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ORIGINAL ARTICLE

Urine Albumin Creatinine Ratio as a Predictor of Acute Kidney Injury in Cirrhotic Patient with Hepatic Encephalopathy

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ABSTRACT

Background: Higher mortality risk is linked with acute kidney injury in hospitalized cases with chronic liver disease; however, early detection and treatment could minimize this risk with better prognosis achieved. Little information is currently available to predict Hepatic Encephalopathy-Acute Kidney Injury (HIE–AKI). In this study, we aimed for evaluation of the role of the urine albumin creatinine ratio to early predict occurrence of acute kidney injury among hepatic encephalopathy patients. **Methods:** This case-control research included forty-eight patients with liver cirrhosis who were categorized into two equal groups: Group I: 24 cirrhotic cases without hepatic encephalopathy and Group II: 24 cirrhotic cases with hepatic encephalopathy. Hepatic encephalopathy was assessed using the West Haven criteria. Urinary albumin creatinine ratio (UACR) was measured on day one of admission. Acute kidney injury was diagnosed following kidney disease: Improving Global Outcomes criteria. **Results:** As regards AKI in the current study, 83.3% developed AKI in cirrhotic patients with HE versus 54.2% in cirrhotic patients without HE, with significant differences among the 2 groups (p=0.029). Urinary creatinine was our study's only predictor for AKI, which was significantly lower among cases with AKI (p=0.013). At the same time, UACR did not differ significantly among HE patients with AKI **Conclusion:** Cases who had cirrhotic hepatic encephalopathy are at higher risk of developing AKI with increased in-hospital mortality. To better understand how UACR predicts hepatic encephalopathy-acute kidney injury, more research is required.

Keywords: Urine Albumin Creatinine Ratio, Acute kidney Injury, Liver Cirrhosis, Hepatic Encephalopathy.

INTRODUCTION

Chronic liver disease is a widespread clinical condition that results from progressive inflammation, destruction and regeneration of liver parenchyma that leads to deterioration of liver function [1]. Acute kidney injury is a widespread complication of liver cirrhosis, which mainly occurs with decompensated cirrhosis rather than compensated cirrhosis; the two most common types of acute kidney injury among chronic liver disease patients are prerenal type and acute tubular necrosis [2]. Higher mortality risk is linked with acute kidney injury in hospitalized cases with chronic liver disease; however, early detection and treatment could minimize this risk with better treatment and prognosis achieved [3].

Evaluation of renal function depending on serum creatinine level is not very accurate in chronic liver disease patients due to diminished protein intake and muscle atrophy. Additionally, there is a lack of accessibility to urine biomarkers such as cystatin C, interleukin 18 (IL18), and neutrophil gelatinase-associated lipocalin [4]. Albuminuria among cases with hepatic encephalopathy and acute kidney injury may be explained by the systemic inflammation that often goes along with the condition. Several clinical researchers have

confirmed a link between inflammation and microalbuminuria [5].

However, novel research in Europe have shown that cirrhotic individuals' kidney damage is characterised by systemic inflammation. The overactivation of endogenous vasoconstrictor systems leads to acute kidney injury when systemic inflammation promotes the nitric oxide-mediated amplification of preexisting splanchnic vasodilation. The renal circulation is one of the vascular beds that experiences substantial vasoconstriction and hypoperfusion as a result of this [6]. Little information is currently available to predict Hepatic Encephalopathy-Acute Kidney Injury (HIE–AKI). In this study, we aimed for evaluation of the role of the urine albumin creatinine ratio to early predict occurrence of acute kidney injury among hepatic encephalopathy patients.

METHODS

This case control study was conducted at the Tropical Department, Faculty of Medicine at Zagazig University Hospitals between February and July of 2023.

Inclusion criteria: Cirrhotic patients; cirrhosis was diagnosed by presence of hepatic nodularity in radiological evaluation or by clinical & laboratory evidence of hepatic decompensation. Hepatic encephalopathy was defined and graded by the West Haven criteria [7].

Exclusion criteria: Patients who had a history of renal disease, diabetes mellitus and hypertension, history of liver transplantation, history of NSAID intake in the last four weeks, hepatocellular carcinoma, hyperbilirubinemia, urinary tract infection, advanced cardiopulmonary disease also, pregnant women were excluded from the study.

Sample size: The present study that was conducted on forty-eight with liver cirrhosis. They were divided into two equal groups: Group I (control group), 24 cirrhotic patients without hepatic encephalopathy, and Group II (case group), 24 cirrhotic patients with hepatic encephalopathy.

Data Collection and Procedures:

All participants were subjected to complete history taking, clinical examination, pelvi- abdominal ultrasound, liver function tests, coagulation profile, complete blood count (CBC), kidney functions & urinary albumin/ creatinine ratio. Evidence of hepatic decompensation by clinical or laboratory evaluation, such as ascites, hepatic encephalopathy, acute variceal hemorrhage, and hypoalbuminemia, in individuals with chronic liver disease, or radiographic evidence of hepatic nodularity, were used for diagnosis of cirrhosis.

Both clinical examination and ultrasound verified the presence of ascites. According to the West Haven standards, HE was defined and assessed. The Model for End-Stage Liver Disease (MELD) as well as the Child Pugh scores were used to evaluate the severity of liver cirrhosis. All patients enrolled in this trial had their serum creatinine levels checked twice daily during their hospital stay: once on the first day (baseline serum creatinine) and again every 24 hours (to detect AKI).

In less than 48 hours, an elevation in serum creatinine (S. Cr) of 0.3 mg/dl or more compared to the baseline serum creatinine level was considered an acute kidney injury. Based on criteria previously specified by EASL, hepatorenal syndrome-AKI was diagnosed [7]. Prerenal acute kidney injury (AKI) was defined as a rise in serum creatinine level of 0.3 mg/dl or more above the baseline level, followed by a decrease in serum creatinine (S. Cr) to ≤1.5 mg/dl within 48 hours of therapy with diuretic withdrawal and intravenous hydration. When serum creatinine levels unexpectedly rise by 0.3 mg/dL or more over baseline, when the patient does not show improvement following 48 hours of volume resuscitation, and when hepatorenal syndrome criteria are not satisfied, this is referred to as intrinsic acute kidney injury [7].

The urinary albumin creatinine ratio was determined on the first day of admission. Completely automated Cobas 8000 was used for the measurement. Albumin was assessed by an immunoturbidimetric test, in which anti-albumin antibodies reacted with the sample's antigen to create antigen/antibody complexes. These complexes were then quantified turbidimetrically after agglutination.

The concentration of creatinine in the specimen was determined using a kinetic assay based on the

Jaffee method. The creatinine concentration was shown to be closely related to the rate of dye production in this experiment, which included establishing a complex between picrate and creatinine in an alkaline solution.

Ethical and administrative considerations: Written informed consent was obtained from all participants after an explanation of the methods and medical research. The research was conducted under the World Medical Association's Code of Ethics (Helsinki Declaration) for human research. This study was carried out after the approval of the Institutional Review Board (IRB) (#10207/6-12-2022).

STATISTICAL ANALYSIS

Microsoft Office Excel 2010 (Microsoft Cor., Redmond, WA, USA), IBM SPSS 22.0 (IBM Inc., Chicago, IL, USA), and MedCalc 13 (IBM Inc., Chicago, IL, USA) were used for data collection, tabulation, and statistical analysis (MedCalc Software bvba, Ostend, Belgium). We utilised the Shapiro-Wall test. Make a distinction between the samples We used Student's t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data to compare two sets of data. When comparing more than two non-normally distributed sets of data, the Kruskal-Wallis H test was used. When comparing categorical data, a chi-square or Fisher's exact test was employed. Using Spearman's rank correlation coefficient, we assessed the study variables that were selected to be correlated with UACR (r). Direct correlation is indicated by the (+) sign, and inverse correlation is marked by the (-) sign. Values close to 1 suggest a strong correlation, whereas values around 0 indicate a weak relationship.

RESULTS

Regarding demographic data and baseline characteristics: The present study revealed non statistically significant differences among the 2 groups as regards age, sex, smoking, HCV Ab and HBVsAg. Regarding the MELD score, a significant difference was revealed between the 2 groups (cirrhotic patients with HE higher than cirrhotic patients without HE with a p-value of 0.013). Regarding Child score, a highly significant difference was revealed between the two groups (cirrhotic patient with HE >cirrhotic patient without HE with a p-value of <0.001). Regarding Child class, 50% of Cirrhotic patients without HE were Class A while 58.3% of Cirrhotic patients With HE were Class C with highly significant differences (with a p-value of <0.001). This can be due to HE being a component of the Child's score. Regarding renal functions, S. Creatinine and UACR were higher in cirrhotic patients with HE. At the same time, Urine Creatinine was lower in cirrhotic patients with HE, with substantial differences among the 2 groups (76.40±36.41 versus 128.07±83.04 with p=0.009). This can be explained by the low muscle bulk of liver disease patients and decreased protein intake (Table 1).

As regards AKI in the current study, 83.3% developed AKI in Cirrhotic patients with HE versus 54.2% in cirrhotic patients without HE, with significant differences among the 2 groups (P<0.05) (Table 2).

Table (3) compares the outcomes of cirrhotic patients without HE and cirrhotic patients with HE. (Length of Hospital stays ≤7 days in 70.8%versus 50%, 8-14 days in 29.2% versus 50%) in cirrhotic patients without HE and cirrhotic patients with HE respectively, Outcome of renal condition (not improved in 69.2% versus 70%, improved in 30.8%versus 30%) in cirrhotic patients without HE and cirrhotic patients with HE respectively, Mortality (25% versus 37.5%) in cirrhotic patients without HE and cirrhotic patients with HE respectively and it demonstrates non statistical significant differences among the 2 groups (P>0.05). Outcome of renal condition was worse among Cirrhotic patient with Hepatic Encephalopathy as they presented with higher basal serum creatinine on admissions which itself affect AKI progression, and the mortality rate was higher among Cirrhotic patient with HE as about 50% of the patient was child C which indicate advanced liver disease.

Table (4) compares patients without AKI and patients with AKI among cirrhotic with HE regarding different characteristics with non-statistically significant differences among the 2 groups (P>0.05), except for protein, prothrombin time and urine creatinine, which were lower among AKI with substantial differences among the 2 groups (p=0.025, 0.028, and 0.013, respectively), urinary creatinine was the only predictor for AKI

in our study. At the same time, UACR was not significant in HE patients with AKI

Table (5) compares patients without AKI and patients with AKI among cirrhotic with HE regarding the outcome with non-statistically significant differences between the 2 groups (P>0.05).

Table (6) showed no significant Correlation, except for urine albumin, which had a positive significant correlation with UACR (P=0.022). Table (7) showed a relationship between Child class, mortality, SBP, AKI and UACR (mg/g) among the studied cirrhotic patients; there was no significant relationship between Child class, mortality, SBP, AKI and UACR (P>0.05).

Table (1): Baseline characters of HE patients versus those without HE.

Demographic data and baseline characteristics	Cirrhotic patients				Test	p-value (Sig.)
	Without HE (N=24)		With HE (N=24)			
	No.	%	No.	%		
Gender						
Male	18	75%	15	62.5%	0.873[a]	**0.350**
Female	6	25%	9	37.5%		**(NS)**
Age (years)						
Mean±SD	58.91±13.98		62.12±5.94		-1.034[b]	**0.309**
Median (Range)	60.50 (19 – 83)		61.50 (54 – 75)			**(NS)**
Alcohol intake						
No	24	100%	24	100%	0.000[a]	**1.000**
Yes	0	0%	0	0%		**(NS)**
Smoking						
No	13	54.2%	14	58.3%	0.085[a]	**0.771**
Yes	11	45.8%	10	41.7%		**(NS)**
HCV Ab						
positive	19	79.2%	22	91.7%	1.505[a]	**0.416**
negative	5	20.8%	2	8.3%		**(NS)**
HBV sAg						
Negative	24	100%	24	100%	0.000[a]	**1.000**
Positive	0	0%	0	0%		**(NS)**
MELD score						
Mean±SD	15.79±7.24		22.33±10.07		-2.583[b]	**0.013**
Median (Range)	17.50 (7 – 32)		25.50 (6 – 36)			**(S)**
Child score						
Mean±SD	7.04±2.13		9.62±1.71		-3.910[c]	**<0.001**
Median (Range)	6.50 (4 – 12)		10 (5 – 12)			**(HS)**
Child class						
Class A	12	50%	1	4.2%	16.425[a]	**<0.001**
Class B	9	37.5%	9	37.5%		**(HS)**
Class C	3	12.5%	14	58.3%		
Ascitic fluid analysis	**Cirrhotic patients**				**Test**	**p-value (Sig.)**
	Without HE (N=24)		**With HE (N=24)**			
	No.	**%**	**No.**	**%**		
SBP	**(N=9)**		**(N=13)**			
Absent	6	66.7%	4	30.8%	2.764[a]	**0.192**
Present	3	33.3%	9	69.2%		**(NS)**
Ascites						
Absent	15	62.5%	10	41.7%	2.087[a]	**0.149**
Present	9	37.5%	14	58.3%		**(NS)**

Laboratory findings	Cirrhotic patients		Test	p-value (Sig.)
	Without HE (N=24)	With HE (N=24)		
Hemoglobin (g/dl)				
Mean±SD	9.03±1.27	9.81±1.83	-1.708[b]	**0.094**
Median (Range)	8.90 (6.80 – 11.00)	9.95 (6.30 – 12.80)		**(NS)**
WBCs count (x10^3/cc)				
Mean±SD	9.39±7.65	10.45±6.70	-1.072[c]	**0.284**
Median (Range)	5.95 (3.10 – 34.50)	8.60 (3.50 – 25.50)		**(NS)**
Platelets count (x10^3/cc)				
Mean±SD	183.70±110.84	151.95±74.30	1.166[b]	**0.251**
Median (Range)	155 (39 – 412)	142.50 (41 – 315)		**(NS)**
ALT (u/l)				
Mean±SD	98.62±309.96	32.53±15.71	-0.052[c]	**0.959**
Median (Range)	29.00 (5 – 1549)	30.50 (12 – 60)		**(NS)**
AST (u/l)				
Mean±SD	129.11±263.49	79.33±43.30	-1.567[c]	**0.117**
Median (Range)	41.20 (12.30 – 1229)	63.25 (10.00 – 153)		**(NS)**
Protein (g/dl)				
Mean±SD	6.90±0.80	5.99±0.50	0.487[b]	**0.629**
Median (Range)	6 (4.90 – 7.50)	6 (5.00 – 7.00)		**(NS)**
Albumin (g/dl)				
Mean±SD	2.66±0.83	2.49±0.49	-0.186[c]	**0.852**
Median (Range)	2.45 (1.40 – 4.30)	2.40 (1.50 – 3.90)		**(NS)**
INR				
Mean±SD	1.37±0.34	1.58±0.52	-1.647[b]	**0.106**
Median (Range)	1.38 (0.89 – 2.00)	1.50 (1.00 – 3.70)		**(NS)**
PT (sec.)				
Mean±SD	15.59±3.78	19.49±3.19	-3.447[c]	**0.001**
Median (Range)	14.50 (11.00 – 24)	19.35 (13.30 – 25)		**(S)**
PTT (sec.)				
Mean±SD	47.08±12.81	41.25±8.25	1.874[b]	**0.068**
Median (Range)	42.00 (33 – 80)	39.50 (32 – 62)		**(NS)**
ESR (mm/hr)				
Mean±SD	74.87±31.45	75.75±40.66	-0.083[b]	**0.934**
Median (Range)	75 (10 – 130)	75 (15 – 150)		**(NS)**
CRP (mg/mL)				
Mean±SD	42.48±55.47	91.26±99.28	-2.619[c]	**0.009**
Median (Range)	26.50 (0.60 – 203)	54 (11.30 – 353)		**(S)**
Procalcitonin (ng/mL)				
Mean±SD	1.01±3.47	1.50±2.65	-1.439[c]	0.150
Median (Range)	0.30 (0.10 – 17.30)	0.40 (0.10 – 9.80)		(NS)

S. Creatinine (mg/dl)				
Mean±SD	1.23±0.62	1.68±1.63	-0.392[c]	0.695
Median (Range)	0.95 (0.50 – 2.90)	1.25 (0.2 – 6.60)		(NS)
EGFR (mg/hr)				
Mean±SD	65.68±38.04	70.13±44.58	-0.289[c]	0.773
Median (Range)	49.46 (8.40 – 129.05)	62.90 (8.68 – 163.40)		(NS)
Urine Creatinine (mg/dl)				
Mean±SD	128.07±83.04	76.40±36.41	2.792[b]	0.009
Median (Range)	112.70 (6 – 357.80)	70.35 (6 – 145.40)		(S)
UACR (mg/g)				
Mean±SD	89.30±93.98	167.35±277.33	-0.516[c]	0.606
Median (Range)	66.95 (0.10 – 360.80)	65.30 (0.40 – 1342.40)		(NS)

SBP: Spontaneous bacterial peritonitis, HCV Ab: Hepatitis C virus antibody, HBV sAg: Hepatitis B virus Serum Antigen, WBCS: White blood cells, ALT: Alanine transaminase, AST: Aspartate aminotransferase, INR: International Normalized Ratio, PT: Prothrombin time, PTT: Partial Thromboplastin Time, CRP: C reactive Protein, S. Creatinine: Serum Creatinine, EGFR: Estimated glomerular filtration rate, UACR: Urine albumin creatinine ratio.

Categorical variables were expressed as number (percentage); Continuous variables were expressed as mean ± SD & median (range); a: Chi-square test; b: Independent samples Student's t-test; c: Mann Whitney U test; p-value<0.05 is significant; Sig.: Significance

Table (2): Comparison between cirrhotic patients without HE and cirrhotic patients with HE regarding acute kidney injury (AKI) and cause of AKI.

Acute kidney injury (AKI) and cause of AKI	**Cirrhotic patients**				**Test[a]**	**p-value (Sig.)**
	Without HE (N=24)		With HE (N=24)			
	No.	%	No.	%		
AKI						
Absent	11	45.8%	4	16.7%	4.752	**0.029**
Present	13	54.2%	20	83.3%		**(S)**
Cause of AKI						
Absent	11	45.8%	4	16.7%	4.868	**0.088**
Pre-renal	7	29.2%	12	50%		**(NS)**
Intrinsic renal	**6**	**25%**	**8**	**33.3%**		

Table (3): Comparison between cirrhotic patients without HE and cirrhotic patients with HE regarding outcome.

Outcome	Cirrhotic patients				Test	p-value (Sig.)
	Without HE (N=24)		With HE (N=24)			
	No.	%	No.	%		
Length of Hospital stays						
≤7 days	17	70.8%	12	50%	2.178[a]	**0.140**
8-14 days	7	29.2%	12	50%		**(NS)**
Length of Hospital stays (days)						
Mean±SD	5.83±3.59		7.25±3.65		-1.685[c]	**0.092**
Median (Range)	5 (3 – 14)		6.50 (3 – 14)			**(NS)**
Outcome of renal condition	(N=13)		(N=20)			
Not improved	9	69.2%	14	70%	0.002[a]	**1.000**
Improved	4	30.8%	6	30%		**(NS)**
Mortality						
Alive	18	75%	15	62.5%	0.873[a]	**0.350**
Died	**6**	**25%**	**9**	**37.5%**		**(NS)**

Categorical variables were expressed as number (percentage); Continuous variables were expressed as mean ± SD & median (range); a: Chi-square test; c: Mann Whitney U test; p-value<0.05 is significant; Sig.: Significance.

Table (4): Relationship between demographic data/baseline characteristics, Laboratory findings and AKI among cirrhotic patients with HE.

Demographic data & Baseline characteristics	N	AKI				Test	p-value (Sig.)
		Absent (N=4)		Present (N=20)			
		No.	%	No.	%		
Gender							
Male	15	2	13.3%	13	86.7%	0.320[a]	**0.615**
Female	9	2	22.2%	7	77.8%		**(NS)**
Age (years)							
Mean±SD		58.50±5.91		62.85±5.82		-1.398[c]	**0.162**
Median (Range)		56.50 (54 – 67)		62 (54 – 75)			**(NS)**
Smoking							
No	14	2	14.3%	12	85.7%	0.137[a]	**1.000**
Yes	10	2	20%	8	80%		**(NS)**
HCV Ab							
Negative	2	1	50%	1	50%	1.745[a]	**0.312**
Positive	22	3	13.6%	19	86.4%		**(NS)**
MELD score							
Mean±SD		21.75±8.73		22.45±10.52		-0.155[c]	**0.877**
Median (Range)		20.50 (14 – 32)		25.50 (6 – 36)			**(NS)**
Child score							
Mean±SD		9.50±1.73		9.65±1.75		-0.678[c]	**0.498**
Median (Range)		9 (8 – 12)		10 (5 – 12)			**(NS)**
Child class							
Class A	1	0	0%	1	100%	2.914[a]	**0.233**
Class B	9	3	33.3%	6	66.7%		**(NS)**
Class C	**14**	**1**	**7.1%**	**13**	**92.9%**		
Ascites							
Absent	13	1	7.7%	12	92.3%	1.645[a]	0.300
Present	11	3	27.3%	8	72.7%		(NS)

Laboratory findings	AKI		Test[c]	p-value (Sig.)
	Absent (N=4)	Present (N=20)		
Hemoglobin (g/dl)				
Mean±SD	10.55±0.68	9.66±1.96	-1.046	**0.295**
Median (Range)	10.65 (9.70 – 11.20)	9.85 (6.30 – 12.80)		**(NS)**
WBCs count (x10^3/cc)				
Mean±SD	14.70±7.49	9.60±6.40	-1.472	**0.141**
Median (Range)	12.55 (8.20 – 25.50)	7.55 (3.50 – 23)		**(NS)**
Platelets count (x10^3/cc)				
Mean±SD	189.25±74.86	144.50±73.80	-1.007	**0.314**
Median (Range)	198 (106 – 255)	132 (41 – 315)		**(NS)**
ALT (u/l)				
Mean±SD	32.75±9.35	32.49±16.88	-0.310	**0.756**
Median (Range)	30.50 (24 – 46)	29 (12 – 60)		**(NS)**
AST (u/l)				
Mean±SD	103.02±18.65	74.60±45.53	-1.279	**0.201**
Median (Range)	96.05 (90 – 130)	62 (10 – 153)		**(NS)**
Laboratory findings	**Absent (N=4)**	**Present (N=20)**	**Test[c]**	**p-value (Sig.)**
Protein (g/dl)				
Mean±SD	6.52±0.41	5.89±0.45	-2.240	**0.025**
Median (Range)	6.55 (6 – 7)	6 (5 – 6.90)		**(S)**
Albumin (g/dl)				
Mean±SD	2.60±0.18	2.47±0.53	-1.089	**0.276**
Median (Range)	2.60 (2.40 – 2.80)	2.40 (1.50 – 3.90)		**(NS)**
INR				
Mean±SD	1.40±0.38	1.62±0.55	-0.777	**0.437**
Median (Range)	1.30 (1.10 – 1.90)	1.54 (1.00 – 3.70)		**(NS)**
PT (sec.)				
Mean±SD	23±2.82	18.79±2.82	-2.250	**0.024**
Median (Range)	24 (19 – 25)	18.60 (13.30 – 24.50)		**(S)**
PTT (sec.)				
Mean±SD	44.50±11.70	40.60±7.63	-0.468	**0.640**
Median (Range)	39 (38 – 62)	39.50 (32 – 60)		**(NS)**
ESR (mm/hr)				
Mean±SD	94.50±24.51	72±42.64	-1.009	**0.313**
Median (Range)	100 (60 – 118)	64.50 (15 – 150)		**(NS)**
CRP (mg/mL)				
Mean±SD	120.77±82.23	85.35±103.17	-1.472	**0.141**
Median (Range)	81.05 (77 – 244)	51.30 (11.30 – 353)		**(NS)**
Procalcitonin (ng/mL)				
Mean±SD	0.27±0.09	1.75±2.85	-1.405	0.160
S. Creatinine on admission (mg/dl)				
Mean±SD	0.82±0.42	1.86±1.73	-1.397	0.162
Median (Range)	0.70 (0.50 – 1.40)	1.40 (0.20 – 6.60)		(NS)
EGFR (mg/hr)				
Mean±SD	91.04±34.51	65.95±45.90	-1.201	0.230
Median (Range)	92.80 (56.56 – 122)	53.80 (8.68 – 163.40)		(NS)

Laboratory findings	Absent (N=4)	Present (N=20)	Test[c]	p-value (Sig.)
Urine albumin (mg/dl)				
Mean±SD	29.42±16.62	23.77±28.40	-0.930	0.352
Median (Range)	37.50 (4.50 – 38.20)	6.10 (0.30 – 84.80)		(NS)
Urine creatinine (mg/dl)				
Mean±SD	117.72±32.16	68.14±31.79	-2.481	0.013
Median (Range)	125 (75.50 – 145.40)	68.50 (6 – 117.20)		(S)
UACR (mg/g)				
Mean±SD	230.82±120.17	154.66±299.68	-1.627	0.104
Median (Range)	261.35 (59.60 – 341)	60.05 (0.40 – 1342.40)		(NS)

SBP: Spontaneous bacterial peritonitis, HCV Ab: Hepatitis C virus antibody, HBV sAg: Hepatitis B virus Serum Antigen, WBCS: White blood cells, ALT: Alanine transaminase, AST: Aspartate aminotransferase, INR: International Normalized Ratio, PT: Prothrombin time, PTT: Partial Thromboplastin Time, CRP: C reactive Protein, S. Creatinine: Serum Creatinine, EGFR: Estimated glomerular filtration rate, UACR: Urine albumin creatinine ratio, ESR: Erythrocyte sedimentation rate.
Categorical variables were expressed as number (percentage); Continuous variables were expressed as mean ± SD & median (range); a: Chi-square test; b: Independent samples Student's t-test; c: Mann Whitney U test; p-value<0.05 is significant; Sig.: Significance.

Table 5: Comparison between patients without AKI and patients with AKI among cirrhotic with HE regarding outcome.

Outcome	AKI				Test	p-value (Sig.)
	Absent (N=4)		Present (N=20)			
	No.	%	No.	%		
Length of Hospital stays						
≤7 days	3	75%	9	45%	1.200[a]	**0.590**
8-14 days	1	25%	11	55%		**(NS)**
Length of Hospital stays (days)						
Mean±SD	6.25±1.89		7.45±3.91		-0.195[c]	**0.845**
Median (Range)	5.50 (5 – 9)		7 (3 – 14)			**(NS)**
Outcome of renal condition						
Not improved			14	70%		
Improved			6	30%		
Mortality						
Alive	3	75%	12	60%	0.320[a]	**1.00**
Died	**1**	**25%**	**8**	**40%**		**(NS)**

Categorical variables were expressed as number (percentage); Continuous variables were expressed as mean ± SD & median (range); a: Chi-square test; c: Mann Whitney U test; p-value<0.05 is significant; Sig.: Significance.

Table 6: Correlation between UACR (mg/g) and selected study variables among the studied cirrhotic patients (N=48).

Variables	UACR (mg/g)	
	r	p-value (Sig.)
Hemoglobin (g/dl)	+0.020	**0.894 (NS)**
S. Creatinine (mg/dl)	+0.186	**0.206 (NS)**
BUN (mg/dl)	+0.005	**0.975 (NS)**
EGFR (mg/hr)	+0.050	**0.735 (NS)**
Urine albumin (mg/dl)	+0.330	**0.022 (S)**
Urine creatinine (mg/dl)	**+0.193**	**0.188 (NS)**

BUN: Blood urea nitrogen, EGFT: Estimated glomerular filtration rate

r: Spearman's rank correlation coefficient; p-value<0.05 is significant; Sig.: Significance.

Table 7: Relationship between Child class, mortality, SBP and UACR (mg/g) among the studied cirrhotic patients (N=48).

	N	UACR (mg/g)				Test	p-value (Sig.)
		Mean	±SD	Median	(Range)		
Child class							
Class A	13	74.46	±99.73	58.50	(0.10 – 360.80)	1.966[d]	**0.374**
Class B	18	120.84	±129.03	71.60	(1.50 – 360.80)		**(NS)**
Class C	17	177.44	±312.57	71.60	(0.40 – 1342.40)		
AKI							
Absent	15	108.32	±128.70	64.10	(0.10 – 360.80)	-0.211[c]	**0.833**
Present	33	137.42	±237.48	68.50	(0.40 – 1342.40)		**(NS)**
Mortality							
Alive	33	134.42	±245.61	62.11	(0.10 – 1342.40)	-0.756[c]	**0.449**
Died	15	114.91	±89.02	90.00	(0.70 – 237.60)		**(NS)**
SBP							
Absent	10	136.05	±97.78	139.05	(0.10 – 237.60)	-0.923[c]	**0.356**
Present	**12**	**86.24**	**±98.46**	**65.60**	**(0.40 – 360.80)**		**(NS)**

SBP: Spontaneous bacterial peritonitis, AKI: Acute kidney injury

Continuous variables were expressed as mean ± SD & median (range); c: Mann Whitney U test; d: Kruskal Wallis H test; p-value<0.05 is significant; Sig.: Significance.

DISCUSSION

Early detection and treatment may improve the prognosis because acute kidney injury is a common consequence in patients hospitalised with chronic liver disease and is linked to a high mortality rate [3]. The study aimed for evaluation of the role of the urine albumin creatinine ratio to early predict occurrence of acute kidney injury among hepatic encephalopathy patients.

Regarding demographic data and baseline characteristics: The present study revealed that there were no significant differences among the 2 groups as regards age, sex, smoking, HCV Ab and HBVsAg. Regarding the MELD score: there were substantial differences between the 2 groups (cirrhotic patients with HE higher than cirrhotic patients without HE with a p-value of 0.013). Regarding Child score, there was a significant difference between the two groups (cirrhotic patient with HE >cirrhotic patient without HE with a p-value of <0.001). Regarding Child class, 50% of cirrhotic patients without HE were Class A while 58.3% of Cirrhotic patients with HE were class C with highly significant differences (with a p-value of <0.001). This can be due to HE being a

component of the Child's score. Similar results were obtained by Licata *et al*. [8], who aimed to compare individuals with cirrhosis. Concerning patients with HE and cirrhosis, in terms of age, sex, clinical and laboratory data (except MELD and Child scores), creatinine clearance, and INR levels, there were no statistically significant differences between the two groups.

Regarding renal functions, S. Creatinine and UACR were higher in cirrhotic patients with HE. In comparison, Urine Creatinine was lower in cirrhotic patients with HE with substantial differences among the 2 groups (76.40±36.41 versus 128.07±83.04 with p=0.009, in agreement with our results, Biadar *et al*. [9] revealed a significant increase of the average ± standard deviation values of urine protein and serum creatinine is reasonable because measuring serum creatinine and increasing proteinuria are recognised to have diagnostic and prognostic significance in confirming the presence of more significant renal disease.

In the current study, 83.3% developed AKI in Cirrhotic patients with HE versus 54.2% in Cirrhotic patients Without HE, with significant differences among the 2 groups (P<0.05). These data agreed with Shahban *et al*. [4], who found that cirrhotic patients with HE had a higher incidence of AKI. There is evidence that 27.9% of chronic liver disease patients experience AKI, according to published literature and additional studies. Gameiro *et al*. [10] found a comparable incidence of 28.0% in their research in Portugal. However, research by Lasheen *et al*. [11] and Lins *et al*. [12] found a prevalence of 43.8% and 53.9%, respectively. The rates we found were higher in our study, and these rates were lower. Possible causes for this variation include differences in patient demographics, the nature and extent of liver disease, the presence of infection, gastrointestinal bleeding, constipation, specific medications, surgery, alcohol consumption, and various serum creatinine thresholds for defining AKI.

The outcome of renal condition (not improved in 69.2% versus 70%, improved in 30.8%versus 30%) in cirrhotic patients without HE and cirrhotic patients with HE, respectively, Mortality (25% versus 37.5%) in cirrhotic patients without HE and cirrhotic patients with HE respectively and it demonstrates that there were no significant differences among the 2 groups (P>0.05). Patients in our study reported a high mortality rate. This may be due to severe stages of AKI, which had higher odds of mortality and underlying liver diseases compared to other studies. Fede *et al*. [13] reported that nearly half of AKI patients with liver cirrhosis die within a month, and another 65% die within a year. Belcher *et al*. [14], in a prospective multicentric study involving 192 cirrhotic patients, reported 26% intra-hospital mortality, while Scott *et al*. [15] reported an intrahospital mortality of 31.8% in their research. Gomes *et al*. [16] and Allegretti *et al*. [17] documented mortality rates of 45% and 46% in their studies, respectively, within 3 months of AKI diagnosis. Wong *et al*. [18] also observed a 34% mortality rate in 30 days.

In the current study, we found that increased length of hospital stay, MELD score and Child score were higher in patients with AKI compared to those without (7.45±3.91 days versus 6.25±1.89 days, 22.45±10.52 versus 21.75±8.73, 9.65±1.75 versus 9.50±1.73 respectively). Patients with AKI had infection and encephalopathy more than those without. However, high MELD and high PT were clinical parameters and scores independent predictors of AKI. There were no significant differences among the 2 groups (P>0.05), except for protein, prothrombin time and urine creatinine, which were lower among AKI with substantial differences among the 2 groups (p=0.025, 0.028, and 0.013, respectively), urinary creatinine was the only predictor for AKI in our study. At the same time, UACR was not significant in HE patients with AKI. The overall rate of death while hospitalized for chronic liver disease is 7.4%. The in-hospital death rates are known to rise in conjunction with the problems caused by concomitant cirrhosis. For example, in cirrhotic HE, HRS was linked to an increased risk of in-hospital mortality. Hirode *et al*. [19] based on these results, a higher in-hospital mortality rate was detected among cirrhotic HE-AKI patients in the current study.

In agreement with the current study, In-hospital mortality rates were significantly higher when AKI occurred in hepatic encephalopathy. Hospitalized cirrhotic individuals with hepatic encephalopathy were more likely to develop AKI if they had elevated blood total bilirubin, creatinine, UACR, CTP score upon admission, and duration of hospital stay [4]. Also, Tariq *et al*. [20] identified MELD, CPS stage C, ascites, and sepsis/septic shock as risk factors for AKI.

Incidence rates of HE-AKI are not well documented. In this investigation, the incidence of AKI was greater in cirrhotic individuals with HE than in those without HE. Renal function impairment (RFI) was found to be a significant predictor of death in cirrhotic HE in a single investigation [4].

This study's urinary/ albumin creatinine ratio also does not correlate with other renal functions such as Baseline S. creatinine, eGFR, and urinary creatinine. In contrast, it was associated with urinary albumin, so in this study, there was no significant albuminuria in AKI patients, and the urinary albumin/ creatinine ratio was not a predictor for AKI in HE patients.

Limitations:

The limitation of this study may be related to the relatively small number of patients and grades of hepatic encephalopathy and stages of AKI needed to be included, as well as follow-up of patients after discharge**.**

CONCLUSION

Patients who had cirrhotic hepatic encephalopathy are at higher risk of developing AKI with increased in-hospital mortality. To better understand how UACR predicts hepatic encephalopathy-acute kidney injury, more research is required.

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