor system. Staging evaluation included physical examination, routine laboratory tests, bone marrow aspirate and biopsy when clinically relevant, computed tomography (CT). Eastern Cooperative Oncology Group performance status (ECOG PS) was recorded at lymphoma diagnosis and during each visit. The International Prognostic Index (IPI) score was calculated for DLBCL patients.[16] Their serum samples were evaluated for HCV, HBV and HIV serologies at lymphoma diagnosis. HCV positive cases were evaluated for HCV viral load. Each patient was planned to be monitored every six months for three years. Investigations were performed after approval received by Mansoura Medical Research Ethics Committee. Written informed consent to participate in the study was obtained from each subject. The study was conducted consistent with Good Clinical Practices (GCP) under the ICH guidelines and applicable national/local regulations.

Laboratory methods. Enzyme-linked immunosorbent assays (ELISA): ELISA assays were used to determine anti-HCV antibodies, Hepatitis B virus (HBV) antibodies and HBsAg and HIV antibodies (BIOTEC, UK) from serum samples of all patients. RNA isolation and quantitative real-time polymerase chain reaction: RNA was extracted from serum samples according to the manufacturer's instructions then RNA was reverse-transcribed and amplified by One Step RT-PCR QIAGEN Kit on a GeneAmp PCR system 9700. Real-time PCR was performed on the StepOne (Life Technologies). Routine laboratory testing: Transaminases (ALT & AST) serum levels were determined and expressed as IU/L, and Rheumatoid factor (RF) were determined for HCV-positive samples by turbid metric methods with cut off value > 25 international unit /ml.

Immunohistochemical testing. For all patients, cyto-histological data regarding B-NHL diagnosis were recorded and categorized according to the WHO 2008 classification. Pathological materials of 22 cases of HCV+ lymphoma samples were reviewed by hematopathologist (DC) who coordinated the review of the ANRS-HC13 Lympho C study. Immunohistochemistry was performed in tumor samples following a three-step immunoperoxidase method. The antibody panel included CD20, CD3, CD5, CD10, Bcl6, Bcl2, MUM1 and Ki67.

Statistical analysis. All statistical computations were performed using SPSS Software version 20 (IBM Corp., Armonk, New York, 2011). Continuous data were represented as the mean ± standard deviation or the median (minimum–maximum), while categorical variables were represented by frequency. Student's t-test, or Mann–Whitney test were used for comparison of continuous variables between groups while categorical data were compared between groups by using chi-square test with Yates correction. A p value of < 0.05 was considered statistically significant. Follow-up was defined from the start of B-NHL diagnosis to the last

follow-up visit. Overall survival (OS) was measured from the lymphoma diagnosis to the last follow-up or the death from any cause. The probability of OS was defined with Kaplan-Meier's method, and differences were compared with the log-rank test.

Results. The study included 110 patients with NHL (**Table 1**). HCV infection was detected in 61% (67/110 patients) of cases. Gender-ratio did not differ between HCV positive and HCV negative patients. HCV positive patients were slightly younger than HCV negative patients (53 versus 58 years, p=0.04). Among 40 HCV positive cases with available HCV viral load, 80 % (32/40) were positive. Rheumatoid factor was positive in 23 patients out of 32 HCV RNA positive patients tested (72%). The main histological subtypes among HCV positive patients were DLBCLs (48/67 (72%)), SLL/CLL (9/67 (13%)), marginal zone lymphoma (5/67 (7.5%)) and follicular lymphoma (5/67 (7.5%)) (**Table 2**). Of note, none of the DLBCL reviewed samples had features of transformation from low-grade lymphoma.

Ann Arbor stage was III–IV in 78% in HCV positive studied patients. ECOG status was 0-1 in 57% of HCV positive patients. ALT and AST serum levels were higher in HCV positive NHL patients in comparison to HCV negative patients (66%versus 49%). LDH was found to be elevated in 82% of HCV positive NHL. Overall, IPI score was high/high intermediate in 78% of HCV positive patients. **Table 3** presents a comparison between HCV positive and HCV negative DLBCL patients. In this subgroup also, HCV-positive patients were younger and had more frequently elevated transaminases than HCV-negative patients.

All patients except eight with DLBCL and four with marginal zone lymphoma were treated with front-line treatment for lymphoma. Lymphoma management was classified according to anthracycline use into

Table 1. Characteristics of HCV positive and HCV negative patients with B-cell Non-Hodgkin Lymphoma (n=110).

	HCV- positive	**HCV- negative**	**p-value**
	***n* = 67 (61%)**	***n*= 43 (39%)**	
Gender ratio (M/F)	37/30(1.2)	26/17(1.5)	0.69
Age (years), mean [±SD]	53[± 13]	58 [± 11]	0.04
Ann Arbor Stage			0.27
1–2	15(22%)	6(14%)	
3–4	52(78%)	37(86%)	
ECOG Scale			0.006
0–1	38(57%)	13(30%)	
2–4	29(43%)	30(70%)	
AAIPI*			0.006
Low, Low-Intermediate	15(22%)	4(9%)	
High, High-intermediate	52(78%)	39(91%)	
Transaminases (ALT&AST)			0.08
Elevated	44(66%)	21(49%)	
Normal	23(34%)	22(51%)	
LDH			0.56
Elevated	35(52%)	25(58%)	
Normal	32(48%)	18(42%)	

*AAIPI : Age Adjusted International Prognostic Index.

Table 2. Comparison of B-NHL histological subtype distributions in HCV positive and HCV negative patients (N=110).

B-NHL histological types	**HCV- positive**	**HCV- negative**
	***n* = 67 (61%)**	***n*= 43 (39%)**
SLL/CLL	9 (13%)	8 (19%)
Mantle cell lymphoma(MCL)	0	1 (2%)
Follicular lymphoma (FL)	5(7.5%)	3 (7%)
Marginal zone lymphoma (MZL)	5(7.5%)	0
Diffuse large B cell lymphoma (DLBCL)	48(72%)	31 (72%)

DLBCL indicates diffuse large B-cell lymphoma; FL: follicular lymphoma, MZL: marginal zone lymphoma; SLL: small lymphocytic lymphoma, MCL: Mantle cell lymphoma.

Table 3. Characteristics of HCV positive and HCV negative patients with DLBCL (n=79).

	DLBCL Patients (N=79)		
	HCV positive n(%) 48(61%)	HCV negative n(%) 31(39%)	P. value
Age (years)			***0.02***
(Means ± SD)	58.6± 10.9	50.8± 13.5	
Sex			0.89
Males	28 (58%)	18 (58%)	
Females	20 (42%)	13 (42%)	
Ann Arbor Stage			0.55
1–2	9 (19%)	4(13%)	
3–4	39(81%)	27(87%)	
ECOG Scale			0.067
0–1	26(54%)	10(32%)	
2–4	22(46%)	21(68%)	
AAIPI*			***0.02***
Low, Low-Intermediate	27(56%)	9(29%)	
High, High-intermediate	21(44%)	22(71%)	
Splenic involvement			0.52
Yes	8 (17%)	3 (10%)	
No	40(83%)	28(90%)	
Extra-nodal sites			0.49
Yes	24(50%)	18(58%)	
No	24(50%)	13(42%)	
Bone marrow involvement			0.06
Yes	13(27%)	6(19%)	
No	28 (58%)	21(68%)	
Not available	7(15%)	4(13%)	
Transaminases (ALT&AST)			***0.01***
Elevated	24(50%)	6 (19%)	
Normal	24(50%)	25(81%)	
LDH			0.63
Elevated	29 (60%)	21 (68%)	
Normal	19(40%)	10(32%)	
Median survival (months)	12.7	23.7	0.26

"Anthracycline containing regimen" 45 patients (67%), "Non-anthracycline containing regimen" 14 patients (24%). Forty-five patients received CHOP, 13 patients received Alkylators ± corticosteroids. Four patients received rituximab in each case associated with CHOP. One MZL patient was treated with interferon alone. With the exception of interferon, no antiviral treatment was given to these patients.

To our knowledge, 24 patients died out of the 67 HCV positive patients (36%). The median OS within the HCV positive group was 13 months (mean 21 ± 2 months) while it was 26 months (mean 25 ± 2.4

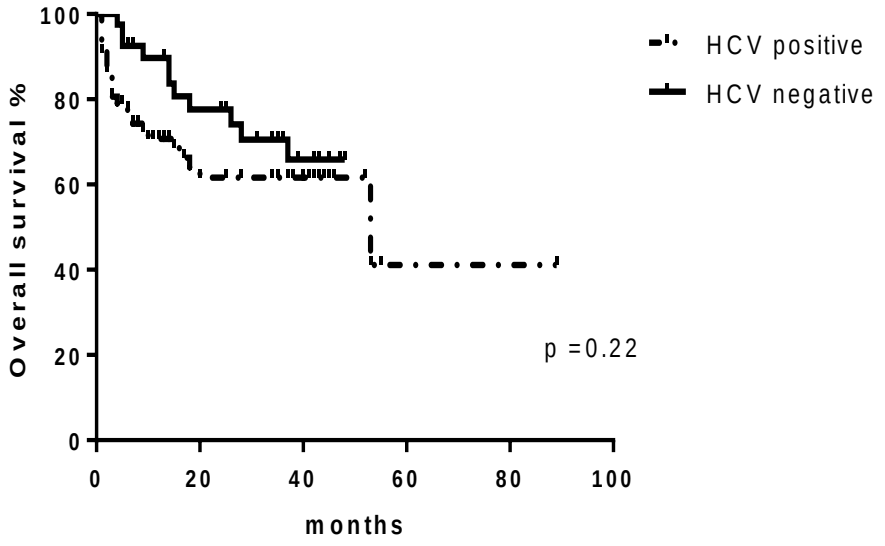

Figure 1. Overall survival of B-cell NHL lymphoma patients according to HCV status. HCV-positive patients (n= 67) HCV-negative patients (n= 43).

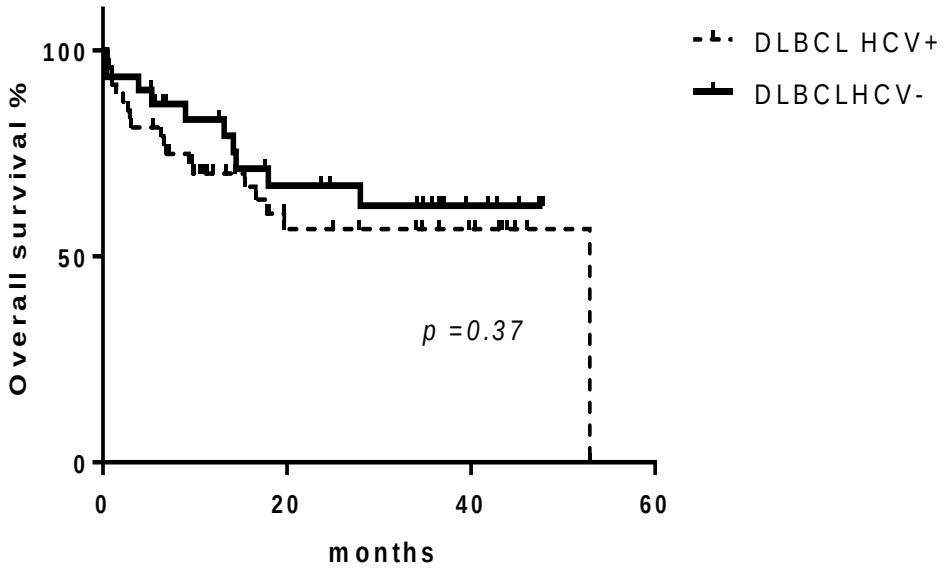

Figure 2. Overall survival of DLBCL patients according to HCV status. HCV-positive DLBCL patients (n= 48) HCV-negative DLBCL patients (n= 31).

months) within the HCV negative patients (p=0.22) (**Figure 1**). The median OS of the HCV positive DLBCL patients was 12.7 months (mean 18.7 ± 15.8 months) and 23.7 months (mean 23.4 ± 15.7 months) within the HCV negative patients (p=0.37) (**Figure 2**).

Discussion. Confirming the role of HCV in lymphoma development, we report a strikingly high rate of HCV infection (61%) among patients with NHL in the Mansoura region, which appears to be the highest reported to our knowledge in the literature. Previous studies on the malignant complications of chronic HCV infection in Egypt or focusing specifically on the association between HCV and NHL reported an HCV prevalence ranging from 40 to 50% among patients with NHL.[19,20,21,23] The higher rate we report in the Delta region may be explained by the higher prevalence of HCV in this region.

In the present study, most of the patients had DLBCL (72%). MZL was rare (7.5%). The distribution of NHL

we report here is similar to previous findings in Egypt[19,20,21] with DLBCL proportions of 55% to 76% among HCV associated NHL, MZL proportion being lower than 10%.[21] Overall, our results are in agreement with many studies that reported HCV association with DLBCL, and MZL.[6,10,24,25] However, in Western/Northern countries most cases of HCV associated NHLs are MZL and DLBCL, being frequently transformed from low-grade lymphomas.[22] In our series, however, we did not identify such cases out of 22 cases reviewed by an expert hematopathologist (DC). The different distribution might be due to the unique environmental background or to differences in access to care. We cannot exclude that patients with low-grade lymphomas are underdiagnosed in Southern countries.

It would be interesting to confirm this finding in a larger number of pathological samples from patients with HCV-associated lymphomas in Southern countries. The low frequency of low-grade lymphoma in the study is consistent with other studies in Egypt although it strongly contrasts with the distribution of HCV associated lymphomas in Northern countries.

We did not find unique clinical or biological characteristics associated with HCV infection in lymphoma patients. This was previously reported in an Egyptian study performed on 132 DLBCL patients among whom 26.5% had HCV. There was indistinguishable demography for this group compared to HCV-negative patients.[21] Additionally, another Egyptian study comparing HCV infected and HCV uninfected patients with NHL showed no statistically significant difference in age, sex, clinical presentation, stage, IPI score, LDH level, pathological type, and chemotherapy regimen.[24] Of note in our population, HCV infected patients were younger and had more frequent elevated transaminases. Rheumatoid factor activity was positive in two-thirds of our population of HCV associated NHL, supporting a role of chronic antigenic stimulation on lymphomagenesis. These observations are similar to those reported in the Lympho C Study.[15] Overall, there was a trend for a pejorative impact of HCV infection on OS.

In our study, only one patient had access to antiviral therapy for their HCV infection. Recently, a subcommittee of the Egyptian National Commission for Viral Hepatitis was assigned to prioritize access to direct antivirals in patients with extrahepatic manifestations. HCV patients with Non-Hodgkin B-cell lymphoma were attributed the highest score according to relative urgency, and expected benefit of treatment.[26] Antiviral approaches should be evaluated in Egypt to improve the outcome of HCV associated NHL patients since many studies in Northern/Western countries demonstrated high rates of response after a successful front-line antiviral treatment (IFN and now Direct Antiviral Agents).[27,28,29]

Conclusions. Our study results confirmed the association between HCV infection and risk of NHL. Prevention and treatment of HCV infection may decrease NHL incidence, especially in areas with a high prevalence of HCV. Patients with NHL and their physicians should be aware of the high prevalence of chronic HCV infection in NHL in Egypt and patients should be routinely screened for HCV infection especially in endemic areas like delta region, Egypt. The access to antiviral drugs should be extended in these regions, and their impact on the clinical course of NHL should be evaluated in Egypt.

Acknowledgments. The ANRS 12263 study was funded by the sponsor ANRS (Agence Nationale de Recherches sur le Sida et les hépatites virales). The sponsor has approved the design of the study, the method and data collection.

References:

1. Campo E, Swerdlow SH, Harris NL, Pileri S, Stein H, Jaffe ES. The 2008 WHO classification of lymphoid neoplasms and beyond: evolving concepts and practical applications. Blood. 2011 May;117(19):5019–32. https://doi.org/10.1182/blood-2011-01-293050 PMid:21300984 PMCid:PMC3109529
2. EASL International Consensus Conference on hepatitis C. Paris, 26-27 February 1999. Consensus statement. J Hepatol. 1999;31 Suppl 1:3–8. PMid:10622553
3. Turner NC, Dusheiko G, Jones A. Hepatitis C and B-cell lymphoma. Ann Oncol Off J Eur Soc Med Oncol. 2003 Sep;14(9):1341–5. https://doi.org/10.1093/annonc/mdg363
4. Morton LM, Slager SL, Cerhan JR, Wang SS, Vajdic CM, Skibola CF, et al. Etiologic heterogeneity among non-Hodgkin lymphoma subtypes: the InterLymph Non-Hodgkin Lymphoma Subtypes Project. J Natl Cancer Inst Monogr. 2014 Aug;2014(48):130–44. https://doi.org/10.1093/jncimonographs/lgu013 PMid:25174034 PMCid:PMC4155467
5. Viswanatha DS, Dogan A. Hepatitis C virus and lymphoma. J Clin Pathol. 2007 Dec;60(12):1378–83. https://doi.org/10.1136/jcp.2007.051870 PMid:18042694 PMCid:PMC2095565
6. Taborelli M, Polesel J, Montella M, Libra M, Tedeschi R, Battiston M, et al. Hepatitis B and C viruses and risk of non-Hodgkin lymphoma : a case-control study in Italy. Infect Agent Cancer [Internet]. 2016;1–6. https://doi.org/10.1186/s13027-016-0073-x
7. de Martel C, Ferlay J, Franceschi S, Vignat J, Bray F, Forman D, et al. Global burden of cancers attributable to infections in 2008: a review and synthetic analysis. Lancet Oncol. 2012 Jun;13(6):607–15. https://doi.org/10.1016/S1470-2045(12)70137-7
8. Giordano TP, Henderson L, Landgren O, Chiao EY, Kramer JR, El-Serag H, et al. Risk of non-Hodgkin lymphoma and lymphoproliferative precursor diseases in US veterans with hepatitis C virus. JAMA. 2007 May;297(18):2010–7. https://doi.org/10.1001/jama.297.18.2010 PMid:17488966
9. Nieters A, Kallinowski B, Brennan P, Ott M, Maynadie M, Benavente Y, et al. Hepatitis C and risk of lymphoma: results of the European multicenter case-control study EPILYMPH. Gastroenterology. 2006 Dec;131(6):1879–86. https://doi.org/10.1053/j.gastro.2006.09.019 PMid:17087949
10. Maso LD, Franceschi S. Hepatitis C Virus and Risk of Lymphoma and Other Lymphoid Neoplasms : A Meta-analysis of Epidemiologic Studies. 2006;15(November):2078–86.
11. Mathers CD, Boschi-pinto C, Lopez AD. Cancer incidence, mortality and survival by site for 14 regions of the world. Glob Program Evid

Heal Policy Discuss Pap No 13. 2001;World Heal.
12. Ezzat S, Abdel-Hamid M, Eissa SA-L, Mokhtar N, Labib NA, El-Ghorory L, et al. Associations of pesticides, HCV, HBV, and hepatocellular carcinoma in Egypt. Int J Hyg Environ Health. 2005;208(5):329–39. https://doi.org/10.1016/j.ijheh.2005.04.003 PMid:16217918
13. Abdel-Aziz F, Habib M, Mohamed MK, Abdel-Hamid M, Gamil F, Madkour S, et al. Hepatitis C virus (HCV) infection in a community in the Nile Delta: population description and HCV prevalence. Hepatology. 2000 Jul;32(1):111–5. https://doi.org/10.1053/jhep.2000.8438 PMid:10869297
14. Darwish MA, Faris R, Clemens JD, Rao MR, Edelman R. High seroprevalence of hepatitis A, B, C, and E viruses in residents in an Egyptian village in The Nile Delta: a pilot study. Am J Trop Med Hyg. 1996 Jun;54(6):554–8. https://doi.org/10.4269/ajtmh.1996.54.554 PMid:8686770
15. Michot J-M, Canioni D, Driss H, Alric L, Cacoub P, Suarez F, et al. Antiviral therapy is associated with a better survival in patients with hepatitis C virus and B-cell non-Hodgkin lymphomas, ANRS HC-13 lympho-C study. Am J Hematol. 2015 Mar;90(3):197–203. https://doi.org/10.1002/ajh.23889 PMid:25417909
16. Armitage JO. Staging Non-Hodgkin Lymphoma. 1993;
17. Besson C, Canioni D, Lepage E, Pol S, Morel P, Lederlin P, et al. Characteristics and outcome of diffuse large B-cell lymphoma in hepatitis C virus-positive patients in LNH 93 and LNH 98 Groupe d'Etude des Lymphomes de l'Adulte programs. J Clin Oncol. 2006 Feb;24(6):953–60. https://doi.org/10.1200/JCO.2005.01.5016 PMid:16418500
18. Farawela H, Khorshied M, Shaheen I, Gouda H, Nasef A, Abulata N. Infection , Genetics and Evolution The association between hepatitis C virus infection , genetic polymorphisms of oxidative stress genes and B-cell non-Hodgkin ' s lymphoma risk in Egypt. Infect Genet Evol [Internet]. 2012;12(6):1189–94. https://doi.org/10.1016/j.meegid.2012.04.007
19. Kadry DY, Khorshed AM, Rashed RA, Mokhtar NM. Association of Viral Infections with Risk of Human Lymphomas, Egypt. 2016;17:1705–12.
20. de Sanjose S, Benavente Y, Vajdic CM, Engels EA, Morton LM, Bracci PM, et al. Hepatitis C and non-Hodgkin lymphoma among 4784 cases and 6269 controls from the International Lymphoma Epidemiology Consortium. Clin Gastroenterol Hepatol. 2008 Apr;6(4):451–8. https://doi.org/10.1016/j.cgh.2008.02.011 PMid:18387498 PMCid:PMC3962672
21. Couronne L, Bachy E, Roulland S, Nadel B, Davi F, Armand M, et al. From hepatitis C virus infection to B-cell lymphoma. Ann Oncol Off J Eur Soc Med Oncol. 2017;(October):1–9.
22. Haggag RM, Abu-Taleb F, Khaled HM. Rituximab-induced hepatitis C virus reactivation in HCV-positive patients with diffuse large B-cell lymphoma. J Clin Oncol [Internet]. 2016 May 20;34(15_suppl): e19039–e19039. https://doi.org/10.1200/JCO.2016.34.15_suppl.e19039
23. El-hefni AM, Elgohary TA, Kotb A, Abu-taleb FM. Efficacy of Ribavirin to Prevent Hepatitis Reactivation in Hepatitis C Virus-Infected Patients Treated for Non-Hodgkin Lymphoma, Single Egyptian Center Study. 2013;2(1):14–21.
24. El-Fishawy H, Saadi G, Hassaballa M, Hussein M, Doss W, Ragab G, et al. Antiviral treatment prioritization in HCV-infected patients with extrahepatic manifestations - An Egyptian perspective. J Adv Res [Internet]. 2016;7(3):391–402. https://doi.org/10.1016/j.jare.2016.02.006
25. Negri E, Little D, Boiocchi M, La Vecchia C, Franceschi S. B-cell non-Hodgkin's lymphoma and hepatitis C virus infection: a systematic review. Int J cancer. 2004 Aug;111(1):1–8. https://doi.org/10.1002/ijc.20205 PMid:15185336
26. Zuckerman E, Zuckerman T, Sahar D, Streichman S, Attias D, Sabo E, et al. The effect of antiviral therapy on t (14 ; 18) translocation and immunoglobulin gene rearrangement in patients with chronic hepatitis C virus infection. Blood. 2001 Mar 15;97(6):1555-9
27. Pozzato G, Mazzaro C, Maso LD, Mauro E, Zorat F, Moratelli G, et al. Hepatitis C virus and non-Hodgkin ' s lymphomas : Meta- analysis of epidemiology data and therapy options. 2016;8(2):107–16.
28. Lim LY, La D, Cserti-gazdewich CM, Shah H, Hpte M. Lymphoma Remission by Interferon-Free HCV Eradication Without Chemotherapy. ACG Case Rep J. 2015 Oct 9;3(1):69-70. doi: 10.14309/crj.2015.104. eCollection 2015 Oct
29. Arcaini L, Besson C, Frigeni M, Visentini M, Torres HA, Loustaud-ratti V, et al. Interferon-free antiviral treatment in B-cell lymphoproliferative disorders associated with hepatitis C virus infection.. Blood. 2016 Nov 24;128(21):2527-2532. DOI: 10.1182/blood-2016-05-714667