HYPERLACTATEMIA IN SEPSIS IN PATIENTS ADMITTED IN INTENSIVE CARE UNIT

By

DR. VIPUL KIRANBHAI PATEL

Dissertation submitted to

SBKS MEDICAL INSTITUTE & RESEARCH CENTRE

SUMANDEEP VIDYAPEETH, PIPARIA, VADODARA

In partial fulfillment
of requirements for the degree of M.D.
in

INTERNAL MEDICINE

Under the Guidance Of

DR. ARTI MULEY

PROFESSOR

M.D. (MEDICINE)

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SBKS MEDICAL INSTITUTE & RESEARCH CENTRE,
PIPARIA, VADODARA.

YEAR 2015-2018

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Dear Dr. Vipul,

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Date: 28th September 2017

STUDY COMPLETION CERTIFICATE

This is to certify that study synopsis entitled: "Hyperlactatemia in Sepsis in Patient Admitted in Intensive Care Unit." Research Project was done by **"Dr. Vipul Patel"** (PG Student, Dept of Medicine, S.B.K.S MI & RC, Dhiraj Hospital, Piparia, Waghodiya road, Vadodara-391760, Gujarat) and it was conducted to the satisfaction of the Sumandeep Vidyapeeth Institutional Ethics committee.

Dr. Niraj Pandit
Member Secretary
SV Institutional Ethics committee

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I hereby declare that this dissertation entitled **"HYPERLACTATEMIA IN SEPSIS IN PATIENTS ADMITTED IN INTENSIVE CARE UNIT"** is a bonafide and genuine research work carried out by me under the guidance of **DR. ARTI MULEY, Professor, Department of MEDICINE, SBKS Medical Institute & Research Centre, Piparia, Vadodara.**

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SUMANDEEP VIDYAPEETH

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Dr. Vipul Kiranbhai Patel

ABSTRACT

Introduction:

Sepsis is a systemic, deleterious host response to infection leading to severe sepsis (acute organ dysfunction secondary to documented or suspected infection) and septic shock. Sepsis is a contributing factor in >200,000 deaths per year in the United States. The incidence of severe sepsis and septic shock has increased over the past 30 years, and the annual number of cases is now >750,000 (~3 per 1000 population). With a population of 1.22 billion, today India is grappling with various health issues. As sepsis is very common in patients admitted to ICU, so the early diagnosis and severity of the sepsis should be an important step in the management of sepsis. It has been suggested that as the level of lactate increase, the severity of sepsis is more. So, we planned to see the lactate level in patients of sepsis, and its correlation with patients of sepsis admitted to our hospital in ICU.

Methodology:

This prospective study was carried out in Medicine department of SBKS Medical Institute and research center, Piparia, Vadodara. A total number of 50 patients of sepsis were included in the study as per the inclusion and exclusion criteria. All included participants were subject to Arterial blood gas analysis for Lactate level, CBC, RFT, LFT, RBS, Urine RM, ESR, chest X-ray, USG Abdomen. Laboratory evaluations were performed in the institutional pathology and biochemistry labs.

Results:

Total 50 patients were included in the study and were analyzed. Most common presenting complaint was fever, breathlessness, altered sensorium. Most common source of sepsis were urinary tract infection, lung, and abdomen. Over all urea and creatinine were increased, and there was increased bilirubin, SGPT, SGOT in most of the patients. The mortality rate was 58.8 % for patients with a lactate level greater than or equal to 2.0 mmol/mm3 clearly demonstrates that a lactate level may be helpful in identifying a high-risk patient population in the ICU, patient who were discharged had significantly lesser lactate level than patients who died (p-0.020).

Conclusion:

Lactate level is a very important prognostic marker in sepsis. If the initial lactate level is high the patient is more likely to die, so according to the level of initial lactate level the risk can be judged.

Keywords: sepsis and lactate.

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INTRODUCTION

"Sepsis is a systemic, mischievous host reaction to infection leading to severe sepsis (acute organ dysfunction secondary to documented or suspected infection) and septic shock." (Acc.to surviving sepsis guideline 2012) Lactic acidosis is the most commonly observed cause of metabolic acidosis in intensive care unit. Lactic acidosis occurs when lactate production exceeds lactate clearance.[1]

Essentially, hyperlactatemia was viewed primarily as the result of anaerobic metabolism due to inadequate tissue oxygen delivery.[2] This understanding persisted for most of the last century, and it was only in the latter half of the last century that the understanding of the significance of elevated serum lactate levels was modified to include disease states other than tissue hypoxia.[3]

Lactate is the end product of glucose metabolism in the cytoplasm (glycolysis)[4] It is formed by reduction of pyruvate in the reaction catalyzed by lactate dehydrogenase (LDH).[4] The lactate exits the cells and is transported to the liver, where it is oxidized back to glucose

Lactate is the marker for the sepsis, it get elevated during the sepsis, and other causes of raised lactate are Hypodynamic shock, Organ ischemia, Hyperglycemia, Hematological malignancy, Liver failure, Shock, Thiamine deficiency.[5]

Sepsis is a contributing factor in >200,000 deaths per year in the United States. The incidence of severe sepsis and septic shock has increased over the past 30 years, and the annual number of cases is now >750,000 (~3 per 1000 population). Approximately two-thirds of the cases occur in patients with significant underlying illness. Sepsis-related incidence and mortality rates increase with age and preexisting

comorbidity. The rising incidence of severe sepsis in the United States has been attributable to the aging of the population, the increasing longevity of patients with chronic diseases, and the relatively high frequency with which sepsis has occurred in patients with AIDS. The widespread use of immunosuppressive drugs, indwelling catheters, and mechanical devices has also played a role. In the aforementioned international ICU prevalence study, the case–fatality rate among infected patients (33%) greatly exceeded that among uninfected patients (15%) [5]

As sepsis is very comman in patient admitted to ICU, so the early diagnosis and severity of the sepsis in patient should be urgent for the management of sepsis, lactate act as the biomarker of sepsis, as the level of lactate increase, the severity of sepsis is more.

With a population of 1.22 billion, today India is grappling with various health issues. One of them is management of illnesses like 'Sepsis', which is taking a toll not only in rural India but is also prominent in urban India. Sepsis is a life-threatening medical condition triggered due to the body's response to an infection. It is often caused by microorganisms invading the body, either limited to a specific body part or can be widespread in the bloodstream.[6]

There are typically four progressive stages of Sepsis namely SIRS (Systematic Inflammatory Response Syndrome), SEPSIS, Septic Shock and MODS (Multiple Organ Dysfunction Syndrome). India currently tackles 750,000 cases of Sepsis every year of which overall mortality rate in ICU patients is 12.08% and in the severe stage Sepsis patients it is 59.26%.

"If empirical treatment for sepsis and bacteremia is holdup it will increase chances of mortality [6] as well as duration of stay [7] and cost [8,] so making timely recognition of infection and initiation of appropriate therapy an important goal so, the need for rapid diagnosis and risk stratification where biomarkers like lactate could be of use". Initial lactate level is very important to tell the prognosis, if the initial lactate level is high the prognosis of the patient is poor, so according to the level of initial lactate level the risk can be judged. After starting the treatment, is patient responding to the treatment can also be judged with consequent lactate level. If the lactate level is increasing the prognosis of the patient is poor and should change the treatment like change in anti-biotics. If the level of lactate is decreasing the prognosis of the patient is improving.[8]

So, we planned to see the lactate level in patient of sepsis, and its co relation with sepsis, admitted to our hospital in ICU.

AIMS AND OBJECTIVES

1. To study incidence of Hyperlactatemia in patients with sepsis on admission in ICU.

2. To study causes of Hyperlactatemia in sepsis.

   (Example, blood sugar, hypoxemia, hypo perfusion etc.)

3. To study ABG changes secondary to sepsis and hyperlactatemia.

4. Vital sign changes and Hyperlactatemia.

REVIEW OF LITERATURE

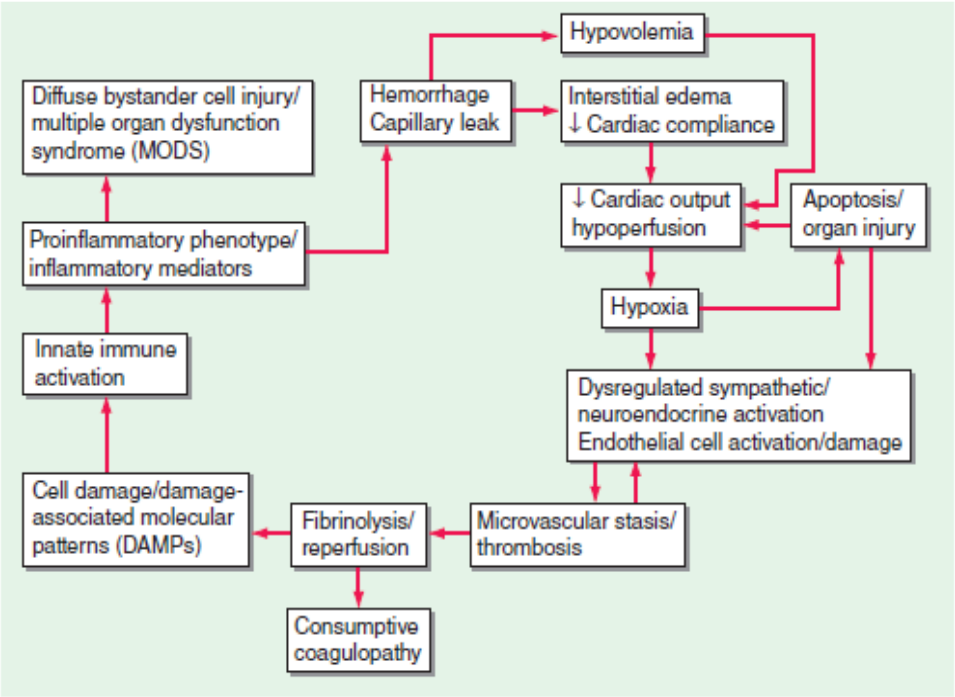
Sepsis:

Sepsis or severe sepsis is a life-hang over condition that arises when the body's reaction to infection causes injury to its own tissues and organs[9]. Fever or hypothermia, leukocytosis or leukopenia, tachypnea, and tachycardia are cardinal signs of the systemic response. Sepsis (Severe sepsis) is the harmful host response to infection, systemic response to proven or suspected infection plus some degree of organ hypofunction, I.e.: 1> Cardiovascular: arterial systolic blood pressure <90 mmHg or mean arterial blood pressure <70 mmHg that respond to administration IV fluids. 2> Renal: Urine output <0.5 ml/kg per hour for 1 hour despite adequate fluid resuscitation. 3> Respiratory: Pao2/Fio2<250 0r, if the lung is the only dysfunctional organ, <200. 4> hematologic: platelet count <80,000/uL or 50% decrease in platelet count from highest value recorded over previous 3 days. 5> unexplained metabolic acidosis: A pH < 7.30 or a base deficit >5.0 mEq/L and plasma Lactate level >1.5 times upper limit of normal for reporting laboratory. Septic shock is Sepsis with hypotension (arterial blood pressure <90 mmHg systolic, or 40 mmHg less than patient's normal blood pressure) for at least 1 h despite adequate fluid resuscitation or Need for vasopressors to maintain systolic blood pressure ≥90 mmHg or mean arterial pressure ≥70 mmHg. Signs of possibly harmful systemic response are Two or more of the following conditions: (1) fever (oral temperature >38°C [>100.4°F]) or hypothermia (<36°C [<96.8°F]); (2) tachypnea (>24 breaths/min); (3) tachycardia (heart rate >90 beats/min); (4) leukocytosis (>12,000/μL), leukopenia (<4000/μL), or >10% bands [10]

Sepsis is caused by an immune response actuate by an infection.[2][3] Most usual, the infection is bacterial, but sepsis can occur also be from fungi, viruses, or parasites.[2] Usual locations for the primary infection include lungs (most common), brain, urinary tract, skin, and abdominal organs in ICU. Risk factors include young or old age, a weakened immune system from conditions such as cancer or diabetes, major trauma, or burns[1]. Fever, chills, rapid breathing and heart rate, rash, confusion and disorientation are most common symptoms. In patients whose blood cultures are negative, the etiologic agent is often established by culture or microscopic examination of infected material from a local site; specific identification of microbial DNA or RNA in blood or tissue samples is also used. In some case series, a majority of patients with a clinical picture of severe sepsis or septic shock have had negative microbiologic data.

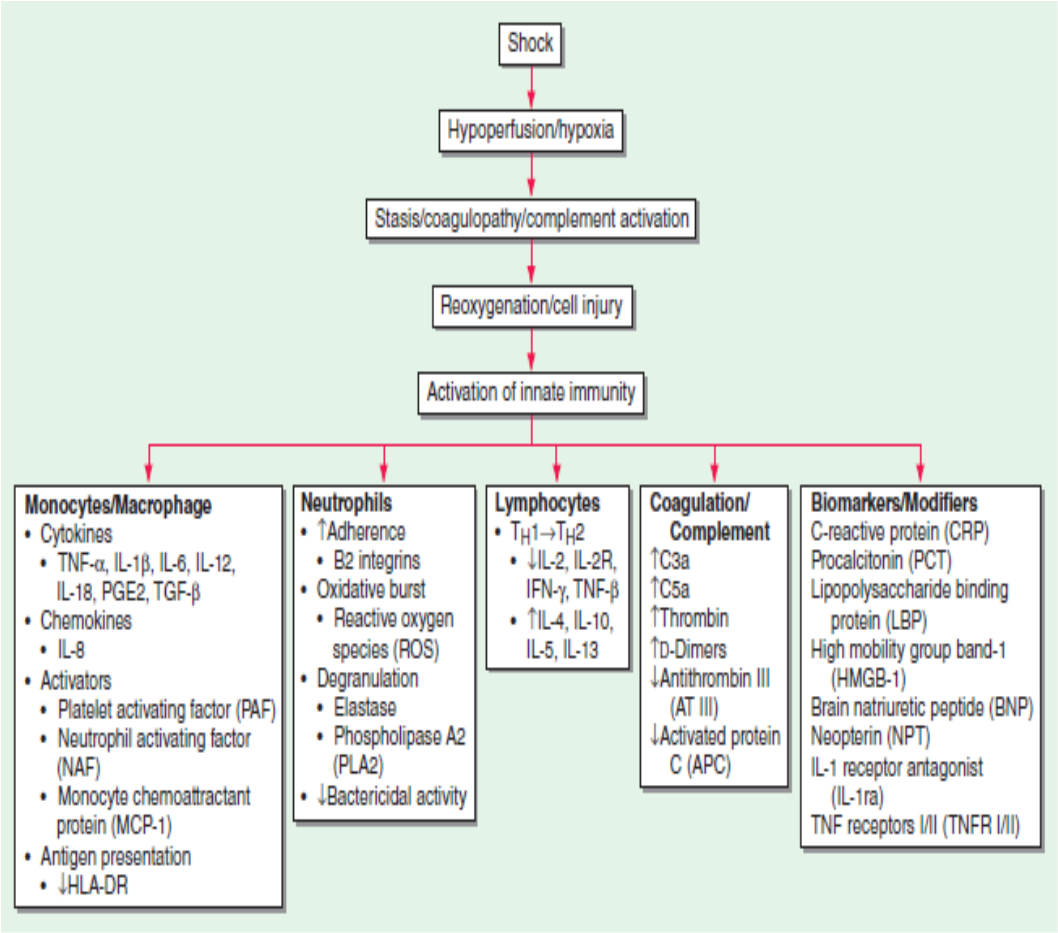
One of most well studied mediators of sepsis is lipopolysaccharide presents in the outer cell membrane of bacteria.[11] Recognition of microbial molecules by tissue phagocytes triggers the production and/or release of numerous host molecules (cytokines, chemokines, prostanoids, leukotrienes, and others) that increase blood flow to the infected tissue (*rubor*), enhance the permeability of local blood vessels (*tumor*), recruit neutrophils and other cells to the site of infection (*calor*), and elicit pain (*dolor*). These reactions are familiar elements of local inflammation, the body's frontline innate immune mechanism for eliminating microbial invaders. Activation of systemic response by neural and/or humoral communication with the hypothalamus and brainstem; these responses enhance local defenses by increasing blood flow to the infected area, increases the number of circulating neutrophils, and increase blood levels of numerous molecules (such as the microbial recognition proteins discussed above) that have anti-infective functions.[12]

Figure 1: Pathophysiology of shock.



Above schematic figure1, shows that in patient of sepsis and septic shock has inflammation leads to increase capillary leak & hypovolemia. As the intravascular volume decreases cardiac compliance decreases & so the cardiac output. This further leads to hypoperfusion & hypoxia of the tissue. Due to hypoxia there will be dysregulation of sympathetic action, neuroendocrine activation and endothelial cell activation & leads to damage. Simultaneously hypoxia also leads to apoptosis & organ injury. Now, as the endothelium is injured, microvascular stasis and development of thrombus occur. Due to this process the fibrinolysis process starts & reperfusion occur. Again the fibrinolysis starts cell damage in response to which innate immunity activates & pro-inflammatory & inflammatory mediators came into action & again the cycle continuous & organ dysfunction & further capillary leak. figure.2

Figure 2: Inflammatory mediators of sepsis.



Sepsis (severe sepsis) and septic shock produces various complication in the body, so sepsis should be identified as early as possible and should start the treatment as early as possible to reduces the mortality, delaying the treatment the mortality will increase.[12]

Complications: It involves multiple systems in body.

In cardiopulmonary system it causes Ventilation-perfusion mismatching produces a fall in arterial Po2 early in the course. Increasing alveolar epithelial injury and capillary permeability result in increased pulmonary water content, which decreases pulmonary compliance and interferes with oxygen exchange. In the absence of

pneumonia or heart failure, progressive diffuse pulmonary infiltrates and arterial hypoxemia occurring within 1 week of a known insult indicate the development of mild acute respiratory distress syndrome (ARDS) (200 mmHg < Pao2/Fio2 ≤ 300 mmHg), moderate ARDS (100 mmHg < Pao2/Fio2 ≤ 200 mmHg), or severe ARDS (Pao2/Fio2 ≤100 mmHg). Acute lung injury or ARDS develops in ~50% of patients with severe sepsis or septic shock. Respiratory muscle fatigue can exacerbate hypoxemia and hypercapnia. An elevated pulmonary capillary wedge pressure (>18 mmHg) suggests fluid volume overload or cardiac failure rather Than ARDS. Sepsis-induced hypotension from hypovolemia, dehydration from Antecedent disease or insensible fluid losses, vomiting or diarrhea, and polyuria. Depression of myocardial function, manifested as increased end diastolic and systolic ventricular volumes with a decreased ejection fraction, develops within 24 h in most patients with severe sepsis[13].

Adrenal Insufficiency The diagnosis of adrenal insufficiency may be very difficult in critically ill patients.

Renal Complications like Oliguria, azotemia, proteinuria, and nonspecific urinary casts are frequently found. Most renal failure is due to acute tubular necrosis induced by hypovolemia, arterial hypotension, or toxic drugs, although some patients also have glomerulonephritis, renal cortical necrosis, or interstitial nephritis.

Coagulopathy- Although thrombocytopenia occurs in 10–30% of patients, the underlying mechanisms are not understood. Platelet counts are usually very low (<50,000/μL) in patients with DIC; these low counts may reflect diffuse endothelial injury or microvascular thrombosis, yet thrombi have only infrequently been found on biopsy of septic.

Neurologic Complications -Delirium (acute encephalopathy) is often an early manifestation of sepsis. Depending on the diagnostic criteria used, it occurs in 10–70% of septic patients at some point during the hospital course**.**

Immunosuppression- Patients with severe sepsis often become profoundly immunosuppressed. Manifestations include loss of delayed type hypersensitivity reactions to common antigens, failure to control the primary infection, and increased risk for secondary infections. [13]

There is no specific diagnostic test for sepsis. Diagnostically sensitive Findings in a patient with suspected or proven infection include fever or hypothermia, tachypnea, tachycardia, and leukocytosis or leukopenia acutely altered mental status, thrombocytopenia, an elevated blood lactate level, respiratory alkalosis, or hypotension also should suggest the diagnosis. Various laboratory investigation to be done are CBC which shows leukocytosis or leukopenia, LFT which shows elevated bilirubin and elevated liver enzymes, urine can shows proteinuria, if thrombocytopenia is severe then there can be elevated prothrombin time, decrease fibrinogen, elevated D-Dimer in case of Disseminated intravascular coagulation, ABG suggestive of respiratory Alkalosis in initial phase, if respiratory muscle become fatigue there will be Metabolic Acidosis with accumulation of Lactate (Lactate Acidosis). X-ray may shows pneumonia and ARDS. USG Abdomen and chest can rule out local collection of fluid if present. CT scan and MRI are also used to rule of cause. Definitive etiologic diagnosis requires identification of the causative microorganism from blood, urine or a local site of infection.[12]

LACTATE:

In 1780 Lactate was first described as a substance in sour milk by the Swedish chemist, Karl Wilhelm Scheele.[14] After this discovery, it was followed by its first portrait in animals in the muscle tissue of hunted stags,by other Swedish chemist, Jons Jacob Berzelius, in 1807[15]. The Japanese chemist, Trasaburo Araki, showed that in states of oxygen deprivation, no matter how, mammals produced and excreted lactate.[16-19] The findings were render in experiments conducted by Hermann Zillessen.[20] The works done by Araki and Zillessen serve as the earliest demonstrations of the relationship between lactate production and tissue hypoxia. The German chemist and physician, Joseph Scherer,[21] in 1843, first showed the presence of lactate in human blood (post mortem) in a series of case reports involving 7 young women who died of puerperal fever. In 1851, he reported the same finding subsequently in the tissue fluids of a patient who had died of leukemia.[22] Carl Folwarczny in 1858 demonstrated of elevated lactate levels in the blood of a living patient .[23] The basis for the understanding of the significance of elevated lactate levels in critically ill patients was made after this observation.

LACTATE PRODUCTION, METABOLISM, AND EXCRETION

For metabolism of glucose, Glycolysis is the first step (Fig. 1), and its end product is pyruvate. After the formation of pyruvate, pyruvate can follow multiple metabolic pathways. It enter in the mitochondrial membranes and produce energy (38 molecules of ATP) by entering into tricarboxylic acid pathway. With the help of lactate dehydrogenase pyruvate can be converted into Lactate. It can be also be used as a substrate in gluconeogenesis for the production of glucose, or it can undergo transamination to alanine. When the pyruvate level is high it is converted to lactate so,

pyruvate to lactate conversion is reserved mainly for high pyruvate levels. pyruvate to lactate conversion is favored during hypoxic tissue (oxygen deprivation) conditions and several other clinically relevant conditions.[20]

Glucose 1 2ADP 1 2NAD1 / 2Pyruvate 1 2ATP 1 2NADH

Pyruvate 1 NADH 1 H1 4 Lactate 1 NAD1

Figure 3: Glycolysis Pathway.

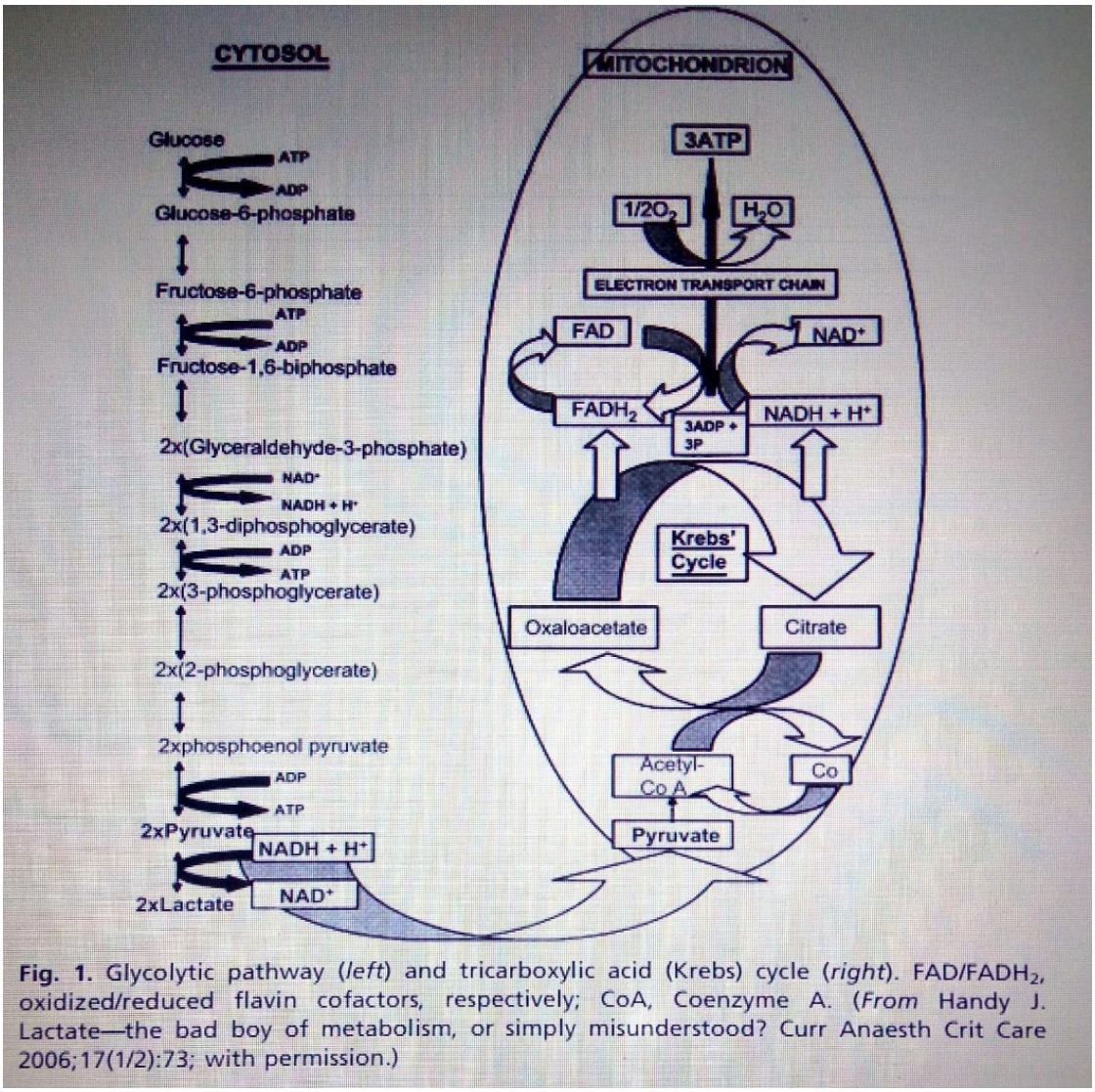


Fig. 1. Glycolytic pathway (*left*) and tricarboxylic acid (Krebs) cycle (*right*). FAD/$FADH_2$, oxidized/reduced flavin cofactors, respectively; CoA, Coenzyme A. (*From* Handy J. Lactate—the bad boy of metabolism, or simply misunderstood? Curr Anaesth Crit Care 2006;17(1/2):73; with permission.)

Conditions which favor the lactate productions from pyruvate are:

- Systemic hypo perfusion (due to any reason) necessitating anaerobic metabolism.
- Regional hypo perfusion (due to any reason) and dysfunction of microcirculation.
- Increased aerobic glycolysis, with pyruvate production aberrantly exceeding pyruvate dehydrogenase capacity. This condition may be seen in reaction to cytokine release, increased circulating catecholamine levels, or the accumulation of leukocytes at the site of inflammation/infection.
- In patient of sepsis and drug toxicity there is Mitochondrial dysfunction in which shunting of pyruvate away from the tricarboxylic acid cycle and formation of lactate.

In patient excessive alcohol use and cofactor deficiency states (beriberi), in which there is Impaired activity of pyruvate dehydrogenase, formation of acetyl coenzyme A from pyruvate is altered, this step is necessary for aerobic pathway to occur, so lactate formation takes place.

In unstressed patients normal blood lactate concentration is 0.5-1 mmol/L. Patients with critical illness those who are admitted to ICU less than 2 mmol/L of Lactate concentration can be consider as normal. Hyperlactatemia can be consider when there is persistent, mild to moderate (2-4 mmol/L) increase in blood lactate concentration without metabolic acidosis (by any cause), whereas lactic acidosis is consider when there is persistently high blood lactate levels (usually >4 mmol/L) in

The serum arterial lactate concentration tells the balance between net lactate production and net lactate consumption/clearance. This lactate concentration is generally less than 2 mmol/L. The amount of daily lactate production is about 1400 mmol, and although majority of the tissues can produce lactate, Lactate production which is physiological mainly produce from skeletal muscle (25%), skin (25%), brain

(20%), intestine (10%), and red blood cells (20%).[28] In pathologic conditions, eloquent lactate production occurs in other organs also.

In the critically ill who are admitted to ICU, lactate is produced in tissues outside the "usual lactate producers (other than physiological production) which includes lungs, white blood cells, and splanchnic organs. Physiologic lactate production by the lungs is very less leading to an arteriovenous difference in lactate levels close to zero across the lungs under physiologic conditions.[29] In critically ill patients who are admitted to ICU , Weil and colleagues[30] observed that venous blood samples from a pulmonary artery catheter yielded lactate concentrations equivalent to those in arterial blood. This finding has been replicated in subsequent works in patients with severe sepsis and acute lung injury/acute respiratory distress syndrome,[31-33] as well as in patients without significant hypoxemia(low oxygen in blood).[34]

Similarly, lactate is also released in supra physiologic amounts from the sites of infection and inflammation and is thought to be related to the increase glycolysis in the recruited and activated leukocytes at the sites of infection. WBC (white blood cell) have a very less capacity for aerobic (mitochondrial) ATP generation. Whenever they are activated, these cells rely mainly on augmented anaerobic glycolysis (low oxygen) to meet energy demands, ultimately leads to the lactate production in high amount not related to oxygen deprivation. In experimental models, there is significant increases were noted in blood lactate levels following exposure to endotoxin[35] and were thought to be a result of increases leukocyte lactate production.

Lactate is metabolized mainly in the liver (60%), kidneys (30%), and heart (10%). The periportal hepatocytes directly use lactate to produce glycogen and

glucose via the Cori cycle in the liver. In patients with chronic liver disease, there may be diminished lactate clearance and this can lead to elevated blood levels.[36,37]

The lactate is also used by renal cortex via the gluconeogenesis pathway to produce glucose.[38] Renal lactate clearance become impaired whenever there is reduction in renal blood flow because the renal cortex is very sensitive less blood through renal artery, in critically ill patients admitted to ICU with compromised renal blood flow, which leads to elevated lactate levels. If the renal threshold is exceeded Lactate can be excreted by the kidney (approximately 5–6 mmol/L). The serum concentration of lactate is generally less than 2 mmol/L; hence, lactate is not excreted in the urine in physiologic states.

Lactate as a bio-marker

A biomarker is defined as "a characteristic that is objectively measured and evaluated as an indicator of normal pathogenic processes, biologic processes, or pharmacologic responses to a therapeutic intervention."[39] The International Sepsis Forum Colloquium on Biomarkers of Sepsis described below.[40]

Uses of biomarkers Screening: It is helpful to identify patients at increased risk of inimical outcome to inform a prophylactic intervention or further diagnostic test

Diagnosis: It is helpful to establish a diagnosis to inform a treatment decision, and to do so more reliably, urgently, or less expensively than available methods

Risk stratification: It is helpful to identify subgroups of patients within a particular diagnostic group, who may experience greater benefit or harm with therapeutic intervention

Monitoring: It is helpful to measure response of the treatment to permit the titration of dose or duration of treatment and manage accordingly.

Surrogate end point: It is helpful to provide a more sensitive measure of the consequences of treatment that can substitute for a direct measure of a patient-centered outcome.

The presence of an elevated serum lactate level is strongly associated with morbidity and mortality in diverse populations of critically ill patients. Clinically, serum lactate is a potentially useful biomarker to risk-stratify patients with severe sepsis presenting to the emergency department (ED). In sepsis, elevated serum lactate level may be due to either impaired lactate clearance or excessive production. It is, therefore, plausible that an elevated serum lactate level is simply a manifestation of organ dysfunction, given that the clearance of lactate is dependent on hepatic and renal functions. Furthermore, investigators demonstrated an association between organ dysfunction and mortality in septic ED patients.[41-56]

Various studies:

In a Daniel et.ol[57] study at Germany of 451 patients, with a mortality of 44.8%; hyperlactatemia without vasopressor need (cryptic shock): 72 patients, mortality 35.3%; no hyperlactatemia with vasopressor need: 331 patients, mortality 27.7%; and absence of hyperlactatemia or overt shock: 134 patients, mortality 14.2% ($P < .001$), so it was concluded hyperlactatemia increases risk of death. Frequencies of the 3 most important sources of infection (abdominal, pulmonary, and urogenital) differed significantly between groups. Limitations- We had no data on comorbid conditions, most important preexisting liver disease, which is a potential confounder in Lactate interpretation and known to be associated with mortality.

The Christie JD et ol.study,[58] was carried out in Pennsylvania from 2005 to 2007: 830 patient were included. Mortality at 28 days was 22.9% and median serum lactate was 2.9 mmol/L. Intermediate (p - 0.024) and high serum lactate levels (p < 0.001) were associated with mortality in the non-shock subgroup. In the shock subgroup, intermediate (p - 0.022) and high serum lactate levels (p -0.001) were also associated with mortality. It was concluded that lactate was associated with mortality independent of clinically apparent organ dysfunction and shock in patients admitted to the ICU with severe sepsis. Limitations- Retrospective cohort study is potentially prone to selection, ascertainment, and misclassification bias, temporal delay potentially exists between the identification of sepsis and the measurement of serum lactate.

IN a Stephen Trzeciak study,[59] of 1,177 patients in Camden, In-hospital mortality was 15%, 25%, and 38% in low, intermediate, and high lactate groups, respectively. So, measurement of lactate in patients with infection and possible sepsis can affect assessment of mortality risk. Specifically, an initial lactate≥4.0mmol/l substantially increases the probability of acute phase death. Limitations: 1>the timing of measuring lactate in relation to the time that a clinician first identified the presence of an acute infection was not available for all subjects in this lactate registry and could only be inferred from a sample of high severity patients who also developed severe sepsis criteria. 2> fact that this study only included patients in whom lactate was measured by a clinician represents an inherent bias in the sample.3> registry did not capture comprehensive clinical information.

In a study of Tim C.Jansen[60], 394 patients in Dutch blood lactate levels at admission to the ICU (LacT0) and the reduction of lactate levels from T - 0 to T- 12 hours (LacT0–12) and from T - 12 to T - 24 hours (LacT12–24), were related to in hospital mortality. Reduction of lactate was associated with a lower mortality only in the sepsis group (LacT0–12: hazard ratio -0.34, p - 0.004 and -LacT12–24: HR 0.24, p - 0.003), but not in the LT group (LacT0–12; HR 0.78, p - 0.52 and LacT12–24; HR 1.30, p - 0.61). The prognostic values of LacT0, LacT0–12, and LacT12–24 were similar in hemodynamically stable and unstable patients (p-0.43). Regardless of the hemodynamic status, lactate reduction during the first 24 hours of ICU stay is associated with improved outcome only in septic patient. Limitation- 1>the group Classification might have changed during the 24 hours. For instance, a trauma patient with a hemorrhagic shock at admission could have developed ischemia-reperfusion damage or sepsis within 24 hours. 2> not collected indices to examine anaerobic or aerobic pathogenesis of hyperlactatemia (e.g., lactate to pyruvate ratio, liver function test, serum catecholamine concentration, or microcirculation imaging) 3>Did not register any form of advanced hemodynamic monitoring, such as cardiac output or SvO2, nor measured oxygen transport.

In a study of Paul A. van Beesta de[61], 74 patients in Europe, lactate levels were prospectively were obtained in a pre-hospital setting. Total population was divided into two groups, that is, a shock group and a non-shock group according to the predefined shock symptoms. The shock group was divided into two groups, that is, a lactate less than 4mmol/l (subgroup I) and a lactate of at least 4mmol/l. In about 50% of possible cases, lactate was measured in the pre-hospital setting. Median lactate in subgroup I (n=74) was 3.2 (1.5–3.9)mmol/l versus 5.0 (4.0–20.0)mmol/l in subgroup II (n=61) (P<0.0001). Significant differences were found in length of stay in

intensive care unit (P=0.03) or hospital (P=0.04) and mortality (subgroup I 12.2% vs. subgroup II 44.3%; P=0.002). In normotensive shock patients showing a lactate of at least 4mmol/l (n=27), the mortality was higher compared with normotensive shock patients with a lactate less than 4mmol/l (n=31) (35 vs. 7%; P<0.001). Limitation-1>this quality improvement project was not powered to yield conclusions pertaining to the obtained lactate measurements. 2>lactate was measured either from venous or capillary blood. 3> The lactate measurements are predominantly made in the Apeldoorn area and reflect such a single-center observation.

In study of Nathan I. Shapiro[62], in Boston 1278 patients, 105 (8.2%) deaths during hospitalization, with 55 (4.3%) of 1,278 deaths occurring in the first 3 days. Mortality rates increased as lactate increased: 43 (4.9%) of 877 of patients with a lactate level between 0 and 2.5 mmol/L died, 24 (9.0%) of 267 patients with a lactate level between 2.5 and 4.0 mmol/L died, and 38 (28.4%) of 134 patients with a lactate level greater than or equal to 4.0 mmol/L died. Lactate level greater than or equal to 4.0 mmol/L was 36% (95% confidence interval [CI] 27% to 45%) sensitive and 92% (95% CI 90% to 93%) specific for any death; it was 55% (95% CI 41% to 68%) sensitive and 91% (95% CI 90% to 93%)specific for death within 3 days. Limitations: collected no data about hemodynamics, comorbidities, or other Clinical conditions like systemic inflammatory response syndrome, severe sepsis, or septic shock.

In this study of Brad S. Karona[63], in USA 501 patient of suspicion sepsis patient, WBC, neutrophil, and IG counts were measured further classified as having severe sepsis or septic shock, There were 267 patients without sepsis; and 234 with sepsis, including 35 patients with severe sepsis or septic shock. Lactate had the highest OR (1.44, 95th% CI 1.20–1.73) for the prediction of sepsis; while WBC,

neutrophil count and percent (neutrophil/WBC) had OR > 1.00 ($p < 0.05$). All biomarkers had AUC < 0.70 and sensitivity and specificity< 70% at the optimal cut-off. Initial lactate was the best biomarker for predicting severe sepsis or septic shock, with an odds ratio (95th% CI) of 2.70 (2.02–3.61) and AUC 0.89 (0.82–0.96).Limitations- Sepsis definitions and guidelines have been updated since the 2012 guidelines were released, However reclassification according to updated definitions was not possible in the scope of the current study.

With a population of 1.22 billion, today India is grappling with various health issues. One of them is management of illnesses like 'Sepsis', which is taking a toll not only in rural India but is also prominent in urban India. Sepsis is a life-threatening medical condition triggered due to the body's response to an infection. It is often caused by microorganisms invading the body, either limited to a specific body part or can be widespread in the bloodstream.[6]

There are typically four progressive stages of Sepsis namely SIRS (Systematic Inflammatory Response Syndrome), SEPSIS, Septic Shock and MODS (Multiple Organ Dysfunction Syndrome). India currently tackles 750,000 cases of Sepsis every year of which overall mortality rate in ICU patients is 12.08% and in the severe stage Sepsis patients it is 59.26%.

"If empirical treatment for sepsis and bacteremia is holdup it will increase chances of mortality [6] as well as duration of stay [7] and cost [8,] so making timely recognition of infection and initiation of appropriate therapy an important goal so, the need for rapid diagnosis and risk stratification where biomarkers like lactate could be of use". Initial lactate level is very important to tell the prognosis, if the initial lactate level is high the prognosis of the patient is poor, so according to the level of initial

lactate level the risk can be judged. After starting the treatment, is patient responding to the treatment can also be judged with consequent lactate level. If the lactate level is increasing the prognosis of the patient is poor and should change the treatment like change in antibiotics. If the level of lactate is decreasing the prognosis of the patient is improving.[8]

MATERIALS AND METHODOLOGY

This study was done to identify the association between sepsis (severe sepsis and septic shock) and hyperlactatemia and clinical and laboratory manifestation of sepsis. . It was conducted for one and a half year from January 2016 to June 2017 in the ICU of Dhiraj hospital, Dept. of medicine of SBKS MI & RC, Sumandeep Vidyapeeth, Piparia. This was cross sectional, observational study. It was started after procuring approval for the study from the Institutional ethics committee.

All suspected and known cases of sepsis (> 18 years in age) coming to ICU of Dhiraj hospital were enrolled for the study. Diagnosis is made by thorough clinical examination and laboratory investigations and patients who gave written, informed consent for participating were included in the study. Drug induced hyperlactatemia, outside treated on the line of sepsis and the patients who did not give consent were excluded from the study.

Data collection: All cases enrolled were subjected to clinical and laboratory investigation for confirmation of sepsis. All included participants were subjected to Arterial blood gas analysis, Lactate level, CBC, RFT, LFT, RBS, Urine RM, ESR, chest X-ray, USG Abdomen. Laboratory evaluations were performed in the institutional pathology and biochemistry labs.

ABG for lactate were done immediately after conformation of sepsis on admission to ICU."

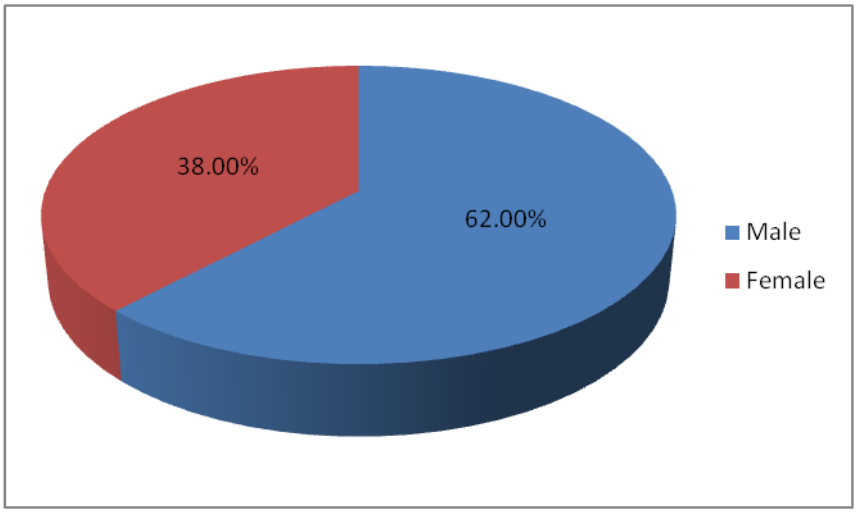
Lactate less than 2 (mmol/mm3) was considered normal.

RESULTS

Total 50 patients were enrolled in the study and were analyzed. Out of 50 patients 31(62%) were male, 19 (38%) were female (Table-1(a)). Past history of Diabetes mellitus was present in 17 (34%) patients, hypertension was present in 13 (26%) patients, tuberculosis in 3(6%) patients, ischemic heart disease in 4 (8%) patients, sickle cell hemoglobinopathies 2 (4%) patients bronchial asthma in 1 (2%) patient and liver disease in 1 patient (2%), (Table 1(b)).

Table 1(a): Demographic characteristic of study population

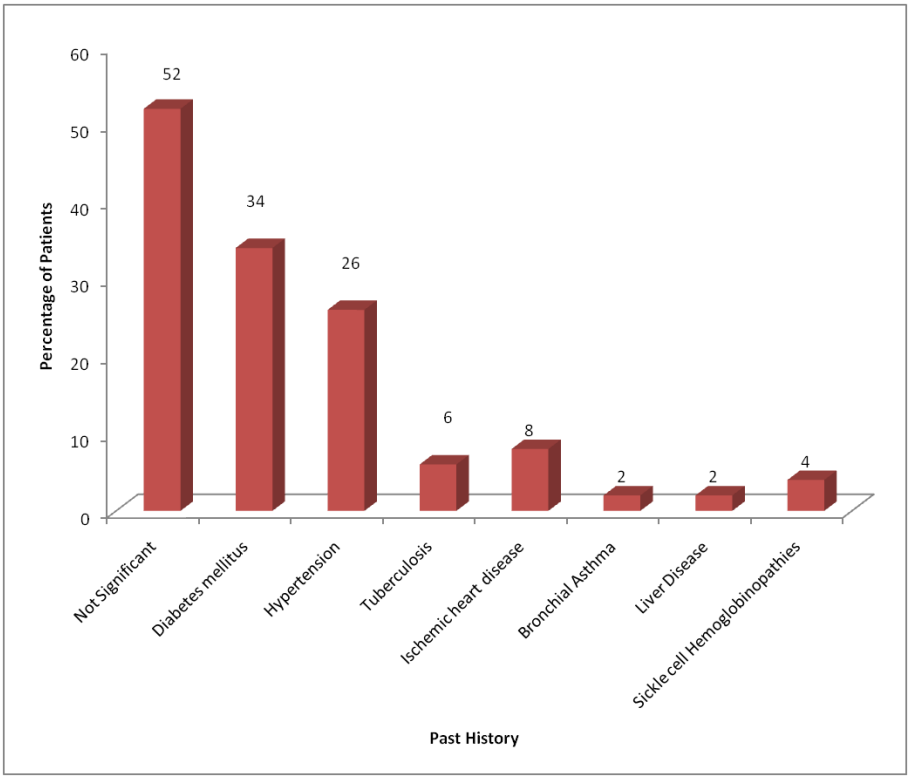
Sex	Frequency	Percent
Male	31	62.0
Female	19	38.0
Total	50	100.0



Graph 1(a): Graph showing Demographic characteristic of study population

Table 1(b): Past history in study population

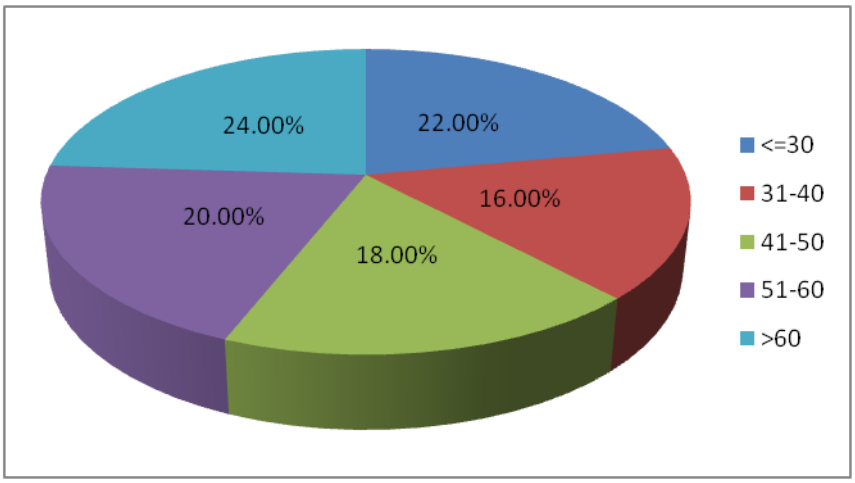
Past History	Frequency	Percent (n=50)
Not Significant	26	52.0
Diabetes mellitus	17	34.0
Hypertension	13	26.0
Tuberculosis	3	6.0
Ischemic heart disease	4	8.0
Bronchial Asthma	1	2.0
Liver Disease	1	2.0
Sickle cell Hemoglobinopathies	2	4.0



Graph 1(b): Graph showing Past history in study population

Table 2: Distribution of participants by their age

Age group	Frequency	Percent
<=30	11	22.0
31-40	8	16.0
41-50	9	18.0
51-60	10	20.0
>60	12	24.0
Total	50	100.0

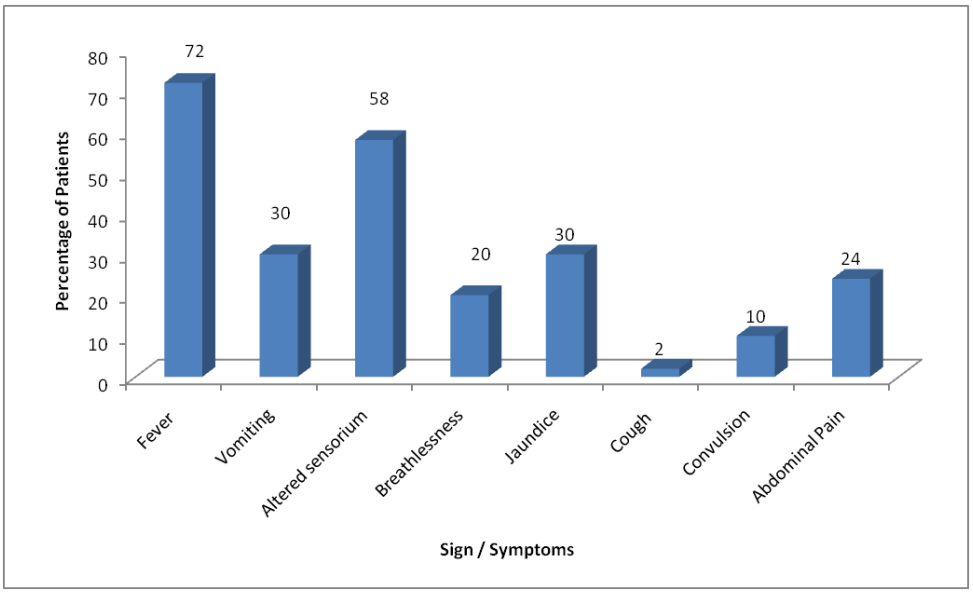


Graph 2: Graph showing Distribution of participants by their age

Out of 50 patients 11 (22%) patients were of age ≤ 30 years, 8 (16%) were between age of 31 to 40 years, 9(18%) patients were between 41 to 50 years of age, 10(20%) patient were between 51-60 years while 12 (24%) patient were >60 years (Table 2) in age. Thus majority of patients were males and were from the elder age groups.

Table 3: Frequency of symptoms/signs in study population.

Sign / symptoms	No of patients	Percentage (n=50)
Fever	36	72.0
Vomiting	15	30.0
Altered sensorium	29	58.0
Breathlessness	10	20.0
Jaundice	15	30.0
Cough	1	2.0
Convulsion	5	10.0
Abdominal Pain	12	24.0



Graph 3: Graph showing Frequency of symptoms/signs in study population

Out of 50 patients, fever was present in 36 (72%), vomiting was present in 15 (30%), altered sensorium was present in 29 (58%), breathlessness was present in 10 (20%), jaundice was seen in 15 patient(30%), cough was present in 1 (2%), convulsion was present in 5 (10%) and abdominal pain was present in 12 patients (24%).(Table 3)

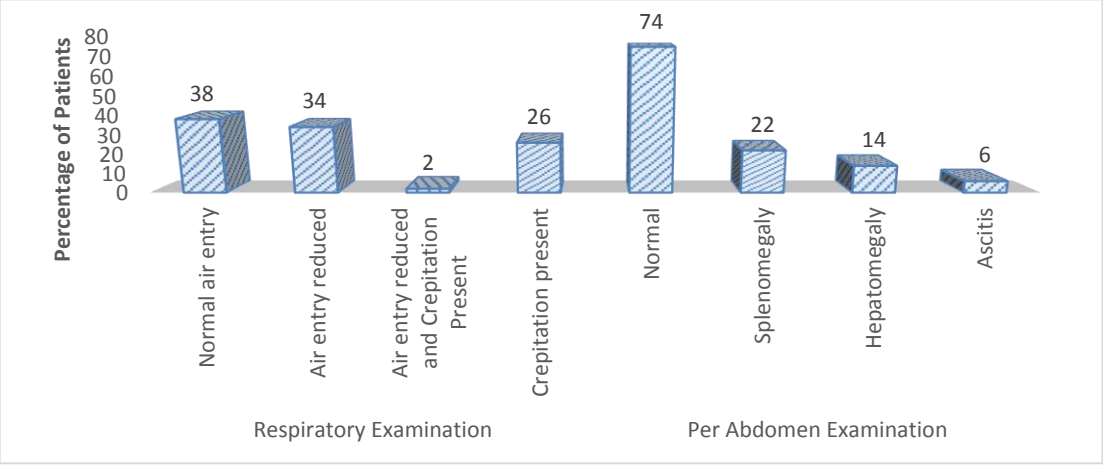
Table 4: Vitals of the study population:

Variable	N	Mean	Std. Deviation
Age in years	50	46.4	17.23
Pulse/ min	50	108.96	17.720
Respiratory Rate/min	50	28.04	5.043
Systolic blood pressure in mmhg	50	101.20	18.428
Diastolic blood pressure in mmhg	50	65.20	12.778

In the study population, mean age was 46.4 ± 17.23 years, mean pulse rate was 108.96 ± 17.72 per minute, mean respiratory rate was 28.04 ± 5.04 per minute, mean systolic blood pressure was 101 ± 18.428 mm Hg, mean Diastolic Blood Pressure 65.20 ± 12.778. Thus, most of the patients were elderly with increased pulse rate and respiratory rate whereas systolic and diastolic blood pressure were at the lower side.(Table 4)

Table 5: Examination findings of study participants:

General Examination	No of patients	Percentage (n=50)
Pallor	18	36.0
Icterus	18	36.0
Cyanosis	0	0
Clubbing	0	0
Lymphadenopathy	0	0
Edema	3	6.0
Abnormal CVS	0	0
Respiratory examination		
Normal air entry	19	38.0
Air entry reduced	17	34.0
Air entry reduced and Crepitation Present	1	2.0
Crepitation present	13	26.0
Normal	37	74.0
Splenomegaly	11	22.0
Hepatomegaly	7	14.0
Ascitis	3	6.0



Graph 4: Graph showing Examination findings of study participants

Out of 50 patients, pallor is present in 18 patients (36%), Icterus is present in 18 patients (36%), Edema is present in 3 patients (6%), cyanosis, clubbing, lymphadenopathy is not present in any patient. In respiratory system examination, normal air entry is present in 19 patients(38%), Air entry reduced in 17 patients(34%), air entry reduced and crepitation is present in 1 patient(2%), crepitation is present in 13 patients(26%). In per Abdomen Examination, normal in 37 patients (74%), splenomegaly is present in 11 patients (22%), Hepatomegaly is present in 7 patients (14%), and Ascites is present in 3 patients (6%) (Table 5)

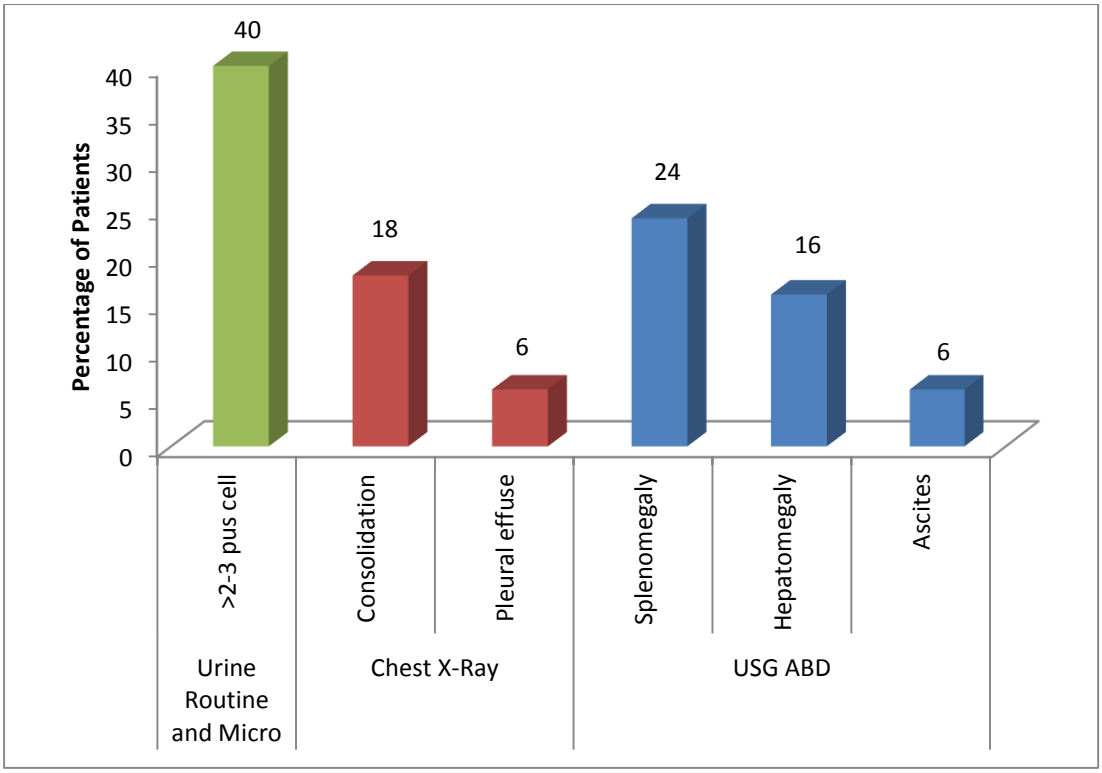
Table 6 (a): Result of investigation in study population

Variables	N	Mean	Std. Deviation
HB (mg/dl)	50	10.992000	2.7441842
TLC(per cumm^3)	50	16936.00	9887.423
Neutrophils	50	78.62	12.355
Lymphocyces	50	14.28	10.377
Monocytes	50	3.24	.960
Eosinophils	50	3.66	1.239
Platelet count(per cumm^3)	50	1.984200	1.2466905
Erythrocytes sedimentation rate	50	49.438	29.0262
Random blood sugar (mg/dl)	50	165.00	80.524
Lactate(mmol/mm3)	50	3.382400	2.1931420
pH	50	7.368980	.1478708
Partial pressure of co2(mm Hg)	50	31.978800	14.3914864
Partial pressure of 02 (mm Hg)	50	70.91	19.36
Bicarbonates (mEq/L)	50	18.912000	6.4374745
Oxygen saturation in blood(%)	50	92.154000	10.4665299
UREA(mg/dl)	50	107.24	95.321
CREATININE (mg/dl)	50	2.362000	1.8728882
BILIRUBIN(mg/dl)	50	2.974000	4.0765036
SGPT(U/l)	50	188.800	561.7456
SGOT(U/l)	50	183.2050	568.75657

Mean hemoglobin was 10.99 ± 2.74 mg/dl, mean total leukocyte count was 16938 ± 9887.423/cumm, mean neutrophils were 78.62 ± 12.35/cumm, mean lymphocytes were 14.28 ± 10.377/cumm, mean eosinophil count was 3.24 ± 0.960/cumm, mean basophil count was 3.66 ± 1.23/cumm, mean platelet count was 1.98 ± 1.24 mg/dl, mean erythrocyte sedimentation rate 49.43± 29.02 mg/dl, mean lactate level was 3.38 ± 2.19 mmol/mm3, mean pH was 7.36 ± o.14, mean partial pressure of carbon di oxide was 31.95 ± 14.39 mm Hg, partial pressure of oxygen was 70.91± 19.36 mm Hg, oxygen saturation of the blood was 92.15 ±10.46%, mean urea was 107.24 ±95.32 mg/dl, creatinine was 2.36 ±1.87 mg/dl, bilirubin was 2.97 ±4.04mg/dl, mean SGPT was 188 ±561.74 U/l while mean SGOT was 83 ±568.75 U/l (Table 6(a))

Table 6 (b) Investigation reports in study population

Urine Routine and micro	Frequency	Percent
>2-3 pus cell	20	40.0
Normal	30	60.0
Total	50	100.0
Chest x-ray		
Normal	38	76.0
Consolidation	9	18.0
Pleural effuse	3	6.0
	50	100%
USG ABD	Frequency	Percent (n=50)
Normal	35	70.0
Splenomegaly	12	24.0
Hepatomegaly	8	2.0
Ascites	3	6.0
	50	100%
Hyperlactatemia (mmol/L)	34	68.0
Normal	16	32.0
Total	50	100.0

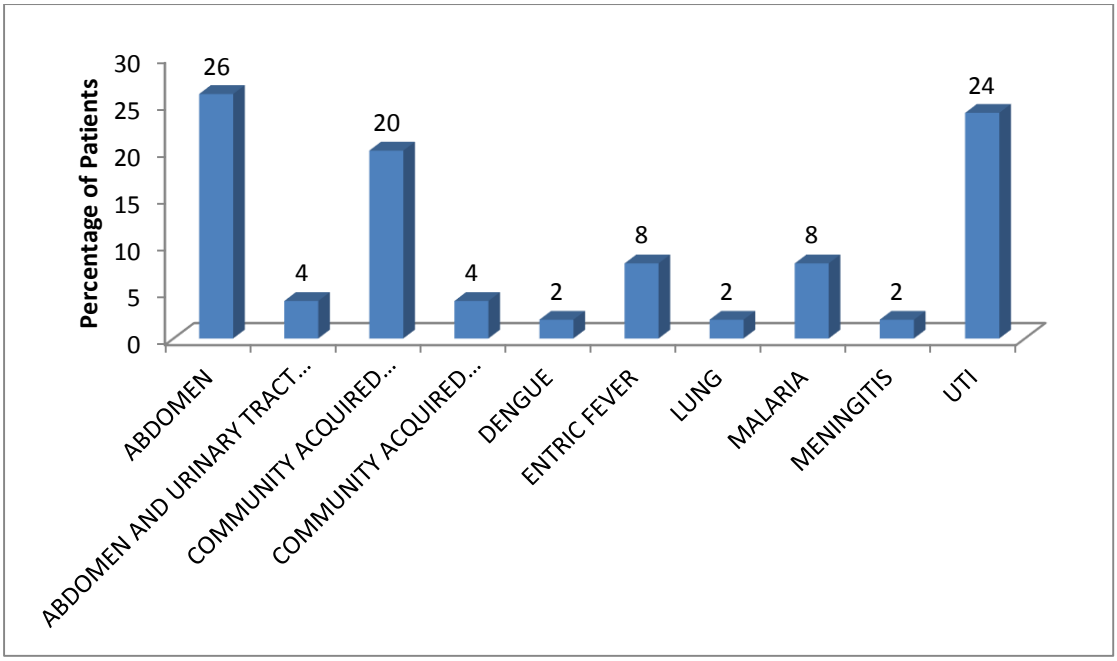


Graph 5: Graph showing Investigation reports in study population

Out of 50 patients urine microscopy showed >2-3 pus cells in 20 patients, chest x ray revealed consolidation in 9 (18%) and pleural effusion in 3 (6%). Ultra Sonography of abdomen revealed splenomegaly in 12 (24%) patients, hepatomegaly in 8 (16%) patients and ascites in 3 (6%) patients. Hyperlactatemia was present in 34 (68 %) patients (>2 mmol/L), in 16 (32%) it was (<2 mmol/L) (Table 6b)

Table 7: Source of infection in study population

Source of Infection	Frequency	Percent
ABDOMEN	13	26.0
ABDOMEN AND URINARY TRACT INFECTION	2	4.0
COMMUNITY ACQUIRED INFECTION	10	20.0
COMMUNITY ACQUIRED INFECTION AND URINARY TRACT	3	4.0
DENGUE	1	2.0
ENTRIC FEVER	4	8.0
LUNG	1	2.0
MALARIA	4	8.0
MENINGITIS	1	2.0
URINARY TRACT INFECTION	12	24.0
Total	50	100.0



Graph 6: Graph showing Source of infection in study population

Out of 50 patients, source of the infection in 13 patients (26%) was abdomen, in 2 patient (4%) source of infection from urinary tract and also from Abdomen, in 10 patients (20%) source of infection from community acquired pneumonia, in 3 patients (6%) source of infection from community acquired pneumonia and urinary tract infection, 1 patient(2%) has Dengue, 4 patients (8%) has Enteric fever, 4 patients (8%) has malaria, 1 patients(2%) has meningitis, in 12 patients (24%) has source of infection urinary tract. (Table 7)

Table 8: Number of patients survived and died

Outcome	Frequency	Percent
Discharge	24	48.0
Death	26	52.0
Total	50	100.0

Out of 50 patients, 24 (48%) patients were Discharge, and Death in 26 (52%) patients. (Table 8)

Table 9: Difference in the lactate level of those who recovered and those who died.

	OUTCOME	N	Mean	Std. Deviation	t-value	p-value
LACTATE (mmol/mm3)	Discharge	24	2.640000	1.6946540	-2.410	0.020
	Death	26	4.067692	2.4016083		

Out of 50 patients, 24 (48%) patients were discharged in whom mean lactate level was 2.64 ± 1.69, and 26 (52%) patients died in whom mean lactate level is 4.06 ± 2.4, p-0.020.

Thus, there was a significant difference in lactate levels of patients who survived and patients who died; p-0.020. It suggests that lactate may act as a biomarker of mortality of the patients in sepsis. (Table 9)

Table 10: Relation of hyperlactatemia with gender

		Hyperlactatemia		**Total**
		Hyperlactatemia	Normal	
SEX	Male	21	10	31
		67.7%	32.3%	100.0%
	Female	13	6	19
		68.4%	31.6%	100.0%
Total		34	16	50
		68.0%	32.0%	100.0%

	Value	**Df**	**P-value**
Pearson Chi-Square	.002	1	.960

Out of 31 male patients, hyperlactatemia was present in 21(67.7%) and in 10(32.3%) lactate level was normal. Amongst 19 females, hyperlactatemia was present in 13 (68.4%) while 6 (31.6%) had normal lactate level, p-0.960. Thus there was no significant difference in lactate levels between male and female patients. (Table 10)

Table 11: Odds of finding, symptoms and signs in patient with hyperlactatemia and without hyperlactatemia

Sign / symptoms	Hyperlactatemia	Normal	Chi-square	p-value	Odds Ratio(OR)
Fever	26(72.2)	10(27.8)	1.053	0.305	1.950
Vomiting	8(53.3)	7(46.7)	2.118	0.146	0.396
Altered sensorium	21(72.4)	8(27.6)	0.618	0.432	1.615
Breathlessness	7(70)	3(30)	0.023	0.880	1.123
Jaundice	11(73.3)	4(26.7)	0.280	0.597	1.435
Abdominal pain	6(50)	6(50)	2.351	0.125	0.357
Pallor	13(72.2)	5(27.8)	0.230	0.631	1.362
Icterus	13(72.2)	5(27.8)	0.230	0.631	1.362

There was no significant difference in odds of finding fever in patients with hyperlactatemia as compared to those with normal lactate level (OR-1.95, p-0.305). There was no significant difference in odds of finding with vomiting in patient with hyperlactatemia as compared to those with normal lactate level (OR-0.39, p-0.14). Similarly, there was no significant difference in odds of finding altered sensorium in patients with hyperlactatemia as compared to those with normal lactate level (OR-1.61, p-0.432), no significant difference in odds of finding with breathlessness in patients with hyperlactatemia as compared to those with normal lactate level (OR-1.123, p-0.880), no significant difference in odds of finding with jaundice in patients

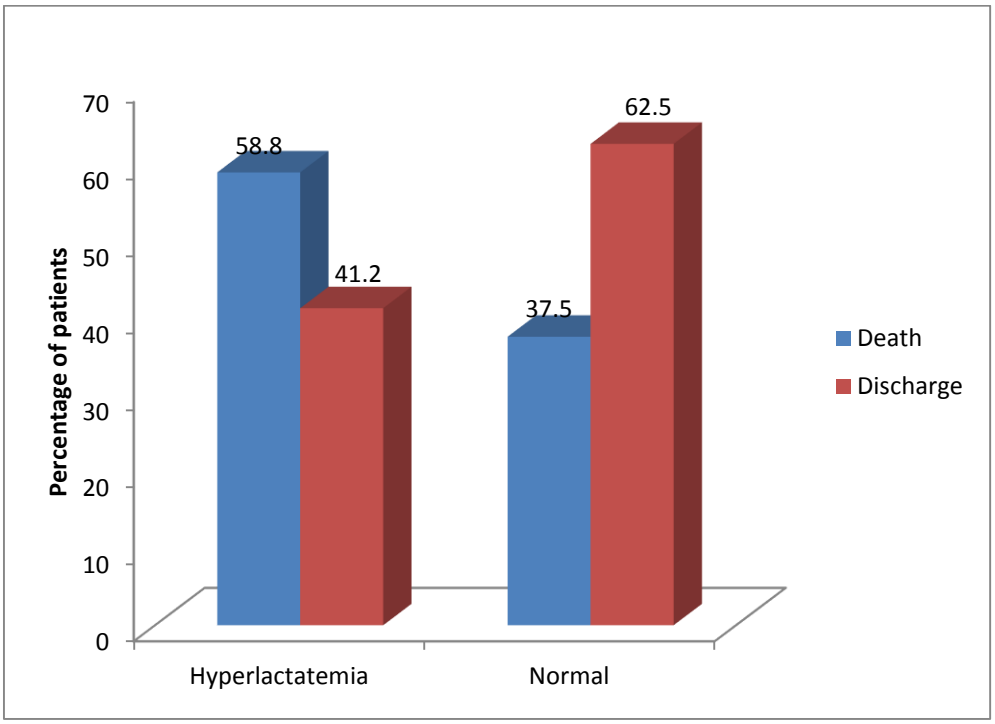
with hyperlactatemia as compared to those with normal lactate level (OR-1.435, p-0.597), no significant difference in odds of finding with abdominal pain in patients with hyperlactatemia as compared to those with normal lactate level (OR-0.357, p-0.125).

Pallor was present in 13 patient with hyperlactatemia while there was no pallor in 5 patients; there was no significant difference in odds of finding with pallor in patient with hyperlactatemia as compared to those with normal lactate level (OR-1.36, p-0.63). Icterus was present in 13 patient with hyperlactatemia and no icterus in 5 patients; thus there was no significant difference in odds of finding icterus in patients with hyperlactatemia as compared to those with normal lactate level (OR-1.36, p-0.631). (Table 11)

Table 12: Odds of death in hyperlactatemia and normal lactate.

Hyperlactatemia	OUTCOME		Total
	Death	Discharge	
Hyperlactatemia (mmol/mm3)	20	14	34
	58.8%	41.2%	100.0%
Normal	6	10	16
	37.5%	62.5%	100.0%
Total	26	24	50
	52.0%	48.0%	100.0%

Chi-Square Value	P-value	OR
1.982	.159	2.381



Graph 7: Graph showing Odds of death in hyperlactatemia and normal lactate.

Odds of death in patients with hyperlactatemia was 2.38 times more than in those with normal lactate; although this did not translate into a statistically significant figure. (p-0.159). (Table 12)

Table 13: Relation of various clinical and laboratory parameters with lactate levels

	Hyperlactatemia	**N**	**Mean**	**Std. Deviation**	**t-value**	**p-value**
AGE	Hyperlactatemia	34	46.79	17.255	.150	.881
	Normal	16	46.00	17.735		
PULSE (per min.)	Hyperlactatemia	34	110.88	16.077	1.121	.268
	Normal	16	104.88	20.759		
RR (per min.)	Hyperlactatemia	34	28.53	4.607	1.000	.322
	Normal	16	27.00	5.888		
SBP in mm Hg	Hyperlactatemia	34	100.18	19.728	-.569	.572
	Normal	16	103.38	15.675		
DBP in mm Hg	Hyperlactatemia	34	64.59	14.376	-.490	.627
	Normal	16	66.50	8.718		
HB (mg/dl)	Hyperlactatemia	34	10.852941	2.9291880	-.518	.607
	Normal	16	11.287500	2.3635778		
TLC per cumm^3	Hyperlactatemia	34	16938.24	10900.126	.002	.998
	Normal	16	16931.25	7613.472		
Neutrophil	Hyperlactatemia	34	77.00	13.755	-1.363	.179
	Normal	16	82.06	7.987		

Lymphocytes	Hyperlactatemia	34	16.21	11.62	1.968	.055
	Normal	16	10.19	5.29		
Monocytes	Hyperlactatemia	34	3.18	.999	-.679	.501
	Normal	16	3.38	.885		
Eosinophils	Hyperlactatemia	34	3.62	1.303	-.349	.728
	Normal	16	3.75	1.125		
Platelet counts per cumm^3	Hyperlactatemia	34	1.864412	1.2309843	-.990	.327
	Normal	16	2.238750	1.2813372		
Erythrocyte sedimentation rate	Hyperlactatemia	34	50.968	28.4927	.539	.592
	Normal	16	46.188	30.8161		
Random blood sugar (mg/dl)	Hyperlactatemia	34	161.76	71.123	-.411	.683
	Normal	16	171.88	99.893		
pH	Hyperlactatemia	34	7.368824	.1528470	-.011	.991
	Normal	16	7.369312	.1415315		
PCO2 (mm Hg)	Hyperlactatemia	34	30.518824	11.7129681	-1.047	.300
	Normal	16	35.081250	18.9644657		
PO2 (mm Hg)	Hyperlactatemia	34	70.12	20.64	-.416	.679
	Normal	16	72.58	16.81		
Bicarbonates (mEq/L)	Hyperlactatemia	34	18.052941	5.8028851	-1.388	.171
	Normal	16	20.737500	7.4876676		

Oxygen saturation in blood	Hyperlactatemia	34	91.285294	12.1620655	-.853	.398
	Normal	16	94.000000	5.2055099		
UREA (mm/dl)	Hyperlactatemia	34	93.62	75.573	-1.491	.142
	Normal	16	136.19	125.706		
CREATININE (mg/dl)	Hyperlactatemia	34	2.247059	1.5435566	-.629	.533
	Normal	16	2.606250	2.4745286		
BILIRUBIN (mg/dl)	Hyperlactatemia	34	3.414706	4.7268500	1.117	.269
	Normal	16	2.037500	1.9376532		
SGPT (U/l)	Hyperlactatemia	34	252.894	673.9582	1.181	.243
	Normal	16	52.600	49.4092		
SGOT (U/l)	Hyperlactatemia	34	230.9162	678.54825	.862	.393
	Normal	16	81.8188	166.28085		

There was no statistically significant difference between patients with hyperlactatemia and normal Lactate levels in respect to terms of Age (p-0.881), pulse rate (p-0.268), respiratory rate (p- 0.322), systolic blood pressure (p- 0.572), diastolic blood pressure (p-0.627), hemoglobin (p-0.607), total leucocyte count (p-0.998), neutrophils (p-0.179), lymphocytes (p-0.353), monocytes (p-0.501), eosinophils (p-0.78), Platelets (p-0.327), erythrocytes sedimentation rate(p-0.592), random blood sugar(p-0.683), pH (p-0.991), partial pressure of carbon-dioxide (p-0.300), partial pressure of oxygen (p-0.922), bicarbonates (p-0.171), oxygen saturation in blood (p-0.398), urea (p-0.142), creatinine (p-0.533), bilirubin (p-0.269), SGPT (p-o.243) and SGOT (p-0.393). (Table 13)

DISCUSSION

Lactate has been studied as a measure of illness severity in circulatory shock for several decades dating back to the 1800's [64, 65]. Although there are various explanations regarding the mechanisms responsible for lactate accumulation in severe sepsis and septic shock, it remains a robust surrogate marker for the development of multi-organ failure and poor outcome [66-70]. Evidence-based guidelines have recommended that an elevated lactate is sufficient to diagnose shock, irrespective of hypotension [69]. Sepsis with lactate level greater than or equal to 4 mmol/L is associated with high mortality and is an indication to initiate treatment protocols and care bundles [70]

We also observed that in patients admitted to ICU with signs and symptoms of sepsis, a single measurement of arterial lactate provides risk-stratification information about in hospital mortality. We measured lactate in a systematic fashion and used the objective endpoint of all-cause mortality. The mortality rate of 58.8 % for patients with a lactate level greater than or equal to 2.0 mmol/mm3 was significantly greater (p-0.020) than that in patients with normal lactate level. Thus, it clearly demonstrates that a lactate level may be helpful in identifying a high-risk patient population in the ICU. This finding was consistent with results in previous studies.

Shapiro et al[62] reported an all-cause mortality rate of 28% for patients with lactate level greater than or equal to 4.0 mmol/mm3 and suggested that serum lactate level may be helpful in identifying a high-risk patient population in the Emergency department. Seminal work by Broder and Weil et al[81] studied 56 patients in shock from a variety of causes and found a mortality rate of 89% when a single lactate value was greater than or equal to 4 mmol/L.

Aduen et al[79] investigated lactate levels in a cross-section of 180 undifferentiated ICU patients. They found that lactate level was significantly higher in non survivors, regardless of blood pressure. Other authors have focused on patients specifically with septic shock.

Bakker et al[82] focused on 48 ICU patients with septic shock and found that initial and serial blood lactate levels were superior to pulmonary arterial catheter–derived data in predicting mortality.

Vincent et al[44], Bakker et al,[42] and Falk et al[78] found that serial lactate levels predicted mortality in ICU patients with septic shock but that initial levels had less of a prognostic ability.

Frequencies of the three most important sources of infection (abdominal, pulmonary, and urosepsis) differed significantly between groups in our study. This might be associated with different strains of pathogens; but, unfortunately, we had no data on the strain of the pathogen. These associations have not been reported before. A larger study, including 1948 patients, showed a higher frequency of pneumonia in severe sepsis and cryptic shock and a higher frequency of urosepsis in dysoxic shock, in contrast to our results [17]. The different patterns may be attributable to the overall different patient population in the study by Ranzani et al [80] who recruited patients admitted to all areas of the hospital (whereas only patients admitted to an ICU were included in our study) with a high proportion of patients without shock, low frequency of abdominal infection, and the study taking place in an emerging nation.

There is no generally accepted cutoff defining hyperlactatemia. A single study reported an increase in mortality for lactate levels more than 1.4 mmol/L [70]; but most

studies use 2 [71, 72, 74, 75] or 2.5 [73, 76, 77] mmol/L as lowest cutoffs to define elevated lactate levels. So we have taken cut off 2mmol/l.

We also observed that there was no association of hyperlactatemia with age, sex like in other studies [57-63], suggesting that age and gender do not affect the lactate levels in cases of sepsis.

In our study we observed that there was no significant difference between patients of sepsis with hyper lactatemia and normal lactate levels in terms of laboratory investigation like hemoglobin, total leukocytes count, platelet, creatinine, SGPT, SGOT, glucose. Other studies like one by *D.O. Thomas et* al[57] have also reported similar observations but they reported deranged leucocytes, creatinine, SGPT, SGOT in majority of the patient of sepsis suggesting the involvement of multiple organ systems.

In our study we didn't find any significant difference in vitals of the patients with high lactate and normal lactate levels in sepsis, but we observed that majority of the patients of sepsis had lower systolic and diastolic blood pressure along with increase in pulse rate.

Daniel O. Thomas-Rueddel reported that patients who had septic shock had the high lactate levels (p-0.01), We also observed that most of the patient of sepsis has low pH (acidosis), and there is low Po2 (hypoxia), high Pco2 (hypercapnia).

SUMMARY

Sepsis is a systemic, deleterious host response to infection leading to severe sepsis (acute organ dysfunction secondary to documented or suspected infection) and septic shock. Sepsis is a contributing factor in >200,000 deaths per year in the United States. The incidence of severe sepsis and septic shock has increased over the past 30 years, and the annual number of cases is now >750,000 (~3 per 1000 population). With a population of 1.22 billion, today India is grappling with various health issues. As sepsis is very common in patients admitted to ICU, so the early diagnosis and severity of the sepsis should be an important step in the management of sepsis. It has been suggested that as the level of lactate increase, the severity of sepsis is more. So, we planned to see the lactate level in patients of sepsis, and its cor relation with patients of sepsis admitted to our hospital in icu.

This prospective study was carried out in Medicine department of SBKS Medical Institute and research center, Piparia, Vadodara. A total number of 50 patients of sepsis were included in the study as per the inclusion and exclusion criteria. . All included participants were subject to Arterial blood gas analysis for Lactate level, CBC, RFT, LFT, RBS, Urine RM, ESR, chest X-ray, USG Abdomen. Laboratory evaluations were performed in the institutional pathology and biochemistry labs.

Total 50 of patients with sepsis were enrolled according to the inclusion and exclusion criteria in this prospective observational study.

Out of 50 patients 31(62%) were male, 19 (38%) were female. , mean age was 46.4 ± 17.23 years. Most of patient has the chief complains of fever, altered sensorium, breathlessness. mean pulse rate was 108.96 ± 17.72 per minute, mean respiratory rate

was 28.04 ± 5.04 per minute, mean systolic blood pressure was 101 ± 18.428 mm Hg, mean Diastolic Blood Pressure 65.20 ± 12.778.

Out of 50 patients, pallor is present in 18 patients (36%), Icterus is present in 18 patients (36%), Edema is present in 3 patients (6%), cyanosis, clubbing, lymphadenopathy is not present in any patient. In respiratory system examination, normal air entry is present in 19 patients(38%), Air entry reduced in 17 patients(34%), air entry reduced and crepitation is present in 1 patient(2%), crepitation is present in 13 patients(26%). In per Abdomen Examination, normal in 37 patients (74%), splenomegaly is present in 11 patients (22%), Hepatomegaly is present in 7 patients (14%), and Ascites is present in 3 patients (6%).

Mean hemoglobin was 10.99 ± 2.74 md/dl, mean total leukocyte count was 16938 ± 9887.423/ cumm, mean neutrophils were 78.62 ± 12.35, mean lymphocytes were 14.28 ± 10.377, mean eosinophil count was 3.24 ± 0.960, mean basophil count was 3.66 ± 1.23, mean platelet count was 1.98 ± 1.24 mg/dl, mean erythrocyte mg/dl, mean lactate level was 3.38 ± 2.19, mean pH was 7.36 ± o.14, mean partial pressure of carbon di oxide was 31.95 ± 14.39, partial pressure of oxygen was 70.91± 19.36, oxygen saturation of the blood was 92.15 ±10.46, mean urea was 107.24 ±95.32 mg/dl, creatinine was 2.36 ±1.87 mg/dl, bilirubin was 2.97 ±4.04mg/dl, mean SGPT was 188 ±561.74 U/l while mean SGOT was 83 ±568.75 U/l

Out of 50 patients source of infection was mainly from urinary tract, community acquired pneumonia, abdomen.

Out of 50 patients, 24 (48%) patients were discharged in whom mean lactate level was 2.64 ± 1.69, and 26 (52%) patients died in whom mean lactate level is 4.06 ± 2.4, p-0.020.

Thus, there was a significant difference in lactate levels of patients who survived and patients who died; p-0.020.

So, it was concluded that elevated levels of lactate in serum are associated with higher mortality and poor prognosis. Serum lactate serves as the biological marker of prognosis and mortality in patients of sepsis.

CONCLUSION

In patients of sepsis, elevated levels of lactate in serum are associated with higher mortality and poor prognosis. Serum lactate serves as the biological marker of prognosis and mortality in patients of sepsis.

BIBLIOGRAPHY

1. Suetrong B, Walley KR .Chest 2015 Sep 17. Doi: 10.1378/chest.15-1703.
2. Mizock BA, Falk JL. Lactic acidosis in critical illness. Crit Care Med 1992;20(1): 80–93.
3. Woods HF, Cohen R. Clinical and biochemical aspects of lactic acidosis. Oxford (UK): Blackwell Scientific; 1976.
4. Thomas GW, Mains CW, Slone DS, et al. Potential dysregulation of the pyruvate dehydrogenase complex by bacterial toxins and insulin. J trauma 2009; 67:628-633.
5. *Kasper D,Fauci, Hauser s, Longo D, Jameson J, Loscalzo J, Harrison principle of internal medicine, 19th ed. USA, Minion pro cenveu publisher, services; 2015.p.1745-1747.*
6. M. A. Puskarich, S. Trzeciak, N. I. Shapiro et al., "Association between timing of antibiotic administration and mortality from septic shock in patients treated with a quantitative resuscitation protocol," Critical Care Medicine, vol. 39, no. 9, pp. 2066–2071, 2011.
7. A. F. Shorr, S. T. Micek, E. C. Welch, J. A. Doherty, R. M. Reichley, and M. H. Kollef, "Inappropriate antibiotic therapy in Gram-negative sepsis increases hospital length of stay," Critical Care Medicine, vol. 39, no. 1, pp. 46–51, 2011.
8. A. L. Cheah, T. Spelman, D. Liew et al., "Enterococcal bacteraemia: factors influencing mortality, length of stay and costs of hospitalization," Clinical Microbiology and Infection, vol. 19, no. 4, pp. E181–E189, 2013.

9. *Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, Hotchkiss RS, Levy MM, Marshall JC, Martin GS, Opal SM, Rubenfeld GD, van der Poll T, Vincent JL, Angus DC (February 23, 2016).* "The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)". *JAMA. 315: 801–10*

10. *Kasper D,Fauci, Hauser s, Longo D, Jameson J, Loscalzo J, Harrison principle of internal medicine, 19th ed. USA, Minion pro cenveu publisher, services; 2015.p.1751-1752.*

11. John Marx, Robert Hockberger, Ron Walls, Rosen's Emergency Medicine Concepts and Clinical Practice, 8th ed. USA, Elsevier publisher, services; 2014.p.68

12. *Kasper D,Fauci, Hauser s, Longo D, Jameson J, Loscalzo J, Harrison principle od internal medicine, 19th ed. USA, Minion pro cenveu publisher, services; 2015.p.1744-1750.*

13. John Marx, Robert Hockberger, Ron Walls, Rosen's Emergency Medicine Concepts and Clinical Practice, 8th ed. USA, Elsevier publisher, services; 2014.p.69-70.

14. Scheele KW. Opuscula chemica et physica. Leipzig (Germany): Kessinger Publishing Company; 1789. p. 316.

15. Philosophical Magazine Series 4. Taylor & Francis; 1851.

16. Araki T. Ueber die Bildung von Milchsa ¨ure und Glycose im Organismus bei Sauerstoffmangel. Z Physiol Chem 1891;15:335–70 [in German].

17. Araki T. Ueber die Bildung von Milchsa ¨ure und Glycose im Organismus bei Sauerstoffmangel. Zweite Mittheilung: Ueber die Wirkung von Morphium, Amylnitrit, Cocain. Z Physiol Chem 1891;15:546–61 [in German].

18. Araki T. Ueber die Bildung von Milchsa ¨ure und Glycose im Organismus bei Sauerstoffmangel. Dritte Mittheilung. Z Physiol Chem 1892;16:453–9 [in German].

19. Araki T. Ueber Bildung von Glycose und Milchsa ¨ure bei Sauerstoff mangel. Entgegnung. Z Physiol Chem 1892;16:201–4.

20. Zillessen H. Ueber die Bildung von Milchsa ¨ure und Glykose in den Organen beigesto ¨rter Circulation und bei der Blausa ¨urevergiftung. Z Physiol Chem 1891;15:387–404 [in German].

21. Scherer JJ. Chemische und Mikroskopische Untersuchungen zur Pathologie angestellt an den Kliniken des Julius-Hospitales zu Wu ¨rzburg. Heidelberg (Germany): C.F. Winter; 1843.

22. Scherer JJ. Eine Untersuchung des Blutes bei Leuka ¨mie. Verhandlungen der Physikalisch-Medicinischen Gesellschaft im Wu ¨rzburg 1851;2:321–5 [in German].Lactate: Biomarker and Potential Therapeutic Target 321

23. Folwarczny Carl. Handbuch Der Physiologischen Chemie, Mit Ru ¨cksicht Auf Pathologische Chemie Und Analytische Methoden. Wien (Switzerland): Verlag von Sallmayer & Comp; 1863.

24. Mizock BA, Falk JL. Lactic acidosis in critical illness. Crit Care Med 1992;20(1): 80–93.

25. Woods HF, Cohen R. Clinical and biochemical aspects of lactic acidosis. Oxford (UK): Blackwell Scientific; 1976.

26. Thomas GW, Mains CW, Slone DS, et al. Potential dysregulation of the pyruvate dehydrogenase complex by bacterial toxins and insulin. J trauma 2009; 67:628-633.

27. Uribarri J, oh MS, Carroll HJ. D-lactic acidosis.A review of clinical presentation ,biochemical features, and pathophysiologic mechanism.1998 Mar. 77(2):73-82.

28. Levy B. Lactate and shock state: the metabolic view. Curr Opin Crit Care 2006; 12(4):315–21.

29. Harris P, Bailey T, Bateman M, et al. Lactate, pyruvate, glucose, and free fatty acid in mixed venous and arterial blood. J Appl Physiol 1963;18:933–6.

30. Weil MH, Michaels S, Rackow EC. Comparison of blood lactate concentrations in central venous, pulmonary artery, and arterial blood. Crit Care Med 1987;15: 489–90.

31. Nimmo GR, Armstrong IR, Grant IS. Sampling site for blood lactate estimation: arterial or mixed venous? Clin Intensive Care 1993;4:8–9.

32. Brown SD, Clark C, Gutierrez G. Pulmonary lactate release in patients with sepsis and the adult respiratory distress syndrome. J Crit Care 1996;11:2–8.

33. Douzinas EE, Tsidemiadou PD, Pitaridis MT, et al. The regional production of cytokines and lactate in sepsis-related multiple organ failure. Am J Respir Crit Care Med 1997;155:53–9.

34. De Backer D, Creteur J, Zhang H, et al. Lactate production by the lungs in acute lung injury. Am J Respir Crit Care Med 1997;156(4 Pt 1):1099–104.

35. Haji-Michael PG, Ladriere L, Senerb A, et al. Leukocyte glycolysis and lactate output in animal sepsis and ex vive human blood. Metabolism 1999;48(6):779–85.

36. Mizock BA. Hyperlactatemia in acute liver failure: decreased clearance versus increased production. Crit Care Med 2001;29(11):2225–6.

37. Bihari D, Gimson AE, Lindridge J, et al. Lactic acidosis in fulminant hepatic failure. Some aspects of pathogenesis and prognosis. J Hepatol 1985;1(4):405–16.

38. Zhang H, Vincent JL. Oxygen extraction is altered by endotoxin during tamponade-induced stagnant hypoxia in the dog. Circ Shock 1993;40(3):168–76.

39. Biomarkers Definitions Working Group. Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. Clin Pharmacol Ther 2001;69: 89–95.

40. Marshall JC, Reinhart K, International Sepsis Forum. Biomarkers of sepsis. Crit Care Med 2009;37(7):2290–8.

41. AduenJ, Bernstein WK, KhastgirT, etal: The use and clinical importance of a substratespecific electrode for rapid determination of blood lactate concentrations. JAMA 1994; 272:1678–1685

42. Bakker J, Gris P, Coffernils M, et al: Serial blood lactate levels can predict the development of multiple organ failure following septic shock. Am J Surg 1996; 171:221–226

43. Abramson D, Scalea TM, Hitchcock R, et al: Lactate clearance and survival following injury. J Trauma 1993; 35:584–589

44. Vincent JL, Dufaye P, Berre J, et al: Serial lactate determinations during circulatory shock. Crit Care Med 1983; 11:449–451

45. Manikis P, Jankowski S, Zhang H, et al: Correlation of serial blood lactate levels to organ failure and mortality after trauma. Am J Emerg Med 1995; 13:619–622

46. Schulman AM, Claridge JA, Carr G, et al: Predictors of patients who will develop prolonged occult hypoperfusion following blunt trauma. J Trauma 2004; 57:795–800

47. Nguyen HB, Rivers EP, Knoblich BP, et al: Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. Crit Care Med 2004; 32:1637–1642

48. Shapiro NI, Howell MD, Talmor D, et al: Serum lactate as a predictor of mortality in emergency department patients with infection. Ann Emerg Med 2005; 45:524–528

49. Trzeciak S, Dellinger RP, Chansky ME, et al: Serum lactate as a predictor of mortality in patients with infection. Intensive Care Med 2007; 33:970–977

50. Howell MD, Donnino M, Clardy P, et al: Occult hypoperfusion and mortality in patients with suspected infection. Intensive Care Med 2007; 33:1892–1899

51. Levraut J, Ciebiera JP, Chave S, et al: Mild hyperlactatemia in stable septic patients is due to impaired lactate clearance rather than overproduction. Am J Respir Crit Care Med 1998; 151:1021–1026

52. Revelly JP, Tappy L, Martinez A, et al: Lactate and glucose metabolism in severe sepsis and cardiogenic shock. Crit Care Med 2005; 33: 2235–2240

53. Duke T: Dysoxia and lactate. Arch Dis Child 1999; 81:343–350

54. Laski ME, Wesson DE: Lactic acidosis. In: Acid-Base and Electrolyte Disorders: A Companion to Brenner and Rector's the Kidney. Dubose TD, Hamm LL (Eds). Philadelphia, WB Saunders, 2000, pp 83–107

55. Shapiro N, Howell MD, Bates DW, et al: The association of sepsis syndrome and organ dysfunction with mortality in emergency department patients with suspected infection. Ann Emerg Med 2006; 48:583–590

56. Bone RC, Balk RA, Cerra FB, et al: Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Chest 1992; 101:1644–1655.

57. Daniel O. Thomas-Rueddel, MD, Bernhard Poidinger, MD, Manfred Weiss, MD, Friedhelm Bach, MD, Karin Dey, MD, Helene Häberle, MDf, Udo Kaisers, MD , Hendrik Rüddel, MD, Dirk Schädler, MD, Christian Scheer, MD, Torsten Schreiber, MD, Tobias Schürholz, MD, Philipp Simon, MD, Armin Sommerer, MD, Daniel Schwarzkopf, MSc, Andreas Weyland, MD, Gabriele Wöbker, MD, Konrad Reinhart,MD, Frank Bloos, MD, PhD Hyperlactatemia is an independent predictor of mortality and denotes distinct subtypes of severe sepsis and septic shock. J Crit Care (2014)203-207.

58. Mikkelsen ME[1], Miltiades AN, Gaieski DF, Goyal M, Fuchs BD, Shah CV, Bellamy SL, Christie JD: Mark E. Mikkelsen, MD, MS; Andrea N. Miltiades, BA; David F. Gaieski, MD; Munish Goyal, MD; Barry D. Fuchs, MD; Chirag V. Shah, MD, MS; Scarlett L. Bellamy, ScD; Jason D. Christie, MD, M. Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. Crit Care Med 2009 Vol. 37, No. 5

59. Stephen Trzeciak R.Phillip Dellinger MichaelE. Chansky RyanC. Arnold Christa Schorr Barry Milcarek StevenM. Hollenberg JosephE. Parrillo. Serum lactate as a predictor of mortality in patients with infection. Intensive Care Med (2007) 33:970–97

60. Tim C. Jansen, MD, Jasper van Bommel, MD, PhD, Paul G. Mulder, PhD, Alexandre P. Lima, MD, Ben van der Hoven, MD, Johannes H. Rommes, MD, PhD, Ferdinand T. F. Snellen, MD, and Jan Bakker, MD, PhD. Prognostic Value

of Blood Lactate Levels: Does the Clinical Diagnosis at Admission Matter?.J Trauma. 2009; 66:377–385

61. Paul A. van Beesta,d,e, Peter Jan Mulderc, Suparto Bambang Oetomoc, Bert van den Broeke, Michael A. Kuiperd,f and Peter E. Spronkb,f.Measurement of lactate in a prehospital setting is related to outcome. European Journal of Emergency Medicine 2009, 16:318–32

62. Nathan I. Shapiro, MD, MPH Michael D. Howell, MD Daniel Talmor, MD, MPH Larry A. Nathanson, MD Alan Lisbon, MD Richard E. Wolfe, MD J. Woodrow Weiss, MD.Serum Lactate as a Predictor of Mortality in Emergency Department Patients With Infection. Ann Emerg Med. 2005;45:524-528.

63. Brad S. Karona, Nicole V. Tolana, Amy M. Wockenfusa, Darci R. Blocka, Nikola A. Baumanna, Sandra C. Bryantb, Casey M. Clementsc. Evaluation of lactate, white blood cell count, neutrophil count, procalcitonin and immature granulocyte count as biomarkers for sepsis in emergency department patiens. 2017, Published by Elsevier.

64. Weil MH, Afifi AA: Experimental and clinical studies on lactate and pyruvate as indicators of the severity of acute circulatory failure (shock). Circulation 1970, 41:989-1001.

65. Kompanje EJ, Jansen TC, Hoven van der B, Bakker J: The first demonstration of lactic acid in human blood in shock by Johann Joseph Scherer (1814-1869) in January 1843. Intensive. Care Med 2007, 33:1967-71.

66. Vincent JL, Dufaye P, Berre J, Leeman M, Degaute JP, Kahn RJ: Serial lactate determinations during circulatory shock. Crit Care Med 1983, 11:449-51.

67. Bakker J, Gris P, Coffernils M, Kahn RJ, Vincent JL: Serial blood lactate levels can predict the development of multiple organ failure following septic shock. Am J Surg 1996, 171:221-6.

68. James JH, Luchette FA, McCarter FD, Fischer JE: Lactate is an unreliable indicator of tissue hypoxia in injury or sepsis. Lancet 1999, 354:505-8.

69. Mikkelsen ME, Miltiades AN, Gaieski DF, Goyal M, Fuchs BD, Shah CV, Bellamy SL, Christie JD: Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. Crit Care Med 2009, 37:1670-7.

70. Yang CS, Qiu HB, Huang YZ, Xie JF, Mo M, Liu SQ, Yang Y: Prospective research on the prognosis of septic shock based on the change of lactate concentration in arterial blood. Zhonghua Wai Ke Za Zhi 2009, 47:685-8.

71. Ranzani OT, Monteiro MB, Ferreira EM, Santos SR, Machado FR, Noritomi DT. Reclassifying the spectrum of septic patients using lactate: severe sepsis, cryptic

72. Sterling SA, Puskarich MA, Shapiro NI, Trzeciak S, Kline JA, Summers RL, et al. Characteristics and outcomes of patients with vasoplegic versus tissue dysoxic septic shock, vasoplegic shock and dysoxic shock. Rev Bras Ter Intensiva 2013;25:270–8..

73. Marchick MR, Kline JA, Jones AE. The significance of non-sustained hypotension in emergency department patients with sepsis. Intensive Care Med 2009;35:1261–4.

74. Trzeciak S, Dellinger RP, Chansky ME, Arnold RC, Schorr C, Milcarek B, et al. Serum lactate as a predictor of mortality in patients with infection. Intensive Care Med 2007;33:970–7.

75. Mikkelsen ME, Miltiades AN, Gaieski DF, Goyal M, Fuchs BD, Shah CV, et al. Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. Crit Care Med 2009;37:1670–7.

76. Hernandez G, Bruhn A, Castro R, Pedreros C, Rovegno M, Kattan E, et al. Persistent sepsis-induced hypotension without hyperlactatemia: a distinct clinical and physiological profile within the spectrum of septic shock. Crit Care Res Pract 2012;2012:536852.

77. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving Sepsis Campaign: international guidelines formanagement of severe sepsis and septic shock, 2012. Intensive Care Med 2013;39:165–228.

78. Falk JL, Rackow EC, Leavy J, et al. Delayed lactate clearance in patients surviving circulatory shock. Acute Care. 1985;11: 212-215.

79. Aduen J, Bernstein WK, Khastgir T, et al. The use and clinical importance of a substrate-specific electrode for rapid determination of blood lactate concentrations. JAMA. 1994;272:1678-1685.

80. Ranzani OT, Monteiro MB, Ferreira EM, Santos SR, Machado FR, Noritomi DT. Reclassifying the spectrum of septic patients using lactate: severe sepsis, cryptic shock, vasoplegic shock and dysoxic shock. Rev Bras Ter Intensiva 2013;25:270–8.

81. Broder G, Weil MH. Excess lactate: an index of reversibility of shock in human patients. Science. 1964;143:1457-1459.

82. Bakker J, Coffernils M, Leon M, et al. Blood lactate levels are superior to oxygen-derived variables in predicting outcome in human septic shock. Chest. 1991;99:956-962.

ANNEXURE I:

LIST OF ABBREVIATIONS

MD = Medical Doctor

Hb = Haemoglobin

Pc = Platelets

TLC= Total leucocytes count

CBC = Complete Blood Count

SBP = Systolic Blood Pressure

DBP = Diastolic Blood Pressure

RFT= Renal function test

LFT= Liver function test

ABG= Arterial Blood Gas

LAC= Lactate

pH = Potential of Hydrogen

Pco2 = Partial pressure of carbon dioxide

Po2 = patial pressure of oxygen

Spo2 = oxygen saturation of blood

SBP- systolic Blood pressure

DBP- diastolic blood pressure

ANNEXURE II:

PARTICIPANT INFORMATION SHEET

Study Title: Hyperlactatemia In Sepsis In Patients Admitted In Intensive Care Unit

1. Introduction:

   Sepsis is a systemic, deleterious host response to infection leading to severe sepsis (acute organ dysfunction secondary to documented or suspected infection) and septic shock. Lactate was earlier known as a marker of tissue hypoxia and has recently emerged to be a marker of sepsis. So we planned to study the hyperlactatemia in patients of sepsis to see its significance and to also find out other cause of hyperlactatemia.

2. What is the purpose of this study?

   To study incidence and causes of Hyperlactatemia in patients with sepsis on admission in ICU and to see ABG changes secondary to sepsis.

3. Why have I been chosen?

   Having sepsis and no other history of hyperglycemia, drug induced hyperlactatemia and outside not treated on the line of sepsis.

4. Do I have to take part?

   Yes, only for few tests that has to be done.

5. How long will the study last?

   Study will last for 1.5 – 2 years.

6. What will happen to me if I take part?

You will be subjected to some questions about and related to the symptoms and the necessary investigations. This will carry no harm in any way.

7. What do I have to do?

Co-operate for giving real fact for questions and allow investigator to complete the investigations needed.

8. What are the benefits of the study?

Benefits of the study is, the early diagnosis of sepsis to decrease the mortality rate.

9. What if new information becomes available?

No new data would affect the study and if any changes occur it would be priorly informed.

10. What happens when the study stops?

When study stops data gathered during the study wil be evaluated and inference would be made accordingly.

11. What if something goes wrong?

There is as such no risk to any participant because it does not include any human or animal experimentation.

12. Will my taking part be kept confidential?

Yes, all data collected will be kept confidential.

13. What else should I know?

Whole study is on voluntary basis, no extra financial burden would be levied on participant.

14. Who to call with questions?

Dr. Vipul Patel, Mobile No. 9879172606

સહભાગીતાનું સંમતિ પત્રક

અભ્યાસનું શીર્ષક :- ઈન્ટેસીવ કેર યુનિટમાં દાખલ થયેલા દર્દીઓમાં ગુમડા/સડાને કારણે હાઈપર બેક્ટેટેમીયાનો અભ્યાસ

પ્રસ્તાવના :-

૧. સડો/ગુમડાએ થતાં સંક્રમણની પ્રતિક્રિયા છે જેનાથી અતિશય ગંભીર સડો કે સેપ્ટીક શોક થવાની શક્યતા છે. (જેમાં અંગનું કામ કરતું બંધ થવું જેવી ઘટનાઓ પણ સામેલ છે.) લેક્ટેટને પૂર્વ ટીસ્યુ હાઈપોક્સિયાના લક્ષણ તરીકે ઓળખવામાં આવતું જ્યારે હાલમાં તે સડાના પ્રાથડમિક લક્ષણ તરીકે જોવાય છે. તેથી સડા/ગુમડાના દર્દીઓમાં હાઈપરલેક્ટેટેમીયાનો પ્રભાવ તેમજ અસરો અને તેના થવાના કારણોનો અભ્યાસ કરવાનું નક્કી કરેલ છે.

૨. આ અભ્યાસનો હેતુ શું છે?

૧૦૦ માં દાખલ થયેલ ગુમડા કે સડા વાળા દર્દીઓમાં હાઈપર લેક્ટેટીયા થવાના કારણો તેમજ A,B,G ના સડા કે ગુમડામાં થયેલ ગૌણ પરિવર્તનોની તપાસ કરી.

૩. મારી પસંદગી શા માટે ?

તમને સડો/ગુમડા કે તેમજ હાઈપર લેક્ટેટેમીયા હોવાનો તબીબી ઈતિહાસ છે. સડા કે ગુમડા માટે તમને કોઈ હાઈપર લેક્ટેટેમીયાને લગતી દવા આપવામાં નથી આવી.

૪. મારે ભાગ લેવાનો છે?

હા, થોડાક તબીબી પરિક્ષણો પૂરતો તમારે ભાગ લેવાનો છે.

૫. અભ્યાસ કેટલો સમય ચાલશે ?

અભ્યાસ દોઢ થી બે વર્ષ સુધી ચાલશે.

૬. હું ભાગ લઈશ તો શું થશે ?

તમને એક સહભાગીદાર તરીકે માત્રને માત્ર પ્રશ્નો પૂછવાના હોવાથી તમને પ્રશ્નોના વિગતરે જવાબ આપવામાં કોઈ જ તકલીફ પડવાની નથી. તમને કોઈ નુકશાન પણ નથી થવાનું.

૭. મારે શું કરવાનું રહેશે ?

તમને જે પણ પૂછવામાં આવે તે બાબતે વિગતે, સાચી માહિતી આપવાની છે તેમજ સંશોધને સહકાર આપવાનો રહેશે.

૮. અભ્યાસના ફાયદા શું શું છે ?

સડો કે નિદાનમઅં સરળતા રહેશે, સમય પહેલા નિદાન કરી શકશે તેમજ તેનાથી થતાં મૃત્યુદરને ઘટાડી શકશે.

૯. જો કોઈ નવી માહિતી ઉપલબ્ધ થશે તો ?

નવી માહિતીથી અભ્યાસને કોઈ અસર થવાની નથી તેમજ જો કોઈ પરિવર્તન આવશે તો તેની તમને વચ્ચે જ અગાઉથી જાણ કરવામાં આવશે.

૧૦. જો અભ્યાસ વચ્ચે જ રોકાઈ જાય કે બંધ થઈ જાય તો ?

અભ્યાસ રોકાઈ ગયેથી જે પણ માહિતી એકત્ર કરવામાં આવી છે તે માહિતીનું વિશ્લેષણ કરવામાં આવશે તેમજ જે તે પ્રભાવની યોગ્ય નોંધ કરવામાં આવશે.

૧૧. કંઈ ખોટું થાય તો ?

સહભાગીદારીને કશું ક થવાનું નથી કારણ કે, અહીં માનવી કે પ્રાણી ઉપર કોઈપણ પ્રકારનો અખતરો કે પ્રયોગ થવાનો જ નથી.

૧૨. હું ભાગ લઉં છું તે ગોપનીય રખાશે ?

હા,તમારી સહભાગીતા તેમજ દ્વારા મળેલ માહિતીને ગોપનીય રખાશે.

૧૩. મારે બીજું શું જાણવાનું રહેશે ?

સમગ્ર અભ્યાસમાં આપની ભાગીદારી સ્વૈચ્છીક છે તેમજ તમારે કોઈપણ પ્રકારનું આર્થિક ભારણ ઉપાડવાનું નથી.

૧૪. કોઈપણ મૂઝવણ કે પ્રશ્ન ઉદ્‌ભવે તો કોનો સંપર્ક કરવો ?

ડૉ. વિપુલ પટેલ : મો.નં. ૯૮૭૯૧૭૨૬૦૬

सहभागीताका जानकारी पत्रक

अभ्यास का शीर्षक :– इन्सेन्टीव केअर युनिटमें दाखील होने वाले मरीजोंमें सडे के कारण होनेवाले लेक्टेटेमीया की जाँच.

प्रास्ताविक :

१. सडा होना यह होनेवाले संक्रमण की प्रतिक्रिया है, जीससे गंभीर प्रकार के सडे या सेप्टीक शोक होने की संभावना है। (जैसे की शरीरके कीसीभी अंगका काम कर देना बंध हो जाए।) लेक्टेट को पूर्व टीस्यु हाईपोक्सिया के लक्षण के रुपमें जाना जाता था जबकी अब उसे सडे के प्राथमिक लक्षण के तौर पर जाना जाता है। इसलिए सडे के मरीजोंमें हाईपरलेक्टेटेमीया का प्रभाव व उसकी असर व होनेवाले कारणो की जाँच करना तय कीया गया है।

२. इस अभ्यास का हेतु क्या है ?

१०० में दाखील होनेवाले सडे वाले मरीजोंमें हाइपरलेक्टेटेमीया होने के कारणो की जाँच व A,B,G के सडे मे हुए गौण परिवर्तन की जाँच करना.

३. मेरा ही चयन क्यों ?

आपकी जाँचमें सडा पाया गया है और हाइपरलेक्टेटेमीया होने का इतिहास भी है सडे या हाइपरलेक्टेटेमीया से जुडी हुई कोई दवाई आपको नहीं दी गइ हैं।

४. मुझे हिस्सा लेना है ?

हाँ, कुछ टेस्ट करने के हेतु आपको हिस्सा लेना होगा।

५. अभ्यास कब तक चलेगा ?

तकरीबन डेढ से दो साल तक अभ्यास चलेगा।

६. अगर में हिस्सा लेता हुँ तो क्या होगा ?

आपको एक सहभागीदार के रुपमें सिर्फ और प्रश्न पूछे जाएगें इससे आपको और कोई नुकशान नहीं होनेवाला है। और आपको कोइ दिक्कत भी नहीं होगी।

७. मुझे क्या करना होगा ?

आपको संशोधक को सहयोग देना होगा और जो भी आपसे पूछा जाए उसकाि सही सही विस्तार से देना होगा।

८. इस अभ्यास से क्या क्या फायदे होंगे ?

सडा या फुँसीयो के निदान च समय से पूर्व उसके उपचारमें सफलता मीलेगी और होनेवाली जान के नुकशान को रोका जा सकेगा।

९. यदी कोई नई जानकारी उपलब्ध होगी तो ?

नई जानकारी से को फर्क नहीं पडनेवाला, और यदी कोई परिवर्तन है तो आपको पहेले से इसकी जानकारी दी जाएगी।

१०. अगर अभ्यास बीचमें रुकता है या बंध होता है तो ?

एसेमें जोभी जानकारी उपलब्ध है उसका विश्लेषण कीया जाएगा और जोभी प्रभाव या कोई परिबल से अभ्यास प्रभावित हुआ है उसकी टीप्पणी रखी जाएगी।

११. अगर कुछ गलत हुआ तो ?

यहाँ कोइ भी प्राणी या इन्सान के उपर कीसीभी प्रकारका कोई भी प्रयोग या कीसी दवाई की जाँच नहीं हो रही है इसलीए आपके साथ कुछ गलत होने की संभावना ही नहीं है।

१२. में जो हिस्सा लेने जा रहा हुँ उसे गोपनीय रखा जाएगा ?

हाँ, आपका हिस्सा लेना व आपके द्वारा प्राप्त जानकारीको पूर्व रुपसे गोपनीय रखा जाएगा।

१३. मुझे और क्या जानना है ?

यह अभ्यासमें हिस्सा लेना पूर्व रुपसे स्वैच्छीक है और इसके लीए कोई खर्च नहीं उठाना है।

१४. अगर कोई दिक्कत या प्रश्न है तो किसका संपर्क करे ?

डॉ. विपुल पटेल मो.न. ९८७९१७२६०६

ANNEXURE III:

INFORMED CONSENT FORM

Informed Consent Form (ICF) for Participants in Research Programs involving studies on human beings

Study Title: - **Hyperlactatemia In Sepsis In Patients Admitted In Intensive Care Unit**

Please initial box
(Subject)

(i) I confirm that I have read and understood the information sheet dated ……....….for the above study and have had the opportunity to ask questions. ☐

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

(iii) I understand that the Sponsor of the clinical trial, others

working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, ☐

Even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. ☐

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) ☐

(v) I agree to take part in the above study. ☐

P.T.O

Signature/Thumb impression of the participant _____

Legally acceptable representative _____

Signatory's Name _____ Date _____

Signature of the investigator _____ Date _____

Study Investigator's Name _____ Date _____

Signature of the impartial witness _____Date _____

Name of the witness _____

અભ્યાસ શીર્ષક : ઈન્ટેસીવ કેર યુનિટમાં દાખલ થયેલા દર્દીઓમાં ગુમડા/સડાને કારણે હાઈપર બેક્ટેટેમીયાનો અભ્યાસ

સહભાગીનું મિતાક્ષરી : ..... સહભાગીનું નામ : .....

જન્મ તારીખ / ઉંમર : .....

સહયોગીનું સરનામું : .....

લાયકાત : .....

વ્યવસાય : વિદ્યાર્થી/સ્વરોજગાર/નોકરી/ગૃહિણી/અન્ય

(યોગ્ય વિકલ્પ પર નિશાની કરો)

અભ્યાસ પાત્રની વાર્ષિક આવક : .....

વારસદાર(રો)ની વિગત

વારસદારનું નામ : .....

વારસદારનું સરનામું : .....

અભ્યાસપાત્ર / સહયોગી સાથે સંબંધ : .....

કૃપા કરી માં હકો જવાબ આપો.

૧. હું ખાતરી આપુ છું કે આ અભ્યાસનું ..... તારીખની માહિતી પત્રક મે વાંચ્યું છે અને સમજ્યો છું તેમજ મને પ્રશ્નો પૂછવાની તક મળેલ છે.

૨. હું સમજું છું કે આ અભ્યાસમાં માન અધ્યોગિતા સ્પૈચ્છિક છે અને હું કોઇ પણ સમયે કારણ દર્શાવ, વિના જ મુક્તિ થઇ શકુ છું તેથી મારી તબીબી ચિકિત્સા કે કાયદાકીય હક્કો પર કોઇ પ્રભાવ પડશે નહીં.

૩. હું સમજુ છું કે અભ્યાસના અન્વેષક, તંબ્બોના વતી કાર્ય કરનાર હિતરક્ષક સમિતિ અને નિયામક સતાઓને જાણ વર્તમાન કે ભાવિ સંશોધન જે મારી સહભાગિતા પછી મૈત્રી લીધા પછી પણ જાનનો બંને કિસ્સામાં મારી સ્વાસ્થ્ય માટેની જોવા મારી પરવાનગીની આવશ્યકતા નથી. હું તેના ઉદ્ઘોપક લેવામાં સહમત છું જો કે હું સમજૂ છું કે માહિત વ્યક્તિ કે પ્રકાશન દ્વારા મારી ઓળખ રજૂ કરવામાં આવશે નહીં.

૪. હું કોઇ પણ માહિતી કે પરિણામ જે માપ આવા વૈજ્ઞાનિક હેતુસર ઉપલબ્ધ કરાવાય છે તેના ઉપયોગમાં અવરોધ ન કરવા માટે સંમત છું.

૫. હું ઉપયોગ અભ્યાસમાં સહભાગી થવા સંમત છું.

અભ્યાસપાત્રની સહી / અંગૂઠાનું નિશાન .....

તારીખ : .....

સહી કરનારનું નામ : .....

અન્વેષકની સહી : .....

તારીખ : .....

અભ્યાસ અન્વેષકનું નામ : .....

સાક્ષીની સહી : .....

તારીખ : .....

સાક્ષીનું નામ : .....

દર્દી માહિતી પત્રક અને ભરેલું, માહિતી સંમતિ પત્ર અભ્યાસ સમાન કે તેની આપેલ વ્યક્તિ વ્યક્તિ આપવું.

प्रतियोगी

अभ्यासमे सहभागी होते समयका

अनुमति– संमति पत्र

अभ्यास का नाम : इन्सेन्टीव केअर युनिटमें दाखील होने वाले मरीजोंमें सडे के कारण होनेवाले

लेक्टेटेमीया की जाँच.

अभ्यास क्रमांक दिनांक

प्रतियोगी की जन्मतारीख / आयु

१) में सत्यापित करता हुं की ता..... से..... उपरोकत अभ्यास के विषयमें जानकारी पढने की एवं प्रश्न करने के अवसर प्रदान किये गये है ।

२) में जानती/ जानता हुं की इस अभ्यासमें सहभागीता करना मेरे लिये स्वैच्छि है, और कोइ भी कारण प्रद्धति किये बिना किसी भी समय इस में से मुक्त होने की स्वतंत्रता है, ऐसा करने से मेरे दाकतरी हस्सो से उपर कोई प्रभाव नहीं होगा ।

३) मे जानती/ जानता हुं कि यह अभ्यासकर्ता, उनसे सहयोगी और जुथ और उनकी उमरीयों से मेरे स्वास्थ्य संबंधी किसी भी जानकारी प्राप्त करने में मेरी अनुमति की आवश्यकता नहीं है, भले ही मे उस अभ्यास से मुक्त हो गई हुँ । मे जानती/ जानता हुं कि मेरी इस प्रसार की जानकारी अन्य किसी भी प्रसार से प्रसाशित नहीं की जाएगी ।

४) इस अभ्यास के दौरान अथवा उसके प्राप्त जानकारी विज्ञानकयोग के हेतु उपयोग करने स्वतंत्र है ।

५) में इस अभ्यासमें जूडने / सहभागी होने के लिये सहमत हुं ।

अभ्यासने सहयोगी की सही या अंगुठे का निशान

तारीख .....

कानुनी अन्वेष्कके सही .....तारीख .....

अन्वे का नाम .....

साक्षी / गवाह की सही ..... तारीख .....

गवाह / साक्षी का नाम .....

ANNEXURE: IV

PROFORMA

Name: Age/sex:

OPD No: IPD NO:

Residence:

Occupation: ` Religion:

Socio-economic status:

Contact no:

Chief complains: IF YES

		Duration
1. Fever	Yes/no	( )
2. Altered sensorium	Yes/no	( )
3. Vomiting	Yes/no	( )
4. Breathlessness	Yes/no	( )
5. Jaundice	Yes/no	( )
6. Cough	Yes/no	( )
7. Convulsion	Yes/no	( )
8. Pain in Abdomen	Yes/no	( )

Past history:

Family history:

Menstrual history: (in case of a female patient)

Personal history:

- Diet : Mixed/Pure veg
- Appetite: Normal/Disturbed
- Sleep: Normal/Disturbed
- Bladder: Normal/Disturbed
- Bowel: Normal/Disturbed
- H/o any addiction:

General examination:

- Temp: Afebrile/Febrile
- Pulse:……/min, Blood pressure:……mm of hg
- Pallor: Present/Absent
- Icterus: Present/Absent
- Lymphadenopathy: Present/Absent
- Clubbing: Present/Absent
- Cyanosis: Present/Absent
- Oedema: Present/Absent

Systemic examination:

- Respiratory system:

- Cardiovascular system:

- Per abdomen:

- Central nervous system:

Diagnosis:

Lactate:

pH :

Pco2:

Po2:

So2:

Haemogram,:

Hemoglobin	13-17 gm%	
W.B.C	4000-11000cell/cumm	
Neutrophils	60-70%	
Lymphocytes	20-35%	
Eosinophils	1-4%	
Monocytes	2-6%	
Basophils	0-1%	
Total Platelets	1.5-4.5 lacs/cumm	

ESR:

Electro cardiogram:

X ray chest:

Urine routine examination:

Albumin	
Sugar	
Pus Cells	
R.B.C	
Epithelial Cells	
Crystals	
Cast	
Other	

Chest x-ray:

USG abdomen:

Liver function test,

SGPT	Up to 40 IU/I	
SGOT	Up to 40 IU/I	
Total Bilirubin	0.2-1.0 mg%	
Direct Bilirubin	0.1-0.4 mg%	
Indirect Bilirubin	0.2-0.8 mg%	

Renal function test,

Urea	11-45 mg%	
Creatinine	0.6-1.3 mg%	

Random blood sugar.

ANNEXURE: V

KEY MASTER CHART

SR	-	serial number
AS	-	Altered sensorium (1-not present, 2- present)
Fever	-	(1-absent, 2- present)
BRT	-	breathlessness (1-absent, 2-present)
JAUN	-	jaundice (1-absent, 2-present)
CNV	-	convulsion(1-absent, 2-present)
ABD PAIN	-	Abdominal pain(1-absent, 2-present)
PAST	-	Past history(1-not significant, 2-known case of DM 3- known case of hypertension, 4- history of tuberculosis 5-k/c/o ischemic heart disease 6- k/c/o bronchial asthma) 7-k/c/o liver disease 8-k/c/o sickle cell hemoglobinopathies
FAMI	-	family history (1-not significant)
P	-	pulse/minutes
B.P	-	blood pressure in mmHg
PALLOR	-	(1-absent, 2-present)
ICT	-	icterus (1-absent, 2-present)
CYAN	-	cyanosis (1-absent, 2-present
CLUB	-	clubbing(1-absent, 2-present))
LYMP	-	lymphadenopathy (1-absent, 2-present)
R/S	-	respiratory system(1-normal air entry, 2-air entry reduced 3- crepts present, 4 rhonchi present)
CVS	-	cardiovascular system- (1-normal
CNS	-	central nervous system-(1-glasgow coma scale=15 2-glasgow coma scale=<15)
P/A	-	Per abdomen examination(1-normal, 2-splenomegaly 3-hepatomegaly,4-Ascitis)

HB	-	Hemoglobin
TLC	-	Total leucocyte count
DC	-	Differential count (neutrophils, lymphocytes, basophil, eosinophils)
PLT	-	Platelet
UNINE R/M	-	Urine routine micro(1-normal 2-pus cell>2-3)
RBS	-	Random blood sugar
ESR	-	Erythrocyte sedimentation rate
pH	-	Potential of hydrogen
PCo2	-	Partial pressure of carbon dioxide in blood
PO2	-	Partial pressure of oxygen
HCO3	-	Sodium bicarbonate in blood
SO2	-	Oxygen saturation in blood
CXR	-	Chest x-ray (1-normal, 2-consolidation, 3-pleural effusion
USG ABS	-	ultra sonography of abdomen (1-normal, 2-splenomegaly 3-hepatomegaly,4-Ascitis)
SOI	-	SOURCE OF INFECTION
OUTCOME	-	(1- DISCHAGE, 2- DEATH)
T.HOS ST	-	TOTAL HOSPITAL STAY IN DAYS

MASTER CHART

SR NO.	AGE	SEX	FEVER	VMT	AS	BRT	JAUN	COUGH	CNV	ABD PAIN	PAST	FAMI	TEMP	PULSE	RR	BP	PALOR	ICTERUS	CYANOSIS	CLUBBING	LYMP	EDEMA	RS	CVS	CNS	PA	HB	TLC	DC	PC	ESR	RBS	LACTATE	PH	PCO2	PO2	HCO3	SO2	UREA	CREATININE	BILIRUBIN	SGPT	SGOT	URINE-RM	CXR	USG-ABD	SOI	OUTCOME	T.HOS.ST
1	60	F	1	1	2	1	2	1	2	1	2,3	1	1	98	26	70/40	1	2	1	1	1	2	1	1	2	1	12.1	22900	85/11/2/2	1.53	70	202	7	7.09	28	43	8.5	61.1	121	4.4	0.7	1047	17	1	1	1	ABDOMEN	2	1
2	70	F	2	1	1	2	1	2	1	1	2,5	1	2	130	30	NOT RECORDABLE	1	1	1	1	1	1	3	1	1	1	11.6	12800	82/14/3/1	1.97	46	126	4.98	7.35	40.7	31	22.7	83.1	46	1	0.8	54	111	1	1	1	CAP	2	2
3	47	M	1	1	2	1	1	1	1	1	2,3	1	1	116	27	110/70	1	1	1	1	1	1	2	1	2	1	15.3	10300	90/6/2/2	2.7	12	235	2.86	7.57	27.9	70	25.6	99.9	11	0.8	1.5	19	34	2	1	1	CAP	2	1
4	19	F	2	1	2	1	1	1	1	1	2,4	1	2	120	36	86/50	1	1	1	1	1	1	3	1	2	1	12.5	46000	72/19/4/5	5	40	166	2.46	7.3	13.3	86	6.3	98.7	46	1.3	0.5	15	20	2	2	1	CAP AND UTI	1	6
5	65	M	2	1	2	1	1	1	1	1	2	1	2	130	34	90/60	1	1	1	1	1	1	1	1	2	1	13.6	7900	67/24/4/5	2.75	32	285	5.8	7.32	38.7	64	20.1	98.8	29	0.8	0.4	15	19	2	1	1	UTI	1	17
6	45	M	2	2	2	1	1	1	1	1	1	1	1	130	30	84/50	1	1	1	1	1	1	3	1	2	1	13.6	12100	66/25/4/5	2.26	20	175	4.85	7.63	18	100	19.1	99	222	3.2	1.3	32	90	1	1	1	MENINGITIS	2	3
7	31	F	1	1	2	2	1	1	1	1	4	1	1	146	36	90/64	1	1	1	1	1	1	2	1	2	1	12.1	10900	89/10/4/5	3.21	97	220	2.63	7.45	32.3	75	22.9	98.4	52	1.3	0.4	19	40	1	3	1	CAP	2	5
8	52	M	2	1	2	1	1	1	2	1	2,3,5	1	2	90	24	80/50	1	1	1	1	1	1	3	1	2	1	12	13000	89/6/3/4	0.6	15	271	2.94	7.44	26.4	55	18	90	62	2.2	1.1	74	54	1	1	1	MALARIA	1	16
9	55	F	2	1	2	1	1	1	2	1	1	1	1	100	22	96/60	1	1	1	1	1	1	1	1	2	1	10.6	13300	76/16/4/4	4.19	36	265	4.23	7.44	32.5	90.8	22.6	97.5	39	0.9	0.4	14	11	2	1	1	UTI	2	1
10	58	M	1	1	2	1	1	1	1	1	2	1	1	120	26	110/70	1	1	1	1	1	1	2	1	1	1	13.4	18000	76/14/5/4	1.8	44	128	4.09	7.5	22.5	89	18.6	98.6	23	1	0.7	43	26	2	1	1	UTI	1	10
11	50	F	2	1	1	1	1	1	1	1	1	1	2	110	30	96/70	1	2	1	1	1	2	2	1	1	1	10	16700	65/26/4/5	O.40	40	106	4.17	7.46	21	78.7	15.2	96.6	109	2.5	8.7	531	303	1	1	1	ABDOMEN	2	3
12	36	F	1	1	2	1	2	1	1	1	1	1	1	84	28	70 SYSTOLIC	2	2	1	1	1	1	2	1	2	2	9.3	9800	74/14/4/5	1	86	112	7.11	7.33	27.2	57	14.5	99.2	123	3.8	11.3	181	625	1	1	2	ABDOMEN	2	2
13	37	F	1	1	2	1	1	1	1	1	2	1	2	150	40	140/90	2	1	1	1	1	1	1	1	2	1	9.4	17500	74/17/4/5	4.21	36	303	0.75	7.099	12.7	90	3.9	96.9	18	0.6	0.4	35	25	2	1	1	UTI	1	27
14	68	M	2	2	2	1	1	1	1	2	1	1	1	86	20	80/50	1	1	1	1	1	1	2	1	2	1	12.9	10300	85/6/4/5	1.06	27	116	0.71	7.13	45.6	78	15.5	98.8	246	3.9	0.4	182	683	1	1	1	ABDOMEN	2	5
15	18	M	2	1	1	2	2	1	1	1	1	1	1	132	34	96/70	1	2	1	1	1	1	2	1	1	1	10.5	6300	86/8/3/3	1.4	88	103	1.55	7.48	36.3	94.7	27.5	98	28	0.6	3.3	58	52	2	1	1	CAP	1	24
16	65	M	2	1	2	1	2	1	1	1	4	1	2	120	30	7O/40	2	2	1	1	1	1	2	1	2	2,3,4	6.5	20000	86/10/2/2	0.3	119	160	7.66	7.5	19.5	85.5	15.5	97.7	141	1.7	5.5	72	69	1	1	2,3,4	ABDOMEN	2	4
17	30	M	2	1	1	1	2	1	1	1	1	1	2	134	34	98/70	2	2	1	1	1	1	1	1	1	1	8.4	13000	41/50/4/5	0.6	34	253	4.07	7.48	34.6	31.3	26	65.9	36	1.6	3.4	94	338	1	1	1	MALARIA	2	1
18	68	M	2	1	2	2	1	1	1	1	3,6	1	1	100	36	NOT RECORDABLE	1	1	1	1	1	1	2	1	2	1	13.8	14000	90/6/2/2	1.2	80	96	4.13	7.18	59.1	59.7	22.2	82.9	86	1.3	0.7	33	87	2	2	1	PNEUMONIA	2	7
19	40	M	2	1	2	1	2	1	1	1	1	1	1	70	18	96/70	1	2	1	1	1	1	1	1	2	1	10.5	9100	88/4/4/4	0.3	28	122	1.23	7.39	22.3	80	13.8	99	230	4.3	2.2	112	100	1	1	1	MALARIA	1	13
20	36	M	2	1	2	2	2	1	1	1	1	1	2	116	30	110/40	2	2	1	1	1	1	2	1	2	2,3	7.3	7600	68/28/2/2	0.1	57	108	5	7.3	28.7	59	15.1	91.5	265	5.8	3.5	33	108	1	1	2,3	MALARIA	2	15
21	58	M	2	1	2	1	1	1	1	1	3	1	1	112	32	160/90	1	1	1	1	1	1	1	1	2	1	16.8	10900	77/14/4/5	1.61	50	203	2.46	7.54	33.6	49	29.3	99.5	28	1	1.2	66	39	2	1	1	UTI	2	11
22	20	F	1	1	2	1	1	1	2	2	1	1	1	122	28	100/70	1	1	1	1	1	1	1	1	2	1	11.4	30000	82/10/4/4	2.12	43	95	3.74	7.3	22.5	87.9	13.6	96.9	56	1.2	0.5	230	262	1	1	1	ABDOMEN	1	8
23	58	M	2	1	1	1	1	1	1	2	1	1	2	74	18	92/60	1	1	1	1	1	1	3	1	2	1	11.7	1300	51/40/4/5	1.82	22	129	6.06	7	68.4	70	20.7	60.3	140	2.1	1.2	41	68	1	2	1	CAP	2	1
24	19	M	2	2	2	1	2	1	1	1	1	1	1	108	25	90/60	1	2	1	1	1	1	2	1	2	2	14.8	11600	52/26/4/5	1.5	26	83	5.43	7.5	33	99	26.7	98.8	32	0.6	10.4	3042	984	1	1	2	ABDOMEN	2	4
25	50	F	2	1	2	1	1	1	1	2	2,3	1	1	114	32	114/70	1	2	1	1	1	1	3	1	1	2,3	9.3	24000	86/10/2/2	1.52	94	245	1.9	7.35	23.4	96	18	88	169	2.8	5.5	50	27	2	3	2,3	UTI AND CAP	1	12
26	70	M	1	1	2	2	1	1	1	1	1	1	1	108	32	90/60	2	1	1	1	1	1	2,3	1	2	1	9.6	22000	90/5/2/3	1	109	126	0.77	7.143	98	58	33.6	93.1	122	1.7	1.1	130	181	1	2	1	CAP	2	2
27	21	F	2	1	2	1	2	1	1	1	1	1	1	130	36	70/40	2	2	1	1	1	1	3	1	2	1	8.4	50000	91/4/2/3	3.52	32	80	5.48	7.25	25.1	35.4	10.8	59.7	123	2.8	2.7	35	60	1	2	1	UTI	1	1
28	55	F	2	2	1	1	1	1	1	1	1	1	1	102	26	74/60	1	1	1	1	1	1	1	1	1	1	11.7	1300	51/40/4/5	1.82	100	126	4.9	7.35	40	49	22.7	83.1	140	2.1	1.2	0.9	0.3	2	1	3	ABDOMEN	1	7
29	22	F	2	1	2	1	1	1	2	1	1	1	1	114	30	116/70	1	1	1	1	1	1	3	1	2	1	11.2	13000	80/11/4/5	1.2	21	112	0.51	7.58	25.4	49	24	99.1	38	0.7	1.2	0.4	0.8	2	1	1	ENTERIC FEVER	2	7
30	42	F	1	2	2	1	1	1	1	1	1	1	1	86	20	70 SYSTOLIC	2	1	1	1		1	2	1	2	1	9.5	16000	73/21/3/3	1.63	90	118	10	6.92	19.7	77	5.7	92	24	1.5	0.6	19	19	2	1	1	UTI	2	1
31	70	F	1	1	1	2	1	1	1	2	2,3,5	1	1	76	22	96/64	2	1	1	1	1	1	3	1	1	2	9.2	18500	81/11/4/4	2.99	80	279	1.64	7.44	30.4	55	21.1	93.7	106	2.2	0.8	33	25	2	1	2	BDOMEN AND U	1	7
32	48	M	2	1	1	2	1	1	1	1	2,7	1	2	112	26	100/60	2	1	1	1	1	1	3	1	1	1	8.6	18000	90/5/2/3	0.5	75	110	5.55	7.43	23.9	96	16	98.1	90	1.8	2.2	30	24	1	2	2	CAP	2	4
33	18	M	2	1	1	1	2	1	1	1	1	1	2	102	30	96/70	2	2	1	1	1	1	1	1	1	2,3	5	18000	04/04/8018	2.95	40	120	2.1	7.3	46.7	57	20	99	332	5.1	12.6	97	169	1	1	2,3	ENTRIC FEVER	1	8
34	24	M	2	1	1	1	2	1	1	2	1	1	2	100	26	100/70	1	2	1	1	1	1	2	1	2	2	4.1	13000	74/20/2/3	0.4	36	118	5.6	7.41	12.8	88	8	90	27	1.4	21.3	13.5	7.85	2	1	2	TI AND ABDOME	2	1
35	40	M	2	2	1	1	2	1	1	1	8	1	2	86	26	100/70	2	2	1	1	1	1	3	1	1	1	7	20000	60/32/4/4	4.7	30	96	1.32	7.38	37.4	49	22.3	80	206	2.2	6.2	46	39	1	2	1	CAP	2	3
36	20	M	2	1	1	1	2	1	1	1	8	1	2	118	26	98/60	2	2	1	1	1	1	1	1	1	2,3	9.7	13200	71/20/4/5	1.53	62	118	0.54	7.434	35.5	65	23.8	99.3	19	0.7	5	30	51	1	1	2,3	ENTERIC FEVER	1	11
37	45	M	1	2	2	1	1	1	1	2	1	1	1	102	22	130/70	1	1	1	1	1	1	1	1	2	1	15.4	14100	81/10/4/5	2.28	20	108	0.56	7.41	39.6	57.6	25.6	90	34	1	0.4	36	20	1	1	1	ABDOMEN	1	15
38	48	F	1	2	1	1	1	1	1	2	1	1	2	100	24	100/70	1	1	1	1	1	1	1	1	1	1	14.3	39500	90/5/2/3	4.28	26	142	1.5	7.27	19.9	77	8.9	90	161	2.1	0.5	0.2	0.3	1	1	1	ABDOMEN	1	7
39	63	M	2	1	1	2	1	1	1	1	1	1	2	96	24	100/70	1	1	1	1	1	1	1	1	1	1	12.2	20000	90/5/2/3	0.5	95	116	6.55	7.37	21.7	58	12.8	96.8	114	4.6	1.4	61	112	2	1	1	UTI	1	8
40	65	M	1	1	2	1	1	1	1	1	2,3,5	1	1	132	34	130/90	1	1	1	1	1	1	2	1	2	1	15	14000	87/5/4/4	2.46	56	168	3.37	7.41	31.04	49	20	98	41	1.1	0.8	18	36	1	2	1	CAP	2	2
41	70	M	1	1	2	1	1	1	1	1	2,3	1	2	114	30	110/70	1	1	1	1	1	1	2	1	2	1	14.4	17000	84/8/4/4	2.81	46	447	1.38	7.373	33.3	69.8	19.4	93.5	458	8	2	26	20	2	1	1	UTI	2	1
42	60	F	2	2	1	1	1	1	1	1	3	1	2	88	22	108/60	1	1	1	1	1	1	1	1	1	1	11.7	17400	90/6/2/2	2.17	39	216	1.92	7.42	43.6	63.6	28.6	92	32	0.9	0.5	11	17	1	1	1	ABDOMEN	1	6
43	72	F	2	1	2	1	1	1	1	1	2,3	1	2	100	32	130/90	2	1	1	1	1	1	3	1	2	1	8.6	14000	84/8/4/4	1.4	82	400	2.41	7.26	41.4	53.7	18.6	82.6	121	4.4	0.3	26	21	2	2	1	UTI	2	3
44	65	M	2	2	1	1	1	1	1	1	2,3	1	2	96	26	110/70	2	1	1	1	1	1	3	1	1	1	8.8	28000	95/2/2/1	2.56	42	161	3	7.44	28.9	85	19.3	97	232	5.9	0.4	38	51	2	1	1	UTI	1	12
45	40	M	2	2	1	1	1	1	1	1	1	1	2	102	24	90/60	1	1	1	1	1	1	2	1	1	1	14.2	16000	82/10/4/4	2.44	28	121	1.5	7.53	29.2	100	24.3	96	26	1.5	1.2	26	20	1	3	1	LUNG	2	2
46	52	M	2	1	1	1	1	1	1	2	2,3	1	2	112	26	100/70	2	2	1	1	1	2	2	1	1	2	8	38,000	90/6/2/2	3.99	2.9	186	2.9	7.46	30.2	71	21.4	98	86	2.1	3.3	18	32	1	1	2	ABDOMEN	1	9
47	38	M	2	2	1	1	1	1	1	2	1	1	2	118	30	90/60	1	1	1	1	1	1	1	1	1	2,3	11.3	13000	85/10/3/2	1.93	5	96	0.51	7.48	28.7	78.6	21.5	96.6	286	8.5	1.9	66	48	1	1	2,3	ENTERIC FEVER	1	7
48	21	F	2	2	1	1	2	1	1	2	1	1	2	112	28	86/50	1	2	1	1	1	1	1	1	1	4	10.6	3500	61/30/4/5	2.21	40	96	2.6	7.36	40	93	22	98	26	0.7	9.8	2528	3906	1	1	4	DENGUE	1	9
49	45	M	2	2	1	1	1	1	1	1	1	1	2	114	24	98/64	2	1	1	1	1	1	1	1	1	1	9.7	18000	86/10/2/3	2.59	40	122	2.1	7.38	24.9	95	14.5	98	77	3.4	0.8	20	25	2	1	1	UTI	1	8
50	58	m	2	2	2	2	2	1	1	2	2	1	1	116	30	90/58	2	2	1	1	1	1	1	1	2	3,4	12	22000	88/8/2/3	0.2	33	161	2.6	7.52	23.4	96	18.8	99	83	1	4.5	39	83	1	1	3,4	ABDOMEN	1	7