

## Dysfunctioning of Kidney as Utility or Futility to Define Acute or Chronic Liver Failure

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### Abstract:

**Background:** Acute on chronic liver failure (ACLF) is a relatively new disease entity, evolving over from last 2 decades. ACLF disease process has multiple definitions, but till now no one is universally accepted. Definition of ACLF by European Association for Study of the Liver (EASL) is widely accepted, which defines ACLF grade 1 as either kidney failure or kidney dysfunction as must criteria. So, validation of fact that patient of ACLF in grade 1 may not necessarily to present with kidney dysfunction/failure is compared in our study.

**Materials and Methods:** In this prospective observational study, from September 2019 to August 2020, in which 46 patients of ACLF were included in study as per definition by "The Asian Pacific Association for the Study of the Liver" (APASL).

All patients included in study were assessed for kidney functioning for conclusion of kidney failure or dysfunction associated with ACLF.

**Results:** Majority of ACLF patients included in study does not have kidney dysfunction or kidney failure.

**Conclusion:** Kidney dysfunctioning may not be associated with ACLF. So kidney failure/dysfunctioning not the characteristic feature of ACLF. Kidney failure is not the utility to define ACLF.

**Key Word:** ACLF, kidney dysfunctioning, kidney failure, EASL ACLF grade

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### I. Introduction

Acute-on-chronic liver failure (ACLF) is acute deterioration of liver functioning in patients with chronic liver disease. Prevalence of ACLF is not clear, due to different types of definitions and diagnosis criteria. Nevertheless, based on hospital registries it is reasonable to estimate that ACLF is present in between 24% and 40% of patients with cirrhosis admitted to the hospital.<sup>[1][2][3]</sup>

Widely accepted definition for ACLF in different parts of world is:

European Association for Study of the Liver (EASL): "An acute deterioration of pre-existing chronic liver disease, usually related to a precipitating event and associated with increased mortality at 12 weeks due to multisystem organ failure".<sup>1</sup> ACLF Grading by EASL:

Grade 1: Single organ failure as kidney or

Single organ failure other than kidney, but serum creatinine level of must be 1.5 to 1.9 mg/dL

Grade 2: Two organs failure.

Grade 3: Three or more organs failure.

The major deficiency of the EASL definition is that, criteria for liver dysfunctioning in missing and to define grade I ACLF patient must have kidney failure or dysfunctioning (serum creatinine level of must be 1.5 to 1.9 mg/dL).<sup>[4]</sup>

### AIMS AND OBJECTIVES :

To study the involvement of kidney as dysfunction or failure in patients of ACLF and evaluate the necessity of kidney dysfunctioning or failure to define the disease of ACLF.

### II. Material And Methods

This prospective observational study was carried out in patients admitted to department of General Medicine and Gastroenterology department at Pradyumna Bal Memorial Hospital, KIMS, Bhubaneswar, during the period from September 2019 to August 2020. During study 49 consecutive patients diagnosed as ACLF as per APASL criteria<sup>[5]</sup> were enrolled in study. Out of which, 3 of these patients were excluded due to age < 18 year. So, finally 43 patients were included in the study. Informed consent was taken from all the patients. All

patient were investigated with liver function test, PT- INR and serum creatinine. There findings were recorded in study Performa.

**Study Design:** Prospective observational study.

**Study Duration:** September 2019 to August 2020.

**Sample Size:** 46 patients admitted under medicine and gastroenterology department.

**Subjects:** The study population were diagnosed cases of ACLF admitted under General Medicine and Gastroenterology department as per APASL definition.

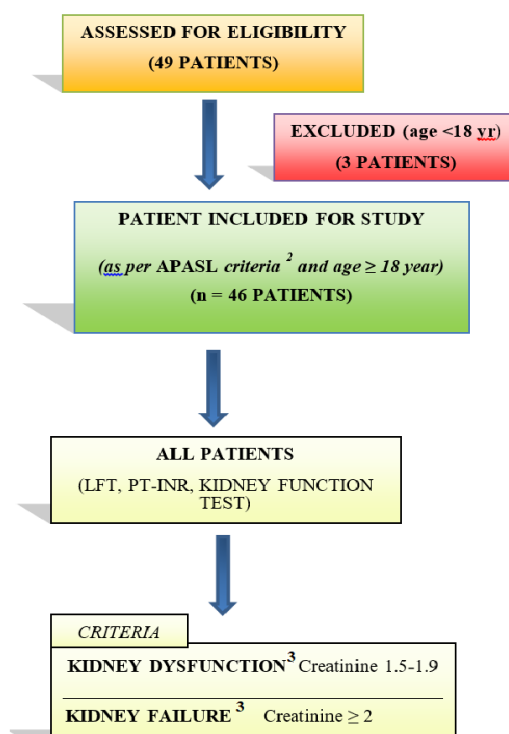
ACLF is defined by Asian Pacific Association for Study of Liver (APASL) as “an acute hepatic insult manifesting as jaundice (total bilirubin  $\geq 5$  mg/dl) and coagulopathy (INR  $\geq 1.5$ ), complicated within four weeks by ascites and/or encephalopathy in a patient with chronic liver disease”.<sup>[5]</sup>

**Inclusion criteria:**

- A) Age 18 years or more
- B) Serum total bilirubin  $\geq 5$  mg/dL (as per consensus recommendations of APASL)
- C) INR  $\geq 1.5$  (as per consensus recommendations of the APASL)
- D) Informed consent

**Exclusion criteria:**

- A) Age less than 18 year
- B) Patients with previous kidney disease
- C) Patients with previous diabetes.



**Figure 1 CONSORT FLOW DIAGRAM**

**Procedure Methodology:**

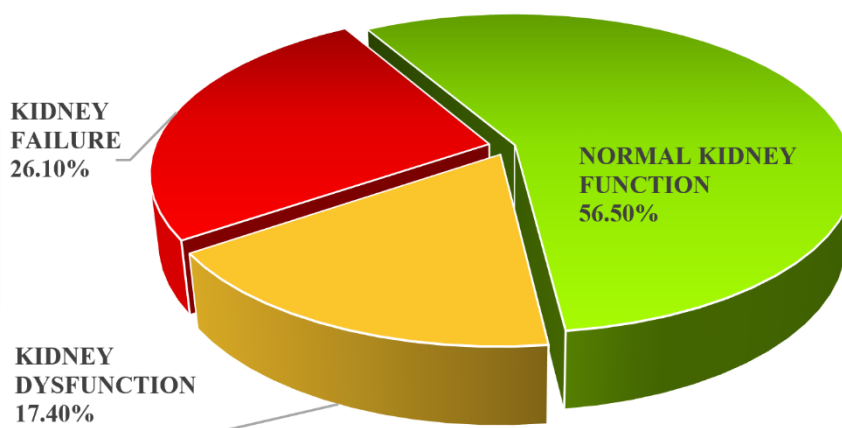
Patients included in study have given written informed consent for participation. Patients were diagnosed with ACLF as per APASL definition of ACLF.<sup>[5]</sup> All patients included in study were investigated for kidney functioning by kidney function test on day of admission.

Patients were categorized into three group as normal kidney functioning, kidney dysfunctioning and kidney failure. The diagnosis criteria used for kidney dysfunctioning was based on serum creatinine level 1.5 mg/dL to 1.9 mg/dL and diagnosis criteria for kidney failure was based on serum creatinine level  $\geq 2$  mg/dL as per renal failure criteria of the EASL-CLIF.<sup>[6]</sup>

The incidence of kidney dysfunction and kidney failure associated with ACLF was assessed to conclude that alternation in kidney functioning for defining the ACLF as grade 1 is necessary or not.

### III. Observations and Results

Out of 46 patients of ACLF included in study, twenty six patients (56.50%) had serum creatinine less than 1.5 mg/dL, eight patients (17.40%) of ACLF had serum creatinine between 1.5 mg/dL to 1.9 mg/dL and twelve patients (26.10%) had serum creatinine  $\geq 2$  mg/dL. Majority of ACLF patients, twenty six (56.50%) out of 46 patients has no kidney dysfunction. ACLF patients with associated altered kidney functioning include dysfunction and failure contributes were observed in twenty patient (43.50%).



*Figure 2: Kidney dysfunctioning and failure in patients of ACLF*

### IV. Discussion

In our study, association of kidney dysfunctioning (with serum creatinine between 1.5 mg/dL to 1.9 mg/dL) with ACLF, accounts for 17.40% of patients only. Patients of ACLF associated with kidney failure, having serum creatinine  $\geq 2$  mg/dL accounts for 26.10%. So alternation in kidney functioning including dysfunction and failure, associated with ACLF was seen in less than the half number of patients.

In our study, majority of patients of ACLF (56.50%) does not have kidney dysfunctioning or kidney failure. So, our study does not support the EASL criteria for definition of ACLF grade I for having either single organ failure as kidney or any other organ failure along with kidney dysfunctioning.



*Figure 3: Incidence of normal kidney functioning and altered functioning in ACLF patients (diagnosed by APASL definition).*

## V. Conclusion

Kidney dysfunctioning/failure may not be associated with ACLF. Loss of kidney function may be a sequelae of the disease, but not the characteristic feature of ACLF. Conclusion of the study is that the kidney dysfunctioning or failure should not be used as must criteria for defining ACLF grade 1, otherwise it will exclude many patients who actually have the disease. Kidney failure is not the utility to define ACLF.

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