

Factors Associated with Acute Kidney Injury in Cirrhotics Patients at the Departmental University Hospital of Borgou and Alibori (Benin)

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Abstract

Introduction: Acute kidney injury is one of the major complications that can occur during liver cirrhosis.

Objective: to study the frequency and factors associated with acute kidney injury in CHUD-B/A cirrhotic patients in 2022.

Patients and methods: This was a cross-sectional, descriptive study with prospective data collection over a period from February 1 to June 30, 2022. A systematic recruitment of cirrhotic patients received in consultation and in hospitalization was made. AKI was defined according to the ADQI- IAC classification. Statistical analysis was performed using SPSS 21 software. The association between the identified factors and the variable of interest was determined by the Odds Ratio (OR) and its 95% confidence interval.

Results: A total of 73 cirrhotic patients were included and 14 of them had AKI. The frequency of AKI in cirrhotics was 19.2%. The mean age was 48.6 ± 16.9 years with a sex ratio of 13. Factors associated with AKI were hepatic encephalopathy ($p=0.006$) and Child-Pugh C score ($p=0.031$).

Conclusion: Acute kidney injury among cirrhotic patients is highly frequent. Its screening should be systematic for cirrhosis patients in order to improve their medical care and survival.

Introduction

Acute kidney injury (AKI) is one of the most serious complications that can occur during cirrhotic liver¹. In cirrhosis, AKI is mainly due to hypovolemia but it can also be of infectious origin or induced by taking some medications (diuretics and nephrotoxic medications)². It leads to rapid progression to death when a liver transplant is not performed³.

AKI was observed in 14 to 50% of patients with cirrhosis in the United States of America in 2014². In Asia, the frequency of AKI in cirrhosis was 20 to 50% in Nepal⁴, 19% in Korea⁵ and 22.83% in Taiwan in hospitalized patients⁶. In Europe, it was noted in 53% of cirrhotic patients in Spain³, in Guadeloupe in 19% of patients with decompensated cirrhosis⁷ and in 40 to 80% of hospitalizations in

cirrhosis patients at the Lille University Hospital in France in 2018².

In Africa, few studies concerning AKI in cirrhosis patients are available in the literature⁸. In Parakou in Benin, the frequency of AKI was determined in several groups of the population and was high. Indeed, it was 44.31% among patients hospitalized for preeclampsia in the gynecology-obstetrics department in 2019⁹; and 44.19% among people living with the human immunodeficiency virus in 2016¹⁰. This frequency is not known in the population of cirrhotics patients. This research work was initiated with the aim of studying the frequency and factors associated with acute kidney injury in cirrhosis at the Departmental University Hospital Center of Borgou and Alibori (CHUD-B/A) in 2022.

Patients and Methods

This was a cross-sectional study carried out in the hepato-gastroenterology unit of the Departmental University Hospital Center of Borgou and Alibori (CHUD-B/A) from February 1st to June 30th, 2022. Were included in the study included all patients with hepatic cirrhosis who had given verbal consent. Patients with known pre-existing renal insufficiency were not included. Excluded from the study were cirrhotics patients who were unable to obtain serum creatinine on admission or control and those who died or were discharged against medical advice less than 48 hours after their admission.

The dependent variable was the presence of acute kidney injury in the cirrhotics patients. Acute kidney injury was selected according to the criteria of the Acute Dialysis Quality Initiative (ADQI) and the International Ascites Club (IAC)⁵, namely due to an increase in serum creatinine following the diagnostic criteria proposed for renal dysfunction in cirrhosis. This was an increase in serum creatinine ≥ 3 mg/L within 48 hours of admission or > 1.5 times the basal serum creatinine measured in the previous 7 days.

The independent variables consisted of sociodemographic data (age and sex), those relating to medication intake, history and lifestyle, clinical and paraclinical data (complications and etiology of cirrhosis, Child Pugh score¹¹ for the occasional assessment of the severity of cirrhosis).

Data was collected via the Kobo Collect app; they were cleared and processed with the SPSS 21 French version software.

Qualitative variables were described as proportions, and quantitative variables expressed as means \pm standard deviation. In bivariate analysis, percentages were compared with the uncorrected Karl Pearson Chi-square (χ^2) test, or Fisher's exact test as appropriate. The association between the identified factors and the variable of interest was

determined by the Odds Ratio (OR), the prevalence ratio (PR) and its 95% confidence interval. A threshold of $p < 0.05$ was retained as statistically significant.

Results

During the data collection period, 88 patients were seen in consultation and/or hospitalized in the hepato-gastroenterology unit of CHUD-B/A presented with liver cirrhosis and 73 among them were retained for the following study according to the eligibility criteria.

Data on selected cirrhotic patients

Sociodemographic data on cirrhotic patients

The mean age of the cirrhotic patients was 44.2 ± 14.8 years. Fifty-two patients were male (71.2%), giving a sex ratio of 2.5. In terms of education and socio-professional status, 32 patients (43.8%) were uneducated and 28 patients (38.4%) were farmers. Table 1 shows the sociodemographic distribution of cirrhotic patients.

Causes, complications, modes of decompensation and prognosis of cirrhosis

Of the 73 patients included, hepatic cirrhosis was due to viral hepatitis B in 48 patients (65.8%). Complications and modes of decompensation

Table 1: Distribution of cirrhotic patients included according to sociodemographic data (CHUD-B/A, Parakou, 2022, N=73)

| | | Number | Percentage |
|----------------------------------|------------------------------|--------|------------|
| Age (years) | < 25 | 4 | 5.4 |
| | [25-35[| 18 | 24.7 |
| | [35-45[[| 18 | 24.7 |
| | [45-55[| 12 | 16.4 |
| | ≥ 55 | 21 | 28.8 |
| | Sex | Female | 21 |
| Male | | 52 | 71.2 |
| Level of education | No education | 32 | 43.8 |
| | Primary | 24 | 32.9 |
| | Secondary | 10 | 13.7 |
| | University | 7 | 9.6 |
| Socio-professional status | Farmer | 28 | 38.4 |
| | Housewife | 12 | 16.4 |
| | Shopkeeper | 11 | 15.1 |
| | Employee (public or private) | 10 | 13.7 |
| | Craftsman/Worker | 6 | 8.2 |
| | Pupil/student | 3 | 4.1 |
| | breeder | 2 | 2.7 |
| | Vehicle driver | 1 | 1.4 |

Table 2: Distribution of cirrhotic patients according to the different causes, complications, modes of decompensation and prognosis of cirrhosis (CHUD-B/A, Parakou, 2022, N=73)

| | Number | Percentage |
|-------------------------------------|--------|------------|
| Causes | | |
| Viral hepatitis B | 48 | 65.8 |
| Undetermined | 17 | 23.3 |
| Alcohol | 5 | 6.8 |
| Viral hepatitis C | 3 | 4.1 |
| Complications | | |
| Ascites | 54 | 77.1 |
| Hepatocellular carcinoma | 30 | 42.9 |
| Acute kidney injury | 14 | 19.2 |
| Digestive haemorrhage | 9 | 12.9 |
| Hydrothorax | 7 | 10.0 |
| Hepatic encephalopathy | 3 | 4.3 |
| Prognosis / Child-Pugh stage | | |
| A | 13 | 17.8 |
| B | 33 | 45.2 |
| C | 27 | 37.0 |

At least one complication or mode of decompensation was found in 70 patients (95.9%). In terms of prognosis, 27 patients (37%) were classified as Child-Pugh C. Table 2 presents the different causes, complications, modes of decompensation and prognosis of cirrhosis.

Données paracliniques

Among the 73 patients, a cytolysis syndrome was found in 90.41% with an increase in transaminases. The mean values for AST were 345.25 ± 34.81 IU and for ALT 378.22 ± 46.81 IU. Total bilirubinemia was elevated in 56 (76.71%) patients. The mean bilirubin level was 78.99 ± 13.44 mg/l. On admission, serum creatinine levels were elevated in 31 (42.47%) patients, with a mean of 45.56 ± 12.33 mg/l. Mean uraemia was 1.67 ± 0.67 g/l.

Of the 73 cirrhotic patients, 42.46% had hypocalcaemia, 90.41% anaemia, 84.93% normal kalaemia, 39;72% hyponatraemia and 56.64% hypochloremia.

Frequency of acute kidney injury in retained cirrhotics patients

Among the 73 patients included with liver cirrhosis, 14 presented with AKI, representing a frequency of 19.2%.

All 14 patients had an increase in serum creatinine of more than 3 mg/l in 48 hours. The extremes of the increased serum creatinine values were 6.22 mg/l and 21.14 mg/l.

Types of acute kidney injury

Of the 73 cirrhotic patients, AKI was found in eight (11.0%) cases of the organic type (parenchymal) and six (8.2%) cases of the functional type in a context of hypovolaemia.

Table 3: distribution of cirrhotics patients with AKI according to the stage of progression of acute kidney injury (CHUD-B/A, Parakou, 2022, n=14)

| | Number | Percentage |
|----------|--------|------------|
| Stage 1A | 2 | 14.3 |
| Stage 1B | 3 | 21.4 |
| Stage 2 | 5 | 35.7 |
| Stage 3 | 4 | 28.6 |

Acute kidney injury stages

Five patients (35.7%) out of the 14 cirrhotic patients presenting AKI were at stage 2. Table 3 below presents the stages of progression of AKI in the patients.

Sociodemographic, clinical and prognostic data of included cirrhotics patients with AKI

The average age of cirrhotic patients presenting with AKI was 48.6 ± 16.9 years [range 25 years and 76 years]. Thirteen of the 14 patients were male, giving a sex ratio of 13.

Among cirrhotics patients with AKI, 7 had a primary education level (50%) and 6 were farmers (42.9%). Among the 14 cirrhotic patients presenting with AKI, 4 patients (28.6%) were considered alcoholics, 2 patients (14.3%) were tobacco users. Of the 14 cirrhotic patients with AKI, viral hepatitis B was the cause of cirrhosis in 8 of them (57.1%) and ascites was found in 11 patients (78.6%).

From a prognostic point of view, 9 of the 14 patients were classified as Child Pugh stage C.

Identification of factors associated with AKI in cirrhotic patients

AKI was not associated with any sociodemographic factor ($p > 0.05$), patients lifestyle ($p > 0.05$) or previous treatments received by the patient ($p > 0.05$). AKI was also not associated with the clinical characteristics of liver cirrhosis or its etiology ($p > 0.05$).

Lifestyle and defects

The proportions of some habits and defects were determined among the cirrhotics selected for the study and compared with those among the cirrhotics patients with AKI. The result is presented in Table 4. No patient among those surveyed was diabetic or had heart disease.

Lifestyle and defects were not statistically associated with the occurrence of AKI ($p > 0.05$).

Previous treatments

The proportions of cirrhotics selected for the study having received previous treatment were determined and compared with those among cirrhotic patients with AKI. The result is presented in Table 5.

Table 4: Relationship between AKI in cirrhotics patients and lifestyle defects, the previous treatments received and the etiology of liver cirrhosis, (CHUD-B/A, Parakou, 2022, N=73).

| | Total | AKI | | OR [IC95%] | p |
|------------------------------|-------|-----|------|--------------------|-------|
| | | n | % | | |
| Chronic Alcoholism | | | | | 0.449 |
| Yes | 14 | 4 | 28.6 | 1.96 [0.51-7.52] | - |
| No | 59 | 10 | 16.9 | 1 | - |
| Smoking | | | | | 0.645 |
| Yes | 8 | 2 | 25.0 | 1.47 [0.26-8.21] | - |
| No | 65 | 12 | 18.5 | 1 | - |
| Arterial Hypertension | | | | | 0.080 |
| Yes | 6 | 3 | 50.0 | 5.09 [0.91-28.6] | - |
| No | 67 | 11 | 16.4 | 1 | - |
| Diuretics | | | | | 0.999 |
| Yes | 11 | 2 | 18.2 | 0.93 [0.18-4.85] | |
| No | 62 | 12 | 19.4 | 1 | |
| Phytotherapy | | | | | 0.721 |
| Yes | 16 | 2 | 12.5 | 0.54 [0.11-2.69] | |
| No | 57 | 12 | 21.1 | 1 | |
| Viral hepatitis B | | | | | 0.535 |
| Yes | 48 | 8 | 16.7 | 0.63 [0.19-2.08] | |
| No | 25 | 6 | 24.0 | 1 | |
| Viral hepatitis C | | | | | 0.092 |
| Yes | 3 | 2 | 66.7 | 9.67 [0.81-115.39] | |
| No | 70 | 12 | 17.1 | 1 | |
| Alcoholism | | | | | 0.999 |
| Yes | 5 | 1 | 20.0 | 1.06 [0.11-10.27] | |
| No | 68 | 13 | 19.1 | 1 | |
| Undetermined | | | | | 0.999 |
| Yes | 18 | 3 | 16.7 | 0.80 [0.20-3.26] | |
| No | 55 | 11 | 20.0 | 1 | |

Etiology of liver cirrhosis

The etiologies of liver cirrhosis in cirrhotics selected for the study were determined and the proportions were compared with those among cirrhotics patients with AKI. The result is presented in Table 5

Complications and modes of decompensation

The proportions of cirrhotics selected for the study who presented complications and modes of decompensation were determined and compared with those among cirrhotic patients with AKI. The result is presented in Table 6.

Prognosis of liver cirrhosis (Child Pugh score)

The Child Pugh score was calculated and the proportions among cirrhotics selected for the study were compared with those among cirrhotics patients with AKI. The result is presented in Table 6.

In the present study, multivariate analysis could not be performed due to the small sample size.

Table 5: Relationship between AKI and complications, modes of decompensation (CHUD-B/A, Parakou, 2022, N=73).

| | N | AKI | | OR [IC95%] | p |
|----------------------------------|----|-----|-------|-------------------|-------|
| | | n | % | | |
| Ascite | | | | | 0.999 |
| Yes | 54 | 11 | 20.4 | 1.36 [0.34-5.53] | |
| No | 19 | 3 | 15.8 | 1 | |
| Gastrointestinal bleeding | | | | | 0.360 |
| Yes | 9 | 3 | 33.3 | 2.41 [0.52-11.13] | |
| No | 64 | 11 | 17.2 | 1 | |
| Hepatic encephalopathy | | | | | 0.006 |
| Yes | 3 | 3 | 100.0 | 6.37 [3.70-10.95] | |
| No | 70 | 11 | 15.7 | 1 | |
| Hepatocellular carcinoma | | | | | 0.134 |
| Yes | 30 | 3 | 10.0 | 0.32 [0.08-1.28] | |
| No | 43 | 11 | 25.6 | 1 | |
| Hydrothorax | | | | | 0.124 |
| Yes | 7 | 3 | 42.9 | 3.75 [0.73-19.16] | |
| No | 66 | 11 | 16.7 | 1 | |

Table 6: Relationship between AKI and the prognosis of cirrhosis (CHUD-B/A, Parakou, 2022, n=73).

| | N | AKI | | OR [IC95%] | p |
|------------------|----|-----|------|------------------|-------|
| | | n | % | | |
| Prognosis | | | | | 0.031 |
| Child Pugh A | 13 | 0 | 0.0 | - | |
| Child Pugh B | 33 | 5 | 15.2 | 1 | |
| Child Pugh C | 27 | 9 | 33.3 | 2.80 [0.81-9.70] | |

Discussion

Limitations

This study has the merit of addressing a question that has been little studied nationally and in Africa. One of the weaknesses of this study is the small size of the sample, which can be explained by the length of the data collection period (4 months). However, the statistical tests are valid. The study has certain limitations, in particular those relating to the source of some of the data collected through patient self-reporting and the inability of some patients to undergo the necessary biological and imaging tests. The study was not funded. It was a cross-sectional study. A longitudinal study would have enabled us to identify the evolution of acute kidney injury in cirrhotic patients.

Nevertheless, this study remains valid and constitutes a reference in the field to serve as a basis for more in-depth studies and better management of cirrhotic patients.

Comparison of results with those of other authors

AKI is a complication that worsens the vital prognosis of cirrhotic patients. Its frequency in cirrhotics is differently appreciated depending on the region where the study was carried out.

In the present study (19.2%) is close to the frequency reported by Choi et al.⁵ in Korea and Garcia-Tsao et al.⁷ in Guadeloupe who both found a frequency of 19%. Angeli et al.¹² in 2014 in Spain also found a frequency of 19.2%. At the Lomé University Hospital Campus in Togo, a country bordering Benin, Bouglouga et al.¹³ found a lower frequency of 10.4%. On the other hand, many studies carried out in different regions have reported frequencies higher than ours. This was Pan et al.⁶ in Taiwan in 2016, by Huelin et al.¹⁴ in 2017 in Italy and Spain and Jaques et al.¹⁵ in 2018 in Switzerland who found frequencies of 22.83%, 53% and 52.3% respectively.

The mean age of cirrhotic patients with AKI in the present study, 48.6 ± 16.9 years, is similar to those found by Cholongitas et al.¹⁶ in 2009 in the United Kingdom and Prakash et al.¹⁷ in India in 2011 in their work which were 49.3 years and 48.5 years respectively. In other studies the average ages were higher as in those of Tandon et al.¹⁸ in 2016 in Canada, by du Cheyron et al.¹⁹ in 2005 in France and Zhou et al.²⁰ in China in 2017 who reported average ages of 60.4 years, 56.4 years and 55.7 years respectively.

In the present study, the male gender was the most represented (92%) in accordance with the literature; thus, Jindal et al.²¹ in 2015 in India and Huelin et al.¹⁴ in 2017 in Italy and Spain, also found a male predominance (85.5% and 67% respectively).

In this study, the most common cause of cirrhosis in patients with AKI was viral hepatitis B (57.1%), as was the case in other cirrhotics patients as well. The study taking place in an area where viral hepatitis is highly endemic could explain this. However, none of the etiologies found in the present study were statistically associated with the occurrence of AKI.

Among the complications and modes of decompensation determined in the present study, only hepatic encephalopathy was statistically associated with the occurrence of AKI (p -value=0.006). Belcher et al.³ in 2011 in the United States and Angeli et al.¹² in 2014 in Spain found the same association (p -value=0.02 and p -value=0.01). Ascites was the most frequently observed mode of decompensation in cirrhotic patients but was not a factor associated with the occurrence of AKI in the present study.

Class C of the Child-Pugh score was the most represented in cirrhotics patients with AKI in this study with a frequency of 64%. This result is consistent with that of Choi et al.²² in Korea in 2014 who also found a predominance of class C of the Child-Pugh score with a frequency of 31.7%. Membership in class C of the Child-Pugh score was statistically associated with the presence of acute kidney injury in cirrhotics (p =0.031). Angeli et al.¹² in 2014 and Khatua et al.²³ also found an association between the

Child-Pugh score and the presence of acute kidney injury in cirrhotics (p -value=0.0001). Child-Pugh stage C reflects an advanced stage of cirrhosis at the time of diagnosis. At this stage the prognosis for the disease becomes darker. The occurrence of acute kidney injury further darkens the prognosis.

Conclusion

Acute kidney injury is common in cirrhotics patients. The occurrence of AKI depends on severe complications. It is necessary to act on the factors in order to prevent acute kidney injury in cirrhotics and therefore to improve the survival of these patients.

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