RESEARCH ARTICLE

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Association of Interleukin-27 (IL-27) *rs181206 T/C* and *rs17855750 T/G* Gene Polymorphisms and the Risk of Hepatitis B Infection among Egyptians

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Abstract

Background and Objective: HBsAg incidence in Egypt is at a range of 2 to 7%. Antiviral immunity is linked to interleukin-27 (IL27), a cytokine that is produced by two genes: *EBI3* and *p28*. *IL-27* gene SNPs can alter the susceptibility to infection of HVB by impacting the production and/or function of cytokines. The study aimed to examine the impact of the IL-27 SNPs on the progression of HBV infection among Egyptian individuals. **Materials and Methods:** This study included a total 112 patients infected with HBV, and 50 healthy individuals served as controls. The link between the IL-27 SNPs (rs181206 T/C and rs17855750 T/G) and HBV was investigated using real-time PCR. **Results:** There was no significant correlation between fibrosis stages and the distribution of IL-27 rs181206 *T/C* and rs17855750 T/G genotypes among HBV patients. Results indicated minimal disparity in the distribution of haplotypes among the study groups. No significant difference in the frequency of the CG, CT, TT, TG, and haplotypes between the groups. **Conclusion:** This study found no correlation between the presence of IL-27 rs1812006 and IL-27 rs17855750 SNPs and the HBV chronicity.

Keywords: SNPs- *IL-27 rs181206 T/C- rs17855750 T/G*- Haplotype- HBV

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Introduction

The Hepatitis B virus (HBV) is the predominant and prototypical member of the Hepadnaviridae family and the Orthohepadnavirus genus. The phenomenon is often seen in several populations and results in the development of chronic disorders [1]. HBV infection may lead to several medical disorders, such as HBV without showing symptoms, acute and chronic hepatitis, liver cirrhosis, and primary Hepatocellular carcinoma (HCC) [2].

There are roughly 400 million instances of chronic HBV infection globally, which leads to more than one million deaths annually. Thus, HBV infection is in the top 10 primary contributors to mortality worldwide. A significant proportion of individuals infected with HBV are unable to eradicate the virus, resulting in a persistent infection that might potentially result in liver damage. The precise processes responsible for the different symptoms are yet not completely understood. Nevertheless, it is thought that the immune system of the host may have a role in the eventual consequences [3].

A chronic HBV infection is diagnosed when the HBsAg is detectable in the plasma for a minimum duration of six months. The mean duration for detecting HBsAg is 30 days, with a variation between 6 and 60 days. The progression of HBV infection through clinical phases is influenced by a multitude of variables, such as genetic, viral, environmental, immunological, and host influences [4].

The exact immunological mechanism responsible for the various symptoms of chronic HBV infection is not yet fully understood. However, there is significant evidence to support the idea that cellular immunity, namely CD4+ Th cells, may play a crucial role in the progression of HBV infection. These particular cell types produce cytokines and provide support to cytotoxic T cells [5].

Cytokines, which are a component of the immune system, govern viral infections in humans. SNPs affect

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the production of cytokines in affected people. SNPs occurring in cytokine genes result in differences in a single nucleotide, which subsequently affect the production and functions of cytokines. The disruption of the immune response to viral infections has the capacity to contribute to the formation of HCC [6].

Activated antigen presentation cells (APCs) are the primary producers of interleukin-27 (IL-27), a recently identified protein belonging to the IL-12 family. IL-27 consists of two subunits, namely p28 and the EBV-induced gene 3 protein [7]. The *IL-27* gene in humans is situated on chromosome 16p11 and is composed of five exons and four introns. This entity's main function is to act as an intermediary between the innate and adaptive immune systems [8].

Owakind and his colleagues performed a study demonstrating that IL-27 is secreted by APCs that have been stimulated in response to viral infections [9]. Consequently, this cytokine triggers the activation of Th 1 cells, leading to an immunological response against viruses. Furthermore, this activation induces the production of IL-10, resulting in an anti-inflammatory reaction [10].

IL-27, in low concentrations, promotes the production of IFN-δ in natural killer (NK) cells. This combination, together with a microbial agent, activates antigen-presenting APCs. During the subsequent adaptive phase of the immune response, this leads to the production of much higher levels of IL-27, which impacts both local and systemic APCs or lymphocytes [11].

IL-27 mutations have been linked to several diseases such as asthma, Crohn's disease (CD), rheumatoid arthritis (RA), colorectal, nasopharyngeal, throat, and ovarian cancers. Prior studies have definitively demonstrated a direct association between two specific IL-27 SNPs; 964A/G [rs153109], and 4730 T/C (rs181206). Recent research discovered a strong correlation between the IL-27 SNPs with the probability of developing CD in the Chinese Han population [5]. Furthermore, a distinct inquiry uncovered that rs153109 is linked to a decreased incidence of lymph node metastases in cases of papillary thyroid cancer [12]. The existence of may function as a protective measure against the occurrence of breast cancer in premenopausal women [13].

SNP is a specific sort of genetic variation in DNA sequences that is especially appropriate for identifying genetic markers associated with disease risks. The cause of this phenomenon is attributed to alterations in the DNA involving two nucleotides. Studying the relationship between SNPs and disease features might provide significant advantages in terms of advancing scientific knowledge, improving genetic diagnostics, and enhancing gene therapy [14].

The study aimed to evaluate the correlation between the risk of HBV infection and SNPs on the *IL-27* gene and to examine the correlation between IL-27 rs181206 T/C and rs17855750 T/G SNPs and fibrosis stages in Egyptian HBV patients.

Materials and Methods

Subjects

The research group consisted of 112 individuals who were diagnosed with chronic HBV at the National Liver Institute, Kafer El-Sheikh University, Egypt. The male population accounted for 73.2%, and the female population accounted for 27.8%. The average age was 46.42 ± 8.93 years. Furthermore, there were 50 individuals in the healthy control group. Of them, 34% were male and 66% were female, with an average age of 46.08 ± 11.47 years. The controls had no history of autoimmune, infectious, or malignant disorders, and they also did not have any liver or renal problems.

Patients' ethics declaration

The study received approval from the National Research Centre, Medical Research Ethical Committee (MREC) (ID: 44512012023). Additionally, all subjects provided written informed consent.

Blood samples

A sterile 6-milliliter blood sample was obtained from each patient. Divided into three equal sections. EDTA was used to extract genomic DNA for the IL27 SNPs from a 2 ml sample. The serum from the second part of the blood was processed to isolate it for routine laboratory tests, including liver function evaluation with an autoanalyzer and AFP detection with ELISA. A complete blood count measurement was taken from the third part of the sample.

Extraction of peripheral blood DNA

Two ml of venous blood withdraw from each participant into sterile anticoagulant Ethylenediaminetetraacetic acid (EDTA) tubes for genomic DNA isolation. Gene JET whole blood genomic DNA purification micro kit (Thermo Scientific, K0781) was used to extract the genomic DNA following the manufacturer's instructions. A Nano-drop spectrophotometer (Quawell, Q-500, Scribner, USA) was used to measure the genomic DNA samples ultraviolet absorbance at 260 nm before they were used in a real -time PCR. The DNA was stored at -80°C until further analysis [15].

Genotyping of the interleukin-27 rs 181206 T/C and rs17855750 T/G gene polymorphisms

The allelic discrimination test on IL-27 rs 181206 T/C and rs17855750 T/G detected the SNPs using a real-time PCR approach. This procedure made use of Applied Biosystems prevalidated TaqMan™ MGB probe probe. The following was combined: 1.25 µL of a 40X combined primer and probe mix (cat. Number: 4351379) (ABI/Life Technologies, USA) was added to 12.5 µL of 2X TaqMan Universal PCR master mix (cat. Number: 4371353) (ABI/Life technologies, USA) in a 25 µL final volume of DNAse/ RNAse-free water (Invitrogen/ Life Technologies,USA) and template. The PCR cycle parameters were as follows: a denaturation step at 95°C for 15 seconds, a denaturation phase at 10 minutes, and an annealing step at 60°C for 1 minute. In the subsequent two stages, a total forty repetitions were offered. The Max3005P qPCR System, made by Agilent Biotechnology in the USA and distributed by Stratagene, was used to

conduct the PCR test.

Statistical analysis

The statistical software SPSS 20.0 from IBM (Armonk, NY) was used for data analysis. The Kolmogorov-Smirnov test verified the distribution is normally distributed. Range, median, interquartile range, standard deviation, and mean were the quantitative data definitions. The findings were evaluated using a significance level of 5%. Analysis of quantitative and categorical data sets by means of separate student t-tests. The relative linkage disequilibrium (D) and haplotype pairing correlation (r^2) were computed. The chi-square test was used to compare categorical data between the groups. For every genotype, the odds ratios (ORs) and 95% confidence intervals (CIs) for HBV were calculated using logistic regression analysis. A statistically significant result was defined as a p-value < 0.05.

Results

General characteristics of studied groups

Despite negative results for HCV antibodies, every patient in the group tested positive for HBsAg and HBV-DNA. The levels of HBsAg, HCV antibodies, and HBV-DNA were all negative in the control group. In the clinical data set, fibrosis was not present in 49.1% of HBV patients; fatty liver was present in 22.3%, cirrhosis in 19.6%, and HCC in 8.9%.

Table 1 shows the biochemical features of the age-matched patients and controls in this study. Compared to the healthy control group, the number of male patients in the fibrosis phases was significantly higher (P=0.001).

On the other hand, the fibrosis groups were equally male- and female-dominated. Elevated ALT levels were statistically significant (P = 0.012) when comparing the HCC group to the control group. The fibrosis phase was also characterized by a significant rise in ALT levels, especially in the HCC group. The fibrosis-stage groups showed markedly higher levels of albumin, total bilirubin, AST, HB, and INR as compared to the control group. The fibrosis groups did not vary significantly in terms of total bilirubin, albumin, HB, or INR, however.

During the fibrosis stages, WBC and direct bilirubin levels were significantly lower than those in the control group (P = 0.001 and 0.007, respectively). In addition, AFP levels were significantly higher in the F0-F1 and F1-F2 groups when contrasted with the F2-F3 and HCC groups, respectively (P = 0.012 and 0.022). Across the board, AFP levels were significantly greater in the fibrosis group than in the control group (P = 0.001).

Distribution of IL-27 (rs181206) and (rs17855750) according to fibrosis stages in HBV patients

The Hardy-Weinberg equilibrium was satisfied by the tested groups' IL-27 rs181206 T/C and rs17855750 T/G genotypes distributions, indicating that these genotypes were typical of the study groups.

Hardy-Weinberg equilibrium equation: $P^2 + 2pq + q^2 = 1$, P represents the dominating allele frequency and q the recessive allele frequency.

Table 2 and Figure 1 show the results of an analysis of the distribution of the IL-27 (rs181206) and (rs17855750) genotypes in relation to the stages of fibrosis. There was no statistically significant correlation between the distribution of IL-27 (rs181206) genotypes and the stages of fibrosis in HBV patients (p = 0.580). The prevalence of the CT genotype was 4.2% in HCC patients, the lowest in the F0-1 group, and 52.1% in the other group. The frequency of TT was lowest (12.9%) among HCC patients and highest (45.2%) among F0-F1 patients. There was no statistically significant correlation between the fibrosis stages and the IL-27 (rs17855750) genotype distribution in HBV patients (P = 0.780). In the F0-1 group, the TG genotype was most common (64.7% frequency), but in the HCC group, it was

Table 1. Baseline and Clinical Characteristics of HBV Cases with Different Fibrosis Stages and Healthy Control

Factors	F0–F1 (n= 55)	F1–F2 (n= 25)	F2–F3 (n= 22)	HCC (n= 10)	Control (n= 50)	P-value
Gender						
Male	37(67.3%)*	19(76.0 %)*	19(86.4%)*	7(70.0%)	17(34.0%)	
Female	18(32.7%)	6(24.0%)	3(13.6%)	3(30.0)	33(66.0%)	0.001
Age /years Mean ± SD.	46.31 ± 9.40	46.76 ± 8.84	46.14 ± 7.66	46.80 ± 10.39	46.08 ± 11.47	0.99
ALT(IU/L)Mean ± SD	32.69 ± 11.74	30.88 ±10.28	30.41 ± 12.36	41.30 ± 12.43*	30.02 ± 1.97	0.041*
AST (IU/L)Mean ± SD	35.87 ± 14.79*	38.16 ± 22.35*	32.27 ± 15.02*	38.30 ± 22.01*	23.96 ± 3.02	0.001*
T.bilirubin (mg/dL)Mean ± SD	1.04 ± 0.95*	0.73 ± 0.13	0.80 ± 0.19	1.06 ± 0.40	0.83 ± 0.07	0.001*
D.Bilirubin (mg/dL)Mean ± SD	0.20 ± 0.15*	0.15 ± 0.06*	0.17 ± 0.06*	0.26 ± 0.24*	0.59 ± 0.07	0.001*
Albumin (g/dL) Mean ± SD	4.43 ± 0.47*	4.25 ± 0.54	4.49 ± 0.58*	4.36 ± 0.46	3.99 ± 0.27	0.001*
HB (%) Mean ± SD	13.75 ± 1.61*	14.10 ± 1.43*	14.23 ± 1.87*	13.56 ± 1.56*	12.49 ± 0.98	0.001*
WBC ($x10^3/mm^3$)	6.47 ± 1.76	6.00 ± 1.58*	7.51 ± 2.12	6.80 ± 1.52	7.19 ± 1.35	0.007
Platelets ($x10^3/mm^3$)	203. ± 53.22	228. ± 72.13	191.9 ± 52.84	250.1 ± 44.67	215.6 ± 44.81	0.019
INR Mean ± SD	1.11 ± 0.08*	1.12 ± 0.09*	1.18 ± 0.13*	1.17 ± 0.13*	0.98 ± 0.06	0.001*
AFP (IU/L) Mean ± SD	4.82 ± 2.39*	5.69 ± 2.37*	3.96 ± 2.14	3.64 ± 2.27	3.40 ± 1.82	0.001*

F, F for One way ANOVA test; HCC, Hepatocellular carcinoma; HBV, Hepatitis B virus; P-value, The probability value; SD, standard deviation; ALT, alanine aminotransferase; AST, aspartate aminotransferase; T. bilirubin, total bilirubin; D. bilirubin, direct bilirubin; HB, hemoglobin; WBC, white blood cells; INR, international normalised ratio; AFP, alfa fetoprotein; *, Statistically significant at p ≤ 0.05.

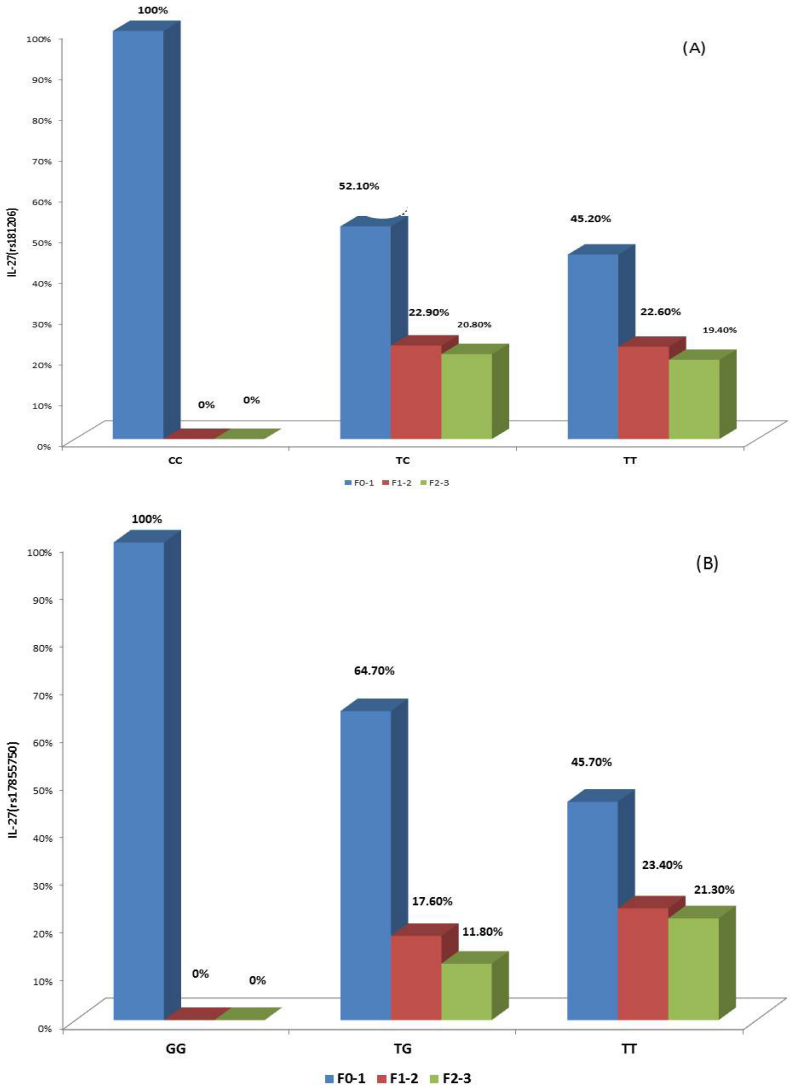

Figure 1. A&B, Distribution of SNPs genotypes according to fibrosis

least common (5.9% frequency).

Patients with F0-F1 had the highest incidence of TT at 45.7%, while those with HCC had the lowest frequency at 9.6%.Among HBV patients, the results showed no statistically significant correlation between the fibrosis stages and the distribution of IL-27 (rs181206) genotypes (P = 0.580). The prevalence of the CT genotype was 4.2% in HCC patients, the lowest in the F0-1 group, and 52.1% in the other group. The frequency of TT was lowest (12.9%) among HCC patients and highest (45.2%) among F0-F1 patients.

Table 3 displays the results of the association analysis between fibrosis and the IL-27 (rs181206) and (rs17855750) genotypes. The frequency of fibrosis stages F1-2, F2-3, and F3-4 was not significantly correlated with the TT genotype compared to the CC+TC genotype. These connections were associated with odds ratios (OR) of 0.815 (95% CI: 0.315-2.108, p = 0.673), 0.864 (95% CI: 0.321-2.330, p = 0.773), and 0.259 (95% CI: 0.050-1.330, p = 0.077), respectively. In contrast to the GG+TG

Table 2. Distribution of SNPs Genotypes According to Fibrosis

SNPs	Genotypes	F0-1	F1-2	F2-3	HCC	P-value
IL-27 (rs181206) gene polymorphism	CC	2(100%)	0 (0%)	0 (0%)	0 (0%)	0.58
	TC	25 (52.1%)	11 (22.9%)	10 (20.8%)	2 (4.2%)	
	TT	28 (45.2%)	14 (22.6%)	12 (19.4%)	8 (12.9%)	
IL-27 (rs17855750) gene polymorphism	GG	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0.784
	TG	11 (64.70%)	3 (17.6%)	2 (11.8%)	1 (5.9%)	
	TT	43 (45.7%)	22 (23.4%)	20 (21.3%)	9 (9.6%)	

SNPs, Single nucleotide polymorphisms; IL-27, Interleukin-27; F, F for One way ANOVA test; HCC, Hepatocellular carcinoma; P, p value for comparing between the different studied groups

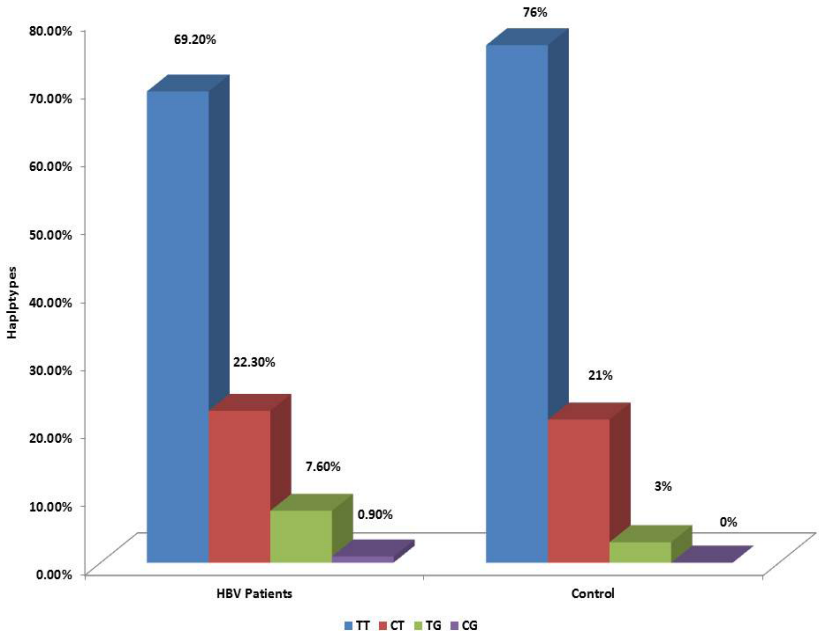

Figure 2. Analysis of IL-27 Haplotype Frequencies with the Risk of HBV

Table 3. Relation between IL-27 Genotype Distribution and Fibrosis in HBV Patients

	TT	(CC+TC)	OR	95% CI	P-value
IL-27 (rs181206)gene polymorphism					
F0-1	28 (51%)	27(49%)	----	----	----
F1-2	14 (56%)	11 (44%)	0.815	0.315-2.108	0.673
F2-3	12 (55%)	10 (45%)	0.864	0.231-2.330	0.773
F3-4	8 (80%)	2 (20%)	0.259	0.050-1.333	0.077
IL-27 (rs17855750) gene polymorphism	TT	TG+GG	OR	95% CI	P-value
F0-1	43 (78%)	12 (22%)	----	----	----
F1-2	33 (91.7%)	3 (8.3%)	0.489	0.125-1.914	0.281
F2-3	20 (90.9%)	2 (9.1%)	0.358	0.073-1.754	0.358
F3-4	9 (90%)	1(10%)	0.398	0.046-3.462	0.358

IL-27, Interleukin-27; HBV, Hepatitis B virus; F, F for One way ANOVA test; P, p value for comparing between the different studied groups;OR, Odd's ratio; CI, Confidence interval.

Table 4. Linkage Equilibrium Analysis of IL-27 (rs181206) and IL-27 (rs17855750) Polymorphism

D statistical	0.045
D' statistical	0.5964
r statistical	0.3829
P value	<0.05

IL-27, Interleukin-27; D, The relative linkage disequilibrium; r, haplotype pairing correlation; P, p value for comparing between the different studied groups.

genotypes, the TT genotype did not show a statistically significant link with the advancement of fibrosis stages F1-2, F2-3, and F3-4. F1-2 had an odds ratio (OR) of 0.489 (95% CI: 0.125-1.914, P = 0.281), F2-3 had an OR of 0.358 (95% CI: 0.073-1.754, P = 0.167), and F3-4 had an OR of 0.398 (95% CI: 0.046-3.462, P = 0.358).

Haplotype analysis of IL-27 genotypes and risk of HBV patients

Table 5. Analysis of IL-27 Haplotype Frequencies with the Risk of HBV

		Cases		Controls		OR (95% CI), p-value
		N	%	N	%	
Haplotypes	TT	155 (69.2%)		76 (76.0%)		r
	CT	50 (22.3%)		21 (21.0%)		1.167 (0.654-2.083), 0.600
	TG	17 (7.6%)		3 (3.0%)		2.778 (0.891-9.804), 0.111
	CG	2 (0.9%)		0 (0/0%)		-----

IL-27, Interleukin-27; HBV, Hepatitis B virus; OR, Odd's ratio; CI, Confidence interval; P-value, The probability value; N, Number; %, Percent; r, Haplotype pairing correlation

The enhanced analytical capabilities of genotype-based analysis are making it a popular tool for enhancing SNP genotyping. To look for a possible link between a mix of IL27 SNPs and HBV infection, we performed a haplotype analysis on the IL27 SNPs. A D' value of 0.5964 and an r^2 value of 0.1466 indicate that the 181206T/C and 17855750 T/G SNPs exhibit LD, according to an LD test that are shown in Table 4. Four possible haplotype frequencies are shown in Table 5 and Figure 2. The results demonstrated that the populations being studied had a somewhat different distribution of haplotypes. All four haplotypes (TT, CT, TG, and CG) were equally common between groups.

Discussion

The HBV poses a substantial risk to worldwide public health, especially in underdeveloped nations. Egypt has a significant prevalence rate of HCV, being among the highest globally [16]. However, the exact prevalence of HBV in Egypt over the whole country is still uncertain. Based on 2019 projections, the global prevalence of HBV infections was approximately 296 million individuals. Unfortunately, the illness led to the deaths of about 820,000 persons due to its likely repercussions. In 2019, the WHO indicated that it is crucial to completely eliminate the HBV by the year 2030. Liver transplantation may be necessary in cases with HBV infection leading to severe liver impairment. The reappearance of HBV in liver transplant patients who have weakened immune systems may greatly elevate the likelihood of graft failure [17].

An important part of inflammation is the production of cytokines, which are powerful chemicals that control the immune system. It is possible to use cytokines to assess the state of the microenvironment in the liver [18]. Initiating and sustaining an adequate immunological and inflammatory response to HBV infection is greatly aided by cytokines, which suppress viral replication in several ways [19]. Research on the effects of cytokine SNPs on infectious illness prognoses, vaccination responses, and treatment outcomes has therefore been extensive in recent years [20–23]. The existence of SNPs in the genes that code for cytokines is the primary cause of the observed variation in clinical presentation across individuals. People with a higher risk of HCC and chronic hepatitis may be identified using these SNPs [24].

HBsAg prevalence in Egypt remains around 2-7% despite the successful prevention of HBV in 1992 [1]. The current study found that a higher percentage of males (ranging from 70% to 81.25%) were included in the fibrosis degree groups compared to females (ranging from 19.75% to 30%). This finding is consistent with previous research [25, 26] that suggests a potential gender bias in HBV infection.

AST, direct bilirubin, albumin, WBCs, and HB levels did not show any noticeable differences between individuals with lower and higher degrees of fibrosis in the ongoing analysis. However, when comparing to milder levels of fibrosis, there was a notable increase in ALT, total bilirubin, and platelets with more severe levels of fibrosis.

An important part of inflammation is the production of cytokines, which are powerful chemicals that control the immune system. It is possible to use cytokines to assess the state of the microenvironment in the liver [27]. Initiating and sustaining an adequate immunological and inflammatory response to HBV infection is greatly aided by cytokines, which suppress viral replication in several ways [28]. Research on the effects of cytokine SNPs on infectious illness prognoses, vaccination responses, and treatment outcomes has therefore been extensive in recent years [25, 26].

The existence of SNPs in the genes that code for cytokines is the primary cause of the observed variation in clinical presentation across individuals. People with a higher risk of HCC and patients with advanced fibrosis compared to those with early stages had higher AST and ALT levels, according to the research by Demir et al. [27]. There was a positive association between liver fibrosis and liver enzymes, but a negative link between fibrosis score and serum albumin [27]. In an independent study, there was no significant difference in AST levels across the different fibrosis groups. In contrast, total bilirubin and INR levels were much greater, and albumin levels were much lower in patients with advanced liver fibrosis [28].

After being activated by naïve cells and NK cells, IL-27 and IL-12 work together to create IFN-δ, which is the primary effect of IL-27 on immature T-lymphocytes. For IL-27 to provide its primary function, it must boost Th1 activity against tumor cells. This involvement has been validated by studies conducted on animals [29].

By reducing the expression of the receptors specific to TNF-α and IL-1, IL-27 may reduce the reactivity of human macrophages to these cytokines [30]. One possible explanation for the higher risk of fatal hepatitis in HBV patients is the elevated production of IL-27. For one thing, IL-27 is crucial for Th1 response promotion, and secondly, chronic Th1 response expansion could produce tissue damage that is out of control and an excess of cell-mediated immune reactions [31].

Evidence from animal studies supports IL-27's principal role, which is to enhance T lymphocyte helper 1 activity against malignant cells. Consequently, SNPs in the IL-27 promoter region may affect IL-27 function in HCC patients. Research on the association between IL-27 SNPs and HBV risk is limited [32, 33].

The researchers in this study set out to determine if and how certain SNPs in the *IL-27* gene affected the development of HBV infection in Egyptian subjects. The scientists looked into the Egyptian population to see whether there was a connection between fibrosis and two SNPs, IL-27 rs181206 T/C and rs17855750 T/G, in individuals with HBV infection.

Statistical analysis of the link between fibrosis phases and the distribution of IL-27 (rs181206) and (rs17855750) genotypes in HBV people was not conducted in the current research.

People who have tested positive for HBV are more likely to have elevated blood levels of IL-27. This increase is associated with liver damage in HBV-positive individuals. According to previous research [34–36]. IL-27 contributes to the immunopathogenesis of HBV infection by increasing inflammation. Also, compared to

both uninfected people and controls, patients with HBV infections who had liver transplants had significantly higher levels of the *interleukin-27* gene, according to a study conducted in 2016 [3].

Ali et al. discovered in 2014 that the frequency and genotyping of the IL-27p28 SNPs (964A/G, 2905T/G, and 4730T/C) in the Egyptian population with respect to HBV infection were only slightly different from one another [37]. Further, neither the genotype nor the allele frequencies of the *IL-27* gene (964A/G and 2905T/G) were significantly different between healthy controls and Chinese individuals with chronic HBV [38]. According to research published in 2016 by Mokhtari et al. [39], SNPs of IL-27 SNP 153109A/G did not contribute to Iranians' increased vulnerability to chronic HBV infection. In the Iraqi population, there is a correlation between HBV infection and elevated plasma levels of IL-27 [40].

In 2019, Tharwat et al. [41] discovered a resemblance in the IL-27 p28 genotypes among patients with HCC and patients with fibrosis (due to the advancement of HCV infection), as well as the healthy control group [41]. People with cirrhosis and HCC who tested positive for HCV in 2020 had significantly higher levels of IL-27 in their blood serum, according to a separate study. There is a significant association between the IL-27 rs153109 G allele with cases of HCC and cirrhosis when compared to a healthy control group [29].

According to the research by Fawzy et al., IL-27 p28 rs153109 SNPa has been identified as a potential genetic biomarker for HCV infection prognosis [41]. No evidence to associate IL-27 with chronic HCV infection among Iranians was found in the 2020 trial conducted by Taghinejad et al. [42]. The IL27 T4730C SNP has been the subject of research on the potential link between heredity and the onset or progression of certain autoimmune diseases. Graves' disease, multiple sclerosis, and Hashimoto's thyroiditis are autoimmune thyroid disorders that are not linked to the SNPs [43, 44].

Treatment effectiveness was also positively correlated with IL-27p28 SNPs rs153109 [45] in those who tested positive for HCV RNA. Systemic lupus erythematosus patients were more likely to have the G allele and the TG genotype (IL-27 p28 +2905 T/G), according to research by Ali et al. [46]. People with the TG genotype and the IL-27 p28 G allele (+2905 T/G) seem to be more likely to develop SLE, according to these results. A p-value of less than 0.01 indicates that the correlation is statistically significant [46].

There is evidence that some IL-27 SNPs, such as rs153109 and rs17855750, increase susceptibility to acute lymphoblastic leukemia. According to the findings, IL-27 is an important factor in the pathophysiology and therapeutic response of this type of leukemia [47].

A new research links the development of allergic rhinitis to decreased IL-27 levels in the blood. On the other hand, the IL-27 p28 gene *rs181206* and *rs153109 SNPs* have not been linked to an increased risk of allergic rhinitis [48].

Among those infected with HBV, the TT haplotype was more prevalent (69.2% vs. 76% in the control group). Research by Peng et al., failed to establish a correlation between IL-27p28 haplotype frequencies and patients with chronic HBV [38].

In conclusion, the current investigation discovered no correlation between IL-27 SNPs rs181206 and rs17855750 and the chronicity of HBV. The research's limited sample size of the population under study may have a possible impact on the results. Subsequent research should take into account the use of more extensive sample sizes.

Author Contribution Statement

Noha E. Ibrahim: contributed to the building of the hypothesis, performing the molecular techniques and biochemical analysis, and participated in writing the manuscript, and made significant revisions to the drafts, and studied the paper before the proposal. Abd El-Gaffar Sabry Oluyemi performed the molecular techniques and biochemical analysis, contributed to doing statistics, contributed to writing, studied the manuscript, and made significant revisions to the drafts and revised the object proposal. Mohamed M. S. Farag and Adel Abd El Basset Mousa: participated in following up on patients and performing the medical tests recommended for them; contributed to reviewing the manuscript. Menha Swellam: Participated in biochemical analysis, examination and interpretation of data, and critical revision. All authors have read and approved the final form of the manuscript.

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Availability of data (if applicable to your research)

All data generated or analyzed during this study are included in this published article (and its supplementary information files).

Conflict of interest

All authors declare no conflict of interest.

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