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DIFFERENCES IN CLINICAL AND BIOCHEMICAL PROFILES BETWEEN ACUTE AND CHRONIC HEPATITIS B AND C PATIENTS

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ABSTRACT

The aim of this study was to compare biochemical and clinical characteristics of patients with acute Hepatitis B & C infections, with those suffering from chronic Hepatitis B & C infections. Two hundred patients were randomly selected from Medicine ward at Jinnah Postgraduate Medical Center, Karachi. Patients were classified in two groups; acute hepatitis and chronic hepatitis. Anthropometric measurements and vitals were recorded. Blood samples were investigated for complete blood counts, blood chemistry, liver function test, and lipid profile. Results from ultrasound of abdomen and liver biopsy were also recorded. Most of the complications that were evaluated in this study were found to be significantly associated with chronic infections. There is a considerable difference in Liver Function Test between both groups. Furthermore, there is a significant relationship between progression of duration of disease and serum lipoproteins, cholesterol and triglycerides– suggesting liver dysfunction ($p<0.05$).There is a need to educate general population regarding the prevention of HBV and HCV infections. Lipid levels of the patients with advanced HBV and HCV should be monitored to prevent further complications.

KEYWORDS: Hepatitis B infection, Hepatitis C infection, Liver function test, Lipid profile.

INTRODUCTION

More than 240 million people globally are victimized by HBV chronically. More than 900,000 deaths have been associated with chronic HBV and HCV infections, more commonly due to cirrhosis and hepatocellular carcinoma (Perz *et al*., 2006).These dreadful viruses have strong potential to bring about certain histopathological changes in liver specifically; inflammation (portal and lobular), necrosis (piecemeal, spotty and bridging), fibrosis (septal, portal and peri-portal), steatosis, formation of inflammatory lymphoid infiltrates and cirrhosis (Alam *et al*., 2011).

A panel of blood markers termed as Liver Function Test (LFT) is useful in reflecting suspected liver diseases, state of hepatic malignancy, metabolic abnormalities or other liver impairments. In both HBV and HCV chronic cases, indices of biochemical markers demonstrate high extrapolative values for necro-inflammatory and fibrotic lesions in liver (Alavian *et al*., 2010). Aminotransferase (ALT and AST) levels are considered the clinical indicators of liver health. Not all persons with elevated aminotransferase activity have liver disease. However, some studies indicate that more advanced liver disease, including cirrhosis, may be detected from seemingly slight aminotransferase elevations (Ruhl *et al*., 2003). Since alkaline phosphatase does not only originate in liver, but is also produced by bones, intestine and placenta, therefore, isolated elevation of this index certainly cannot predict liver dysfunction (Mauro *et al*., 2006). Declination in serum albumin levels associated with progressive liver disease is suggestive of decreased albumin synthesis by the affected liver. First-line global screening tests such as the prothrombin time (PT) and the activated partial thromboplastin time (aPTT) are used widely to assess risk of bleeding in patients undergoing chronic liver disease (Siddiqui *et al*., 2011).

The liver being a major site for synthesizing lipoproteins plays an important role in maintaining a dynamic balance between lipoprotein synthesis and metabolism. Studies have demonstrated close interactions of HBV and HCV with lipid metabolism. The entry, and then the assembly of HCV are responsible for exploiting lipid metabolism in liver cell (Popescu and Dubuisson, 2010).

In patients infected with chronic HCV, a fraction viral particles are associated with host triacylglycerol-rich lipoproteins, forming lipo-viroparticles (LVPs). As a result, up regulation of LDL receptors is implicated with HCV entry and replication with profound evidence that LVPs behave as ligands of the LDL receptor.

The literature also demonstrates well the importance of HCV- Lipid interactions clinically. A community based cohort study in Egypt, demonstrated low lipid levels in patients with HCV infections than those who were never infected. Two independent National Health and Nutrition Examination Survey (NHANES) cohorts of United States of America suggest a possible influence of sex hormones on host lipid response to HCV infection (Lao *et al*., 2011). Additionally, a study on Hepatitis B virus transgenic mice (HBV-Tg mice) reveals the alterations in regulatory proteins can impair host cell lipid metabolism.

HBx (Hepatitis B virus protein X) has been studied to boost the recruitment of a transcriptional co-activator that controls lipid metabolism "ASC2" (activation signal co-integrator 2) to LXRE (Liver X Response Element) with LXRα (Liver X Receptor α) (Kim *et al*., 2008). Furthermore, HBx can directly inhibit the production of Apo B (vital component of LDL-C and VLDL-C) through over expression of N-acetylglucosaminyltransferase III. These studies support the notion that there must a relationship between the progression of hepatitis and lipid profile.

The main aim of this study is to identify the differences in clinical and biochemical characteristics of patients with acute Hepatitis B and C infections, with those suffering from chronic Hepatitis B and C infections.

METHODOLOGY

Study site and population: In this cross-sectional study, a sample of 200 patients diagnosed with Hepatitis B virus (HBV) or Hepatitis C virus (HCV) infections was selected randomly from the medical ward of Jinnah Postgraduate Medical Centre (JPMC), Karachi. Case definitions of HBV and HCV were made on the basis of serological markers and time duration. Patients were further classified in two groups; Acute Hepatitis and Chronic Hepatitis. The former included acute HBV and HCV infected patients while the latter included chronic HBV and HCV infected patients.

Exclusion criteria: Patients with history of renal, cardiac, liver or endocrinological disorders and patients with known malabsorption, malnutrition and immunoglobulin disorders were excluded from the study.

Study measures: Personal interviews were conducted using pre–tested structured questionnaires. The questionnaire comprised questions on demographic and socioeconomic attributes, potential parenteral exposures to blood or blood productsand household exposure to hepatitis. Anthropometric measurements and vitals were recorded. Blood samples were investigated for complete blood counts, blood chemistry (Sodium, Potassium, Urea, Creatinine, Chloride, Bicarbonate and Glucose), liver function test (Aspartate transaminase (AST), Adenosine triphosphate (ALT), Alkaline Phosphatase (ALP), Total Bilirubin, Direct Bilirubin, Gamma-glutamyltransferase (GGT), Prothrombin time (PT), Activated Partial Thromboplastin Time (aPTT), Albumin and Globulin),and lipid profile (Total Cholesterol (TC), Triglycerides (TG), LDL and HDL) using Randox® kits. Results from ultrasound abdomen and liver biopsy were obtained from patients' records for evaluating hepatocellular carcinoma and cirrhosis. Informed consent was obtained from all study participants.

Statistical analysis: Data were entered and analyzed in the Statistical Package for Social Sciences (SPSS version 17.0) and MS Excel 2007. For categorical variables (gender, occupation, marital status, ethnicity, residence, sign and symptoms and complications) descriptive statistics were computed. Inferential statistics for these variables were done using chi–square test of significance. Descriptive statistics for numerical variables (age, number of households, income per month, anthropometric measurements, vitals, complete blood counts, blood chemistry, liver function tests and lipid profile) were done by computing mean ± SEM. Independent t–test was applied to compare the significant differences between acute hepatitis and chronic hepatitis. Correlation between Lipid Profile and duration of illness was determined using Pearson Product–Moment Correlation (r). A p–value < 0.05 was considered statistically significant.

RESULTS

Two hundred patients diagnosed with HBV or HCV were enrolled in the study. Out of which 94 (47%) patients were suffering from HBV (acute cases 40 and chronic cases 54) and 106 (53%) were infected with HCV (acute cases 44 and chronic cases 62). Thus from a total of 200, 84 patients had acute hepatitis while 116 had chronic hepatitis. Mean (± SEM) age of patients with acute hepatitis was found to be 35 (±1.45) and of patients with chronic hepatitis was 38.17 (± 1.26). There was no significant difference in mean ages of acute and chronic hepatitis patients (p-value 0.102). There were 106 (53%) males and 94 (47%) females indicating the male gender was slightly more associated with the disease. 72% (144) patients of all were ever married whereas 28% (56) were never married. Chronically infected patients had significantly lower weight and BMI than the acute ones.

Complete blood counts of patients with acute and chronic hepatitis showed significant differences (Table 1).

Table 1. Complete blood counts of patients with acute and chronic hepatitis B and hepatitis C infections.

Complete blood counts	Mean ± SEM		–value*
	Acute (n = 84)	Chronic (n = 116)	
Hemoglobin (mg/dl)	11.01 ± 0.2326	8.96 ± 0.1724	0.000
Hematocrit (%)	33.17 ± 0.7101	26.98 ± 0.5173	0.000
Platelets / mm^3	$1.5 \times 10^5 \pm 5.35 \times 10^3$	$1.3 \times 10^5 \pm 3.75 \times 10^3$	0.02
TLC / mm^3	$5.3 \times 10^4 \pm 4.4 \times 10^3$	$3.9 \times 10^4 \pm 2.8 \times 10^3$	0.010

* p–value <0.05 significant (calculated by independent t–test)

Mean ± SEM AST levels were found to be elevated in acute patients than chronic ones but the difference remained statistically insignificant. ALT levels were also high in acute patients than chronic cases but this time a statistically significant difference existed (Table 2).

Table 2. Liver function tests of patients with acute and chronic hepatitis B and hepatitis C infections.

Liver function test	Mean ± SEM		p–value*
	Acute (n = 84)	Chronic(n = 116)	
AST (IU/L)	199.42 ± 15.92	172.83 ± 6.76	0.092
ALT (IU/L)	442.36 ± 26.56	124.83 ± 6.18	0.000
ALP(IU/L)	56.10 ± 3.20	98.45 ± 12.48	0.001
GGT (IU/L)	49.95 ± 3.77	134.33 ± 19.31	0.000
Total Bilirubin (mg/dL)	2.47 ± 0.087	2.23 ± 0.076	0.045
Direct Bilirubin (mg/dL)	1.52 ± 0.066	2.52 ± 0.823	0.306
PT (s)	12.21 ± 0.198	14.74 ± 0.279	0.000
aPTT(s)	35.79 ± 0.761	45.39 ± 0.806	0.000
Albumin (A) (g/dL)	3.77 ± 0.0219	2.99 ± 0.0485	0.000
Globulin (G) (g/dL)	3.53 ± 0.035	3.63 ± 0.037	0.063
A/G Ratio	1.07 ± 0.081	0.84 ± 0.020	0.000

* p–value <0.05 significant (calculated by independent t–test)

With regards to plasma cholesterol (total, HDL and LDL) and triglycerides levels, all four variables showed to decline significantly with the progression of duration of hepatitis. There was a significant negative correlation between the progression of duration of disease and lipid indices.

DISCUSSION

Hepatitis is one of the most 10 reportable diseases in Pakistan. The prevalence rate is very high and Pakistan falls in the intermediate to high endemicity zone of hepatitis prevalence. The reason may stand for lack of proper health facilities, poor economic status and less public awareness about the transmission of major communicable diseases including HBV, HCV and HIV. The clinical course and sequel of acute and chronic hepatitis vary among individuals, ranging from asymptomatic carrier state to self-limiting infection or fulminant hepatic failure, chronic hepatitis with progression to cirrhosis, and hepatocellular carcinoma.

A 13-year study in Pakistan revealed that hepatitis B antigen prevalence in pediatric populations is as much as 5.5% and for hepatitis C antibody is as much as 5.4%. A weighted average of hepatitis B antigen prevalence among healthy adults was found to be 2.4% whereas for hepatitis C antibody was 3.0% (Ali *et al*., 2009). Different data suggest a moderate to high prevalence of hepatitis B and hepatitis C in different areas of Pakistan (Khattak *et al*., 2002).

Thrombopoietin produced by liver is a dominant cytokine for controlling the development of megakaryocyte and platelet production and hepatitis is also associated with another hematological abnormality other than anemia that is thrombocytopenia. Olariu *et al*., 2010 identified that several potential mechanisms can contribute to thrombocytopenia in chronic HCV infection, like elevated platelet clearance due to an immune complex disease or a decreased platelet production due to direct marrow suppression and chronic hepatitis C may be associated with variable degrees of thrombocytopenia (Olariu *et al*., 2010). Hepatocellular damage and hepatic fibrosis are strongly correlated with thrombocytopenia (Wang *et al*., 2004). Adinolfi demonstrated an inverse correlation between the spleen size and platelet count accounting for one of the reason for splenomegaly in these patients (Adinolfi *et al*., 2001). This study also shows significant differences in CBC among acute and chronic hepatitis.

Chronic liver disease is often diagnosed by detecting asymptomatic elevations in serum aminotransferases. One study found a statistically significant positive association between liver stiffness and both types of aminotransferases among acutely infected patients of viral hepatitis. ALT and AST levels have shown to increase significantly in patients infected with HBV and HCV. ALP increment has been associated with HBV hepatitis in comparison with healthy control group. GGT enzyme seems to be useful as an indirect marker of more advanced liver disease in chronic hepatitis C (Silva *et al*., 2004). HBV with acute flare revealed that patients with acute hepatitis B showed higher level of serum GGT accompanied with higher levels of ALT and total bilirubin than chronic cases (Han *et al*., 2008). Our study has also demonstrated quite similar results for AST, ALT, ALP and GGT for patients infected with acute and chronic hepatitis B and C. However, significant difference for the elevation of these enzymes between acute and chronic cases appeared for ALT, ALP and GGT. Albumin synthesis is an important function of the liver and it is most abundant protein in human blood plasma which is produced in liver. No or little reduction in serum albumin levels are seen in patients with acute liver disease as the fractional clearance remains quite low. However, Chronic Liver Diseases may cause a severe reduction in serum Albumin levels due to increased parenchymal liver cell damage (Abou *et al*., 2009). Furthermore, coexistence of mutant variant of viruses with higher pathogenicity and replication ability may result in progressive liver disease and thus low serum albumin levels in these patients (Peng *et al*., 2005). Serum immunoglobulin levels are often

found elevated in hepatitis infection. There is a strong association between levels of serum globulin and immunoglobulin G and extent of hepatic fibrosis in patients with chronic HBV infection. Hypergammaglobulinaemia is a common finding (67%) in patients with cirrhosis associated with severe active liver disease. Perhaps our study demonstrated that globulins rise more frequently in chronic patients than acute ones but the p-value remained insignificant indicating the existence of no difference in elevations among acute and chronic patients (Table 2).Coagulation abnormalities as a result of chronic liver diseases are often measured via prolongation of screening tests such as the PT and PTT. A study conducted at Liaquat University Hospital, Jamshoro during the study period of one year showed that out of all the patients admitted during the study time 88% with chronic liver disease had elevated PT and while 71% had elevated aPTT (Siddique *et al*., 2011). In this regard, our study has documented significant elevation of PT and aPTT in chronic hepatitis patients than the acute ones (Table 2).

The liver is an important organ in maintaining dynamic balance of metabolism of cholesterol and triglycerides. Most of the lipoproteins and endogenous lipids are prepared by liver and therefore the homeostatic metabolism is quite dependent upon the integrity of the liver cells. A prominent decline is seen in plasma cholesterol and triglyceride levels in patients with severe hepatitis and hepatic failure because of reduction of lipoprotein biosynthesis (Mehboob *et al*., 2010). Acute or chronic malfunction of liver because of viral hepatitis, non-viral hepatitis, liver cirrhosis and other diseases may also induce hyperlipidemia. Furthermore, a study conducted in Iran showed that HDL, LDL, TG and total cholesterol in cirrhotic patients appeared to be significantly lower than at in healthy individuals. This study has also shown that the more severe the liver damage is, the more decline in lipid levels can be detected (Ghadir *et al*., 2010). In support of this finale, our study has presented significantly that with the progression of infection LDL, HDL, TG and total cholesterol levels in serum decrease (Figs. 1-4).

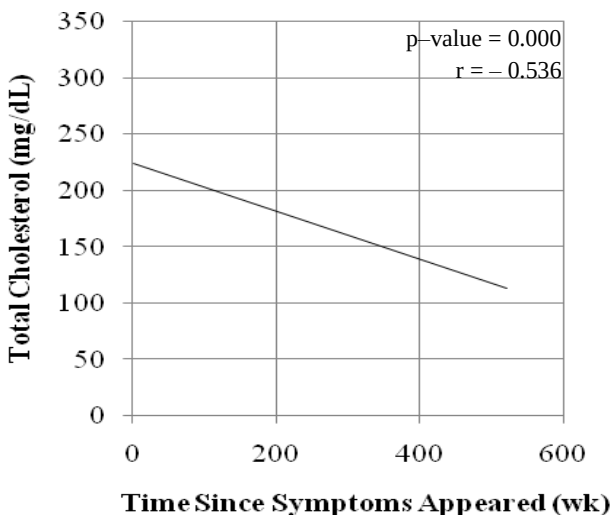

Fig. 1

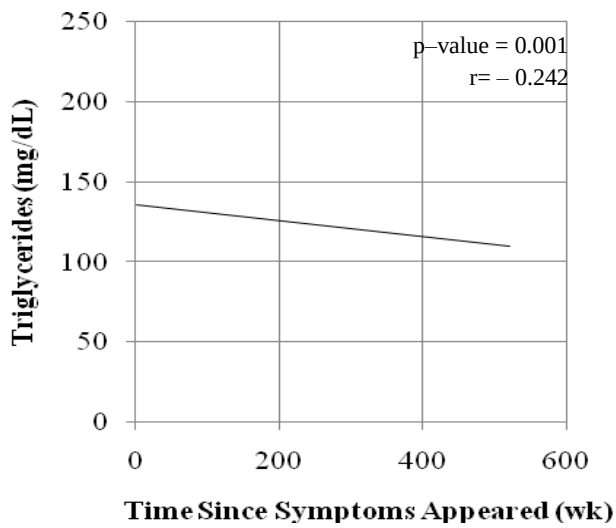

Fig. 2

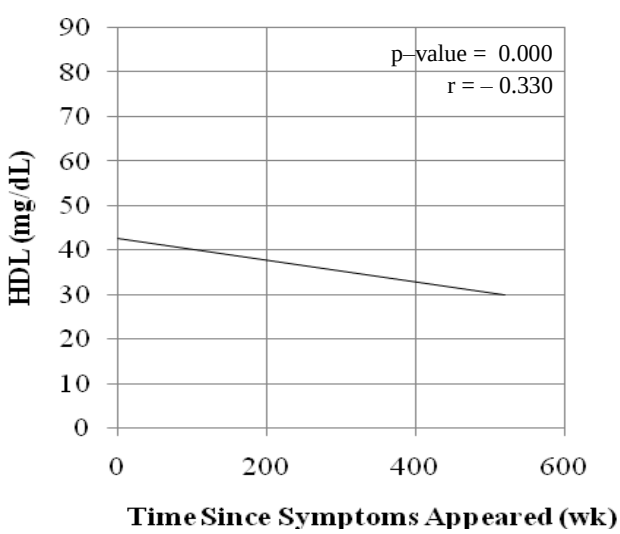

Fig. 3

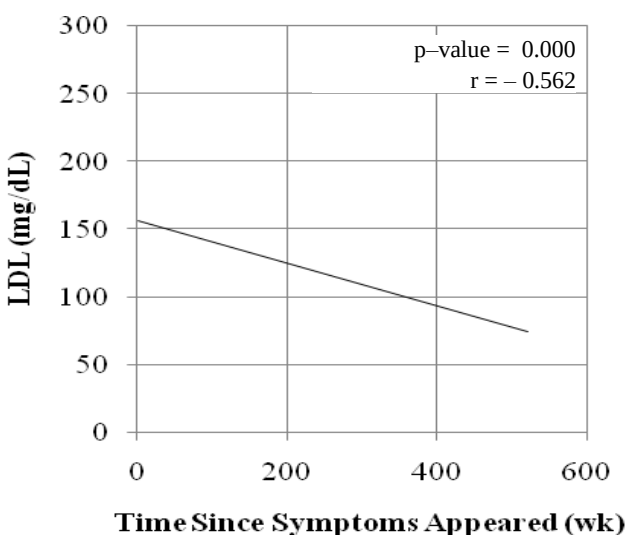

Fig. 4

Figs. 1-4. Correlation between lipid profile and duration of hepatitis B and hepatitis C infections.

CONCLUSION

It is suggested from this study that awareness regarding the prevention of HBV and HCV infections should be created among the population at risk. Importance of HB vaccination should be promoted and patients with chronic infections should be monitored for their lipid levels in order to prevent further complications.

Ethical Considerations

Ethical issues (including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

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