JMCJMS

DOI: https://doi.org/10.3126/jmcjms.v14i02.98083

ISSN: 2091-2242
eISSN: 2091-2358

OPEN ACCESS

Original Research

Patterns and Outcomes of Hepatic Dysfunction among Intensive Care Unit Patients: A Prospective Observational Study

Niraj Kumar Keyal[1*], Alok Kumar Singh[2], Jeetendra Kumar Mishra[3], Achutanand Lal Karn[3], Gaurav Gupta[4], Aananda Bhatta[5], Shishir Saurabh[5]

[1]Department of General Practice & Emergency Medicine-Critical Care Medicine Unit, National Medical College, Birgunj, Nepal
[2]Department of Internal Medicine, National Medical College, Birgunj, Nepal
[3]Department of Cardiology, National Medical College, Birgunj, Nepal
[4] Department of Orthopaedics, National Medical College, Birgunj, Nepal
[5] Department of General Practice and Emergency Medicine, National Medical College, Birgunj, Nepal

Correspondence to:
Dr Niraj Kumar Keyal
National Medical College, Birgunj, Nepal
Email: nirajkumarkeyal@gmail.com

Received: 29 March 2026
Revised: 22 July 2026
Accepted: 25 July 2026

Citation:
Keyal NK, Singh AK, Mishra JK, et al. Patterns and Outcomes of Hepatic Dysfunction among Intensive Care Unit Patients: A Prospective Observational Study. Janaki Med Coll J Med Sci. 2026;14(2):29-37

ABSTRACT:

Background & Objectives: Acute liver dysfunction is a common reason for admission to the intensive care unit. This study was conducted to know the pattern of liver dysfunction and outcome in the semi-closed intensive care unit.

Materials and Methods: This descriptive cross-sectional study was conducted over 2 years in 982 patients aged ≥18 years who were admitted to the mixed intensive care unit of a tertiary care hospital for more than 24 hours with altered liver function tests. The outcomes of the patients were defined as being shifted to the ward, expired or left against medical advice. All data were transferred to an Excel sheet and to a statistical package for the social sciences version-20.

Results: Among 982 patients, 658(67%) were males and 324(33%) were females. All 982(100%) patients were community-acquired, and the majority, 968(98.5%), were admitted

from the emergency having medical reasons, 962(98%) as a cause of acute liver dysfunction. The mean age, APACHE II, SOFA, MELD score, and duration of illness of the patients were 52.59±17.65 years, 4.45±7.4, 10.84± 6.84, 11.76± 7.91 and 2.5±1.63 days. 441(44.9%) developed a mixed type of acute liver dysfunction. Only 74(7.5%) cases underwent mechanical ventilation. 762(77.5%) patients were shifted to ward and 132(13.5%) expired. The mean length of stay and duration of mechanical ventilation were 3.66 ±1.78 and 2.1±0.94 days, respectively.

Conclusions: Medical causes (mostly Infective) were the most common cause of ICU admissions in patients who had liver dysfunction. Mixed type of liver dysfunction was more common in patients who developed acute liver dysfunction. The burden of acute liver dysfunction in critically ill patients admitted to our ICU is high.

Keywords: Cholestasis; Intensive Care Units; Liver failure.

INTRODUCTION

The liver plays a key role in the synthesis of various types of proteins, bile, urea, gluconeogenesis, metabolism of toxins and drugs, and in modulation of immunity [1]. Liver dysfunction is more common than in other organs in patients admitted to the intensive care units. [2,3]. The liver is at risk of injury due to polypharmacy, critical illness, older age and comorbid conditions [4,5]. These patients may or may not have pre-existing liver disease or have an acute primary liver injury. It is always challenging to identify hepatic dysfunction due to a lack of specific laboratory investigations. Liver dysfunction occurs in 13-85.2% of patients admitted to the Intensive Care Unit (ICU) [1-6,11]. It is one of the major causes of increased mortality, length of stay and increased days of mechanical ventilation in the ICU [6,7].

A variation in the cause, incidence, prevalence, and outcome of hepatic dysfunction has been reported globally [8-17]. There are limited studies that include all groups of patients under different medical and surgical specialities on the epidemiology of hepatic dysfunction in the ICU. This study was conducted to know the prevalence and outcome of hepatic dysfunction in patients admitted to the level III mixed intensive care unit of a medical college.

MATERIALS AND METHODS

It was a time-frame-based descriptive cross-sectional study at a level three intensive care unit (based on guidelines of Nepalese Society of Critical Care Medicine) of the National Medical College between 3rd April 2023 and 2nd April 2025. The ethical approval from the Institutional Review Committee was obtained before enrolment. The ethical approval number was F-NMC/645/079-080. All patients ≥18 years admitted to the mixed level III intensive care unit with altered liver function test (LFT) were included in this study after written informed consent was obtained from the patients or surrogate decision-makers.

Altered LFT was defined as a) total bilirubin >2 mg/dL and/or b) Aspartate aminotransferase (AST)/alanine aminotransferase (ALT) >1.5 times the upper limit of normal value and/or c) alkaline phosphatase (ALP) >2 times upper limit of normal value and/or d) International normalized ratio (INR) >1.3 (without anticoagulation) [1].

Patients who were <18 years or those who/ their surrogate decision maker did not give written informed consent, and patients who were on anticoagulants were excluded from this study. The following information was collected from each patient meeting inclusion criteria on the day of study. Age, sex, ethnicity, occupation, duration of illness, speciality, Acute physiology and chronic health evaluation II (APACHE), Sequential organ failure assessment (SOFA), Model for end-stage liver disease (MELD),diagnosis, temperature, symptoms like fever, nausea and vomiting, altered sensorium, shortness of breath, jaundice, bleeding,, hemoglobin, hematocrit, serum sodium, potassium, magnesium, calcium, blood sugar, creatinine, urea, albumin, total bilirubin, direct bilirubin, aspartate aminotransferase(AST), alanine aminotransferase (ALT), alkaline phosphate (ALP), total protein, prothrombin time, international normalized ratio (INR), bicarbonate, $_{P}H$, partial pressure of oxygen(Po_2), partial pressure of carbon dioxide(PCo_2), lactate, urine, examination, viral markers (anti-HAV IgM, anti-HEV IgM, HBsAg, anti-HCV, HIV), ascitic fluid examination, chest X ray, ultrasound of abdomen and blood culture.

Fever profile (rapid malaria antigen test, leptospirosis IgM antibody, dengue NS1 antigen, IgM antibody, Brucella IgM antibody, Scrub IgM antibody, peripheral smear for malarial parasite) was done wherever required in patients who had a history of fever or developed it. Other information like co-morbidities, causes, types of hepatic dysfunction and requirement of renal replacement therapy were also recorded.

Hepatic dysfunction was defined as derangement of liver function test. [8,9] Hepatic dysfunction was divided into cholestasis, hepatotoxic or mixed types. The criteria for cholestasis were serum bilirubin>2.5mg/dl, an increase in alkaline phosphatase (ALP) greater than 2 times the upper limit of normal (ULN) and/or an alanine aminotransferase (ALT)/ALP ratio of less than 2 and R value <2, Hepatocellular and mixed hepatitis was classified according to R value which was >5 and 2-5 respectively. The R ratio is calculated by the formula R = (ALT value÷ ALT ULN) ÷ (ALP value÷ ALP ULN) [17-19].

Patients were also evaluated for acute liver failure (ALF) and acute on chronic liver failure (ACLF) depending on the presence or absence of preexisting liver disease. Acute liver failure (ALF) was defined as the presence of hepatic encephalopathy, INR>1.5, duration <26 weeks and absence of previous liver injury and was further classified into acute, sub-acute and hyperacute according to the interval between the appearance of jaundice and the onset of hepatic encephalopathy, i.e. 1-4, 5-12 and <1 week, respectively [8,9].

Acute on chronic liver failure (ACLF) was defined as acute deterioration related to a precipitating event from extrahepatic origin or secondary to superimposed liver injury in patients with a preexisting liver disease or chronic liver disease. Extrahepatic failure was defined according to the SOFA score [8,9].

Patients were followed clinically until the patient was discharged, went on leave against medical advice (LAMA) or expired during ICU stay. Similarly, the duration of mechanical ventilation, length of stay in the ICU, requirement of renal replacement therapy, and use of vasopressor in the ICU were recorded at the time of discharge from the ICU. The outcome of the study was discharge,

death or LAMA from the ICU. Although this was a time frame–based prospective observational study, a priori sample size calculation was performed during the study design to determine the minimum number of participants required to achieve adequate precision for the primary study objective. The sample size was calculated using the formula.

$n = Z^2 * pq/e^2$

$= (1.96)^2 * 0.61 * 0.39/(0.03)^2$

$= 951$

Considering a drop-out rate of 3.2%, Sample size is 982.

Where, n= minimum required sample size, Z= 1.96 at 95% Confidence interval (CI), p= prevalence from a previous study, [2] q= 1-p, e= margin of error, 3%. Prevalence is taken from a study by Thomson et al. [2]. Bias was reduced by collecting data from all groups of patients.

During the study period, a total of 2,826 patients were admitted to the intensive care unit (ICU). Of these, 274 patients were aged below 18 years, 10 patients were excluded because their surrogate decision-makers did not provide consent, and 6 patients did not provide consent. Additionally, 1,554 patients did not have acute liver dysfunction and were therefore excluded from the study. Consequently, 982 patients were included in the final analysis.

Data collection was done in a pre-formed sheet. The pre-formed sheet included all physiologic variables and demographic variables. All data were transferred to the Excel sheet and transferred to SPSS-16. The descriptive data are presented as the number and percentage for categorical data and mean ± standard deviation for continuous data according to their distribution.

RESULTS

Table 1 shows the demographic characteristics of the study population. Middle-aged patients were admitted more than younger and older patients. 658(67%) were males and 324(33%) were females. Most of the patients in this study were Hindus and farmers. The minimum, maximum, and mean age of the patients who developed liver dysfunction were 18, 90, and 52.59±17.65 years respectively.

Table 2 shows the clinical characteristics of the study population. The majority of patients at the time of admission had APACHE II of 31-40 and SOFA score of 0-6 and did not require mechanical ventilation. 968(98.5%) were admitted from Emergency, 785(80%) did not require inotropes and 982(100%) had community-acquired liver dysfunction, Medical 962(98%) cause was the most common cause for liver dysfunction. The duration of illness was less than 2 days in 585(59.5%) patients.

Table 3 shows the laboratory parameters of patients that were included in this study. Laboratory parameters showed wide variation among patients with acute liver dysfunction. The mean ALT and AST levels were 111.09±317.37 U/L and 186.60±590.99 U/L, respectively, while the mean serum albumin, bilirubin, and INR were 3.36±0.79 g/dL, 1.68±3.45 mg/dL, and 1.14±0.36, respectively. The mean sodium, creatinine, and lactate levels were 133.26±6.28 mmol/L, 1.62±1.50 mg/dL, and 1.65±1.29 mmol/L, respectively.

Table 1. The demographic characteristics of the study population

Parameters	n (%)	Mean ± SD
Age (Years)		
18-35	176(18)	52.59±17.65 years
36-60	441(45)	
>60	365(37)	
Sex		
Male	658(67)	
Female	324(33)	
Ethnicity		
Hindu	845(86)	
Muslim	137(14)	
Occupation		
Businessman	30(3)	
Farmer	412(42)	
Shopkeeper	240(24)	
Student	9(1)	
Worker	44(5)	
Other	245(25)	

Table 2: Clinical characteristics of the study population

Parameters	n (%)
APACHE II Score at time of admission	
3-10	64(6.5)
11-20	374(38)
21-30	58(6)
31-40	486(49.5)
SOFA Score at time of admission	
0-6	775(79)
7-12	158(16)
13-18	35(3.5)
19-24	14(1.5)
MELD Score at time of admission	
0-9	540(55)
10-19	225(23)
20-29	138(14)
30-39	25(2.5)
42	54(5.5)
Mechanical Ventilation	
Yes	74(7.5)
No	908(92.5)
Source of patients	
Emergency	968(98.5)
Ward	15(1.5)
Inotropes	
Yes	197(20)
No	785(80)
Nature of acute Liver dysfunction	
Community	982(100)
Hospital	0
Cause of acute Liver dysfunction	
Medical	962(98)
Surgical	10(1)
Obstetric	5(0.5)
Trauma	5(0.5)
Duration of illness	
<2	585(59.5)
>2	397(40.5)

(APACHE II: Acute physiology and chronic health evaluation, MELD: Model for End-Stage Liver Disease, SOFA: Sequential organ failure assessment)

Table 3: Laboratory parameters of patients with Acute Liver Dysfunction

Characteristics	Minimum	Maximum	Mean±SD
Haemoglobin, g/dl	1.13	16	11.69±2.51
Packed Cell Volume, %	6.14	54	35±8.64
Sodium (mmol/L)	105	148	133.26±6.28
Potassium (mmol/L)	1.86	7.2	4.11±0.92
Creatinine (mg/dl)	0.48	10.4	1.62±1.50
Urea (mg/dl)	10	260	52.35 ±41.28
Bilirubin (mg/dl)	0.063	40.52	1.68±3.45
Serum Albumin (g/dl)	0.99	6.5	3.36±0.79
ALT (U/L)	1.4	3515.6	111.09±317.37
AST (U/L)	0.366	6881.63	186.60±590.99
Blood sugar, mg/dl	52	440	140.47±70.01
PH	6.8	8	7.35±0.12
Bicarbonate(mEq/L)	4.5	49.7	23.92±6.84
PCO_2(mmHg)	12.2	120	40.17±16.44
PO_2(mmHg)	21	310	114.25±55.04
Lactate(mmol/L)	0.3	10.9	1.65±1.29
CBC(/mm^3)	1400	45000	13406.48±6729.87
Platelets (/mm^3)	10100	520000	192836.5±96970.99
Bilirubin/Albumin Ratio	0.4	8.13	0.60±0.94
Direct Bilirubin, (mg/dL)	0.03	35	1.21±3.09
Alkaline Phosphatae(IU/L)	39	670	114.68±58.27
Total Protein (gm/dL)	1.81	8.3	5.08±1.48
PT, sec	10	28	14.43±1.96
INR	1	4	1.14±0.36

(ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CBC: Complete blood count, dL: Deciliter, gm: Gram, INR: International normalized ratio, L: Liter, mEq: Milliequivalent, mg: Milligram, mmHg: Millimeter of mercury, mmol: Millimol, PCO_2: Partial pressure of Carbondioxide, PO_2: Partial pressure of Oxygen, PT: Prothrombin time, sec: Seconds, U: Unit)

Table 4: Duration of Illness and Severity Scores among Patients with Acute Liver Dysfunction

Clinical parameters	Minimum	Maximum	Mean ± SD
Duration of illness(days)	1	13	2.50 ± 1.63
APACHE II score	0	23	4.45 ± 7.40
SOFA score	0	35	10.84 ± 6.84
MELD score	1	39	11.76 ± 7.91

Table 4 indicates that among the patients who developed acute liver dysfunction, the duration of illness and severity scores showed considerable variation. The duration of illness ranged from 1 to 13 days, with a mean of 2.50 ± 1.63 days. The corresponding ranges and mean ± SD values for the APACHE II, SOFA, and MELD scores were 0–23 (4.45 ± 7.40), 0–35 (10.84 ± 6.84), and 1–39 (11.76 ± 7.91), respectively.

Table 5 shows the classification of acute liver dysfunction with speciality. The majority of patients were from the medical 495(50.5%) speciality. 441(44.9%) of patients developed mixed type of liver dysfunction.

Table 6 shows the management and outcome of acute liver dysfunction. All patients were managed conservatively 851(96%), and 762(77.5%) were shifted to the ward. Among the patients who developed acute liver dysfunction, the ICU stay ranged from 1 to 12 days, with a mean duration of 3.66 ± 1.78 days. The duration of mechanical ventilation ranged from 1 to 3 days, with a mean duration of 2.10 ± 0.94 days.

Table 5: The Classification of acute liver dysfunction with speciality

Parameters	n(%)
Specialty	
Medical	495(50.5)
Surgical	15(1.5)
Obstetric	10(1)
Neurosurgery	142(14.5)
Orthopedics	30(3)
Psychiatry	10(1)
Cardiology	280(28.5)
Type of Acute Liver dysfunction	
Cholestasis	290(29.53)
Hepatotoxic	251(25.56)
Mixed	441(44.9)
Acute liver failure	25(2.54%)
Acute on chronic liver failure	80(8.14%)

Table 6: Management and outcome of Acute Liver dysfunction

Parameters	n (%)
Management	
Conservative	982(100%)
Liver transplantation	0(0%)
Outcome	
Shift to ward	762(77.5)
LAMA	88(9)
Expired	132(13.5)

(LAMA: Leave Against Medical Advice)

DISCUSSION

In our study, the prevalence of acute liver dysfunction was found to be 45.014%, while in other studies it ranges from 2.9 % to 55.54%. [1,3,4,6,12,15,16]. These differences may be due to differences in the study population and the primary disease-causing acute liver dysfunction. The mean age of the study population in our study was 52.59 years, which is similar to the study by Tanaka et al. [6], while in the study by Patel et al [1] it was 37 years. Males were more common in our study, which is similar to other studies [4,6,12], while in a study by Lee SY [15] female were most common. These differences may be due to differences in the study populations.

The mean MELD score in our study was 11.76, while in a study by Patel et al [1] it was 8.97. This difference may be because we have included all groups of patients, while only medical patients were included by Patel et al. [1] In our study, 7.5% of patients underwent mechanical ventilation, while in the study by Patel et al [1] it was 43.1%. This difference may be due to differences in the study population, primary disease, and management of patients by a full-time intensivist.

In our study, 20% of patients required inotropes, while in a study by Patel et al [1] it was 41.4%. These differences may be due to differences in the group of patients, delayed presentation, primary disease, and management of patients by a full-time intensivist. This study has shown that medical reasons are a common cause of liver dysfunction which is similar to a study by Patel et al. [1] and Kopczynska et al. [12], while in a study by Shrestha et al. [4] surgical cause was the most common. This may be due to differences in the group of patients that are studied in different studies and patient care that is provided in different hospitals.

Acute on chronic liver failure was present in 8.14% of patients in our study, while in a study by Patel et al. [1] and Shrestha et al. [4] it was 85.2% and 29%, respectively. These differences may be due to differences in the study population, and medical patients are more predisposed to liver failure than surgical patients. This study has shown that mixed types of liver were present in 44.9% of patients while a study by Tanaka S [6] cholestasis was the most common. These differences may be due to differences in the study population, and the type of liver dysfunction depends on the primary disease.

The mortality in our study was 13.5%, while in other studies it varied from 26% to 56.4%. [1,4,8-16]. These differences may be because all groups of patients were included in our study, and medical patients are more predisposed to death than surgical patients. This study has shown that 77.5% of patients were shifted to the ward, while in a study by Patel et al. [1] it was 26.2%. These differences may be because all groups of patients were included in our study, medical patients are more predisposed to death than surgical patients, and management of patients by a full-time intensivist in a semi-closed ICU.

The present study has a few limitations. First, it was a study done in a single ICU setting, which may not represent patients who develop liver dysfunction in other ICUs around the country. Second, these patients represent different types of liver dysfunction and need further follow-up for potential recovery or death. Also, being a purely descriptive study, inferential statistics were not applied. Hence, studies with longer duration of follow-up and inferential statistics would be recommended for better representation of the outcome and risk factors associated with liver dysfunction in the ICU.

CONCLUSIONS

Medical reason was the most common cause of ICU admissions in patients who developed liver dysfunction. Mixed type of liver dysfunction was more common in patients who developed acute liver dysfunction. The burden of acute liver dysfunction in critically ill patients admitted to our ICU is high.

ACKNOWLEDGEMENT

We are thankful to National Medical College, Birgunj, Nepal for all the logistic support during this study.

AUTHOR'S CONTRIBUTION:

Conceptualization, data collection, formal analysis, writing, original draft preparation- **NKK**; Methodology and writing review and editing- **AKS**; Investigation, data collection, and writing, review and editing- **JKM, ALK, AB, GG**, **SS**. All authors have read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

CONFLICT OF INTEREST: None declared

FUNDING: Self

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