SERUM LIPOPOLYSACCHARIDE BINDING PROTEIN AS A PREDICTOR AND PROGNOSTIC BIOMARKER FOR CIRRHOSIS RELATED ACUTE KIDNEY INJURY

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INTRODUCTION

- Acute kidney injury (AKI), defined as an increase in serum creatinine ≥ 0.3 mg/dL (26.5 µmoL/L) ≤ 48 hours, or a 50% increase from baseline, is one of the most serious complications of liver cirrhosis. It occurs in about 19% of hospitalized cases with liver cirrhosis and it carries a bad prognosis. The acute kidney dysfunction is associated with mortality in cases with cirrhosis. Moreover, it usually occurs concomitantly with other cirrhosis related complications like spontaneous bacterial peritonitis (SBP) and bleeding varices.
- Multiple factors could increase the risk for this complication including infections, hypovolemia, use of vasodilators, and non-steroidal anti-inflammatory drugs. Because of its unfavorable prognosis, potential triggers for AKI should be identified and removed in such cases. This includes correction of hypovolemia, discontinuation of nephrotoxic drugs, eradication of infections and management of other complications like variceal bleeding.
- Lipopolysaccharide binding protein (LBP) is an acute phase protein that is synthesized by the liver. It is secreted into the blood stream in response to infection with Gram-negative bacteria. Recent studies have reported that LBP is an important mediator of AKI in critically ill patients. However, after intensive online research, the current literature had poor data regarding the role of that biomarker in AKI in cirrhotic patients.

AIM OF THE WORK

- This study was conducted to study the serum level of LBP in patients having decompensated cirrhosis with or without cirrhosis related AKI, and find out the prognostic value of LBP in relation to renal outcomes along with all-cause mortality.

PATIENTS & METHODS

- This prospective study included 80 patients with decompensated cirrhosis (jaundice, encephalopathy, coagulopathy or variceal hemorrhage). They were divided into two groups; Group I (40 cases – no AKI) and Group II (40 cases – AKI). Patients with compensated cirrhosis, postrenal AKI, contrast nephropathy, or history of chronic kidney disease were excluded.
- The included cases were subjected to full history taking and thorough clinical examination. A pelviabdominal ultrasonography was ordered for all cases with special emphasis on the urological system. An ascitic tap was also performed and analyzed.
- Laboratory investigations included complete blood count, daily urea and creatinine, hepatological viral markers. Regarding LBP assessment, it was measured by ELISA within 24 hours from admission in Group I, and within 24 hours of AKI detection in Group II.

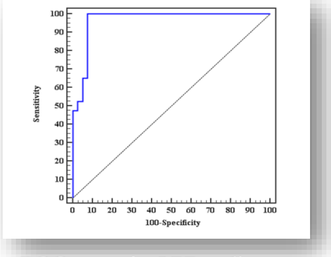
RESULTS

- LBP was significantly higher in group II compared to group I. It had mean values of 13.51 and 31.52 in groups I and II respectively. It had sensitivity and specificity of 100 and 92.5% respectively for identifying cirrhotic cases with cirrhosis related AKI using a cut off value of 17.5 ng/ml. Serum LBP was significantly elevated in cases with persistent disease (42.08) vs. cases with recovery (28.88) (p = 0.003). Nevertheless, no significant difference was detected between living and deceased cases regarding LBP levels.

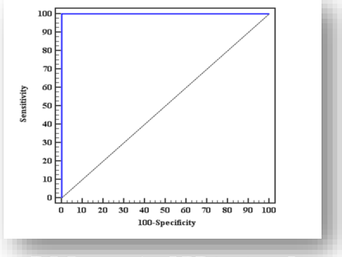
History, clinical and laboratory characteristics of the study groups

	Group I (n = 40)	Group II (n = 40)	p
Sex			
Male	21 (52.5%)	20 (50%)	0.823
Female	19 (47.5%)	20 (50%)	
Age			
Mean ± SD.	58.3 ± 8.4	60.8 ± 8.7	0.204
Median (Min. – Max.)	58 (30 – 76)	60 (45 – 85)	
Cause of cirrhosis			
Viral Hepatitis	33 (82.5%)	31 (77.5%)	0.576
Autoimmune hepatitis	0 (0%)	0 (0%)	–
Cardiac Cirrhosis	0 (0%)	0 (0%)	–
Cryptogenic	2 (5%)	1 (2.5%)	1.000
Periportal fibrosis	6 (15%)	10 (25%)	0.264
Steatohepatitis	1 (2.5%)	0 (0%)	1.000
Signs of decompensation			
Jaundice	25 (62.5%)	33 (82.5%)	0.045*
Encephalopathy	9 (22.5%)	18 (45%)	0.033*
Coagulopathy	31 (77.5%)	26 (65%)	0.217
Ascites	35 (87.5%)	34 (85%)	0.745
Variceal hemorrhage	20 (50%)	13 (32.5%)	0.112
Urea			
Day 1			
Mean ± SD.	35.2 ± 14.8	115.4 ± 30	<0.001*
Median (Min. – Max.)	34 (15 – 79)	114.5 (54 – 182)	
Day 2			
Mean ± SD.	36.3 ± 18.7	124 ± 31.7	<0.001*
Median (Min. – Max.)	31 (15 – 86)	127 (38 – 199)	
Day 3			
Mean ± SD.	38.3 ± 20.9	116.7 ± 33.1	<0.001*
Median (Min. – Max.)	30 (15 – 98)	122 (30 – 208)	
Creatinine			
Day 1			
Mean ± SD.	0.9 ± 0.3	2 ± 0.5	<0.001*
Median (Min. – Max.)	1 (0.4 – 1.2)	1.9 (1.3 – 3.6)	
Day 2			
Mean ± SD.	0.9 ± 0.3	1.9 ± 0.4	<0.001*
Median (Min. – Max.)	0.9 (0.4 – 1.7)	1.7 (1.1 – 2.9)	
Day 3			
Mean ± SD.	0.9 ± 0.3	1.5 ± 0.5	<0.001*
Median (Min. – Max.)	1 (0.5 – 1.7)	1.4 (0.8 – 2.9)	
SBP			
No	35 (87.5%)	33 (82.5%)	0.531
Yes	5 (12.5%)	7 (17.5%)	

	Group I (n = 40)	Group II (n = 40)	p
Lipopoly saccharide			
Mean ± SD.	13.5 ± 4.8	31.5 ± 9.9	<0.001*
Median (Min. – Max.)	12.9 (8.2 – 29.7)	29 (17.9 – 54.7)	
Renal outcome			
Recovery	1 (2.5%)	32 (80%)	<0.001*
Persistence	2 (5%)	8 (20%)	0.043*
Need for RRT	0 (0%)	0 (0%)	–
Rise of serum creatinine			
Mean ± SD.	0.1 ± 0.1	0.9 ± 0.4	<0.001*
Median (Min. – Max.)	0 (0 – 0.5)	0.8 (0.3 – 2.3)	
Stage			
Negative	37 (92.5%)	0 (0%)	<0.001*
Stage 1	3 (7.5%)	31 (77.5%)	
Stage 2	0 (0%)	9 (22.5%)	
All-cause mortality			
Died	2 (5%)	9 (22.5%)	0.023*
Alive	38 (95%)	31 (77.5%)	



ROC curve for LBP to diagnose patients with cirrhosis related AKI



ROC curve for LBP to stage I (n=3/40)

CONCLUSIONS

- Based on the previous findings, LBP appears to be a sensitive biomarker for the diagnosis of AKI in cirrhotic patients. Besides, higher levels are associated with an increased risk of persistent renal disease.