Comparison between clinical and biochemical versus interleukin 28B as a predictive factor of virological response to direct antiviral drugs without interferone in treatment of hepatitis C virus patients

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Abstract
Introduction: for SNP, the CC is associated with a higher SVR after DAAs/RBV therapy while, the genotype TT is a risk factor for non-response.
Aim of the work: this study aimed to assess the value of SNP (rs8099917) as a predictor of SVR.
Methodology: this study was a retrospective controlled study and was performed on a total number of 150 patients who were treated by DAAs/RBV for 12 weeks and SNP was done for all the patients.
Results: CC genotype was more prevalent in SVR group than CT and TT genotypes.
Conclusion: determination of SNP before starting antiviral therapy may serve as a good response predictor.

Keywords: HCV-direct acting antiviral drugs, interleukin 28b SNP.
treatment for HCV. They were treated with DAAs plus ribavirin. Duration of treatment was 3 months; PCR was done after 3 months from discontinuation of treatment. The study was approved by the Ethics Board of Al-Azhar University.

Patients Selection:
1- Patients were screened for their eligibility to participate in the study.
2- Eligible patients signed an informed consent.
3- Medical history and possible routes of acquiring HCV infection were taken, as blood transfusion, surgeries, dental care, needle pricks and tattoos.
4- They had through clinical examination and ultrasonography for detection of any signs of decompensation as (jaundice, shrunken liver, hepatic focal lesion and ascites) before treatment.

Patients Inclusion criteria:
1- Chronically infected HCV patients aged 18 to 75 years old.
2- Serological and virological diagnosis of chronic HCV.
3- Detectable HCV RNA by polymerase chain reaction.
4- Quantitative HCV PCR will be done before treatment and after the end of treatment qualitative HCV PCR at 24th weeks.

Patients exclusion criteria:
1- Decompensated liver disease.
2- Hemoglobin <9 g/dL for men and women, white blood cell count of <3,000/mm3, neutrophil count of <1500/mm3, or platelet count of < 50,000/mm3.
3- Patients with hepatitis B surface antigen (HBsAg) sero positivity or infected with the human immunodeficiency virus (HIV).
4- Active schistosomiasis.
5- Serum creatinine above upper limit of normal was excluded.
6- Poorly controlled diabetes mellitus, hypertension, or psychiatric diseases.
7- Thyroid stimulating hormone (TSH) out of normal range (0.5-5 million units/l).

Specimen collection:
Morning blood samples were collected; 6 ml venous samples were withdrawn and divided into 2 tubes under aseptic conditions from patients and after obtaining their written consent as follows:
- Three milliliters (3ml) blood were left for 10 minutes to clot and then centrifuged at 2000 Xg for 5 minutes. The serum was then separated for determination of all serological tests as well as HCV-RNA Quantitation.
- Three milliliters (3ml) blood on EDTA using a sterile tube, the EDTA samples were stored at -80°C to be used for molecular biology techniques.

Methods:
Laboratory Tests:
I. Routine tests:
1. Complete blood picture.
2. Liver biochemical profile: Serum bilirubin (total and direct), transaminases (ALT and AST), alkaline phosphatase, GGT, total protein, serum albumin and Prothrombin time and concentration.

II. Serological tests for chronic hepatitis markers:
a- Anti-HCV EIA: the third generation Abbott HCV EIA 3.o was used (Abbott Laboratories, Ludwigshafen, Germany).
b- HBsAg EIA: According to Abbott Monoclonal EIA (Abbott Laboratories, Ludwigshafen, Germany)
c- Anti-HBc EIA: the Abbott CoRZYMME commercial assay for qualitative detection of antibodies to HBV core protein (IgG and IgM) was used (Abbott Laboratory, Ludwigshafen, Germany and Abbott Park, II).

III. HCV RNA using real time quantitative PCR Technique:
It was done for all patients to detect the viral load. Pretreatment and PCR was done after 3 months of discontinuation of treatment.

IV. Analysis of Interleukin 28B polymorphism by Real time PCR technique using TaqMan SNP genotyping assay:
Extraction of genomic DNA from sterile EDTA anti-coagulated blood samples was done using QIAamp DNA blood Mini kit (Qiagen, Hilden, Germany) by silica-gel spin columns. Real-time PCR allelic discrimination was designed using Taq-Man SNP Genotyping Assays (Applied Biosystems) and performed on Step one™ Real Time PCR System (Applied Biosystems, Foster City, CA) by using the fluorogenic 5´nuclease with TaqMan minor groove binder (MGB) probes to define interleukin 28B gene SNP (rs809997). The final volume of each reaction was 25ul, consisting of 12.5 uTaqMan Universal PCR Master Mix (2X) which contained AmpliTaq-Gold DNA polymerase, 1.25ul assay mix (2oX) contained primers and probes, 5ul genomic DNA, and 6.25ul nuclease free water. Negative control (no DNA template) was run to ensure that there was no amplification of contaminating DNA. The amplification reactions were carried out with initial hold step at 95 °C for 10 min for activation of AmpliTaq-Gold DNA polymerase followed by 40 cycles of three-step PCR: denaturation at 92 °C for 15 sec, annealing at 60 °C for 30 sec and extension at 60 °C for 30 sec. The fluorescence signal increases when the probe with the exact sequence match binds to the single stranded template DNA and is digested by the 5´nuclease activity of AmpliTaq-Gold DNA polymerase. Digestion of the probe releases the fluorescent reporter dye (either FAM or VIC) from the quencher dye.

**Statistical methods:**
Data were statistically described in terms of mean ± standard deviation (± SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student t test for independent samples. For comparing categorical data, Chi square ($\chi^2$) test was performed. Exact test was used instead when the expected frequency is less than 5. p values less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

**Results**
A total of 150 Egyptian patients were included in this study. All patients were infected with HCV. All of them was treated with DAAs (Sofusbuvir and Daclatsuvir) plus ribavirin. The 150 included patients had median age of 44 years ranging from 20 years to 65 years old. 22.3% (33 patients) of them were female and 77.7% (117 patients) were male.

### Table 1: classification of the studied patients according to their sex

<table>
<thead>
<tr>
<th>Sex</th>
<th>Frequency (n=604)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>117</td>
<td>77.7</td>
</tr>
<tr>
<td>Female</td>
<td>33</td>
<td>22.3</td>
</tr>
</tbody>
</table>

### Table 2: baseline demographic, biochemical and virological characteristics of all studied patients

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAI score</td>
<td>6.6 ± 2.9</td>
<td>4 - 8</td>
</tr>
<tr>
<td>Age</td>
<td>42.3 ± 10.1</td>
<td>35 - 50</td>
</tr>
<tr>
<td>BMI</td>
<td>27.5 ± 4.7</td>
<td>24.2 - 30.4</td>
</tr>
<tr>
<td>AST</td>
<td>45.7 ± 2.7</td>
<td>24 - 57.8</td>
</tr>
<tr>
<td>ALT</td>
<td>47.4 ± 6.9</td>
<td>22 - 60.8</td>
</tr>
<tr>
<td>T. Bilirubin</td>
<td>0.8 ± 0.1</td>
<td>0.6 - 0.9</td>
</tr>
<tr>
<td>S. albumin</td>
<td>4.1 ± 0.5</td>
<td>3.8 - 4.4</td>
</tr>
<tr>
<td>AlkPhosp</td>
<td>134.6 ± 9.3</td>
<td>95 - 167.8</td>
</tr>
<tr>
<td>PC</td>
<td>87.5 ± 9.3</td>
<td>91 - 95</td>
</tr>
<tr>
<td>PT</td>
<td>12.8 ± 0.7</td>
<td>12.3 - 13</td>
</tr>
<tr>
<td>INR</td>
<td>1.10 ± 0.09</td>
<td>1.01 - 1.13</td>
</tr>
<tr>
<td>TSH</td>
<td>1.61 ± 0.09</td>
<td>0.91 - 2.10</td>
</tr>
<tr>
<td>Hb</td>
<td>13.85 ± 1.54</td>
<td>12.80 - 14.90</td>
</tr>
<tr>
<td>TLC</td>
<td>6.28 ± 1.39</td>
<td>4.80 - 7.30</td>
</tr>
<tr>
<td>Platelet</td>
<td>204.26 ± 4.27</td>
<td>158.00 - 240.75</td>
</tr>
<tr>
<td>PCR before</td>
<td>1,237,569.5 ± 5,160,643.3</td>
<td>62,600.0 - 811,000.0</td>
</tr>
</tbody>
</table>

SD= standard deviation, IQR = interquartile range (25th percentile – 75th percentile)
Table 3: baseline demographic, biochemical, virological data of patients according to their response to treatment

<table>
<thead>
<tr>
<th></th>
<th>Responders</th>
<th>N0n-responders</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>39.9 ± 10.3</td>
<td>45.6 ± 8.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>26.3 ± 4.2</td>
<td>29.0 ± 4.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAI score</td>
<td>6.3 ± 2.7</td>
<td>7.0 ± 3.1</td>
<td>0.002</td>
</tr>
<tr>
<td>AST</td>
<td>34.3 ± 2.6</td>
<td>60.7 ± 7.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ALT</td>
<td>33.8 ± 4.5</td>
<td>65.3 ± 2.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T. Bilirubin</td>
<td>0.80 ± 0.03</td>
<td>0.77 ± 0.02</td>
<td>0.194</td>
</tr>
<tr>
<td>S. albumin</td>
<td>4.00 ± 0.48</td>
<td>4.16 ± 0.40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alk. Phosp</td>
<td>149.3 ± 2.7</td>
<td>115.3 ± 2.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PC</td>
<td>87.97 ± 8.76</td>
<td>86.94 ± 10.02</td>
<td>0.188</td>
</tr>
<tr>
<td>PT</td>
<td>12.77 ± 0.73</td>
<td>12.72 ± 0.59</td>
<td>0.375</td>
</tr>
<tr>
<td>INR</td>
<td>1.10 ± 0.09</td>
<td>1.09 ± 0.09</td>
<td>0.469</td>
</tr>
<tr>
<td>TSH</td>
<td>1.62 ± 0.09</td>
<td>1.60 ± 0.09</td>
<td>0.727</td>
</tr>
<tr>
<td>Hb</td>
<td>13.99 ± 1.54</td>
<td>13.66 ± 1.52</td>
<td>0.01</td>
</tr>
<tr>
<td>TLC</td>
<td>6.51 ± 1.78</td>
<td>5.97 ± 1.70</td>
<td>0.005</td>
</tr>
<tr>
<td>Platelet</td>
<td>199.5 ± 64.2</td>
<td>210.6 ± 63.9</td>
<td>0.035</td>
</tr>
<tr>
<td>PCR before</td>
<td>211,000</td>
<td>324,228</td>
<td>0.019</td>
</tr>
</tbody>
</table>

Table 4: classification of the studied patients according to their sex and its relation to response to treatment

<table>
<thead>
<tr>
<th></th>
<th>Responders (n=96)</th>
<th>N0n-responders (n=54)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>80</td>
<td>37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>16</td>
<td>17</td>
<td></td>
</tr>
</tbody>
</table>

Table 4 showed that 33 patients (22.3%) from all studied patients were females, while 117 patients (77.7%) were males. Only 16 female patients were responder (16.7% from responsive patients), while 17 female patients didn't achieve response (31.5% from non-responsive patients), while 80 male patients were responder (83.3% from responsive patients), while 37 male patients didn't achieve response (68.5% from non-responsive patients). This means that male sex was associated with higher response than female sex with significant p value (p< 0.001).

Table 5: comparison between naive patients and experience patients who take INF before

<table>
<thead>
<tr>
<th>Groups</th>
<th>Responders (n=96)</th>
<th>Non-responders (n=54)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naïve</td>
<td>90</td>
<td>30</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Experience</td>
<td>6</td>
<td>24</td>
<td></td>
</tr>
</tbody>
</table>

It means that naïve patients were associated with higher response than experience patients.
• P value was significant

Table 6: relation between responses of chronic hepatitis C patients treated with DDAs and bilirubin

<table>
<thead>
<tr>
<th>Groups (bilirubin)</th>
<th>total</th>
<th>Responders</th>
<th>Non-responders</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5 MG/DL&lt;</td>
<td>85</td>
<td>72</td>
<td>13</td>
<td>0.02</td>
</tr>
<tr>
<td>1.5MG/DL&gt;</td>
<td>65</td>
<td>24</td>
<td>41</td>
<td>0.02</td>
</tr>
</tbody>
</table>

• It was found that there was higher response with patients have normal bilirubin than patients with high bilirubin.
• P value was significant
Comparison between clinical and biochemical versus interleukin 28B as a predictive factor…

Table 7: relation between responses of chronic hepatitis C patients treated with DDAs and albumin

<table>
<thead>
<tr>
<th>Groups (albumin)</th>
<th>total</th>
<th>Responders</th>
<th>Non-responders</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.6mg/dl&gt;</td>
<td>90</td>
<td>82</td>
<td>91.1%</td>
<td>8.9%</td>
</tr>
<tr>
<td>2.6Mg/dl&lt;</td>
<td>60</td>
<td>14</td>
<td>23.3%</td>
<td>46</td>
</tr>
</tbody>
</table>

- It was found that there was high response with high concentration of albumin.
- P value was significant

Table 8: relation between response of chronic hepatitis C patients treated with DDAs and anemia

<table>
<thead>
<tr>
<th>Groups (HB %)</th>
<th>Total</th>
<th>Responders</th>
<th>Non-responders</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 mg/dl &gt;</td>
<td>120</td>
<td>91</td>
<td>75.8%</td>
<td>29</td>
</tr>
<tr>
<td>12Mg/dl–9.4mg/dl</td>
<td>30</td>
<td>5</td>
<td>16.7%</td>
<td>25</td>
</tr>
</tbody>
</table>

- It was found that there was low response with patients with anemia.
- P value was significant

Table 9: relation between responses of chronic hepatitis C patients treated with DDAs and PC

<table>
<thead>
<tr>
<th>Groups(PC)</th>
<th>total</th>
<th>Responders</th>
<th>Non-responders</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>65%&gt;</td>
<td>99</td>
<td>79</td>
<td>79.8%</td>
<td>20</td>
</tr>
<tr>
<td>%65&lt;</td>
<td>51</td>
<td>17</td>
<td>33.3%</td>
<td>34</td>
</tr>
</tbody>
</table>

- It was found that patients with PC greater than 65% have higher response than patients with PC lower than 65%.
- P value was significant

Table 10: relation between response of chronic hepatitis C patients treated with DDAs and count of platelets

<table>
<thead>
<tr>
<th>Groups (platelets)</th>
<th>total</th>
<th>Responders</th>
<th>Non-responders</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50.000&gt;</td>
<td>110</td>
<td>80</td>
<td>72.7%</td>
<td>30</td>
</tr>
<tr>
<td>&lt;50.000&gt;</td>
<td>40</td>
<td>16</td>
<td>40%</td>
<td>24</td>
</tr>
</tbody>
</table>

- It was found that patients with high count of platelets have higher response than patients with low count of platelets.
- P value was significant

Table 11: the relationship between bodyweight and response for treatment

<table>
<thead>
<tr>
<th>Groups</th>
<th>total</th>
<th>Responders</th>
<th>Non-responders</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal weight</td>
<td>110</td>
<td>90</td>
<td>81.8%</td>
<td>20</td>
</tr>
<tr>
<td>Overweight</td>
<td>10</td>
<td>4</td>
<td>40%</td>
<td>6</td>
</tr>
<tr>
<td>Obese</td>
<td>30</td>
<td>2</td>
<td>6.7%</td>
<td>28</td>
</tr>
</tbody>
</table>

- It was found that high response for treatment among normal weight (81.8%) , decrease among overweight (40%) and decrease more among obese (6.7%) .
- P value was significant

Table 12: relation between responses of chronic hepatitis C patients treated with DDAs and alpha FP

<table>
<thead>
<tr>
<th>Groups (alpha FP)</th>
<th>total</th>
<th>Responders</th>
<th>Non-responders</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50&lt;</td>
<td>132</td>
<td>82</td>
<td>62.1%</td>
<td>50</td>
</tr>
<tr>
<td>&gt;50</td>
<td>18</td>
<td>14</td>
<td>77.8%</td>
<td>4</td>
</tr>
</tbody>
</table>

- The ratio was insignificant
- P value was insignificant
Table 13: patients who were developed hepatocellular carcinoma

<table>
<thead>
<tr>
<th>Groups</th>
<th>Cirrhotic (45)</th>
<th>Non-cirrhotic (105)</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Responder</td>
<td>Non-responder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal hepatocellular</td>
<td>10</td>
<td>35</td>
<td>150</td>
<td>0.03</td>
</tr>
<tr>
<td>Hepatocellular cancer</td>
<td>4</td>
<td>1</td>
<td>5</td>
<td>0.03</td>
</tr>
</tbody>
</table>

It was found that hepatocellular carcinoma developed with cirrhotic responder patients. So, Its proved that carcinoma occurred due to presence of cirrhosis not due to presence of the virus.

It was found that hepatocellular carcinoma developed with cirrhotic responder patients. So, Its proved that carcinoma occurred due to presence of cirrhosis not due to presence of the virus.

Le The cirrhosis was trigger factor for developing of carcinoma.

- **P value was significant**

**Discussion**

In 2009 and 2010, four independent Genome-wide association studies on response to treatment of chronic hepatitis C with DAAs and ribavirin were published (4). In each of these GWAS, only SNPs around the IL28B gene reached genome-wide significance for the association with treatment outcome. All identified IL28B SNPs correlate with each other and can, therefore, be clustered in haplotypes.

Our study was conducted on 150 Egyptian patients who were infected with HCV. Patients were selected from HCV patients that attend National Hepatology and Tropical Medicine Research Institute for receiving treatment for HCV. They were treated with DAAs plus ribavirin. Duration of treatment was adjusted according to their response which was determined using quantitative PCR for HCV at the 12th and 24th weeks from treatment. Genotyping of rs8099917 polymorphisms near the IL28B gene was performed for all patients.

In the present study, the impact of rs8099917 genetic polymorphisms near the IL28B gene on response of chronic HCV patients to standard treatment was investigated by analyzing the association between genetic polymorphisms and sustained virological response (SVR) after administering DAAs and ribavirin. We studied also multiple factors that were associated with SVR to combination therapy with DAAs and ribavirin, including age, sex, body weight, Alpha fetoprotein. We demonstrated that carriers with the TT genotype of rs8099917, located 8 kb upstream of IL-28B, are less likely to achieve SVR with HCV infected Egyptian patients after standard treatment. We found that the rate of SVR was significantly higher (32.7% vs. 11.3% with p = 0.001) in patients with the IL28B major allele (CC, wild type) compared to those with TT type.

Our study reconfirmed the previously reported findings in various populations around the world in a large cohort of HCV mono-infected patients with chronic hepatitis C genotype (GT) 1 (6), but our observation was to Egyptian patients who are mainly infected with HCV GT4. Stättermayer et al. (7) studied 102 Egyptian patients infected with HCV (GT 4) and they found that the major allele CC was associated with significant SVR (p = 0.0036), also they observed that low base line viral load (≤ 800,000 IU/ml) had significant effects on the outcome SVR (p = 0.0085). Furthermore, findings from the initial genome-wide association study suggested that IL-28B may play a role in determining whether acute HCV infection leads to spontaneous clearance or chronic infection.

Ge et al. (6) first noted that the presence of the C allele rs12979860 was lower in patients with chronic genotype 1 HCV infection compared to matched healthy controls, suggesting that the C allele may be associated with spontaneous resolution. The same finding had been noted in additional studies, including a large study of over 1,000 individuals in which the prevalence of the rs12979860 genotype was investigated in patients who achieved spontaneous resolution and those who developed chronic HCV infection (8). These studies found that the C allele occurred more frequently in patients who spontaneously cleared HCV. Individuals with the C/C genotype had a 3-fold greater likelihood of spontaneous HCV clearance compared to patients who had the T/C or T/T genotype. Additionally, the strong association between C/C genotype and spontaneous clearance was present in both whites and blacks. By studying other factors that may have relation to response to treatment, our study found that the comparison between the age and the response to treatment had significant statistically difference (p <0.001).

Also, Stättermayer et al. (7) found that age of patients had significant effect on the outcome SVR to standard combination
treatment for which younger patients had better SVR (p = 0.003), however there was no significant correlation between sex and SVR. Also, et al. (9) found that young HCV infected patients had higher SVR to standard combination treatment than older patients (p = 0.0003), but there was no difference in response to treatment between males and females. But, in our study male sex was associated with high response than female sex with significant p value (p<0.001), also young age of the patients is associated with high response than the old age of the patients . (p value is 0.−1), so p value is significant. We assessed the response of the patients in relation to degree of cirrhosis by sonar and lab, it was clear that patients with no cirrhosis by sonar and lab had significant higher rates of SVR than patients with advanced cirrhosis.( p < 0.0001). And by assessing the response of the chronic hepatitis C patients treated with DAAs in relation to α fetoprotein <5o showed that 82 patients (62.1% patients) had achieved SVR while 50 of patients (37.9% patients) were non-responders. But with α fetoprotein > 5o, it was found that 14 patients (77.8% patients) had achieved SVR and 4 patients (22.2% patients) were non-responders. It was clear that the relation between serum α fetoprotein and response to treatment was statistically non-significant with p value (p <0.6). In our study, the relation between response of HCV patients treated with DAAs and obesity was statistically significant because there was high response for treatment among normal weight (81.8%) while decrease among overweight (40%) and decrease more in obese patients (2%) with P value is significant (<0.03). Our findings showed that the IL28B genotype SNP rs8099917 is a useful baseline predictor of virological response which should be used for selecting the treatment for patients with DAAs and RBV or to wait for more effective another therapy and another regimen of DAAs. Also, in our study patients with low viremia were associated with high response for treatment by DAAs 60 patients (62.5%) vs high viremia was associated with low response 36(37.5%). It was found that the response in naïve patients was associated with higher response 9o(75%) than experience patients 6(20%). It was also found that there was higher response with patients with normal bilirubin <1.5 mg/dl 72(84.1%) than patients with high bilirubin 24(36.9%). Also, in our study patients with concentration of albumin higher than 2.6 gm/dl were associated with high response for treatment by DAAs 82 patients (91.1%) versus patients with low concentration of albumin lower than 2.6 gm/dl is associated with low response 14(23.3%). Also, this study showed low response with patients with anemia 5(16.7%) versus high response with normal haemoglobin 91(75.8%). High response for treatment with prothrombin concentration above 65% 79(79.8%) versus low response with PC <65% 17(33.3%) The thrombocytopenia (<50000) was associated with low response 16(40%) compared with high response for treatment in patients with platelet count (>50000) 80 (72.7%). We can say that the patients with cirrhotic liver i.e disturbed synthetic functions, albumin, bilirubin and prothrombin concentration were associated with low response for treatment by new DAAs and RBV. Also, patients with cirrhotic liver by sonar were associated with lower response for treatment by new DAAs and RBV than patients with normal liver. In our study, TSH and Alpha FP count were insignificant for response by DAAs and RBV treatment. Decisions of treatment may be based on the possibility of a response against a potential risk of adverse events and the cost of the therapy or disease progression while waiting for future therapy (10).

Conclusion

IL-28B polymorphism single nucleotide polymorphism (SNP) was a strong pretreatment predictor of response to DAAs and ribavirin in Egyptian patients chronically infected with HCV genotype 4. This study confirmed the strong impact of IL-28B (SNP) on SVR.

Recommendations

1. Before the start of the treatment by DAAs we must make IL B-28 for all patients to determine the genotype CC, CT or TT.
2. We chose sofosbuvir (Sovaldi) and daclatasvir (Daclanza) to treat patients with CC and CT genotype.
3. If the patient has TT genotype we must give another regimen as Simeprevir (olyso) and sofosbuvir (Sovaldi) or ombitasvir, paritaprevir and ritonavir (Qurevo).
4. Future studies are needed to explore whether the combination of baseline IL28B genotype and response-guided
approach further improves the optimization of treatment duration.

References


