Correlation Of Biochemical Parameters In Viral Hepatitis Patients

Habibullah Shaikh[1], Yasmin Shaikh[2], Ghulam Mustafa Dahri[3], Ghulam Sarwar Shaikh[4].

1. Habibullah Shaikh
M.B.B.S; M.Phil
Professor,
Department of Biochemistry,
Peoples University of
Medical & HealthSciences
for Women, Nawabshah.
2. Yasmin Shaikh
M.B.B.S; M.Phil
Senior Lecturer,
Department of
Pharmacology,
Peoples University of
Medical & HealthSciences
for Women, Nawabshah.
3. Ghulam Mustafa Dahri
M.B.B.S; M.Phil
Professor,
Department of
Pharmacology,
Peoples University of
Medical & Health Sciences
for Women, Nawabshah.
4. Ghulam Sarwar Shaikh
M.B.B.S; PhD
Associate Professor,
Department of Biochemistry,
SMBBMU, Larkana
Address of Correspondence
Prof. Dr. Habibullah Shaikh,
Professor, Department of
Biochemistry, Peoples
University of Medical & Health
Sciences for Women,
Nawabshah.
Cell No. 0333-7026326;
e-mail:
shaikhh24@gmail.com

ABSTRACT

Objective: Observation of biochemical parameters in the subjects with viral hepatitis in relation to their cause and stage of disease.

Design: Observational study.

Place & Duration: The research was performed at the Department of Biochemistry in Basic Medical Sciences Institute (B.M.S.I), situated at the J.P.M.C. Karachi, for the period of twelve months.

Material & Methods: The patients diagnosed with viral hepatitis B or hepatitis C infection were incorporated in current research. Selection of subjects was done after diagnosis by ELISA method of their disease. Controls for the study were selected those subjects who were negative for Hepatitis B and Hepatitis C. Serum insulin levels were estimated by ELISA method. While blood glucose by Hexokinase method and prothrombin time (PT) was estimated by one stage coagulation technique. However liver enzymes were assayed by enzymatic method. For paired and correlation data analysis, all comparisons, up to 0.05 P value was considered significant.

Result: The mean values of fasting blood glucose, insulin and albumin as compared to control were statistically significant ($P<0.05$). In all groups, the mean values of AST and ALT were found statistically highly significant ($P<0.01$), which indicates liver damage progression with subsequent rise in serum levels of insulin in these subjects.

Conclusion: The patients diagnosed positive either for viral hepatitis B and C, should also be screened for insulin in addition to hepatic profile to decrease fatal outcome of the co-morbid condition.

Key Words: Viral hepatitis, liver enzymes, co-morbid, cirrhosis, ELISA method, prothrombin time.

Shaikh H[1], Shaikh Y[2], Dahri GM[3], Shaikh GS[4]. **Correlation Of Biochemical Parameters In Viral Hepatitis Patients.** JPUMHS:2020;10(02)180-185
http://doi.org/10.46536/jpumhs/2020/10.02.314

INTRODUCTION

Hepatitis in general is referred to the liver inflammation. It may be caused by several factors.[1]Depending upon cause; it may be divided into two big groups viz infectious and noninfectious. Infectious may be due to viruses, bacteria, fungi and different parasites, while alcohol intake, different drugs, metabolic and autoimmune diseases can be noninfectious causes.[2] Different viruses may cause the disorder.[3] About 350 million population in the world is infected by hepatitis B virus which highlight it as major global health problem.[4,5]

Acute viral hepatitis is defined as an inflammatory process of liver lasting less than 6 months, commonly caused by viruses.[6] Hepatitis B and C viruses may remain asymptomatic for many years and progress to development of chronic hepatitis.[3] They may further progress to development of cirrhosis and hepatocellular carcinoma. Worldwide it remains a major public health threat mainly in developing countries with increased morbidity and mortality.[7,8,9] Chronically infected patients may transmit the disease for many years. It is more common in HCV infections than in HBV infections.[3,10]

Traditionally, the development of diabetes is observed as closely associated with aging, obesity and lack of physical activity.[11] In Prediabetes mellitus there is abnormal glucose homeostasis with deficiency or resistance to insulin as the hallmark.

Prediabetes mellitus may lead to the development of type II diabetes mellitus (T2DM).[12] It is more observed in patients of HCV as compared to patients with other risk factors to development of diabetes.[13,14]

The liver is a major organ of the body and have key role for maintaining metabolic homeostasis. The liver is largely involved with the synthesis and regulation of various lipids, lipoproteins and apolipoproteins.[15]

Therefore in perspective of the crucial outcome of comorbid state, the study was intended to observe the correlation of bio-chemical factors in the patients of viral hepatitis in relation to their cause and stage of disease.

MATERIAL AND METHOD:

This observational study was carried out at the B.M.S.I. Biochemistry Department situated at the JPMC Karachi. The study was performed in twelve months period. Patients were selected with the association of Hepato-gastroenterology department and Medical Units of J.P.M.C. Karachi. Eighty patients of either gender were selected for the study with an established diagnosis of the disease. The age of patients selected ranged 20-59 years with mean age of 39 years. These were divided equally and placed in separate groups in accordance to their disease type and cause. Group I and III hepatitis B positive with or without cirrhosis respectively. While group II and IV were hepatitis C positive with or without cirrhosis respectively. Patients having any other accompanying chronic disorder and viral coinfection were not included in study.

RESULTS:

Observations of current study highlighted statistically significant ($P<0.01$) values for fasting blood glucose, insulin, albumin and lipoproteins (a), while statistically extremely significant for AST and ALT with ($P<0.001$) mean values in all the groups. The difference was less significant in groups III and IV ($P<0.05$) of prothrombin time, globulin and A/G ratio, whereas as compared to control, it was found non-significant in groups I and II. Total proteins showed statistically non-significant in all groups (Table 1). While comparing observations between hepatitis B virus infected groups, AST and A/G ratio were significant ($P<0.01$) and other parameters remains less significant. Also in hepatitis C group II and IV, A/G ratio and AST levels found significant (Figure I).

In the group I, fasting blood glucose levels, insulin, prothrombin time, AST, ALT and globulin showing a significant negative correlation, whereas total proteins and albumin were positively correlated in group I and II only. Finally A/G ratio was the only finding significant in group III with Lp (a) (Table 2).

In the group II, fasting levels of blood glucose, insulin, PT (prothrombin time), AST and ALT were showing a significant negative correlation, whereas total proteins, albumin and globulin showed weak correlation. While In the group III, all the parameters showed a significant negative correlation. However in the group IV, fasting blood glucose levels, insulin, prothrombin time, AST, ALT, total proteins, albumin as well as globulin were showing a significant negative correlation, whereas A/G ratio showed weak correlation (Figure 2).

These findings reflect that lipoprotein (a) can be a good indicator of hepatic derangement in viral hepatitis irrespective of cause.

DISCUSSION:

In our study, parameters of diabetes have been observed along with biochemical parameters of hepatic function. The mean values of insulin showed statistically significant increased serum level in various groups in comparison to controls which indicates insulin resistance in the patients (Table 1). This hyperinsulinemia occurs because of decrease in insulin catabolism.[16]

The mean fasting blood glucose and insulin value has a statistically good positive correlation in all groups. The observations of Alizadeh et al and Mason et al.are similar to observations noted in our study.[16, 17] As lipoprotein (a) is synthesized in the liver, the mean values of lipoprotein (a) in all groups were found statistically significantly diminished.

TABLE # 1: COMPARISON OF PARAMETERS (BIOCHEMICAL) AMONG VARIOUS GROUPS					
Parameter	**Group I (n 20)**	**Group II (n 20)**	**GroupIII (n 20)**	**Group IV (n 20)**	**Control (n 20)**
Insulin (µU/ml)	13.9±1.12*$^{\Delta}$	19.2±1.69*$^{\lozenge}$	25.60±3.87*	24.3±4.57*	3.8±0.45
Fasting Blood Glucose (mg/dl)	89±3.60$^{\Delta}$	94±4.80 $^{\lozenge\lozenge}$	117±10.87*	134±15.85*	88±3.40
Lipoprotein (a) (mg/dl)	6.4±1.58*$^{\Delta}$	7.8±1.45*$^{\lozenge}$	3.5±0.98*	2.4±0.73*	13.6±0.62
Prothrombin time (Control: 11 to 16 sec)	17.2±1.02$^{\Delta}$	16.1±0.69$^{\lozenge}$	19.4±1.28*	19.6±0.95*	13.7±0.38
AST (U/L)	76.6±7.36**$^{\Delta\Delta}$	72.9±5.95**$^{\lozenge\lozenge}$	123.7±17.41***	128.2±15.65***	15.2±1.08
ALT (U/L)	81.6±7.94**	79.4±5.90**	95.6±10.42***	87.1±10.65***	27.4±1.25
Total protein (gm/dl)	6.7±0.18$^{\Delta}$	6.5±0.15$^{\lozenge}$	7.4±0.22 ^{NS}	7.6±0.15 ^{NS}	7.2±0.14
Albumin (gm/dl)	3.86±0.11*$^{\Delta}$	3.56±0.15*$^{\lozenge}$	2.87±0.08**	2.88±0.06**	4.66±0.14
Globulin (gm/dl)	2.9±0.11$^{\Delta}$	2.7±0.06$^{\lozenge}$	4.5±0.20**	4.7±0.12**	2.5±0.06
A/G ratio	1.34±0.05*$^{\Delta\Delta}$	1.38±0.04*$^{\lozenge\lozenge}$	0.65±0.02***	0.60±0.02***	1.88±0.07

TABLE # 2: CORRELATION COEFFICIENT WITHIN CASES										
ations = Total	Lipoprotein (mg/dl)	Insulin (uU/ml)	Glucose (mg/dl)	AST (U/L)	ALT (U/L)	Total Protein (g/dl)	Albumin (g/dl)	Globulin (g/dl)	A/G Ratio	PT (sec)
Lipoprotein (mg/dl)	1.00	-0.52	-0.53	-0.70	-0.69	-0.13	0.39	-0.35	0.37	-0.78
Insulin (uU/ml)	-0.52	1.00	0.93	0.80	0.70	0.41	-0.11	0.46	-0.32	0.66
Glucose (mg/dl)	-0.53	0.93	1.00	0.77	0.63	0.42	-0.18	0.49	-0.38	0.63
Diabetes mellitus	-0.45	0.55	0.40	0.53	0.62	0.04	0.02	0.01	0.11	0.55
AST (U/L)	-0.70	0.80	0.77	1.00	0.90	0.53	-0.21	0.61	-0.46	0.89
ALT (U/L)	-0.69	0.70	0.63	0.90	1.00	0.23	-0.10	0.28	-0.17	0.87
Total Protein (gm/dl)	-0.13	0.41	0.42	0.53	0.23	1.00	0.10	0.82	-0.52	0.33
Albumin (gm/dl)	0.39	-0.11	-0.18	-0.21	-0.10	0.10	1.00	-0.38	0.68	-0.24
Globulin (gm/dl)	-0.35	0.46	0.49	0.61	0.28	0.82	-0.38	1.00	-0.88	0.46
A/G Ratio	0.37	-0.32	-0.38	-0.46	-0.17	-0.52	0.68	-0.88	1.00	-0.35
Prothrombin Time (sec)	-0.78	0.66	0.63	0.89	0.87	0.33	-0.24	0.46	-0.35	1.00

FIGURE # 1: COMPARISON OF BIOCHEMICAL PARAMETERS BETWEEN DIFFERENT GROUPS

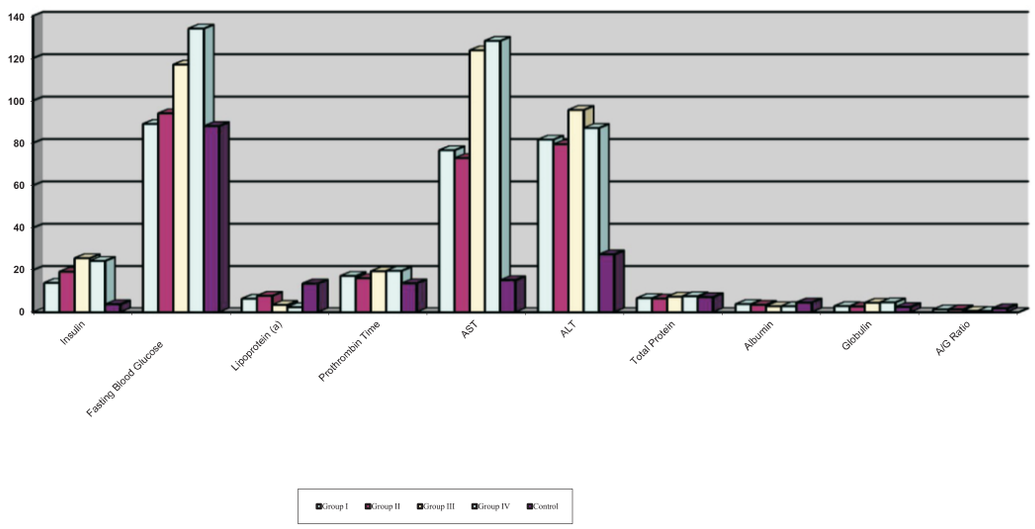
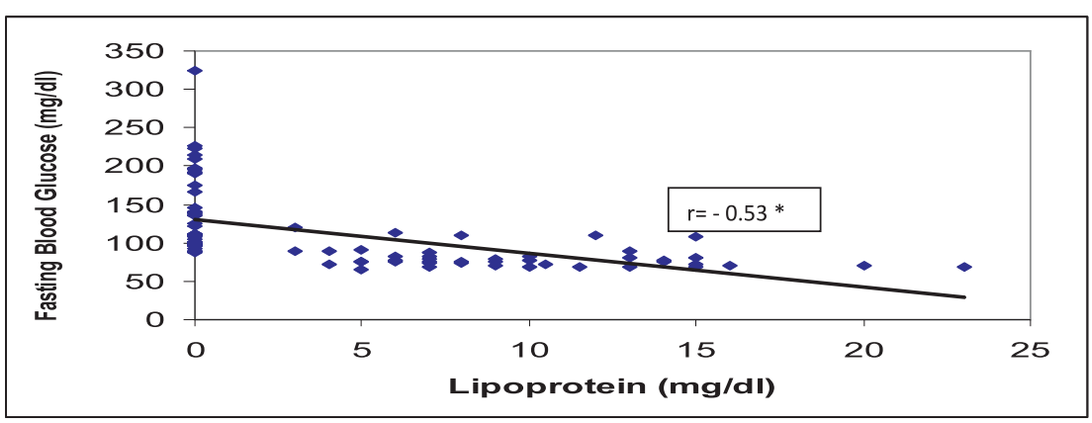


FIGURE # 2: Correlation Coefficient between Lipoprotein a (mg/dl**) and F.B. Glucose** (mg/dl)



* p<0.01

It showed a significant negative correlation with fasting levels of blood glucose, insulin, PT (Prothrombin Time), AST as well as with ALT, whereas with other parameters it showed a non-significant correlation. These findings are similar to findings analysed by Irshad[18] and Geiss et al[19] but contradict with the observation of Feely et al.[20]

Coagulation abnormalities are not uncommon in chronic viral hepatitis. There was significantly negative correlation of PT (prothrombin time) with lipoprotein (a) in all patients, while a significantly positive correlation was found with insulin, fasting blood glucose, AST and ALT. However with other parameters statistically non-significant correlation was observed. The results were in resemblance with the conclusions of Siddiqi et al (2007).[21]

The increase in serum level of hepatic enzymes i.e. transaminases (AST and ALT) are the markers of liver disorders. ALT is a specific enzyme of liver, while AST is also found in other tissues of the body along with liver. In all patients they show a significantly negative correlation with lipoprotein (a), whereas with fasting blood glucose levels, insulin, and PT (prothrombin time) a significantly positive correlation was observed. Non-significant correlation was also observed with other parameters. These results match closely with the observations of Giannini et al (2003),[22] Butt et al (2001)[23] and Rehman and Sarwar (2006).[24]

The liver has extensive synthetic capacity, play a role in protein synthesis, occurring on the rough endoplasmic reticulum of the hepatocytes. Disturbance of protein synthesis occurs as a consequence of impaired hepatic functions.

Significant decrease in serum total protein may not develop obvious until chronic or severe hepatic disorders. There is statistically significant positive correlation of total proteins with albumin in all patients, while it is statistically non- significant with other parameters. These observations are supported with the findings of Lin et al (2008)[25] and Bugianesi et al (2006).[26]

Conclusion: The chronic viral hepatitis B and C subjects, with progression of ailment may develop type 2 diabetes along with derangement of hepatic function, even with no family history or other predisposing factors.

Recommendation: Those patients who are diagnosed as viral hepatitis B or C positive should get screened out for presence or absence of diabetes, to decrease morbidity and mortality in concurrent condition of chronic liver disorder by treating the condition at earlier stage of development.

REFERENCES

1. Birajdar SV, Chavan SV, Mundhe SA, Bhosale MG. Clinical and biochemical profile of patients with viral hepatitis at tertiary care centre. Int J Adv Med. 2017;4(2):412-6.
2. Fazlul-Karim SM, Rezwanur-Rahman M, Shermin S, Sultana S. Correlation between Aminotransferase Ratio (AST/ALT) and Other Biochemical Parameters in Chronic Liver Disease of Viral Origin. Delta Med Col J. 2015;3(1):13-17
3. Chamberlain NR. Viral Hepatitis. Blood-Borne Hepatitis. Overview [Internet]. 2013 October 10 [cited 2014 March 20]. Available from: http://www.atsu.edu/faculty/ chamberlain /website/ lectures/lecture/hepatit2.htm.
4. Xing Y-F, Zhou D-Q, He J-S, Wei C-S, Zhong W-C, Han Z-Y et al. Clinical and histopathological features of chronic hepatitis B virus infected patients with high HBV-DNA viral load and normal alanine aminotransferase level: A multicenter-based study in China. PLoS ONE 2018;13(9): e0203220 https://doi.org/10.1371/journal.pone.0203220 .
5. Di-Bisceglie AM, Lombardero M, Teckman J, Roberts L, Janssen LSA et al. Determination of hepatitis B phenotype using biochemical and serological markers. J Viral Hepat. 2017;24(4):320-9.
6. Libo L, Xiangke P, Yongzhong W. Impaired plasma lipid profile in acute hepatitis. Lipids Health Dis. 2010;9:1-6.
7. Mokdad AA, Lopez AD, Shahaz S, Lozano R, Mokdad AH, Stanaway J et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. BMC Med 2014;12:145. DOI:10.1186/s12916-014-0145-y.
8. Hong YS, Chang Y, Ryu S, Cainzos-Achirica M, Kwon M, Zhang Y et al. Hepatitis B and C virus infection and diabetes mellitus: A cohort study. Scientific Reports | 7: 4606 | DOI:10.1038/s41598-017-04206-6)
9. Wasley A, Grytdal S, Gallagher K. Surveillance for Acute Viral Hepatitis-United States, 2006. MMWR Surveill Summ. 2008;57(2):1-24.
10. Seeff LB. Natural History of Hepatitis C. Am J Med.1999;107(suppl S2):10S-15S.
11. Lu J, Hou X, Tu H, Tang Z, Xiang Y, Bao Y et al. Chronic hepatitis B virus infection status is more prevalent in patients with type 2 diabetes. J Diab Investig. 2017;8(4):619-25.
12. El-Soud AA, El-Deeb GS, Essa AAS, Ahmed NSS. Study of frequency of prediabetes in Egyptian patients with chronic hepatitis C virus infection Menofuia Med J. 2014;27:453–7.
13. Gualerzi A, Bellan M, Smirne C, Minh MT, Rigamonti C, Burlone ME. Improvement of insulin sensitivity in diabetic and non-diabetic patients with chronic hepatitis C treated with direct antiviral agents. PLoS ONE 2018;13(12):e0209216. https://doi.org/10.1371/journal.pone.0209216 .
14. Ghouri A, Kumar S, Khan SA, Ghani MH, Aslam S, Asadullah. Frequency of type 2 diabetes mellitus in patients with chronic hepatitis C virus infection. JLUMHS. 2014;13(2):51-6.
15. Patil B, Amareshwar M, Sreekantha, Avinash SS. Comparison of lipid parameters in acute viral hepatitis and normal individuals. Int J Clin Biochem Res. 2019;6(1):105–10.
16. Alizadeh AHM, Fallahian F, Alavian SM, Ranjbar M. Insulin resistance in chronic hepatitis B and C. Ind J Gastroentrol. 2006;25(4):286-9.
17. Mason AL, Johnson YNL, Hoang N, Qian K, Alexander GJM, Xu L. Association of diabetes mellitus and chronic hepatitis C virus infection. Hepatology. 1999;29(2):328-33.
18. Irshad M. Serum Lipoprotein (a) level in liver disease caused by hepatitis. Ind J Med Res. 2004;120:542-5.
19. Geiss HC, Ritter MM, Richter WO. Low Lipoprotein(a) levels during acute viral hepatitis. Hepatology. 1996;24(6):1334-7.
20. Feely J, Barry M, Keeling PWN, Weir DG, Cooke T. Lipoprotein (a) in cirrhosis. BMJ. 1992;304:545-6.

21. Siddiqi AI, Siddiqeh M, Mehmood A, Siddiqi AM. ALT/AST ratio reversal and prolonged prothrombin time: a specific indicator of hepatic cirrhosis. J Ayub Med Coll. 2007;19(3):22-4.

22. Giannini EG, Testa R, Savarino V. Liver enzymes alteration. CMAJ. 2005;172(3):367-79

23. Butt AR, Ahmed S, Haider N, Tayyab M. Evaluation of AST/ALT ratio in patients with liver disease. Pak J Med Sci. 2001;17(4):1-9.

24. Rehman H, Sarwar M. AST/ALT ratio predicts cirrhosis in patients with chronic hepatitis C. Pak Arm Forc Med J. 2006;56(1):23-7.

25. Lin CS, Chang CS, Yang SS, Yeh HZ, Lin CW. Retrospective evaluation of serum markers APRI and AST/ALT for assessing liver fibrosis and cirrhosis in chronic hepatitis B and C patients. Inter Med. 2008;47:569-75.

26. Bugianesi E, Marchesini G, Genticlore E, Cua IHY, Vanni E, Rizetto M, George J. Fibrosis in genotype 3 chronic hepatitis C and non-alcoholic fatty liver disease. Hepatology. 2006;44(6):1648-55.