Evaluation of IL-10 and IL-12B Gene Polymorphisms on the Response to the Standard of Care Therapy in Chronic Hepatitis C Patients: An Egyptian Cohort Study

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Authors’ contributions

This work was carried out in collaboration between all authors. Design of the study and writing the protocol: Authors EM, HS. Patients’ enrollment and clinical evaluation: Authors DO, TE, AR. Medical Biochemical study, and statistics: Author HF. First drafting of the manuscript: Authors RM, ZZ. Revision of the manuscript: Author NZ. Final approval of the manuscript: Authors EM, HF.

ABSTRACT

Background: Interleukin-10 (IL-10) and IL-12B single nucleotide polymorphisms (SNPs) are confirmed to influence the natural history of hepatitis C virus (HCV) infection, and the response to treatment. This work aimed at evaluating the impact of SNPs in IL-10 gene at positions _1082, _819, and _592 and IL-12B gene on the response to the standard of care (SOC) treatment in Egyptian patients with chronic HCV.

Methods: Eighty seven patients with chronic HCV treated by SOC therapy and 20 healthy controls were tested for SNPs in IL-10 at _1082 G/A, _819 C/T and _592 C/A and in IL-12B (30-UTR 1188-A/C) by polymerase chain reaction (PCR). Patients were divided according to their virologic response into 2 groups; group I=patients who achieved sustained virologic response (SVR) and group Π = non responder (NR) patients.

Results: SNPs of IL-10 at _1082 G/A and _819 C/T showed that; GA and TT genotypes were significantly related to SVR (P=0.001 and 0.007 respectively). IL-12 gene

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polymorphisms showed that; CC genotype was significantly related to SVR group ($P=0.01$) while AA genotype was significantly related to NR ($P=0.01$).

**Conclusions:** Studying SNPs of IL-10_1082 G/A, IL-10_819 C/T and IL-12B (30-UTR 1188-C/A) proved GA, TT and CC genotypes, respectively, to be good predictors for SVR. Conversely, SNPs of IL-12 C/A proved AA genotype to be good predictor for NR.

**Keywords:** Hepatitis C virus (HCV); sustained virologic response (SVR); non responder (NR); standard of care (SOC); single nucleotide polymorphism (SNP).

### 1. INTRODUCTION

Hepatitis C virus (HCV) is a global disease with significant impact. Chronic infection is estimated around 170 million individuals, and annual mortality rate more than 350 000 patients with evident geographic differences [1]. The highest prevalence of HCV infection (15%) is reported in Egypt[1], mostly (90%) by genotype 4 [2].

Combined therapy of pegylated interferon alfa (PEG-IFNα) and ribavirin (RBV) are the base for HCV treatment, therefore defined as standard of care (SOC) [3]. Unfortunately, many HCV patients experience significant adverse effects and fail to respond to SOC treatment, therefore, identifying predictors of response is beneficial for both patients clinically and economically [4].

Interleukin (IL)-12 and IL-10, the immunoregulatory cytokines, have an antagonistic effect of the T-helper (Th) 1/Th2 cytokine balance and link between innate and adaptive immune responses [5]. Moreover, HCV-specific Th1 response with its strong cytokine release is pivotal for the viral recovery, whether spontaneous or treatment-induced [6–9]. Excess IL-10 inhibits Th1 protective immune responses which facilitate viral eradication, therefore, favouring viral persistence [10].

Single nucleotide polymorphisms (SNPs) are inherited single-base alteration in a known genetic location occurring in at least 1% of the population, around one per 1000bp in the human genome. Most of variations in the human genome are attributed to SNPs[11].

IL-10 SNPs affect the progression of HCV–induced hepatic affection. IL-10 level is related to transaminases as well as histopathological scores determining the severity of hepatic disease [12]. The IL-10 SNP affect the progression of HCV-induced hepatic affection and particularly at position _1082 G/A (rs1800896) affect IL-10 production [13]. Similarly, IL-12 SNP affects IL-12 production [14–16].

**1.1 Aim of the Work**

The impact of SNPs in IL-10 gene at promoter positions_1082, 819, and _592, and in IL-12B gene on the response of Egyptian patients with chronic HCV to the standard of care (SOC) treatment.

### 2. PATIENTS AND METHODS

This prospective study included 87 patients with chronic HCV and 20 healthy subjects.
Inclusion criteria:

- Adult (≥ 18 years old),
- Naïve chronic HCV infection diagnosed by seropositivity to its 3rd generation antibody testing and nucleic acid (RNA) detection.

Exclusion criteria:

- Previous SOC therapy,
- Other aetiology of liver disease e.g other viral, metabolic, cholestatic, immune.
- Decompensated hepatic cirrhosis
- Hepatocellular carcinoma (HCC).

Control subjects: Healthy subjects clinically and negative for markers of HCV and HBV.

All enrolled patients were subjected to: a) Detailed history, b) Thorough clinical examination, c) Basic laboratory tests: [Complete blood count (CBC), liver biochemical profile (LBP), renal function (urea and creatinine), blood glucose], d) Specific HCV testing [i.) Third generation enzyme-linked immunosorbent assay (ELISA) and ii.) HCV RNA by reverse transcription–polymerase chain reaction (RT-PCR), iii). Viral load was measured by quantitative serum HCV RNA b DNA assay (Bayer, USA) according to the manufacturer’s instructions. The PCR product was digested by the restriction enzymes HhaI (R6441), PvuII (R6331) and Taq-1 (R6151) supplied by: Promega (Southampton, UK) at 65ºC for 120min using the specific enzyme buffer. The amplified products were analyzed on 2% agarose gel. The minimum quantification limit of HCV RNA assay is 60 copies/mL serum, e) Tests done prior to SOC to select candidates: [alpha fetoprotein (AFP), thyroid stimulating hormone (TSH), antinuclear antibody (ANA)], f) Abdominal ultrasound (US), g) Histological examination via US guided liver biopsy, applying METAVIR scoring system [17] to assess grade of hepatitis activity (A) and stage of fibrosis (F), and h) Specific tests for the study: IL-10 and IL-12B (SNPs were detected using DNA extraction from mononuclear cell layer using QIAamp kit supplied by Qiagen (USA, catalogue number 51306). The three biallelic IL-10 SNPs at promoter positions _1082 G/A, _819 C/T, and _592 A/C were detected by PCR using primers as shown in (Table 1), provided that the wild genotypes are GA,TT and AA respectively. CC genotype is the wild form of IL-12B (30 untranslated region UTR 1188-C/A).

Patients received SOC therapy, according to the AASLD guidelines, 2009 [18] in the form of Peg-IFN α 2a (180µg SC once weekly) and RBV (13-15mg/kg) for 48 weeks, at Railway hospital in Cairo, and were followed up for another 24 weeks after cessation of therapy to assess SVR. The patients were then divided into 2 groups according to their virologic response: group I; those who achieved SVR and group II; those who did not i.e NR as defined by Ghany et al. [18].

The study was approved by the institutional ethical committee, and all patients provided an informed consent.

2.1 Statistical Analysis

Patients' data were analyzed using SPSS 17.0 for windows 7. All quantitative variables were expressed by mean and Standard errors mean (SEM) and compared using unpaired t-student test and Mann-Whitney test. Spearman rank order test was used for correlating quantitative variables. Qualitative variables were expressed by numbers (Frequency) and
percent compared between groups using Chi-square test. P value was considered to be significant if <0.05 and highly significant if <0.001.

Table 1. Primers for SNPs at promoter positions _1082 G/A, _819 C/T, and _592 C/A

<table>
<thead>
<tr>
<th>Polymorphism/allele location</th>
<th>Primer</th>
<th>Sequence</th>
<th>Product size (bp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-10_1082</td>
<td>Genetic primer</td>
<td>5-CAGTGCCAACTGAGAATTTGG-3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Primer G(sense)</td>
<td>5-CTACTAAGGCTTCTTGGAG-3</td>
<td>258</td>
</tr>
<tr>
<td></td>
<td>Primer A(sense)</td>
<td>5-ACTACTAAGGCTTCTTGGGAA-3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Genetic primer</td>
<td>5-AGGATGTGTTCCAGGCTCCT-3</td>
<td></td>
</tr>
<tr>
<td>IL-10_819/_592</td>
<td>Primer C (sense)</td>
<td>5-CCCTTGTACAGGTGATGTAAC-3</td>
<td>233</td>
</tr>
<tr>
<td></td>
<td>Primer T (sense)</td>
<td>5-ACCCCTGTACAGGTGATGTAAT-3</td>
<td></td>
</tr>
<tr>
<td>Internal control</td>
<td>Primer 1</td>
<td>5-GCTTCCCAACCATTCETTA-3</td>
<td></td>
</tr>
<tr>
<td>Internal control</td>
<td>Primer 2</td>
<td>5-TCACGGATTCTGTTGTTTTC-3</td>
<td>429</td>
</tr>
</tbody>
</table>

3. RESULTS

This prospective study was conducted on 87 patients with chronic HCV who received SOC therapy at Railway hospital, and 20 healthy control persons. This study was conducted from May 2011 to May 2013.

The selected patients were classified into 2 groups according to their virologic response; group (I): included 48 patients (55.2%) who achieved SVR, and group (II): included 39 patients (44.8%) who were non responders (NR).

3.1 Demographic Features and Baseline Laboratory Results

The demographic features and pre-treatment laboratory results, including histopathological examination, of the studied patients are shown in (Table 2). None of the baseline laboratory parameters, including histopathological examination, recorded a statistically significant relation to any of the studied groups except for bilirubin which was significantly higher in NR than in SVR groups.

3.2 SNPs of IL-10 and IL-12 in HCV Cases and Control Subjects

The distribution of IL-10 and IL-12 SNPs at the genotype and at allele levels in the studied HCV cases and control subjects are shown in (Table 3). GG genotype at IL-10_1082 G/A, and CC and CT genotypes at _819 C/A were significantly related to HCV patients (P =0.001, 0.02 and 0.01 respectively). Conversely TT genotype of the latter position was significantly related to control subjects (P =0.01).

3.3 SNPs of IL-10 and IL-12 in HCV Cases, Responders and Non-responders

The distribution of SNPs of IL-10 and IL-12- at the genotype level (individually and when comparing the wild versus the mutant forms), and at allele level - in groups I and II, is shown in (Table 4), and (Figs. 1-4). SNPs at IL-10_1082 G/A showed that GA, the wild genotype
form, was significantly related to SVR group \( (P=0.001) \). SNPs at IL-10_819 C/T showed that TT, the wild genotype form, was significantly related to SVR \( (P=0.007) \). SNPs at IL-10_592 C/A showed that none of the genotypes showed a statistical significant relation with either group I or group II, however allele study showed that A allele significantly favours SVR \( (P=0.02) \). On the other hand, IL-12B SNPs showed that CC, the wild genotype form, was significantly related to SVR group \( (P=0.01) \), while AA genotype, was significantly related to group II \( (P=0.01) \), which was confirmed by allele study.

### Table 2. Demographic features and pre-treatment laboratory results of the studied patients

<table>
<thead>
<tr>
<th>Demographic features</th>
<th>Group (I) SVR, ( n=48 )</th>
<th>Group (II) NR, ( n=39 )</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (mean±SD)</td>
<td>45.1±8.3</td>
<td>40.7±9.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Gender</td>
<td>Male/female</td>
<td>41/7</td>
<td>32/7</td>
</tr>
</tbody>
</table>

**Laboratory Results:**(mean±SD)

- **CBC**
  - WBC\( (4-11 \times 10^3/mm^3) \): 5.698±1.7
  - Hemoglobin \( (12-16g/dl) \): 113.517±1.5
  - Platelet \( (150-400 \times 10^3/mm^3) \): 213.17±60.5
- **LBP**
  - Albumin \( (3.5-5g/dl) \): 4.09±0.34
  - Bilirubin \( (0.3-1.2mg/dl) \): 0.758±0.171
  - AST \( \leq 40 IU/L \): 42.25±17.99
  - ALT \( \leq 40 IU/L \): 50.75±20.95
  - PC \( (80-100\%) \): 90.14±8.03
- **AFP** \(<10ng/ml\): 6.86±6.76
- **TSH** \( (0.5-4.5 mIU/L) \): 1.49±0.911
- **HCV_RNA** \( (x10^6 copies/ml) \): 1.0864 ±1.4985
- **Histo-pathology** Activity: A1/ A2/ A3 |
  - Fibrosis: F1/ F2/ F3/ F4 |

**CBC:** Complete blood count, **WBC:** White blood count, **LBP:** Liver biochemical profile, **AST:** Aspartate aminotransferase, **ALT:** Alanine aminotransferase, **PC:** Prothrombin concentration, **AFP:** Alpha feto protein, **TSH:** Thyroid stimulating hormone, A: Activity, F: Fibrosis

### Table 3. Distribution of different SNPs of IL-10 and IL-12 in the studied HCV cases and control subjects

<table>
<thead>
<tr>
<th>Studied SNPs</th>
<th>Genotypes</th>
<th>Cases, ( n=87 ) (%)</th>
<th>Controls, ( n=20 ) (%)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IL-10_1082G/A:</strong></td>
<td>AA/GA/GG</td>
<td>8/62/17 (9.2)/(71.3)/(19.5)</td>
<td>1/19/0 (5)/(95)/(0)</td>
<td>0.09/0.08/0.001</td>
</tr>
<tr>
<td></td>
<td>G/A</td>
<td>96/78 (55.2)/(44.8)</td>
<td>19/21 (47.5)/(52.5)</td>
<td>0.12/0.07</td>
</tr>
<tr>
<td><strong>IL-10_819C/T:</strong></td>
<td>CC/CT/TT</td>
<td>16/67/4 (18.4)/(77.01)/(4.5)</td>
<td>0/9/11 (0)/(45)/(55)</td>
<td>0.02/0.01/0.01</td>
</tr>
<tr>
<td></td>
<td>T/C</td>
<td>75/99 (43.1)/(56.9)</td>
<td>31/9 (77.5)/(22.5)</td>
<td>0.047/0.049</td>
</tr>
<tr>
<td><strong>IL-10_592A/C:</strong></td>
<td>AA/AC/CC</td>
<td>28/43/16 (32.2)/(49.4)/(18.4)</td>
<td>10/8/2 (50)/(40)/(10)</td>
<td>0.047/0.06/0.07</td>
</tr>
<tr>
<td></td>
<td>A/C</td>
<td>99/75 (56.9)/(43.1)</td>
<td>28/12 (70)/(30)</td>
<td>0.048/0.078/0.09</td>
</tr>
<tr>
<td><strong>IL-12B C/A:</strong></td>
<td>CC/AC/AA</td>
<td>34/29/24 (39)/(33.3)/(27.6)</td>
<td>10/6/4 (50)/(30)/(20)</td>
<td>0.08/0.09/0.07</td>
</tr>
<tr>
<td></td>
<td>C/A</td>
<td>97/77 (55.7)/(44.2)</td>
<td>26/14 (65)/(35)</td>
<td>0.09/0.06</td>
</tr>
</tbody>
</table>

**SNPs:** Single nucleotide polymorphisms, **IL:** Interleukin
Table 4. SNPs of IL-10 and IL-12 in groups I and II

<table>
<thead>
<tr>
<th>Studied SNPs</th>
<th>Geno-types</th>
<th>Group (I) SVR, n=48(%)</th>
<th>Group (II) NR, n=39(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-10_1082 G/A:</td>
<td>AA/GA/GG</td>
<td>4(8.3)/41(85.4)/3(6.2)</td>
<td>4(10.2)/21(53.8)/14(35.9)</td>
<td>0.09/0.08/0.047</td>
</tr>
<tr>
<td></td>
<td>GA-AA+GG</td>
<td>41(85.5)/7(14.5)</td>
<td>21(53.8)/18(46.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>A/G</td>
<td></td>
<td>49(51)/47(49)</td>
<td>29(37.2)/49(26.8)</td>
<td>0.048/0.03</td>
</tr>
<tr>
<td>IL-10_819 C/T:</td>
<td>CC/CT/TT</td>
<td>11(22.9)/33(79.7)/4(8.3)</td>
<td>5(12.8)/34(87.2)/0(0)</td>
<td>0.07/0.08/0.02</td>
</tr>
<tr>
<td></td>
<td>TT/CT+CC</td>
<td>4(8.3)/44(91.7)</td>
<td>0(0)/39(100)</td>
<td>0.007</td>
</tr>
<tr>
<td>C/T</td>
<td></td>
<td>55(57.3)/41(42.7)</td>
<td>44(56.5)/34(43.5)</td>
<td>0.06/0.07</td>
</tr>
<tr>
<td>IL-10_592 A/C:</td>
<td>AA/AC/CC</td>
<td>17(35.4)/26(54.2)/5(10.4)</td>
<td>11(28.2)/17(43.6)/11(28.2)</td>
<td>0.09/0.08/0.10</td>
</tr>
<tr>
<td></td>
<td>AA/AC+CC</td>
<td>17(35.4)/31(64.6)</td>
<td>11(28.2)/28(71.2)</td>
<td>0.47</td>
</tr>
<tr>
<td>A/C</td>
<td></td>
<td>60(62.5)/36(37.5)</td>
<td>39(50)/39(50)</td>
<td>0.02/0.02</td>
</tr>
<tr>
<td>IL-12B C/A:</td>
<td>CC/CA/AA</td>
<td>23(47.9)/17(35.4)/8(16.6)</td>
<td>11(28.2)/12(30.7)/16(41)</td>
<td>0.01/0.07/0.01</td>
</tr>
<tr>
<td></td>
<td>CC/AA+CA</td>
<td>23(48)/25(52)</td>
<td>11(28.2)/28(71.8)</td>
<td>0.1</td>
</tr>
<tr>
<td>C/A</td>
<td></td>
<td>63(65.6)/33(34.4)</td>
<td>34(43.6)/44(56.4)</td>
<td>0.01/0.01</td>
</tr>
</tbody>
</table>

SNP: Single nucleotide polymorphism, IL: Interleukin, SVR: Sustained virologic response, NR: Non responder
Fig. 1. SNPs of IL-10_1082 G/A in the studied patients at genotype level

Fig. 2. SNPs of IL-10_819 C/T in the studied patients at the genotype level
Fig. 3. SNPs of IL-10_592 A/C in the studied patients at the genotype level

Fig. 4. SNPs of IL-12B C/A in the studied patients at the genotype level
4. DISCUSSION

IL-10 plays a major role in HCV pathogenesis [19]. IL-10 SNPs influence HCV infection; clinical and histopathological outcome [20,21], and virologic response as well [22].

Interleukin 12 is an important immunoregulatory cytokine and its expression during infection regulates innate responses and determines the type of adaptive immune responses [23].

In this study, SVR was achieved in 48 patients; 55.2%. This incidence is higher than that reported by Poynard et al. 48% [24], and lower than Thakeb et al. 70% [25]. It is close to figures reported by other previous studies: 50% [26] and 60% [27] and 63% [28].

Relationship between baseline parameters in the selected patients and their virologic response showed that patients who showed SVR were significantly older than non responders (45.1 and 40.7 years respectively, \(P=0.02\)). It was confirmed that SVR is negatively correlated with age [29,30]. Our result was contradictory to other previous studies [31,32]. This may be explained by the fact that all the enrolled patients were attendants of Railway hospital, middle aged patients being members of Railway Association employees, drivers, workers and their wives. There was male predominance in groups I and II (85.4% and 82.1% respectively) with no statistically significant difference (\(P=0.671\)). This agrees with the fact that female gender is favored for HCV clearance [3,30,32,33].

On analyzing viral load; group II had high viral load (almost double that recorded in group I). This coincides with many studies documenting low baseline viral load to be a significant predictor of SVR, regardless the genotype [30-32]. Meanwhile, transaminases, in group II were higher than in group I but without recording a significant relation. This agrees with the fact that low baseline transaminases is a predictor for SVR [30]. Also, neither HAI nor fibrosis was significantly related to either SVR or NR groups. This is contrary to Derbala et al. [29] who found a positive association between SVR and pretreatment histopathological injury. Only one cirrhotic patient was included but did not respond to SOC therapy. This agrees with previous studies which identified absence of cirrhosis and bridging fibrosis are independent predictors related to SVR [30,32].

Studying the prevalence of SNPs at IL-10 _1082G/A in all studied groups i.e HCV patients and control subjects showed that; GA genotype, the wild form, was the most frequent genotype at all; in both cases and control groups but higher in prevalence among control subjects (62/87 patients; 71.3% and 19/20 subjects; 95% respectively). This is similar to Afzal et al. [34] who found GA genotype in 93% of controls versus 75% of HCV Pakistani patients (\(P=0.001\)) suggesting its possible protective effect. Similarly, Gao suggested its relation with the reduced risk of persistent HCV infection [20]. However, allele study did not show significant relation with either of them. Other studies found no statistical relation between HCV patients and controls either at allele or genotype levels [35-37]. On the other hand, GG genotype, was not detected at all in any of the control group (\(P=0.001\)). This is similar to Afzal et al. [34] and Vidigal et al. [38] who found GG genotype to be more common in HCV patients than in controls (\(p=0.001\) and 0.048 respectively) suggesting favouring susceptibility to chronic HCV infection. Whereas AA genotype was the least detected in all studied groups (8/87 patients; 9.2% and 1/20 subjects; 5%). This was different from Abbas and Moatter who found GG genotype the least detected genotype [39]. Meanwhile, AA was mostly i.e 88.9% (8 patients/total 9) present in HCV patients. This agrees with Afzal et al. who found AA genotype more frequently detected in HCV patients than in controls [34].
SNPs of IL-10_819 C/T showed that; CC genotype was not detected at all in control group ($P=0.02$). This is similar to Afzal et al. [34] who showed a higher frequency of this genotype in HCV patients compared to healthy group. Conversely, TT genotype was significantly higher in control group ($P=0.01$).

On the other hand, SNPs of IL-10_592 showed no significant relation with either cases or control, however, AA genotype, the wild form, was more prevalent in control group (10/20 subjects; 50%) than in HCV cases group (28/87 patients; 32.2%). This is different from Lu et al. who studied these SNPs in Asian population, and found them significantly related to HCV infection susceptibility [37].

While SNPs of IL-12B showed that, neither genotypes nor alleles showed significant relation with either cases or control. This agrees with Mueller et al. [40] who clearly excluded a major influence of overall genotype distribution and allele frequency of IL-12B polymorphisms on the natural course of HCV infection.

Studying the prevalence of SNPs at IL-10_1082G/A in HCV patients revealed; GA, the wild genotype form, was the most frequent genotype in groups I and II (41/48 patients; 85.4% and 21/39 patients; 53.8%). This agrees with Abbas and Moatter who found GA genotype, the commonest form in their patients (52%) [39]. Meanwhile it was significantly higher in SVR in comparison to NR when compared amongst other mutant forms (41/62 patients; 66.1% versus 21/39 patients; 33.9%, $P=0.001$), that was significantly attributed to G allele ($P=0.03$). This is in concordance with Knapp who found G allele, an influencing factor for SVR [22]. GG genotype was significantly higher in NR (14/39 patients; 35.9%) than in SVR (3/48 patients; 6.3%, $P=0.02$). This agrees with Knapp who found GG genotype association with persistent HCV infection [22]. And also Vidigal who found this to be related to resistance to SOC therapy [38]. On the contrary, Dogra found GG genotype more frequently detected in responders compared to NRs [36]. AA genotype was equally detected in both groups (4 patients/total 8 in each group). This equivocal result was different from Gao et al. [20] who concluded that AA genotype is associated with higher risk of chronic HCV infection. On the contrary, Yee found it more related to SVR [19]. On the other hand, Kusumoto found no association between IL-10 SNPs and HCV eradication [41]. Also, Afzal et al. [34] found IL-10 SNPs at the allele level, not the genotype distribution, was correlated with HCV infection.

SNPs of IL-10_819 C/T in HCV patients showed that; TT genotype, the wild type, was the least present (4 patients; 4.6%), all belonged to group I ($p=0.007$). This agrees with Yee et al. [19] who stated that homozygous genotype at SNP at _819T is correlated with SVR.

On the other hand, SNPs of IL-10_592 C/A in HCV patients; none of the genotypes showed a statistical significant relation with either groups. This was contrary to Lu et al. [40] who found a significant relation between these SNPs and HCV infection susceptibility in Asian population. However, allele study proved A allele significantly favoured SVR ($P=0.02$) while C one significantly favoured NR ($P=0.02$). This is similar to Yee et al. [19] who detected higher prevalence of IL-10 _592AA in responders than in NRs.

While SNPs of IL-12B in HCV patients, CC genotype was significantly related to SVR group ($P=0.01$). This was confirmed by allele study i.e C allele significantly favoured SVR ($P=0.01$) while A one significantly favoured NR ($P=0.01$). This agrees with Mueller et al. who found CC genotype present in greater frequency among responders than in the non-responder group (55% versus 46% respectively) [40]. This is consistent with Quiroga et al. [42] and
Amaraa et al. [43] that showed that HCV adult patients carrying the CC genotype have greater chance of SVR than patients with CA/AA genotypes.

The reasons of these differing results appear to be caused by several factors e.g. studied populations, different cultural, ethnic and environmental background, factors affecting SVR particularly varying HCV genotypes, and study designs [44].

5. CONCLUSION

Studying SNPs of IL-10_1082 G/A, IL-10_819 C/A and IL-12B (30-UTR 1188-AC) proved GA, TT and CC genotypes, respectively, to be good predictors for SVR. Conversely, SNPs of IL-12 C/A proved AA genotype to be good predictor for NR. On the other hand, SNPs at _592 A/C was not related to response to therapy. These findings suggest that these genotypes may be a suitable genetic tool to predict higher response rates in Egyptian patients with chronic HCV.

CONSENT

All authors declare that ‘written informed consent was obtained from the enrolled patients.

ETHICAL APPROVAL

This study was approved by the Endemic Medicine and Hepatology Department ethical committee, Faculty of Medicine, Cairo University in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

ACKNOWLEDGMENT

We would like to express our gratitude to Railway hospital medical staff for their outstanding cooperation.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES


