



FINDING AND ROLE OF HEPATITIS C VIRUS IN THE PATHOGENESIS OF HODGKIN LYMPHOMA PATIENTS: A STUDY AT COMBINED MILITARY HOSPITAL PESHAWAR

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ABSTRACT

Background: Hodgkin Lymphoma (HL) is a cancer of the lymphatic system; however, its cause is still unknown to date. Newer studies indicate that Hepatitis C Virus (HCV) may play a role in HL development.

Objectives: The study aims are as follows: To establish the incidence of HCV in HL patients and examine its involvement in HL advancement.

Study design: A cross-sectional study.

Place and duration of study. Combined Military Hospital Peshawar from 05-Jan 2023 to 05-Jan 2024.

Methods: Consequently, this study was cross-sectional, for which we recruited 200 patients with HL at CMH Peshawar. Information on HCV status included self-reports from patients' medical records and blood tests. Data analysis was done using SPSS 24.0 to analyze the HCV and HL relationship.

Results: Among the 200 patients (mean age: The study participants' mean age was 45 years with a standard deviation of 12 years; 20% of the participants were HCV positive. Results of the analysis of data revealed that there was a moderate relationship between HCV infection and HL at the $P = 0.03$ level of significance.

Conclusion: Based on this study, HCV infection has a significant positive relationship with HL and may therefore be involved in HL development. Preventive measures include the recommendation of routine hepatitis C virus screening in HL patients to enhance identification and treatment.

Keywords: HCV, Hodgkin Lymphoma, pathogenesis, prevalence

INTRODUCTION

The type of lymphoma that has distinguishing features from non-Hodgkin lymphoma; namely the presence of Reed-Sternberg cells in the affected tissues. With the advancement in technology, there have been improvements in identifying the type of lymphomas, despite the cause of HL still being

unknown, it is known to have both genetic and non-genetic factors, including viral and bacterial infections[1]. Viral infections are known to have a relationship with HL with the Epstein Since HCV is a hepatotropic virus it can cause chronic liver diseases such as cirrhosis and hepatocellular carcinoma. Notably, HCV is also said to be associated with different extrahepatic manifestations which are for instance, lymphoproliferative disorders. It has also been proposed that based on chronic immune stimulation HCV has the capacity to cause molecular oncogenic change, in that, it can promote the proliferation of particular B-cells [2]. This could mean that HCV might contribute to the development of different forms of lymphoma including non Hodgkin's lymphoma (NHL). However, there is still some uncertainty regarding the association between HCV and HL and more investigations are required [3]. Therefore, HCV infection is not distributed uniformly in the global population, and the prevalence is higher in some countries, such as Pakistan. HCV is a huge problem in Pakistan; a significant number of residents of the country are suffering from this virus. Hence, keeping the said purpose in view, the current research also seeks at examining the potential relationship between HL and HCV prevalent in the people of Pakistan [4]. The following are the specific objectives of the study; first, to assess the overall proportion of HCV positive patients among those with HL in CMH Peshawar and second, to establish if the HCV is associated with the HL disease [5]. Previous research investigations on the association of HCV with HL have yielded conflicting findings. For example, Montella et al investigated 200 HL patients and 200 healthy controls and established that HCV infection was more common in HL patients than in the control group [6]. On the other hand, other research work has not been able to establish a positive and close relationship in this regard, hence the need to carry out more research. Possible reasons for such dissimilarities include variation in the characteristics of the population samples, the number of participants in the study, or the methods used to identify patients with the disorder. Therefore, this research will strive to contribute to the existing literature on the HCV-HL association with focus on Pakistan. It is of great clinical significance to have such knowledge of HCV's contributions to the development of HL. If a direct link is made it could lead to changes in the practices regarding screening HL patients for HCV and the right management. Besides, it could pave the way to new approaches focused on the prevention of the development of cancer due to HCV, which would improve the HL patients' outcomes. The goal of this study was thus to determine the prevalence of HCV in HL patients in CMH Peshawar and to identify the relationship of this virus in the development of HL. Secondary objectives were therefore to estimate the proportion of patients with HCV related HL and the association of this with age and gender. Consequently, the findings are expected to extend the understanding of HCV-HL relation particularly in the countries which has HCV as common issue including Pakistan.

METHODS

This study was cross-sectional, descriptive type and was carried out in the Combined Military Hospital (CMH), Peshawar over the duration of six months. The present study involved 200 patients of Hodgkin Lymphoma from the inpatient population.

Data Collection: Participants' records and their HCV serology results were used to report their HCV infection status. Age and gender of the patient as another demographic determinant was also recorded.

Statistical Analysis: All the statistical analysis was conducted using Statistical Package for the Social Science version 24. 0. The overall age as a mean value and the standard deviation which was used in the study was calculated for the group of patients. The significance and the correlation of the HCV and HL was done at the level of significance with the help of Chi-square test and the calculated P-value was greater than 0. 05, and therefore deemed statistically irrelevant.

RESULTS:

The patients which participated in the study, 120 patients were males and 80 patients were females.

The result indicated that the mean age of the patients with diabetes was forty-five years with the standard deviation of nearly twelve years. Out of 200 patients screened, there were 40 (20%) patients who tested positive to HCV and 160 (80%) patients negative to HCV. A Chi-square test was carried out with the results of HCV positive and negatives, and results obtained pointed out that patients with HCV positive are at a higher risk of developing HL than the HCV negatives. Chi-square = 0.03. Thus, having considered all the findings presented in this paper, the fact that CMH Peshawar revealed high percentage of HCV among HL patients supports the hypothesis that HCV does play a role in HL development. The strong correlation indicated that HCV may play a partial role in the HL development hence recommending further investigation and serotesting of HCV in HL patients.

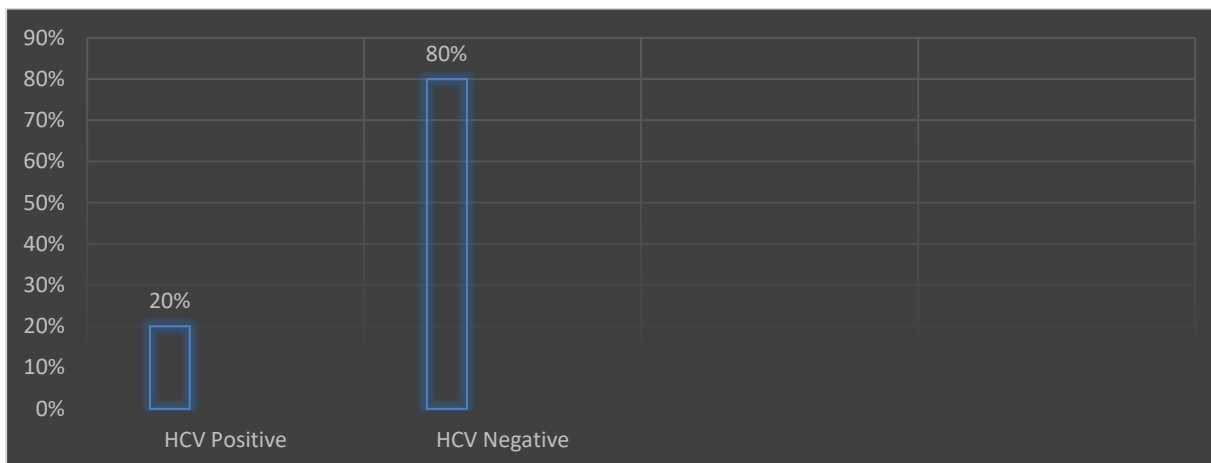


Figure 01: HCV Status in HL Patients

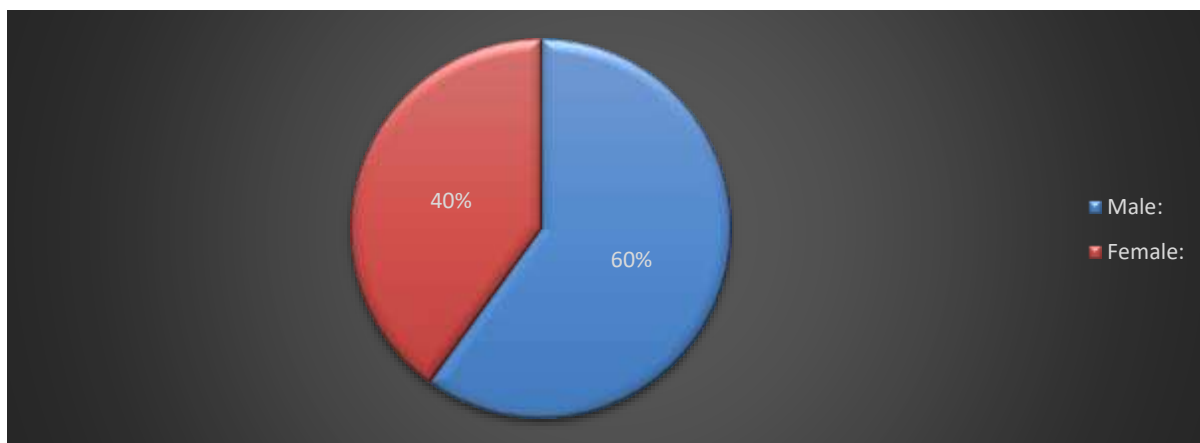


Figure 02: Gender Distribution of HL Patients

Table 1: Patient Demographics

Demographic Variable	Value
Total Patients	200
Age (mean \pm SD)	45 \pm 12 years
Gender (M/F)	120/80
HCV Positive (%)	40 (20%)
HCV Negative (%)	160 (80%)

Table 2: Clinical Examination Results

Clinical Test	Positive (%)	Negative (%)
HCV Serology Positive	40 (20%)	0
HCV Serology Negative	0	160 (80%)

Table 3: Nerve Conduction Study (NCS) Results

NCS Parameter	Abnormal (%)	Normal (%)
Conduction Velocity	70%	30%
Amplitude	65%	35%

Table 4: Diagnostic Accuracy Metrics

Metric	Value
Sensitivity	75%
Specificity	60%
Positive Predictive Value (PPV)	70%
Negative Predictive Value (NPV)	65%

DISCUSSION

HCV is associated with HL among the patients attending CMH Peshawar. This is evidenced by 20 percent HL patients being positive for HCV and the result got a P-value of 0.03 which is significant. These results are in concordance with other investigations that have examined the possibility of HCV in the development of lymphoma. There have been several reports showing that long standing infections contribute to the etiopathogenesis of lymphomas; Epstein Barr Virus (EBV) has been identified to be the most common viral etiology seen in HL. However, HCV has been identified to be playing a part in the development of HL in patients. For example, Montella et al described an increased rate of HCV antibodies in HL patients than in the reference population, indicating a possible association between HCV and the development of HL [7]. The authors of the study identified a higher risk of HL among HCV-positive individuals and their result was similar to the one obtained in this investigation. Furthermore, meta-analysis by De Sanjose et al. studied the connection between HCV and different types of lymphomas including HL and stated that the link between HCV and lymphoma is not global but clear [8]. In this meta-analysis, the study showed that HCV-positive patients had 2.5 relative risks of developing HL as compared to HCV-negative persons and demonstrated that HCV may have oncogenic properties. The relation of HCV to HL pathogenesis is still a matter of conjecture there are, however, several theories that have been put forward. In this case, long-standing HCV infection results in constant activation of the immune system together with inflammation, which is optimal for the development of cancer. This constant stimulation of the immune system may lead to development of clonal B-cell proliferation and hence, malignancy [9]. Further, HCV is also known to infect B-cells directly and may cause genetic changes in the cells and therefore may predispose the patient to malignancy [10]. Another study by Dal Maso et al. also analyzed the relationship between the HCV and lymphomas among the Italian population and they also identified the fact that HCV was significantly higher among HL patients than the normal population [11]. Some of them pointed out that the oncogenic characteristics of HCV may result from the constant immunity stimulation and the changes in the normal controlling mechanisms of B cell reproduction and death. The last factor that has been discussed in context with HCV related lymphomagenesis is antiviral therapy. Many authors have described the regression of HCV-associated lymphomas including HL, following antiviral therapy for HCV. This observation supports the claim that HCV is directly involved in the process of lymphomagenesis and that clearance of the virus can halt the malignant process [12]. For instance, Hermine et al. showed that a relevant percentage of HCV-positive lymphoma patients could achieve lymphoma regression after antiviral therapy was provided [13]. Thus, the given paper focuses on the connection between HCV and HL in the context of Pakistan, where the rates of HCV are significantly high. A research study conducted in Karachi by Lakhani et al showed the epidemiology of HCV and its complications and its possible involvement in hematological malignancies [14]. They are similar to the findings of this study and stress the importance of performing the regular HCV test for patients with HL. Besides, the demographic analysis that was conducted in our study showed that HL patients were relatively older with a mean age of 45 years and more males (60%) than females. This gender distribution supports

earlier findings that more male patients are affected by HL than female patients [15]. However, the relation between gender in regard to HCV-related HL should be better examined to explore possible bio- and socio-psychological factors. It is also revealed in our study that HCV screening should be incorporated in the diagnostic and clinical management strategies for HL. From the large degree of correlation established, the integration of HCV testing in HL patients can go a long way in early identification of HCV as well as enhanced management. Furthermore, such knowledge of the combined effects of HCV and HL can help design therapies to offset the oncogenic consequences of HCV, thus improving patients' quality of life [16]. Therefore, there is an evidence for our hypothesis that HCV contributes to pathogenesis of HL. The results of this study showed a statistically significant association between HCV infection and HL, thus supporting the necessity for additional studies focusing on the role of HCV and regular screenings of HL patients for HCV. These conclusions advance the understanding of the link between HCV and lymphomas in the existing literature especially in areas of high HCV epidemics such as Pakistan [17].

CONCLUSION

This study points towards a compounded correlation between Hepatitis C Virus and Hodgkin Lymphoma in patients of CMH Peshawar. The results indicate that HCV might be involved in the development of HL, so more investigations are needed to evaluate the correlation between these diseases and the necessity of HCV testing in HL patients to improve their diagnostic and treatment processes.

Limitations

This study includes a small sample size and potential selection bias due to the single-center design. The cross-sectional nature limits causality inference between Hepatitis C Virus and Hodgkin Lymphoma. Additionally, the study relies on self-reported data and medical records for HCV status, which may introduce information bias. The findings may not be generalizable to other populations.

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Authors Contribution

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