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# BIOCHEMICAL PARAMETERS IN RELATION TO SERUM ALPHA FETOPROTEIN & LEPTIN LEVELS IN IRAQI PATIENTS WITH CHRONIC LIVER DISEASES

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## ABSTRACT

**Background:** Hepatitis B and C virus is a leading cause of chronic liver disease. Elevated serum alpha-fetoprotein (AFP) has been used as a marker for hepatic regeneration after the destruction of hopatocyte in viral hepatitis. Also Leptin level may be important to determined in patients with chronic hepatitis B and C.
**Aims:** This study aimed to examine the association between serum AFP, serum leptin levels and some other biochemical parameters in patients with chronic liver disease (B and C).
**Materials and methods:** Serum AFP, leptin, total serum protein TSP ,lipid profile, transaminases, alkaline phophatase ALP, total serum bilirubin levels TSB were measured in 61 patients (31 HBV, 30 HCV) and compared with 30 control subject.
**Results:** In comparison to controls, a significant increase in the serum AFP , Leptin, TSP, AST, ALT,ALP & TSB levels ($p < 0.00$) and a significant decrease in Albumin, cholesterol , Triglyceride, (HDL), (VLDL) & (LDL) levels ($p < 0.00$) compared to control subject. Also Serum AFP levels showed positive correlation with Prothrombin time (PT) ($r=0.384$, $p=0.048$) & with Leptin($r=0.531$, $p=0.005$) in HBV patients.
**Conclusions:** AFP and Leptin can be used as dependent predictors in Patients with HBV, HCV.

**Key words:** HBV, HCV, AFP, Leptin, liver function , ALP.

## INTRODUCTION

Hepatitis means inflammation of the liver. There are many reasons for the liver to be inflamed by viral, toxic, metabolic, pharmacologic, or immune-mediated attack on the liver [(1)]. Viral hepatitis is a major glob health problem all over the world [(2, 3)]. The infection with chronic hepatitis B (HBV) and C (HCV) viruses, and alcoholic and non-alcoholic fatty liver disease are the major etiologies. Chronic hepatitis B and C are the leading causes of cirrhosis and of hepatocellular carcinoma (HCC) worldwide. Approximately 400 million people are chronically infected with HBV and 25%-40% of them die of cirrhosis and of its end-stage complications [(3)]. Alpha-fetoprotein (AFP) is a glycoprotein with a molecular Weight of approximately 70,000 Daltons, represents the major serum protein during fetal life [(4)]. AFP is normally produced during fetal and neonatal development by the liver, yolk sac, and in small concentrations by the gastrointestinal tract [(5)]. After birth, serum AFP concentrations decrease rapidly, and by the second year of life and thereafter only trace amounts are normally detected in serum (typically <10 ng/ml) [(6)]. High levels of AFP are observed during adulthood only under certain

conditions, such as hepatocellular carcinoma -HCC, germ-cell tumors, and liver diseases [7]. Elevation of AFP in chronic hepatitis B and C virus infections and cirrhosis without malignancy is even less clear. There is a growing number of evidence that AFP levels are significantly raised in anti-HCV-positive in comparison with HBsAg-positive patients [8]. Leptin, a 16 kDa peptide hormone (146 amino acid residues , non glycosylated protein ) , derived mainly from the adipose tissue is a prominent biological factor of energy homeostasis by regulation of energy intake and energy expenditure including regulation of appetite, glucose homeostasis and body fat [9, 10], also implicated in many actions including liver fibrogenesis [11 ,12 ,13]. Leptin first linked to obesity but latter found to be implicated in the pathogenesis of a wide variety of disease like inflammation [10]. The results of serum leptin levels in patients with chronic hepatitis C and particular in those with more severe fibrosis or cirrhosis have conflicting [14, 15, 16]. The percent of Iraqi patients with chronic hepatitis B & C during 2008 to 2011 summarized in table (1). This study was designed aimed to evaluate the levels of serum leptin and AFP in sera target population (chronic hepatitis B & C) compared with healthy subject and its correlation with some biochemical parameters.

**Table 1**

***percent of Iraqi patients with chronic hepatitis B&C during (2008, 2009, 2010, and 2011)***

| Years (donor) % | HBV (donor) % | HCV (danger) % | HBV (danger) % | HCV % | HBV Total | HCV Total |
|---|---|---|---|---|---|---|
| 2008 | 1.07 | 0.29 | 2.37 | 2.57 | 3.44 | 2.86 |
| 2009 | 0.53 | 0.16 | 1.62 | 1.36 | 2.15 | 1.52 |
| 2010 | 0.49 | 0.18 | 1.29 | 1.55 | 1.78 | 1.73 |
| 2011 | 0.47 | 0.14 | 1.19 | 0.80 | 1.66 | 0.94 |

## MATERIALS AND METHODS

The study was carried out on 91 subjects, 31 of them with HBV, 30 with HCV, and 30 healthy volunteers as a control group (with no clinical or laboratory evidence of liver diseases). None of those 91 subjects had received any medications. The duration of the study was from September 2011 to March 2012. After ethical clearance the study was carried out in the Gastroenterology and Hepatology teaching hospital / Baghdad. The process of collecting specimens by withdraw about 10 ml of venous blood using plastic disposable syringes.1.8 ml from whole blood add to 0.2 ml (200 µl) trisodium citrate in test tube to obtained plasma for PT test, the remaining Blood samples (8.2 ml) were left for 30 minutes at room temperature. After coagulation, the sera were separated by centrifugation at 704 xg for 10 min. Hemolysed samples were discarded and the sera were stored and frozen about -20C°until analysis. All patients and healthy group were screened for HBsAg and Anti HCV-Ab using (HBsAg ELISA TEST KIT (PLASMATEC LABORATORY PRODUCTS) &HCV ELISA TEST KIT), respectively and the positive cases were confirmed by confirmatory tests. All cases were tested for Prothrombin time (PT) using NEOPLASTINE® CI PLUS kits, serum levels of bilirubin, Alanine aminotransferase(ALT), asparagine aminotransferase (AST ), and TSB by RANDOX kit, alkaline phophatase (ALP) by bioMerieux® kit , total serum protein (TSP ), and serum albumin(ALB) by SPINREACT kit , total cholesterol , Triglyceride and HDL-C were measured enzymatically with commercial Linear Chemicals S.L. kits, VLDL was calculated using the Friedwald formula:(1/5(triglyceride), and LDL-C was calculated also by using the Friedwald formula:(total cholesterol)-(HDL-C)-1/5(triglycerides) [9]. All sera samples were tested for the presence of alpha-fetoprotein using

(HUMAN AFP ELISA kit), and leptin using DRG Leptin ELISA kit.

***Statistical analysis***

For a statistical analysis of quantitative variables, the mean and standard deviation were calculated. One-sample t-tests were performed; comparisons were done with the independent-samples T Test and paired –samples T Test. All values are presented as mean ± SD. Data regarding age, sex,liver function test, lipid profile,AFP test, HBV,HCV and control. Statistical software was SPSS, version 11. It would be significant if $p \leq 0.05$.

## RESULTS

The distribution of the studied groups according to age & sex are summarized in table (2). From a total of 91 subjects 49 (53.84%) were male and 42 (46.15%) were female. Hepatitis B and C was present in 61 (67.03%) cases. Out of these positive cases 31 (50.81%) were suffering from hepatitis B and 30 (49.18%) were suffering from hepatitis C, and in 30 (32.96%) cases were healthy (control). Among the 31 patients suffering from HBS, 17 (54.83%) were male and 14 (45.16%) were female. Out of 30 hepatitis C patients 17 (56.66%) were male and 13 (43.33%) were female patients. Clinical &Lab. data for the studied groups are given in table 3. Serum AFP levels were significantly higher in HBV (14.69 ± 5.279ng/ml) and HCV (16.56 ± 6.954ng/ml) ($p < 0.05$) in comparison with control group (7.54 ± 1.196ng/mL) and there were a non significant difference in HBV patients compared to HCV ($p > 0.05$). Serum leptin levels were significantly higher in HBV (17.99 ± 3.280 ng/ml) and HCV (23.77 ± 5.898 ng/ml) ($p < 0.05$) in comparison with control group (5.34 ± 1.2ng/mL) and non significant decrease in HBV patients compared to HCV ($p < 0.05$). Patients with HBV & HCV had also a significant higher total protein, AST, ALT, ALP & TSB ($p < 0.00$) and significant lower cholesterol, Triglyceride, HDL, VLDL & LDL compared to control as clear in table 3. The relationship between serum leptin, AFP and other biochemical parameters for HBV and HCV are shown in tables 4 and 5 respectively. The results indicated that there were a positive correlation between serum AFP levels & Prothrombin time (PT) ($r=0.384$, $p=0.048$) & with Leptin($r=0.531$, $p=0.005$) in HBV patients .

**Table 2**

***Distribution of the patients and control groups according to age & sex***

| Groups (year) | HBV | | HCV | | control |
|---|---|---|---|---|---|
| | male | female | male | female | male female |
| < 20 | 2 | 1 | 1 | 0 | 2 1 |
| 20 – 29 | 3 | 4 | 1 | 2 | 2 4 |
| 30 – 39 | 5 | 2 | 5 | 4 | 3 5 |
| 40 – 49 | 5 | 2 | 2 | 4 | 4 3 |
| 50 – 59 | 1 | 2 | 7 | 2 | 2 1 |
| ≥ 60 | 1 | 3 | 1 | 1 | 2 1 |
| Sub Total | 17 | 14 | 17 | 13 | 15 |
| Net Total | 31 | | 30 | | 30 |
| Total = 91 | | | | | |

**Table 3**
***clinical and laboratory data of patients with HCB, HBV and control***

| | HCV patients | HBV patients | control | P HCV | PHBV |
|---|---|---|---|---|---|
| N | 30 | 31 | 30 | ------- | -------- |
| Gender (F/M) | 17/13 | 17/14 | 15/15 | ------- | -------- |
| Age | 42.53 ± 11.880 | 38.64 ± 14.947 | 37.53 ± 13.525 | 0.111 | 0.762 |
| PT (Sec) | 13.43 ± 0.747 | 13.27 ± 0.719 | 13.29 ± 0.329 | 0.390 | 0.913 |
| TSP (g/dl) | 9.37 ± 1.624 | 9.29 ± 2.426 | 7.19 ± 0.662 | 0.000 | 0.000 |
| ALB (g/dl) | 2.54 ± 0.170 | 2.63 ± 0.237 | 4.61 ± 0.578 | 0.000 | 0.000 |
| AST (U/L) | 9.63 ± 3.805 | 8.65 ± 4.423 | 5.69 ± 1.995 | 0.000 | 0.002 |
| ALT (U/L) | 16.54 ± 9.252 | 15.75 ± 9.306 | 6.92 ± 1.539 | 0.000 | 0.000 |
| ALP (U/L) | 90.59 ± 17.402 | 91.08 ± 17.133 | 50.83 ± 11.635 | 0.000 | 0.000 |
| TSB (mg/dl) | 1.01 ± 0.786 | 0.89 ± 0.838 | 0.42 ± 0.073 | 0.000 | 0.003 |
| TC (mg/dl) | 93.52 ± 31.257 | 97.07 ± 26.358 | 166.66 ± 13.330 | 0.000 | 0.000 |
| TG (mg/dl) | 102.14 ± 63.587 | 103.45 ± 51.305 | 254.52 ± 26.49 | 0.000 | 0.000 |
| HDL (mg/dl) | 22.41 ± 8.507 | 22.37 ± 5.784 | 46.82 ± 11.633 | 0.000 | 0.000 |
| VLDL (mg/dl) | 20.40 ± 12.621 | 21.05 ± 10.593 | 50.90 ± 5.298 | 0.000 | 0.000 |
| LDL (mg/dl) | 50.74 ± 21.893 | 52.41 ± 22.282 | 68.77 ± 3.584 | 0.000 | 0.000 |
| AFP (ng/ml) | 14.69 ± 5.279 | 16.56 ± 6.954 | 7.54 ± 1.196 | 0.000 | 0.000 |
| Leptin (ng/ml) | 23.77 ± 5.898 | 17.99 ± 3.280 | 5.34 ± 1.200 | 0.000 | 0.000 |

**TABLE 4**
***Spearman's Correlation Analysis between Serum AFP and patients with (HCV& HBV) and Biochemical Variables of the Study Subjects***

| Parameter | HCV patients N=(30) | p-value | HBV patients N=(31) | p-value |
|---|---|---|---|---|
| Age Years | 0.043 | 0.823 | 0.235 | 0.238 |
| PT (Sec) | -0.152 | 0.431 | 0.384* | 0.048 |
| TSP (g/dl) | 0.114 | 0.555 | -0.269 | 0.174 |
| ALB (g/dl) | 0.066 | 0.735 | -0.083 | 0.681 |
| AST (U/L) | -0.205 | 0.445 | 0.287 | 0.153 |
| ALT (U/L) | -0.126 | 0.516 | -0.273 | 0.168 |
| ALP (U/L) | -0.251 | 0.189 | -0.210 | 0.294 |
| TSB (mg/dl) | 0.052 | 0.787 | 0.081 | 0.688 |
| TC (mg/dl) | 0.053 | 0.784 | -0.288 | 0.145 |
| TG (mg/dl) | -0.232 | 0.225 | 0.094 | 0.641 |
| HDL (mg/dl) | -0.312 | 0.099 | -0.265 | 0.182 |
| VLDL (mg/dl) | -0.230 | 0.229 | 0.060 | 0.767 |
| LDL (mg/dl) | 0.062 | 0.751 | -0.304 | 0.123 |
| Leptin (ng/ml) | -0.149 | 0.441 | 0.531** | 0.005 |

****. Correlation is significant at the 0.05 level (2-tailed).***
*****. Correlation is significant at the 0.01 level (2-tailed).***

**TABLE 5**
***Spearman's Correlation Analysis between Serum Leptin and patients with (HCV& HBV) and Biochemical Variables of the Study Subjects***

| Parameter | HCV patients N=(30) | p-value | HBV patients N=(31) | p-value |
|---|---|---|---|---|
| Age Years | 0.165 | 0.383 | 0.071 | 0.718 |
| PT (Sec) | 0.076 | 0.688 | -0.034 | 0.862 |
| TSP (g/dl) | -0.174 | 0.357 | -0.124 | 0.530 |
| ALB (g/dl) | 0.347 | 0.060 | -0.349 | 0.068 |
| AST (U/L) | 0.244 | 0.194 | 0.019 | 0.922 |
| ALT (U/L) | -0.018 | 0.927 | -0.052 | 0.793 |
| ALP (U/L) | -0.038 | 0.842 | -0.259 | 0.183 |
| TSB (mg/dl) | 0.067 | 0.726 | 0.048 | 0.808 |
| TC (mg/dl) | 0.206 | 0.274 | -0.309 | 0.110 |
| TG (mg/dl) | -0.022 | 0.909 | -0.157 | 0.426 |
| HDL (mg/dl) | 0.001 | 0.997 | -0.142 | 0.426 |
| VLDL (mg/dl) | -0.017 | 0.930 | -0.163 | 0.408 |
| LDL (mg/dl) | 0.278 | 0.137 | -0.215 | 0.272 |
| AFP (ng/ml) | -0.149 | 0.441 | 0.531** | 0.005 |

***. Correlation is significant at the 0.05 level (2-tailed).***
****. Correlation is significant at the 0.01 level (2-tailed).***

# DISCUSSION

Viral HBV and HCV infections are the greatest infectious disease problems among the world's , about 350 million people have chronic hepatitis B virus (HBV) infection, and about 125 million have been infected with hepatitis C virus (HCV) , therefore these diseases are important candidates for public health measures aimed at prevention , early diagnosis and treatment [18] , also Individuals with chronic hepatitis especially through HBV and HCV, are at highest risk to progress to cirrhosis hepatocellular carcinoma (HCC) [19, 20]. In the present study patients with chronic liver diseases (HBV & HCV) were compared with control subjects in term of age , hematological parameters , liver functions , AFP and leptin .interestingly , HBV & HCV patients were commonly found in ages ranged between 20-49 years , the median of patients age was 4 years older than that of the control subjects , these findings are related to the author observed that infection with HCV were most prevalent among people age between 30 to 49 years [21] . The results also shown that the gender in HBV patients were about (54.8% male & 45.2% female) and in HCV patients were about (56.6% male & 43.3% female) , Tungtrongchitr et al[22], in their study on Thailand patients with HBV , HCV & non – alcoholic steatosis hepatitis found that most subjects were males since liver disease is more common among men . In clinical practice, AFP levels are elevated in various clinical situations, which include hepatocellular carcinoma, acute or chronic viral hepatitis, chronic liver disease, and gonadal tumors [23]. The levels of AFP among patients with chronic HBV & HCV were determined and compared to control subjects , the results in the current study indicated that the serum AFP levels were significantly higher in HBV and HCV patients ($p < 0.05$) in comparison with control subjects and non significant difference in HBV patients compared to HCV ($p > 0.05$) , Our results were consistent with the previous studies [24, 25, 26, 27] which revealed that their were an increase in AFP level in viral hepatitis (HBV &HCV) and liver cirrhosis without evidence of HCC . The ALT ,AST and ALP activities were important as a biological markers that are widely used for liver diseases. This study revealed that their were a significant increase in ALT , AST and ALP activities in patients with HBV & HCV , damaged liver cells may be the result of increase these

enzymes activities[28 ].The behavior of leptin concentrations in the course of liver disease due to HBV & HCV infection is still under investigation , in this study serum leptin levels were significantly high in both patients groups as compared to control subjects , which is in consistent with previous reports from other countries[29, 30, 31, 32, 33, 34]. Finally, there were a positive correlation between serum AFP levels & leptin, also there were no correlation between AFP , leptin and lipid profile , transaminases , ALP bilirubin that used in this study , this might be argues against the potential role played by AFP and leptin in pathogenesis of human chronic liver disease or may be from the small number of subjects in this study so further studies on larger sample size are being planned to confirm these observations.

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