The Relationship between Interleukin-6 Polymorphism and Susceptibility to Hepatitis C-virus Infected Patients

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Abstract

Introduction: Raised levels of the interleukin (IL-6) have been reported in patients with Hepatitis C Virus (HCV), but it remains debatable whether they are influenced by IL-6 promoter polymorphisms. Therefore, this current study sought to assess whether IL-6 (-174G/C), (-597G/A), and (-572G/C) promoter polymorphisms are associated with serum IL-6 levels in HCV patients..

Methods: Total 102 patients and 103 healthy controls were involved. IL-6 (-174G/C) was genotyped using Mutagenically separated Polymerase Chain Reaction (MS-PCR) while sequence specific primers-PCR(SSP-PCR) was used for (-572G/C) and (-597G/A). The levels of IL-6 in serum samples were determined by enzyme linked immunosorbent assay (ELISA).

Result: The most frequent genotypes were (-174GG) in both groups. (-572GG) in patients while (-572GC) in the control group and (-597GG) in patients and (–579GA) in control. A significant increase (P<0.001) in (-174GG), (-572GG) and (-597GG); respectively in the HCV group against controls, however (-572GC) and (-597GA) genotype was significantly decreased (P<0.001) in patients. A significant increase in G alleles in all polymorphism. Detection and differentiation of levels of IL6 were significantly higher (P=0.028) in patients infected with (HCV) compared with normal group. In serum IL-6 level, A significant increase was observed in (-174G/C) IL-6.

Conclusions: our results indicate that a predisposition to chronic HCV infection is associated with a particular IL-6 polymorphism (-174 G/C), (-597G/A), and (-572 G/C) in an Egyptian population and may affect the level of IL-6.

Keywords: Polymorphism, Interleukin-6, HCV.

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Introduction

The hepatitis C virus (HCV) is a single stranded RNA virus belonging to the flaviviridae family which mostly impacts the live. It is estimated about 185 million people are infected with HCV throughout the world.[1] Approximately 70% of people infected with HCV develop chronic infection and the remaining 30% are known to spontaneously clear the infection; but these rates vary by ethnicity, gender, and other factors.[2,3]Cytokines have a key role in differentiation, maturation, and functional activation of immune cells, cytokines influence the

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defense against hepatitis viruses and the immune response against hepatitis infections.[4,5]It is involved in the regulation of different cellular processes, including proliferation and differentiation and plays a functional essential role in acute phase response and in the control of the equation between pro-inflammatory and anti-inflammatory pathways, which could affect the result of antiviral treatment.[6,7,8] The human IL6gene encoded on chromosome 7p21 contains five exons and four introns.[9] Recently, several polymorphisms, at most single nucleotide polymorphisms (SNPs), with biological importance have been reported in the IL-6 gene. These polymorphisms affect the level of interleukin-6 production. Production of IL-6 is regulated at the transcriptional, posttranscriptional and translational levels. [10, 11] Different single-nucleotide polymorphisms in the IL-6 gene have been described to include in its transcriptional regulation, such as the (-174G/C) polymorphism[12], the (-597G/A) polymorphism, and the (-572G/C) polymorphism.[13] It is shown that a polymorphism in the promoter region of IL-6 (position -174 G/C), would influence the level of IL6 expression.[14] Prior studies have shown the association between (-174G/C) rs1800795 polymorphism and HCV infection. [15,16] On the other hand, (−572C/G) rs1800796, and (−596G/A) rs1800797, have been reported to be related to a wide range of diseases, including cancer, autoimmune diseases and hepatitis.[17,18, 19,20] There are only few studies dealing with the relationship between IL-6 promoter polymorphisms and chronic HCV infection, and their results have been contadictory. Therefore the aim of our study was to investigate whether a predisposition to chronic HCV infection is associated with a particular IL-6 polymorphism in an Egyptian population and to correlate the polymorphism with the level of serum IL-6.

Patients and Methods

A sample of 102 consecutive Egyptian individuals; 74 males and 28 females; with confirmed chronic HCV. Patients were from the Oncology Hospital, Shebein El-kom, Menoufia Governorate, Menoufia University, Egypt. Also, a 103 unrelated healthy blood donors; 60 males and 43 females served as normal controls. The medical history, complete blood count, liver, renal function tests, Thyroid-Stimulating Hormone (TSH), and Alpha-fetoprotein (AFP) were tested in all participates.

This study was previously approved by the Ethical Committee of The Institute of Genetic Engineering and Biotechnology Research. Written informed consent was obtained from all patients.

DNA Extraction:

Blood samples were collected in EDTA sterile tubes. Genomic DNA was isolated from whole blood, according to the manufacturer's instructions (Qiagen Ltd., UK).

SNP typing:

For the detection of the IL-6 polymorphisms, Mutagenically Seperated polymerase chain reaction (MS-PCR) for IL-6 (-174G/C) was used as previously described by Talaat et al [21]. The product of PCR resulted in 136 bp (C allele) and 121 bp (G allele). The size of PCR products were analyzed by electrophoresis in 4% agarose gel after staining with ethidium bromide and valuated in comparison to 25 bp DNA ladder (Fermentas, Thermo Fisher Scientific Inc.). PCR sequence-specific primer method (PCR-SSP) was used for IL-6 (-572 G/C and -597 G/A) SNPs. The primers for IL6 (-572 G/C and -597 G/A) were newly designed by using the aid of NCBI Primer-Blast Tool (http://www.ncbi.

nlm.nih.gov/ tools/ primer-blast) (Table 1). For every SNP, the reaction was done in two separated tubes, one for each allele, with 25 final reaction volume. The PCR mixtures composed of the DreamTaq Green Master Mix 2x (Fermentas, Thermo Fisher Scientific Inc.),10 pmoles of each allele-specific primer, 10 pmoles of reverse primer, and 100 ng of DNA. PCR conditions regarding both polymorphisms were performed as follows: 94°C for 2 min (1 cycle), followed by 96°C for 25 s, 70°C for 45 s, and 72°C for 20 s (5 cycles); followed by 96°C for 25 s, 65°C for 50 s, and 72°C for 45 s (11cycles); and finally 96◦C for 25 s, 55◦C for 60 s, and 72°C for 2 min (15 cycles).The size of PCR products were analyzed by electrophoresis in 2% agarose gel after staining with ethidium bromide and valuated in comparison to 100 bp DNA ladder (Fermentas, Thermo Fisher Scientific Inc.) (Figure 1 b&c). All PCR reactions were produced in the Biometra thermal cycler (Biometra GmbH, Germany).

Measurement of Serum IL-6 by (ELISA):

Total concentrations of IL-6 in serum samples were measured using a commercial ELISA kit (R&D System, Inc., Minneapolis, MN), according to the manufacturer's instructions. The intensity of the developed color was measured by reading optical absorbance at 450 nm using a microplate reader (SunriseTM, Tecan Group Ltd. Ma¨ nnedorf, Switzerland)) Results were expressed as pictogram of cytokine per milliliter plasma (pg/ml). [22]

Statistical Analysis:

Data was analyzed using IBM SPSS software package version 20.0. Qualitative data was described using numbers and percent. Quantitative data was described using range (minimum and maximum), mean, standard deviation and median. A significance of the obtained results was judged at the 5% level.

Comparisons between both groups were performed by Chi-square test for categorical variables to compare between the different groups, Student t-test for normally quantitative variables to compare between two studied groups, Mann Whitney test for abnormally quantitative variables to compare between the two studied groups.

Table 1.Primers used to detect polymorphisms of IL-6 in HCV patients and controls.

Primer	Product size
IL-6 (-174) G/C	
Forward G: 5'-GCACTTTTCCCCCTAGTTGTGTCTTACG-3'	121 bp
Forward C: 5'GACGACCTAAGCTTTACTTTTCCCCCTAGTTGTGTCTTGAC-3'	136 bp
Reverse: 5'-ATAAATCTTTGTTGGAGGGTGAGG-3'	
IL-6 (-572) G/C	
Forward G: 5'-GGCCAGGCAGTTCTACAACAGCCG-3'	
Forward C: 5'-GGCCAGGCAGTTCTACAACAGCCC-3	325bp
Reverse: 5'-ATTAGTGACTCAGCACTTTGG-3'	
IL-6 (-597) G/A	
Forward G: 5'-AAGTAACTGCACGAAATTTGAGGG-3'	
Forward A: 5'-AAGTAACTGCACGAAATTTGAGGA-3'	473 bp
Reverse: 5'-TGTGCAATGTGACGTCCTTTA-3'	

Results

Patients' characteristics:

Table (2) demonstrates the number, age, and the results of different biochemical parameters carried out in this study, including, different liver function tests, TSH, AFP as well as different parameters of blood picture of individuals from all investigated groups**.** In the HCV patient group there were 74 (72.5%) male and 28 (27.5%) females patients and in the control group there were 55 (53.4%) males and females 48 (46.6%). The median age of HCV patients was 48.0 years (range: 23.0 – 69.0 years) and 26 (range: 19.0-54.0).HCV patients had significantly higher levels of Creatinine, AST, ALT, and AFP than in control cases (P<0.01), No significant difference was found in the Hub and TSH.

Table (2): Comparison between the two studied groups according to different parameters

	Patients (n=102)	Control (n=103)	p
Gender			
Female	28 (27.5%)	48 (46.6%)	0.005*
Male	74 (72.5%)	55 (53.4%)	
Age	45.42 ± 10.01	28.89 ± 8.40	<0.001*
TLC	5.35 (2.20 – 33.0)	5.60 (4.20 – 10.10)	0.013*
Creatinin	0.90 ± 0.24	0.76 ± 0.18	<0.001*
Hemoglobin	13.06 ± 1.92	13.16 ± 0.94	0.640
AST	46.50 (12.0 – 209.0)	23.0 (10.0 – 40.0)	<0.001*
ALT	51.0 (12.0 – 318.0)	22.0 (10.0 – 37.0)	<0.001*
Alb	4.22 ± 0.61	4.45 ± 0.30	0.001*
TSH	2.20 (0.03 – 36.49)	2.0 (0.40 – 4.20)	0.616
AFP	3.10 (1.20 – 2109.0)	2.0 (0.90 – 8.0)	<0.001*
IL-6	29.0 (4.0 – 1086.0)	29.30 (3.70 – 139.0)	0.028*

Qualitative data were described using number and percent and was compared using Chi square test, while normally quantitative data was expressed in mean ± SD and was compared using student t-test, abnormally distributed data was expressed in median (Min. - Max.) and was compared using Mann Whitney test

*: Statistically significant at $p \leq 0.05$

IL-6 polymorphism

IL-6 (-174G/C, -572G/C and -597G/A) allele and genotype frequencies in HCV patients and healthy control are shown in Table (3). Genotype frequencies of the 3 SNPs of IL-6 were significantly different between the HCV patients and controls. The frequencies of GG, GC and CC genotypes in IL-6 -174G/C were 95 (93.1%), 7 (6.9%) and 0 (0.00%) cases in HCV patients, respectively; and were 76 (73.8%), 26 (25.2%) and 1 (1.0%) cases in the controls respectively.IL-6 -174 G/C showed significant genotypic and allelic associations (P<0.001) -174 GG was the most prevalent genotype in the population while CC genotype was not detected in HCV patients and was represented by one case in the control group. IL-6 -174G allele showed a significant association (P<0.001) with HCV when compared to control. The frequencies of GG, GC and CC genotypes in IL-6 -572G/C were 75 (73.5%), 27

(26.5%) and 0 (0.0%) cases in HCV patients respectively, and were 33 (32.0%), 68 (66.0%) and 2 (1.9%) cases in the controls.

A significant increase (P<0.001) in -572GG genotype was observed in HCV group compared to controls, while GC genotype and C allele showed a significant increase (P<0.001, for both) in the same group. The frequencies of GG, GA and AA genotypes in IL-6 -597G/A were 59 (57.8%), 42 (41.2%) and 1 (1.0%) cases in HCV patients respectively and were 32 (31.1%), 70 (68.0%) and 1(1.0%) cases in the controls, respectively. No genotypic were observed for IL6-174CC and IL 6 -572AA in the present study. Analysis of IL-6 (-597G/A) SNP pointed to a significant increase (P<0.001) in GG genotypes in the HCV group versus a significant decrease (P<0.001) in the same genotype in the control group.-597GA genotype increased significantly (P<0.001) in the control group. -597 AA genotype was rare in both controls and HCV cases (1.0% for both). A significant increase (p<0.001) in the A allele was observed in the control group compared to HCV.

Table 3. Genotype distribution and allelic frequency of IL-6 (-174 G/C, -572 G/C and -597 G/A) in controls and HCV patients.

Cytokine gene	Patients (n=102)	Control (n=103)	P
IL6-174			
G/G	95 (93.1%)	76 (73.8%)	
G/C	7 (6.9%)	26 (25.2%)	0.001*
C/C	0 (0.0%)	1 (1.0%)	
Allele			
G	197 (96.6%)	178 (86.4%)	<0.001*
C	7 (3.4%)	28 (13.6%)	
IL 6 -597			
G/G	59 (57.8%)	32 (31.1%)	
G/A	42 (41.2%)	70 (68.0%)	<0.001*
A/A	1 (1.0%)	1 (1.0%)	
Allele			
G	160 (78.4%)	134 (65.0%)	0.003*
A	44 (21.6%)	72 (35.0%)	
IL 6 -572			
G/G	75 (73.5%)	33 (32.0%)	
G/C	27 (26.5%)	68 (66.0%)	<0.001*
C/C	0 (0.0%)	2 (1.9%)	
Allele			
G	177 (86.8%)	134 (65.0%)	<0.001*
C	27 (13.2%)	72 (35.0%)	

Qualitative data were described using number and percent and was compared using Chi square test, while normally quantitative data was expressed in mean ± SD and was compared using student t-test, abnormally distributed data was expressed in median (Min. - Max.) and was compared using Mann Whitney test

*: Statistically significant at $p \leq 0.05$

Table (4): Relation between IL-6 level according to IL-6 (-174 G/C, -572 G/C and -597 G/A) in controls and HCV patients

	IL-6 level						
	Patients				Control		
	N	Median	Min. – Max	p	N	Median	Min. – Max	p
IL6-174								
G/G	95	30.0	4.0 – 1086.0		76	31.05	8.0 – 139.0	
G/C	7	29.0	6.0 – 671.0	0.323	26	22.75	3.70 – 64.0	0.019*
CC	0	-	-		1#	7.80		
Allele								
G	197	29.0	4.0 –1086.0	0.330	178	30.5	3.7 - 139.0	0.008*
C	7	29.0	6.0 – 671.0		28	20.0	3.7 - 64.0	
IL 6 -597								
G/G	59	29.0	4.0 – 1086.0		32	26.80	5.20 – 134.0	
G/A	42	31.0	5.0 – 987.0	0.860	70	30.95	3.70 – 139.0	0.773
A/A	1#	10.0			1#	25.70		
Allele								
G	160	29.0	4.0 – 1086.0	0.635	134	28.6	3.7 – 139.0	0.887
A	44	29.5	5.0 – 987.0		72	30.5	3.7 – 139.0	
IL 6 -572								
G/G	75	29.0	4.0 – 1086.0		33	26.80	5.20 – 134.60	
G/C	27	42.0	7.0 – 987.0	0.205	68	30.45	3.70 – 93.90	0.274
C/C	0	-			2	85.25	31.50 – 139.0	
Allele								
G	177	29.0	4.0 – 1086.0	0.243	134	28.3	3.7 – 134.6	0.446
C	27	42.0	7.0 – 987.0		72	31.0	3.7 – 139.0	

Abnormally distributed data was expressed in median (Min. - Max.) and was compared using Mann Whitney test

*: Statistically significant at $p \leq 0.05$

Serum levels of IL-6 in infected HCV patients:

A statistically significant increase of IL-6 ($p \leq 0.05$) in infected HCV patients compared to healthy controls, 29.0± (4.0 – 1086.0) versus 29.30± (3.70 – 139.0) was demonstrated. The disease was significantly correlated with elevation of IL-6 secretion level, table (1).

Relation between IL-6 level according to IL-6 (-174 G/C, -572 G/C and -597 G/A) in controls and HCV patients

Table (4) demonstrated the correlation between the level of IL-6 and the different polymorphism, the mean serum concentration of IL-6 (-174 G/C) was increased significantly ($p \leq 0.05$; $p \leq 0.01$ respectively) in HCV patients with GG genotype and G allele; respectively. In IL-6 (-572G/C),GC genotype, G and C alleles were not significant despite the increase of IL-6 levels in the patients. The same results were observed in IL-6 (-597 G/A) where IL-6 increased in the patients.

Discussion

Studies on the cytokine gene polymorphisms [22, 23] suggest that inheritance of some genotypes related to polymorphisms of cytokine genes, such as the IL-6 genotypes, which become clear to affect cytokine production, may be host genetic factors associated with the progression of HCV. With this overview, the present study was planned to identify the relationship between SNPs of IL-6 gene (-174G/C, -572G/C, and -597G/A) genotypes, and plasma levels and susceptibility to chronic hepatitis C virus (HCV) infection in a Minufiya Egyptian population. This study exhibited that the G allele and G/G genotype at the IL6 -174 position had higher distribution among Egyptian HCV patients (96.6% and 93.1 %, respectively) in comparison to controls (86.4% and 73.8 % respectively) (Table 2). The majority of the patients (93.1%) revealed the potential for producing G/G genotype was significantly increased (P<0.001) compared to (86.4 %) of the control group (p=0.001); showing a positive correlation with HCV infection.

The -174 G/C genotype and C allele were significantly decreased (P<0.001) in the patient group showing a negative correlation with the infection(P<0.001). These results agree with the results of Falleti et al. [24], who reported a correlation between the presence of the high-producer genotype (GG) in IL6 – 174 polymorphism and a worse evolution of the HCV infection[25]. In addition, our result agrees with Cussigh et al. who analyzed that(−174G/C) polymorphism in IL-6 can influence the establishment and course of chronic HCV infection[16].On the other hand, Fabrício-Silva et al., found influence of the IL-6 (−174) C allele on the clearance of HCVwith no evidence for genetic association between IL-6 (-174G/C) SNP and the susceptibility to HCV infection.[25] However, Fabrício-Silva's result is in contrast with the results published by Pereira et al. who didn't find any difference in allele and genotype frequencies of the −174 polymorphism in a South American cohort with chronic HCV infection in comparison to controls,[26] and with Minton et al.,who didn't support a role for IL-6 (-174G/C) SNP in HCV clearance,[27]in addition to Park et al., in a Korean population,[28] Ribeiro et al., in a Brazilian population,[29]Migita et al., [30] and in Chang et al., in the meta-analysis study,[31] who demonstrated that there is no association between (-147G/C) IL-6 polymorphisms and outcome of chronic HCV infection may be entirely accounted for by the almost absence of the C allele of -174GC polymorphism in east Asian and South American populations, which agree with our result. few studies examined the association between the IL-6 (-597G/A, -572G/C) SNP and HCV infection risk. In the present study, the frequencies of the IL-6 -572 GG genotype in our patients were higher distribution in HCV patients (73.5%) versus (32.0%) in controls.In correspondence with us, the results of Cussigh et al., [16] who pointed that the GG genotype was distributed about (86.8%) in patients, and Sarsu et al., who reported that -572GG genotype was distributed (89.3%) in inflammatory patients. [32] On the other hand, -572GC genotype distribution is higher in different studies (49.02%, 85.2%, respectively) in patients. [34, 35]

The significant increase *(*P<0.001*)* of-572GG genotype in our HCV patients pointed that (-572G/C) SNP in IL-6 gene was associated with an increased risk of HCV infection in G allele (86.8%) in patients versus (65.0%) in control. This result disagrees with Lu et al., who indicated that the IL-6 -572 allele

G may be beneficial for spontaneous clearance of HBV. [35]In conformity with these findings, some studies demonstrated that the IL-6 (-572G/C) might be related to the risk of HCV infection, [36, 37] while other studies could not demonstrate the link between the IL6-572 G/C SNP and hepatitis viral infection. [16, 38] The distribution analysis of IL-6 (-597G/A) showed IL-6 -597 GG genotype had higher distribution in HCV patients (57.8%) versus (31.1%) in controls, while GA genotype had (41.2%) distribution in HCV patients versus (68.0%) in controls. On the other hand, there was a rarity in the IL-6-597 AA Genotype in both groups (1.0%). This result matches Falleti et al., who observed that the IL-6, -597 G/A polymorphism was related to the presence and outcome of HCV infection. [24] Cussigh et al. also reported (−597G/A) as appearing to favor a progressive HCV disease.[16] In contrast to our study, Lu et al., demonstrated that no significant differences in the(−597G/A) allele or genotype frequencies between HCV patients and control group were observed. [35]However, The different results of IL-6 promoter SNPs (-174 G/C,-572G/C and -597 G/A) of different studies have been inconsistent. This may be due to the great ethnic diversity in the world, as further studies with subjects from different genetic and ethnic backgrounds would provide important information to understand the commonalities between host and viral factors responsible for HCV pathogenesis and the clinical course of infection.[25, 38] Our study demonstrated a significant increase in the IL-6 level in HCV patients compared to controls. In comparison with healthy people, the serum level of IL-6 in patients with HCV is controversial. Comanescu et al.,[39] and Fallahi et al., [40] reported that IL-6 levels in patients with HCV were significantly higher than those in healthy controls. Serum IL-6 levels related to viral load and histological index. [41] Also the rapid serum clearance of IL-6 may give differing results in the level of this inflammatory cytokine.[42] As it follows, lower levels of IL-6 were associated with sustained virologic response, at most, in men.[8] In our group of patients, we found significant differences between serum levels of IL-6 in male versus female (p=0.006) in contrast to Comanescu et al.[39]

In the analysis of IL-6 SNPs with level of expression, the C allele appears to be associated with significantly lower levels of serum IL-6, whereas the GG and GC genotypes appear to have higher levels of serum IL-6. This suggests a possible connection of IL-6 status with the therapy outcome. The putative low producing IL-6 phenotype may play a protective role against HCV infection by helping to clear the viral particles during standard therapy. This result agrees with Fishman et al., Lapinski et al, and Ben Ari et al. [14, 43, 44] However, our result showed increases in the level of IL-6 (-572G/C), as we observed a high production of IL-6 GC genotype compared to GG and CC genotypes in the patient group, although it did not match the statistical significance indicated in different studies, proving that an IL-6 -572GG genotype is associated with lower IL-6 levels, while the -572 CC genotype is associated with high levels of IL-6. [45, 46] In the case of (-597G/A) we observed a high level of IL-6 GA genotype compared to GA and AA despite the statistic significance. This finding agrees with the report of Saxena et al., showing no significant difference in IL-6 levels in any of the genotypes of IL-6 -597G/A.[33]

Conclusion

Our results investigated the predisposition to chronic HCV infection in association with a

particular IL-6 polymorphism (-597G/A, -572 G/C and -174 G/C) in an Egyptian population and the effect of polymorphism in IL-6 level. There is a significant increase in G alleles in all polymorphism. Detection and differentiation of levels of IL6 were significantly higher in patients infected with (HCV) compared with the normal group. Further studies with a larger sample size are greatly needed to confirm the findings of our study.

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التعدد الجيني للانترلوكين –6 في المرضى المصريين بالالتهاب الكبدي الوبائي –س

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الملخص

التهاب الكبد الفيروسي (س): هو مرض معدٍ يصيب الكبد ويتسبب به فيروس الكبد (س)، يعد التهاب الكبد الفيروسي (س) من الأسباب المهمة لالتهاب الكبد المزمن. يتميز مرض الالتهاب الكبد الوبائي بارتفاع نسب الانترلوكين 6 في الدم وهو بروتين محفز للالتهابات و يساعده على زيادة انتاج الاجسام المضادة في جسم الانسان كما يتميز الانترلوكين 6 بتعدد الجينات الشكلية المكونة له مثل (G/C, 147- G/A, 597- G/C, 572-) و يؤدي التعدد الجيني الى اختلاف تأثيره على خلايا جسم الانسان ومن هنا تأتي هذه الدراسة التي تهدف الى تقييم مدى ارتباط التعدد الجيني (G/A, 597- G/C, 572- G/C, 147-) للانترلوكين–6بمستوياته في الدم عند مرضى الالتهاب الكبدي الوبائي– س. حيث تم اجراء هذه الدراسة على مجموعتين، المجموعة الاولى تشمل 102 مريض بالالتهاب الكبدي الوبائي– س والمجموعة الثانية تشمل 103 شخص كمجموعة ضابطة. وتم قياس مستوى الانترلوكين–6 في المجموعتين باستخدام تقنية الاليزا (ELISA).

ولمعرفة الأشكال الجينية للانترلوكين–6 للمجموعتين تم استخدام تقنية تفاعل البلمرة المتسلسل ((SSP-PCR) لتحديد التعدد الجيني (572- G/C, 597- G/A) وتقنية تفاعل المتسلسل (MS-PCR) لتحديد التعدد الجيني (G/C 147-).و قد تم تحليل البيانات الاحصائية باستخدام برنامج SPSS. و قد اظهرت النتائج ارتفاع نسبة الانترلوكين–6 في مرضى الالتهاب الكبد الوبائي مقارنة بالمجموعة الضابطة. لقد أوضحت الدراسة ان الشكل الجيني للأنترلوكين–6 (GG 174-) كان الأكثر انتشارا لدى المجموعتين / المرضى و المجموعة الضابطة. كما اوضحت النتائج ان الشكل الجيني للانترلوكين–6 (597GG-) كان الاكثر انتشارا في مرضى الالتهاب الكبدي الوبائي في حين ان الشكل الجيني للانترلوكين–6 (597GA-) كان الاكثر تواجدا في المجموعة الضابطة. بالاضافة الى ان الشكل الجيني للأنترلوكين –6 (572GG-) كان الاكثر انتشارا لدى المرضى في حين ان الشكل الجيني للأنترلوكين –6 (572GC-) كان الاكثر تواجدا في المجموعة الضابطة.

الكلمات الدالة: التعدد الجيني للانترلوكين –6، التهاب الكبد الفيروسي (س)، الاجسام المضادة.