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Research Article

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Platelets as a Possible Reservoir of HCV And Predictor of Response to Treatment

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Abstract

In the era of new Hepatitis C Virus (HCV) therapy, and the detection of extrahepatic HCV reservoirs such as peripheral blood mononuclear cells and platelets, it is important to understand the factors underlying resistance to treatment. Detection and quantitation of HCV-RNA in platelets or leucocytes from patients under antiviral therapy is poorly studied and the limited studies generated contradictory results.

Aim: To detect and quantify HCV-RNA in platelets, and to evaluate the relation between HCV-RNA in the serum and the kinetics of HCV-RNA in platelets, in response to treatment.

Method: Viral kinetic was tested in 20 chronic HCV genotype4, during the course of therapy.

Results: HCV-RNA was detected in sera of all infected patients. The baseline platelet viral load was significantly lower in responders compared to non-responders. Platelet viral load was also related to serum viral load (t=3.39, p=0.001), but not related to platelet count (t=-0.56, p=0.58). ROC curve analysis revealed that in general, platelet viral load at different time points was a better predictor of SVR compared to serum viral load.

Conclusion: HCV RNA analysis in whole blood may be more sensitive than platelet-poor plasma, which might underestimate circulating viral load. Early eradication of viremia from platelets is associated with higher rates of SVR. Our data, reconfirm higher HCV-RNA levels in serum compared to platelets. Thrombocytopenia occurring during interferon-based therapy might be a manifestation of viral eradication rather than adverse effects. Our findings warrant testing the sensitivity of platelet viral load as a predictor of poor response.

Keywords

Hepatitis; HCV; Platelets; Response to treatment

Background

Hepatitis C virus (HCV) is one of the most important causes of chronic hepatitis around the globe, particularly in Egypt, where genotype 4 (G4) is the predominant one, and it has been detected at extrahepatic sites [1]. Although HCV has hepatic tropism, viral RNA was found in extrahepatic compartments. A few recent studies have demonstrated that in individuals infected with HCV, viral RNA is associated with platelets which act as carriers of the virus in the circulation leading to persistence of the virus. Consequently, platelet- associated viral particles would exert a limiting effect on the efficiency of antiviral therapy. Cytopenias associated with HCV infection is another limiting factor by delaying or may be interrupting the course of treatment [2], and directly interact with platelets and platelet dysfunction and thrombocytopenia [3].

HCV- associated thrombocytopenia is complex and multifactorial in origin. Interaction of platelets with HCV is presumed to be one of the pathogenic mechanisms implicated in HCV-associated thrombocytopenia. Also, autoimmune thrombocytopenia in chronic HCV infection and detection of anti-platelet antibodies, have been reported [4]. Specific glycoprotein antibodies [5], and immune complex bound to the platelet, have been reported [6]. Furthermore, the finding that thrombocytopenia is reversed by a selective thrombin receptor agonist, indicates that HCV-induced thrombocytopenia might be related to platelet activation due to the infection related inflammation [7]. Paradoxically, thrombocytopenia is not usually associated with bleeding tendency during treatment of hepatitis C with interferon and ribavirin [8].

The recently approved targeted therapy with Direct Acting Antiviral (DAAs), changed the treatment paradigm and raised the hope of better treatment, it offers a new era of high safety and efficacy to a variety of patients suffering from chronic HCV infection [9]. However, the current treatment course still involves the drugs, pegylated interferon and ribavirin (PEG-IFN/RBV) in certain regimens. Also, at these expensive prices, these treatments will remain unaffordable for most patients who need treatment. So, PEG-IFN- based therapy will remain for sometimes in low-income settings. Both HCV infection and its treatment with PEG-IFN/RBV therapy were reported to be associated with decreased several blood cells, such as; white blood cells (neutropenia), red blood cells (anemia), and platelets (thrombocytopenia), which can delay or prevent treatment [10]. We suggested, in our previous study, that pretreatment neutrophil count and the degree of decline can be useful in predicting how HCV genotype 4 patients would respond to therapy. We also postulated that neutropenia during PEG-IFN therapy, could reflect viral clearance of infected neutrophil rather than being an adverse effect [11]. Other studies reported that, HCV is directly involved in the process that, at least in part, leads to thrombocytopenia [12].

Detection of HCV has been reported in extrahepatic sites such as peripheral blood mononuclear cells and platelets, the quantitation of HCV-RNA in platelets or leucocyte components from patients under antiviral therapy is rarely studied and generated contradictory results. Since the complex function of platelets' HCV-RNA and platelets count in predicting response to therapy has not been well characterized, we decided to explore the possible interplay between response to treatment with platelets count and platelets' HCV-RNA viral load in 20 chronically HCV-G4 infected patients. Therefore, we examined and quantified the presence of HCV-RNA in platelet. In addition, we evaluated the relation between HCV-RNA in the serum and the kinetics of HCV-RNA in platelet in response to treatment.

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Materials and Methods

Sample population

Twenty chronic HCV genotype 4 patients who were scheduled to receive treatment at the Hepatology clinic at Hamad General Hospital (HGH) were selected. The prescribed treatment consisted of PEG-IFN and RBV according to body weight. Patients were considered to have chronic HCV infection if they had sustained increase in alanine aminotransferase (ALT), positive anti-HCV serology, detectable HCV-RNA, and histopathological evidence of chronic active hepatitis. Patients were excluded from the study if they had any other disease or receiving treatment which may affect platelet count. The treatment regimen was 48-week a once weekly subcutaneos, 180 µg of Peginterferon-2a (Pegasys®, Hoffmann-La Roche, Basel, Switzerland) and 1000 mg (body weight ≤ 75 kg) or 1200 mg (body weight ≥ 75 mg) of oral Ribavirin (COPEGUS®; Hoffmann-La Roche). We defined end of treatment response (ETR) and sustained viral response (SVR) as undetectable serum HCV RNA at the end of treatment (48 week) and at the end of follow up (72 week) respectively.The study started after obtaining the approval of the ethics research committee of the Hamad Medical Corporation. All patients provided written informed consent the study was funded by UREP grant 09-065-3-010, QNRF.

Sample collection

A total of 14 mL blood was collected at each time point. More specifically, 10 mL whole blood samples were collected and added to 3.2% ACD vacutainer tubes; and additional 4 mL blood samples were collected without anticoagulant agent for serum preparation. Blood samples were collected at the following time points: pre-treatment, 4, 12, and 48 weeks post-treatment. To detect sustained virological response to treatment, serum samples were also collected on week 72.

Sample laboratory analysis

Platelet rich plasma was prepared by centrifuging citrated whole blood sample at 150xg for 10min. The plasma was transferred to another plain tube and then re-centrifuged at 150xg for 10min to obtain a platelet pellet. The pellet was washed seven times with Tyrode's solution, which helped to maintain a healthy platelet population and prevented further cell disruption. HCV-RNA extraction was completed promptly using the QIAamp Viral RNA and RNeasy Mini kit (QIAGEN, Hilden, Germany) according to manufacturer's instructions. Briefly, samples were homogenized and cells were lysed using the RLT buffer supplied with the kit. To each sample 70% ethanol was applied to enhance clean up. Each sample was then passed through a specialized column that binds the total RNA. Before elution, the samples were cleaned up from any residual DNA by applying DNAse, and then the sample was eluted and collected by spinning at × 10,000 RPM using a table top centrifuge. The final concentration of the extracted RNA was measured using spectrophotometry.

Statistical analysis

Individuals were classified as having rapid viral response (RVR), early viral response (EVR), end of treatment response (ETR), and sustained viral response (SVR) if they had undetectable HCV-RNA at weeks 4, 12, 48, and 72 respectively. Bivariate associations were tested using t-tests and chi-square tests. In addition, we examined Spearman correlations between various variables. To adjust for covariates, multivariable regression models were employed using generalized estimating equation (GEE) models, and mixed models to examine predictors of SVR and viral loads accounting for repeated measurements on the same individual and covariates. Subsequently, we examined whether platelet count, or platelets viral load is superior to serum viral load in predicting SVR using ROC curve method. SAS 9.32 (SAS Inc., Cary, North Carolina, USA) was used for all analyses.

Results

The study included 20 HCV-G4 patients who received PEG-IFN/RBV therapy. Most of the study participants were men (95%), with a baseline median (interquartile range) age 46 (38.5,50.5) years, platelet counts 166 (150.5,222), log10 serum viral load 7.56 (6.43,8.10) and log10 platelet viral load 3.52 (0.0,5.09). RVR, EVR, ETR, and SVR were observed in 35%, 70%, 75% and 55% respectively. Approximately 27% of those who had ETR, relapsed at 72 weeks, with an overall relapse rate of 20%, and nonresponse of 25%.In the bivariate unadjusted analysis, only baseline platelet viral load was significantly different between those who had SVR and non-responders, while there were no age, serum viral load, platelet count, spleen size, inflammation or fibrosis significant differences (Table 1).

While, patients experiencing RVR had sharp reductions in serum viral load by week 4 of ~zero, which remained around zero levels through week 48, which is followed by a slight increase at week 72 in some individuals (Figure 1). In contrast, non-responders had a slower decline in serum viral loads to reach the lowest values at 48 weeks and then showed an increase by 72 weeks. On the other hand, platelet viral load among RVR showed a sharp decline by week 4 but did not reach zero levels, and remained almost constant afterward. Individuals with non-RVR had a steeper decline in platelet viral load until week 12, which was followed by an increase by week 48. Platelet count tended to be lower among those with RVR compared to those with non-RVR throughout the follow up. Of note, among individuals with RVR platelet counts declined slightly by week 4 and week 12 then gradually increased to reach pre-treatment levels by week 48, but there was no similar decline among patients who did not achieve RVR (Figure 2).

As illustrated in Figure 1, patients with EVR experienced sharp reduction of serum viral load to reach ~zero by week 12 and week 48, which was followed by an increase by week 72. EVR group also demonstrated a drop in platelet viral load by week 4, which remained almost constant through the remaining follow up (Figure 2). In addition, patients with EVR had a decline in platelet count to reach the lowest level at week 12 followed by an increase in platelet count by week 48 (Figure 3). In contrast to patients with EVR, patients who did not achieve EVR had a very slow reduction in serum viral load to reach the lowest values by 48 weeks which was followed by an increase (Figure 1). We also observed no change in platelets' viral load by week 4, followed by reaching its lowest levels at week 12 which was followed by an excess by week 48 (Figure 2). Interestingly individuals with no-EVR had a progressive increase in platelet count to reach the highest level at week 12, and then were followed by decline (Figure 3).

By week 4, platelets' viral load showed sharp declines among SVR to reach approximately zero and remains ~0 throughout the follow up. On the other hand, among non-SVR, the platelets' viral load decline continues until the 12th week, and then an increase in the platelets' viral load is observed throughout the remaining period of follow up (Figure 2). In comparison, the observed decline in serum viral load (Figure 1) is steeper than the decline in platelet viral load (Figure 2), such that both SVR and non-SVR show steep decline in serum viral load until the 12th week where the responders viral load

Table 1: Selected pretreatment characteristics by SVR status.

	All N=20	No SVR N=9	SVR N=11	P value
Age median (IQR)	46 (38.5,50.5)	46 (44,50)	46 (35,53)	0.91
Baseline serum log10 viral load median (IQR)	7.56 (6.43,8.10)	7.67 (6.63,8.06)	7.52 (6.42,8.14)	0.76
Baseline platelet viral load median (IQR)	3.52 (0.0,5.09)	4.44 (3.86,5.14)	0.00 (0.00,4.90)	0.04
Baseline platelet count median (IQR)	166 (150.5,222)	162 (150-215)	169 (151,250)	0.87
Spleen size median (IQR)	11.35 (9.60,14.15)	13.0 (11.1,15.0)	11.1 (9.6,13.2)	0.31
Inflammation N (%)				
I & II	14 (77.78%)	5 (35.7%)	9 (64.3%)	0.61
III & IV	4 (22.22%)	2 (50.0%)	2 (50.0%)	
Fibrosis N (%)				
I & II	10 (55.56%)	2 (20.0%)	8 (80.0%)	0.07
III & IV	5 (44.44%)	5 (62.5%)	3 (37.5%)	

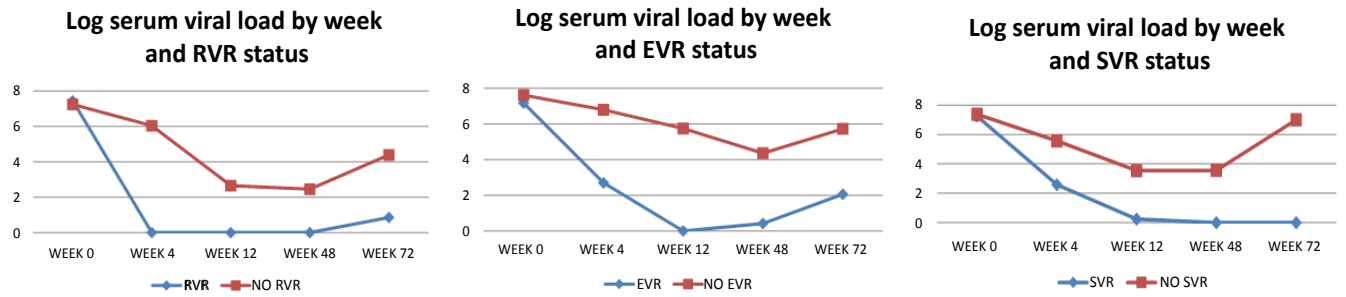

Figure 1: Mean serum log viral load over time by response status.

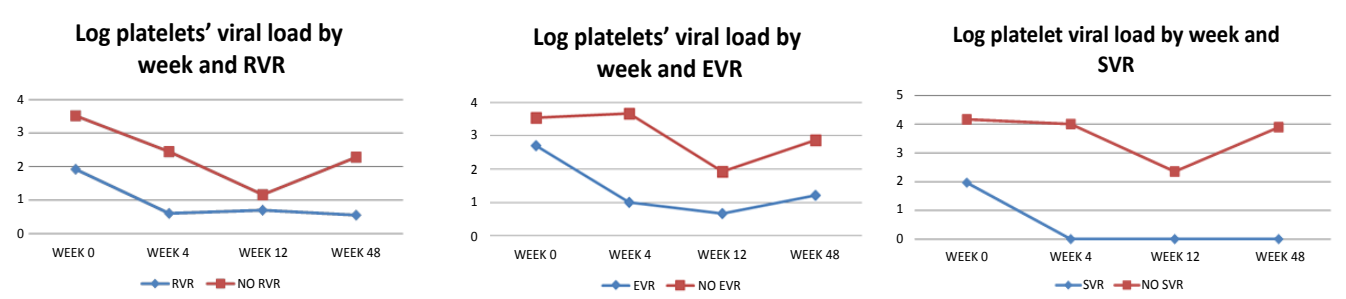

Figure 2: Mean platelet log viral load over time by the response status.

become very close to zero, whereas afterwards non-SVR viral load remains high but steady until the 48th week, then it increase again (Figure 1). Platelet count remained almost constant over time, among non-SVR, but among SVR it should steady small decline until week 12, then it started to increase to pre-treatment levels (Figure 3).

As shown in Table 2, platelet viral load at week 4 significantly positively correlated with platelet viral loads, and serum viral loads at successive time points, but significantly negatively correlated with EVR, and SVR. Platelet viral load at week 12 significantly positively correlated with platelet viral load at week 48, and serum viral load at week 72, but significantly negatively correlated with SVR. Similarly, platelet viral load at the 48th week was significantly correlated with serum viral loads at the 48th and 72nd weeks and negatively correlated with SVR. Serum viral load at 12th weeks significantly correlated with viral loads at the 4th, 48th, and 72nd weeks and negatively correlated with RVR, EVR, and SVR. Serum viral load at week 48 significantly correlated with serum viral load at the 72nd week, as well as negatively correlated with RVR, EVR and SVR. Platelets count at any time point positively significantly correlated with platelet count at any other time point, but did not correlate with platelet or serum viral loads or treatment responses (Table 2).

A more detailed examination of the relapsed cases, revealed that all those patients had a one or more visit where serum viral load was undetectable, but the platelet viral load was still detectable (Table 3). We further examined whether the serum viral load, platelet viral load and platelet count values measured over time predicted SVR or not.

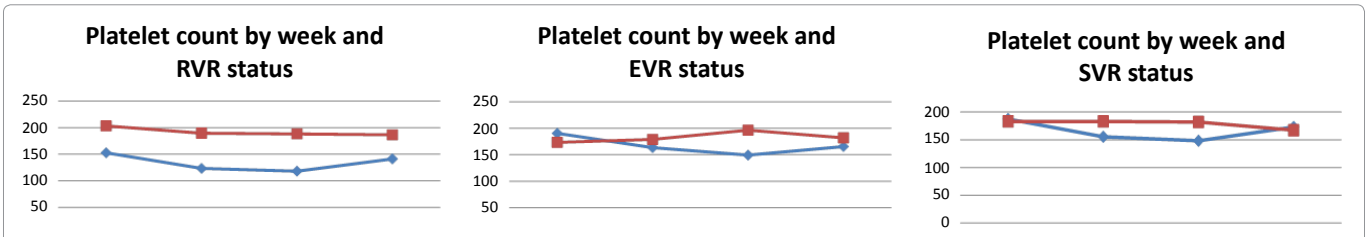

Figure 3: Mean platelets count over time by the response status.

Serum viral load, significantly predicted SVR, such that for each unit increase in log serum viral load, the odds of SVR decreased by 27% (OR 0.73 95% CI 0.64, 0.83, P<.0001). Similarly, platelet viral load predicted SVR such that for each unit decrease in log platelet viral load, the odds of SVR increase by ~2.13 times (P<.0001). Platelet count over time did not significantly predict SVR (Table 4).

Mixed models were run to examine predictors of serum and platelet viral load accounting for the time of sample collection. The serum viral load was positively associated with platelet viral load (t=3.58, p=0.001), and platelet count (t=6.79, p=0.02). The Platelet viral load was related to serum viral load (t=3.39, p=0.001), but not related to platelet count (t=-0.56, p=0.58), or weak levels (t=0.64, p=0.52). Platelet count was significantly positively associated with log serum viral load (t=10.25, p=0.002), but not with log platelet viral load (t=-0.97, p=0.33), or week (t=1.27, p=0.21).

ROC curve analysis revealed that in general platelet viral load at different time points were better predictors of SVR compared to serum viral load. More specifically, platelet viral loads at baseline, week 4, week 12, and week 48 had AUC of 81%, 93%, 79%, and 100% respectively. In contrast, serum viral loads at baseline, week 4, week 12, and week 48 had AUC of 58%, 71%, 69%, and 71% respectively. Since serum viral load is usually used to predict SVR, we compared ROC curves of each of the indicators to ROC curve of serum viral load at baseline. The ROC curve of platelet viral load at week 4 and week 48 were significantly better than ROC curve of serum viral load at baseline, therefore, platelet viral loads are better clinical predictors of response to treatment (Table 5).

Discussion

Detection of HCV-RNA in different in mononuclear subpopulation and platelet, has been documented in a few studies, which was hampered by small size samples [12]. Similar to de Almeida [13], all our patients harbor HCV-RNA in their platelets before and throughout the course of therapy, independent of pre-treatment viral load or platelet counts. As shown in our study, HCV-RNA levels were higher in serum than in platelets, regardless of time of antiviral therapy, which was in agreement with previous studies [14]. This confirms that platelets may serve as reservoirs of HCV and protect virions from immune recognition. Whether, this immune escape will play a role in developing viral mutations in HCV with resistance to the recently approved protease and non-nucleoside inhibitors.

This reported detection of HCV-RNA in peripheral blood components; raise the question about the correlation between response and/or relapse with the detectable viral genome in the platelet. Despite HCV-RNA elimination from blood serum during treatment in some patients, HCV viremia appears again after the completion of therapy. Despite hepatocytes being the primary target cells of HCV, however, HCV-RNA has been detected in other cells, such as platelets, which have been described as carriers of the virus in the circulation of infected patients. Some studies have suggested that PBMC could serve as a reservoir for virus resistant to IFN therapy, therefore, could be one of the mediating mechanisms of relapse [15]. In the current study, we found that patients with undetectable serum HCV-RNA but have detectable HCV-RNA in their platelets after completion of anti-viral therapy, would be at greater risk of HCV relapse compared to those without HCV-RNA in their platelets. We also found that, those who relapsed had detectable HCV-RNA in their platelets in spite of being negative in peripheral blood. Platelets do not express CD81 or the classical LDL-R, suggesting that other receptors/molecules are involved in the entry of HCV-RNA to the platelets [16]. HCV interaction with the platelet membrane glycoprotein VI, might explain the viral binding to platelets in infected patients [17]. According to our findings, any effective treatment should be effective in clearance if infected platelets, as platelets act as reservoirs for the virus and HCV is known to replicate in megakaryocytes

Although the majority of sustained responders eventually loses HCV RNA from PBMCs [18], it should be noted that patients with detectable HCV-RNA in platelets or PBMCs represents a potential source of HCV spread, even if they were HCV-RNA serum negative. While including the RBC fraction of the tested sample was reported not to increase assay sensitivity [19], our data indicated that a significant proportion of HCV RNA in peripheral blood is not identified by standard plasma RNA detection methods. Thus measuring HCV-RNA in serum or plasma may underestimate the true HCV burden. The importance of the early detection of relapse is of paramount importance in PEG-IFN based therapy, as well as with the more expensive IFN-free direct acting therapy, when considering a prolonged course of 24 weeks or to shift to a mixture of antiviral drugs.

Conclusion

Our data reconfirm higher HCV-RNA levels in serum compared to platelet, independent of time point of antiviral therapy. We suggest that, the HCV RNA analysis in plasma, may underestimate circulating virus load. Thrombocytopenia occurring during interferon-based therapy might be manifestation of viral eradication rather than adverse effects. Our findings warrant testing the sensitivity of platelet viral load as a predictor of poor response in a larger sample size, and that early eradication of HCV-RNA from platelet, is associated with higher rates of SVR.

References

1. Di Lello FA Culasso AC, Parodi C, Baré P, Campos RH, et al. (2014) New evidence of replication of hepatitis C virus in short-term peripheral blood mononuclear cell cultures. Virus Res 191: 1-9.
2. Giannini EG, Marenco S, Fazio V, Pieri G, Savarino V, et al.(2012) Peripheral blood cytopaenia limiting initiation of treatment in chronic hepatitis C patients otherwise eligible for antiviral therapy. Liver Int 32:1113-1119.

Table 2: Correlation between serum viral load, platelet viral load, platelets counts and responses to treatment.

	LOG PLTVL W0	LOG PLTVL W4	LOG PLTVL W12	LOG PLTVL W48	Log Serum VL W0	Log Serum W4	Log Serum W12	Log Serum W48	Log Serum W72	PLT_N W0	PLT_N W4	PLT_N W12	PLT_N W48	RVR	EVR	SVR
LOG PLTVL W0	1															
LOG PLTVL W4	0.4	1														
	0.08															
LOG PLTVL W12	0.36	0.95	1													
	0.18	<0.01														
LOG PLTVL W48	0.45	0.82	0.79	1												
	0.05	<0.0001	0.0001													
Log Serum VL W0	-0.17	0.24	0.01	0.19	1											
	0.48	0.31	0.97	0.44												
Log Serum VL W4	0.38	0.51	0.23	0.39	-0.02	1										
	0.1	0.01	0.34	0.1	0.94											
Log Serum VL W12	0.25	0.54	0.34	0.36	0.1	0.73	1									
	0.28	0.01	0.16	0.13	0.66	<0.001										
Log Serum VL W48	0.21	0.39	0.4	0.39	-0.22	0.54	0.76	1								
	0.36	0.09	0.09	0.03	0.36	0.01	0.0001									
Log Serum VL W72	0.49	0.79	0.47	0.77	-0.05	0.45	0.46	0.51								
	0.03	<0.0001	0.04	0.0001	0.85	0.05	0.04	0.01	1							
PLT N W0	0.14	-0.21	-0.29	-0.07	-0.05	0.19	-0.26	-0.16	-0.01	1						
	0.56	0.37	0.22	0.79	0.84	0.42	0.28	0.49	0.96							
PLT N W4	0.38	0.03	0.08	0.29	-0.07	0.29	0.004	0.13	0.2	0.8	1					
	0.11	0.9	0.77	0.24	0.78	0.22	0.99	0.59	0.41	<0.0001						
PLT N W12	0.19	-0.03	0.17	0.27	0.03	0.29	0.13	0.25	0.09	0.68	0.84	1				
	0.42	0.91	0.49	0.26	0.88	0.22	0.57	0.28	0.7	0.01	<0.0001					
PLT N W48	0.37	-0.22	-0.07	-0.06	-0.33	0.27	0.08	0.18	-0.02	0.74	0.84	0.77	1			
	0.11	0.34	0.78	0.82	0.15	0.26	0.75	0.45	0.94	<0.001	<0.0001	<0.0001				
RVR	-0.33	-0.4	-0.11	0.37	0.1	-0.85	-0.47	-0.42	-0.51	-0.34	-0.38	-0.38	-0.28	1		
	0.16	0.08	0.56	0.12	0.67	<0.0001	0.04	0.07	0.02	0.15	0.11	0.11	0.23			
EVR	-0.25	-0.52	-0.31	-0.35	-0.21	-0.73	-0.98	-0.67	-0.41	0.23	-0.03	-0.17	-0.08	0.48	1	
	0.29	0.02	0.2	0.14	0.38	<0.001	<0.0001	0.001	0.07	0.34	0.9	0.47	0.75	0.03		
SVR	-0.44	-0.87	-0.6	-0.87	-0.06	-0.47	-0.55	-0.63	-0.94	0.13	-0.16	-0.1	0.08	0.45	0.5	1
	0.05	<0.0001	<0.01	<0.0001	0.8	0.04	0.01	<0.01	<0.0001	0.58	0.5	0.69	0.74	0.04	0.02	

3. Ariede JR, Pardini MI, Silva GF, Grotto RM (2015) Platelets can be a biological compartment for the Hepatitis C Virus. Braz J Microbiol 46: 627-629.

4. de Almeida AJ, Campos-de-Magalhaes M, Antonietti CL, Brandao-Mello CE, da Silva ML, et al.(2009) Autoimmune thrombocytopenia related to chronic hepatitis C virus infection. Hematology 14:49-58.

5. Zhang W, Nardi MA, Borkowsky W, Li Z, Karpatkin S(2009) Role of molecular mimicry of hepatitis C virus protein with platelet GPIIIa in hepatitis C-related immunologic thrombocytopenia. Blood 113:4086-4093.

6. Weksler BB (2007) Review article: the pathophysiology of thrombocytopenia in hepatitis C virus infection and chronic liver disease. Aliment Pharmacol Ther 26 Suppl 1: 13-19.

7. McHutchison JG, Dusheiko G, Shiffman ML, Rodriguez-Torres M,

Table 3: Platelet and serum viral load among relapsers.

Patients	LOG PLT VL W0	LOG SRM VL W0	LOG PLT VL W4	LOG SRM VL W4	LOG PLT VL W12	LOG SRM VL W12	LOG PLT VL W48	LOG SRM VL W48	LOG SRM VL W72
Patient 1	3.18	8.06	4.24	0.00	4.88	0.00	3.86	0.00	5.96
Patient 2	3.86	8.33	4.71	4.99	0.00	0.00	4.88	0.00	6.50
Patient 3	5.04	6.63	5.06	5.40	4.30	0.00	5.06	0.00	8.39
Patient 4	5.83	8.78	5.92	7.84	0.00	4.66	3.19	0.00	7.57

Table 4: The association between serum viral load, platelet viral load and platelet count overtime and SVR.

	OR*	OR 95% CI	Chi-square	P value	
Serum viral load	0.73	0.64	0.83	24.77	<.0001
Platelet viral load	0.47	0.35	0.63	25.5	<.0001
Platelet count	1	0.99	1.01	0.2	0.652
*Interpreted as the change in the odds of SVR for each unit increase of continuous predictors.					

Table 5: Area under the curve of different possible predictors of SVR.

	AUC	AUC 95% CI	Contrast	Chi-square	P value	
Platelet VL W0	0.8052	0.5945	1	0.2208	1.4431	0.2296
Platelet VL W4	0.9286	0.7886	1	0.3442	7.8919	0.005
Platelet VL W12	0.7857	0.5877	0.9837	0.2013	1.1392	0.2858
Platelet VL W48	1	1	1	0.4156	7.9751	0.0047
Serum VL W0	0.5844	0.296	0.8728	ref	ref	ref
Serum VL W4	0.7143	0.4601	0.9685	0.1299	0.4703	0.4928
Serum VL W12	0.6883	0.4664	0.9102	0.1039	0.4611	0.4971
Serum VL W48	0.7143	0.5163	0.9123	0.1299	0.371	0.5425

Sigal S, et al. (2007) Eltrombopag for thrombocytopenia in patients with cirrhosis associated with hepatitis C. N Engl J Med 357: 2227-2236.

8. Jimenez-Saenz M, Rojas M, Pinar A, Salas E, Rebollo J, Carmona I, et al.(2000) Sustained response to combination therapy in a patient with chronic hepatitis C and thrombocytopenia secondary to alpha-interferon. J Gastroenterol Hepatol 15:567-569.

9. Wiegand J, Schiefke I, Stein K, Berg T, Kullig U, et al. (2016) Interferon-free treatment of chronic hepatitis C virus infection in patients with inherited bleeding disorders. Hamostaseologie 36.

10. Hajder J, Stanisavljevic N, Markovic O, Marisavljevic D (2010) [Late onset of severe thrombocytopenia during interferon treatment for chronic hepatitis C infection--case report]. Srp Arh Celok Lek 138:240-243.

11. Amer A, Shebl F, Derbala M (2014) Neutropenia and viral load decline during treatment of hepatitis C virus genotype-4. Turk J Gastroenterol 25: 15-19.

12. de Almeida AJ, Campos-de-Magalhães M, de Melo Marçal OP, Brandão-Mello CE, Okawa MY, et al. (2004) Hepatitis C virus-associated thrombocytopenia: a controlled prospective, virological study. Ann Hematol 83: 434-440.

13. de Almeida AJ, Campos-de-Magalhaes M, Brandao-Mello CE, de Oliveira RV, do Espirito-Santo MP, Yoshida CF, et al. (2009) Detection of hepatitis C virus in platelets: evaluating its relationship to antiviral therapy outcome. Hepatogastroenterology 56:429-436.

14. Espírito-Santo MP, Brandão-Mello CE, Marques VA, Lampe E, Almeida AJ (2013) Analysis of hepatitis C virus (HCV) RNA load in platelets of HCV-monoinfected patients receiving antiviral therapy. Ann Hepatol 12: 373-379.

15. Zignego AL, Giannini C, Monti M, Gragnani L (2007) Hepatitis C virus lymphotropism: lessons from a decade of studies. Dig Liver Dis 39: 38-45.

16. Padovani JL, Corvino SM, Drexler JF, Silva GF, Pardini MI, et al. (2013) In vitro detection of hepatitis C virus in platelets from uninfected individuals exposed to the virus. Rev Soc Bras Med Trop 46: 154-155.

17. Zahn A, Jennings N, Ouwehand WH, Allain JP (2006) Hepatitis C virus interacts with human platelet glycoprotein VI. J Gen Virol 87: 2243-2251.

18. Garcia-Bengoechea M, Basaras M, Barrio J, Arrese E, Montalvo II, et al.(1999) Late disappearance of hepatitis C virus RNA from peripheral blood mononuclear cells in patients with chronic hepatitis C in sustained response after alpha-interferon therapy. Am J Gastroenterol 94:1902-1905.

19. Schmidt WN, Wu P, Han JQ, Perino MJ, LaBrecque DR, et al. (1997) Distribution of hepatitis C virus (HCV) RNA in whole blood and blood cell fractions: plasma HCV RNA analysis underestimates circulating virus load. J Infect Dis 176: 20-26.

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