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EVALUATION OF ALTERATION OF SERUM TOTAL BILIRUBIN, GAMMA GLUTAMYL TRANSFERASE (GGT), BLOOD UREA NITROGEN (BUN), SERUM CREATININE AS POTENTIAL MARKERS OF KIDNEY FUNCTION IN HEPATITIS C INFECTED INDIVIDUALS

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ABSTRACT

Objective: The objective of present study is to evaluate the alternation in serum total bilirubin, Gamma glutamyl transferase, blood urea nitrogen, serum creatinine levels in patients suffering from HCV. The approach is to see the effect of Hepatitis C on kidneys.

Design of Study: These tests were performed on 25 individuals with confirm HCV by ELISA. These tests were also performed on 25 normal healthy individuals for the purpose of comparison.

Setting: Institute of Molecular biology and Biotechnology, The University of Lahore, Raiwund, Lahore. Samples were collected from Shaukat Khanum Memorial Cancer Hospital and Research Centre**.**

Period: July 2012-August 2012.

Material and Methods: Patients suffering from HCV were included in the present study. Diabetic patients, patient suffering from blood cancer, patient suffering from renal failure, patient suffering from Hypertension, patient suffering from cardiac disease, patient suffering from HCV plus any other disorder were excluded from the present study to evaluate the biochemical alteration in serum total bilirubin, Gamma GT, BUN, serum creatinine in patients suffering from HCV.

Statistical Analysis: Statistical analysis was performed using the statistical package for social studies (SPSS) version 16 for windows. For comparison between the patient's *vs.* healthy controls, Student's *t* test was applied to evaluate differences in proportions. P value <0.05 was considered significant.

Results: The observed mean ±SD value of serum total bilirubin level, Gamma glutamyl transferase, BUN, serum creatinine in normal healthy individuals was 0.4609±0.17, 24.6±13.1, 13.5±3.5, 0.75±0.18 while that in HCV +ve individuals was 0.54±0.36, 49.2±41.4, 13.8±3.05, 0.89±0.25. According to Independent T-test overall significant difference ($p < 0.05$) was observed in gamma glutamyltransferase and serum creatinine but serum creatinine were still in normal range in HCV patient as compare to normal individuals, While insignificant difference ($p > 0.05$) was observed in serum total bilirubin and blood urea nitrogen (BUN) in HCV patient as compare to control group.

Conclusions: The outcomes of the present study showed that overall insignificant alteration was observed in all the parameters related to kidney function. It is therefore inferred that Hepatitis C infection has no or very little effect on kidney function.

KEYWORDS: Chronic Liver Disease**,** Blood Urea Nitrogen, Kidneys

INTRODUCTION

In Pakistan more than 10 million people are living with Hepatitis C virus (HCV) with high morbidity and mortality. Pakistan is a developing country of 170 million people with low health and educational standards. According to the human development index of the United Nations, it was ranked 134th out 174 countries. In Pakistan 10 million people are presumed to be infected with HCV[1].

Most people with hepatitis C feel well and have no specific findings on physical examination that would lead a health care provider to suspect liver disease. Even the vast majority of people with liver disease that has advanced to cirrhosis have a normal physical examination. Therefore, the evaluation and treatment of liver disease, in particular hepatitis C, places a large emphasis on laboratory tests results to diagnose, stage and predict and evaluate response to therapy. The degree of elevation may be important in acute disease but is unimportant in chronic disease. Bilirubin is the final breakdown product of heme, the majority of which comes from hemoglobin. Bilirubin can be elevated in many liver-related and non-liver- related conditions and it may be elevated in conditions which lead to liver cell damage and cholestasis. The level of serum bilirubin is not a sensitive indicator of liver function and it may not accurately reflect the degree of liver damage[2].

Chronic hepatitis C Virus (HCV) is often called a silent disease because the liver can suffer a lot of damage and still function pretty well[3]. In some cases of Hepatitis C, the kidneys can be damaged because of a condition known as cryoglobulinemia. Cryoglobulinemia is the presence of abnormal proteins in the blood called cryoglobulins. Cryoglobulins is a term for proteins in the blood that become solid at low temperatures. When cryoglobulins thicken or become gel-like, they block blood vessels throughout the body which may lead to complications ranging from skin rashes to kidney failure[4].

The kidneys are also affected in some patients with hepatitis C. The mechanism is still unclear, but some studies suggest that it is caused by circulating complexes of antibodies and HCV particles directly causing damage to the kidneys as they are deposited in the glomerulus and tubules of the kidneys[5]. A blood creatinine test may be done along with a BUN test to indicate the working of the kidneys[6].

Gamma-glutamyltransferase (GGT) is another enzyme that occurs in liver cells. A high level of this enzyme is particularly associated with heavy alcohol drinking. Gamma glutamyl transferase is used in the diagnosis and monitoring of hepatobillary diseases. It is found in many tissues, the most notable one being the liver, and has significance in medicine as a diagnostic marker. Elevated serum GGT activity can be found in diseases of the liver, biliary system, and pancreas[7].

Thus the objective of present study is to evaluate the alternation in serum total bilirubin, Gamma glutamyl transferase, BUN, serum creatinine.

MATERIALS AND METHODS

These tests were performed on 25 individuals with confirm HCV by ELISA. These tests were also performed on 25 normal healthy individuals for the purpose of comparison.

PLACE OF WORK

Biochemical analysis was done at Institute of Biochemistry and Biotechnology (IMBB), University of Lahore. Samples were collected from Shaukat Khanum Memorial Cancer Hospital and Research Centre during the period of July 2012 to August 2012. Samples were stored at 2-8 °C and protected from light until analysis. Samples were centrifuged

at 10,000 rpm for 10 minutes. Samples were analyzed within 2 days of sample collection. Samples were free from hemolysis, icteric, lipemic nature. Samples were collected in vaccutee grenier Bio one gel clot activator tubes. All cases were selected by taking history and laboratory investigations following the exclusion or inclusion criteria.

INCLUSION CRITERIA

Patient suffering from HCV were included in the present study.

EXCLUSION CRITERIA

Diabetic patients, patient suffering from blood cancer, patient suffering from renal failure, patient suffering from Hypertension, patient suffering from cardiac disease, patient suffering from HCV plus any other disorder were excluded from the present study to evaluate the biochemical alteration in serum total bilirubin, Gamma GT, BUN, Serum Creatinine in patients suffering from HCV.

STATISTICAL ANALYSIS

Statistical analysis was performed using the statistical package for social studies (SPSS) version 16 for windows. For comparison between the patient's *vs* healthy controls, Student's *t* test was applied to evaluate differences in proportions. P value <0.05 was considered significant.

RESULTS

The alternation in serum total bilirubin, serum gamma glutamyltransferase, Blood Urea Nitrogen, Serum Creatinine levels in patients suffering from HCV was evaluated. Following results were obtained.

Table1: Descriptive Statistics of Total Bilirubin (Mg/Dl), Gamma Glutamyl Transferase (U/L), Blood Urea Nitrogen (Mg/Dl), Serum Creatinine (Mg/Dl)

Parameters Analyzed	Group	Mean	Range (Mean ±std. Deviation)
Serum total Bilirubin (mg/dL)	Normal	.4609	.4609 ± .17200
	HCV Patients	.5396	.5396 ± .36362
Serum Gamma glutamyltransferase (U/L)	Normal	24.6061	24.6061 ± 13.12664
	HCV Patients	49.1923	49.1923 ± 41.38987
Blood urea nitrogen (mg/dL)	Normal	13.5324	13.5324 ± 3.49585
	HCV Patients	13.8481	13.8481 ± 2.99677
Serum creatinine (mg/dL)	Normal	.7497	.7497 ± .17615
	HCV Patients	.8908	.8908 ± .24717

The observed mean value of serum total bilirubin level in normal healthy individuals was 0.4609±0.17, while that in HCV +ve individuals was 0.54±0.36. Insignificant increase ($P > 0.05$) was observed in serum total bilirubin level of HCV +ve individuals as compare to normal individuals.

The recorded mean value of serum gamma glutamyltransferase level in normal healthy individuals was 24.6±13.1, while that in HCV+ ve individuals was 49.2±41.4. Significant increase ($P < 0.05$) was observed in serum gamma glutamyltransferase level of HCV +ve individuals as compared to normal healthy individuals.

The observed mean value of Blood Urea Nitrogen level in normal healthy individuals was 13.5±3.5, while that in HCV +ve individuals was 13.8±3.05. Insignificant difference ($P > 0.05$) was observed in Blood Urea Nitrogen level of HCV +ve individuals as compared to normal individuals.

The observed mean value of serum creatinine level in normal healthy individuals was 0.75±0.18, while that in HCV +ve individuals was 0.89±0.25. Significant increase was observed in serum creatinine level of HCV +ve individuals as compared to normal healthy individuals.

Table 2: Independent Samples Test

		Levene's Test for Equality of Variances		T-Test for Equality of Means		
		F	Sig.	T	Df	P Value
Serum total bilirubin	Equal variances assumed	6.757	0.012	-1.1	57	0.276
	Equal variances not assumed			-1.02	33.77	0.316
Serum Gamma glutamyltransferase	Equal variances assumed	13.1	0.001	-3.22	57	0.002
	Equal variances not assumed			-2.92	28.98	0.007
Blood urea Nitrogen	Equal variances assumed	1.832	0.181	-0.37	57	0.716
	Equal variances not assumed			-0.37	56.56	0.71
Serum creatinine	Equal variances assumed	0	0.983	-2.56	57	0.013
	Equal variances not assumed			-2.46	43.56	0.018

According to Independent T-test overall significant difference ($p < 0.05$) was observed in gamma glutamyltransferase and serum creatinine in HCV patient as compare to normal individuals, While insignificant difference ($p > 0.05$) was observed in serum total bilirubin and blood urea nitrogen (BUN) in HCV patient as compare to control group.

DISCUSSIONS

The present study was carried out to assess the severity of effect of HCV viral hepatitis in respect to different biochemical changes on kidneys. 25 diagnosed patients of HCV and 25 normal healthy individuals were selected for study. Insignificantly high levels ($P > 0.05$) of serum total bilirubin were obtained in HCV +ve patients as compared to normal individuals which was correlated with the study of Ashraf *et al.* (2010)[8], where they observed the insignificant differences in bilirubin level of normal healthy individuals and HCV positive individuals. The level of serum bilirubin is not a sensitive indicator of liver function and it may not accurately reflect the degree of liver damage. Chronic hepatitis C Virus is also called a silent disease because the liver can suffer a lot of damage and still function pretty well, so that was the reason for not too high elevation of serum total bilirubin in HCV +ve patients as compared to normal individuals (Lucinda and Porter, 2011)[3].

Significantly high levels ($P < 0.05$) of serum Gamma Glutamyl transferase (gamma GT) were observed in HCV patients as compared to normal individuals. The outcomes were in line with the work of Silva *et al.* (2004)[9], where they observed significant high levels of Gamma Glutamyl transferase in HCV +ve patients as compared to normal healthy individuals. Gamma Glutamyl transferase is reasonably specific to the liver and may be elevated with even minor, sub-clinical levels of liver dysfunction, so that why significant increase level of Gamma Glutamyl transferase was observed in HCV +ve patients as compared to normal individual (Lee and Mary, 2009)[10].

In the present study blood urea nitrogen (BUN) levels were also studied and it was observed that in HCV +ve patients BUN levels raised insignificantly ($P > 0.05$) as compared to normal individuals which were in line with the work of Bushra *et al.* (2011)[11]. They observed the insignificant differences in BUN level of normal healthy individuals and HCV positive individuals. Hepatitis is a condition of inflammation of the liver and it was not related to kidney dysfunction so BUN levels did not get changed significantly in HCV patients as compare to normal individuals (Gupta *et al*., 1972)[6].

Significant high levels ($P < 0.05$) of serum creatinine levels were observed in HCV patients as compare to normal individuals, which were highly correlated with the work of Bushra *et al.*, (2011)[11], where they observed significant differences in creatinine levels of normal healthy individuals and HCV positive patients. The kidneys might also be affected in some patients with hepatitis C. The mechanism is still unclear, but some studies suggest that it is caused by circulating complexes of antibodies and HCV particles directly causing damage to the kidneys as they are deposited in the glomerulus and tubules of the kidneys. So that's why significant increase in serum creatinine levels were observed in HCV patients as compared to normal healthy individuals (Johnson *et al.*, 1993)[5].

CONCLUSIONS

The outcomes of the present study showed significant alteration in serum Gamma glutamyl transferase and serum creatinine levels in HCV patients as compare to control group, but serum creatinine levels were still in normal range in HCV patients, where as insignificant alteration in serum total bilirubin and blood urea nitrogen is observed in HCV patients as compare to control group. Overall insignificant alteration was observed in all the parameters related to kidney function. It is therefore inferred that Hepatitis C infection has no or very little effect on kidney function.

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