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The Effect of Immune responses In Pathogenesis of Hepatitis B Virus Patients

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Abstract

Study attempts to estimate immune molecules CD45- R & CD79 and cytokines TNF-α and IL-6 in patients infected with HBV

A total of (100) seropositive patients for HBV 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-HBV antibodies directly choose to show level of TNF-α & IL-6 in serum of patient and show expression of CD45-R and CD79. Results showed that serum samples were analyzed for IL-6 & TNF-α by ELISA , showed highly significant increases ($p<0.05$) in serum level of HBV patients as compared with healthy control groups , acute HBV revealed high as well as , increases in serum level of TNF-α significantly($p<0.05$) ,while chronic liver disease patients express high increase in serum level of IL-6 significantly($p<0.05$).Activated markers study revealed high expression of CD79 & CD45-R in HBV patients as compared with healthy normal groups

Keywords: *CD79, CD45-R, Hepatitis B, HBV.*

I. Introduction

Hepatitis B virus (HBV) was first exposed by Blumberg et al in 1965 (1), and the connection between HBV and acute hepatitis after blood transfusion was stated by (2). At that time, most trainings were based on immunological and serological means. Molecular-based studies progressed rapidly after the HBV element was exposed and the HBV genome cloned (3). (4). HBV is the major source of non-digestive hepatitis. The most common of HBV 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 HBV [5,6]. Both sexual & Prenatal transmission are quite infrequent. Anyway, the track of contamination is secretive in almost 50% of people having HBV.

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 [7,8]

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The occurrence of vital CD8+ and CD4+ T responses in patient blood suffers from acute disease looks related with retrieval[9].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 [10]. The regulator of acute disease is linked with a decreasing HBV variety, imitating a "enclosing" of HBV variety with a positive resistant reaction, while chronicity is related with quasi-species extension [11].

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 [12]T helper-1 cytokines, like IL-2 & IFN-ϑ, 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 [13].

II. Materials &Methods

Patients

The study enrolled 100 HCV patient , admitted at the public health laboratory and with yellowish color or signs and symptoms sensitive of critical and chronic HBV patients and showed seropositive for anti HBV antibody.

Samples Collection

(100) blood samples (5-10) ml was pinched from every medical patients(HbV seropositive). then the blood samples were centrifuged at (4700 RPM) for (5 min.) to gain blood serum to estimate the cytokines and immune molecules.

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 ($\chi 2$) 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 important.

III. Results & Discussion

1-Medical Remarks

Medical marks in HBV 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 sings	15	15%
2	Chronic Liver disease	5	5%
3	Chronic liver disease (asymptomatic signs)	80	80%

Our results of this study showed that 15(15%) cases showed signs of vomiting ,fever ,loss of appetite and abdominal pains ,while 80 (80%) cases showed asymptomatic and 5(5%) develop into chronic liver disease separately. According to F- exam the variation in medical marks were substantial ($p<0.05$) . Symptoms of acute phase of HbV disease leftovers clinically silent for most patients, and only (15% - 20%) of people progressing medical marks [14]. Our results of this study showed that 15(15%) cases showed signs of vomiting ,fever ,loss of appetite and abdominal pains ,while 80 (80%) cases showed asymptomatic and 5(5%) develop into chronic liver disease separately. According to F- exam the variation in medical marks were substantial ($p<0.05$) . Symptoms of acute phase of HbV disease remains clinically quiet for most patients, and only (15% - 20%) of people succeeding medical grades [14]. Symptoms of acute HBV infection are nonspecific and include fatigue, poor appetite, nausea, vomiting, abdominal pain, low-grade fever, jaundice, and dark urine. Clinical signs include liver tenderness, hepatomegaly, and splenomegaly.(15,16). While the majority of these (80–90%) have cirrhosis at the time of diagnosis of HCC, it may occasionally follow without the presence of cirrhosis; this is principally real for HCC due to HBV(17)

2. IL-6 in hepatitis patients

Serum of all patients with HBV and those with acute or asymptomatic disease action contain higher level of IL-6 than healthy control group . IL-6 concentration was mostly increased in patients with chronic liver disease and asymptomatic patients , correspondingly than acute HBV disease

T-test ,showed that there was an increased arithmetical substantial differences among asymptomatic , chronic liver disease and acute infection group ($p<0.05$) as table (2)

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

Group	NO.	Serum level of IL-6		
		Mean ±SE	Minimum	Maximum
Asymptomatic	80	934.82±62.85	190.00	2300.00
Acute HCV	15	478.20±81.94	124.00	994.00
Chronic liver disease	5	1414.60±225.50	1209.00	1440.00
Control	10	67.50±1.49	70.00	85.00
Total	110	713.21±59.65	61.00	2300.00

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[18].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 [19]. 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-6 aids to stimulate the motivation of neutrophils and monocytes [20]. Neutrophils offer the principal-route of defense in contrast to attacking different pathogens as virus. These cells discharge inflammatory cytokines such as IL-6, 10 &12 ,create irritable oxygen species. IL-8 excretion effects in an elevated employment of neut rophils into li ver that lead to the ri ses of hep atic altitudes of this cytokine and worsens the necro- inflammatory manner [21]. Liver I L -6 is noticed at less preservation grade at acute stage of H BV impurity, while noticable rises in blood serum and liver grade can be detected in H BV patients with advanced infection & scarring as matched to controls .This rise in liver & bordering I L-6 associates completely with an elevated in T NF - α as well as developing rate of fibrosis as noted by tissue action guide [24,25].

3- concentration of TNF

Current study showed that all patients with H BV cover higher level of TNF-α than healthy control group , T NF-α concentration was improved particularly with acute H CV patients ,asymptomatic patients(81.43± 5.00) and liver cirrhosis patients correspondingly .Analysis of variance among acute H CV , asymptomatic, liver cirrhosis , and control people ($p<0.001$) .T- test exhibited that there was great statistical significant alteration among acute HCV and asymptomatic, liver chronic disease group ($p<0.001$)table(3)

Table(3) The Awareness of TNF-α in patients and controls

Group	NO.	Serum level of TNF-α		
		Mean ±SE	Minimum	Maximum
Asymptomatic	80	82.43±5.00	28.28	230.46
Acute HCV	15	583.64±17.43	503.00	699.00
Chronic liver disease	5	18.71±0.84	17.77	19.45
Control	10	14.56±1.05	8.08	18.58

In acute agreeing infections, the response of the innate and adaptive

Immune system to *HBV* is capable and well-timed.(26) Viral clearance involves the generation of a stout adaptive T cell retort inducing both a cytolytic(27,28)

4- CD45-R expression in HBV positive patients

Results shown that there was highly significant differences in mean of CD 45-R expression among HBV patients and healthy control groups ($p<0.005$) ,the cell surface CD45-R was over expressed in acute HBV compared to asymptomatic HBV patients, liver cirrhosis and healthy control groups respectively the high expression seen in acute HCV disease.

The hepatic vascular opinion is doubled known past vesseles that frequency into web definite tubes well-known as hepatic sinusoids[29] .These sinusoids are creased with pored endothelial cells (E Cs) & luminal Kupffer cells (K Cs), & track same organized via liver parenchyma passing conveying blood stream gorgeous with O2 as well as nutrition & Ag to body tissue [30].On reoccurrence run, "blood" provide to prime vessels then liver strains formerly retiring complete the spare hepatic poorer venacava [29,30) The result of acute infection is usually prepared in the major 6 months and ultimately be commission on the scope, time and specific of the adaptive immune reaction[31].Acute shaping infections are considered thru primary widening of "poly clonal C D 4+andCD8 + T –cell" occupants that unremitting over budget[32]. On other hand, elongated infections are associated with fleeting stuck comebacks that are feeble and objective a slim arrangement of MHC class I and II restricted epitopes [33]

5- Expression of CD79 in HBV positive patients

The results demonstrated in table (4) shows there was high statistically important difference in mean of CD79 expressions among HBV patients and healthy control groups ($p<0.005$),and the higher percentage of expression was found in acute patients , chronic liver disease followed by asymptomatic patients and control groups respectively .

T –test results showed that there was high important variance among acute HBV ,asymptomatic and liver chronic liver disease groups($p<0.05$).

To get rid of hepatitis (H BV) is related with vital multi-vague C D 4+ and C D 8+ T cell responses ,while persons that progress chronic infection likely to have fragile, slimly dedicated responses [34]. Revisions on chimpanzees have exposed that reduction of C D4+ or C D 8+ cells inhibits H B V allowance[10]. In H B 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 [35].Hepatocytes usually never precise MHC session 2 ,while medical case, abnormal session appearance arises [35]. The determination of liver pathogens is frequently attended thru frail "CD8+ T cell response " antigens subsequent[36]. We exasperated to conclude the pathogenic status of C D79 over comparing of its expression during infection , our results make it clear that robust up-regulation of both C D45&C D79 manage a tough mark that lymphocytes in peripheral blood of H CV persons within formal of immune dysregulation. [37]. Though, CD79 lately was establish to show an extra protagonist "assistant-signaling molecule". MQ proves great-empathy linking to the pro-inflammatory "MI F" necessary " M IF-mediated M APK activation and cell proliferation" [38].Furthermore, the *"Helicobacter pylori"* revealed link to it over stomach tissue and to activate "IL -6" construction[39].

Table(4.) The Concentration of CD45-R in patients and controls

Group	NO.	Serum level of CD45		
		Mean ±SE	Minimum	Maximum
asymptomatic	80	8.03±0.271	4.51	11.30
Acute HCV	15	12.47±0.322	11.23	13.80
Chronic liver disease	5	5.65±0.418	5.14	6.18
Control	10	3.16±0.110	0.80	4.17

Table(5) The Concentration of CD79 in patients and controls

Group	NO.	Serum level of CD79		
		Mean ±SE	Minimum	Maximum
asymptomatic	80	7.16±0.244	6.00	19.00
Acute HCV	15	42.16±4.31	17.23	44.60
Chronic liver disease	5	13.16±1.00	10.69	12.69

Control	10	6.11±0.219	5.0	8.0

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