The association of early combined lactate and glucose levels and hospital mortality in critically ill patients

Prof. Dr. Bahaa Elden Eweas Hassan, Dr. Dina Salah Elden Mouhamed, Dr. Mai Mohsen Abdlaziz Gadallah, Ahmed Ramadn Abdlaziz Abdlgawad.

Anesthesia and Postsurgical ICU, Faculty of Medicine, Ain Shams University, Egypt
Ahmedelemery1@gmail.com

Abstract: Since early 1960s, blood lactate concentrations have been used widely as a marker of altered tissue perfusion in critically ill patients. Hyperlactatemia is a hallmark characteristic of shock states and the degree of increase in lactate concentrations is directly related to the severity of the shock state and to mortality rates. On the other hand, both hyperglycemia and hypoglycemia in the intensive care unit (ICU) patient have long been associated with increased morbidity and mortality. The worsened outcome from hyperglycemia occurs not only in patients with diabetes, but also in non-diabetics when enhanced glycogenolysis and gluconeogenesis combined with impaired glucose consumption and impaired glycogen production lead to stress-induced hyperglycemia. Recently, a growing body of evidence has suggested that abnormal combined lactate and glucose levels may provide an early indication of organ dysfunction in ICU patients. Therefore, we conducted the present retrospective study in order to investigate whether the risks of morbidities and mortality are higher in ICU patients with hyperlactatemia and higher/lower glycemic level. In the present study, we included 100 cases that had an ICU stay of at least 12 hours. The mean age of the included patients was 46.2 ±15.4 year; while the majority of them were males (58%) and smokers (62%). Notably, the mortality rate in the present study was 37%. In the present study, the median lactate level decreased significantly from 2.3 (1.3-5) mg/dL at first six hours of ICU admission to reach 1.4 (0.9–3.8) mg/dL after 24 hours (p <0.001). Forty-eight perent of the patients had hyperlactatemia at admission. Our analysis showed that the serum lactate level was significantly higher in dead patients than the patients who survived (p <0.001). Moreover, the proportion of dead patients were significantly higher in hyperlactatemia group than normal lactate level at admission group (p <0.001). On the other hand, our analysis showed thatthe random blood sugar level was not significantly different between dead patients and the patients who survived (p =0.58). However, a statistically significant higher proportion of patients with hyperglycemia were dead compared to patients with normal glycaemia at admission (p =0.007). With regard to our primary outcome, 40% of the patients in the present study had combined hyperlactatemia and hyperglycemia at admission; while 11% had combined hyperlactatemia and hypoglycemia. Notably, statistically signifcant higher proportions of patients in combined hyperlactatemia and hyperglycemia required mechanical ventilation (p =0.049), had higher APACHE IV (p= 0.026), longer length of hospital stay (p =0.013), and higher mortalitly than patients with normal lactate and normal blood glucose levels. In conclusion, patients admitted to ICU with combine hyperlactatemia and hyperglycemia are at increased risk of adverse outcomes than patients without this combination. Our study showed that patients with combine hyperlactatemia and hyperglycemia were more likely to require mechanical ventilation, had higher APACHE IV, and longer length of hospital stay than patients with normal lactate and normal blood glucose levels.
[Bahaa Elden Eweas Hassan, Dina Salah Elden Mouhamed, Mai Mohsen Abdlaziz Gadallah, Ahmed Ramadn Abdlaziz Abdlgawad. **The association of early combined lactate and glucose levels and hospital mortality in critically ill patients.** *J Am Sci* 2019;15(6):17-26]. ISSN 1545-1003 (print); ISSN 2375-7264 (online). http://www.jofamericanscience.org. 3. doi:10.7537/marsjas150619.03.

Keywords: association; lactate; glucose; level; mortality; ill; patient

1. Introduction

Derangements of lactate and glucose levels are common in critically ill Patients**.** In the routinely available laboratory measurements, lactate has the strongest relation with outcome in a broad variety of clinical settings. As a result, it is increasingly used to monitor the effectiveness of instituted therapy. Since lactate and glucose monitoring has steadily gained popularity, optimal understanding of changes in glyco-metabolism, may improve interpretation of acute clinical Change. Lactate and glucose are linked through both glycolysis and gluconeogenesis and both pathways are part of the Cori cycle. Gluconeogenesis which is performed by the liver and the kidney recycles circulating lactate into glucose. Mild hypoglycemia can be the result of dysfunction of the gluconeogenetic organs and it has been associated with impaired renal and liver function which affects outcome. **(Vincent et al., 2016)**

Most frequently, the stress reaction that accompanies acute critical illness directly induces both hyperlactatemia and hyperglycemia. Thus hyperlactatemia without hyperglycemia might constitute already an abnormal response in the face of stress. Therefore we hypothesized that the combination of an elevated lactate with even a 'normal' glucose, might be associated with an increased incidence of renal or liver dysfunction and hospital mortality. Most observational and retrospective studies have reported that hyperglycemia in patients with severe disease, is associated with an increased risk of complications, longer ICU stay and higher mortality rates. Hyperlactatemia is common among patients requiring critical care, and lactate levels and their trend may be reliable markers of illness severity and mortality. Abnormal combined lactate and glucose measurements may provide an early indication of organ dysfunction. In critically ill patients a 'normal' glucose with an elevated lactate should not be considered desirable, as this combination is related with increased mortality. **(Pedro Fr et al., 2017)**

Aim of the Work

This study aims to clarify the role of early measurement of glucose & lactate level and its role in mortality & morbidities in critically ill patient. It is confirming that Increased organ dysfunction is found more in patients with hyperlactatemia with higher & or lower glycemic level and it is less with mid glycemic control.

It also clarifies that Aggressive control of hyperglycemia is associated with incidence of hypoglycemia and therefore increasing the mortality rates. It aims to prove that Hospital mortality and organ dysfunction improved with better lactate monitoring & glycemic control.

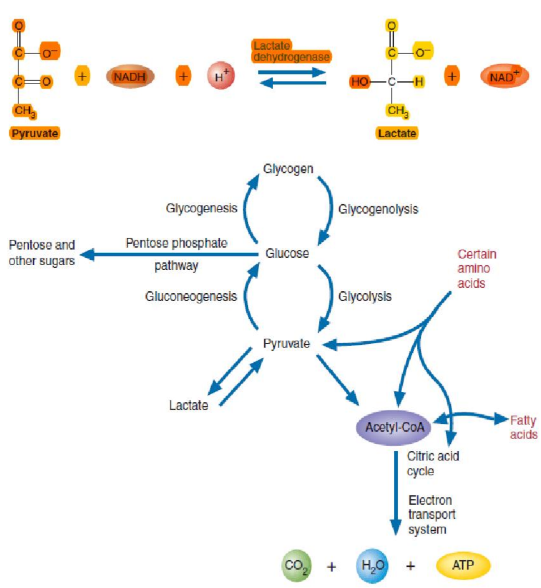

Figure (1) showing: Pyruvate + NADH + H+⇌ lactate + NAD and Glycolysis in the absence and presence of oxygen (Bakker et al., 2016).

The lactate production every day in resting humans is estimated as 20 mmol/kg and Production is primarily from highly glycolytic tissues like skeletal muscles. (**Shigeki Ku et al., 2016)**

Pyruvate is generated in large amount by anaerobic glycolysis. The redox-coupled inter conversion of pyruvate and lactate, occurs in the cytosol and is catalyzed by lactate dehydrogenase. The blood lactate: pyruvate ratio is maintained at approximately 10:1; therefore, any condition that increase pyruvate generation will increase lactate generation (Figure 2).

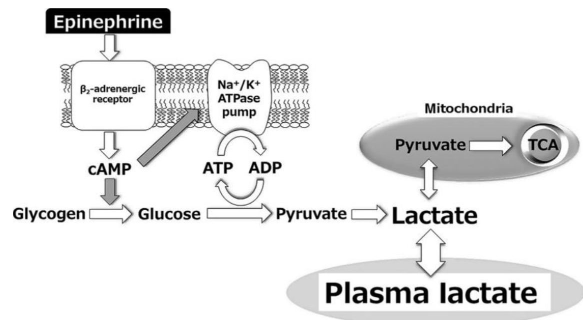

Figure (2) showing: Epinephrine-induced lactate production **(Shigeki Ku et al., 2016)**

Lactate can be metabolized by the liver and the kidneys either through direct oxidation or as a source of glucose. The liver accounts for up to 70% of whole body lactate clearance. Under normal conditions, the generation and consumption of lactate are equivalent, which results in a stable concentration of lactate in the blood. Lactate is reconverted to pyruvate and it is metabolized in the liver, kidney, and other tissues through the Cori cycle, that generates glucose and consumes adenosine triphosphate (ATP) (gluconeogenesis) (Figure 3). Lactate is also metabolized through the tricarboxylic acid cycle and oxidative phosphorylation in the liver, kidney, muscle, heart, brain, and other tissues, generating ATP, when pyruvate is oxidized to carbon dioxide and water. Half of lactate is metabolized through oxidation at rest and 75–80% during exercise. In contrast, lactate production by muscle and other tissues is coupled with its conversion to glucose. **(Satoshi Ak et al, 2016).**

During strenuous exercise, lactate is produced anaerobically in muscle cells. After passing through blood to the liver, lactate is converted to glucose by gluconeogenesis. Lactate is an important precursor of gluconeogenesis and a key source of glucose. Under stress conditions, lactate has been suggested to act as a biofuel, which eliminates blood glucose use and provides additional glucose. Therefore, hyperlactatemia may indicate a protective response to stress under critical conditions. **(Miller BF et al., 2002).**

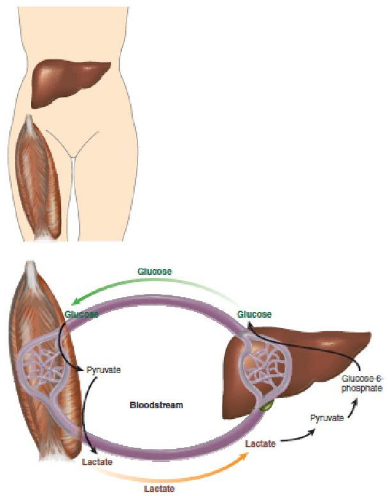

Figure (3) showing: The Cori Cycle (Mensonides F. I.C et al, 2000).

The relationship between stressful situations in critically ill patients (CIPs) and acute hyperglycemia was first described in the late 19th Century. Stress-induced hyperglycemia was thought of as an adaptive and even beneficial neuro-hormonal response, to support the energy requirements of insulin-independent cell types, such as brain cells and phagocytes. With high prevalence, hyperglycemia and insulin resistance are associated with poor outcome in a wide spectrum of CIPs that why tight glycemic control could improve the prognosis of these patients and decrease adverse events. Insulin resistance and hyperglycemia are common in critical illness due to an alteration in the immune-neuroendocrine axis and subsequent alteration in lipid and carbohydrate metabolisms. **(Andreelli et al., 2006)**

Disturbances in cross-taking between endocrine, immune and neural systems, which are highly interrelated with each other, and alteration in their complex interactions during critical illnesses, would finally result in metabolic instabilities. Pre-existing conditions, such as diabetes mellitus (DM), pancreatitis and cirrhosis, will increase the risk of hyperglycemia in the intensive care setting. Iatrogenic causes of hyperglycemia, including administration of steroids, sympathomimetic.

(e.g., catecholamines [ChAs]), total parenteral nutrition (TPN) and particularly, excess administration of dextrose must also be considered. Stress is a response to any situation that threatens homeostasis, and usually results in the activation of the hypothalamic–pituitary–adrenal (HPA) axis and sympathetic autonomic nervous system. **(Mechanick et al., 2006)**

Neuroendocrine involvements and stimulation of the HPA axis, which is characterized by hypercortisolemia during critical illnesses, play a major role in the occurrence of hyperglycemia. Activation of the HPA axis is associated with activation of the corticotrophin-releasing factor (CRF) adrenocorticotrophic hormone (ACTH) axis via cytokines such as interleukin (IL)-1, IL-6 and tumor necrosis factor (TNF) α, which are primed by monocytes, lymphocytes and other chief endocrine factors, and eventually results in increased secretion of glucocorticoids from the adrenal cortex, that influence the immune accessory cells, a bidirectional interaction of immune-neuroendocrine systems. Stimulation of the sympathetic nervous system leads to release of Chas and hormonal modulation. Increased level of counter regulatory hormones (e.g., glucagon and growth hormone), cortisol, Chas and pro-inflammatory cytokines cause insulin resistance and hyperglycemia by different mechanisms. **(Farshad Ka et al., 2007)**

Methodology

The study population (n=100) included 58 males (58%) and 42 females (42%), their ages range from (19 years) to (75 years) with the mean age was 46.2 ±15.4, were selected from critically ill patients admitted to Benisuef general hospital general ICU in the period 2016-2018.

Inclusion criteria:

- Age between 18 to 70 yrs.
- Both sexes.
- Diabetic patients & not diabetic patients.
- Any patient with a disease process which causes physiological instability leading to death or disability.
- Patients who had an ICU Stay of at least 12hr were included.

Exclusion criteria:

- Any patient with a disease process causing abnormal changes in lactate & glucose levels but without causing physiological instability.
- advanced Malignancy
- Patients on immunosuppressive drugs.
- Patients with renal dysfunction.
- Patients with hepatic dysfunction.
- Post-arrest patients

Methods

All patients underwent the following:

1) History taking:

IF the patient had chronic Heath Condition like

A) Diabetes

B) Hypertension

C) Immunosuppression drugs.

D) Previous admission to the ICU.

2) Examination:

General examination:

- Checking G.C.S of the patient to assess conscious level and recording on day zero and day seven.
- If the patient had any respiratory problems or not.
- If the patient had Cardiac arrhythmias or not.

Local examination:

- searching in post-traumatic patients for wounds, organ injury and lacerations.
- Scars of previous operation.

3) Investigation:

- Complete blood count.
- Hepatic function test (ALT, AST, bilirubin Total, Direct) on day zero & day seven.
-Renal function test (urea, creatinine) on day zero & day seven.
-Serial blood glucose & lactate levels.
- Serial daily ABGS for monitoring Pao2, Paco2 and lactate level.

3. Results

Statistical Analysis:

An Excel spreadsheet was established for the entry of data. We used validation checks on numerical variables and option-based data entry method for categorical variables to reduce potential errors. The analyses were carried with SPSS software (Statistical Package for the Social Sciences, version 24, SSPS Inc, Chicago, IL, USA). The normality of the data were assessed using Shapiro-Wilk Test. Numerical data were described as mean ±SD if normally distributed; or median and interquartile range [IQR] if not normally distributed. Frequency tables with percentages were used for categorical variables. Independent Student t-test and paired t-test were used to compare parametric quantitative variables; while Mann-Whitney tests and Wilcoxon matched pairs test were used to compare non-parametric quantitative variables. Chi-square test or McNemar-Bowker tests were used to analyze categorical variables. Multilinear logistic regression was undertaken to assess the predictors of mortality. A p-value < 0.05 is considered statistically significant.

The present retrospective study was conducted at Ain Shams university hospital and general hospital of Beni-Suef. One hundred cases who had an ICU stay of at least 12 hours were included. The mean age of the included patients was 46.2 ±15.4 year; while the majority of them were males (58%). In addition, 62% of patients were smokers and 42% of them were diabetic.

Table 1: The baseline demographic characteristics of the included patients

Variables	**Patients (N =100)**
Age in years	
- Mean ±SD	46.2 ±15.4
Gender	
- Male	58 (58%)
- Female	42 (42%)
Smoker, No (%)	
- Yes	38 (38%)
- No	62 (62%)
DM, No (%)	
- Yes	42 (42)
- No	58 (58)
CRF, No (%)	
- Yes	0
- No	100 (100%)
Readmission, No (%)	
- Yes	34 (34%)
- No	66 (66%)
Pre ICU LOS, in days	
- Median (IQR)	2 (2 - 2)
- Range	1 - 14

Data are presented as mean ±SD, median (IQR), or number (%). DM: Diabetes meliitus; CRF: Chronic renal failure

Regarding the physical examination findings, the mean temperature of the included patients was 37.58 ±0.84C and the average mean arterial pressure was 64.8 ±21.57mmHg. In addition, the mean heart rate was 109.5 ±20.6 beats/minutes and the mean respiratory rate was 25.6 ±10.3/minutes.

Table 2: Vital sings of the included patients at admission

Variables, mean ±SD	**Patients (N =100)**
Temperature in C	37.58 ±0.84
MAP in mmHg	64.8 ±21.57
HR in beats/min	109.5 ±20.6
RR per minutes	25.6 ±10.3

Data are presented as mean ±SD. MAP: mean arterial pressure; HR: heart rate; RR: respiratory rate.

The ABG analysis showed that the mean PaO2 was 87.2 ±13.7mmHg and the mean PaCO2 was 41.9 ±15.6mmHg. Likewise, the mean PH was 7.3 ±0.11.

Table 3: ABG of the included patients at admission

Variables, mean ±SD	**Patients (N =100)**
PaO2 in mmHg.	87.2 ±13.7
PaCO2 in mmHg.	41.9 ±15.6
PH	7.3 ±0.11

Data are presented as mean ±SD, median (IQR), or number (%). PaO2: Partial pressure of oxygen; PaCO2: Partial pressure of carbon dioxide.

In terms of laboratory findings, the mean urine output was 1611 ±633.57ml/day and the median creatinine was 1.25 (0.9 – 1.7) mg/dL. In addition, the median urea level was 44 (36 – 60) mg/dL; while the mean albumin was 3.4 ±0.58g/dL.

Table 4: Laboratory findings of the included patients at admission

Variables, mean ±SD	Patients (N =100)
Urine Output ml/day	1611 ±633.57
Creatinine mg/dL	1.25 (0.9 – 1.7)*
Urea mg/dL	44 (36 – 60)*
Albumin in g/dL	3.4 ±0.58
Bilirubin in g/dL	1 (0.8 – 1.1)*

Data presented as median (IQR)

The mean hematocrit value was 35.5 ±5.6% and the median white blood cells was 12.25 (9 - 17) cell/mm^3.

Table 5: CBC Profile of the included patients at admission

Variables, mean ±SD	Patients (N =100)
Ht%	35.5 ±5.6
WBCs	12.25 (9 - 17)*

Data presented as median (IQR). WBCs: white blood cells.

Regarding the ICU outcomes, half of the patients required mechanical ventilation; while the median APACHE IV was 59 (40 -90). The median length of hospital stay was 5.75 (3.3 – 6.7) days. In addition, 52% of patients required insulin therapy. Notably, the mortality rates was 37%.

Table 6: Outcomes of the included patients

Variables	Patients (N =100)
Ventilated, No (%)	
1. Yes	50 (50%)
2. No	50 (50%)
APACHE IV	
1. Median (IQR)	59 (40 -90)
2. Range	16 - 153
LOS in days	
1. Median (IQR)	5.75 (3.3 – 6.7)
2. Range	1.3 – 10.5
Insulin Therapy, No (%)	
1. Yes	52 (52%)
2. No	48 (48%)
Mortality rate, No (%)	
1. Dead	37 (37%)
2. Alive	63 (63%)

Data are presented as mean ±SD, median (IQR), or number (%). LOS: length of stay; APACHE: Acute Physiology and Chronic Health Evaluation IV.

Ove the length of hospital stay, the median lactate level decreased significantly from 2.3 (1.3 - 5)mg/dL at first six hours of admission to reach 1.4 (0.9 – 3.8)mg/dL after 24 hours (p <0.001). Similarly, the median random blood sugar increased significantly from 130 (111 - 203)mg/dL at first six hours of admission to reach 138 (108 - 180)mg/dL after 24 hours (p =0.004).

Table 7: The changes in creatinine and RBS level of the included patients

Variables	Patients (N =100)				P-value
	1st 6 hours	2nd 6 hours	3rd 6hours	4th 6 hours	
Lactate level in mg/dL					
1- Median (IQR)	2.3 (1.3 - 5)	2 (1.4 - 5)	1.9 (1 – 4.8)	1.4 (0.9 – 3.8)	
2- Range	0.4 - 12	0.6 - 12	0.5 - 10	0.5 - 9	<0.001
Random blood Sugar in mg/dL					
1- Median (IQR)	130 (111 - 203)	143 (109 - 207)	150 (107 - 201)	138 (108 - 180)	
2- Range	30 - 450	40 - 530	50 - 560	60 - 430	0.004

Data are presented as median (IQR)

Forty-eight percent of the patients had hyperlactatemia on admission and 59% of the patients had hyperglycemia at admission. In addition, 14% of the patients had iatrogenic hypoglycemia at end of 24 hours. Notably, 40% of the patients had combined hyperlactatemia and hyperglycemia at admission and 11% had combined hyperlactatemia and hypoglycemia.

Table 8: shows the frequency of hyperlactatemia, hyperglycemia, and hypoglycemia

Variables, No (%)	Patients (N =100)
Hyperlactatemia at admission	
1. Yes	48 (48%)
2. No	52 (52%)
Hyperglycemia at admission	
1. Yes	59 (59%)
2. No	41 (41%)
Hypoglycemia at end of 24 hour	
1. Yes	14 (14%)
2. No	86 (86%)
Hyperlactatemia & Hyperglycemia & Hypoglycemia at admission	
1. Yes	51 (51%)
2. No	49 (49%)

Data are presented as number (%).

In addition, there were statistically significant differences between hyperlactatemia & hyperglycemia group and the other group in terms of ventilation (P =0.049), APACHE IV (P= 0.026), LOS (P =0.013), and mortality rate (P <0.001).

Table 9: Effect of combined hyperlactatemia and hyperglycemia on the Outcomes of the included patients

Variables	HHH group (N =51)	Control group (N =49)	P –value
Ventilated, No (%)			
1. Yes	32 (62.5%)	20 (40.9%)	0.049
2. No	19 (37.5%)	29 (59.1%)	
APACHE IV			
1. Median (IQR)	82 (54 - 94)	54 (32 - 82)	0.026
2. Range	42 – 106	16 - 153	
LOS			
1. Median (IQR)	6.5 (4.5 – 8.1)	4.8 (2.9 – 7.4)	0.013
2. Range	2.6 – 9.6	1.3 – 10.5	
Mortality rate, No (%)			
1. Dead	31 (60.7%)	6 (13.1%)	<0.001
2. Alive	20 (39.3%)	43 (86.9%)	

Data are presented as mean ±SD, median (IQR), or number (%). HHH: Hyperlactatemia & Hyperglycemia & Hypoglycemia at admission

The analysis showed that the serum lactate level was significantly higher in dead patients than the patients who survived (p <0.001). In contrary, the random blood sugar level was not significantly different between dead patients and the patients who survived (p =0.58).

Table 10: The association between lactate and RBS levels at admission with mortality

Variables	Mortality		P-value
	Dead (N =37)	Alive (= 63)	
Lactate level in mg/dL			
- Median (IQR)	4.75 (2.3 – 7)	1.5 (1.12 – 3.37)	
- Range	0.6 - 12	0.4 - 11	<0.001
Random blood Sugar in mg/dL			
- Median (IQR)	118.5 (107.25 – 238.25)	150 (112 - 200)	
- Range	30 - 450	89- 290	0.58

*Data are presented as median (IQR).

Similarly, there was statistically significant difference in mortality rates between patients with hyperlactatemia and patients with normal lactate level at admission. Almost 73% of the patients with hyperlactatemia were dead compared to only 27% in the normal lactate groups (p <0.001). Similarly, a statistically significant higher proportion of patients with hyperglycemia were dead compared to patients with normal glycaemia at admission (p =0.007)

Table 11: shows the association between normal glucose and lactate at admission with mortality

Variables, No (%)	Dead (N =37)	Alive (=63)	P-value
Lactate level at admission			
- Hyperlactatemia	38 (73.1%)	10 (20.8%)	<0.001
- Normal	`14 (26.9%)	38 (79.2%)	
Glucose level at admission			
- Normal	24 (46.2%)	35 (72.9%)	0.007
- Hyperglycemia	28 (53.8%)	13 (27.1%)	

*Data are presented as number (%).

Table 12: Multivariate analysis of factors associated with mortality.

	Odds ratio	95% confidence interval	P- Value
Age in years	0.948	0.908- 1.98	0.114
LOS	0.785	0.611 – 1.008	0.058
RBG at admission	0.997	0.989 – 1.005	0.455
Lactate at admission	1.045	0.779 – 1.42	0.771

*Data are presented as odds ratio and 95% confidence interval

4. Discussion:

In the present examination we found a solid connection among lactate and glucose levels and result and consolidated appraisal of early lactate and glucose would give extra data on metabolic hindrance and high lactate joined with a low glucose was related with the most noteworthy danger of AKI, liver brokenness, and medical clinic mortality.

There were measurably huge contrasts between hyperlactatemia and hyperglycemia gathering and the other gathering as far as ventilation (P =0.049), APACHE IV (P= 0.026), LOS (P =0.013), and death rate (P <0.001) as indicated by table (10). Thus, there was factually noteworthy contrast in death rates between patients with hyperlactatemia and patients with ordinary lactate level at affirmation. Practically 73% of the patients with hyperlactatemia were dead contrasted with just 27% in the typical lactate gatherings (p <0.001). Also, a factually critical higher extent of patients with hyperglycemia were dead contrasted with patients with ordinary glycaemia at affirmation (p =0.007) as indicated by table (12)

Since mid-1960s, blood lactate focuses have been utilized generally as a marker of adjusted tissue perfusion in fundamentally sick patients. It was accounted for those even minor increments in lactate focuses to >1.5 mEq/l are related with higher death rates. The precise pathophysiologic components of hyperlactatemia have been abundantly discussed, on the grounds that the condition does not in every case essentially mirror the improvement of anaerobic digestion. Despite these instruments, hyperlactatemia is a trademark normal for stun states and the level of increment in lactate focuses is straightforwardly identified with the seriousness of the stun state and to death rates. In addition, late examinations have featured the significance of observing lactate levels and alter treatment to the adjustment in lactate levels in early revival. As lactate levels can be estimated quickly at the bedside from different sources, it was stressed that organized lactate estimations ought to be fused in revival conventions.(**Vincent et al., 2016**)

A conceivable clarification for the signifcant job of lactate level in anticipating the in-emergency clinic mortality is the way that hyperlactatemia is normal may mirror a lopsidedness between neighborhood or foundational oxygen supply (DO2) and oxygen utilization (VO2); hyperlactatemia likewise might be found amid expanded vigorous glycolysis in hypermetabolic states from different causes. Subsequently, raised lactate levels are related with the improvement of various organ brokenness and passing. (**Zhang et al., 2014**)

Then again, both hyperglycemia and hypoglycemia in the emergency unit quiet have for quite some time been related with expanded grimness and mortality. The compounded result from hyperglycemia happens in patients with diabetes, yet additionally in non-diabetics when upgraded glycogenolysis and gluconeogenesis joined with disabled glucose utilization and impeded glycogen creation lead to pressure initiated hyperglycemia. Moreover, patients with hyperglycemia are at a more serious hazard for wound diseases, bacteremia, septicemia, and ischemic occasions. While iatrogenic hypoglycemia has since been accounted for to be an autonomous hazard factor for mortality and multi-organ framework grimness in the ICU populace.(**D'Ancona et al.**, **2011**)

Hypoglycemia implies that plasma glucose fixation < 70 mg/dL which is the most widely recognized edge used to characterize. In any case, the vast majority of the investigations including glucose control in the ICU have characterized extreme hypoglycemia discretionarily as qualities < 40 mg/dL whether the patients had related side effects. Developing information propose that hypoglycemia may negatively affect the clinical status and result of ICU patients. ICU patients may endure hypoglycemia ineffectively and furthermore show impeded counter-administrative reactions or have postponed location of hypoglycemia. The most extreme entanglements of serious hypoglycemia, for example, seizures and demise, are anything but difficult to gauge; progressively unpretentious signs of neuro-glycopenia, for example, migraines, weakness, disarray, dysarthria, or hindered judgment, might be troublesome or difficult to analyze in fundamentally sick patients. **(BrunkhorstFM.,2008)**

In light of the Leuven consider in 2001, serious insulin treatment was generally utilized in numerous ICUs. Numerous investigations have appeared escalated insulin treatment is related with altogether a greater number of scenes of extreme hypoglycemia than ordinary insulin treatment. In the VISEP and GLUCOCONTROL preliminaries (2001), the examinations were ended early in light of fundamentally increasingly hypoglycemic scenes in the escalated insulin treatment gathering. In two meta-investigations thinks about, escalated insulin treatment additionally demonstrated an altogether expanded danger of hypoglycemia.

Since escalated insulin treatment has been related with a fundamentally higher danger of hypoglycemia, there is expanded worry about the security of serious insulin treatment, which has turned into a deterrent to severe glycemic control. **(GriesdaleDE.,2009)**

As of late, a developing collection of proof has recommended that strange joined lactate and glucose levels may give an early sign of organ brokenness in ICU patients. The pressure reaction related with organ brokenness can prompt huge rise in lactate and glucose creation. In this manner, they are both immovable and can, in mix, anticipate morbidities and mortality. In any case, there is a shortage in the distributed writing that evaluates the prescient job of consolidated anomalous lactate and glucose levels in ICU setting.(**Marik et al.**, **2013**)

Therefore, we conducted the present retrospective study in order to investigate whether the risks of morbidities and mortality are higher in ICU patients with Alongthese lines, we directed the present review contemplate so as to research whether the dangers of morbidities and mortality are higher in ICU patients with hyperlactatemia and higher/lower glycemic level. Seniority is related with perpetual restorative maladies and practical disability, which may prompt expanded rate and seriousness of intense basic ailments and to admission to the ICU. While smoking and undesirable liquor use are general medical issues that ordinarily result in basic disease.(**Polmear et al.**, **2017**)

In the present investigation, the middle lactate level diminished fundamentally from 2.3 (1.3-5) mg/dL at initial six hours of ICU admission to achieve 1.4 (0.9 – 3.8)mg/dL following 24 hours ($p < 0.001$). Forty-eight perent of the patients had hyperlactatemia at confirmation. Our investigation demonstrated that the serum lactate level was essentially higher in non enduring patients than the patients who endure ($p < 0.001$). In addition, the extent of dead patients were essentially higher in hyperlactatemia bunch than typical lactate level at affirmation gathering ($p < 0.001$).

In concordane with our discoveries, a review observational investigation performed at 11 ICUs between 1 April 2011 and 28 February 2013 and included14,040 ICU patients. The outcomes demonstrated that the death rate in patients with serious hyperlactatemia was 78.2 % which was signifcantly higher than the death rate in patients with typical lactate. Hyperlactatemia was related with death in the ICU [odds proportion 1.35 (95 % CI 1.23; 1.49; $p < 0.001$)]. (**Haas et al.**, **2016**)

Simialrly, an ongoing single-focus, review learn at a tertiary consideration medical clinic recrutied patients who exhibited to the ICU somewhere in the range of 2014 and 2016. A sum of 450 patients were incorporated into the examination. While changing for all factors, patients with intermediate and high lactate had higher in-medical clinic death rates. Another review ponder found that hyperlactatemia is related with in-emergency clinic mortality in a heterogeneous ICU populace.(**Bou Chebl et al.**, **2017**)

In a directed methodical survey to investigate the symptomatic exactness of lactate leeway in anticipating mortality in basically or intensely sick patients. An aggregate of 15 unique articles were incorporated into the investigation and the pooled impact gauges showed that lactate leeway is prescient of lower death rate in fundamentally sick patients, and its indicative execution is ideal for clinical utility. (**Zhang et al.**, **2014**)

Then again, the present investigation demonstrated that measurably higher death rates in patients with hyperglycemia contrasted with patients with ordinary glycaemia at confirmation (p =0.007). As led a review companion investigation of an absolute 1,224 subjects (guys, 798; females, 426) admitted to ICU from 1 January 2009 to 31 December 2010. Their outcomes recommend that serum glucose levels upon entrance into ICU is related with clinical results in ICU patients. Serious hypergylcemia at the season of ICU confirmation could anticipate medical clinic mortality among fundamentally sick patients. (**Park et al.**, **2013**)

Moreover, one investigation of 6,891 network procured pneumonia patients, those with mellow hyperglycemia upon confirmation (serum glucose levels, 108 to 198 mg/dL) had an essentially expanded danger of death at 90 days (risk proportion, 1.56), which expanded to 2.37 when affirmation blood glucose levels were ≥252 mg/dL. (**Lepper et al.**, **2012**)

In another investigation of 1,550 fundamentally sick youngsters, patients with high serum glucose level in the main day of pediatric ICU confirmation (>200 mg/dL) had longer mechanical ventilation days, longer pediatric ICU length of remain, and lower level of survival than those with typical serum glucose (≤200 mg/dL). Besides, patients with confirmation hyperglycemia (>135 mg/dL) had higher medical clinic mortality than those with normoglycemia (<100 mg/dL) in polytraumatised patients.(**Kreutziger et al.**, **2009**)

As referenced previously, the huge job of consolidated height of lactate and glucose levels in foreseeing the in-medical clinic mortality can be expalined by the reality the raised lactate and glucose levels recognize distinctive glycometabolic states. A state with both hyperlactatemia and hyperglycemia could be translated as a pressure reaction where the body still can produce 'versatile' hyperglycemia. Conversely, a state with raised lactate without hyperglycemia may be translated as state where the body is unfit to create hyperglycemia regardless of a pressure reaction. (**Freire Jorge et al.**, **2017**)

As to the present investigation essential result, 40% of the patients in the present examination had consolidated hyperlactatemia and hyperglycemia at affirmation; while 11% had joined hyperlactatemia and hypoglycemia. Eminently, factually signifcant higher extents of patients in joined hyperlactatemia and hyperglycemia required mechanical ventilation (p =0.049), had higher APACHE IV (p= 0.026), and longer length of clinic remain (p =0.013) than patients with ordinary lactate and typical blood glucose levels.

In concurrence with our discoveries, a review ponder performed over a 4-year time frame (2011 to 2014) to included grown-up patients admitted to clinic ICU for at any rate 12 hours. Lactate and glucose estimations were gathered from 6 h before to 24 h after ICU confirmation. In general, 9074 patients were incorporated who demonstrated that the consolidated lactate and glucose measurments were fundamentally connected with longer length of medical clinic remain (p ≤ 0.001). (**Freire Jorge et al.**, **2017**)

Notwithstanding, we found a staistically signifcant relationship between consolidated hyperlactatemia and changes in blood glucose level (hyperglycemia or hypoglycemia) with death rate (P <0.055). In opposite, found that the consolidated lactate and glucose measurments were fundamentally connected with ICU mortality (p ≤ 0.001). (**Freire Jorge et al.**, (**2017**)

Prominently, the death rate in the present investigation was 37%. In concordance with our discoveries, an imminent engaging investigation performed in patients of Assiut emergency clinic who were admitted to ICU for over one day (247 patients) amid the period from April 2010 to March 2012. The creators detailed that the moratlaity rate was 41%. (**El-Shahat et al.**, **2015**)

Conclusion

In conclusion, patients admitted to ICU with combine hyperlactatemia and hyperglycemia is at increased risk of adverse outcomes than patients without this combination. Our study showed that patients with combine hyperlactatemia and hyperglycemia were more likely to require mechanical ventilation, had higher APACHE IV, and longer length of hospital stay than patients with normal lactate and normal blood glucose levels. Nevertheless, further trials that assess the usefulness of continuous lactate and glucose monitoring in at-risk patients are still needed. The measurement of combined lactate/glucose levels at the point-of-care may provide a more complete picture of carbohydrate metabolism in critically ill patients.

References

1. Andreelli, F., Jacquier, D., and Troy, S., (2006). Molecular aspects of insulin therapy in critically ill patients. Curr. Opin. Clin. Nutr. Metab. *Care* 9(2), 124–130.
2. Bakker, J., Nijsten, MW., and Jansen, TC (2013). Clinical use of lactate monitoring in critically ill patients. Ann Intensive Care (3), 12.
3. Bou Chebl, R., El Khuri, C., and Shami, A., et al (2017). Serum lactate is an independent predictor of hospital mortality in critically ill patients in the emergency department: a retrospective study.

Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine, 25(1), 69.
4. D'Ancona, G., Bertuzzi, F., and Sacchi, L., et al (2011). Iatrogenic hypoglycemia secondary to tight glucose control is an independent determinant for mortality and cardiac morbidity. European Journal of Cardio-Thoracic Surgery: Official Journal of the European Association for Cardio-Thoracic Surgery.
5. El-Shahat, H., Salama, S., and Wafy, S., et al (2015). Risk factors for hospital mortality among mechanically ventilated patients in respiratory ICU. Egyptian Journal of Bronchology, *9*(3), 231.
6. Farshad, Kajbaf., Mojtaba, Mojtahedzadeh., and Mohammad, Abdollahi (2007). Mechanisms underlying stress-induced hyperglycemia in critically ill patients. Future Medicine Ltd ISSN. 4(1), 97–106.
7. Freire Jorge, P., Wieringa, N., and de Felice, E., et al (2017). The association of early combined lactate and glucose levels with subsequent renal and liver dysfunction and hospital mortality in critically ill patients. Critical Care.
8. Haas, SA., Lange, T., and Saugel, B., et al (2016). Severe hyperlactatemia, lactate clearance and mortality in unselected critically ill patients. Intensive Care Med 10(42), 202.
9. Miller, BF., Fattor, JA., and Jacobs, KA et al (2002). Lactate and glucose interactions during rest and exercise in men: effect of exogenous lactate infusion. J. Physiol (544), 963.
10. Mechanick, JI., (2006). Metabolic mechanisms of stress hyperglycemia. J. Parenter. Enteral. Nutr. 30(2), 157–163.
11. Pedro, Freire Jorge., Nienke., and Wieringa., et al (2017). The association of early combined lactate and glucose levels with subsequent renal and liver dysfunction and hospital mortality in critically ill patients. Critical Care (21), 218.
12. Park, B. S., Yoon, J. S., and Moon, J. S., et al (2013). Predicting mortality of critically ill patients by blood glucose levels. Diabetes and Metabolism Journal.
13. Polmear, C. M., Nathan, H., and Bates, S., et al (2017). The effect of intensive care unit admission on smokers' attitudes and their likelihood of quitting smoking. Anaesthesia and Intensive Care, *45*(6), 720–726.
14. Shigeki, Kushimoto., Satoshi, Akaishi., and Takeaki, Sato., (2016). Lactate, a useful marker for disease mortality and severity but an unreliable marker of tissue hypoxia/hypo perfusion in critically ill patients. Acute Medicine & Surgery (3), 293–297.
15. Vincent, J.-L., Quintairos e Silva, A., and Couto, L., et al (2016). The value of blood lactate kinetics in critically ill patients: a systematic review. Critical Care, *20*(1), 257.
16. Zhang, Z., Xu, X., and Chen, K., (2014). Lactate clearance as a useful biomarker for the prediction of all-cause mortality in critically ill patients: A systematic review study protocol. BMJ Open.

6/10/2019