



## A Study on Acid Base Disorders in Acute Hepatic Failure

Authors

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### Abstract

**Introduction:** *Alongside the kidneys and lungs, the liver has been recognized as an important regulator of acid-base homeostasis. The most common acid-base disorder with liver disorder is respiratory alkalosis. However, metabolic alkalosis, respiratory acidosis, metabolic acidosis all can be seen.*

**Objectives:** *To determine whether the acid-base state is destabilized in critically ill patients with cirrhosis and whether this is associated with mortality.*

**Materials and Methods:** *A prospective analytical study from July 2016 to July 2017 was done including 50 patients admitted in medical intensive care unit in Darbhanga Medical College and Hospital with hepatic failure. Patients with history of concomitant other drug or alcohol consumption, known history of cardiac, respiratory, renal disorder, any neurological disease, infectious disease, Known cirrhosis were excluded. Clinical, demographic, biochemical data were collected. Patients were followed till intensive care unit stay or death. All data were analysed using appropriate statistical test.*

**Results:** *Abnormality in blood pH was noted in 35(70%) patients. Alkalosis was commonest finding (40%) followed by acidosis (30%). Blood lactate was significantly higher and blood pH was significantly lower in non survivors in comparison to survivors.*

**Conclusion:** *Various complex metabolic acid-base disorders may occur with liver dysfunction. When patients with liver cirrhosis become critically ill metabolic acidosis may ensue. Thus, further research regarding pathophysiology and prognostic importance of various acid-base disturbances in patients with liver disease is necessary.*

### Introduction

Alongside the kidneys and lungs, the liver has been recognized as an important regulator of acid-base homeostasis. In patients with well-compensated cirrhosis, the abnormality may not be evident clinically. In the setting of acute derangement of hepatic function, compensatory mechanisms often fail to maintain equilibrium resulting in detectable acid base and electrolytes abnormality.

A number of factors contribute to acid-base imbalance in liver disease: impaired gluconeogenesis reduces the metabolism of lactic acid and leads to metabolic acidosis, abnormalities in the efficiency of the urea cycle can cause a reduction in bicarbonate use, and a reduction in protein synthesis and primarily albumin in the setting of liver disease all contribute to changes in acid-base balance.

Respiratory alkalosis is probably the most common acid base derangement found in patients with liver disease. Proposed causative factors for respiratory alkalosis include an increase in blood ammonia and hyperventilation. Hypoxemia in the setting of massive ascites, anemia, hepatopulmonary syndrome, hepatic hydrothorax, or bacterial infection also often play contributory role. the exact cause of hyperventilation remains obscure, but increased level of progesterone in liver failure seems to be an explanation. Metabolic alkalosis often occurs from treatment with loop diuretics resulting in increased distal secretion of H<sup>+</sup> ion. A study by Haussinger et al suggested that metabolic alkalosis occurs as a result of abnormal hepatic bicarbonate disposal and urea synthesis in cirrhosis. Metabolic alkalosis also exacerbates hepatic encephalopathy promoting conversion of ammonium to lipid soluble ammonia which diffuses to brain easily.

Metabolic acidosis develops with progressively severe liver disease. Increased anion gap metabolic acidosis may be seen in 10% to 20% of patients with chronic liver disease.

Hyperchloraemic acidosis, characterized by replacement of bicarbonate with chloride often occurs as a compensatory mechanism to chronic respiratory alkalosis. HCO<sub>3</sub> loss and Cl retention also cause hyperchloraemic acidosis, especially in patients on lactulose therapy or in patients with alcoholic diarrhoea. Distal renal tubular acidosis (RTA Type D) may happen in patients with cholestatic disorders, such as primary biliary cholangitis (PBC), Wilson's disease, amyloidosis and glycogen storage disorders. Spironolactone therapy may contribute in occurrence of renal tubular acidosis type IV. critically ill patients with hepatic failure often show net metabolic acidosis, owing to unmeasured anions, lactic acidosis and mild dilutional acidosis. Complex disturbances of lactate metabolism can be found in acute and chronic liver disease. While the healthy liver has a huge functional reserve of metabolising lactate, lactate clearance is impaired in chronic liver diseases because of a decrease in the functional

hepatocyte mass. A dysfunctional liver may even become a net lactate producer during period of acute illness. Splanchnic area is considered to be a major source of lactate production in patients with sepsis and acute liver dysfunction. Defects in hepatic pyruvate metabolism with a reduction in hepatic gluconeogenesis also play a role.

### Objectives

The purpose of this study was to determine whether the acid-base state is destabilized in critically ill patients with cirrhosis and whether this is associated with mortality.

### Materials and Methods

**Setting of Study:** Darbhanga Medical of Medicine, Laheriasarai, Bihar

**Design:** Prospective analytical study.

**Ethical Committee Permission:** Taken

**Period of Study:** From July 2016 to July 2017 patients were enrolled and each of them was followed upto intensive care unit staying or death.

**Sample Size:** 50

**Inclusion Criteria:** Patients diagnosed with acute hepatic failure defined as

Occurrence of coagulopathy (INR > 1.5)

Onset of encephalopathy

Within 26 weeks of acute liver insult due to any etiology in absence of any preexisting liver disease.

Patients with pre-existing Wilson disease, vertically acquired HBV or autoimmune hepatitis were also included in the study if their disease has only been recognised for < 26 weeks.

**Exclusion Criteria:** History of concomitant other drug or alcohol consumption, known history of cardiac, respiratory, renal disorder, any neurological disease, infectious disease, Known cirrhosis.

**Study Protocol:** All patients were seen on admission by study doctors. Data were collected prospectively by the study doctors, who recorded examination findings, including pulse, blood pressure, pupil size, and Glasgow coma score (GCS), cardio respiratory findings. This

examination took place during initial resuscitation by a different set of doctors. All patients underwent biochemical investigation including Blood Glucose, LFT, KFT, PT (INR), serum electrolytes. Arterial blood was collected by direct puncture from femoral artery, Blood gas analysis and lactate estimation was done. All patients received standard medical treatment under the direction of the hospitals' consultant physicians.

**Statistical Analysis**

The statistical software SPSS version 20 has been used for analysis.

An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it has been considered as significant.

**Results**

Total 50 patients were included in the study.

A low paCO<sub>2</sub> was the commonest abnormality found in 38(76%) patients. Among them 15 (39.47%) had blood pH in alkine range (>7.44), 12 (31.57%) had blood pH in acidic range (<7.34), 11 (28.94%) had blood pH in normal range.

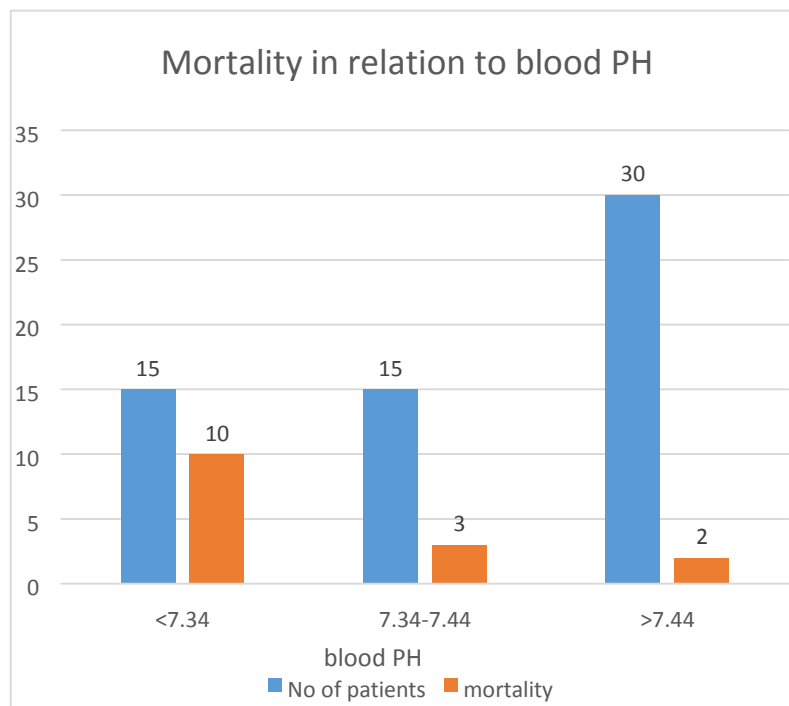
Blood lactate level ranged between 1.04 to 15.54 mmol/L with a mean of 5.45+/4.27.

Mortality was 30%.

Higher mortality was noted in patients with acidosis.

**Table 1:** Mortality in relation to blood PH

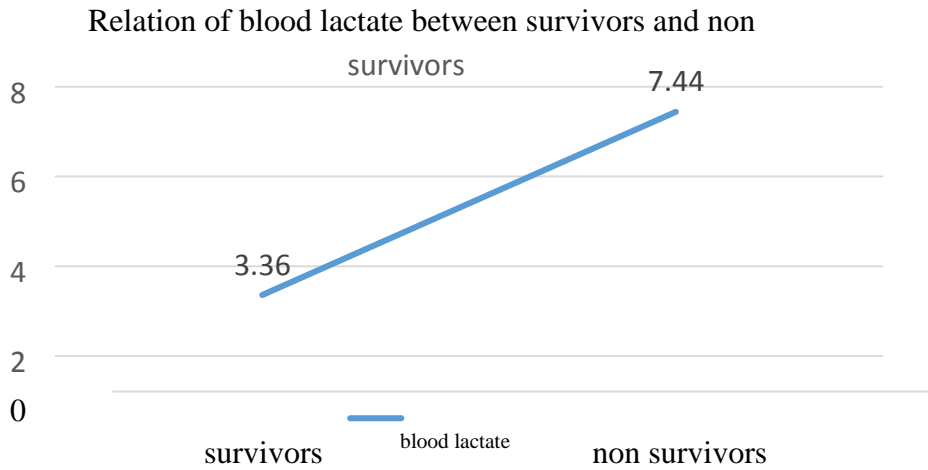
BLOOD PH	NO. OF PATIENTS(n=50)	MORTALITY (n=15)	PROBABILITY
<7.34	15(30%)	10(66.66%)	P value=0.0085 (significant)
7.34-7.44	15(30%)	3(20%)	
>7.44	30(40%)	2(10%)	



**Figure 1**

**Table 2:** Comparison of mean blood lactate between survivors and non survivors

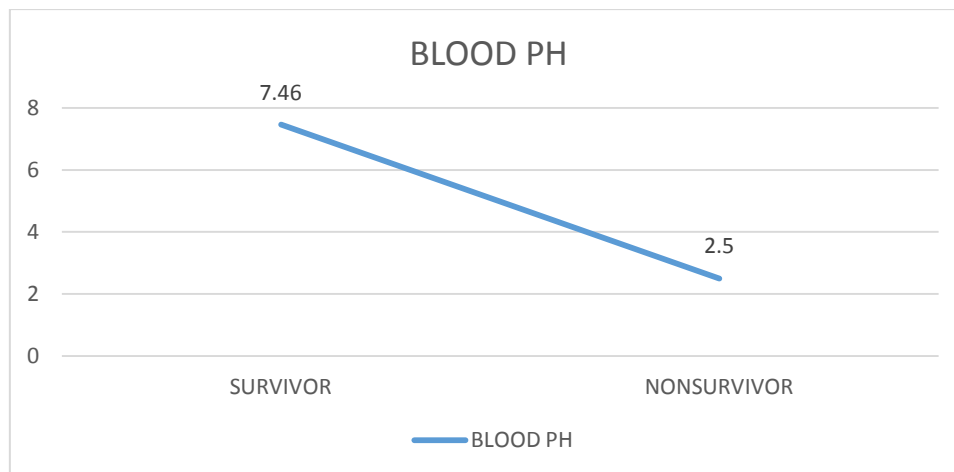
	Survivors	Non survivors	Probability
Blood lactate	3.36+/- 1.81	7.44 +/- 3.14	P =<0.001 (significant)



**Figure 2**

**Table 3:** Relation of mean blood PH between survivors and non survivors

	Survivors	Non survivors	Probability
Blood PH	7.46+/-0.12	7.27+/-0.23	P =<0.01 (significant)



**Figure 3**

**Discussion**

Acid base disorders are well recognized in hepatic coma due to chronic liver disease. In fulminant liver failure hyperventilation and both respiratory and metabolic alkalosis have been reported. Lactic acidosis has been recognized in both acute and chronic liver disease. Lactic acidosis has been

reported in fulminant hepatic failure by Smadja et al (1972); most of their patients were in peripheral circulatory failure. Liver dysfunction was thought to be of etiological importance in 18 of the 71 cases of lactic acidosis described by Tranquada (1964). A low paCO<sub>2</sub> with alkalemia was most common acid base disorder found in our study

which was similar to finding of Opolon, Hadchouel, Del Corso, And Caroli, (1970) and C.O. Record, R.A. Iles, R.D. Cohen, and Roger Williams(1975).A study by Lustik et al. showed a correlation between increased progesterone and oestradiol levels (caused by impaired hepatic metabolism in advanced liver disease) that may directly stimulate ventilation by the activation of progesterone receptors in the central nervous system leading to hyperventilation. Aspiration of gastric contents and vomiting were supposed to be the principal cause of the metabolic alkalosis in patients described by Opolon et al. Alternative sources of metabolic alkalosis which should be considered are accumulation of bases in the circulation, movement of hydrogen ions into the intracellular space or failure of normal metabolic pumping of hydrogen ions from cells. Patients had net metabolic acidosis owing to unmeasured anions and owing to hyperchloraemic, dilutional and lactic acidosis. Elevation of lactate may be mediated through a pH dependent stimulation of glycolysis, particularly in subjects with respiratory alkalosis. The Healthy liver acts as the main consumer of lactate and contributes to 30–70% of lactate metabolism. Experimental data indicated that liver lactate consumption is directly related to arterial lactate concentrations, rather than liver blood flow. Keto acids are produced in the mitochondria of the liver when carbohydrate or fat is incompletely oxidised. Therefore, the net production of keto acids as well as their urinary excretion is controlled by a feedback mechanism, leading to reduced endogenous acid production if pH decreases and increased keto acid production if pH rises. This up- or down regulation applies both to hepatic ketogenesis and lactate production. Hepatic ketogenesis and its regulation are negligible and do not cause relevant acidosis under normal conditions. However, starvation or massive alcohol consumption can cause ketogenesis with substantial metabolic acidosis. Interestingly, even though patients with acute liver failure show significantly elevated lactate levels, often, no overt acid-base disorder can be

Found probably because of the offsetting hypoalbuminaemia.

### Limitation and Scope for Future Studies

- 1) Cause and type of acidosis or alkalosis was not analysed.
- 2) Difference in anion gap and its effect on outcome was not analysed.
- 3) Urinary PH measurement helps in differential diagnosis of metabolic derangement, which was not considered under analysis.
- 4) Difference in findings according to etiology of liver failure was not analysed.

### Conclusion

Acid-base disorders in the setting of liver disease are frequent and complex; mixed acid-base disturbances are not uncommon in the setting of the underlying disease process and the therapy used to treat it. Different treatment modality may worsen the stability of acid base disorder in this milieu. So vigilance regarding acid base status is important in making of therapeutic decision.

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