ORIGINAL ARTICLE

PROGRESSION OF SERUM MARKERS IN CHRONIC LIVER DISEASE PRODUCED BY CHRONIC VIRAL HEPATITIS B, C AND CO-INFECTION

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ABSTRACT

Background: Chronic liver disease represents a major cause of morbidity and mortality worldwide. The objectives of the study were to determine and compare values of serum markers in subgroups; category-wise (MCTP scoring system) as well as infection-wise among patients of HBV, HBC and co-infections.

Material & Methods: A cross-sectional study was conducted in the Department of Medicine, Lahore General Hospital, Lahore in 2010. Sample size was patients of chronic HBV, HCV, and co-infections. The patients were grouped with 25 subjects each in HB, HC and co-infection. Non-probability-convenience sampling was used for data collection. Demographic variables were sex and age in years. Research variables were AST/ALT ratio, prothrombin time, platelet conunt, serum albumin and serum bilirubin. Continuous variables like biochemical markers were analyzed as mean ±standard deviation (±SD) whereas categorical variables were analyzed as count and percentages using SPSS version 20.0. One-way ANOVA was applied to observe group mean differences.

Results: Out of the 75 subjects, 51(68.0%) were males and 24(32.0%) were females. The mean ±SD age was 44.69 ±7.423 years. There was a significant difference in AST/ALT ratio in chronic HBV group only ($p < 0.05$). Platelet count significantly decreased in co-infection group only from (MCTP) class A-D ($p<0.05$). PT and serum bilirubin significantly increased, while serum albumin significantly decreased in all groups from MCTP class A-D ($p<0.05$). In class wise comparison amongst all groups, none of the biochemical markers was statistically different ($p>0.05$).

Conclusion: There was statistically significant differences of the values of serum markers among subgroups category-wise A-D (MCTP classes) of chronic liver disease produced by chronic HBV, HCV, and co-infection. There was no statistically significant difference of these values between subgroups infection-wise.

KEY WORDS: chronic liver disease; viral hepatitis; serum markers; modified Child-Turcotte-Pugh score.

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INTRODUCTION

Liver diseases due to hepatitis B virus (HBV) have been a constant problem worldwide leading to more than 1 million deaths per year.[1] It is a critical communal well-being issue in Pakistan.[2] Almost 3% of humans are infected by HCV worldwide.[3] In 80% cases, acute viral hepatitis C becomes chronic and progresses fibrosis into cirrhosis in next twenty years.[4] Chronic HBV, HCV, and co-infection develop 90% cases of chronic liver disease (CLD) in Pakistan.[5] The global prevalence of co-infection is still anonymous and underestimated.[6] Altered Prothrombin time (PT), serum albumin, and serum bilirubin are evident of well-being of liver. The routine markers of hepatic damage are aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Hepatitis B, hepatitis C, ethanol, iron (hemochromatosis), autoimmune hepatitis, drugs or toxins, fatty liver, and copper (Wilson's disease) are causes of raised serum AST and ALT.[7]

Serum albumin level can guide about hepatic synthetic ability. Both PT and serum albumin levels are frequently recognized as "tests of liver function". Bilirubin level rises when liver loses about half of its excretory capacity. Similarly, raised bilirubin level is

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MODIFIED CHILD-TURCOTTE-PUGH SCORING SYSTEM

	1 point	2 points	3 points	4 points
Bilirubin (mg/dl)	< 2	2-3	3.1-8	> 8
Albumin (g/dl)	> 3.5	2.8-3.5	2.3-2.7	< 2.3
PT prolong (sec)	< 4	4-6	6-11	> 11
Ascites	None	Easily controlled	Poorly controlled	---
Encephalopathy	None	Grade 1-2	Grade 3-4	---

considered as a sign of hepatic dysfunction.[8-9] Modified Child-Turcotte-Pugh (MCTP) scoring system has scores for albumin, bilirubin, prothrombin time, ascites, and hepatic encephalopathy which are related to prognosis of stage. It is classified from class A-D and based on the same parameters i.e. albumin, bilirubin, prothrombin time, ascites, and hepatic encephalopathy.[10,11] The objectives of the study were to determine and compare values of serum markers in subgroups; category-wise (MCTP scoring system) as well as infection-wise among patients of HBV, HBC and co-infections.

MATERIAL AND METHODS

A cross-sectional study was conducted in the Department of Medicine, Lahore General Hospital, Lahore in 2010. Seventy five patients of chronic HBV, HCV, and co-infection of either sex, aged 35 years or above were selected. The patients were grouped with 25 subjects each in HB, HC and co-infection. Non-probability-convenience sampling was used for data collection. Demographic variables were sex and age in years. Research variables were AST/ALT ratio, prothrombin time, platelet conunt, serum albumin and serum bilirubin. A specimen of 5 ml of blood was collected in 5ml disposable syringe from each subject by venepuncture with aseptic measures. 1.8 ml of this sample was transferred in PT bottle and 1 ml was mixed with ethylene diamine tetra acetate (EDTA) in test tube. Serum in the syringe was transferred in serum cups. After collection of blood samples, PT bottles, test tubes, and serum cups were marked for identification of a subject. Grouping of the patients was done according to MCTP scoring system. Serum AST and ALT was measured by kinetic method. Platelet count was measured on Hematology analyzer. Serum bilirubin was measured by Colorimetric method. Serum albumin was measured by Bromcresol Green method. PT was measured by coagulation method. Continuous variables like biochemical markers were analyzed as mean ± standard deviation (±SD) whereas categorical variables were analyzed as count and percentages. Data was entered in the SPSS version 20.0. Data was presented in tables. One-way ANOVA was applied to observe group mean differences. Level of 5 % ($p < 0.05$) was used for significance testing.

RESULTS

Seventy five subjects were included in the study. 51 (68.0%) were males and 24 (32.0%) were females. The age of the selected CLD patients was ranged from 35 to 65 years while the mean ± SD age was 44.69 ±7.423.

In chronic HBV group, there was a significant increase in AST/ALT ratio, PT, and serum bilirubin from class A-D ($p < 0.05$). While serum albumin significantly decreased from class A-D ($p < 0.05$). There was a non-significant decrease in platelet count ($p > 0.05$) (Table 1). In chronic HCV group, there was also a significant increase in PT and serum bilirubin from class A-D ($p < 0.05$). While serum albumin significantly decreased from class A-D ($p < 0.05$). There was also a non-significant increase in AST/ALT ratio and decrease in platelet count ($p > 0.05$) (Table 2). AST/ALT ratio, PT, platelets count, serum albumin, and serum bilirubin were also studied in the co-infection group. There was also a significant increase in PT and serum bilirubin from class A-D ($p < 0.05$). While serum albumin significantly decreased from

Table 1: Comparison of serum markers of MCTP classes in chronic HBV group (n=25)

MCTP class	AST/ALT ratio	Prothrombin time in second	Platelet count (/ cmm)	Serum albumin (g/dl)	Serum bilirubin (mg/dl)
MCTP class A	1.03 ±0.257	4.71 ±0.951	139.71 ±76.275	5.24 ±0.723	1.63 ±0.298
MCTP class B	1.08 ±0.144	15.67 ±6.653	139.50 ±19.087	5.00 ±0.639	1.77 ±0.137
MCTP class C	1.48 ±0.617	21.17 ±5.636	120.00 ±25.401	3.83 ±0.889	2.85 ±1.484
MCTP class D	1.94 ±0.710	34.33 ±8.042	98.67 ±31.066	2.17 ±0.367	6.05 ±2.692
p - value	0.018*	0.000*	0.368	0.000*	0.000*

*Significant

Table 2: Comparison of serum markers of MCTP classes in chronic HCV group (n=25)

MCTP class	AST/ALT ratio	Prothrombin time in second	Platelet count (/cmm)	Serum albumin (g/dl)	Serum bilirubin (mg/dl)
MCTP class A	0.99 ±0.279	4.56 ±0.952	138.57 ±91.471	5.49 ±1.042	1.50 ±0.379
MCTP class B	1.11 ±0.216	16.83 ±9.218	133.17 ±21.803	5.18 ±0.556	1.62 ±0.264
MCTP class C	1.50 ±0.693	21.15 ±4.584	112.00 ±24.528	3.88 ±0.781	3.13 ±1.782
MCTP class D	1.85 ±1.022	36.33 ±9.832	99.17 ±32.738	2.28 ±0.417	6.20 ±2.768
p - value	0.096	0.000*	0.543	0.000*	0.000*

Table 3: Comparison of serum markers of MCTP classes in co- infection group (n=25)

MCTP class	AST/ALT ratio	Prothrombin time in second	Platelet count (/cmm)	Serum albumin (g/dl)	Serum bilirubin (mg/dl)
MCTP class A	1.06 ±0.243	4.43 ±0.787	166.14 ±69.487	5.50 ±1.041	1.47 ±0.325
MCTP class B	1.13 ±0.185	15.67 ±7.891	138.33 ±17.282	5.08 ±0.595	1.62 ±0.194
MCTP class C	1.43 ±0.629	19.00 ±2.608	121.50 ±19.003	4.13 ±0.589	2.87 ±1.208
MCTP class D	1.84 ±0.933	35.17 ±10.187	97.00 ±29.469	2.15 ±0.356	6.15 ±2.554
p - value	0.097	0.000*	0.047	0.000*	0.000*

*Significant

Table 4: Comparison of serum markers of MCTP class 'A' in all groups (chronic HBV, HCV, and co-infection) (n=21)

Type of infection	AST/ALT ratio	Prothrombin time in second	Platelet count (/cmm)	Serum albumin (g/dl)	Serum bilirubin (mg/dl)
HBV	1.03 ±0.257	4.71 ±0.951	139.71 ±76.275	5.24 ±0.723	1.63 ±0.298
HCV	0.99 ±0.279	4.56 ±0.952	138.57 ±91.471	5.49 ±1.042	1.50 ±0.379
Co-infection	1.06 ±0.243	4.43 ±0.787	166.14 ±69.487	5.50 ±1.041	1.47 ±0.325
p - value	0.905	0.839	0.767	0.851	0.654

Table 5: Comparison of serum markers of MCTP class 'B' in all groups (chronic HBV, HCV, and co-infection) (n=18)

Type of infection	AST/ALT ratio	Prothrombin time in second	Platelet count (/cmm)	Serum albumin (g/dl)	Serum bilirubin (mg/dl)
HBV	1.08 ±0.144	15.67 ±6.653	139.50 ±19.087	5.00 ±0.639	1.77 ±0.137
HCV	1.11 ±0.216	16.83 ±9.218	133.17 ±21.803	5.18 ±0.556	1.62 ±0.264
Co-infection	1.13 ±0.185	15.67 ±7.891	138.33 ±17.282	5.08 ±0.595	1.62 ±0.194
p - value	0.905	0.958	0.837	0.869	0.367

Table 6: Comparison of serum markers of MCTP class 'C' in all groups (chronic HBV, HCV, and co-infection) (n=18)

Type of infection	AST/ALT ratio	Prothrombin time in second	Platelet count (/cmm)	Serum albumin (g/dl)	Serum bilirubin (mg/dl)
HBV	1.48 ±0.617	21.17 ±5.636	120.00 ±25.401	3.83 ±0.889	2.85 ±1.484
HCV	1.50 ±0.693	21.15 ±4.584	112.00 ±24.528	3.88 ±0.781	3.13 ±1.782
Co-infection	1.43 ±0.629	19.00 ±2.608	121.50 ±19.003	4.13 ±0.589	2.87 ±1.208
p - value	0.979	0.634	0.751	0.770	0.936

Table 7: Comparison of serum markers of MCTP class 'D' in all groups (chronic HBV, HCV, and co-infection) (n=18)

Type of infection	AST/ALT ratio	Prothrombin time (/sec)	Platelet count (/cmm)	Serum albumin (g/dl)	Serum bilirubin (mg/dl)
HBV	1.94 ±0.710	34.33 ±8.042	98.67 ±31.066	2.17 ±0.367	6.05 ±2.692
HCV	1.85 ±1.022	36.33 ±9.832	99.17 ±32.738	2.28 ±0.417	6.20 ±2.768
Co-infection	1.84 ±0.933	35.17 ±10.187	97.00 ±29.469	2.15 ±0.356	6.15 ±2.554
p - value	0.977	0.934	0.992	0.806	0.995

class A-D ($p < 0.05$). There was also a non-significant increase in AST/ALT ratio and decrease in platelet count ($p > 0.05$) (Table 3). Serum markers of each MCTP class from A-D were also evaluated amongst chronic HBV, HCV and co- infection groups. There was no statistically significant difference in AST/ALT ratio, PT, platelet count, serum albumin, and serum albumin amongst all groups ($p > 0.05$) (Table 4-7).

DISCUSSION

In chronic HBV group, data showed progressive increase in AST/ALT ratio from class A-D with a significant difference in AST/ALT ratio amongst MCTP classes ($p < 0.05$). In chronic HCV and co-infection groups, AST/ALT ratio progressively increased from class A-D with no significant difference amongst MCTP classes ($p > 0.05$). In other study, Imperiale et al. concluded that AST/ALT ratio of ≥ 1 is significant to diagnose cases of cirrhosis produced by chronic viral hepatitis C. [12] In this study, AST/ALT ratio ≥ 1 has shown value for the diagnosis of cirrhosis in chronic HCV group, while AST/ALT > 1 predicted cirrhosis in chronic HBV group. In co-infection group, platelet counts decreased significantly from class A-D but showed no significant difference amongst MCTP classes in all groups ($p > 0.05$). Karasu et al concluded that platelet count decreased more significantly in patients with chronic HCV but not in chronic HBV. [13] AST/ALT ratio increases significantly in HCV patients with fibrosis. Serum AST and ALT levels can be described as more useful than other parameters to predict significant fibrosis. The platelet counts may be lower in cases with advanced hepatic fibrosis or cirrhosis.[14]

However, PT and serum bilirubin progressively increased in all groups from class A-D with a significant difference amongst MCTP classes ($p < 0.05$). Giannini et al. concluded raised prothrombin levels in cases of chronic viral hepatitis B, C, and co-infection. Decreased hepatic synthesis of coagulation factors (I, II, V, VII, X) leads to increased PT levels. Bilirubin level rises when liver loses about half of its excretory capacity. Therefore, raised level of serum bilirubin indicates hepatic damage.[8-9] In this study, the increase in PT was not significantly different amongst MCTP classes in both groups ($p > 0.05$). In all groups, serum albumin progressively decreased from class A-D with a significant difference amongst MCTP classes ($p < 0.05$). Mano et al. concluded negative correlation of serum albumin level with progressive liver dysfunction.[15] In our study, serum albumin was highly decreased in MCTP classes A, B, and C in chronic HBV group, while in end-stage liver disease. The progressive decrease in serum albumin was not significantly different amongst MCTP classes in both groups ($p > 0.05$).

CONCLUSION

There was statistically significant differences of the values of serum markers among subgroups category-wise A-D (MCTP classes) of chronic liver disease produced by chronic HBV, HCV, and co-infection. There was no statistically significant difference of these values between subgroups infection-wise.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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None declared.

AUTHORS' CONTRIBUTION

Conception and Design:	AN, AT
Data collection, analysis & interpretation:	AN, AT, RN
Manuscript writing:	AN, RN, SNQ