

# DETECTION AND CORRELATION ANALYSIS OF SERUM CYTOKINE LEVELS IN CHRONIC HEPATITIS C VIRUS INFECTION

## AUTHORS

Ismail Che Noh (1,2), Asma Abdullah Nurul (3), Imran Ahmad (4) and Abu Bakar Ruzilawati (1)

## AFFILIATIONS

1 Department of Pharmacology, School of Medical Sciences, Universiti Sains Malaysia, Kota Bharu, Kelantan, Malaysia  
2 Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia  
3 Biomedicine Programme, School of Health Sciences, Universiti Sains Malaysia, Kota Bharu, Kelantan, Malaysia  
4 Department of Family Medicine, School of Medical Sciences, Universiti Sains Malaysia, Kota Bharu, Kelantan, Malaysia

## INTRODUCTION

Hepatitis C virus (HCV) infection is identified as one of the major causes of chronic liver disease and is the leading indication for a liver transplant. It is estimated that about 58 million people are currently burdened by chronic HCV infection, with 1.5 million new infections recorded every year. Approximately 60%–80% of acute HCV infections progress to chronic HCV infection, with symptoms presenting when liver damage progresses. The pathophysiology of chronic HCV infection is unclear. However, numerous studies have suggested that the progression of chronic hepatitis C lesions is associated with an imbalance of T helper (Th) 1 and 2—that is, upregulation of intrahepatic Th1 cytokines (e.g., interleukin-12, interleukin-18, tumor necrosis factor [TNF]- $\alpha$  and interferon [IFN]- $\gamma$ ) and as well as upregulation of Th2 cytokines (e.g., interleukin [IL]-4 and IL-10).

## OBJECTIVE

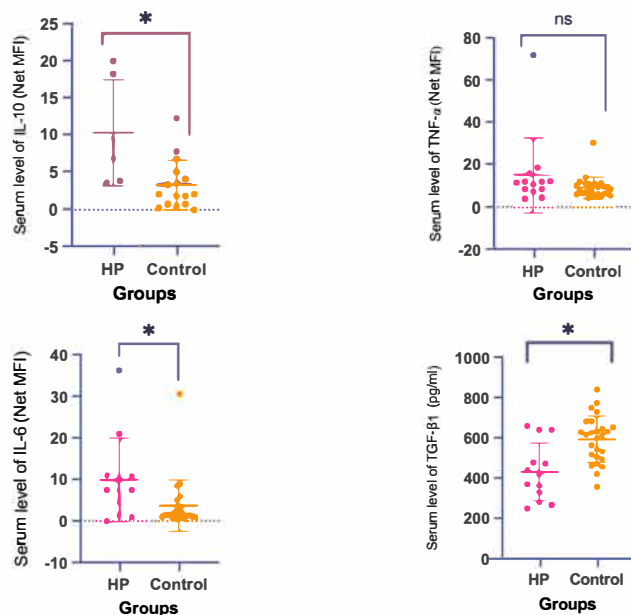
The aim of this study was to assess and correlate serum cytokine levels of IL-10, IL-6, TNF- $\alpha$  and TGF- $\beta$ 1 with chronic HCV infection among Malay male subjects.

## METHODOLOGY

A total of 39 adult male subjects were enrolled in this study and recruited from various health clinics in the state of Kelantan, Malaysia, from July 2019 to December 2020. Study subjects were divided into two groups: 13 patients with chronic HCV infection (HP) and 26 control subjects (HS). Blood samples were collected from each study subject by venipuncture under aseptic conditions. The blood samples were centrifuged at 1000  $\times$  g for 15 min at room temperature for serum separation. The sera were aliquoted into 1.5 ml microcentrifuge tubes and stored in a freezer at  $-70^{\circ}\text{C}$ . The serum levels of the IL-10, IL-6, TNF- $\alpha$  were simultaneously determined using human premixed multi-analyte kits (catalog number LXSAMM) on a Luminex 200 analyzer (R&D System, Minneapolis, USA). The serum level for TGF- $\beta$ 1 was determined using a Quantikine ELISA kit (R&D System, Minneapolis, USA). The sample for TGF- $\beta$ 1 measurement involved pre-activation with NHCl and kept at  $4^{\circ}\text{C}$ . to avoid measuring bio-active TGF- $\beta$ 1.

## RESULTS

- There were statistically significant differences in the mean serum levels of IL-10, IL-6, and TGF- $\beta$ 1 in the chronic HCV-infected patients compared to healthy subjects ( $p = 0.0096$ ,  $p = 0.0180$ , and  $p = 0.0005$ , respectively). No significant observation made in the mean serum level of TNF- $\alpha$ .
- In the chronic HCV-infected patients, the concentration of TNF- $\alpha$  has shown significant positive correlation with the serum level of ALP ( $r = 0.868$ ,  $p = 0.0001$ ) and gamma glutamyl transpeptidase (GGT) ( $r = 0.658$ ,  $p = 0.014$ ). The serum level of TGF- $\beta$ 1 also showed a significant positive correlation with serum GGT ( $r = 0.714$ ,  $p = 0.006$ ).
- In the healthy control group, there were significant negative correlations between the levels of IL-6 and total protein ( $r = -0.505$ ,  $p = 0.0119$ ) and albumin ( $r = -0.617$ ,  $p = 0.0013$ ); TNF- $\alpha$  and the total protein ( $r = -0.636$ ,  $p = 0.0005$ ), albumin ( $r = -0.634$ ,  $p = 0.0005$ ) and total bilirubin ( $r = 0.404$ ,  $p = 0.0041$ ).



\*Significant difference between the groups of HCV-infected patients (HP) and healthy controls with  $p < 0.05$

## CONCLUSION

Serum levels of IL-10 and IL-6 is associated with chronic HCV infection. However, serum level of TGF- $\beta$ 1 was negatively associated with chronic HCV infection and there was no significant association observed for TNF- $\alpha$ .

## REFERENCES

1. World Health Organization. Hepatitis C Available online <https://www.who.int/news-room/fact-sheets/detail/hepatitis-c> (accessed on 6 March 2021).
2. Modi, AA, Liang TJ. Hepatitis C: A Clinical Review. *Oral Diseases* 2008, 14, 10–14.
3. Fan XG, Liu WE, Li CZ, Wang ZC, Luo LX, Tan DM, Hu GL, Zhang Z. Circulating Th1 and Th2 cytokines in patients with hepatitis C virus infection. *Mediators of inflammation*. 1998 Jan 1;7(4):295–7.
4. Velazquez-Salinas L, Verdugo-Rodriguez A, Rodriguez LL, Borca MV. The Role of Interleukin 6 during Viral Infections. *Frontiers in Microbiology* 2019, 10.
5. Moura AS, Andrade Carmo R, Teixeira AL, Otávio Da Costa Rocha M. Soluble Inflammatory Markers as Predictors of Hepatocellular Damage and Therapeutic Response in Chronic Hepatitis C; 2009; Vol. 13.