



PREVALENCE AND RISK FACTORS OF HEPATITIS C VIRUS INFECTION AMONG LYMPHOMA PATIENTS IN SANA'A CITY, YEMEN

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ABSTRACT

Back ground: Hepatitis C virus (HCV) has been postulated to be an etiological agent for lymphoid malignancies. People infected with the hepatitis C virus are at an increased risk of developing certain lymphomas. In developing country like Yemen, there is a scarcity of data to show either a positive or a negative association between HCV infection among patients with lymphoma.

Objective: To determine the prevalence of HCV by antibody testing and predisposing factors that may lead to HCV infection among patients with lymphoma at the National Oncology Center, Military Hospital Sana'a, Yemen.

Methods: Cross-sectional study was conducted on 144 lymphoma patients within period from May 2014 -April 2015. Blood samples were collected from lymphoma patients, then serum were separated and tested for detection of hepatitis C virus antibodies using commercially available kits for an advanced serological diagnostic of Chemiluminescent Microparticle Immunoassay (CMIA).

Results: HCV seropositivity was 2.8 %, where the male and female seropositivity were 3.0 % and 2.2% respectively, and based on age group categories the high rate was found among male young middle age 4.3%, and the HCV seropositivity was 3.2% among patients under chemotherapy. Risk factor for contracting HCV infection with dental visit, blood transfusion and clinic visit which ranged in descending order from higher 3.7% to lower 3.5% respectively. According to type of lymphoma the prevalence rate was 3.9% of HCV among the non-hodgkin's lymphoma (NHL), particularly B-cell NHL types and the geographical variations rate 3.7% was found among patients from Taiz province.

Conclusions: HCV prevalence in patients with B-NHL is approximately 3.9% suggesting a role of HCV in the etiology of B-NHL. This study will be helpful to the health care policy makers to design strategies plan for controlling and eradication of Hepatitis C infection in Yemen and more efforts are needed to provide proper educating and training of the ideal infection control measures for dental clinic.

KEYWORDS : Hepatitis C Virus, Non-Hodgkin lymphoma, Chemiluminescent Microparticle Immunoassay, Yemen

INTRODUCTION

Nowadays Hepatitis C virus (HCV) infection has been reported to be a prevalent disease and consider as a global health problem affecting 3% of the world population and 180 million people since earlier of the 21th century. Cirrhosis and hepatocellular cancer are the most common complications of HCV. However, HCV related health problems are not limited to the liver, hematological problems like type II mixed cryoglobulinemia (MC) or B-NHL may be seen in cases infected with HCV¹. The infection spread to the general population in some developed and developing countries such as Japan, Italy, and Egypt, with prevalence estimates ranging from 5% to 10%. In other developed countries the infection largely has been limited to individuals who have received blood transfusions or are intravenous drug users with population prevalence estimates ranging from 1% to 2%^{2,3}.

A causal role of HCV infection in cirrhosis and hepatocellular carcinoma is well established. Also, HCV has been linked to lymphomagenesis in people with and without type II mixed cryoglobulinemia⁴. However, in the majority of lymphoma studies, small sample sizes have prevented an analysis of the relationship between HCV and single lymphoma subtypes. Increasing evidence indicates that the association between HCV infection and lymphoma may be owing to viral infection-related chronic antigenic stimulation similar to that reported for *Helicobacter pylori* and gastric mucosa-associated lymphoid tissue lymphoma⁵. The chronic inflammation pathway would be consistent with the association between HCV and several types of lymphomas and with the regression of some lymphomas after eradicating the HCV

infection^{6,7}. The aims of this study were to determine the prevalence and analysis of the association between non-Hodgkin lymphoma (NHL) and HCV among Yemeni lymphoma patients which were determined using a rapid and advanced chemiluminescent microparticle immunoassay to measure HCV antibodies.

MATERIALS AND METHODS

Cross-sectional study was conducted on 144 lymphoma patients within a period from May 2014 -April 2015. About 3 cc blood is collected from each individual in gel vacutainer tube. All subjects had previously been informed about the HCV study, and had provided written informed consent for use of their sera for this study. The predesigned questionnaire was on Socio-demographic data as age, sex, chemotherapy and risk factor associated such as blood transfusion, dental visit, clinic visit.

Sample processing

The samples allowed to clot at room temperature and were centrifuged at high speed about 8000 rpm for 5 minutes in order to obtain a clear supernatant serum. All samples were run on Architect system which is fully diagnostic services of automated immuno analyser Architect i2000 analyser, by (Abbott Diagnostics, Illinois, USA).

Chemiluminescent Microparticle Immuno Assay (CMIA)

Chemiluminescent Microparticle Immuno Assay is slightly modified and advanced form of the Enzyme Linked Immuno Sorbant Assay (ELISA) technique. Architect system is designed to detect antibodies to putative structural and non-structural protein (HCr-43, c-100,

NS3, NS4) of HCV genome⁷. In the final reaction of Anti HCV detection, bound achrindinylated conjugates were used to generate chemiluminescent signals. Results were obtained automatically by the software by comparing the chemiluminescent signals obtained from the reaction product of the sample with the signal of the cut off value previously obtained by Anti HCV calibration. The overall specificity and sensitivity of this method was 99.6% and 99.7% respectively.

Statistical analysis

Data was analyzed statistically using the Epi Info statistical program version 6 (CDC, Atlanta, USA). The Chi-square test was used to analysed, the qualitative data, p value < 0.05 was considered as significant and Odds ratio with 95% confidence interval was used to evaluate the association of various age groups with respect to HCV status of male/female population.

RESULTS

HCV seropositivity was 2.8 %, where the male and female seropositivity were 3.0% and 2.2%, respectively with no associated OR for contracting HCV infection (OR=0.44) among male while among female it was associated OR (OR= 2.26). The age specific prevalence rates were ranged from 0 % - 4.3 %. Age group of ≤5 years was not detected. Based on the age group categories the higher rate 4.3% was among age group of 16-25 years, in which it was with associated OR for contracting HCV infection equal to 1.79 (p=0.61) where the lower rate was 2.6% among age group 6-15 years and age group of ≤5 years it was not detected as shown in Table 1.

Table 1: Seropositivity rate of HCV among Lymphomas patients according to sex and age

Characters	Positive HCV n=4		OR	CI	χ ²	P
	No.	%				
Sex						
Male n = 99	3	3.0	0.44	0.04-4.6	0.67	0.41
Female n = 45	1	2.2	2.26	0.23-23.3	0.7	0.41
Age groups/ Years						
≤ 5 (n=19)	ND	ND	ND	0-10.7	0.63	0.42
6 – 15 (n=39)	1	2.6	0.89	0.1-8.3	0.01	0.92
16 – 25 (n=23)	1	4.3	1.79	0.2 -16	0.25	0.61
26 – 35 (n=35)	1	2.9	1.04	0.11- 9.7	0.0	0.97
≥ 36 (n=28)	1	3.6	1.4	0.15 -	0.08	0.77

OR Odds ratio >1 (at risk) ,CI Confidence intervals, χ² Chi-square ≥3.9 (significant), p Probability value ≤0.05 (significant), Seropositivity rate of HCV was 3.2% among lymphoma patients under chemotherapy as shown in Table 2.

Table 2: The rate of HCV among patients of Lymphomas under chemotherapy sitting at National Oncology Center, Sana'a city

Variables	Positive HCV=4		OR	Ci	χ ²	p
	No.	%				
Under chemotherapy n=126	4	3.2	Undefined		0.59	0.44
Not under chemotherapy n=18	ND	0	0.00	0-11.4	0.59	0.43
Diabetic n=6 (4.2%)	ND	0				Undefined
Tuberculosis n=2 (1.4%)	ND	0				Undefined
Bilharzias n= 0 (0%)	ND	0				Undefined

OR Odds ratio >1 (at risk) ,CI Confidence intervals, χ² Chi-square ≥3.9 (significant), p Probability value ≤0.05 (significant), ND Not Detected

Table 3. Show the risk factor for contracting HCV infection with dental visit, blood transfusion and clinic visit which arranged in descending order from higher 3.7% to lower 3.5% respectively. In

addition there was no occurrence for other potential risk factors as contact to injected drug abuse, travel abroad, cupping, tattooing, etc. in our patients.

Table 3. Risk factors of contacting HCV among Lymphomas patients attending to National Oncology Center, Sana'a city

Factors	Positive HCV = 4		OR	CI	χ ²	P
	No.	%				
Blood transfusion n=86 of 144 (59.7%)	3/4	3.5	2.1	0.2-52	0.4	0.52
Dental visit n=81 of 144 (56.3%)	3/4	3.7	2.3	0.21-61	0.59	0.42
Clinic visits n=85 of 144 (59%)	3/4	3.5	2.2	0.2-54.3	0.43	0.51
Hemodialysis n=0	0	0				Not present
Injection drug abuse n=0	0	0				Not present
Cupping n=0	0	0				Not present
Tattooing n=0	0	0				Not present
Shared shaving bald n=0	0	0				Not present
Travel abroad n=0	0	0				Not present
Out marriage intercourse n=0	0	0				Not present

OR Odds ratio >1 (at risk), CI Confidence intervals, χ² Chi-square ≥3.9 (significant), p Probability value ≤0.05 (significant), Table 4. Show the prevalence rate of HCV according to type of lymphoma which found all the cases of HCV were among the Non- Hodgkin lymphoma especially in B-cell NHL types, with prevalence rate equal to 3.9%.

Table 4: Prevalence of HCV seropositivity in different types of lymphoma patients

Disease	Positive HCV=4		OR	CI	χ ²	p
	No.	%				
Hodgkin lymphomas (HL) n= 37 (26.7%)	ND	0	0	0-4.5	1.42	0.23
All Non-Hodgkin lymphomas n= 107 (74.3%)	4	3.7	Undefined		1.42	0.23
T-cell NHL (T-NHL) n= 06	0	0	0	0-4.5	0.1	0.67
B-cell NHL (B-NHL) n=101	4	3.9	Undefined		1.75	0.18

OR Odds ratio >1 (at risk) ,CI Confidence intervals, χ² Chi-square ≥3.9 (significant), p Probability value ≤0.05 (significant), ND Not Detected

DISCUSSION

Hepatitis C virus (HCV) is a hepatotropic and lymphotropic virus and is a global health problem. Cirrhosis and hepatocellular cancer are the most common complications of HCV and the association between HCV and B cell non-Hodgkin lymphomas (B-NHL) has been shown in epidemiological studies in the last 20 years⁹. Although incidence rates of non-Hodgkin lymphoma (NHL) have increased dramatically over the past several decades throughout the world, the etiology of NHL remains largely unknown¹⁰. Epidemiologic studies have proposed a link between hepatitis C virus (HCV) infection and both benign and malignant lymphoproliferative diseases, including mixed cryoglobulinemia¹¹. Also, previous epidemiologic studies of HCV infection and B-cell non-Hodgkin lymphoma (B-NHL) have yielded conflicting results.

In the current study, prevalence of HCV seropositivity was lower 2.8% among the 144 lymphomas patients, this result has contrasted with previous study performed among Yemeni patients with non-Hodgkin's lymphoma by Salem¹² in which the rate was 15.1%, also lower than Egypt (26-48%), Italy (9-34%), Roma (29.5%), Japan (22.2%), USA (22%), and Saudi Arabia (21%)^{13,14}. On the other hand, our low rate was similar to previous results reported from different European and Middle East countries such as Germany (4.3%), France (1.85%), Iran (0.7%) and Turkey (5%)^{10, 13}. Factors that might be attributed to low prevalence rate of this study in contrast to higher HCV rates it could be due to the geographic ethnic differentiation of the populations studied and HCV genotype as another reason of low prevalence it has been suggested that different HCV genotypes might be have variable degrees of lymphotropism or oncogenic potential for the development of NHL, On the other hand, not all lymphoma types are associated with HCV infection¹⁵.

The prevalence rate of HCV was higher in the age group of 16–25 years (15.9%) without statistical significant, and this may be due to receive a contaminated blood product, or due to lack of dental clinic hygienic. However, some studies showed the highest prevalence of HCV infection among Lymphoma patients and were observed at the age groups above 40 years^{12,16}. Slightly higher prevalent rate of HCV infection of this study among male lymphoma patients rather than female lymphoma patients, which was 3.0 % versus 2.2%, this finding was agreed with that reported in Yemen (4.3% versus 3.5 %) and Canada (2.4% versus 0.6%)^{12,17}.

Higher prevalent rate of HCV infection among lymphoma patients who were under chemotherapy which was 3.2% in our study, that may be due to increase times of blood products receiving in patients who under chemotherapy on the other hand, there was no any significant prevalence of HCV among lymphoma patients with another risk factors such as Diabetes, Tuberculosis and Bilharzias. According to obtained results, the risk factors contracting for HCV infection among lymphoma patients showed that the highest prevalent rate was noted among those who under prior blood transfusion, and this result is agree with some of studies finding performed in British Columbia¹⁷.

While some of previous studies did not show a significant association between history of blood transfusion for lymphoma patients and HCV prevalence¹⁵. Meanwhile the highest prevalent rate of HCV infection was noted among lymphoma patients who went to dental and general clinic for visit. In addition, there was no occurrence for other potential risk factors as contact to injected drug abuse, travel abroad, cupping, tattooing, etc in our patients.

According to lymphoma subgroups (classification), the high rate of HCV infection was found among lymphoma patients with non-hodgkin's lymphoma, especially B-cell type rather than Hodgkin's lymphoma, in which four seropositive for HCV infection (3.9%) suggesting a role of HCV in the etiology of B-NHL. This result is similar with a conducted meta-analysis review reported by Gisbert¹⁵ in which the mean prevalence of HCV infection in B-NHL cases has reported 13%, although it's higher than our finding. Moreover, this is agree with a study that performed in British Columbia and which reported 18 seropositive for HCV infection from 699 patients with B-cell NHL and only one seropositive for HCV infection from 77 patients with T-cell NHL¹⁷.

The main limitation of our study of HCV and NHL may not be used of a comparison population that may accurately reflect the background prevalence of HCV in the population, creating uncertainty about the relationship between HCV and NHL and this study didn't cover all Yemeni province where all cases were our study was cross sectional study focusing on the cases that present in the National Oncology Center during survey where this center receiving the majority cases from all provinces of Yemen.

CONCLUSION

The prevalence of HCV infection in patients with lymphomas in

Sana'a city was low in comparison with other studies globally, while the highest rate of HCV infection was found among male and young middle age population of this country as the higher risk of HCV ailments compared to the other age groups. This study will be helpful to the health care policy makers to design strategies for controlling and eradication of Hepatitis C infection in Yemen, and therefore, we recommended to implement of infection control and prevention guidelines among all types of Health services. Additionally, Effective and efficient control system to be put in place for screening of blood donors at health facilities throughout the country is highly recommended.

Conflict of Interest.

The authors declare that there is no conflict of interests regarding the publication of this paper.

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