RESEARCH ARTICLE

Editorial Process: Submission:02/02/2025 Acceptance:07/14/2025

Epidermal Growth Factor (*EGF rs4444903*) Gene Polymorphism and Risk of HCC in Egyptian HCV Cirrhotic Patients

Ehab Mabrouk Abd EL-Maksoud[1], Noha E. Ibrahim[2], Mohamed M. S. Farag[3,4,5], Fatima G. Yehia[6], Eman E. Mohamed[6], Menha Swellam[7]*

Abstract

Background: Hepatocellular carcinoma (HCC) is the most prevalent form of primary liver cancer in Egypt, largely due to the widespread presence of hepatitis C virus. Symptoms of HCC often appear only at an advanced stage, making early detection essential through advanced methods. This study aimed to explore the association between the *rs4444903* gene polymorphism in the epidermal growth factor and the likelihood of developing HCC in individuals with cirrhosis. **Methods:** This study involved 152 ethnically homogeneous Egyptians, categorized into three groups: 49 patients with Hepatitis C Virus (HCV) with Hepatocellular Carcinoma (HCC), 52 patients with HCV but without HCC, and 51 control subjects. DNA was extracted from blood samples, and the *SNP EGF rs4444903* was detected using a genotyping assay. **Results:** The presence of the EGF G allele was significantly more common in patients with hepatocellular carcinoma and chronic hepatitis C compared to the control group (P = 0.006 and P = 0.018, respectively). **Conclusion:** The G allele of the *EGF rs4444903* gene polymorphism is significantly associated with an increased risk of hepatocellular carcinoma (HCC) in Egyptian patients with hepatitis C virus (HCV) infection, identifying it as a potential pathogenic variant. In contrast, the A allele appears to have a protective role. Individuals carrying the G allele may benefit from regular surveillance to enable early detection and timely intervention. Understanding the molecular mechanisms by which EGF polymorphisms contribute to HCC development may provide valuable insights for risk stratification and inform the design of targeted therapeutic strategies.

Keywords: *HCC- EGF-* gene polymorphism

Asian Pac J Cancer Prev, **26 (7)**, 2577-2584

Introduction

Hepatocellular carcinoma (HCC) is the most prevalent type of primary liver cancer globally, primarily affecting individuals with liver cirrhosis resulting from chronic liver disease [1]. The leading risk factors for HCC include chronic infections with hepatitis B and C viruses, excessive alcohol consumption, heavy smoking, and exposure to aflatoxin B1 [2]. Nonetheless, only a minority of those exposed to these risk factors actually develop liver cancer, indicating a multifactorial etiology involving both environmental and genetic components [3].

In Egypt, HCC represents a significant public health challenge [4]. Historically, Egypt had one of the highest prevalence rates of hepatitis C virus (HCV) worldwide, contributing substantially to its HCC burden [5]. In response, the Egyptian government launched large-scale initiatives such as the "100 Million Healthy Lives" campaign in 2018, which dramatically reduced HCV prevalence and led Egypt to become the first country to meet the WHO's hepatitis C elimination targets [6]. Despite this success, HCC incidence remains high due to long-term liver damage and emerging risk factors. As part of continued efforts to combat liver cancer, Egypt has implemented national programs focused on early detection and treatment of HCC, aiming to reduce mortality through enhanced screening and disease management strategies [7].

Many clinicians use the AFP test and abdominal ultrasound for diagnosing HCC, which often leads to a

*[1]Department of Clinical Hematology Laboratory, Suez Canal Authority Hospital, Ismailia, Egypt. [2]Department of Microbial Biotechnology, Biotechnology Research Institute, National Research Centre, El-Bohouth St. (former El-Tahrir St.), Dokki, Giza, P.O.12622, Egypt. [3]Department of Botany and Microbiology, Faculty of Science, Al- Azhar University, Cairo, Egypt. [4]Biomedical Research Department Armed Forces Collage of Medicine (AFCM), Cairo, Egypt. [5]The Regional Center for Mycology and Biotechnology, Al-Azhar University, Cairo, Egypt. [6] Department of Clinical Pathology, Faculty of Medicine (for Girls), Al-Azhar University, Cairo, Egypt. [7]Department of Biochemistry, Biotechnology Research Institute, High Throughput Molecular and Genetic laboratory, Center for Excellences for Advanced Sciences, National Research Centre, Dokki, Giza, Egypt. *For Correspondence: menhamswellam@gmail.com*

delayed diagnosis [8]. Traditional tests for liver disease lack sensitivity and specialization [9], highlighting the need for molecular markers to detect the disease early and accelerate treatment or prevent infection [10]. One such marker is the *EGF rs4444903A/G* gene polymorphism, which has been investigated for its possible association with increased HCC risk, although findings remain debated and inconclusive [11].

HCV infection is known to be a major risk factor for liver cancer, with patients infected with HCV having a higher incidence of liver cancer compared to those with hepatitis B virus [12]. In Egypt, HCV is the primary risk factor for HCC, which is the fourth most common cancer among Egyptians. Recent data show a doubling in HCC cases among patients with chronic liver disease in the country [13]. Liver carcinogenesis is typically linked to ongoing inflammation and hepatocyte regeneration, often associated with chronic hepatitis and cirrhosis [14-16].

The Epidermal Growth Factor Receptor (EGFR) system plays a crucial role in the tumor microenvironment by activating tyrosine kinase, which influences cell proliferation and differentiation, thereby promoting tumor growth [17]. Consequently, the authors aimed to explore the relationship between *EGF (rs4444903) A/G* gene polymorphism and the risk of HCC in Egyptian patients with cirrhotic liver disease due to HCV.

Materials and Methods

Study Design and Population

This case-control study was conducted on a total of 152 ethnically homogeneous Egyptian participants who were categorized into three distinct groups. Group I consisted of 49 individuals diagnosed with chronic hepatitis C virus (HCV) infection and hepatocellular carcinoma (HCC). Group II included 52 patients with chronic HCV infection without evidence of carcinoma. Group III comprised of 51 healthy individuals who served as the control group and were confirmed to be negative for HCV infection.

All participants, including patients and controls, were tested for HCV using both anti-HCV antibody detection and quantitative real-time PCR for HCV RNA. The control subjects were verified to be free from HCV infection by testing negative on both assays.

Patients with HCC were recruited from the HCC clinic at the National Liver Institute Hospital, Menofia University. Patients with HCV but without carcinoma and healthy control subjects were enrolled from the Suez Canal Authority Hospital.

Exclusion criteria applied uniformly across all groups ruled out individuals with co-infections such as hepatitis B virus (HBV) or human immunodeficiency virus (HIV), any malignancy other than HCC, a history of immunosuppressive therapy, organ transplantation, autoimmune disease, diabetes mellitus, or alcohol abuse.

Sample Collection and Clinical Evaluation

Approximately 3 ml of venous blood was collected from each subject into EDTA-containing tubes and immediately stored at -80°C for subsequent analysis. All participants underwent a detailed clinical history, physical examination, and abdominal ultrasonography. For HCC patients, additional diagnostic confirmation was provided through computed tomography imaging.

Laboratory Investigations

A comprehensive panel of biochemical and hematological tests was performed. Liver and renal function tests were conducted using the Dimension Xpand Plus autoanalyzer (Siemens Healthineers, Germany). The coagulation profile, including prothrombin time (PT) and international normalized ratio (INR), was assessed using the Sysmex CA-600 System (Siemens, Germany). Complete blood count analysis was performed with the Sysmex XN-1000 Hematology Analyzer (Sysmex Corp., Japan). Serum alpha-fetoprotein (AFP) levels were measured using the Ortho VITROS 5600 Integrated System (Ortho Clinical Diagnostics, UK). Quantification of HCV RNA was carried out using the Abbott m2000sp/m2000rt Real-Time PCR system (Abbott Molecular, USA).

DNA Extraction

Genomic DNA was extracted from whole blood samples using the GeneJET Whole Blood Genomic DNA Purification Mini Kit (Thermo Scientific™, Cat. No. K0781), following the manufacturer's protocol. DNA purity and concentration were assessed using a NanoDrop™ 2000 spectrophotometer (Thermo Scientific™). All extracted DNA samples were stored at −80°C until used for genotyping.

Epidermal Growth Factor (EGF rs4444903) Genotyping Assay

The rs4444903 single nucleotide polymorphism (SNP) in the epidermal growth factor (*EGF*) gene, involving an A>G substitution, was genotyped using the TaqMan® SNP Genotyping Assay (Assay ID: C__27031637_30; Thermo Fisher Scientific, TaqMan™ Genotyping Master Mix, Cat. No. 4371355) on the Stratagene Mx3005P Real-Time PCR System (Agilent Technologies, USA).

PCR amplification was carried out in a final reaction volume of 20 µL, consisting of 10 µL of TaqMan® Universal Genotyping Master Mix (2X), 0.5 µL of the TaqMan® SNP Genotyping Assay Mix (20X), 5 µL of genomic DNA (10–50 ng), and 4.5 µL of nuclease-free water. The thermal cycling conditions included an initial denaturation step at 95°C for 10 minutes, followed by 40 cycles of denaturation at 95°C for 15 seconds and annealing/extension at 60°C for 1 minute.

Allelic discrimination was performed using the Mx3005P system's integrated software, which automatically classified genotypes as AA, AG, or GG.

Statistical Analysis

Data were statistically analyzed using SPSS version 25.0 (IBM Corp., USA). Categorical variables were compared using the Chi-square (χ^2) test, while continuous variables were analyzed using analysis of variance (ANOVA). Genotype distributions were tested for Hardy-Weinberg Equilibrium (HWE). The association between EGF genotypes and the risk of HCC was evaluated

by calculating odds ratios (ORs) and 95% confidence intervals (CIs). A P-value less than 0.05 was considered statistically significant.

Results

This case-control study involved 101 patients with cirrhotic hepatitis C virus (HCV) infection, divided into two groups: 49 with cirrhotic HCV and hepatocellular carcinoma (HCC), 52 with cirrhotic HCV without HCC, and 51 healthy controls.

Characteristics of the Study Participants

Table 1 showed the general characteristics of the participants. Significant age differences were observed between Egyptian HCV-infected patients (both chronic hepatitis C and HCC) compared to the controls, but gender differences were not significant. No notable difference in bleeding frequency was found between the HCV patients and the healthy controls (P=0.089). However, patients with HCC showed significantly higher levels of ALT, AST, total bilirubin, white blood cells, and alpha-fetoprotein (AFP), alongside lower levels of albumin and platelets, compared to controls.The mean AFP levels were 320± 196 ng/ml for HCC patients, 4.3 ± 2.53 ng/ml for patients without HCC, and 3.37 ± 1.8 ng/ml for controls. AFP levels were significantly higher in HCC patients compared to both non-HCC cirrhotic patients (P < 0.001) and controls (P < 0.001). Liver function tests (ALT, AST, and total bilirubin) were significantly elevated in the HCC group compared to controls, while albumin levels were significantly lower in the HCC group compared to controls (P < 0.001).

Hematological parameters such as INR, hemoglobin, and platelet counts were significantly higher in cirrhotic HCV patients with HCC compared to controls (P < 0.001), and WBC counts were also significantly different. No significant difference was observed between cirrhotic patients without HCC and controls. Platelet counts were significantly different between HCC and non-HCC cirrhotic patients (P < 0.001), while WBC counts did not differ significantly (P < 0.48).

Hardy-Weinberg Equilibrium (HWE) of the Polymorphisms

The genotype distributions for the epidermal growth factor (*EGF (rs4444903) A/G*) gene polymorphisms in the studied groups were consistent with Hardy-Weinberg equilibrium, as indicated in Table 2.

EGF rs4444903 A>G SNP Frequency and risk factors

The EGF genotypes were distributed as follows: AA genotype in 14% of HCC patients, 15% of non-HCC cirrhotic patients, and 29% of controls; AG genotype in 45% of HCC patients, 48% of non-HCC cirrhotic patients, and 53% of controls; GG genotype in 41% of HCC patients, 37% of non-HCC cirrhotic patients, and 18% of controls (Figure 1). Statistically significant differences were found between HCC patients and controls (P=0.0084), and between cirrhotic HCV patients and controls (P = 0.018).

The A allele was present in 37% of HCC patients, 39% of cirrhotic HCV patients, and 56% of controls, while the G allele was found in 63% of HCC patients, 61% of cirrhotic HCV patients, and 44% of controls. Compared to controls, the G allele significantly increased the risk of developing HCC (OR (95% CI) = 2.18, P= 0.006), and was associated with HCC risk in cirrhotic HCV patients (P = 0.018). In recessive models, the GG genotype was significantly associated with HCC risk compared to the AG+AA genotypes (P= 0.0107) and cirrhotic patients without HCC (P= 0.0312), while the dominant model showed less significance (P= 0.06795 for HCC, P= 0.08745 for non-HCC cirrhotic) (Table 3).

EGF gene polymorphism and clinical features

The study found no significant differences between different EGF genotypes and liver function tests, hemoglobin levels, or platelet counts among the groups, as detailed in Tables 4, 5, and 6.

Table 1. Demographic Features, Biochemical Parameters of Egyptian HCV-infected Patients and Control Group

Parameters (Mean ± SD)	Healthy (Control group) n = 51))	HCV –related Cirrhosis (n=101)	F	Sig
Age	46.37 ± 11.5	58.04 ± 8.18	18.38	0
BMI	29.27 ± 1.65	29.07 ± 3.55	10.561	0.001
ALT (IU/L)	30.02 ± 1.95	36.18 ± 20.4	40.79	0
AST(IU/L)	23.98 ± 2.99	39.19 ± 24.7	50.076	0
AFP(IU/L)	3.37 ± 1.80	98.58 ± 243.1	27.89	0
Albumin(g/dl)	3.99 ± 0.26	3.43 ± 0.49	11.68	0.001
Total Bilirubin (mg/dL)	0.831 ± 0.07	1.043 ± 0.73	28.93	0
INR Value	0.98 ± 0.05	1.19 ± 0.87	2.928	0.089
HB	12.5 ± 1.03	13.2 ± 1.84	8.766	0.004
WBCs $x10^3/mm^3$	7.17 ± 1.33	6.89 ± 2.27	9.18	0.003
ANC	2.29 ± 0.32	3.36 ± 1.50	40.8	0
Platelets $x10^3/mm^3$	216.2 ± 44.6	175.3 ± 78.8	16.15	0

% points to percent within group; a points to ANOVA test; Person chi-square test; NS points to Non-significant at p –value ≥ 0.05; SD points to Standard deviation; n points to number of patients; HCC points to Hepatocellular carcinoma; Min points to Minimum; Max points to Maximum.

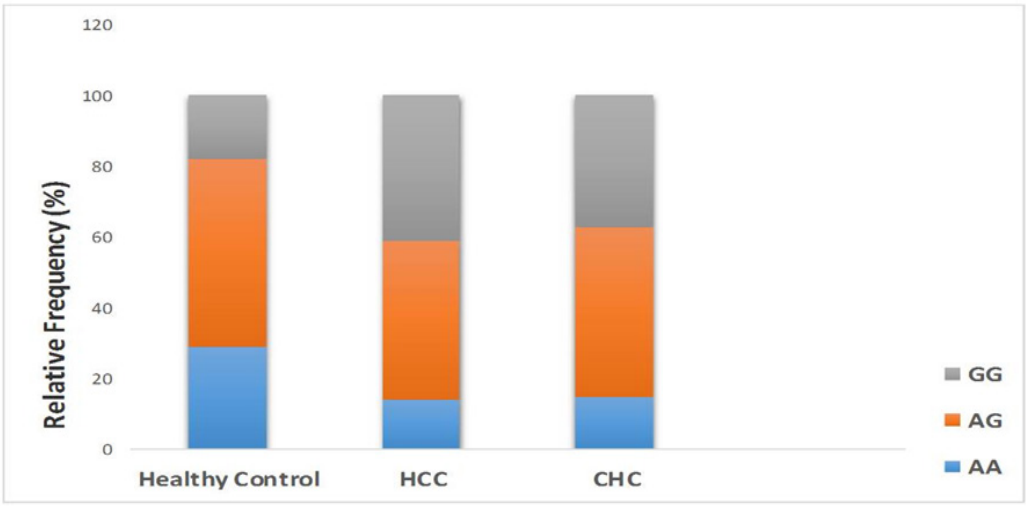

Figure 1. Distribution of *EGF rs4444903* Genotypes among Groups

Table 2. Hardy-Weinberg Equilibrium for *EGF (rs4444903) A/G* Gene Polymorphism

Genotypes	Observed	Expected	X^2	P
HCC patients (n = 49)				
AA	7	6.6		
AG	22	22.8	0.056	0.811
GG	20	19.6		
Chronic hepatitis C (n=52)				
AA	8	7.9	0.002	0.96
AG	25	25.1		
GG	19	19.9		
Control (n = 51)				
AA	15	15.9		
AG	27	25.1	0.27	0.59
GG	9	9.9		

Discussion

The development of hepatocellular carcinoma (HCC) is a multifactorial process influenced by environmental factors, viral infections, and genetic predispositions. Advances in hepatitis C treatment, particularly with direct-acting antivirals (DAAs), have been accompanied by increasing research into the genetic factors contributing to liver cancer progression, including single nucleotide polymorphisms (SNPs) like EGF rs4444903 [18,19].

Liver cirrhosis, a common precursor to HCC, is primarily driven by chronic infections with hepatitis B virus (HBV) and hepatitis C virus (HCV), as well as alcohol use. While not all individuals with these risk factors develop HCC, a subset of patients without them still progress to liver cancer, underscoring the potential role of genetic susceptibility [20].

Recent Egyptian data suggest that treatment with DAAs does not significantly increase HCC recurrence risk, though continuous surveillance remains essential [21]. In Egypt, hepatocellular carcinoma constitutes approximately 70% of primary liver tumors [22], with molecular mechanisms involving dysregulated signaling pathways, particularly the epidermal growth factor (EGF) and its receptor (EGFR) pathway [23–24].

The *EGF rs4444903* gene polymorphism, characterized by an A>G substitution in the 5' untranslated region, has been implicated in various cancers and the epidermal growth factor (EGF) through the EGFR pathway is known to stimulate cell proliferation and differentiation [25-26]. This SNP may influence EGF secretion either by altering mRNA stability, thereby increasing transcription or through linkage with other functional polymorphisms [27]. Elevated EGF levels can promote hepatic inflammation, regeneration, and ultimately carcinogenesis.

We hypothesized that the G allele, especially in GG genotype carriers, may be associated with increased susceptibility to HCC. Our study investigated the association between the EGF rs4444903 polymorphism and HCC risk in HCV-infected Egyptian patients. Although global studies have examined this polymorphism's role in HCC development [28–30], few have specifically addressed its impact in Egyptian populations.

Our findings revealed that the AG genotype was the most prevalent among both HCC patients (45%) and HCV-infected cirrhotic patients without HCC (48%), followed by the GG genotype (41% and 37%, respectively). A statistically significant association was observed between

HCC patients and healthy controls, as well as between cirrhotic patients and controls, suggesting a role of the G allele in liver cancer susceptibility.

These results are consistent with those of Bothina et al. [31], who found AG to be the most common genotype in HCC patients, followed by GG. Interestingly, our study observed a higher frequency of the GG genotype among cirrhotic HCV patients without HCC, a finding that contrasts with El Sergany et al. [32] but aligns with Suenaga et al. [33]. These discrepancies likely reflect population specific genetic variation or gene environment interactions. Supporting our results, a recent PRISMAcompliant metaanalysis incorporating 18 studies (2,692 cases, 5,835 controls) confirmed that the G allele of *EGF rs4444903* significantly increases virusrelated HCC risk across all genetic models (G vs. A: OR1.15, 95% CI 1.02-1.29; GG vs. AA: OR 1.72, 95% CI 1.19-2.48) [34]. Another large case-control study in Chinese Han HCVcirrhotic patients reported that carriers of GG (vs. AA) had a 1.53fold higher HCC risk (P = 0.02) [35].

Conversely, a newly published multiinstitutional analysis found no significant association between rs4444903 and HCC in HBV/HCV coinfected patients (n = 1,200; p = 0.48) [36]. Similarly, a 2021 pooled evaluation across 18 cohorts showed no difference in Gallele frequency between HBV carriers and healthy controls, although GG did predispose to cirrhosis (OR 1.42, 95% CI 1.10–1.82) [37].

Importantly, a 2024 Egyptian cohort confirmed that the G allele elevates HCC risk (dominant model OR 2.83, 95% CI 1.05-7.60) among HCV cirrhotic patients [38]. In contrast, Chinese patients with chronic HBV showed no allele disease correlation (p > 0.05) [39], while an Iranian study identified the A allele as the risk variant (AA vs. GG: OR 1.72, 95% CI 1.02-2.90) [40].

These divergent findings underscore the critical role of ethnic and regional genetic variability in modulating EGF rs4444903's impact on hepatocarcinogenesis. Recent Egyptian studies have reinforced the link between this polymorphism and HCC risk. Bahnasy et al. reported a strong association between the GG genotype and increased HCC risk among cirrhotic HCV patients [41]. Similarly, El-Sayed et al. and El-Mahdy et al. confirmed the prognostic value of this SNP in predicting HCC progression in Egyptian cohorts [42, 43]. Additionally, a 2022 meta-analysis by Zhao et al. validated the broader relevance of EGF rs4444903 in virus-related HCC across multiple populations [44]. Beyond HCC, the G allele has also been linked to an elevated risk of cholangiocarcinoma in Egyptian patients, suggesting a broader oncogenic role [45].

Taken together, our findings, in concordance with regional and international studies, support the hypothesis that *EGF rs4444903* G allele, especially the GG genotype may serve as a genetic marker for increased HCC risk in HCV-infected individuals. These insights underscore the potential utility of EGF polymorphism screening as part of personalized risk assessment in Egyptian populations and call for further research across diverse ethnic groups to validate these associations.

Table 3. Distribution of Genotypes and Allele Frequencies of *EGF (rs4444903) A/G* Gene Polymorphism in Chronic Hepatitis C and HCC Patients Compared to Controls

Alleles /Genotypes	Healthy control	HCC	CHC	Control VS. HCC			Control vs. CHC			HCC VS. CHC		
EGF rs4444903	(n=51) n%	(n=49) n%	(n=52) n%	P	OR	95% CI Lower -Upper	P	OR	95% CI Lower -Upper	P	OR	95% CI Lower -Upper
AA	15(29%)	7(14%)	8(15%)	1 Ref								
AG	27(53%)	22(45%)	25(48%)	0.301	1.74	(0.605- 5.035)	0.286	1.73	(0.628-4.79)	0.992	1.005	(0.313- 3.224)
GG	9(18%)	20(41%)	19(37%)	0.008	4.76	(1.444- 15.703)	0.018	3.958	(1.230- 12.734)	0.763	1.203	(0.364- 3.966)
Alleles A	57(56%)	36(37%)	41(39%)	1 Ref								
G	45(44%)	62(63%)	63(61%)	0.006	1.8	(0.94- 3.4)	0.018	1.1	(0.62-2.04)	0.69	1.6	(0.82-3.02)
Dominant Model AG+GGVSAA	36(70.6%)	42(85.7%)	44(84.6%)	0.067	2.5	(0.918- 6.806)	0.087	2.29	(0.873- 6.012)	0.876	1.09	(0.363- 3.274)
Recessive Model GGVS AA+AG	9(17.64%)	20(40.8%)	19(36.53%)	0.01	3.21	(1.28- 8.06)	0.312	2.686	(01.076- 6.7)	0.659	1.197	(0.537- 2.67)
HWE P Value	0.598	0.811	0.962									

Ref, refers to the reference group; CI, signifies confidence interval; AOR, denotes Adjusted odds ratio; P-value≤ 0.05 Significant; SNP, stands for single-nucleotide polymorphism, and n represents the number.

Table 4. Distribution of Genotypes and Lab Investigations in the Healthy Control Group.

Parameters	AA (n = 15)	AG (n= 26)	GG (n=10)	F	Sig
Age	47.93 ± 9.91	45.42 ± 12.68	46.5 ± 11.59	0.218	0.805
BMI	29.4 ± 1.54	28.8 ± 1.704	30.1 ± 1.44	2.1	0.132
ALT (IU/L)	30.6 ± 1.639	29.88 ± 2.179	29.5 ± 1.716	1.08	0.348
AST(IU/L)	24 ± 3.317	23.92 ± 3.032	2.6 ± 1.173	1.18	0.316
AFP(IU/L)	3.66 ± 1.98	3.5 ± 1.88	2.6 ±1.17	1.181	0.316
Albumin(g/dl)	4.013 ± 0.23	3.96 ± 0.28	4.03 ± 0.283	0.274	0.762
Total Bilirubin (mg/dL)	0.833 ± 0.07	0.823 ± 0.071	0.850 ± 0.07	0.522	0.597
INR Value	0.98 ± 0.04	0.99 ± 0.06	0.985 ± .055	0.283	0.754
HB	12.3 ± 0.89	12.6 ± 1.15	12.54 ± 0.92	0.367	0.695
WBCs $x10^3/mm^3$	7.1 ± 1.36	7.26 ± 1.408	7.05 ± 1.212	0.127	0.881
Platelets $x10^3/mm^3$	219.6 ± 28.5	212.8 ± 57.09	220 ± 25.8	0.148	0.863

% points to percent within group; a points to ANOVA test; Person chi-square test; NS points to Non-significant at p –value ≥ 0.05; SD points to Standard deviation; n points to number of healthy control; Min points to Minimum; Max points to Maximum.

Table 5. Distribution of Genotypes and Lab Investigations in Chronic Hepatitis without HCC

Parameters of CHC	AA (n = 8)	AG (n= 25)	GG (n=19)	F	Sig
Age	53.13 ± 12.3	60 ± 9.904	57.26 ± 9.46	1.46	0.241
BMI	31 ± 3.207	29.5 ± 2.8	28.89 ± 3.61	1.23	0.3
ALT (IU/L)	43.2 ± 46.4	29.5 ± 13.93	29.6 ± 13.04	1.35	0.267
AST(IU/L)	34.38 ± 36.3	27.84 ± 13.43	24.8 ± 10.6	0.804	0.453
AFP(IU/L)	4 ± 2.26	4.7 ± 3.01	3.93 ± 1.97	0.556	0.577
Albumin(g/dl)	3.463 ± 0.42	3.45 ± 0.336	3.532 ± 0.384	0.262	0.771
Total Bilirubin (mg/dL)	0.575 ± 0.22	0.760 ± 0.334	0.758 ± 0362	1.041	0.361
INR Value	1.011 ± 0.13	1.39 ± 1.73	1.03 ± 0.122	0.591	0.558
HB	13.47 ± 1.94	13.28 ± 1.9	13.9 ± 1.8	0.802	0.454
WBCs $x10^3/mm^3$	6.625 ± 1.24	6.93 ± 2.23	8.13 ± 2.45	2.086	0.135
Platelets $x10^3/mm^3$	257.2 ± 84.3	209.8 ± 26.8	201.6 ± 82.6	1.43	0.249

% points to percent within group; a points to ANOVA test; Person chi-square test; NS points to Non-significant at p –value ≥ 0.05; SD points to Standard deviation; n points to number of patients; HCC points to Hepatocellular carcinoma; Min points to Minimum; Max points to Maximum.

Table 6. Distribution of Genotypes and Lab Investigations in Chronic Hepatitis with HCC.

Parameters of HCC	AA (n =7)	AG (n= 24)	GG (n=18)	F	Sig
Age	59.57 ± 4.31	57.75 ± 5.29	58.11 ± 5.88	0.308	0.736
BMI	30.28 ± 1.88	27.4 ± 2.71	29.5 ± 5.20	2.46	0.096
ALT (IU/L)	36.7 ± 26.5	41.08 ± 18.5	42.39 ± 13.73	0.245	0.783
AST(IU/L)	51.8 ± 45.86	51.79 ± 22.9	50.5 ± 19.3	0.014	0.986
AFP(IU/L)	138.9 ± 346	187 ± 281	232 ± 370	0.226	0.798
Albumin(g/dl)	3.32 ± 0.368	3.5 ± 0.638	3.24 ± 0.656	0.975	0.385
Total Bilirubin (mg/dL)	1.657 ± 0.83	1.37 ± 1.15	1.25 ± 0.389	0.504	0.608
INR Value	1.34 ± 0.18	1.15 ± 0.14	1.18 ± 0.24	2.611	0.084
HB	13.2 ± 2.2	12.7 ± 2.04	12.98 ± 1.97	0.219	0.804
WBCs $x10^3/mm^3$	7.38 ± 2.7	6.44 ± 2.18	6.039 ± 2.88	0.924	0.404
Platelets $x10^3/mm^3$	114 ± 52.28	142.2 ± 46.5	131 ± 13.8	0.842	0.437

% points to percent within group; a points to ANOVA test; Person chi-square test; NS points to Non-significant at p –value ≥ 0.05; SD points to Standard deviation; n points to number of patients; HCC points to Hepatocellular carcinoma; Min points to Minimum; Max points to Maximum.

Author Contribution Statement

NEI played a major role in formulating the hypothesis, performing molecular techniques, biochemical analyses, manuscript writing, editing and final review. EMA conducted molecular techniques, biochemical analyses, statistical work, manuscript writing, review, and final editing. MMSF managed patient care and clinical examinations and contributed to manuscript review. FGY,

EEM contributed to biochemical analyses and contributed to manuscript review. MS contributed to biochemical analysis, data interpretation, and manuscript revisions. All authors reviewed and approved the final manuscript.

Acknowledgements

The instruments used in this study were procured with funding from the Science and Technology Development Fund (STDF) through the Capacity Building Grant Fund (CBG).

Approval

Ethical approval was granted by the Medical Ethical Committee of the National Research Centre, Dokki, Giza [No. 05430123].

Conflict of Interest

The authors declare no conflicts of interest related to this work.

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