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Research Article

Prevalence of Rheumatoid Factor Positivity in Hepatitis C Patients.

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Abstract

Introduction: Rheumatoid Factor (RF) positivity is common in patients with Hepatitis C virus (HCV) infection, occurring in 50-70% of cases, and can also be associated with autoimmune symptoms. In view of its high prevalence, an RF test alone is not sufficient to diagnose rheumatoid arthritis (RA) in a patient with HCV. A positive RF test in an HCV patient could be due to the HCV infection itself, or it could indicate a co-occurring RA diagnosis.
Aim of study: To estimate prevalence of Rheumatoid Factor positivity in Hepatitis C patients at tertiary care center of Northern India.
Material and Methods: This study was conducted at Medical Gastroenterology Department at PGIMS, Rohtak. It was a prospective study done over one year, from 01.10.2024 to 30.09.2025, during which 500 confirmed hepatitis C patients were tested for Rheumatoid factor positivity or negativity. All hepatitis C patients were confirmed on anti HCV antibody test on Enzyme linked immunosorbent assay (ELISA) test and HCV RNA Quantitative test on Polymerase chain reaction test (PCR).
Observation and Results: On prospective analysis of 500 confirmed hepatitis C patients, males were 290 (58%) and females were 210 (42%). Out of total pool of 500 HCV patients, 250 (50%) were having rheumatoid factor positive and 250 (50%) were negative. Out of 250 rheumatoid factor positive patients, 133 were males (53.20%) and 117 (46.80%) were females. Out of these 133 rheumatoid factor positive males, 85 (63.90%) were having F0-F2 fibrosis, 12 (9.02%) were having F2-F3 fibrosis and 36 (27.06%) were cirrhotic. Out of total 117 rheumatoid factor positive females, 63 (53.84%) were having F0-F2 fibrosis, 32 (27.35%) were having F2-F3 and 22 (18.80%) were cirrhotic. Out of 250 rheumatoid factor negative patients, 155 were males (62%) and 95 (38%) were females. Out of these 155 rheumatoid factor negative males, 71 (45.80%) were having F0-F2 fibrosis, 60 (38.70%) were having F2-F3 fibrosis and 24 (15.48%) were cirrhotic. Out of total 95 rheumatoid factor negative females, 107 (74.30%) were having F0-F2 fibrosis, 22 (15.27%) were having F2-F3 fibrosis and 15 (10.43%) were cirrhotic. Out of total 250 rheumatoid factor positive patients, 163 (65.20%) were having symptoms of joint pains and rest 87 patients (34.80%) were asymptomatic.
Conclusion: The hepatitis C patients need to be evaluated not only from hepatic point of view but also its extra hepatic impact, of which musculoskeletal system is integral part and every HCV patient should be tested for RF and if positive then confirmation for Rheumatoid arthritis. It holds true in reverse also, meaning by that every RA patient should be checked for HBV and HCV infection.

Key words: Hepatitis C, Anti HCV antibody, HCV RNA Quantitative, Rheumatoid Factor, Rheumatoid arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic inflammatory autoimmune disease characterized by chronic and destructive arthritis [1]. Patients infected with Hepatitis C Virus (HCV) often present with rheumatic symptoms, but its link to rheumatoid arthritis (RA) remains unclear. Although RA pathogenesis is incompletely understood, chronic viral infections may be one of the triggers for its onset [2]. Hepatitis C virus (HCV) infection is a major global public health issue and a leading cause of chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma [3]. According to the World Health Organization, an estimated 170 million people worldwide are chronically infected with HCV, and 40-74% of these patients exhibit extrahepatic clinical manifestations, such as joint pain and arthritis [4,5]. The prevalence of Rheumatoid factor (RF) positivity is significantly higher in HCV patients compared to the general population, which decreases the specificity of RF for diagnosing RA. However, only a limited number of studies have found an association between HCV and RA [6,7]. Possible mechanisms include that HCV infection involves B cell expansion producing a pathogenic IgM with

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rheumatoid factor (RF) activity [8]. An RF test alone does not help distinguish between RA and HCV-associated rheumatic symptoms. In contrast to RF, anti-cyclic citrullinated peptide (anti-CCP) antibodies are much more specific for RA and their presence is not significantly increased in HCV infection alone. Therefore, anti-CCP testing is a more useful tool for diagnosing RA in patients with HCV. RF positivity in HCV patients is also significantly correlated with the presence of mixed cryoglobulinemia, which can have significant health consequences.

AIM OF STUDY

To estimate prevalence of Rheumatoid Factor positivity in Hepatitis C patients at tertiary care center of Northern India.

MATERIAL AND METHODS

This study was conducted at Medical Gastroenterology Department at PGIMS, Rohtak. It was a prospective study done over eight months, from 01.01.2025 to 31.08.2025, during which 500 confirmed hepatitis B patients were tested for Rheumatoid factor positivity or negativity. All hepatitis C patients were confirmed on HbsAg on Enzyme linked immunosorbent assay (ELISA) test and HCV RNA Quantitative test on Polymerase chain reaction test (PCR).

OBSERVATION AND RESULTS

On prospective analysis of 500 confirmed hepatitis C patients, males were 290 (58%) and females were 210 (42%). Out of total pool of 500 HCV patients, 250 (50%) were having rheumatoid factor positive and 250 (50%) were negative. Out of 250 rheumatoid factor positive patients, 133 were males (53.20%) and 117 (46.80%) were females. Out of these 133 rheumatoid factor positive males, 85 (63.90%) were having F0-F2 fibrosis, 12 (9.02%) were having F2-F3 fibrosis and 36 (27.06%) were cirrhotic. Out of total 117 rheumatoid factor positive females, 63 (53.84%) were having F0-F2 fibrosis, 32 (27.35%) were having F2-F3 and 22 (18.80%) were cirrhotic. Out of 250 rheumatoid factor negative patients, 155 were males (62%) and 95 (38%) were females. Out of these 157 rheumatoid factor negative males, 72 (45.85%) were having F0-F2 fibrosis, 60 (38.21%) were having F2-F3 fibrosis and 25 (15.92%) were cirrhotic. Out of total 93 rheumatoid factor negative females, 58 (62.36%) were having F0-F2 fibrosis, 12 (12.90%) were having F2-F3 fibrosis and 23 (24.74%) were cirrhotic. Out of total 250 rheumatoid factor positive patients, 163 (65.20%) were having symptoms of joint pains and rest 87 patients (34.80%) were asymptomatic.

Table 1. Showing Sex and Rheumatoid Factor Distribution in HCV Patients

Total HCV Patients	Males	Females	Rheumatoid Factor Positive	Rheumatoid Factor Negative
500	290 (58%)	210 (42%)	250 (50%)	250 (50%)

Table 2. Showing Sex Distribution in Rheumatoid Factor Positive HCV Patients

Total Rheumatoid Factor (RA) Positive HCV Patients	Males	Females
250	133 (53.20%)	117 (46.80%)

Table 3. Showing Fibrosis and Cirrhosis Distribution in RA Positive HCV Male Patients

Total RA Positive HCV Male Patients	F0-F2 Fibrosis	F2 -F3 fibrosis	Cirrhosis (F4)
133	85 (63.90%)	12 (9.02%)	36 (27.06%)

Table 4. Showing Fibrosis and Cirrhosis Distribution in RA Negative HCV Male Patients

Total RA Negative HCV Male Patients	F0-F2 Fibrosis	F2 -F3 fibrosis	Cirrhosis (F4)
157	72 (45.85%)	60 (38.21%)	25 (15.94%)

Table 5. Showing Fibrosis and Cirrhosis Distribution in RA Positive HCV Female Patients

Total RA Positive HCV Female Patients	F0-F2 Fibrosis	F2 -F3 fibrosis	Cirrhosis (F4)
117	63 (53.84%)	32 (27.35%)	22 (18.81%)

Table 6. Showing Fibrosis and Cirrhosis Distribution in RA Negative HCV Female Patients

Total RA Negative HCV Female Patients	F0-F2 Fibrosis	F2 -F3 fibrosis	Cirrhosis (F4)
93	58 (62.36%)	12 (12.90%)	23 (24.24%)

Table 7. Showing Distribution of RA Positive HCV Patients on Basis of Symptoms

Total RA Positive HCV Patients	Symptomatic Patients	Asymptomatic Patients
250	163 (65.20%)	87 (34.80%)

DISCUSSION

HCV infection is usually asymptomatic and may be detected incidentally; it also induces immunological extra-hepatic manifestations including arthralgia and arthritis which can mimic RA, and discrimination is really difficult without observing the erosions [9]. Along with anti-CCP, a new marker, anti-mutated citrullinated vimentin (anti-MCV) came into question. Anti-MCV antibodies have been linked mainly to connective tissue diseases recently [10-12]. In one study on hepatitis C patients, RF was positive in 46.7%, anti-CCP was positive in 3.3%, and anti-MCV was positive in 30% of the group [13]. There were no differences between the active and mild active patients regarding RF, anti-CCP and anti-MCV levels. There are studies suggesting a significant correlation with disease activity [11] while some others did not find any correlation [14]. It is well known that auto-antibodies may be positive in HCV infection without clinical involvement. HCV infection also establishes a linkage between extra-hepatic involvement and autoimmunity causing further confusion in evaluating the autoantibody responses [15]. Many studies have discussed about the extrahepatic involvement of HCV, such as Sjogren's Syndrome [16], arthritis [17], fibromyalgia [18], and cryoglobulinemia [19]. There were also many studies which described the autoantibody production of HCV, such as cryoglobulins, rheumatoid factor (RF) [20], antinuclear antibodies [21], antiphospholipid antibodies [22], anti-smooth muscle antibodies [23], and anti-extractable nuclear antigens antibodies [24]. The rheumatoid factor is one of the highest prevalent autoantibodies in patients with HCV and present in 50-80% of cases [25] and same 50% was observed in our Study group, which had a good number of 500 patients. It is much higher than 26.80% seen in HBV patients [26]. The overall predominance of males in HCV pool was reflected in rheumatoid factor positivity also. In both male and female group majority of patients who were rheumatoid factor positive were having normal liver without any significant fibrosis or cirrhosis which is same as seen in HBV patients [26]. It implies that advancement in stage of liver disease does not predict the positivity of rheumatoid factor positivity. Majority of rheumatoid factor positive patients including both male and female were symptomatic, same as was seen in HBV patients [26].

CONCLUSION

The hepatitis C patients need to be evaluated not only from hepatic point of view but also its extra hepatic impact, of which musculoskeletal system is integral part and every HCV patient should be tested for RF and if positive then confirmation for Rheumatoid arthritis because mere prescence of RA factor positivity does not mean Rheumatoid arthritis. It holds true in reverse also, meaning by that every RA patient should be checked for HCV and HCV infection.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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