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ORIGINAL ARTICLE

Evaluation of Role of Hepatitis C Virus in the Pathogenesis of Hodgkin Lymphoma Patients

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ABSTRACT

Background and Aim: Hepatitis C is a viral infection that cause liver's inflammation. Numerous studies have found a significant frequency of hepatitis C virus (HCV) infection in non-lymphoma Hodgkin's patients. B-cell non-Hodgkin's lymphoma (B-NHL) development could be significantly caused by HCV. The purpose of the current study was to investigate the hepatitis C virus role in the pathogenesis Hodgkin lymphoma patients.

Patients and Methods: This prospective study was carried out on 60 B-cell non-Hodgkin's lymphoma. (B-NHL) and 30 (healthy) control group in PAF Hospital Lahore Department of Internal Medicine and Oncology Department CMH, Lahore from May 2022 to October 2022. Study protocol was approved by institute ethical committee. Each individual provided written informed consent. All the patients were subjected to history taking, clinical examination, CBCs, kidney and liver function assessment, B2 microglobine, erythrocyte sedimentation rate determination, serum uric acid, abdominal ultrasound for lymphadenopathy and organomegaly, serum LDH, proper diagnosis and staging through CT abdomen, PCR, biopsy of bone marrow, and ELISA. Data analysis was done using SPSS version 27.

Results: Of the total 60 B-NHL patients, there were 32 (53.3%) male and 28 (46.7%) females. The overall mean age was 42.8± 10.8 years with an age range 16-65 years. There were 20 (66.7%) male and 10 (33.3%) females in control group and their mean age was 28.4± 11.6 years with an age range 12-60 years. Based on ELISA test, the incidence of for positive and negative anti-HCV antibodies were 34 (56.7%) and 26 (43.3%) respectively. The incidence of positive and negative anti-HCV RNA was 36 (60%) and 24 (40%) respectively.

Conclusion: The present study revealed that higher incidence of HCV infection play significant role in the pathogenesis of Hodgkin's lymphoma patients. This increases the likelihood of HCV infection playing a role in the development of B-NHL.

Keywords: Hepatitis C virus, Hodgkin lymphoma, Pathogenesis

INTRODUCTION

Hepatitis C virus (HCV) infection is related with a greater incidence as well as different clinical features and prognosis in B-cell Hodgkin lymphoma [1]. Globally, the incidence of HCV infections was 3% as a leading cause of chronic liver disease [2]. HCV infections have been related to different extrahepatic symptoms such as vasculitis, glomerulonephritis, and a wide spectrum of lymphoproliferative diseases, resulting in additional morbidities and deaths [3, 4]. A previous study found that unique prognosis and clinical presentation of B-cell non-Hodgkin lymphoma (NHL) has been associated with HCV infection [5-8]. Initially, cell-mediated and humoral responses are triggers by HCV infections, but these responses appear to be inadequate to prevent persistent viremia and chronic infection mostly patients. HCV positive patients may develop a number of localized or systemic autoimmune disease [9].

The majority of HCV infections cause acute disease, but up to 80% might progress to chronic hepatitis [10]. Almost all the patients produce a robust cell-mediated immune and antibody-mediated responses contributing to the liver damage and fail the viral infection eradicate. Chronic liver disease spontaneously resolves is extremely rare, and are at risk of developing hepatocellular carcinoma. Nevertheless, other investigations have shown that infection, at least in some groups, may have a more benign consequence [11]. HCV infection affects the B-lymphocyte compartment, resulting in B-cell proliferative diseases. Hodgkin lymphoma (HL) is an uncommon cancer in that the tumor cells mostly composed of a mixed cellular infiltration. Mature B cells missing B cell receptors would ordinarily perish by apoptosis, thus HRS cells must have acquired survival strategies. The resistance to apoptosis and transcriptional reprogramming of HRS cells are related and appear to be important in disease etiology [12].

Numerous epidemiological evidence associated the NHL with HCV infections and pathogenesis that leads to proliferation of clonal B-cell and eventual malignant alteration are just now being unraveled [13]. The recurrence of quiescent NHLs following HCV eradication supports the causative involvement of HCV in lymphomagenesis [14]. Several retrospective investigations have demonstrated a substantial HCV prevalence in individuals with diffuse big B-NHL [15, 16]. The current study aimed to establish the prevalence of HCV infection in B-NHL patients and compare them to seemingly healthy volunteers.

METHODOLOGY

This prospective study was carried out on 60 B-cell non-Hodgkin's lymphoma. (B-NHL) and 30 (healthy) control group in PAF Hospital Lahore Department of Internal Medicine and Oncology Department CMH, Lahore from May 2022 to October 2022. Study protocol was approved by institutes' ethical committee. Each individual provided written informed consent. All the patients were subjected to history taking, clinical examination, CBCs, kidney and liver function assessment, B2 microglobine, erythrocyte sedimentation rate determination, serum uric acid, abdominal ultrasound for lymphadenopathy and organomegaly, serum LDH, proper diagnosis and staging through CT abdomen, PCR, biopsy of bone marrow, and ELISA. Venous blood samples of two millimeter were taken from each individual to plain tubes for detection of anti-HCV antibodies using the ELISA commercial kit in sterile EDTA vacutainer. Ficoll-density centrifugation was used to separate mononuclear cells; a portion of this sample (RNA) was reverse transcribed and amplified using the One-Step RT-PCR Kit.

SPSS version 27 was used for data analysis. Numerical data were described as mean and standard deviation. Qualitative parameters were described as percentages. The $\chi 2$-test was used for comparing the clinical data and independent test was used for laboratory data. For the comparison of quantitative measurement data, Pearson's correlation was employed. All the data analysis was done using 5% level of significance.

RESULTS

Out of 60 B-NHL patients, there were 32 (53.3%) male and 28 (46.7%) females. The overall mean age was 42.8± 10.8 years with an age range 16-65 years. There were 20 (66.7%) male and 10 (33.3%) females in control group and their mean age was 28.4±

11.6 years with an age range 12-60 years. Based on ELISA test, the incidence of for positive and negative anti-HCV antibodies were 34 (56.7%) and 26 (43.3%) respectively. The incidence of positive and negative anti-HCV RNA was 36 (60%) and 24 (40%) respectively. Table-I shows the comparison of laboratory and clinical data in both study and control group. Liver function of study and healthy patients are compared in Table-II. Comparison of clinical and laboratory data with anti-HCV antibody and HCV RNA RT-PCR findings in the patient groups are shown in Table-III.

Table-1: comparison of laboratory and clinical data in both study and control group

Parameters	Study group	Control group	P-value
Age (years) (ms±SD)	42.8± 10.8	28.4± 11.6	<0.0001
Gender N (%) Male Female	 32 (53.3) 28 (46.7)	 20 (66.7) 10 (33.3)	0.0105
Hepatomegaly	30 (50)	7 (23.3)	0.0221
Lymphadenopathy	32 (53.3)	12 (40)	0.2831
Splenomegaly	52 (86.7)	8 (26.7)	<0.0001
Hemoglobin (g %)	10.5 ± 2.6	9.7 ± 1.6	0.0891
Total leukocytic count (10^3 mm^3)	9.7 ± 2.7	21.6 ± 2.6	<0.0001
Platelet count (10^3 mm^3)	171.6 ± 102.6	134.8 ± 66.4	0.0743

Table-2: comparison of Liver function of study and healthy patients

Liver function	Study group	Control group	P-value
AST (IU/dl)	40.6 ± 36.8	28.9 ± 20	0.0937
Bilirubin (mg/dl)	0.81 ± 0.59	1.2 ± 0.9	0.0279
ALT (IU/dl)	33.8 ± 28.7	32.6 ± 20	0.9372
Total protein (mg/dl)	3.19 ± 1.02	4.8 ± 0.1	<0.0001

Table-3: Comparison of clinical and laboratory data with anti-HCV antibody and HCV RNA RT-PCR findings in the patient groups

Variables	Study group r (P-value)	Control group r (P-value)
Age (years)	0.089 (0.532)	0.079 (0.623)
Hb (g %)	0.021 (0.936)	0.093 (0.492)
Platelet count (10^3 mm^3)	0.006 (0.959)	0.015 (0.872)
TLC (10^3 mm^3)	0.072 (0.562)	0.117 (0.372)
AST (IU/dl)	0.121 (0.389)	0.053 (0.749)
ALT (IU/dl)	0.020 (0.976)	0.236 (0.109)
Bilirubin (mg/dl)	0.062 (0.718)	0.024 (0.789)

DISCUSSION

The current study compared the role of HCV infection in B-NHL patients to that of ostensibly healthy volunteers. The regression of indolent NHLs following HCV elimination supports the causative involvement of HCV in lymphomagenesis. Several retrospective investigations have demonstrated that individuals with diffuse B-NHL had a significant HCV seroprevalence [17, 18]. HCV infection has been linked to a variety of extrahepatic symptoms [19], with lymphoproliferative diseases being the most closely linked to HCV infection [20]. As a result, it has been established that chronic HCV infection might cause clonal expansion of B cells and that continued proliferation of B cells would enhance the incidence of genetic alterations.

Several hypothetical models have been proposed to determine the HCV infection putative pathologic function in aggressive B-cell lymphoma (B-NHL). One type of concept that accounts for HCV-associated lymphomagenesis is the direct transformation process. In vitro, HCV infection causes somatic mutations in multiple oncogenes and tumour suppressor genes, including p53, betacatenin, and Bcl6 [21]. On the contrary, several investigations suggest HCV's involvement causing lymphoma by continuously boosting B-cell immunologic response. Lymphoma risk is predicted to be 35 times greater in individuals with HCV-associated cryoglobulinemia than in the general population [22].

Previous investigations found that HCV-infected DLBCL patients had different clinical characteristics. During diagnosis, an older age (> or =60) was linked with a larger percentage of HCV-positive DLBCL patients than HCV-negative DLBCL cases [23]. HCV-positive individuals showed greater extra nodal involvement [24] and higher levels of LDH [25]. Our findings are consistent with those of Wei et al. [26], who discovered that the incidence of HCV infection was higher in patients with B-cell lymphoma than in two groups of controls, which included patients with other malignant hematologic conditions and patients with general medical conditions.

The discovery of a link between HCV infection and B-cell lymphoma raises the idea that HCV plays a pathogenic role. Yi et al. [27] identified a significant incidence of clonal B-cell growth in HCV-infected individuals, even in the absence of cryoglobulinemia, lending more credence to the putative link between clonal B-cell expansions with HCV infection. Based on these findings, it is possible that chronic HCV infection, alone or in combination with other factors, may result in B-lymphoid expansion. A later transforming event may result in malignant lymphoma [28].

In contrast to our findings, Gragnani et al. [29] found no HCV antibodies in 60 individuals with B-cell lymphoma. These disparities may be due to the diverse geographic origins and ethnicities of the people investigated. Another possibility for the low HCV prevalence in the lymphoma group in this study is that not all lymphoma types are associated with HCV infection.

According to several research, the NHL association with prognosis of HCV-positive aggressive is comparable to that of HCV-negative aggressive NHL [30]. Some studies, however, have demonstrated that anti-HCV-positive patients with diffuse large B-cell lymphomas had a poorer prognosis in terms of overall survival and disease-free survival compared to HCV-negative individuals [31].

CONCLUSION

The present study revealed that higher incidence of HCV infection play significant role in the pathogenesis of Hodgkin's lymphoma patients. This increases the likelihood of HCV infection playing a role in the development of B-NHL.

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