Correlation between lipid profile and Rapid Virologic Response to treatment of HCV

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Abstract: Background: Egypt has the highest prevalence of HCV worldwide13.8 %. The classic effective treatment is Interferon alpha (IFN-α) in combination with ribavirin. As these therapies have side effects and high costs, it is important to identify patients having the best chance to respond before initiation of therapy. **Objective:** to study the relationship between the lipid profile of the patient before starting treatment and the rapid virologic response (RVR). **Patients &Methods**: This study was conducted on 56 non-cirrhotic HCV positive patients, they were divided into 2 groups, group I with 27 patients with normal lipid profile and group II with 29 patients with high lipid profile. Both groups were treated with peg-IFN (2b) plus RBV, HCV viral load was measured before therapy and after 4 weeks of therapy. **Results:** pretreatment cholesterol and LDL levels were significantly higher in group (II), while the triglycerides levels were significantly higher in group (I). RVR in group II was 58.6%, while it was only 22.2% in group I, *p* value =0.0056. **Conclusion:** Our data suggest that pretreatment cholesterol and LDL is strongly associated with RVR. Assessing the lipid profile in all chronic HCV patients at baseline would be a useful tool in predicting RVR.

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1. Introduction

Chronic hepatitis C virus is a major health problem affects ~ 170 million individuals worldwide, Egypt has one of the highest HCV prevalence in the world***(1,2)***An accurate early predictor of a patient's response to interferon therapy could reduce unnecessary and ineffective treatments, permit greater flexibility in tailoring therapy on an individual basis, and enhance the cost-effectiveness of treatment(3)**.**

The rapid virologic response (RVR), defined as HCV RNA negative at four weeks is a strong predictor of an SVR and may be an important factor when deciding how long treatment should be continued(4)**.**There is a strong correlation between blood lipids and HCV in its different stages of its life cycle. However, little is known about its general relevance to response to interferon therapy. We therefore conducted this prospective study, to determine the relationship between blood lipids as a pretreatment variable to the RVR, which will be useful for tailoring anti-viral regimens.

2.Patients and methods:

This study was performed in kasr El Aini university hospital after the approval of the local scientific ethical committee, 56 non-diabetic, non-hypertensive, non-cirrhotic Egyptian patients, with chronic HCV infection who had not been previously treated with interferon alpha and/or ribavirin and arecandidates for therapy were prospectively enrolled in our study. After signing a written informed consent patients with decompensated liver disease, Co infection with HBV or HIV, autoimmune disorders, clinically significant cardiac or cardiovascular abnormalities, Renal impairment, Hypersensitivity to Peg-interferon alpha & Ribavirin, Pregnancy or breast feeding, Hemoglobinopathy (hemoglobin concentration of 10 g / dl or less), absolute neutrophilcount (ANC) < 1,500 / µ l, thrombocytopenia (80,000 / µ l or less), or those with previous history of cerebrovascular event were excluded from our study.

Patients were categorized into two groups according to their lipid profile, where patients with normal lipid profile belongs to group (I) (n=27), while those with high cholesterol and LDL levels belongs to group (II) (n=29).All patients were subjected to detailed medical history,clinical examination, biochemical and hematological investigations, blood lipids profile including serum triglycerides, cholesterol, LDL and HDL. Anti-HCV antibodies using a third generation enzyme immunoassay EIA (Abbott HCV 3.0 Elisa) and Serum HCV-RNA levels by using quantitative reverse-transcription polymerase chain reaction (PCR) (Amplicor Monitor HCV v. 2.0; Roche Molecular Systems, Mannheim, Germany). Measurement of HCV-PCR base line and after 4 weeks of starting interferon based therapy. Hepatitis B surface antigen, anti-hepatitis B core antibody, and

anti-HIV were tested by using commercially available kits (Abbott Laboratories, Chicago, IL). Abdominal Ultrasonography, assessment of fibrosis via Liver biopsy.Patients were treated with Peg-IFN (2b) (Peg-Intron; Schering-Plough K.K., Kenilworth, NJ), which was given in weekly doses adjusted to body weight according to the manufacturer's instructions at 1.5 µg / kg / week, plus RBV (Rebetol; Schering-Plough K.K.), which was given in daily doses adjusted to body weight (800 mg for weights < 50 kg, 1,000 mg for weights 50 – 65 kg, 1,200 mg for weight 65 – 80 kg, and 1,400 mg for weights > 80 kg) and orally administered with food in three divided doses per day.

Statistical analysis

Statistical analysis was performed using SPSS statistical software(Version 16,SPSS Inc. USA) and Microsoft Excel 2007. Results are expressed as mean ± SD. Group).Also Medical program is used in ROC curve. *p*-value ≤ 0.05 was considered significant.

3.Results:

Our study is a prospective study that included 56 patients (75% males and 25% females) with age ranging between 27 and 60 years,with a mean age of 48.85±10.25 years in group I and 51.14 years in group II, the data of both groups were compared in table (1).

Our results showed that the cholesterol , and the LDL levels were higher in group II than those in group I , while the triglycerides levels are higher in group I than that of group II and this difference is statistically significant. No statistically significant difference detected between both groups regarding the baseline viral load.

After 4 weeks of therapy 58.6% (17 patients) of group II showed RVR while only 22.2% (6 patients) of group I showed RVR and this difference is statistically significant with *p*-value=0.0056, denoting that there is assciation between high cholesterol and LDL levels and RVR .

In group I, 3 cases of total 10 of the female cases responded to treatment with a percentage of 30 % while in males 3 cases of total 17 responded with a percentage of 17.4 %, while in group II, the number of female cases who responded to treatment was 2 out of 4 cases with a percentage of 50 % and in case of males 15 out of 25 cases responded with percentage of 60 %. Thus, it is obvious that the percentage of response to treatment among males and females increased markedly in group 2(Figure 1)

It was reported that in patients showing RVR in group Ithe least of them decreased with log 2.17, the highest decreased with log 4.7 , while in group II the least of them decreased with log 3, the highest decreased with log 5.9 (Figures 2 & 3).

Table (1): Comaprison between the two studied groups.

	Group I n= 27	**Group II n= 29**	***P* value**
	Mean±S.D	**Mean ± S.D**	
Age (yrs)	48.8519± 10.26	51.1379± 8.79	**> 0.05**
BMI kg/m^2	28.6211 ± 6.25	28.74±3.77	**> 0.05**
Hbgm/dl	13.2074± 1.77	13.7172± 1.46	**> 0.05**
TLC10^3/cmm	5.7311 ± 1.89894	4.62 ± 0.93306	**< 0.01**
Platelets10^3/cmm	171.5185± 66.63642	160.5172± 58.02008	**> 0.05**
ASTU/L	70.1481± 46.1775	53.069 ± 42.80431	**> 0.05**
ALTU/L	74.2222 ± 61.80262	61.6552± 52.27761	**> 0.05**
T. Bilirubinmg/dl	1.3122 ± 0.92178	1.1814± 1.25439	**> 0.05**
Albumingm/dl	3.3407± 0.85766	3.6962± 0.87879	**> 0.05**
Creatinine	0.9378 ± 0.19995	0.8621 ± 0.18208	**> 0.05**
Cholesterol	160.7778 ± 18.58108	255.0345 ± 33.56921	**< 0.01**
Triglycerides	124.2593 ± 20.04532	91.6207± 12.81019	**< 0.01**
LDL	92.4444± 13.24135	175.034± 21.39006	**< 0.01**
HDL	37.2593 ± 6.95918	34.5172 ± 2.97154	**> 0.05**
HCV base line	629126.92± 870493.04	1000669.28±1858898.3	**> 0.05**

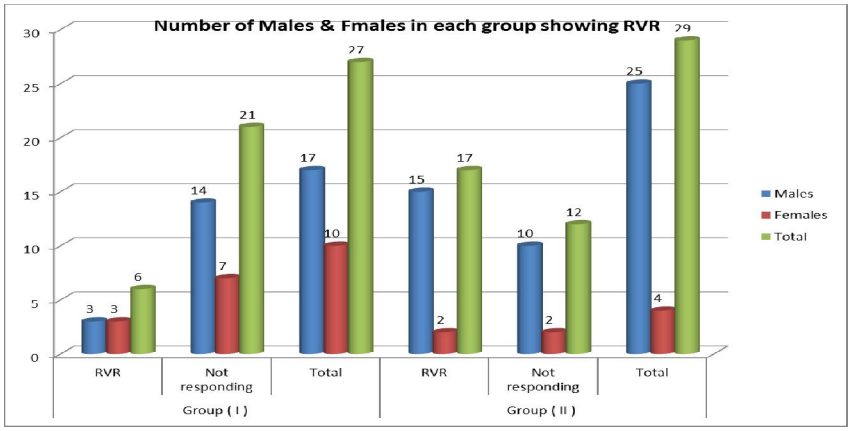

Figure (1): Number of males and females in each group that show RVR

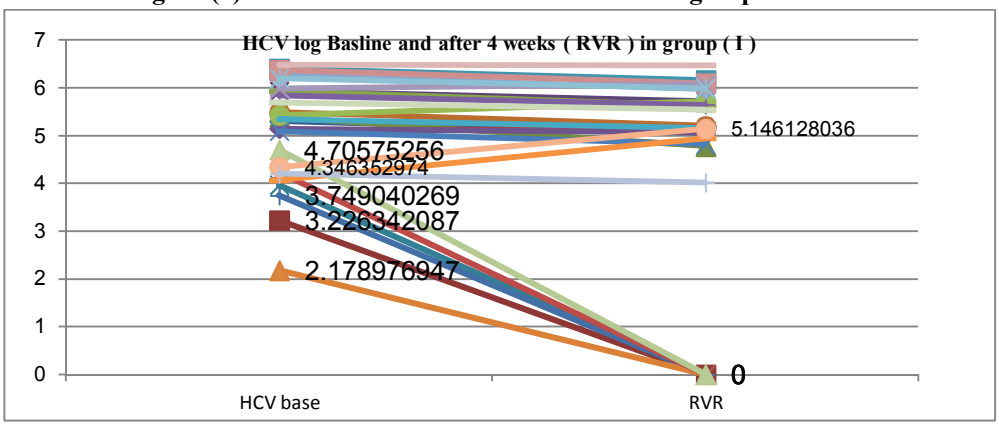

Figure (2): HCV log at baseline and after 4 weeks of treatment in group I.

The chart represents the RVR in group (I) showing that there are only 7 of 27 cases with complete RVR reaching 0 after 4 weeks with a percentage of 22.22 % .The least of them decreased with log 2.17, the highest decreased with log 4.7 . This group have a mean cholesterol of 160.78± 18.58 mg/dl and a mean LDL 92.44 ± 13.24 mg/dl.

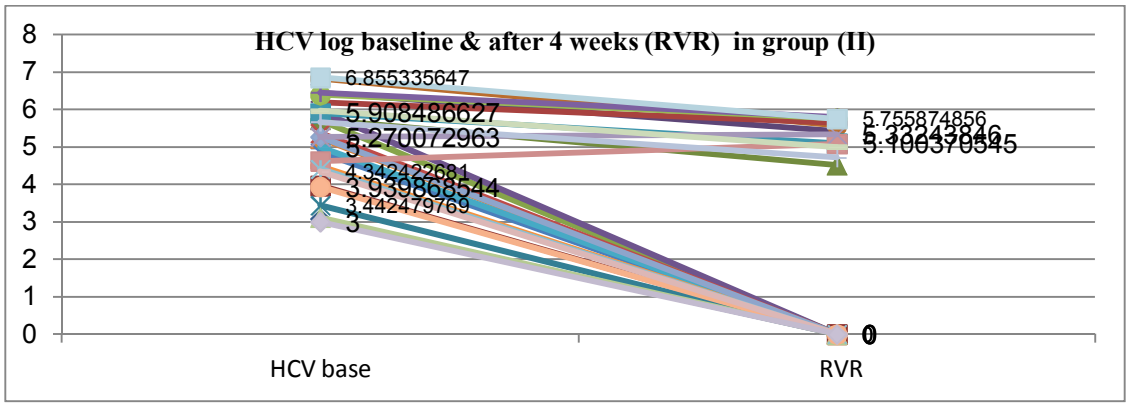

Figure (3): HCV log at baseline and after 4 weeks of treatment in group II.

The chart represents the RVR in group (II) showing that there are 17 of 29 cases with complete RVR reaching 0 after 4 weeks with percentage of 58.6 %. The least of them decreased with log 3, the highest decreased with log 5.9. This group has mean cholesterol of 255.03 ±33.56 mg/dl and a mean LDL 175.035 ± 21.39 mg/dl.

4.Discussion

A substantial proportion of patients infected with HCV still do not respond to peg-IFN/ribavirin therapy, therefore predictive factors that identify potential non responders are needed to limit drug exposure in patients unlikely to benefit from treatment and to save healthcare resources. Patients who become HCV-RNA negative after 4 weeks have the best chance of achieving an SVR (5). The rapidity of viral elimination may be a useful guide to tailoring how long treatment should be continued in patients with an RVR or EVR and outcome of therapy (6).

Host predictive factors have a low negative predictive valuein contrast; viral predictive factors have a high precision in predicting outcome of therapy. the fact that the direct relationship between LDL and SVR that may partially be explained bycompetition for LDL receptor sites preventing viralentry into hepatocytes, increasing exposure of HCV tothe host immune response in the serum(7) *explains the findings of our study where* the higher the level of LDL and cholesterol prior to treatment, the more significant was the RVR to treatment. Also other studies *concluded* that an LDL level > 86mg/dL was an independent predictor in a multivariate logistic regression analysis of EVR and SVR in patients treated with PEG-IFN and RBV for 48 weeks (8), but the fact that HCV needs lipid particles to thrive, replicate and be more infectious (9) could be contradictory to our results,that high levels of pretreatment LDL are associated with RVR.

In this study no statistically significant association reported between HDL or triglycerides with RVR , which doesn't go with what was reported in other studies that high concentrations of triglycerides at the time of acute infection compete with HCV for binding to the hepatocyte receptors, resulting in lower hepatocyte entry andeasier infection clearance among those with high triglyceride levels(10,11).

The hypothesis concerning better RVR with high LDL and cholesterol would perhaps argue against the advantage of statin use in the treatment of hepatitis C. An earlier pilot study(12)suggested that improved SVRrates might be obtained with the use of statins. Statins function by inhibiting the rate-limiting enzyme in hepatocyte cholesterol synthesis, 3-hydroxy-3-methylglutarylcoenzyme A reductase. Intuitively, one might suspect that inhibiting this enzyme would result in more LDL receptors appearing on the cell membrane and thus potentially increase cell infectivity. In fact, a pilotstudy in patients coinfected with human immunodeficiency virus and HCV did show an increase in HCVRNA levels after 4 weeks of fluvastatin (13).

Recommendation: Larger prospective studies are needed to support and confirm our results in genotype 4 patients, especially regarding correlation between HDL and Triglycerides and RVR.

Conclusion:

Together with other factors, baseline lipid profile may help in selecting patients prior to initiation of treatment. This will help a lot in cutting costs and in prioritization of patients.

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