

# Further Insights into the Causes of Thrombocytopenia in Chronic Hepatitis C

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Thrombocytopenia is likely the most common and prevalent haematological abnormality that can be found in patients affected by chronic liver disease [1]. A recent systematic review has shown that, in patients chronically infected with the hepatitis C virus (HCV), the prevalence of thrombocytopenia may vary from 0.16% in a cohort study that identified patients with severe autoimmune cytopenia alone to 45.4% in a study that included only patients with compensated cirrhosis [2-4]. In particular, the results of this review showed that the prevalence of thrombocytopenia in chronic HCV infection depends upon several factors, mainly the threshold used to define the haematological abnormality and the severity of the underlying liver disease in the studied population [4]. However, the most important evidence “hidden” in the data reviewed indirectly pointed to a multi-factorial aetiology of thrombocytopenia in chronic hepatitis C [5].

In the article published in this issue of the Journal of Gastrointestinal and Liver Diseases, Olariu and colleagues evaluated the prevalence of several possible causes for thrombocytopenia in a series of patients with chronic hepatitis C in Romania [6]. The authors provided no information regarding the prevalence of thrombocytopenia in the chronic hepatitis C patients population referred to their centre, but used the most common definition of thrombocytopenia (i.e., platelet count  $<150 \times 10^9/L$ ), subdivided their study population according to various platelet cut-offs, and excluded patients on interferon-based antiviral therapy as well as patients with cirrhosis [6]. Although the majority of patients evaluated (97.5%) had at least significant fibrosis and half of them had significant fibrosis – and increasing fibrosis stages have been associated with more prevalent thrombocytopenia [7, 8] – the

exclusion of cirrhotic patients ruled out portal hypertension as a potential aetiological factor for thrombocytopenia in the study population. Overall, evaluating the association between decreased platelet count and demographic, biochemical, virological, and histological parameters the authors found that the severity of thrombocytopenia increased with increasing age and severity of fibrosis stage. Interestingly enough, they also found that all patients with thrombocytopenia had evidence of fibrosis at histology, and up to 18.5% of the study cohort had a platelet count below  $100 \times 10^9/L$ . These latter findings emphasise the fact that in a population where interferon-based antiviral treatment may be indicated the prevalence and degree of thrombocytopenia may be an obstacle to initiating and maintaining therapy [9, 10]. Furthermore, antiviral therapy in chronic hepatitis C patients with severe thrombocytopenia may be burdened by an increased risk of bleeding [11].

One of the characteristics that increase the yield of the present study is that both bone marrow biopsy and assessment of anti-platelet antibodies were performed in all patients [6]. In fact, although the definitions used to diagnose autoimmune and “central” causes of thrombocytopenia may be arbitrary, these assessments provided the opportunity to evaluate the relative weight of these possible causes of thrombocytopenia in the study population. Furthermore, the prevalence of anti-platelet antibodies and of bone marrow findings compatible with decreased megakaryocytopoiesis were evaluated according to various platelet count subgroups. This analysis showed that both peripheral and central causes of thrombocytopenia were present in patients with platelet counts  $<100 \times 10^9/L$ , while the presence of anti-platelet antibodies alone was more prevalent among patients with a platelet count between  $126 \times 10^9/L$  and  $149 \times 10^9/L$ . As the datum regarding the distribution of fibrosis stages in these sub-groups of patients is missing, we are left without a more comprehensive analysis of the inter-relationships among all the possible aetiological factors for thrombocytopenia in chronic hepatitis C. Furthermore, this analysis should be interpreted with caution as the majority (64%) of patients included in this study were females, and this might have led to the inclusion of patients with chronic hepatitis C and

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immune thrombocytopenia. Lastly, thrombopoietin serum levels were not assessed in this study, and this does not allow us to evaluate how the decreased megakaryocytopoiesis may have been related to decreased bone marrow stimulation.

**In conclusion**, the study by Olariu and colleagues provides us a further insight into the aetiology of thrombocytopenia in chronic hepatitis C, and underscores the multifaceted aspects of this haematological abnormality in patients with chronic liver disease reminding us that only a comprehensive and thorough evaluation may help identify the possible cause(s) for decreased platelet count in the single patient.

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