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Clinical Implication of Lactate Monitoring in Intensive Care Unit: An Observational Study

(Research Article)

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Abstract

Introduction: *Lactate is common parameter in critically ill patients. It is mainly used to diagnose inadequate tissue oxygenation; other processes are not related to tissue oxygenation may increase lactate level. In critically ill patients increase glycolysis may be an important cause of hyperlactemia. The presence of increase lactate has significant implication for morbidity and mortality. Lactate play important role in early resuscitation. lactate can be measure bedside rapidly.*

Aim: *1) To study the significance of lactate level in critically ill patients.2) to study the role of lactate in early resuscitation.*

Material and Methods: *It is a simple random sampling study of 100 patients admitted to intensive care unit of index hospital from 2014 to 2015. Patients lactate level are studied by arterial blood gas analysis and their correlation with spo_2;PH and Pao_2 and $PaCO_2$ and glucose is studied.*

Result: *lactate level are increased in critically ill patients and it is related to tissue hypoxia and it leads to significant morbidity and mortality.*

Conclusion: *lactate level may be an epiphenomena of severity of disease .clinician can interpret hyperlactemia as warning signal that patients are deteroiting in spite of stable hemodynamic parameters and take as early marker of resuscitatory measure.*

Keywords: *lactate, intensive care unit, resuscitation, prognosis.*

Review

Introduction

Many variables measured in critically ill patients have been used to estimate the severity of disease, prognosis, morbidity, mortality and finally indicate specific treatment and monitor adequacy of treatment. No single parameter measurement can replace all the conditions, but Lactate is related to many physiological metabolic processes, tissue hypoxia and subject to disturbances in different clinical situations. The use of lactate as a clinical prognostic tool was first suggested in 1964 by Broder and Weil when they observed that a lactate excess of > 4 mmol/L was associated with poor outcomes in patients with undifferentiated shock.[1]

Aim of the study

The importance of lactate monitoring in arterial blood gas analysis in critically ill patients.

Objectives of the study

1. Significance of lactate monitoring in critically ill patients.
2. Role of lactate level in resuscitation& management.

Material and Methods

It is a simple observational study of a total of 100 patients admitted to intensive care unit in Index hospital from july 2014 to july 2015.

Lactate levels of these patients were monitored by a simple bed side test i.e arterial blood gas analysis by using ABG Analyzer. The lactate level were taken at the time of admission and monitored for 8 hours and also taken at the time of discharge.

It was found that hyperlacticacidemia found in 64 patients and mortality was found in 36 patients, which is clinically as well as statistically significant.

Mortality is more common in patients with hyperlacticacidemia with lactate level >5 mmol/l i.e 18 out of 36 patients which is 50% and with PH<7.2 in 20 patients out of 64 patients which is 31.25 %.

Statistical Analysis

It is observational study of 100 patients admitted in ICU. Out of 100 patients studied 26 patients were in septic shock and 24 patients were diabetic and 19 patients were COPD ,14 patients were in renal failure,8 patients were in cardiac failure and 5 patients were of chronic liver parenchymal disease and rest classified as others.

Out of which 64 patients were found to have hyperlacticacidemia and they were graded into mild, moderate and severe hyperlacticacidemia. And the lactate level correlation was found with PH, SPO_2, $paCO_2$ and glucose, their correlation tables were made. Out of 64 patients, 21 patients were found to have lactate level more than 5 (i.e in category of moderate and severe hyperlacticacidemia).

Correlation between PH, lactate and SPO_2 are found significant at 0.001 (2-tailed) level. Out of 100 patients, 36 were found to have mortality, among them 18 patients had lactate level(>5 mmol/l), they were in moderate and severe hyperlacticacidemia. Mortality was mainly found in patients with septic shock, DM ,renal failure, acute exacerbation of COPD , respiratory failure ,liver disorders and other causes.The liver is the organ primarily responsible for lactate clearance, and in the presence of significant liver dysfunction lactate clearance may be impaired. 0[2,3] Additionally, studies have shown that the acutely injured liver may itself act as a source of lactate.[4–7]In the absence of thiamine, anaerobic metabolism predominates and lactate production increases.[8]

Patients lactate levels were measured by taking ABG at the time of admission and after 8 hours.It is found that in 43 patients lactate levels were increased after admission and after that patients were managed by the O_2 inhalation, iv fluids, sodium bicarbonates and inotropes as per needed. In patients with severe sepsis or septic shock to determine if impaired lactate clearance could serve as an indicator for use of inotropic support and/or blood transfusion. Specifically, they compared the early goal-directed therapy.[9]

In 38 patients lactate level decreases and patients condition improves &vitals monitored continuously. It is found that although patient hemodynamic parameters were stable, saturation was deranged and on ABG it showed moderate to severe hyperlacticacidemia leading to impaired tissue oxygenation and hypoxia. While the presence of vital sign abnormalities may help to identify shock, their absence does not definitively exclude occult hypoperfusion.[10] Lactate elevation may help identify a patient whose initially normal vital signs may mask ongoing tissue hypoperfusion.[11]

Discussion

The terms lactate and lactic acid are often used interchangeably but lactate (the component measured in blood) is strictly a weak base whereas lactic acid is the corresponding acid. "Lactic acidosis" is often used clinically to describe elevated lactate but should be reserved for cases where there is a corresponding acidosis (pH < 7.35).[36]Lactate is an important metabolite of 2 main energy (ATP) producing processes i.e glycolysis and oxidative phosphorylation(figure1)

Both processes steadily metabolise glucose when the conditions are stable. Pyruvate is a molecule which links both the reactions.

Lactate is produced by most tissues in the human body, with the highest level of production found in muscle.[12,13] Under normal conditions, lactate is rapidly cleared by the liver with a small amount of additional clearance by the kidneys.[12,14] In aerobic conditions, pyruvate is produced via glycolysis and then enters the Krebs cycle, largely bypassing the production of lactate. Under anaerobic conditions, lactate is an end product of glycolysis and feeds into the Cori cycle as a substrate for gluconeogenesis. But in conditions of stress, glycolysis provides energy (ATP) at much faster rate than oxidative phosphorylation, hence it produces more pyruvate which will then accumulate and process will divert toward lactate production.

Lactate is normally metabolized by lactate dehydrogenase (LDH) enzyme. In critical conditions and at the time of cellular stress,large amount of energy is required. Hence lactate acts as critical buffer that accelerates glycolysis.

STEADY STATESTRESSRECOVERY

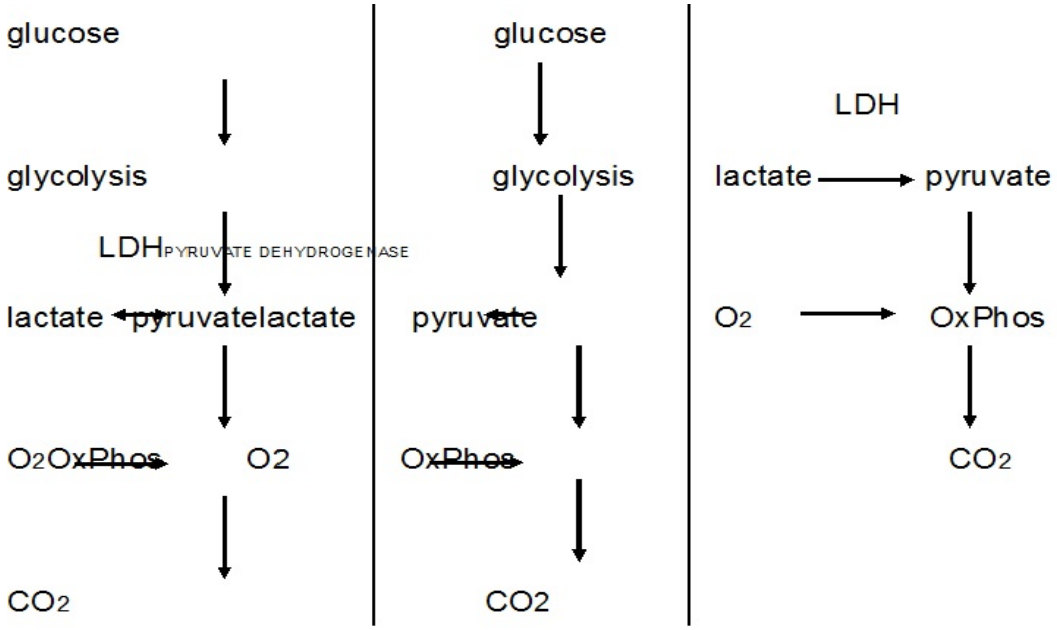


Figure1[35]shows metabolism of glucose in different conditions at cellular level.

Metabolism of glucose during tissue hypoxia results in production of lactate, ATP, water and H+ from hydrolysis of ATP. These H+ in presence O_2 can be used in oxidative phosphorylation and cannot cause acidosis.

Acidosis is dissociation of water to maintain acid-base balance by addition of strong lactate ion to the circulation. The accumulation of lactic acid in the blood is generally associated with metabolic acidosis, increases in the blood lactate concentration may also occur in both metabolic and respiratory alkalosis.[15,16]In these instances, the mechanism of increased lactic acid production has been ascribed to enhanced activity of intracellular enzymes, principally phosphofructokinase, that accelerate lactate production.

Phosphofructokinase is an important regulatory enzyme in the glycolytic pathway, and its activity

is largely controlled by the intracellular pH. As intracellular pH increases with alkalosis, the activity of phosphofructokinase is accelerated, resulting in increased production of lactic acid[15] However the correlation between PH and lactate is significant only at higher level of lactate.The etiology of elevated lactate is perhaps best studied in shock states. Contributing factors appear to include: hypoperfusion due to macro- and/or microcirculatory dysfunction, mitochondrial dysfunction (including potential lack of key enzymatic cofactors) and the presence of a hypermetabolic state, among others.[17-22]

In septic shock:-

A. there is an increase in lactate pyruvate ratio (>20:1)
B. Increases insulin resistance,
C. Decreased lactate clearance,
D. inhibition of pyruvate dehydrogenase enzyme,
E. skeletal and lung tissue will all produce lactate.

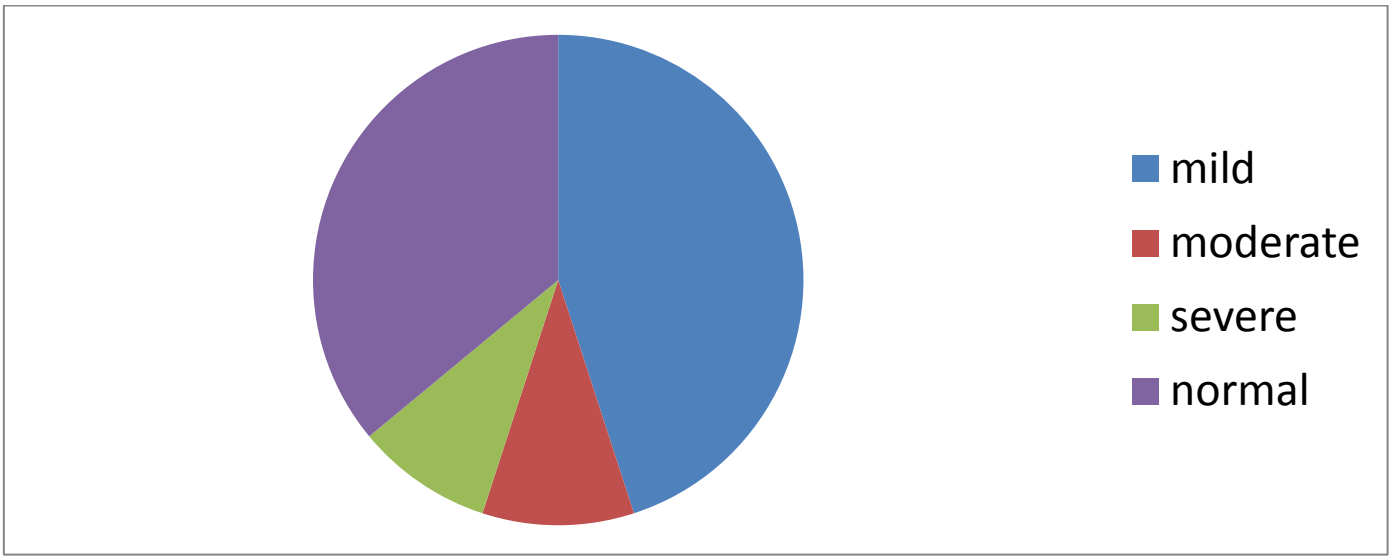
Studies have shown that while anion gap and base excess are associated with lactate, they do not necessarily predict elevated lactate levels accurately.[23,24] There is also impaired lactate clearance in some conditions like liver dysfunction and sepsis after cardiac surgery. Patients are at increased risk of multiple potential causes such as thiamine deficiency or liver dysfunction in septic shock[25], seizures in the setting of alcohol intoxication or drug abuse[26,27] or cyanide/carbon monoxide poisoning in the setting of burns with concurrent smoke inhalation[28]

Frequency table:

TABLE 1: This is table showing frequency cumulative and valid percentage of different categories of hyper lacticacidemia studied in100 patients.

	FREQUENCY	PERCENT	VALID PERCENT	CUMULATIVE PERCENT
MILD	45	45	45.0	45.0
MODERATE	10	10	10.0	55.0
SEVERE	9	9	9.0	100.0
NORMAL	36	36	36.0	91.0
TOTAL	100	100	100.0	

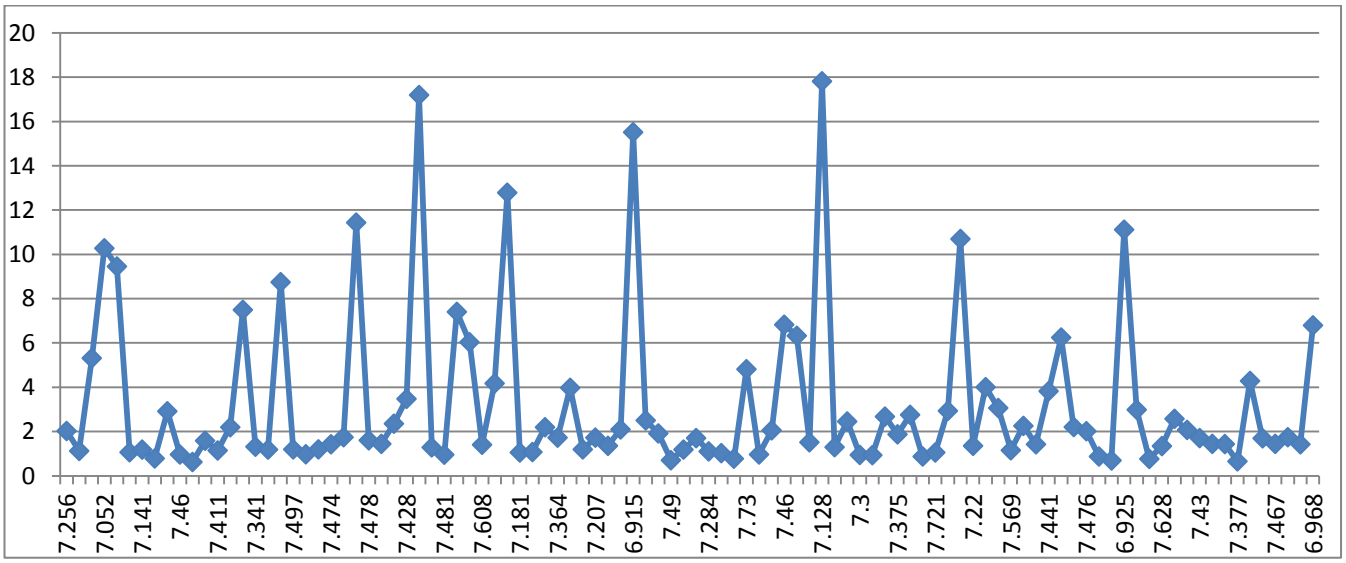
Pie diagram showing hyperlacticacidemia categories:



(Figure-1)

PH and Lactate correlation

Line diagram showing correlation between lactate and PH: only at higher level of lactate PH decreases.
(Figure-2)



Correlation table between PH and lactate (table no 2,3):

Table no 2: showing mean and standard deviation of PH and lactate.

	MEAN	STD DEVIATION	N
PH	7.3735	.18612	100
LACTATE	3.2224	3.61602	100

Table no 3: Correlation is significant at the 0.001 level (2-tailed)

		pH	LACTATE
PH	Pearson Correlation Sig (2-tailed)	1 100	-.400 .000 100
Lactate (0.56-1.39)	Pearson correlation Sig (2-tailed) N	-.410 .000 100	1 100

Correlation table between lactate and SPO_2(table 4,5):

Table no 4: shows mean and standard deviation of lactate and SPO_2

	MEAN	STD DEVIATION	N
LACTATE(0.56-1.39)	3.2224	3.61602	100
SPO_2(90-98)	91.8274	13.64804	100

Table no 5: Correlation Is Significant At 0.01 Level(2-Tailed Significance)

		LACTATE(0.56-1.39)	SPO2(90-98)
LACTATE(0.56-1.39)	PEARSON CORRE-LATION SIG(2-TAILED)	1 100	-.283 .004 100
SPO_2	PEARSON CORRELATION SIG(2-TAILED) N	-.283 0.04 100	1 100

Correlation between lactate, PaO_2 and PCO_2:

Table 6:(shows mean and standard deviation of lactate with PaO2 with high standard deviation of pao2)

	MEAN	STD DEVIATION	N
LACTATE(0.56-1.39)	3.2224	3.61602	100
PO_2	115.9538	80.4622	100

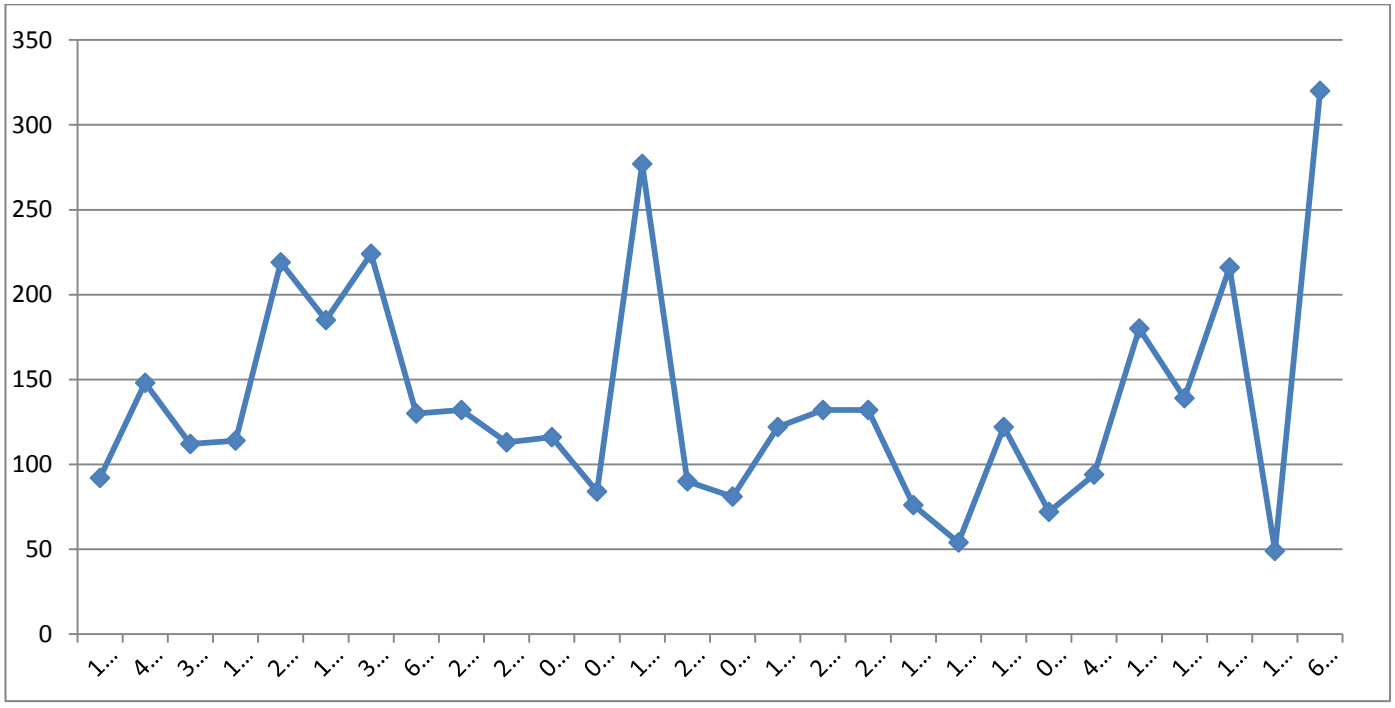
Table no 7: Correlation between lactate,paO_2 and pCO_2 is found significant because of unnecessary supplementation of oxygen in intensive care and this leads to higher standard deviation.

		LACTATE(0.56-1.39)	PaO_2(83-102)glucose
Lactate(0.56-1.39)	Pearson correlation sig (2 tailed) N	1 100	.132 .192 100
PO_2	Pearson correlation sig(2-tailed) N	.132 .192 100	1 100

Correlation between lactate and glucose

Correlation between the lactate and glucose is significant at the time of cellular stress because of accelerated glycolysis.

Lactate should be corrected before putting patient on insulin therapy or oral hypoglycemic drugs.[29]Today, metformin is the only biguanide used clinically for the management of diabetes mellitus. Metformin is thought to increase the risk of elevated lactate, but the correlation remains controversial. The proposed mechanism includes inhibition of gluconeogenesis and mitochondrial impairment.[30]



Line diagram **(figure 3)** showing correlation between glucose and lactate: it shows at only higher level of lactate the glucose level is found elevated.

There are four main causes of mortality found in hyperlacticacidemia patients.

- Septic shock,
- Diabetes mellitus,
- Renal failure &
- Acute exacerbation of COPD.

Septic shock is the main cause of mortality with hyperlacticacidemia,Lactic acid levels have become a useful marker for tissue hypoperfusion and may also serve as an endpoint for resuscitation in patients with sepsis and septic shock.[31,32] DM is another common cause as metabolic acidosis is complicated by ketone bodies accumulation (ketoacidosis).Elevated lactate in DKA may be due not only to hypoperfusion but also to an altered metabolic profile, but further investigation is warranted.[33,34] The elevated lactate observed in metformin users may be related to an exacerbation of their chronic disease or another acute insult and is not necessarily related to metformin.[30,35] Pure metformin-associated elevated lactate is often seen with accumulation due to kidney failure, liver failure or overdose. In cases with renal failure, the suggested treatment is hemodialysis, which will correct the metabolic acidosis and remove metformin.[30]

Mortality causes of hyperlacticacedimia

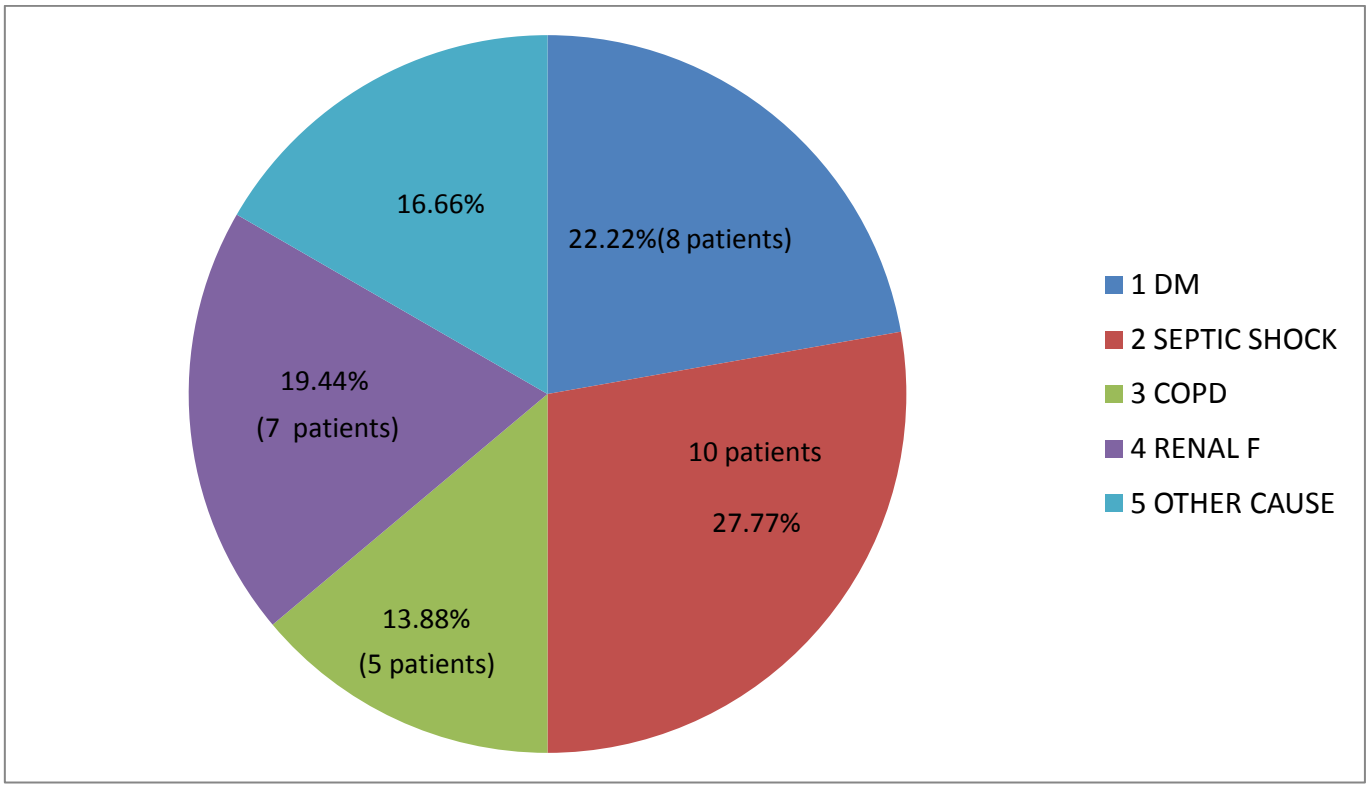


Figure-4: pie diagram showing mortality cause in patients with elevated levels; septic shock,diabetes mellitus and renal failure are 3 most common causes.

Limitations of Study

We could not find exactly at what O2 saturation and after how much duration of tissue hypoxia, will lactate level start increasing.

We described our mortality in hyperlacticacidemia in 5 main groups, could not take every case into consideration.

Recommendations

This study is conducted from July 2014 to 2015 to observe the lactate changes in patients admitted to intensive care unit.

Conclusion

Lactate level may be an epiphenomena of severity of a disease process. Clinician can interpret hyperlacticacidemia as a warning signal or as a

prognostic marker that the patients are deteriorating even in stable hemodynamic parameters.

Hyperlacticacidemia usually increases morbidity and mortality. Use of lactate as goal directed therapy may improve clinical outcome. These findings confirm that lactate is a useful parameter in critically ill patients.

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