Plant Archives Vol. 21, Supplement 1, 2021 pp. 1151-1155 e-ISSN:2581-6063 (online), ISSN:0972-5210

Plant Archives

Journal homepage: http://www.plantarchives.org
doi link : https://doi.org/10.51470/PLANTARCHIVES.2021.v21.S1.179

INFLAMMATORY REACTION OF HEPATITIS C VIRUS IN HCV PATIENTS

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ABSTRACT

Project attempts to estimate the manifestation of stimulated indicators CD54 & CD79 in patients infected with HCV and assessment of gamma -INF and IL-6 in serum ranks in patients with HCV, total of (100) seropositive patients for HCV were screened for this study. Patients attended general lab., because of abdominal pain, jaundice and loss of appetite and other liver complaint, any serum samples expressed positive for anti-HCV antibodies directly choose to show level of gamma -INF & IL-6 in serum of patient and show expression of CD54 and CD79 in blood of HCV patients. Results showed that serum samples were analyzed for IL-6 & gamma -INF by ELISA, showed highly significant increases ($p<0.05$) in serum level of HCV patients as compared with healthy control groups, acute HCV revealed high as well as , increases in serum level of gamma-INF significantly($p<0.05$), while chronic liver disease patients express high increase in serum level of IL-8 significantly($p<0.05$). Activated markers study revealed high expression of CD79 & CD54 in HCV patients as compared with healthy normal groups ,where acute HCV patients were showed significantly($p<0.05$) high expression in CD79 & CD54 compared with other HCV patients.
Keywords: Inflammatory reaction, Hepatitis C Virus, HCV Patients.

Introduction

(HCV) is a hepatotropic RNA virus, It is responsible for acute as well as chronic hepatitis in chimpanzees and humans by a great tendency for chronicity (Twu *et al*., 2019) The life cycle of HCV resembling "viral attachment, entry, fusion, RNA translation, post-translational processing, replication, assembly and release" (Ploss and Dubuisson, 2012) *Hepatitis C virus* consider a *Hepacivirus genus* from *Flaviviridae* family, usually troubled with hepatic infections, HCV is (+Ss RNA) with (6-7) major genotypes and more than 100 subtypes have been consequently distiguished (Irshad *et al* 2010) RNA of HCV consist of an open reading frame ended with 5' and 3' (UTRs) (Pietschmann and Brown, 2019) that codes for a long polyprotein, managed by proteases to develop proteins of HCV (Pietschmann and Brown, 2019)

HCV is the major source of non-digestive hepatitis. The most common of HCV impurities are conveyed by different method of blood, In people having several blood transfusion, like hemophilia or thalassemia patients, are mostly at great danger of having HCV (Zahid *et al*., 2019) Both sexual & Prenatal transmission are quite infrequent. Anyway, the track of contamination is secretive in almost 50% of people having HCV (Williams *et al*., 2011).

The threat of long-lasting hepatitis is raised. Almost seventy five percent of infected people having acute HCV never decrease RNA and develop to chronic phase. Maximum of cases hall progress insistently an increased hepatic enzymes in addition. HCV is develop into chronic in (180) days. Hence only a slight degree of impulsive recovery .The preponderance of people having chronic disease are with no signs or with less common signs if no cirrhosis. The greatest recurrent illness is exhaustion. Then sickness, faintness, joint pain, and weightiness (Crowley *et al*., 2019).

The incidence of T cells may be noticed. When virus enters hepatocyte it will be activated to yield IFN, that prompt K-cells to create MIP–1a, that strengthen NKcells which, in sequence, discharge interferon that then adjusts chemokine which then straight hepatic penetrating cells of lymph to liver parenchyma. Which distinguish MHC-1 peptide compounds over the exterior of infested cells to get red of apoptosis (Racanelli and Rehermann, 2003)

The occurrence of vital CD8+ and CD4+ T responses in patient blood suffers from acute disease looks related with retrieval (Gerlach *et al*., 1999) In compare, decreasing of a response seems to expect the conclusion of chronic disease. Then Ab -mediated reduction, recalling was related with insistent disease, so authorizing the majorpart that CD4+ act in the get rid of serious disease (Grakoui *et al*., 2003). The regulator of acute disease is linked with a decreasing HCV variety, imitating a “enclosing” of HCV variety with a positive resistant reaction, while chronicity is related with quasi-species extension (Coppolino *et al*., 2019).

Cytokines function as the molecules of defense reaction that result in numerous physiological roles and adjust the defensive, provocative and repairing patient reactions, and mostly concealed by mono and lymph cells. cytokines from T cells act essentially in the host response. Stimulated T cells classified into (2) subcategories rendering cytokines manufacturing (Koziel *et al*., 1995). T helper-1 cytokines, like IL-2 & IFN-, to lead to (CMI) response while T helper -2 cytokines as IL-10 and IL-4 are concerned with AMI. Both responses have been revealed to relate in a viral disease and

the inequality among them prefer HIR and depressed adjust CMI, that is essential for immunity beside diseases (Gong *et al*., 2015).

Materials and Methods

Patients

The study enrolled 100 HCV patient, admitted at the public health laboratory and with symptoms sensitive of critical and chronic HCV patients

Samples Collection

100 blood samples (5-10) ml was pinched from every medical patients (HCV seropositive). then the blood samples were centrifuged at (4700 RPM) for (5 min.) to gain blood serum then frozen at (20 °C) until gathered enough total for accomplishment ELISA technique to approximation the HCV patients then detect cytokines level HCV blood patients as termed by manufacture company.

Serum cytokine

Sizes of cytokines in the serum were done by ELISA test (R&D Systems). Absorbance was restrained in copies with a micro plate reader (Beckman Coulter). The last concentration was expressed in pg/ml.

Statistical analysis:

Statistical analysis was showed by using Chi-square (2) test to regulate the statistical changes among diverse groups by using a proposal statistical platform for social science (SPSS 19). The possibility of ($P \leq 0.05$) was measured to be statistically significant. The examined parameters were offered in terms of means ± standard errors (S.E.), and variances between means of patients and controls were calculated by ANOVA test and the Least Significant Difference (LSD). The difference was measured significant when the possibility (P) value were ($\leq 0.05, \leq 0.01$).

Results and Discussion

1. Medical Remarks

Medical marks in HCV patients were comprised vomiting, fever, loss of appetite, while other patients never exposed any of these signs and shows asymptomatic carrier as shown in table (1).

Table 1 : Clinical signs for HCV patient.

No.	Clinical signs	Number	Percentage%
1	Acute	10	10%
2	Chronic Liver disease	5	5%
3	Chronic liver disease (asymptomatic signs)	85	85%

Our results of this study showed that 10(10%) cases showed signs of vomiting, fever, loss of appetite and abdominal pains, while 85 (85%) cases showed asymptomatic and 5(5%) develop into chronic liver disease separately .Symptoms of acute phase of HCV disease leftovers clinically silent for most patients, and only (15% - 20%) of people progressing medical marks(Koretz *et al.*, 1993; Centers for Disease Control and Prevention (1998). When they current, symptoms like mild fever, exhaustion, loss appetite, abdominal aching, sickness, and retching may develop during 6-7 weeks after having HCV then cleared within a few weeks (Marcellin *et al*., 2002; McMahon *et al*., 1989).

2. Results of IL-6 in in hepatitis patients

From results showed high level of IL-6 in chronic liver disease as compared with other and healthy groups.

Table 2 : The Concentration of IL-6 in patients and controls

Group	NO.	Serum level of IL-6		
		Mean	Minimum	Maximum
Asymptomatic	85	913.12	190.00	3100.00
Acute HCV	10	370.20	124.00	914.00
Chronic liver disease	5	1431.50	1008.00	1370.00
Control	10	50.30	70.00	85.00

Chemokines are tiny mole cular mass chemotactic cytokines of 8–10 kDa. They composed of an growing family of 50 ligands and 20 receptors. Chemokines are known and categorized by their efficient and fundamental features. As their name indicates, their action is to prompt the straight passage of cells to the location of inflammation. In relationships of their structure (Radkowski *et al*., 2004) Chemokines apply their biological activity through linking to certain cell surface receptors. An infrequent feature of greatest chemokine receptors is their great attraction for numerous ligands (Apostolakis *et al*., 2006). In vivo, the chemotactic grade can be created by the linking of IL-6 to proteins of basement membrane. This grade helps in getting cells in the direction of the location of inflammation besides preserves them when they are reached. Additionally to conscription, IL-8 aids to stimulate the motivation of neutrophils and monocytes (Remick, 2005). Neutrophils offer the principal-route of defense in contrast to attacking different pathogens as virus. These cells discharge inflammatory cytokines such as IL-8, 6 &12, create irritable oxygen species. IL-8 excretion effects in an elevated employment of neut rophils into liver that lead to the rises of hepatic altitudes of this cytokine and worsens the necro-inflammatory manner (Wisniewska-Ligier *et al*., 2006; Heydtmann and Adams, 2009). Moreover, the discharge of responsive O2- species from granulated cells recognized modifying action previous, thus disturbing "I L–6" appearance. Liver I L -6 is noticed at less preservation grade at acute stage of H CV impurity, while noticeable rises in blood serum and liver grade can be detected in H CV patients with advanced infection & scarring as matched to controls (25) .

3- Concentration of serum gamma -INF

Current study showed that all patients with H CV cover higher level of gamma -INF than healthy control group, gamma -INF concentration was improved particularly with acute H CV patients, asymptomatic patients and liver cirrhosis patients correspondingly .Analysis of variance among acute H CV, asymptomatic, liver cirrhosis and control people ($p<0.001$) table(3)

Table 3 : The Concentration of gamma -INF in patients and controls

Group	NO.	Serum level of gamma -INF		
		Mean	Minimum	Maximum
Asymptomatic	85	85.51	29.00	211.21
Acute HCV	10	581.15	421.01	677.00
Chronic liver disease	5	18.81	17.98	19.00
Control	10	16.16	8.07	20

gamma -INF is a central cytokine to the of inflammatory pathogenesis routes. The gamma -INF pro- inflammatory effect is facilitated via straight initiation of other pro-inflammatory cytokines, free radicals &metalloproteinase, and via variation of the sub population of regulatory T cells (Tregs) (Aggarwal *et al.,* 2012; Biton *et al.,* 2012).

4- CD54 expression in HCV positive patients

Results as in table (4) shown that there was highly significant differences in mean of CD 54 expression among HCV patients and healthy control groups ($p<0.001$), the cell surface CD54 was over expressed in acute HCV compared to asymptomatic HCV patients, liver cirrhosis and healthy control groups respectively seen in acute HCV disease.

The hepatic vascular principle is doubled given via vessels that channel into web specific tubes known as hepatic sinusoids (Knobler and Schattner, 2005). These sinusoids are creased with pored endothelial cells (E Cs) & luminal Kupffer cells (K Cs), & track equivalent together via liver parenchyma permitting delivring blood stream rich with O_2 as well as nutrition & Ag to body tissue (Greuter and Shah, 2016). On reoccurrence flow, "blood" deliver to overriding vessels then liver strains previously departing through the extra hepatic inferior venacava (McCuskey, 2000). Immune-defence investigation and acceptance facilitated via scheme distinctive ramparts. Furthermore, the liver is occupied by whole classic courses of effector and memory t plus b cells along with C D2 5+ Fox P 3+ (Tregs) (Langhans *et al.,* 2013). Severe infections are usually asymptomatic, so revisions of huge portion restricted protected chimpanzees. The result of acute infection is usually organized within the first 6 months and eventually be contingent on the extent, span and precise of the adaptive immune response (Langhans *et al.,* 2013). Acute determining infections are considered thru primary enlargement of "poly clonal C D 4+andCD8 + T –cell" residents that continued over allowance (Levander *et al.*, 2018). On other hand, prolonged infections are related with temporary hindered responses that are frail and goal a slight array of MHC class I and II limited epitopes (Szereday *et al*., 2016).

5- Expression of CD79 in HCV positive patients

The results demonstrated in table (5) shows there was high statistically significant difference in mean of CD79 expression among HCV patients and healthy control groups ($p<0.001$), and the higher percentage of expression was found in acute patients , chronic liver disease followed by asymptomatic patients and control groups

To get rid of hepatitis (H CV) is related with vital multi-vague C D 4+ and C D 8+ T cell responses, while persons that progress chronic infec tion likely to have fragile, slimly dedicated responses (Filskov *et al*., 2017). Revisions on chimpanzees have exposed that reduction of C D4+ or C D 8+ cells inhibits H C V allowance (Grakoui *et al*., 2003). In H C V infected people, C D8+ T C M cells exist in the margin are able of distinguishing into E MC, that are conscripted to the liver. CD8+ effector cells in the liver were initiate to have less serviceable proficiency, as proved by low IF N -y fabrication (Filskov *et al*., 2017) Hepatocytes usually never precise MHC session 2 ,while medical case, abnormal session appearance arises (Filskov *et al.*, 2017) The determination of liver pathogens is frequently attended thru frail "CD8+ T cell response " antigens subsequent (Holz and Rehermann 2015). We exasperated to conclude the pathogenic status of C D74 over comparing of its expression during infection, our results make it clear that robust up-regulation of both C D54&C D79 manage a tough mark that lymphocytes in peripheral blood of H CV persons within formal of immune dysregulation (Stumptner-Cuvelette and Benaroch, 2002 ; Holz and Rehermann 2015). Though, CD79 lately was establish to show an extra protagonist "assistant-signaling molecule" (Leng *et al.,* 2003; Beswick *et al.,* 2005)

Table 4 : The Concentration of CD54 in patients and controls

Group	NO.	Serum level of CD54		
		Mean	Minimum	Maximum
Asymptomatic	85	8.13	4.40	11.21
Acute HCV	10	12.88	11.21	13.70
Chronic liver disease	5	5.89	5.31	6.40
Control	10	2.44	0.80	3.00

Table 5 : The Concentration of CD79 in patients and controls

Group	NO.	Serum level of CD79		
		Mean	Minimum	Maximum
Asymptomatic	85	9.20	6.00	21.00
Acute HCV	10	30.00	19.00	40.00
Chronic liver disease	5	13.00	12.00	14.00
Control	10	5.00	4.00	8.00

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