

## Immunomodulatory Role of Serum Interleukin-37 and Its Association with Biochemical Indicators of Liver Injury in Patients with Chronic HBV and HCV Infections

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### Abstract

**Background:** Chronic viral hepatitis poses a significant health issue in the population because of its progressive capacity to affect liver functioning and the incidence of cirrhosis and hepatocellular carcinoma.

**Purposes:** This study was conducted to identify the levels of interleukin-37 (IL-37) in the blood of patients having chronic hepatitis B or C infections and compare them to the levels of healthy people, and to examine the correlations between levels of IL-37 and signs of liver dysfunction and the prevalence of chronic HBV and HCV infections by age and gender. The participants were compared based on age groups. The level of serum IL-37 was determined by means of enzyme-linked immunosorbent assay (ELISA), and liver function indicators (ALT, AST, ALP, total bilirubin, etc.) were also determined. The gender distribution was counted and evaluated by both sets.

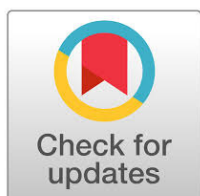
**Findings:** The authors discovered that the majority of the infected people were aged 40–49 (57.7%), with the minimum prevalence being within 50–59 (47.4%). The control group, on the other hand, had the highest frequency in the 50–59 age range (52.6%). Males constituted the majority of the infected patients (61%). The level of IL-37 in the serum of patients with chronic viral hepatitis was significantly greater compared to that in healthy controls (1.064 vs. 0.881 pg/mL,  $P = 0.011$ ). The high levels of liver enzymes (ALT, AST, ALP) and bilirubin indicated liver damage and dysfunction in patients.

**Conclusion:** Interleukin-37 levels are high in chronic HBV and HCV infections and can be used as a biomarker of disease severity, as it helps to regulate the immune system and inflammation of the liver. Explanation of its dual functions requires further research.

### 1. Introduction

The effects of hepatitis viruses are very crucial, particularly in the context of population health; they are a leading cause of morbidity and mortality, and there is a huge amount of spending required on health systems [1,2]. These infectious agents can cause small local outbreaks or large-scale epidemics and can present clinically with either asymptomatic, acute, chronic, or fulminant hepatitis. It is responsible for close to 1.4 million cases annually.

It tops the list of causes of cancer mortality and chief cause of liver cancer records. Chronic liver disease is commonly associated with Hepatocellular carcinoma, which is often a consequence of long-term viral infection resulting in cirrhosis. Distinct viruses that cause liver inflammation upon infection are known as viral hepatitis [3–5]. This has been known since ancient times as epidemic jaundice. It is important to note that viruses, such as the hepatitis B virus (HBV), can integrate their genetic content into the DNA of hepatocytes, leading to chromosomal instability,



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deletions, and rearrangements [8,9]. These changes in the genome can interfere with tumor suppressor genes or activate oncogenes that are critical to cell survival or programmed cell death. The pathogenesis of HBV chronic infection involves repeated liver degeneration and regeneration, with complex interactions between the virus and the host immune system [9,10]. The evolution and maintenance of chronic HBV infection can be considered the result of diverse interactions between the virus and the host immune system. The mechanism of this immune activity is commonly associated with the generation of inflammatory cytokines, such as Interleukin-37 (IL-37) [11,12]. The IL-37 cytokine has been associated with several autoimmune and inflammatory diseases [12,13].

Nevertheless, there are situations where its expression may become deregulated. Some genetic alterations, increased by IL-37 dysfunction, have been linked to a greater risk of severe inflammatory diseases [13]. Of note, IL-37 appears capable of suppressing immune responses. The increase in circulating IL-37 levels has been shown to inversely relate to the progression of hepatocellular carcinoma. In addition, some studies associating protective gene variants of IL-37 with a lower susceptibility to tuberculosis, coronary artery disease, and autoimmune thyroid diseases have been reported. All of these studies together demonstrate the importance of IL-37 as a modulator of inflammatory and immune processes [14,15].

## 2. Study Design

The study involved a case-control cross-sectional study. It involved two key groups: one of patients with chronic hepatitis B (HBV) or hepatitis C (HCV) infection, and a control group of healthy, liver disease-free, and virus-free individuals. The subjects were recruited to the study based on a diagnosis of hepatology and infectious disease clinics, and serum interleukin-37 (IL-37) levels were compared with clinical biochemical indicators of liver damage (including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total bilirubin) in patients and healthy controls. Age and gender data were also collected to assess their distribution and the potential association with disease prevalence.

### 2.1. Subjects, materials, and methods

This research involved a total of 190 biological samples collected from participants for the purposes of the study. The study was conducted over four months (September to December 2022) across multiple healthcare facilities in Al-Anbar province, including General Al-Ramadi Hospital and its dialysis center, the Blood Bank at Al-Anbar Public Health Laboratory, and laboratories in Al-Fallujah city.

### 2.2. Blood collection

Each participant provided 5 mL of venous blood, divided into three aliquots. Three milliliters were placed in a gel

tube, chilled at 4 °C for 15 min to induce clotting, then centrifuged at 3,000 rpm for 5 min at 4 °C. The separated serum was aliquoted into Eppendorf tubes and stored at -20 °C for later analysis of liver function, other parameters, and IL-37.

### 2.2.1. Serum level of interleukin-37

Interleukin-37 (IL-37) ELISA kit remained in stock for sale to assess IL-37 levels in Human serum, plasma, culture media, or any biological fluid, such as urine.

Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin levels were measured using enzymatic colorimetric methods with commercially available diagnostic kits according to the manufacturer's instructions. The analysis was carried out using an automated biochemistry analyzer, and the results were expressed in international units per liter (IU/L) for enzymes and in milligrams per deciliter (mg/dL) for total bilirubin.

### 2.3. Calculation of results

To represent the relationship between the known concentrations of human IL-37 standards and their corresponding optical density (OD) values, both the x-axis (log scale) and y-axis were utilized. The concentration of human IL-37 in each sample was determined by reading the OD value along the y-axis. The initial concentration of each sample was then obtained by multiplying the measured value by the corresponding dilution factor.

### 2.4. Statistical analysis

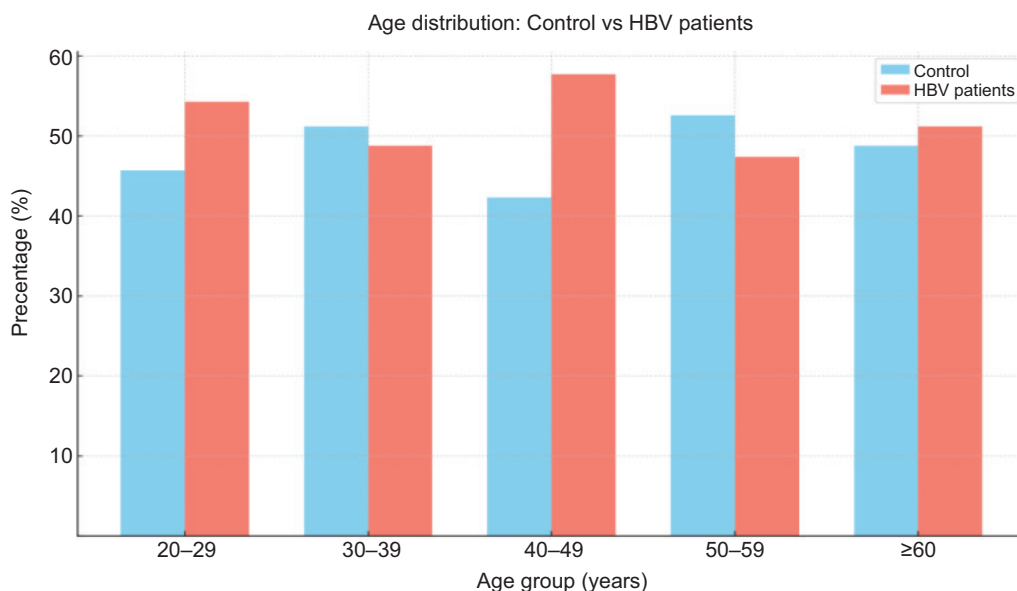
The T-test at the 0.05 level, the running test, test 1.05, the analysis test with SPSS statistical software, and the hosting with an Excel program to show the findings were all employed in the data analysis [20].

## 3. Results and Discussion

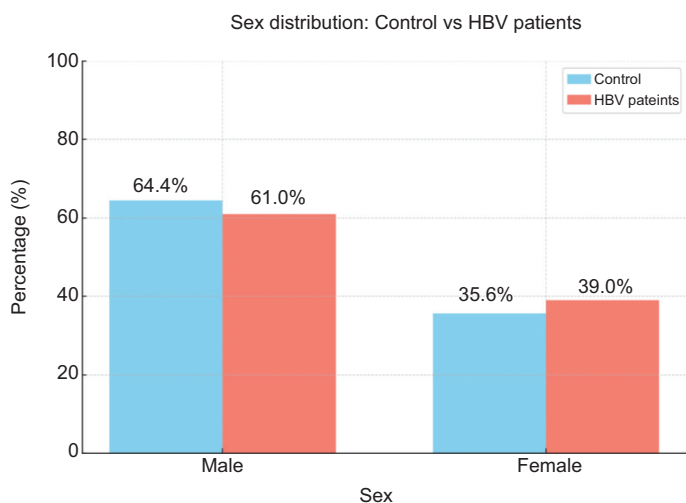
When HBV and HCV patients were categorized according to their ages, it was found that the 40–49 year age group had the highest frequency of 57.7% (30 n), while the 50–59 year age group had the lowest frequency of 47.4% [9], as shown in Figure 1.

Among the HBV and HCV patients recruited, 39% were females, and 61% were males. 64.4% of the control group's members were men and 35.6% were women, the same ratios as those seen in the sick group (Figure 2).

The findings confirmed the age and sex match between HBV cases and controls. However, it was shown that those aged 41–49 were more likely than others to become infected with HBV and HCV. As a result, males were discovered to be more susceptible to HBV and HCV infection. Previous Iraqi research exposed that the majority of HBV patients were under the age of 50 and that males were more likely to be infected than women [21,22]. As a result, male sex and reproductive age may be regarded as risk factors for HBV infection. Higher age, being male, poorer



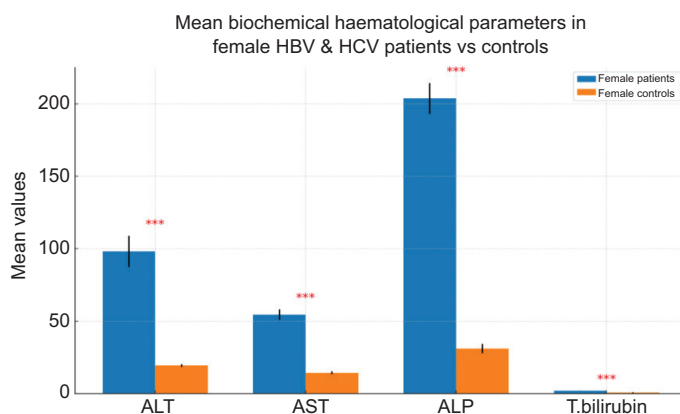
**Figure (1):** Hepatitis B and C virus infected patients divided into age groups.



**Figure (2):** Sex distribution among HBV- and HCV-infected patients.

economic level, a family history of hepatitis, a history of dental treatment, and hospitalization were all risk factors [21]. The current study found a higher prevalence among males than among females, which is consistent with the findings of Hussein [22], who found that males were more at risk of infection depending on their professions [21,23,24]. It was significantly increased in the mean value of hepatitis C and B patients compared to controls (1.064 vs 0.881 pg/mL;  $P = 0.011$ ).

Interleukin-37 (IL-37) was associated with chronic HBV \*infection, indicating the role for IL-37 in the immune pathogenesis of such infections [25]. This investigation did not agree with Zhao's [26] finding that lower IL-37 expression was associated with HCC development. However, it agreed with the findings of Li [25], who stated that higher serum IL-37 levels were seen in individuals infected with hepatitis. IL-37 serum level was enhanced in chronic HIV infection [27] and was connected with infection and the amount of the full viral tank [26]. Figure 3 shows a



**Figure (3):** Mean biochemical hematological parameters in female hepatitis B and C patients and controls.

substantial increase ( $P < 0.001$ ) in the mean values of GPT, GOT, ALP, and total bilirubin. Furthermore, the results show that there is a significant decrease in the mean value of Hb ( $P < 0.001$ ) and PLT ( $P < 0.001$ ) for female hepatitis C and B patients compared with female control groups

In HBV- and HCV-infected individuals, liver function tests (LFTs) are biomarkers that may be used to evaluate hepatic function and disease severity. The current study results show that HBV can alter blood levels of liver enzymes, including ALT, AST, and ALP [30]. Conducted in Falluja, discovered that individuals with chronic hepatitis B showed a substantial rise in blood levels of liver functions (T.S.B., ALT, and AST) [29,30]. While T.S.B. did not demonstrate any significant changes, Mohsen et al.'s [17] study in Baghdad found that chronic HBV patients had higher levels of the liver enzymes AST, ALT, and ALP than controls. Since there was no discernible difference in the blood level of TSB between HBV patients and controls, this serum protein might not be connected to HBV chronicity. Increased levels of TSB are often linked to acute HBV infection rather than chronic infection; hence, these

results may be expected [29]. Acute HBV infection is typically associated with significantly elevated TSB levels, and these studies are consistent with Mohsen et al. [17]. There were no significant differences between the research groups in TSB in chronic HBV patients compared with controls. The current study was in line with earlier research conducted in Iraq, which noted that HCV patients had significantly higher levels of AST, ALT, and bilirubin than the control group [30,31]. Eventually, it was discovered that Ali et al. [31], who had elevated serum ALT levels comparable to those of healthy controls, had acute HCV. ALT is the most commonly used marker for liver activity and is used as a secondary signal for hepatic inflammation or injury. The AST and ALT records were also discovered in certain studies to be the most accurate predictors of liver fibrosis [28].

#### 4. Conclusions

Although serum IL-37 levels were significantly higher in patients with chronic hepatitis B and C compared to healthy controls, suggesting an immunomodulatory role in liver inflammation and disease progression, its clinical application as a diagnostic marker remains limited. The variability in IL-37 levels due to multiple factors, such as disease stage, immune status, and coexisting conditions, limits its reliability as a standalone indicator. However, given its consistent elevation among infected patients, IL-37 may still serve as a supportive or adjunctive biomarker for assessing disease activity and immune response when interpreted alongside conventional biochemical parameters (ALT, AST, ALP, and bilirubin).

#### Authors' contributions

Contributor Role	Degree of Contribution		
	Lead	Equal	Supporting
Conceptualization	RTM	RTM	RTM
Data curation	RTM	RTM	RTM
Formal analysis	RTM	RTM	RTM
Funding acquisition	RTM	RTM	RTM
Investigation	RTM	RTM	RTM
Methodology	RTM	RTM	RTM
Project administration	HS	HS	HS
Resources	HS	HS	HS
Software	HS	HS	HS
Supervision	HS	HS	HS
Validation	HS	HS	HS
Visualization	HS	HS	HS
Writing—original draft	RTM	RTM	RTM
Writing—review & editing	RTM	RTM	RTM

#### Ethical Approval

The ethical approval was provided by the Ministry of Higher Education and Scientific Research, University of

Anbar, Scientific Study Ethics Committee, Number 166, dated June 01, 2022.

#### Data Availability

Data supporting the findings of this study are available upon request from the corresponding author.

#### Funding Resources

No funding resources.

#### Conflict of Interest

The authors declare no conflict of interest with other previous studies.

#### References

- [1] Abutaleb, A.; Kottiril, S., Hepatitis A: epidemiology, natural history, unusual clinical manifestations, and prevention. *Gastroenterol Clin N Am*, 49: 191–199, 2020. <https://doi.org/10.1016/j.gtc.2020.01.002>
- [2] Carty, M.; Guy, C.; Bowie, A.G., Detection of viral infections by innate immunity. *Biochem Pharmacol*, 183: 114316, 2021. <https://doi.org/10.1016/j.bcp.2020.114316>
- [3] Mohsen, R.T.; Iman, A.K.; Alkubaisi, M.R.; Al-Tae, H.Z.; Wafaa, H.H.; Hassanb, S., Hepatitis virus-related microRNA-122 gene and biochemical parameters in Iraqi patients with hepatocellular carcinoma. *Egypt J Med Microbiol*, 34(1): 141–148, 2025. <https://doi.org/10.21608/ejmm.2024.317083.1324>
- [4] Mohsen, R.T.; AL-azzawi, R.H.; Adhiah, A.H., Single-nucleotide polymorphism of IL12A gene (rs582537 A/C/G) and susceptibility to chronic hepatitis B virus infection among Iraqi patients. *Egypt J Med Hum Genet*, 23(1): 1–3, 2022. <https://doi.org/10.1186/s43042-022-00322-9>
- [5] Jefferies, M.; Rauff, B.; Rashid, H.; Lam, T.; Rafiq, S., Update on global epidemiology of viral hepatitis and preventive strategies. *World J Clin Cases*, 6(13): 589, 2018. <https://doi.org/10.12998/wjcc.v6.i13.589>
- [6] Robinson, A.; Wong, R.; Gish, R.G., Chronic hepatitis B virus and hepatitis D virus: new developments. *Clin Liver Dis*, 27: 17–25, 2023. <https://doi.org/10.1016/j.cld.2022.08.001>
- [7] Mohsen, R.T.; Al-Tae, H.Z.; Wafaa, H.H.; Abd-Alazeeza, R.A.; Hassanb, S.; Mohsen, S.T., MicroRNA-122 gene expression in Iraqi patients with hepatocellular carcinoma. *Asia Pac J Mol Biol Biotechnol*, 32(4): 245–250, 2024. <https://doi.org/10.35118/apjmbb.2024.032.4.25>
- [8] Dinarello, C.A.; Nold-Petry, C.; Nold, M.; Fujita, M.; Li, S.; Kim, S.; Bufler, P., Suppression of innate inflammation and immunity by interleukin-37. *Eur J Immunol*, 46: 1067–1081, 2016. <https://doi.org/10.1002/eji.201545828>
- [9] Hassan, S.; Mohsen, R.T.; Farman, S., Interleukin-37 gene single nucleotide polymorphisms and patient susceptibility to hepatitis B and C infection. *Opera Med Physiol*, 11(1): 52–60, 2024. <https://doi.org/10.24412/2500-2295-2024-1-52-60>
- [10] Ding, S.-X.; Ma, J.-B.; Hu, Y.-R.; Hu, A.R.; Shen, Q.; Gao, G.-S., Outcomes of interferon/ribavirin therapy in patients with

- HCV defined by expression of plasma soluble human leukocyte antigen-G but not IL-37. *Med Sci Monit*, 22: 1398–1402, 2016. <https://doi.org/10.12659/msm.895971>
- [11] Iman, A.K.; Anmar, K., Association of microRNA-155 gene polymorphism and the incidence of systemic lupus erythematosus in Iraqi patients. *Asia Pac J Mol Biol Biotechnol*, 31(4): 22–26, 2016. <https://doi.org/10.35118/apjmbb.2023.031.4.10>
- [12] van Deuren, R.C.; Arts, P.; Cavalli, G.; Jaeger, M.; Steehouwer, M.; van de Vorst, M.; et al. Impact of rare and common genetic variation in the interleukin-1 pathway on human cytokine responses. *Genome Med*, 13: 94, 2021. <https://doi.org/10.1186/s13073-021-00907->
- [13] Mohsen, R.T.; AL-azzawi, R.H.; Adhiah, A.H., Serum level of interleukin-35 in patients with chronic hepatitis B virus infection. *Iraqi J Sci*, 61(11): 2860–2865, 2021. <https://doi.org/10.24996/ij.s.2020.61.11.9>
- [14] Zhao, J.J.; Pan, Q.Z.; Pan, K.; Weng, D.S.; Wang, Q.J.; Li, J.J.; et al. Interleukin-37 mediates the antitumor activity in hepatocellular carcinoma: role for CD57+ NK cells. *Sci Rep*, 4: 5177, 2014. <https://doi.org/10.1038/srep05177>
- [15] Allam, G.; Gaber, A.; Othman, S.; Abdel-Moneim, A., The potential role of interleukin-37 in infectious diseases. *Int Rev Immunol*, 39(1): 3–10, 2020. <https://doi.org/10.1080/08830185.2019.1677644>
- [16] Yin, D.; Naji, D.H.; Xia, Y.; Li, S.; Bai, Y.; Jiang, G.; et al. Genomic variant in IL-37 confers a significant risk of coronary artery disease. *Sci Rep*, 7: 42175, 2017. <https://doi.org/10.1038/srep42175>
- [17] Mohsen, R.T.; Al-Azzawi, R.H.; Ad'hiah, A.H., Hepatitis B virus genotypes among chronic hepatitis B patients from Baghdad Iraq and their impact on liver function. *Gene Rep*, 17: 100548, 2019. <https://doi.org/10.1016/j.genrep.2019.100548>
- [18] Li, C.; Ji, H.; Cai, Y.; Ayana, D.A.; Lv, P.; Liu, M.; et al. Serum interleukin-37 concentrations and HBeAg seroconversion in chronic HBV patients during telbivudine treatment. *J Interferon Cytokine Res*, 33(10): 612–618, 2013. <https://doi.org/10.1089/jir.2013.0001>
- [19] Ding, L.; Hong, X.; Liu, D., The role of Interleukin-37 in inflammation: suppression or pro-motion? *J Rheum Dis Treat*, 4: 058, 2018.
- [20] Haaland, P.D., Separating signals from the noise. *Experimental Design in Biotechnology*. CRC Press: Boca Raton, FL, 2020, pp. 61–83. <https://doi.org/10.1201/9781003065968>
- [21] Merza, M.A., Characteristics of chronic hepatitis B virus patients related liver cirrhosis in a tertiary care referral hospital, Duhok, Iraqi Kurdistan. *J Gastroenterol Pancreatol Liver Disord*, 4: 1–5, 2017. <https://doi.org/10.15226/2374-815X/4/5/00199>
- [22] Li, H.; Guo, J.; Cheng, G.; Wei, Y.; Liu, S.; Qi, Y.; et al. Identification and validation of SNP-containing genes with prognostic value in gastric cancer via integrated bioinformatics analysis. *Front Oncol*, 11: 564296, 2021. <https://doi.org/10.3389/fonc.2021.564296>
- [23] Hussein, M.U.; Mohsen, R.T., Evaluation of a plasma torch in the inhibition of *Escherichia coli* bacteria in water. *AIP Conf Proc*, 3051: 020014, 2024. <https://doi.org/10.1063/5.0191668>
- [24] Hussein, M.U.; Mohsen, R.T., Ambient decontamination by non-thermal plasma in atmospheric pressure air. *J Phy Conf Series*, 1032(1): 12032, 2017. <https://doi.org/10.24996/IJS.2022.63.11.9>
- [25] Mohsen, R.T.; Al-Taeae, H.Z.; Wafaa, H.H.; Anmar, K., Iraqi patients with a single-nucleotide polymorphism of interleukin-10 -1082G/A and interleukin-6 -174G/C susceptibility to asthma. *Asia Pac J Mol Biol Biotechnol*, 32(3): 49–55, 2024. <https://doi.org/10.35118/apjmbb.2024.032.3.06>
- [26] Samarani, S.; Abulkhir, A.; Amre, D.; Mehraj, V.; Tremblay, C.; Routy, J.P.; et al. The anti-inflammatory IL-37/SIGIRR axis is functionally compromised in HIV infection. *AIDS*, 33(11): 1693–1703, 2019. <https://doi.org/10.1097/qad.0000000000002271>
- [27] Højen, J.F.; Rasmussen, T.A.; Andersen, K.L.D.; Winckelmann, A.A.; Laursen, R.R.; Gunst, J.D.; et al. Interleukin-37 expression is increased in chronic HIV-1-infected individuals and is associated with inflammation and the size of the total viral reservoir. *Mol Med*, 21: 337–345, 2015. <https://doi.org/10.2119/molmed.2015.00031>
- [28] Mohsen, R.T.; Alsnbl, O.I.; Ahmed, Z.A., Blood group and liver function parameters in pregnant women Infected with *Toxoplasma gondii*. *Samarra J Pure Appl Sci*, 5(3): 121–127, 2021. <https://doi.org/10.54153/sjpas.2023.v5i3.538>
- [29] Saod, W.M.; Zaidan, T.A.; Alfaluji, A.W.A.R., Hepatitis B and renal function of patients with chronic hepatitis B in Fallujah district, Iraq. *Biochem Cell Arch*, 19(1): 1999–2004, 2019. <https://doi.org/10.35124/bca.2019.19.S1.1999>
- [30] Yosur, F.A., Genetic polymorphisms of some interferons associated with chronic viral hepatitis B and C. PhD Thesis, College of Medicine, University of Babylon, Babylon, Iraq, 2018.
- [31] Ali, S.J., A correlative study between haematological and biochemical parameters in hepatitis B. *Ibn Al-Haitham J Pure Appl Sci*, 32(2): 21–29, 2019. <https://doi.org/10.30526/32.2.2127>