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ORIGINAL ARTICLE

Outcome of hepatorenal syndrome - AKI patients in the hepatic care unit in Aswan University Hospital "one year study"

Huda Mubarak Ahmed [1*], Zain El-Abedieen Ahmed Sayed Saleh [2], Wael Abd El Gwad Abd Elaziz [1]

[1]Department of Internal Medicine & Nephrology, Faculty of Medicine, Aswan University

[2]Department of Internal Medicine, Faculty of Medicine, Assuit University

ABSTRACT

Keywords: Acute kidney injury, Cirrhosis and Hepatorenal syndrome.

***Corresponding author:**
Huda Mubarak Ahmed

Email:
dr.hoda7777@gmail.com

Tel: :

01119301119

Background; Cirrhosis of the liver is an enduring medical condition distinguished by the presence of structurally aberrant nodules and fibrosis, which conclude a range of chronic liver diseases histologically. Renal failure ranks among the most significant complications of cirrhosis, which is linked to substantial morbidity & mortality. Hepatorenal syndrome (HRS-AKI) is a distinct kind of kidney failure that specifically arises in the advanced phases of cirrhosis. **Aim of the work:** To evaluate the outcome of HRS - AKI between individuals attending Aswan University Hospital in the hepatic care unit for one-year. **Patients & methods:** This research was a cross-sectional research performed on sixty individuals at the hepatic care unit in Aswan University Hospital, from April 2020 to March 2021. **Result:** Among the studied cases, there were 22 (36.7%) cases with diabetes, 16 (26.7%) cases with hypertension, 8 (13.3%) with hepatocellular carcinoma, 60 (100%) with ascites, 40 (66.7%) with hepatic encephalopathy, 35 (58.3%) spontaneous bacterial peritonitis and 22 (36.7%) with sepsis. There were 25(41.6%) cases improved and 35 (58.3%) cases not improved.**Conclusion:** AKI is frequently observed in cirrhotic patients who are hospitalized to ICU, and it is linked to a notable rate of death during hospitalization. HRS-AKI was the prevailing and severe form of AKI observed in cirrhosis individuals who were hospitalized to ICU.

INTRODUCTION

AKI is distinguished by a fast deterioration in kidney function mostly caused by a reduction in GFR. It is linked to significant short- &long-term problems, which can lead to higher death rates [(4)]. Cirrhosis patients frequently encounter this life-threatening condition [(5)]; in fact, the risk of mortality increases by a factor of seven in those with cirrhotic renal failure, with fifty percent of patients succumbing to their conditions within a month [(3)].

Prerenal azotemia (PRA), acute tubular necrosis (ATN), & hepatorenal syndrome (HRS) are the most frequent causes of AKI in cirrhotic cases. However, there are additional potential causes as

glomerulonephritis, drug toxicity, & abdominal compartment syndrome resulting from tight ascites [6].

HRS is a distinct kind of renal failure caused by reduced blood supply to the kidneys, generally affecting kidneys that are structurally normal [7]. HRS primarily affects individuals with severe cirrhosis and ascites, characterized by significant circulatory dysfunction. It also occurs in people with acute liver failure or alcoholic hepatitis [8].

The majority of evidence about HRS therapies is derived from retrospective analyses, pilot studies, non-randomized investigations, and a limited number of RCTs. The treatment options for HRS include the use of vasoconstrictors such as vasopressin or terlipressin, along with albumin to enhance renal blood flow in patients with cirrhosis. Another option is the trans-jugular intrahepatic Porto systemic stent-shunt (TIPS) procedure. Renal replacement therapy can also be considered. However, liver transplantation remains the most effective therapy for patients with HRS, especially in cases where vasoconstrictors and TIPS are not available or not suitable. It continues to be the preferred treatment for these individuals [9].

We aimed to estimate the outcome of HRS - AKI among patients attending Aswan University Hospital in the hepatic care unit for one-year duration.

PATIENTS & METHODS

This was a cross-sectional research performed in the period from April 2020 to March 2021. All patients aged more than 18 years with known cirrhosis with HRS in Aswan university hospital.

Inclusion criteria: Adult cases (age 18 years or older), cases with AKI with a history of cirrhosis and ascites, and cirrhotic patients with AKI or develop HRS in Aswan University hospital.

Exclusion criteria: Patients aged less than 18 years, those who received renal transplants, pregnant or lactating patients, and cases with renal failure on regular dialysis were excluded from the research.

Methods

All cases were subjected to

Complete history taking & clinical examination: Personal history (age, gender, alcohol consumption and addiction), presenting complaints (mainly: abdominal pain & signs of chronic liver disease (chronic hepatitis & liver cirrhosis), and history of any preceding disease, previous operations and history of bilharziasis.

Clinical examination: including hemodynamic data, abdominal examination (to detect the existence of any mass, organomegaly, and signs of cirrhosis or ascites)

Diagnosis of cirrhosis: confirmed by: LFTs, albumin, prothrombin, INR, hepatitis markers, and abdominal ultrasound.

Investigations: Serum urea, serum creatinine, serum sodium, serum potassium, urine sodium, abdominal Ultrasound, LFTs and PT, PC, INR

Abdominal Ultrasound for Cirrhosis

International recommendations recommend that individuals with cirrhosis have ultrasonography examinations every six months in order to identify HCC at an early stage. Fig 1, 2

In patients with cirrhosis, Doppler ultrasonography may be used to observe the presence of fast-moving blood flow in the enlarged hepatic artery. As the level of fibrosis develops, the artery becomes more twisted & irregular.

Treatment taken: according to the causes of AKI such as (UTI and septic shock treated by antibiotic, gastroenteritis and burn treated by volume expansion……etc.).**Treatment of HRS:** Large volume paracentesis, IV albumin, and terlipressin

Ethical Consideration

Approval of the ethical committee of the Faculty of Medicine, Aswan University to the final protocol had been obtained. Written or verbal consent was obtained from all participants prior to their inclusion in the study. With the cases, the investigation's procedures, objective, potential benefits, & risks had all been described in detail. Ensuring the confidentiality of all data was achieved.

STATISTICAL ANALYSIS

Data management and statistical analysis involved the coding, entering, and analyzing of outcome measures, fundamental clinical examination data, and laboratory investigation data gathered over time using Microsoft Excel. The information was subsequently transferred into version 25.0 of Statistical Package for the Social Sciences (SPSS) software in order to conduct the analysis. In order to determine the significance of differences between qualitative and quantitative groups (represented by number and percentage, respectively, and mean ± standard deviation, respectively), the following tests were applied: Pearson's correlation or Spearman's correlation. 0.05 was designated as the significance level for results, while 0.001 was considered highly significant.

RESULTS

Among the studied cases there were forty four (73.3%) men & sixteen (26.7%) women with average age 56.40 (±11.86 SD) and range (37-77) years. There was no relation between outcome and demographic data. There were 18 (72%) males and 7 (28%) females improved , twenty six (74.3%) men & nine (25.7%) women not improved.Table 1

There was a significant relation among outcome and sepsis (p-value) (Table 2)

The mean length of hospital stay of he studied cases was 18.67 (±9.18 SD) days. There was high significant relation between outcome and lengths of hospital stay (p-value) (Table 3)

The mean arterial blood pressure was 93.56 (±12.63 SD) with no relation between outcome and blood pressure (p-value) (Table 4).

There was no relation between outcome and serum creatinine, there was high significant variance among different periods as regard & serum creatinine (p-value) (Table 5).

There was a noteworthy relation between outcome and treatment (p-value) (Table 6).

DISCUSSION

Since its initial description by **Hecker & Sherlock** in the 1960s, renal dysfunction among individuals with ascites & advanced cirrhosis has commonly been referred to as HRS. This syndrome is characterized by reduction in kidney function primarily caused by the hemodynamic effects of advanced portal hypertension [(10)].

The primary findings of our investigation were as following:

In the current research, there were forty four (73.3%) men & sixteen (26.7%) women with average age 56.40 (±11.86 SD) and range (37-77) years. There was no relation between outcome and demographic data (age & sex).There were 18 (72%) males and 7 (28%) females improved , 26 (74.3%) males and 9 (25.7%) females not improved.

Concurring with our findings, **Piano et al.,** [(11)] stated that there were no significant differences were found among the two groups in terms of age and gender**, Allegretti et al.,** [(6)] showed that No significant variances were found among the examined groups Regarding age & sex, **El-Gebaly et al.,** [(12)] found that there was no relation between the studied groups as regard age and sex.

Similar to our results, **Bashir et al.,** [(13)] found that the average age of examined cases was 55.7 ± 0.61, **KHAIRIA et al.,** [(14)] revealed that the average of age was (51.9 1 ± 5.36).

Hafez et al., [(15)] reported that the age varied from twenty two to eighty five years old with average of 60.38 ± 15.11 years & males constituted 52. 6%.

On the contrary to our findings, **Sheng et al.,** [(16)] stated that gender was positively correlated with mortality of HRS. Moreover, **Lasheen et al.,** [(17)] noted that a significant relation was found among the studied groups as regard age & sex.

In the current study, there were 22 (36.7%) with diabetes, 16 (26.7%) with hypertension, 8 (13.3%) with hepatocellular carcinoma, 60 (100%) with ascites, 40 (66.7%) with hepatic encephalopathy, 35 (58.3%) spontaneous bacterial peritonitis and 22 (36.7%) with sepsis. There was a significant relation between outcome and sepsis.

Concurring with our findings, **Piano et al.,** [(11)] found that no relation among the two groups as regards diabetes and hypertension, Furthermore, **Allegretti et al.,** [(6)] revealed that no relation

among the two groups regarding diabetes, hypertension, spontaneous bacterial peritonitis, hepatic encephalopathy, and ascites. While, **Kumar et al., [18]** showed that the existence of jaundice & hepatic encephalopathy (HE) was allied with poor survival with an adjusted hazard ratio of 3.54 & 2.17, correspondingly. Moreover, **El-Gebaly et al., [12]** found that a substantial relation was found among examined groups concerning spontaneous bacterial peritonitis and hepatic encephalopathy.

Lower than our results, **Hafez et al., [15]** reported that Approximately 45.4 percent of the individuals examined had DM & 46.4 percent had hypertension. 39.2% of the individuals experienced cardiac issues.

In the present research, a significant relation among outcome & the length of hospital stay. Concurring with our findings, **Thapa et al., [19]** stated that The severity of acute kidney injury had a direct impact on the average duration of hospital stay. Individuals who presented with hepatorenal syndrome-associated acute kidney injury exhibited a greater degree of ascites & hyponatremia.

Allegretti et al., [6] supported our results by reporting that Hepatorenal syndrome & acute tubular necrosis have comparable 90-day fatality rates.

In current research, the average systolic blood pressure of studied cases was 129 (±16.54 SD) with range (110-170), the average diastolic blood pressure was 75.83 (±13.19 SD) with range (60-100) and MAP was 93.56 (±12.63 SD) with range (76.7-120). There was no relation between outcome and mean blood pressure. In harmony with our outcomes, **Rodriguez et al., [20]** reported that no significant relation among outcome & mean arterial pressure. However, **Allegretti et al., [6]** showed that there was a noticeable relation between outcome and mean arterial pressure.

The present investigation found no correlation among the result & serum creatinine levels. However, there was a statistically significant variance seen in serum creatinine levels across different time periods.

Consistent with our findings, **Piano et al. [11]** found that those who did not react to treatment had a significantly greater SCr level compared to those who responded, specifically at the time of AKI-HRS diagnosis (219 vs. 183 µmol/L, P = 0.008). However, this difference was not observed prior to the development of AKI-HRS. **Allegretti et al. [6]** demonstrated a considerable disparity in serum creatinine levels across different time periods. Similarly, **El-Gebaly et al. [12]** observed a significant distinction in serum creatinine levels across the groups under study.

Kumar et al., [18] showed that Serum creatinine is the most pragmatic biomarker for assessing renal function, however it presents some constraints in cirrhotic individuals.

While, **Bashir et al., [13]** found that The average of the first serum creatinine level was 0.94 ± 0.14. The mean increase in creatinine levels from the initial value was 1.36 ± 0.08 mg/dl.

And, **KHAIRIA et al., [14]** showed that (63%) of patients have creatinine level ranging between (1.5-2.5) mg/L

In contrast to our outcomes, **Rodriguez et al., [20]** stated that no variance was found among examined groups regarding Serum creatinine.

The current investigation found a strong and statistically significant relationship between the result & the therapy.

Consistent with our research, **Bashir et al., [13]** discovered that 92.3 percent of individuals diagnosed with HRS were administered intravenous fluids, while 75.4 percent got intravenous albumin within forty-eight hours of experiencing a sudden increase in creatinine levels. There was high significant relation between outcome and treatment.

Also, **Nguyen-Tat et al., [21]** supported our results by reporting that The combination of terlipressin and albumin is efficacious in the majority of individuals with HRS, **Ortega et al., [22]** found that The administration of terlipressin & albumin resulted in a significant reduction in blood creatinine levels, an elevation in arterial pressure, & inhibition of the renin-aldosterone system, **Sagi et al., [23]** reported that Terlipressin effectively reverses HRS type 1. The recurrence of HRS is infrequent when medication is administered for a minimum of fourteen days. Severe adverse effects necessitating the cessation of treatment are infrequent. Patients with HRS who were treated with terlipressin exhibited a noticeable improvement in survival rates. A study conducted by **Allegretti**

et al. [6] demonstrated a substantial correlation among the medications taken & the prognosis of the individuals.

CONCLUSION

AKI is frequently observed in cirrhotic patients who are hospitalized to ICU, and it is linked to a notable rate of death during hospitalization. HRS-AKI was the predominant & most severe form of AKI observed in cirrhosis patients who were hospitalized to the ICU. Hepatorenal syndrome is defined by a pronounced systemic inflammatory condition, similar to that observed in non-hepatic inflammatory illnesses, which is associated with outcomes for patients

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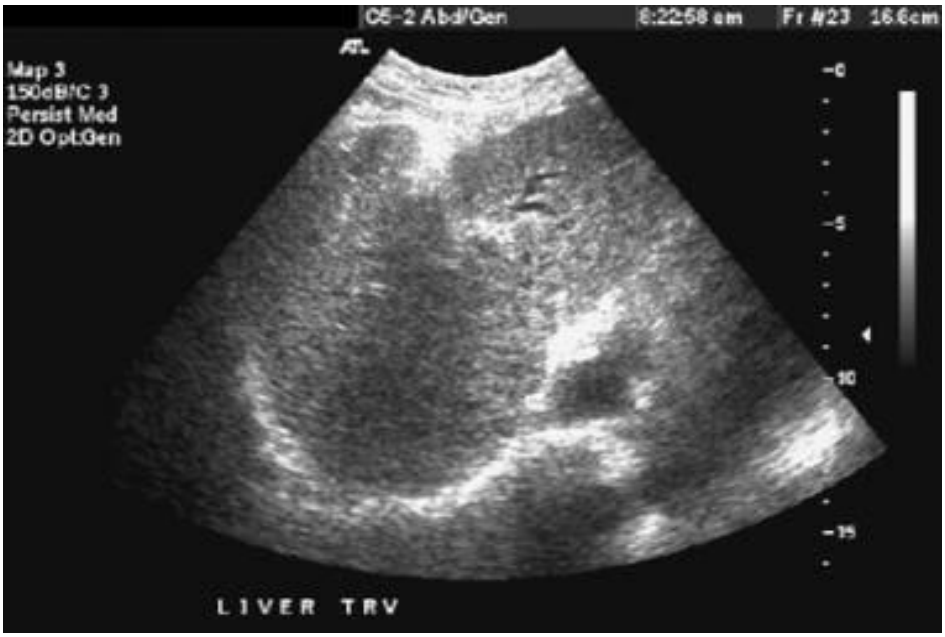

Fig (1): Female patient with cirrhosis showing "coarsened" echo texture and enlarged left lobe of liver

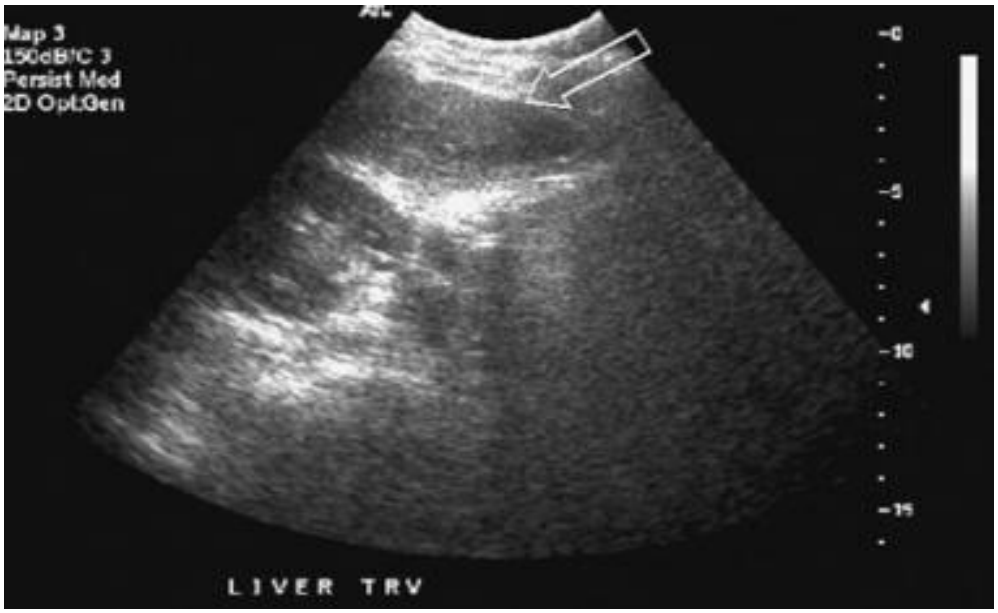

Fig (2): Transverse view, real-time ultrasonogram shows an irregular external contour of the left lobe (arrow)

Table (1): Demographic data of the study population

	Total (n = 60)		Outcome				Test of Sig.	P-value
			Improved (n = 25)		**Not improved (n = 35)**			
	No.	**%**	**No.**	**%**	**No.**	**%**		
Gender								
Male	44	73.3	18	72.0	26	74.3	χ^2= 0.039	0.844
Female	16	26.7	7	28.0	9	25.7		
Age (years)								
Mean ± SD.	56.40 ± 11.86		57.84 ± 11.51		55.37 ± 12.16		t= 0.792	0.431

IQR: Inter quartile rang SD: Standard deviation2: Chi square test t: Student t-test
P value < 0.05 is considered significant

Table (2): Relation between the outcomes of hepatorenal syndrome - AKI with different co-morbidities among the included cases in the hepatic care unit

Co-morbidities	Total (n = 60)		Outcome				χ^2	p
			Improved (n = 25)		**Not improved (n = 35)**			
	No.	**%**	**No.**	**%**	**No.**	**%**		
Diabetus	22	36.7	7	28.0	15	42.9	1.386	0.239
Hypertension	16	26.7	5	20.0	11	31.4	0.974	0.324
Hepatocellular carcinoma	8	13.3	1	4.0	7	20.0	3.231	0.123
Hepatic encephalopathy	40	66.7	15	60.0	25	71.4	0.857	0.355
Spontaneous bacterial peritonitis	35	58.3	11	44.0	24	68.6	3.623	0.057
Sepsis	22	36.7	5	20.0	17	48.6	5.126*	0.024*

Table (3): Relation between outcome of hepatorenal syndrome - AKI in hepatic care and lengths of hospital stay

Lengths of hospital stay (days)	Total (n = 60)	Outcome		U	p
		Improved (n = 25)	**Not improved (n = 35)**		
Mean ± SD.	18.67 ± 9.18	27.40 ± 6.21	12.43 ± 4.79	32.0*	<0.001*

IQR: Inter quartile range SD: Standard deviation U: Mann Whitney test p: p value for comparing between improved and not improved *: Statistically significant at $p \leq 0.05$

Table (4): Relation between outcome of hepatorenal syndrome - AKI in hepatic care and blood pressure

Blood pressure	Total (n = 60)	Outcome		t	p
		Improved (n = 25)	**Not improved (n = 35)**		
Systolic BP					
Mean ± SD.	129.0 ± 16.54	128.0 ± 15.81	129.7 ± 17.23	0.393	0.696
Diastolic BP					
Mean ± SD.	75.83 ± 13.19	76.40 ± 12.87	75.43 ± 13.58	0.279	0.781
MAP (mmHg)					
Mean ± SD.	93.56 ± 12.63	93.60 ± 12.03	93.53 ± 13.21	0.022	0.982

IQR: **Inter quartile range** SD: **Standard deviation t: Student t-test** p: p value for comparing between improved and not improved

Table (5): Relation between outcome of hepatorenal syndrome - AKI in hepatic care and serum Creatinine

Serum Creatinine (umol/L)	Total (n = 60)	Outcome		t	p
		Improved (n = 25)	**Not improved (n = 35)**		
Baseline					
Mean ± SD.	164.5 ± 21.26	163.6 ± 17.96	165.1 ± 23.58	0.263	0.793
After 48 hr.					
Mean ± SD.	175.1 ± 22.20	173.7 ± 19.57	176.0 ± 24.14	0.392	0.696
^{t}p		<0.001*	<0.001*		

IQR: Inter quartile range SD: Standard deviation t: Student t-test p: p value for comparing between improved and not improved p: p value for Paired t-test for comparing between Baseline and after 48 hr. *: Statistically significant at $p \leq 0.05$

Table (6): Relation between outcome of hepatorenal syndrome - AKI in hepatic care and treatment

	Total (n = 60)		Outcome				χ^2	p
			Improved (n = 25)		**Not improved (n = 35)**			
	No.	**%**	**No.**	**%**	**No.**	**%**		
	60	100.0	25	100.0	35	100.0		
Treatment								
IV albumin	14	23.3	1	4.0	13	37.1	20.841*	<0.001*
Terlipressin	32	53.3	22	88.0	10	28.6		
Large volume paracentesis	14	23.3	2	8.0	12	34.3		

2: Chi square test p: p value for comparing between improved and not improved *: Statistically significant at $p \leq 0.05$