Renal Function Status of Fallujah Patients (IRAQ) Infected with Chronic Hepatitis B

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Abstract

The present study focuses on the kidney function in patients with chronic hepatitis B. The patients were divided into two groups including patients with chronic hepatitis B; some of the patients were HBSAg positive, HBeAg positive and HBeAb negative; others were HBSAg positive, HBeAg negative and HBeAb positive. The results were compared to those of healthy individuals.

There were about sixty patients with chronic hepatitis B and thirty healthy individuals. Transaminases (AST and ALT) enzymes activities in patients, T.S.B and amount of albumin in addition to serum electrolyte, urea and creatinine were measured using standard laboratory methods. Viral load (HBV PCR) was also measured in patients.

Results from this study showed low serum albumin and higher serum urea and creatinine with chronic hepatitis B compared to those of healthy individuals. Serum potassium, chloride and phosphorus concentration were higher in the patients with chronic hepatitis B compared to those of healthy individuals (5.25389±.78565)(6.518±.58370); and in comparison to healthy individuals (4.5185 ±.33948) while chloride measures (101.4±10.2682), (104.2821±19.63813) compared to healthy individuals (100.4133±8.32457) while phosphorus measured (36±5.88) (35.6283±11.6) compared to healthy individuals (34.7100±5).While serum sodium was significantly low in patients with chronic hepatitis B compared to those of healthy individuals (143±7.144±6.76) and compared to healthy individuals (145±6.89).The results from this study showed a possible relationship between hepatitis B infection and insufficient renal function.

Keywords: Hepatitis, HBV PCR, renal, electrolytes

الخلاصة

تم التركيز في الدراسة الحالية على وظائف الكلىء لدى مرضى التهاب الكبد الفيروسي تم اختيار مجموعتين من المرضى الاولى تحمل (HBe Ag positive) اما المجموعة الثانية تحمل (HBe Ag negative) بالاضافة الى مجموعة الاصحاء. حوالي ستين عينة دم تم جمعها من مرضئ التهاب الكبد الفيروسي نوع B من مستشفى الفلوجة التعيلمي بالاضافة الى ثلاثين عينة دم من مجموعة الاصحاء وتم تقدير انزيمات الكبد بالاضافة الى اليوريا والكرياتين والالبومين والالكتروليتات الموجبة والسالبة مع حسباب عدد الفايروسات الكلي .اظهرت نتائج الدراسة الحالية انخفاض نسبة الالبومين وارتفاع نسبة اليوريا والكرياتيين مقارنة مع مجموعة الاصحاء وارتفاع تركيز البوتاسيوم وايون الكلوريد والفسفسور بينما انخفض تركيز الصوديوم مقارنة مع مجموعة الاصحاء . وتم الاستنتاج من خلال دراستنا الحالية امكانية وجود تاثير لمرض التهاب الكبد الفيروسي على وظائف الكلئ .

الكلمات المفتاحية:– التهاب الكبد الفايروسي ,عدد الفيروسات الكلي, الكلئ , الالكتروليتات

Introduction

The liver is one of the most important organs in energy metabolism. Most plasma, apolipoproteins , endogenous lipids and lipoproteins are synthesized in the liver. This depends on the integrity of liver cellular function, which ensures homeostasis of lipid and lipoprotein metabolism .Hepatitis B virus (HBV) infection, a major world health problem, is hyper-endemic in South-East Asia and sub-Saharan Africa. Being a major cause of morbidity and mortality (Pungpapong *et al.* 2007).

ALT is found in kidney, heart, muscle and greater concentration in liver compared with other tissues of the body. ALT is purely cytoplasmic catalysing the transamination reaction AST catalyse transamination reaction. AST exist two different isoenzyme forms which are genetically distinct, the mitochondrial and cytoplasm form) (Mauro *et al.*, 2006).The serum albumin level is not a reliable indicator of hepatic protein synthesis in acute liver disease the serum albumin level is

not a reliable indicator of hepatic protein synthesis in acute liver disease. Albumin synthesis is affected not only in liver disease but also by nutritional status, hormonal balance and osmotic pressure. Liver is the only site of synthesis of albumin (Rosalki , *et al.,* 1999) .

The kidneys essential in the urinary system and also erve homeostatic functions such as the regulation of electrolytes, maintenance of acid–base balance, and regulation of blood pressure . They serve the body as a natural filter of the blood, and remove wastes, which are diverted to the urinary bladder (Cotran *et al.,* 2005). Sodium and its anion constitute the primary extracellular solutes determining tonicity.1 Thus, sodium is the major determinant of extracellular fluid volume (ECFV). In normal humans, the kidney is primarily responsible for maintaining the homeostasis of total body sodium (Schrier, 2010) .Urea and creatinine are nitrogenous end products of metabolism. Urea is the primary metabolite derived from dietary protein and tissue protein turnover. Creatinine is the product of muscle creatinine catabolism. (Bauer *et al.,* 1982)

The first symptoms of acute hepatitis B may be non-specific including fever, skin rash and joint pain and inflammation. Other symptoms may include fatigue, loss of appetite, nausea and jaundice (Yim HJ and Lok AS 2006). About 10-20% of people with chronic hepatitis B develop complications in other organs and tissues outside the liver, vascular inflammation and kidney diseases are the two most common complications (Nippo and Gakkai, 2006). Renal function tests include measurement of serum urea, creatinine, creatinine clearance, uric acid, calcium, and phosphorus, electrolytes (sodium, potassium, bicarbonate, lithium and chloride). Hepatitis B infection is usually complicated with nephritic syndrome. During acute hepatitis B infection serum creatinine, urea and some electrolytes are usually elevated, this effects are a signal of on-going kidney disease particularly glomerulonephritis (Ryder, 2001).

Important consideration should be given to the impact of HBV genotype on the risk of hepatocellular carcinoma in this population. The HBV genotypes B and C are the predominant genotypes, and genotype C has been shown to be associated with higher HBV DNA levels and a greater risk of hepatocellular carcinoma , participants with HBV DNA levels of (100 000 copies\Ml) or greater, the frequencies of genotypes B and C were 79.3% and of chronic hepatitis B patients. Randomized controlled trials comparing different therapeutic strategies in patients with elevated serum HBV DNA level but a normal ALT level may further contribute to the development of appropriate treatment guidelines in these patients. These patients, especially those seronegative for HBeAg, account for an increasing majority of chronically infected individuals and are at an increased risk of future hepatocellular carcinoma (Chien-Jen *et al.,* 2010) .

Materials and methods

About sixty patients with hepatitis B virus infection were included in this study, with thirty healthy controls for comparison purposes, which included HBsAg , HBsAb , HBcAb and HBV DNA by PCR technique.

Procedure: Six to eight mL of blood was collected from the vein and protected in evacuated tubes without adding any anticoagulant agent. Prior to this study, patients were not administered antiviral treatment. Collected blood samples were placed in sterile place and allowed to clot. Then blood samples were centrifuged at 300 g for 45 min. Next, the collected sera were stored in plastic vials at–20 C^0 until further analysis (samples were collected from Fallujah teaching Hospital). The individuals in the healthy groups had no history of alcoholism, smoking or viral hepatitis; in addition, there was also an absence of any acute or chronic pathology. Afterwards, the serum was separated and immediately levels of the enzymes namely ALT and AST also S.

Albumin, phosphorus and Chloride were determined by a kit method by spectrophotometric analysis, using the modified Jaffe method (Jaffe, 1886). Levels of urea and creatinine were determined using a strip method on Microlab 300. Finally, serum sodium and potassium were estimated by flame photometry using Flame Photometer.

Result

Table 1: Age , gender and residence distribution of groups for patients with chronic hepatitisB and group healthy.

Characteristics	Control n=30	Patients, *HBeAg (+ve)* n=28	Patients *HBeAg (-ve)* n=30
Age (in years)	11-40	2-23	4-60
Male	21	15	15
Female	9	13	15
Urban	16	8	9
Rural	14	20	21

Table 2: Serum levels T.S.B, ALT and AST of groups for patients with chronic hepatitis B and group healthy.

Parameters	I- Control n=30	II- Patients, HBeAg (+ve)	III- Patients HBeAg (-ve)	p-value
T.S.B (mg/100ml)	0.6995± 0.063**	0.8664±0.21257**	0.8453±0.1973**	I:II=0.000 I: III=0.002 II:III=0.000
ALT(IU/L)	23.662±5.3995**	38.3893±17.5*	31.8567±15.16**	I:II=0.000 I: III=0.024 II:III=0.000
AST(IU/L)	19.759±7.2*	52.46±18.4*	36.3567±16.337*	I:II=0.000 I: III=0.000 II:III=0.000
Albumin(gm/ dl)	4.38±.3357*	4.1719±.43183*	4±.3735*	I:II=0.025 I: III=0.002 II:III=0.025

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

Table 3: Viral load (HBV PCR) of groups for patients with chronic hepatitis B .

Level of HBV DNA, copies/mL	Mean	N
Patients, *HBeAg (+ve)*	472261416.5333	30
Patients *HBeAg (-ve)*	1037788975.2857	28

Table 4:- parameters for patients with chronic hepatitis B and group healthy.

Parameters	I- Control n=30	II_ HBV e Ag (+) n=28	III _HBV e Ag (-) n=30	p-value
Urea (mg/dL)	34.5± 4.76*****	38.6±6.664 ******	42.2467± 6.65*****	I:II=0.012 I: III=0.000 II:III=0.025
Creatinine (mg/dL)	.7933±.08******	.9138±.1398*****	.8537±.14779	I:II=0.000 I: III=0.068 II:III=0.000
Na+ (mmol/L)	145±6.89******	144.1±6.76******	143.2±7.33******	I:II=0.000 I: III=0.000 II:III=0.000
K+ (mmol/L)	4.5185 ±.33948******	5.25389±.78565******	6.518±.58370***v**	I:II=0.000 I: III=0.001 II:III=0.000
Cl- (mmol/L)	100.4133±8.32457	104.2821±19.63813	101.4±10.26826	I:II=0.8 I: III=0.3 II:III=0.9
P(mg\L)	34.7100±5	36±5.88	35.6283±11.6	I:II=0.5 I: III=0.06*. II:III=0.8

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

Table 5:- Pearson product moment correlations between physical parameter and biochemical parameters in patient with chronic hepatitis B (group e Ag +ve).

Parameters	Urea (mg/dL)	Creatinine (mg/dL)	Na+ (mmol/L)	K+ (mmol/L)	Cl- (mmol/L)	P(mg\L)	PCR (copies/mL)
Urea (mg/dL)	1	0.819**	0.143	0.097	-0.013	-0.059	-0.105
Creatinine (mg/dL)		1	0.252	-0.102	0.035	-0.089	-0.166
Na+ (mmol/L)			1	-0.006	-0.515**	0.170	-0.139
K+ (mmol/L)				1	-0.156	-0.385*	0.298
Cl- (mmol/L)					1	-0.300	0.109
P (mg\L)						1	-0.550**
PCR(copies/mL)							1

*. Correlation is significant at the 0.05 level .
**. Correlation is significant at the 0.01 level .

Table 6:- Pearson product moment correlations between physical parameter and biochemical parameters in patient with chronic hepatitis B (group e Ag -ve).

Parameters	Urea (mg/dL)	Creatinine (mg/dL)	Na+ (mmol/L)	K+ (mmol/L)	Cl- (mmol/L)	P(mg\L)	PCR (copies/mL)
Urea (mg/dL)	1	0.383*	0.179	0.150	-0.112	0.175	-0.050
Creatinine (mg/dL)		1	0.210	0.325	-0.421*	0.378*	-0.014
Na+ (mmol/L)			1	0.169	-0.093	0.443*	0.138
K+ (mmol/L)				1	0.115	-0.237	0.036
Cl- (mmol/L)					1	-0.237	0.147
P (mg\L)						1	-0.140
PCR(copies/mL)							1

*. Correlation is significant at the 0.05 level.
**. Correlation is significant at the 0.01 level.

Discussion

The aim of this study is the impact of chronic inflammatory disease *in patients with chronic hepatitis B and* on the functions of various organs of the body especially renal function. Hepatitis B Virus (HBV) is ubiquitous in liver, but it also has been seen to cause persistent infections in many other human organs. However, the evidence of a putative HBV association with other organs needs to be investigated. Liver has been the sole target for research on hepatitis B virus for the past 40 years. Scientists and clinicians had been more interested in knowing the genotypes, their differences in biological properties; the prevalence of hepatitis B virus mutants in various geographic regions; in addition to the clinical outcome and response to antiviral treatment in different population groups (Baig ,2007) , (Baig *et al*.,2007).

The results from this study have shown an increase in mean serum potassium concentration in *patients with chronic hepatitis B* compared to healthy individual's .The serum potassium concentration might increase along with deteriorating renal function. Subsequently, the elevated potassium level might by itself stimulate potassium excretion. As a result, a new steady state develops without medical complications (Gennari and Segal, 2002). There will also be a diminution in glomerular filtration capacity as a renal complication of hepatitis B viral infection. The DNA of the hepatitis B virus was also found in the nearby renal tubules, where urine is concentrated (Lai and Lai, 1991). While serum sodium concentration recorded a significant decrease compared to healthy individuals, this decrease may be due to impaired renal capacity and its inability to excrete solute free water (Agrawal, *et al.,* 2008) . If found that hyponatremia and hypernatremia represented disorders of water balance, or due to impaired renal water excretion and antidiuretic (El–Zawhry, *et al.,* 2013)

Serum transaminases enzymes (ASAT and ALAT) revealed a significant increase in activities among patients with chronic hepatitis B. AST elevations are often predominate in patients with cirrhosis and even in liver diseases that typically have an increased ALT (Panteghini *et al.,* 1983).

A significant decrease in serum levels of albumin in patients with chronic hepatitis B compare to healthy groups may suggest decreased hepatic production due to decreased liver function following hepatocellular disease. However, a low serum albumin concentration is a recent finding in liver disease. When it is present, it suggests chronic disease (Ian *et al.,* 1999).

The relationship among the different biochemical parameters analyzed in HBV e Ag (+ve) and HBV e Ag (-ve) were determined using Pearson product moment correlation analysis. A positive correlation and negative correlation were observed between different variables.

The present study and several other studies including (Olubunmi *et al.*, 2012) suggested that the virus replicates in the tubules of the kidney.

Conclusion

The results of our study will most likely indicate that complications in patients with chronic Hepatitis B might be the cause of renal malfunction or weakness in the organ.

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