EVALUATED OF THE IL-12 AND TNF-A LEVELS IN SERUM OF HCV IRAQI PATIENTS

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Abstract -
Our study aims at detecting the concentration of IL-12 and tumor necrosis factor(TNF-α) in hepatitis C virus patients in ThiQar province compared to the healthy control.
Sixty-eight patients from Thi Qar were randomly selected, 32 males and 36 females aged 23-76 years with 20 healthy individuals with 12 males and 8 females. And for the period from January to December 2017.
ELISA kit from (Takara, China) was used to measure IL-12 and TNF-α concentration.
The result was a high concentration of IL-12 and tumor necrosis factor(TNF-α)in patients (**11.3949 ± 3.93553** ng/ml) and (**150.54 ± 64.01**ng/ml) compared to healthy (**9.6530 ± 0.74842ng/ml**), (**78.78 ± 46.79ng/ml**) Respectively, and significant difference.
Conclusion: In present study, increase the concentration of IL-12 and TNF-α in patients compared with healthy control.

I. INTRODUCTION

The term of Hepatitis consists of two sections, the first is the (hepar) which originated from the Greek, meaning the liver, second the suffix (itis) means inflammation (Dyson *et al*,2014).HCV is a globally prevailing pathogen and a leading cause of morbidity and death (Cooke *et al*,2013). The HCV infections patterns differ temporally and geographic (Alter *et al*,2000).globally, HCV infection is one of the key causes of chronic liver disease (Lavanchy,2011).HCV is both an hepatotropic and a lymphotropic virus (Craxi *et al*,2008).Hepatitis C virus has been known as a reportable disease in Iraq for more than twenty years.

cytokines play a critical role indirecting and regulating immune responses to viral infections, indirectly,by determination of the dominant (T helper 1 \ T helper 2) type of immune response, and directly, through the repression of viral replication (Lalla *et al*,2004; Osburn *et al.*,2013).Cytokines are very essential fraction of host defense network. And cytokines are mediators of cell-to-cell cross-talk and coordinators of innate and acquired immunity. Today it is fully known that HCV upsets cytokine production on various levels (Baskic *et al*.,2017).

Interleukin-12 is an important immunoregulatory cytokine, during infection the production of IL-12 regulates innate immune response and determine the pattern of adaptive immune responses, is produced chiefly by antigen-presenting cells (macrophages, Dendritic Cells (DC) and by NK cells) (Cavalcanti *et al*., 2012; Teng *et al*., 2015).

There are many biological activities to IL-12, such immunoregulation , antiviral and anti-tumor (Wen and Wu.,2003).IL-12 reflects susceptibility of the host body to killing viruses.The production of IL-12 is crucial for stimulation of T helper1 immunity and is drive towards the removal of viruses (Wan *et al*.,2009).TNF-α is a pleiotropic cytokine with important functions in homeostasis and disease pathogenesis,produced in response to infections pathogens.numerous cells have the ability to produce and release it, such as,macrophages, lymphocytes, monocyte ,endothelial cells, smooth muscle cells, fibroblasts, osteoblasts, and epithelial cells. Inflammatory factors, as the infestation of viruses can rapidly stimulate to synthesize and express TNF-α(Tang *et al*.,2005;Tian *et al*.,2015).polymorphism to TNF gene affect serum levels of TNF and to influence tendency to different diseases.TNF- α has a crucial role in regulating cell differentiation,proliferation, and innate and adaptive immune responses (Qidwai and Khan,2011).

II. MATERIAL AND METHODS

Sixty-eight Iraqi patientsfrom Thi Qar were randomly selected, 36females and 32 males aged 23-76 years with 20 healthy individuals with 8females and 12 malesaged 19 - 62 years.And for the period from January to December 2017. IL-12 and TNF-α ELISA kit obtained by (Takara , China) was used to measure IL-12 and TNF-αconcentration.

III. RESULTS

groups	No.	No.%	Mean ± Std. Deviation	P-value
Patients group	68	77.27%	11.3949 ± 3.93553	0.00 HS
Control	20	22.63%	9.6530 ± 0.74842	
total	82	100.0%	10.523 ± 2.341975	

Sig. (2-tailed):(0 .000). (t = 57.681). (df = 19-67).

Table (1) : Concentration IL-12 (ng / ml) between the studied groups.

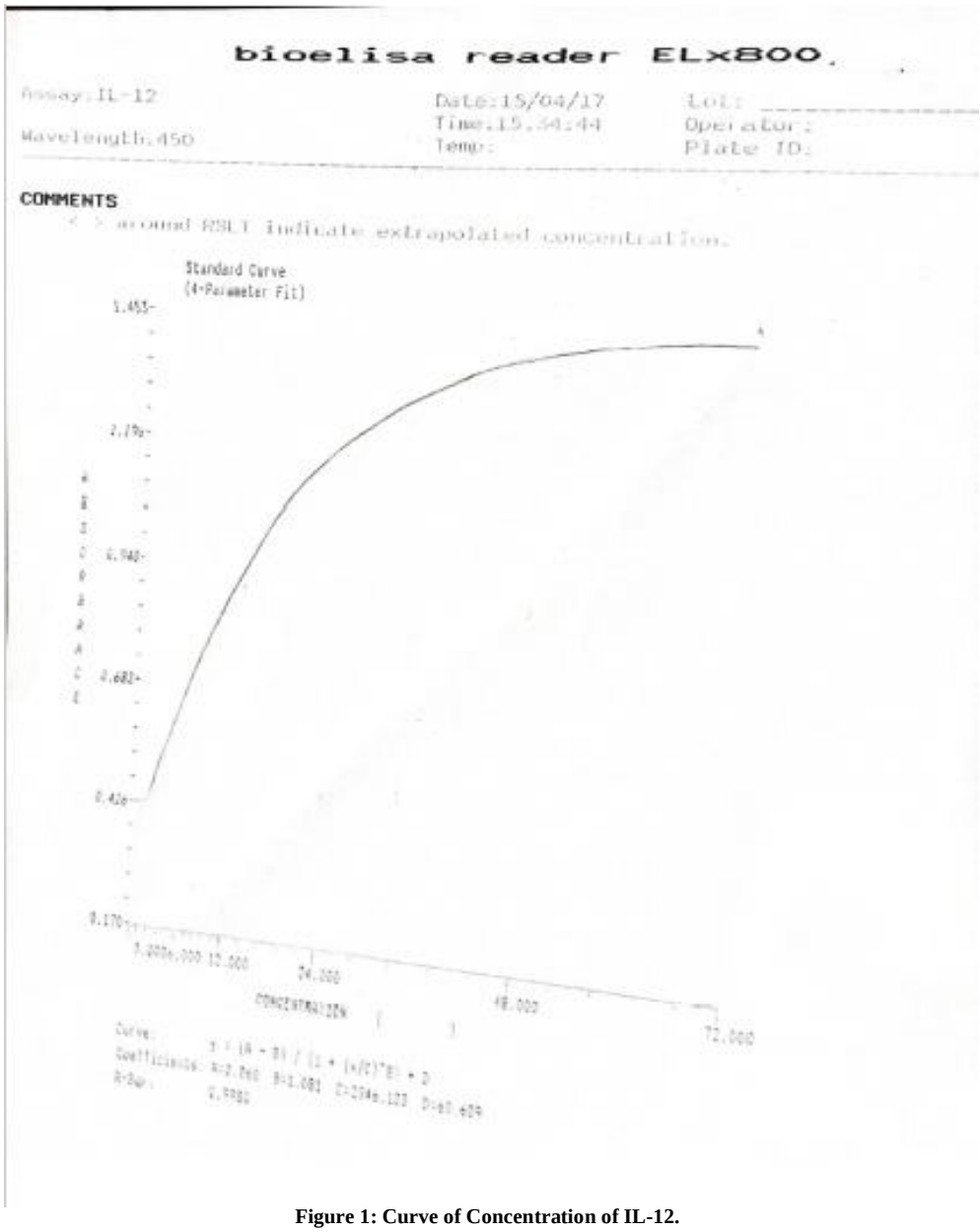

Figure 1: Curve of Concentration of IL-12.

groups	No.	No.%	Mean ± Std. Deviation	P-value
Patients group	68	77.27%	150.54 ± 64.01	0.00 HS
Control	20	22.63%	78.78 ± 46.79	
total	82	100.0%	114.66 ± 55.4	

Sig. (2-tailed):(0 .000). (7.896). (df = 19-67).

Table (2) : Concentration TNF-α (ng / L) between the studied groups.

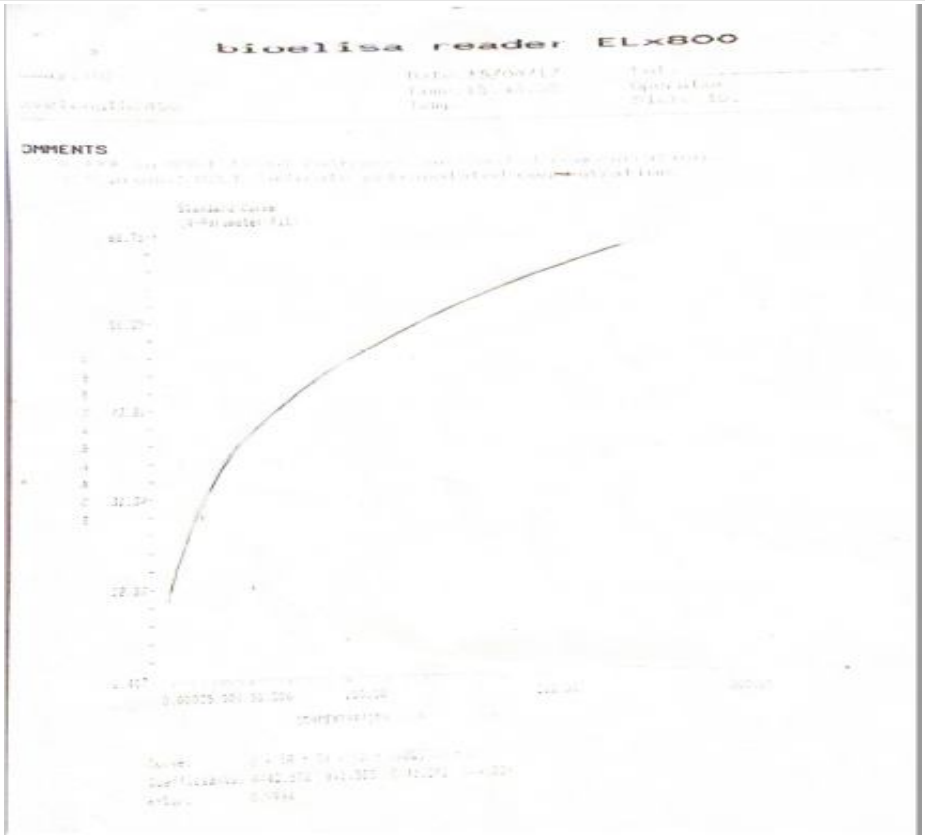

Figure 1: Curve of Concentration of TNF-α

DISCUSSION

Depending on the standard manufacturing curve. IL-12 concentration was measured in serum HCV patients, and there was a significant increase in IL-12 concentration compared to the healthy control group.
the mean concentration of IL-12 in hepatitis C patients was (**11.3949 ± 3.93553**), while the concentration in healthy control was (**9.6530 ± 0.74842**) as shown in the table (1).
The results of our study are consistent with a number of studies such as: (Hamed *et al*.,2017) in Saudi Arabiaand(ElEmshaty *et al*.,2015) in Egypt. This result suggests an intense reaction for eliminating virus at onset of severe hepatitis, particulary in heavy disease patients(Liu *et al*,.2011).
There are many biological activities to IL-12, such immunoregulation, anti-tumor and is a robust antiviral cytokine, adequate in eliminating HCV by binding both innate and adaptive antiviral immune response. Activation of (Toll-Like-Receptor-4) on macrophages surface stimulates expression of IL-12 via Nuclear Factor-κB(NF-κB) and activator protein 1 (AP-1) transcriptional pathway. following expression, IL- 12 releases IFN-γ, which stimulates anti-HCV cytotoxic lymphocytes. (Farooqi *et al*.,2016).
Because it has a higher molecular mass compared with other cytokines, IL-12 has a relatively long serum half-life(Gately,1997). Thus, the potential caption is that IL-12 accumulates in serum after stimulation and release from the target site of infection. Spontaneous secretion of detectable quantities of IL-12 was observed in PBMC from a minority of patients. (Gately & Mulqueen,1996).
Following (IFN-g/LPS) stimulation, the production of IL-12 rises extremely in patients and healthy. but, hepatitis C patients produced significantly more IFN-g/LPS-inducible IL-12 than healthy, maybe because of the chronic inflammatory process. This result indicates that the capacity of PBMC to produce IL-12 in response to specific stimuli is conserved in HCV patients (Chehimi *et al*.,1994).Study of Gigi et al.,2008 indicated that it is, in chronic HCV infections, the robust proinflammatory cytokine response plays a key role in the evolution of hepatic injury. and thus, aloof from engaging in viral clearance, this polarized immunological profile may participate in the pathogenesis of the liver disease.
Depending on the standard manufacturing curve.TNF-α concentration was measured in serum HCV patients, and there was a significant increase in TNF-α concentration compared to the healthy control group.the mean concentration of TNF-α in hepatitis C patients was (**168.337 ±80.906**), while the concentration in healthy control was (**110.176 ± 36.681**) as shown in the table (2).

This result is consistent with a number of studies such as:
(Sabry *et al*.,2015) in Egypt , (Arouch*aet al*.,2013) in Brazil and (Elsammak*et al*.,2005).

This may be because TNF-α stimulating a partly overlapping group of antiviral defense mechanisms and level of TNF-α in serum reverses the progression of inflammation. Increased level TNF-α in patients with chronic hepatitis C may participate to the role of innate immunity in stimulating the adaptive immune responses, so suggest the role of TNF-α in antibody production (Akyűz *et al*.,2005).

Zhang et al. reported that level of TNF-α in the serum of patients was high significantly compared with the healthy group. They suggested that rise serum level of TNF-α is an important mediator in the pathogenesis of liver necrosis and alterations in microcirculation (Zhang *et al*.,1993).

Tilg *et al.* They found elevation significantly in serum level of TNF-α in chronic liver diseases and reaches its maximum in decompensated cirrhosis. They suggested that this increase in the cytokine concentration may be due to liver dysfunction rather than the inflammatory illness (Tilg *et al*.,2002).the infected liver display an important rise in gross macrophage numbers, also Chronic HCV is correlated with immune infiltration, high levels of HCV particles could stimulate macrophages to express TNF- α, create a direct mechanism for the HCV to enhance infection (Fletcher *et al*.,2014).Also Fletcher *et al*.,2014they suggested that hepatitis C stimulates Kupffer Cells(Liver resident macrophages) to express TNF-α.

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