



Assessment of the 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 mainly affects the liver, causing inflammation. Infection with hepatitis C virus (HCV) commonly observed and associated with various clinical manifestations, including a diagnosis in patients with B-cell Hodgkin lymphoma. Worldwide, HCV infection accounts for about 3% of the population and a major cause of chronic liver disease. The study was conducted to investigate the possible role of Hepatitis C virus (HCV) in the development and progress of Hodgkin Lymphoma. **Patients and Methods:** This cross-sectional study investigated 160 Hodgkin lymphoma patients in the department of Medicine of Mayo Hospital, Lahore from January 2024 to December 2024. All patients made a detailed clinical evaluation including taking history, physical examination and relevant laboratory examination. Diagnostic workup included full blood calculation (CBC), liver and kidney function test, B 2-microglobulin level, erythrocyte sedimentation rate (ESR), serum uric acid and serum lactate dehydrogenase (LDH). Abdominal ultrasonography demonstrated to assess lymphadenopathy and organomegaly. For staging and diagnosis, Tomography (CT), Bone Marrow Biopsy, and Polymerase Chain Reaction (PCR) conducted hepatitis C virus (HCV) contrast-comprehensive calculation for RNA. The presence of HCV infection confirmed by the enzyme immunosorbent assay (ELISA) and PCR techniques. Data analysis done using SPSS version 28. **Results:** A total of 160 patients diagnosed with Hodgkin lymphoma were nominated in the study, including 86 (53.8%) male and 74 [46.2%] women, whose average age 46.6±9.6 years with an age range 16-65 years. Hepatitis C virus (HCV) infection was detected in 78 (48.8%), as confirmed by ELISA and PCR. Patients with HCV positivity showed high frequency of advanced-phase (Phase III/IV) compared to HCV-negative patients (P = 0.03). The level of elevated liver enzymes, serum LDH, and B2-microglobulin was quite popular among HCV positive HL cases (P <0.05). Statistical analysis indicated a significant relationship between HCV infection and aggressive disease features, suggesting the possible role of HCV in Hodgkin lymphoma's pathogenesis and clinical progression. **Conclusion:** The present study suggests a potential association between HCV infection and pathogenesis of Hodgkin lymphoma. HCV-positive patient has demonstrated more aggressive disease characteristics, including advanced phase, elevated inflammatory markers, and increased external participation. These results highlight the importance of regular HCV screening in HL patients and suggest that HCV may contribute to the progression of the disease.

INTRODUCTION

Hodgkin lymphoma (HL) is a malignant lymphoproliferative disorder characterized by the presence of reed-sternburg cells within an inflammatory background. Although the accurate etiology of HL remains unclear, various infectious agents have been implicated in its pathogenesis, including Epstein-Bar virus (EBV) and, recently, hepatitis C virus (HCV).

HCV is a hepatotropic and limitropic virus considered as the cause of chronic infection, which is associated with many hematological malformations, especially non-Hodgkin lymphoma [1]. Hepatitis C virus (HCV) has been linked to various types of extrasite manifestations, especially lymphoproliferative disorders [2]. Emerging evidence suggests that chronic immune stimulation caused by HCV infection may induce molecular

oncogenic changes, possibly promoting clonal expansion of the specific B-cell population. This mechanism has been proposed as a contribution factor in the development of various lymphoma, especially non-Hodkin's lymphoma (NHL). However, the relationship between HCV and Hodgkin lymphoma (HL) is not clear and warrant further examines [3, 4]. Importantly, HCV circulation is not uniform worldwide, with some areas, such as Pakistan, is experiencing a high burden. Given the important public health effects of HCV in Pakistan, the purpose of this study is to detect potential relations between HCV infection and HL's pathogenesis within the local population [5].

While many hepatitis C virus (HCV) infections are initially present as acute disease, about 80% progress for chronic hepatitis. Although most patients mount strong cell-mediated and humoral immune responses, these reactions often fail to eliminate the virus, resulting in liver inflammation and damage [6]. The spontaneous resolution of chronic liver disease is rare, and patients have an increase in the risk of development of hepatocellular carcinoma. However, some studies suggest that HCV infection may have less severe clinical courses in some population [7, 8]. Beyond hepatic complications, HCV has also been implicated in B-cell dysregulation, causing a spectrum of lymphoproliferative disorders. Hodgkin lymphoma (HL), although deadly Hodgkin and minority population of Reed characterizes the background of rare, reactive inflammatory cells-Sternberg (HRS) cells [9]. Since mature B cells are deficient in functional B-cell receptors, which usually undergoes apoptosis, HRS cells acquired by the firmness of the cells to avoid strongly avoiding. These include resistance to apoptosis and significant transcriptional reproduction; both considered central for HL's pathogenesis [10].

A growing body of evidence of epidemiological evidence has added the hepatitis C virus (HCV) infection to the development of non-Hodkin lymphoma (NHL), which leads to an insight that emerged in the mechanisms, by which HCV clonal B-cells can run and let out a deadly change [11]. The recurrence of malaise NHL after HCV eradication confirms the possible cause role of HCV in further lymphomas. Additionally, several retrospective studies have reported a particularly high proliferation of HCVs in spreading large B-cell lymphoma (DLBCL), supporting the association [12, 13]. Given HCV's known ability to induce chronic immune stimulation and B-cell proliferation, it is admirable that the virus can also contribute to HL's pathogenesis. In areas like Pakistan, where HCV circulation is quite high, it is special to investigate this possible relationship. Understanding whether HCV infection affects the clinical course, staging, or aggression of HL, can be meaningful implications for initial diagnosis, treatment decisions and patient results.

Therefore, the purpose of this study is to detect the role of HCV in HL pathogenesis within a spatial population.

METHODOLOGY

Study Design and Setting

It was a cross-sectional study performed in the department of Medicine, Mayo hospital, Lahore from January 2024 to December 2024, in a period of one year, from January 2024 to December 2024. The study approved by the Institutional Ethical Review Board, and informed written consent taken from all participants or their legal parents before it joined.

Study Population

A total of 160 patients diagnosed with Hodgkin lymphoma (HL) confirmed through histopathological and immunohistochemical analysis nominated in the study. Patients from both gender and all age groups were included. The exclusion criteria consisted of individuals with co-existing malformations, already receiving antiviral treatment for hepatitis C, or patients with a known history of liver cirrhosis for reasons other than HCV.

Data Collection, Clinical Assessment, and Laboratory Investigations

Each patient made a comprehensive clinical evaluation, including detailed history and physical examination. Baseline demographic data (age, gender), symptoms, performance and staging information recorded. The following laboratory investigations performed for all participants: Complete Blood Count (CBC), Erythrocyte Sedimentation Rate (ESR), Liver Function Tests (LFTs) and Kidney Function Tests (KFTs), Serum Lactate Dehydrogenase (LDH), Serum Uric Acid, β 2-Microglobulin Levels, Hepatitis C Virus Detection: Serological testing for anti-HCV antibodies carried out using Enzyme-Linked Immunosorbent Assay (ELISA). HCV RNA further confirmed through the polymerase chain reaction (PCR) for active infection. All patients involved to undergo imaging to evaluate the range of the disease, including abdominal ultrasound to assess hepatosplenomegaly and lymphadenopathy. Contrast-added CT scan of chest, stomach and pelvis for staging. The bone marrow biopsy was performed in selected cases with advanced-phase or unexplained cytopenias.

Data Analysis

The data was analyzed using SPSS Statistics version 28.0. Quantitative variables expressed as the mean and standard deviation, while the range of variables presented as frequencies and percentage. The relationship between the position of HCV and the various clinicopathological characteristics of HL (eg disease phase, LDH level, extranodal participation and histological sub-availability) was evaluated using a chi-square test or Fisher's exact test. $p < 0.05$ considered a P-value statistically important.

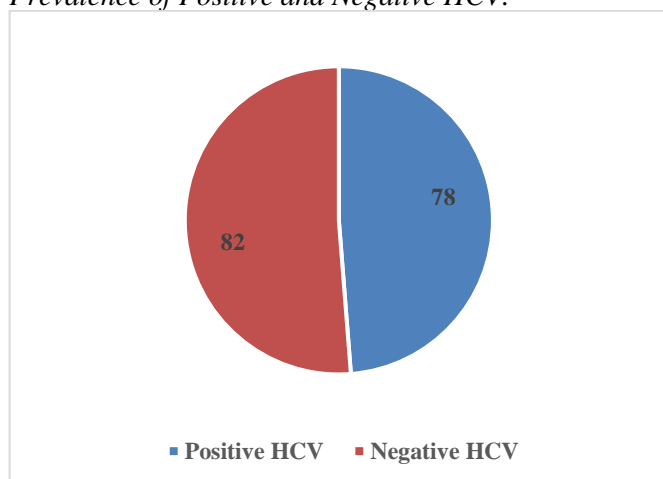
RESULTS

A total of 160 patients diagnosed with Hodgkin lymphoma (HL) nominated in the study. Among them, 86 (53.8%) were male and 74 (46.2%) women were women, whose average age was 46.6 (9.6 years (limit 16-65 years)) Hepatitis C virus (HCV) infection was identified in 78 patients (48.8%) through syllagical tests by Elisa and confirmed by PCR. An important association seen between HCV positivity and advanced disease phase. In particular, a high ratio of HCV-positive patients is presented with phase III or IV HL compared to HCV-negative individuals ($P = 0.03$). In addition, laboratory findings demonstrated that elevated liver enzymes, serum lactate dehydrogenas (LDH), and OB2-microglobulin levels were more prevalent in HCV-positive groups ($P < 0.05$ for all parameters). Overall, statistical analysis revealed a meaningful relationship between HCV infection and many aggressive disease characteristics in HL patients. These findings support Hodgkin lymphoma's potential contributor role in the pathogenesis and clinical progression.

Table 1
Demographic and Clinical Characteristics of Hodgkin Lymphoma Patients

Characteristic	Total (n = 160)	HCV Positive (n = 78)	HCV Negative (n = 82)
Gender			
Male	86 (53.8%)	42 (53.8%)	44 (53.7%)
Female	74 (46.2%)	36 (46.2%)	38 (46.3%)
Average Age (years)	46.6 ± 9.6	46.9 ± 9.8	46.3 ± 9.4
Age Range	16 - 65	16 - 65	16 - 65
HCV Infection Status	160 (100%)	78 (48.8%)	82 (51.2%)
Advanced Disease Stages (Phase III/IV)	45 (28.1%)	30 (38.5%)	15 (18.3%)
Elevated Liver Enzymes (ALT/AST)	22 (13.8%)	18 (23.1%)	4 (4.9%)
Elevated Serum LDH	29 (18.1%)	24 (30.8%)	5 (6.1%)
Elevated B2-Microglobulin	33 (20.6%)	27 (34.6%)	6 (7.3%)

Figure 1
Prevalence of Positive and Negative HCV.



DISCUSSION

The current study explicitly examined the effect of HCV infection in patients with B-cell non-Hodgkin lymphoma (B-NHL). Evidence of pre -studies has shown that the regression of indolent NHL after successful HCV treatment supports a potential cause role for HCV in lymphomagenis. Many retrospective analyses have reported a particularly high seroprevelle of HCV among individuals diagnosed with B-NHL. In addition, HCV is associated with a wide range of extrasite manifestations, in which lymphoprolleptive disorders significantly correlated [14]. Chronic HCV transition considered being a contributing to clonal B-cell expansion, and frequent B-cell proliferation may increase the possibility of accumulating genetic mutations that may eventually lead to malicious malpractices [15].

A key finding in our study was HCV-positive HL patients had a high level of liver enzymes, serum lactate dehydrogenase (LDH), and OB2-microglobulin. These biomarkers often used to monitor the disease activity and signs of systemic inflammation and cellular turnover both increased in viral infections such as HCVs. The relationship between LDH and β 2-microglobulin levels with HCV positivity supports the hypothesis that chronic immune activation caused by HCV can affect tumor microelement, potentially contributes to malaise changes in B-cells and clinical progress of HL [16].

The findings of our study align with the broader body of evidence that suggests that HCV can contribute to lymphomagenis through immune dysfunction. Chronic HCV infection leads to frequent stimulation of the immune system, especially B-cells, which can pass into clonal detail and achieve genetic changes [17]. These genetic changes are likely to facilitate the development of lymphoma. Additionally, previous studies have shown that the regression of indolent lymphoma after successful HCV treatment supports the idea that HCV plays an inspiring role in lymphoma development including HL [18].

However, it is important to note that when our study identifies an important relationship between HCV and HL, the work can definitely not be established without further longitudinal and mechanical studies. The exact mechanism through which HCV affects HL pathogenesis remains unclear. It is possible that chronic inflammation related to HCV can increase the mutant capacity of environment and genetic factors that motivate individuals to lymphoma. In addition, HCV can act as a cofactor that increases the maliciousness of pre -present genetic sensitivity [19].

The identification of a relationship between HCV infection and B-cell lymphoma suggests a possible pathological role for the virus [20]. Depending on these findings, chronic HCV infection, either alone or in combination with other factors, can contribute to B-lymphoid expansion, and later transforming phenomena

may have malignant lymphoma [21]. Unlike our results, an earlier study [22] did not detect HCV antibodies in 40 persons diagnosed with B-cell lymphoma. These anomalies can be attributed to the difference between geographical origin and ethnicity among the study population. Additionally, the low proliferation of HCV in the lymphoma group in this study may be because not all types of lymphoma are associated with HCV infection [23].

Although the relationship between HCV and HL is hypnotic, it remains an area of active investigation. The role of HCV in HL's pathogenesis may be important clinical implications, especially in areas with high HCV proliferation such as Pakistan. If the association confirmed, this novel can give rise to medical strategies, such as an antiviral treatment standard HL remedies, especially in HCV positive individuals.

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CONCLUSION

This study provides valuable insight into the possible role of hepatitis C virus (HCV) in the pathogenesis of Hodgkin lymphoma (HL). Our findings indicate a significant connection between HCV infection and advanced disease stages in HCV patients, high levels of liver enzymes with HCV positive individuals, serum LDH, and β 2-microglobulin, which are usually markers associated with disease progression. These results suggest that HCV infection can contribute to the development and clinical progression of HL, possibly through the mechanisms of chronic immune activation and B-cell proliferation. While this study strengthens the hypothesis that HCV can play a pathological role in HL, further investigation is necessary to clarify the inherent molecular mechanisms connecting HCV to H.

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