Immunologial Study of IL32-gamma in Different Hepatitis B Virus Patient Groups at Alnajaf City

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Abstract

Hepatitis B virus is a member of the Hepadnaviridae family and responsible for causing acute and chronic hepatitis in humans. This review deals with our current understanding of the virology, life cycle and immunopathology effecting of this very important pathogen. the present study show the relationship between HBV infection and the rule of IL32 gamma against it ,all of which are considered essential for current and future approaches to antiviral treatment. The study was conducted on 159 patients [43(53.75%) males and 37(46.25%) females] during December ,2019 to July 2020 at AL-Najaf province. They suffering from signs and symptoms of liver diseases.

Key word: *HBV, IL32 g; health; immunosystyems*

Background

Hepatitis B virus (HBV) infection is a worldwide problem associated with significant morbidity and mortality[1]. It has been estimated that two billion people have had hepatitis B virus exposure and near 400 million have experienced chronic infection [2].The burden of chronic infection due to hepatitis B virus (HBV) is currently estimated at around 250 million worldwide [3], while deaths as a result of the chronic squeal of the disease, such as cirrhosis, hepatocellular carcinoma (HCC) or liver failure, stand at 800,000 annually [4,5].

The virus is most commonly transmitted from mother to child during birth and delivery, as well as through contact with blood or other body fluids, including sex with an infected partner, injection-drug use that involves sharing needles, syringes, or drug-preparation equipment and needle sticks or exposures to sharp instruments.[6,7]

Studies that explain the connection between the Australia antigen, or hepatitis B surface antigen (HBsAg) as it is now known, and HBV, became apparent by 1970 [8,9]. Electron microscopic studies in the early 1970s led to the visualization of the infectious virion or Dane particle [10],This was followed by the characterization of the virus genome, the virion-associated proteins and the detailed definition of the serological pro- files in acute and chronic HBV infection [8–11]. the liver injury caused by HBV infection is principally contributed by immune responses, and the immune-related liver damage is induced by active viral replication [12-13]. It is suggested that HBV-species cytotoxic T lymphocytes (CTLs) initially induce the death of virus-infected hepatocytes. However, CTLs are unable to mediate complete eradication of the virus, and they subsequently recruit HBV-non species in ammatory cells, including by stander T cells, natural killer (NK) cells, and neutrophils, that inevitably cause the immunopathology of Chronic Hepatitis B [14-15]. Recently, IL-32 was found to be associated with membrane vesicles inside the cell and released with buoyant structure via exosome-like vesicle release mechanisms[16]. Therefore, IL-32 may be secreted via the Endoplasmic reticulum/Golgi-independent pathway, non-classical protein secretion pathway like interleukin-33 (IL-33) and high-mobility group box 1 protein (HMGB1) that do not contain a signal peptide and are released through ER/Golgi-independent means [17]. The IL-32 transcript is expressed in various human tissues and organs such as the spleen, thymus, leukocyte, lung, small intestine, colon, prostate, heart,

placenta, liver, muscle, kidney, pancreas, and brain. The expression of IL-32 mRNA is more prominent in immune cells than in non- immune tissues [18].

The expression pattern of each isoform of IL-32 in certain cells or tissues and functional difference of each isoform of IL-32 are a matter to be resolved in the future. For example, only IL-32g isoform possesses a hydrophobic signal peptide in its N-terminus, which is a typical feature of secreted cytokine. IL-32 does not possess transmembrane domain but immunohistochemistry analysis reveals that expressed IL-32 in peripheral blood mononucleare cell(PBMC) by LPS and Mycobacterium. tuberculosis was particularly associated with the cell membrane [19]. the amount of IL-32, IL-1, and IFN- protein in serum from hepatitis B patients was significantly higher than that in healthy volunteers [18].

HBV with risk groups

HBV with cancer

HBV is the most common cause of Hepatocellular Carcinoma (HCC) worldwide, accounting for 54% of the cases, with global mortality rates in 2010 estimated in 786,000 deaths (473,600 deaths for HCC and 312,400 for cirrhosis).[20] The role of HBV in hepatocarcinogenesis was first reported in the 1970s when chronic HBV infection was associated with an increased incidence of HCC in the general population[21].

Risk factors for the development of HCC in these patients are higher HBV DNA levels, HBsAg positivity, higher HBV surface anti- gen levels, HBV genotype C, basal core promoter mutations, older age, male gender, chronic active hepatitis, higher ALT levels and higher alfa-fetoprotein.[22]

The pathogenetic mechanisms underlying HBV carcinogenesis appear complex and the following processes have been demonstrated in playing a role: HBV genome integration, chronic inflammation, epigenetic mechanisms, host immune response and cytokine production promoted by the HBV core protein. [23],there are a suggestion that HBV infection is associated with the risk of non- liver cancers, especially digestive system cancers among adults in China.[23]

HBV with thalassemia and hemolytic dialysis

Transfusion transmitted infections (TTI) are major causes of morbidity and mortality among multi-transfused patients such as thalassemics. [24-25]

Thalassemia's are genetic anemia which result from the reduced synthesis of one or more of the globin subunits of normal hemoglobin . This results in an imbalanced alpha/beta-globin chain ratio [26]. HBV infection is also reported in thalassemia patients. Worldwide, 0.3%–5.7% of thalassemia patients are hepatitis B surface antigen (HBsAg)-positive [21] Repeated blood transfusion in thalassemic patients is necessary for their survival; however, such transfusions increase the exposure to blood-borne viruses (hepatitis B virus (HBV) [27]

Also patients undergoing kidney dialysis or individual with early kidney disease. renal failure (Chronic Renal Failure) patients with hemodialysis are at increased risk for transmission of Hepatitis B virus (HBV) infection. In dialysis environment HBV transmits by transfusion of contaminated blood and blood product exposure to contaminated equipment [28] and contact with infected patients and health staff [29].

Baseline

Study design and participants

Cross sectional study obtained 159 Blood samples (78) male and (81) female age range,10-60 years). the samples were carried out from December 2019 to July 2020 collected from hospitals in Najaf city. The inclusion criteria for hepatitis B patients was: the patients did not receive any antiviral treatment or immunotherapy. Blood samples were collected from patients and controls and centrifuged to obtained supernatants.

Instruments and reagents

Biological cabinet (hood), Eppendorf tube (100ml). Micropipettes 0.5-10,100-1000ml, Micro centrifuge, Plastic test tubes 10 ml. ELISA technique instruments for diagnosis of HBV infection and another ELISA kit and instruments for IL32 gamma level detection.

Detection of HBV infection for all samples

HBsAg was detected for all samples using

commercial ELISA kit in accordance with the manufacturer's instructions.

Detection of IL32g level for all samples

IL32g level was detected for all serum samples samples using commercial ELISA kit in accordance with the manufacturer's instructions.

Statistical analysis

Data are presented as the mean and standard deviation (mean ± SD). All statistical analyses were performed using SPSSv20 .Differences were considered statistically significant at $P < 0.05$.

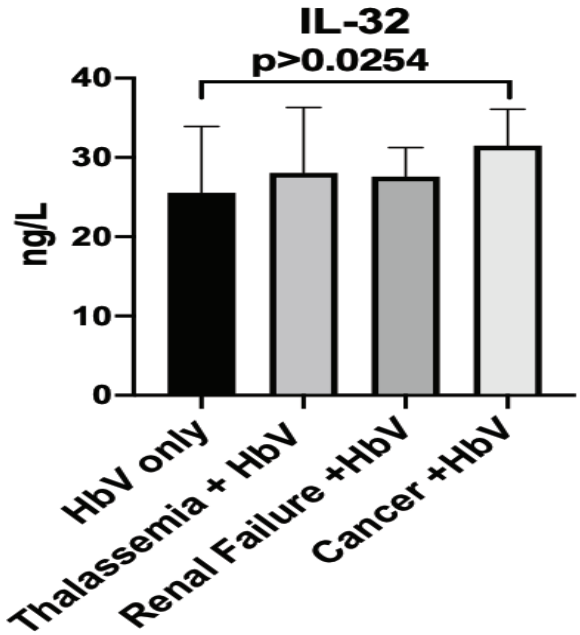
Results & Discussion

80 sample were positive to hepatitis B infection (37 female and 43male and the remain 79 sample were negative to hepatitis B(healthy group).

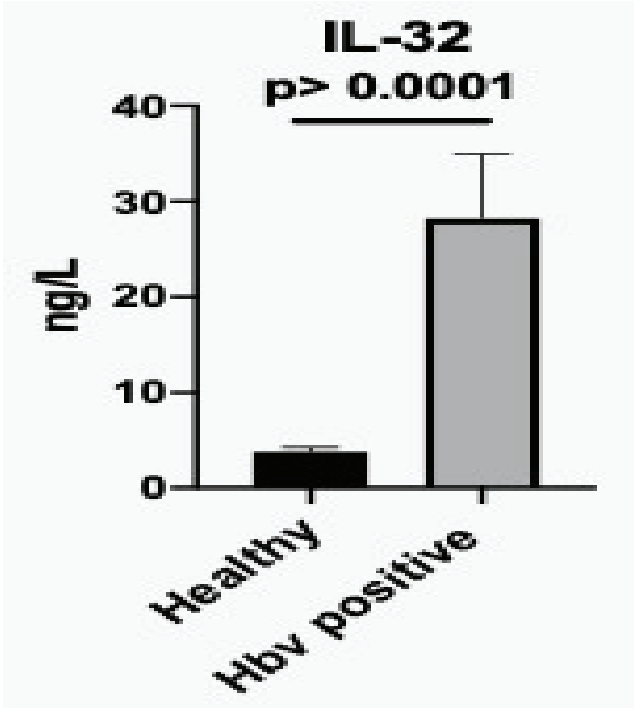
The level of IL32 gamma was significantly higher in hepatitis B patients (for all risk groups) than in healthy group, ($P < 0.05$) is shown in figure (1) and figure (2) this result agrees with (Tian Zhao-ju et al,2019) whom worked on113 patients (79 male and 34 female; age range, 18–68 years) with hepatitis B and from 60 healthy volunteers (33 male and 27 female; age range, 21–60 years). The study prove that IL-32g levels in serum from hepatitis B patients were significantly higher than those in healthy volunteers ($P < 0.05$). (IL32 and HBV) as shown in figure (1)

Distribution of IL32g and HBV infection level were non significantly different between male and female patients with HBV infection ($p < 0.05$) as shown in figure (3).

This result disagree with (mohammed A.Merzah at al ,2019) whom collect data from 2007 to2016 from Karbala hospitals through a federal survey conducted by the Health Directorate of Karbala the result show that Males were higher in having HBV than females. these 3143 were positive for HBV, includes 68.15% males and 31.85% females. Male were observed to be more frequently infected as compared to the female Hepatitis B virus infection among different sex and age groups in Pakistani Punjab. The difference in sample size, natures, livening condition between the present study and other study may be the reason in these disagreements results.



Figure(1): High level of IL32 g in all patients who infected with HBV either only or with other disease .



Figure(2): Significantly high level of IL32 g in patients infected with HBV in compared to healthy volunteers who had low level.

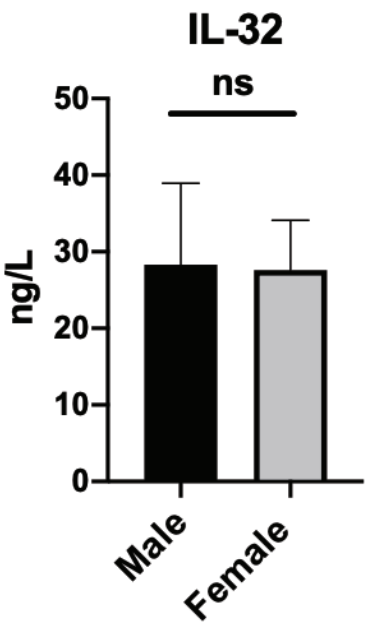


Figure (3):Distribution of IL32 gamma level in infected patients with HBV according to gender

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHSER in Iraq

Conflict of Interest: None

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