

# **The Association OfOligoclonal Mixed Cryoglobulinemia With Cirrhosis In Patients Infected With Hepatitis C Virus**

*Thesis*

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*By*

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Cryoglobulins were noted to be associated with different diseases in the initial study of **Brouet JC et al., 1974**).

More sensitive methodologies were developed since the Brouet classification have detected multiple monoclonal immunoglobulins in cryoglobulins, i.e., oligoclonal immunoglobulins (**Tissot JD et al.,1993**).A new terminology for Oligoclonal cryoglobulins is proposed: Type IIa.( **De Rosa, et al.,2009**).

Estimates of the prevalence of mixed cryoglobulinemia in people with HCV infection vary widely. This is mostly because of unfamiliarity with clinical symptoms, lead-time bias, and mishandling of specimens. The association between cryoglobulinemia and severe liver affection is still a controversial issue.

The aim of the present work is to determine whether a specific cryoglobulin type, type IIa and not mixed cryoglobulins in general associate with cirrhosis & its progression in patients infected with hepatitis C virus.

The study was conducted on 80 patient infected with HCV (with and without cirrhosis). Divided into two groups. **Group 1:** 40 Patients infected with hepatitis C and have evidence of liver cirrhosis. **Group 2:** 40 Patients infected with hepatitis C without cirrhosis.All patients were subjected

to: CBC, ALT&AST, PT, PC, INR, Serum albumin, Bilirubin (total & free) tests. Anti-HCV antibodies, HBsAg. High-resolution, Semi automated Immunofixation Electrophoresis was employed for typing the cryoglobulins. Mixed cryoglobulins Type II, Type IIa (Oligoclonal), or Type III were assessed. HCV infection was confirmed by qualitative or quantitative tests for HCV-RNA PCR.

Data was collected for each patient including age, sex, cryoglobulin characterization, serum HCV-RNA concentration, anti-HCV antibodies, and serum alanine transaminase. Univariate analyses were used to compare demographics, clinical and laboratory data. Differences in proportions to be examined with the Chi-square test or Fisher's exact test. An unpaired T test was used for continuous variables. All calculated P values are 2-tailed and those  $< 0.05$  to be noted.

Our study found that the prevalence of mixed cryoglobulin type IIa test was 25% of studied population, and found high positive correlation between the cryoglobulins positivity and presence of cirrhosis, as we found that only 5 patients (12.5%) of group 1 (patients with no evidence of cirrhosis), while it was positive in 15 patients (37.5%) of group 2 (patients with evidence of cirrhosis) which make P-value (0.01) highly statistically significant. Also we found that

HCV- PCR was significantly elevated in patients without cirrhosis than cirrhotic patients with statistically significant P-value 0.01. Finally, our study did not find any correlation between mixed cryoglobulin type IIa positivity and age, sex, or ALT levels.

By comparing the results of our study, with other studies evaluating the prevalence of cryoglobulins associated with liver cirrhosis in HCV infected patients, we found that:

- The available data and information about the causal link are lacking, and significance of this problem still remains controversial.

- Estimates of the prevalence of mixed cryoglobulinemia in people with HCV infection vary widely. This is because of unfamiliarity with clinical symptoms, lead-time bias, and mishandling of specimens.

- Several studies have shown an epidemiologic association between MC and severe liver damage. However, this matter is still controversial

So, we recommend more comprehensive population-based and multifactorial studies for more evaluation of the significance of this problem.