Plant Archives Vol. 20, Supplement 2, 2020 pp. 4171-4173 **e-ISSN:2581-6063 (online), ISSN:0972-5210**

SERUM LEVELS OF INTERLEUKIN-28B IN IRAQI PATIENTS WITH HEPATITIS C VIRUS INFECTION

Sahib A. Hussein*[1,2] and Raghad H. Al-Azzawi[2]
[1] Ministry of Health, Baghdad Health Alkarkh Directorate, Alfurat Hospital, Iraq
[2] Department of Biology, College of Science, University of Baghdad, Iraq
*Corresponding Author Email : sahb1972sahb@gmail.com

Abstract

Hepatitis C virus (HCV) is a major cause of chronic viral hepatitis that can lead to cirrhosis and hepatocellular carcinoma. This research was conducted to provide further insight into classical risk factors (gender, hypertension , diabetes and smoking). In addition, to obtain further interpretation on the effect of the causal agent to excite inflammatory mediators such as IL-28β. Ninety eight patients with Hepatitis C virus (HCV), 52 without treatment with average age ± SE (45.26 ± 2.97) years and 46 received Harvoni drug their average age ± SE (39.30 ± 3.90) years were involved in this study as well as (80) healthy individuals their average age ± SE (29.40 ± 2.84) as control. These patients were attending to Special Nursing Home Hospital in Baghdad between December 2018 and January 2019. They were identified with this illness by using a real-time PCR to concentrate the viral level. In this research showed that the most patients at the fourth decade of age; female were affected more than male, In general the results showed no positive effect for other risk factors (smoking, Diabetes mellitus and Hypertension) among studied patient groups. IL-28β level detected by enzyme linked immune sorbent assay (ELISA). The recent data exhibited that the concentration of serum IL-28β was raised non-significantly in both groups untreated patient group (181.83 ± 33.27pg/ml) and treated patient group (161.02 ± 8.97 pg/ml) versus apparently healthy volunteers as control group (155.77 ± 9.24pg/ml). Furthermore there was no important variance between untreated patient group and treated patient group. Moreover, the present results was appeared no positive affect of the age and gender on the serum IL-28β concentration. These findings displayed that the Hepatitis C virus plays an essential role in the development of IL-28β stimulation.

Keywords: Hepatitis C virus; Intereukin-28β; Iraqi patients

Introduction

Hepatitis C is a liver disease that acts the lives of the region's 14 million people about one in every 50 people. This is caused by the hepatitis C virus (HCV) and may cause serious complications, including cirrhosis and liver cancer, both acute and chronic infections (WHO, 2019). About more than 120 million, or 3 percent of the world's were HCV-infected people. Depending to the World Health Organization (WHO), nearly 3 - 4 million new cases of Hepatitis C virus infection are reported yearly (Morozov and Lagaye 2018). It is a major cause of hepatic morbidity and mortality by its predisposition to liver fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). Annually, HCV causes about more than 390,000 deaths world-wide, mostly from cirrhosis and hepatocellular carcinoma (Renau and Berenguer 2018). In Iraq, hepatitis C is considered of little endemicity. The prevalence of anti-HCV was little (0.4%) (Hanan *et al.,* 2019). HCV prevalence was with a range of 0.32 % to 7.1 % in Iraqi general people (Abdulghani *et al*., 2016). Innate immune responses are the initial line of defense alongside viral infections and interferons (IFNs) are the main cytokines responsible for inducing an antiviral state in cells and for stimulating and controlling the cellular components of innate immunity, such as natural killer (NK) cells (Stetson and Medzhitov, 2006). There are three members of the IFN- λ family: IFN-λ1, IFN-λ2, and IFN-λ3. The genomic structures of IFN- λ are similar to those of the IL-10 family (Renauld, 2003) and (Langer *et al*., 2004). Thus they were independently qualified as IL-29 (IFN-λ1), IL-28α (IFN-λ2) and IL-28β (IFN-λ3) (Sheppard *et al*., 2003) At the amino acid level and functionally, however, IFN- λs are more correlated to type IFNs than to IL-10. They activate the feature of interferon stimulated response (ISRE) and induce antiviral activity (Kotenko, 2003) and (Li, and Huang, 2007). IFNs are commonly regarded as antiviral cytokines in innate immune responses. In the type III IFN family, IFN-λ1, IFN-λ2 & IFN-λ3 represent antiviral activities against a range of viruses in vitro (Sheppard *et al*., 2003) (Li and Huang, 2007). This rapidly raised questions about the functions of IFN-λs in limiting the replication of major human pathogenic viruses. The first report about the antiviral response of IFN-λs is that IFN-λs can block the replications of hepatitis C virus and hepatitis B virus in vitro (Jian-hua *et al*., 2018).

On the basis of the above, this research aimed to measure serum levels of IL-28β in patients infected with HCV and its relationship with patients' gender and age.

Materials and Methods

Patients and control

Ninety eighty consecutive patients with Hepatitis C virus (HCV) were included in this study. They were admitted to Special Nursing Home Hospital in Baghdad between December 2018 and January 2019. These patients were divided into two clinical subgroups 52 without treatment with average age ± SE (45.26 ± 2.97) years and 46 received Harvoni drug their average age ± SE (39.30 ± 3.90) years. Eighty apparently healthy volunteers included in this study as a control group, with average age ± SE (29.40 ± 2.84) years. The viral load of hepatitis C virus was detected by Real-Time PCR. Serum level of IL-28β was estimated by Elisa kit produced by (Omnikine, U.S.A). The sandwich technique is the scientific principle on which Elisa kit performed. Standard protocols mentioned by the producers were followed in these evaluations.

Results and Discussion

The serum level of IL-28β was assessed in three study groups. As shown in Table 1, the mean of serum IL-28β

concentration in untreated hepatitis patients group (181.83 ± 33.27 pg/ml) was non-significantly higher than both treated hepatitis patients group (161.02 ± 8.97 pg/ml) and healthy controls group (155.77 ± 9.24 pg/ml). Treated hepatitis patients group was also higher than that for healthy controls but with non- significant differences (P > 0.05).

As revealed in Table 2 the age factor is not affected significantly on quantity of serum IL-28β where there were no significant differences among study groups.

In addition there was non-significant difference in serum IL-28β level among searching groups when distributed according to gender (Table 3).

Table 1: Comparison between difference groups in IL-28 level

Groups	Number	Mean ± SE(pg/ml)
Without treatment	52	181.83 ± 33.27
With treatment	46	161.02 ± 8.97
Control	80	155.77 ± 9.24
LSD value	---	53.440 NS*
P-value	---	0.584
*Non-Significant.		

Table 2 : Effect of Age on IL-28β levels among different study groups

Groups	Mean ± SE of IL-28 (pg/ml)		T-test
	Least than 40	40 and more than	
Without treatment	138.27 ± 11.78	209.03 ± 53.08	140.95 NS*
With treatment	154.47 ± 10.76	171.93 ± 16.01	38.56 NS*
Control	147.86 ± 10.46	174.21 ± 18.38	40.445 NS*
LSD value	36.087 NS	124.03 NS*	---
P-value	0.721	0.766	---
*Non-Significant.			

Table 3: Effect of gender on IL-28β levels among different study groups

Groups	Mean ± SE of IL-28 (pg/ml)		T-test
	Male	Female	
Without treatment	157.90 ± 27.78	192.45 ± 46.78	151.16 NS*
With treatment	172.58 ± 17.34	155.24 ± 10.42	39.65 NS*
Control	133.53 ± 13.46	166.48 ± 11.65	38.99 NS*
LSD value	55.946 NS*	75.179 NS*	---
P-value	0.320	0.627	---
*Non-Significant.			

There was a variation in the results of researches with respect to the IL-28β levels for patients infected with HCV; Some of local prior outcomes similar to the present study such as Al-Qahtani *et al*. (2015), Alazzawy, (2018), Yosur, (2018), and other universal studies like Diegelmann *et al*. (2010), Dolganiuc *et al*. (2012) and Lee *et al*. (2014).

Although The recent study exhibited non-significant increase of IL-28β in patient groups may be because of small sample size but agree with the Arabic previous study by Al-Qahtani *et al*. (2015) indicated that serum levels of IL28B have a significant association with the various outcomes of HCV infection, especially among patients with cirrhosis and HCC, where serum levels of IL28 appear to increase with disease progression. Also Alazzawy (2018) who recorded that IL-28β level was amplified in Hepatitis C Virus patients who were negative confirmed by PCR and was a highly substantial relation of IL-28β with the clearance of HCV. In addition the prior research in Iraqi patients by Yosur, (2018) who exhibited that the amount of serum IL28β in patients with HCV infection was bigger (0.14 ± 0.005pg/ml) than that of control group (0.06 ± 0.002pg/ml). Diegelmann, *et al*. (2010), Dolganiuc *et al*. (2012) recorded that the level of IL-28β raised in chronic HCV infected patient versus to apparently healthy volunteers and patient with non-viral liver disease. Lee *et al*. (2014) mentioned that IL-28β transcription is more in patient with HCV than control.

In contrast in Iraq prior study by Sara, (2017) revealed that the level of IL-28β was non significantly decreased in HCV patients (145.578 ± 235.520 pg/ml) compared to control (235.418 ± 173.181 pg/ml). on the other hand Alborzi *et al*. (2017) indicated that the quantity of IL-28β in serum of patient with HCV is significantly less than that in serum of Quality control. Another study when performed comparison among untreated patients with HCV, recovered persons and healthy control was revealed that the level of IL-28β and mRNA transcription were decreased considerably in the untreated group versus clearance and healthy control groups (Shi *et al*., 2012)

Israelow *et al*. (2014) were showed in their research on primary human hepatocytes (PHH) that the HepG2-HFL cells had a strong native immune response to HCV infection related with amplified levels of interferon-λ, cytokine levels and interferon-stimulating gene (ISG). Zhang *et al*. (2011) were recorded that IFNλ3 inhibits HCV reproduction in a dose and time dependent way. IFN-based therapy in HCV-infected hepatocytes decreases the expression of miR-122, and co-treatment of IFN-λ and miR-122 inhibitors leads to enhanced suppression of HCV replication Lee *et al*. (2014).

Interleukin-29, Interleukin-28A and Interleukin-28β belong to cytokine family Group II that induced by infection with virus. In addition to their antivirus activities,

interferons-λs can modulate the effects of inherited immune responses (SNP-19). Interferon-λ3 proteins have ability to modulating immunological functions, up-regulate class I antigen expression of major histocompatibility complex and exhibited strong antitumor and antiviral action (Kotenko, 2003).

References

Abdulghani, M.A.; Gailan, A. and Amina, H.A. (2016). Seroprevalence of Hepatitis C Virus in Iraqi Population. J. Immuno Virology 1(3).

Alazzawy, M.A. (2018). Role of Interleukin-28B in clearance of HCV in acute and chronic hepatitis patients in Kirkuk city. J. KAJR. 2411-7684.

Alborzi, A.; Hashempour, T.; Moayedi, J.; Musavi, Z.; Pouladfar, G. and Merat, S. (2017). Role of serum level and genetic variation of IL-28B in interferon responsiveness and advanced liver disease in chronic hepatitis C patients. J. Med Microbiol Immunol., 206(2): 165-174.

Al-Qahtani, A.; Al-Anazi, M.; Ayman, A.A.; Faisal, M.S.; Al-Hamoudi, W.; Alswat, K.A.; Al-Ashgar, H.I.; Mohammed, Q.K.; Albenmousa, A.; Nisreen, K.; Nisha, V. and Al-Ahdal, M.N. (2015). Correlation between Genetic Variations and Serum Level of Interleukin 28B with Virus Genotypes and Disease Progression in Chronic Hepatitis C Virus Infection. J. Imm. (10).

Diegelmann, J.; Beigel, F.; Zitzmann, K.; Kaul, A.; Goke, B.; Auernhammer, C.; Bartenschlager, R.; Diepolder, H. and Brand S. (2010). Comparative analysis of the lambda-interferons IL-28A and IL-29 regarding their transcriptome and their antiviral properties against hepatitis C virus. PLoS One; 5:e15200.

Dolganiuc, A.; Kodys, K.; Marshall, C.; Saha, B.; Zhang, S.; Bala, S. and Szabo G. (2012). Type III interferons, IL-28 and IL-29, are increased in chronic HCV infection and induce myeloid dendritic cell-mediated FoxP3+ regulatory T cells. PLoS One; 7:e44915.

Hanan, N.N.; Dheyaa, J.K.; Ahmed J. and Dheyaa, A.A. (2019). Depression, Anxiety and Stress Among a Sample of Chronic Hepatitis C Patients in AL-Najaf Province /Iraq. J. Res. Pharm. Sci., 10(4): 3170-3177.

Israelow, B.; Narbus, C.; Sourisseau, M. and Evans M. (2014). HepG2 cells mount an effective antiviral interferon-lambda based innate immune response to hepatitis C virus infection. J. Hepato. 60(4):1170–9.

Jian-hua, Z.; Yi-ning, W.; Qiu-yan, C.; Peng, M.; Yonghao, H. and Xin, C. (2018). Type III Interferons in Viral Infection and Antiviral Immunity. J. Cell Physiol Biochem., 51: 173-185.

Kotenko, S.V. (2003). IFN-lambdas. J. Imm., 23: 583–590.

Langer, J.A.; Cutrone, E.C. and Kotenko, S. (2004). The class II cytokine receptor (CRF2) family: overview and patterns of receptor-ligand interactions. Cytokine Growth Factor. J. Rev. 15: 33–48.

Lee, H.; Narayanan, S.; Park, S.; Seong, S. and Hahn Y. (2014). Transcriptional regulation of IFN-lambda genes in hepatitis C virus-infected hepatocytes via IRF-3.IRF-7.NF-kappaB complex. J Biol Chem; 289: 5310–9.

Li, M. and Huang, D. (2007). On-column refolding purification and characterization of recombinant human interferon-1 produced in Escherichia coli. J. Protein Expr. Purif. 53: 119–123.

Morozov, V.A. and Lagaye, S. (2018). Hepatitis C virus: morphogenesis, infection and therapy. J. of hepat., 10(2):186–186.

Renau, L.P. and Berenguer, M. (2018). Introduction to hepatitis C virus infection: Overview and history of hepatitis C virus therapies. J. Hemodialysis International, 22: 8–21.

Renauld, J.C. (2003). Class II cytokine receptors and their ligands: key antiviral and inflammatory modulators. J. Imm. 3: 667–676.

Sara M.S. (2017). Impact of IL-28β rs-12979860 polymorphism on its serum levels in Hepatitis C patients. M.Sc. thesis College of science. University of Baghdad.

Sheppard, P.; Kindsvogel, W.; Xu, W.; Henderson, K.; Schlutsmeyer, S.; Whitmore, T.E.; Kuestner, R.; Garrigues, U.; Birks, C.; Roraback, J.; Ostrander, C.; Dong, D.; Shin, J.; Presnell, S.; Fox, B.; Haldeman, B.; Cooper, E.; Taft, D.; Gilbert, T.; Grant, F.J.; Tackett, M.; Krivan, W.; McKnight, G.; Clegg, C.; Foster, D. and Klucher, K.M. (2003) IL-28, IL-29 and their class II cytokine receptor IL-28R. Nat. Immunol. 4: 63–68.

Shi, X.; Pan, Y.; Wang, M.; Wang, D.; Li, W.; Jiang, T.; Zhang, P.; Chi, X.; Jiang, Y.; Gao, Y.; Zhong, J.; Sun, B.; Xu, D.; Jiang, J. and Niu J. (2012). IL28B genetic variation is associated with spontaneous clearance of hepatitis C virus, treatment response, serum IL-28B levels in Chinese population. PLoS ONE 7(5): e37054.

Stetson, D.B. and Medzhitov, R. (2006). Type I interferons in host defence. J. Imm. 25: 373–381.

WHO, hepatitis C (2019).

Yusor, F.A. (2018). Genetic polymorphisms of some interferons associated with chronic viral hepatitis B and C. Ph.D. thesis College of Medicine. University of Babylon.

Zhang, L.; Jilg, N.; Shao, R.X.; Lin, W.; Fusco, D.N.; Zhao, H.; Goto, K.; Peng, L.F.; Chen, W.C. and Chung, R.T. (2011). IL28B inhibits hepatitis C virus replication through the JAK-STAT pathway. J. Hepatol. 55: 289 – 298.