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Serum Lactatevis-A-Vis Anion Gap as Prognostic Markers in Sepsis

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ABSTRACT:

Background: According to SOFA criteria, sepsis is characterised as fatal Malfunction of an organ caused by a de-regulated reaction of the host to infection. When infection is first suspected, an in-hospital mortality of over ten percent is associated with even a mild degree of organ failure. Sepsis is a condition that would be dangerous to life in lay terms that happensif such patients, their early diagnosis can alter the prognosis and outcome. Sepsis entails dysfunction of the organ, this indicates that pathology plus an associated inflammatory response alone is more complicated than infection. The concentration of the response team on fatal malfunction of the organ is aligned with the outlook that physiological and biochemical anomalies underlie cell defects within particular Systems for tissues. The word "severe sepsis" appears superfluous in this terminology. Generally, higher stages of Surveillance and involvement are warranted, Inclusive of potential Intensive care admission or facilities of high Dependent unit. In this study serum lactate and anion gap levels estimated in sepsis and they will be tested as to whether they can predict the outcome of sepsis in patients. Justa few studies on this subject have been performedin theIndian setup.

Aim of the study- To study Serum lactate vis-a-vis anion gap as prognostic markers in sepsis in rural tertiary care hospital.

Objectives :

1)To evaluate anion gap values in sepsis syndrome.

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2)To measure the serum lactate levels in sepsis syndrome.
3) To correlate the anion gap and serum lactate values with outcome of sepsis syndrome.{▪ Severity of sepsis ▪ septic shock ▪ septic shock and death▪ recovery from sepsis}

Material and method-In this prospective observational study,160 patients were enrolled and diagnosed on the basis of SOFA(sequential organ failure assessment).Patient were admitted in ICU under medicine department, Acharya Vinoba Bhave Hospital, Sawangi (Meghe) associated to Datta Meghe institute of Medical sciences, Wardha from November 2020 to April 2022.

Keywords-Serum lactate, Aniongap, prognosticmarkers, sepsis

INTRODUCTION:

According to SOFA criteria, sepsis is characterised as mortal dysfunction of organ triggered by a de-regulated reaction from host to infection. When infection is first suspected, even a mild degree of organ failure is related to in-hospital fatalities of over 10 percent. Sepsis is a state that is fatal Malfunction of the Organ in lay terms that occurs when the reaction of the body to an infection destroys its own tissue and organ. Therefore,recognition of this condition merits timelyadequate and prompt response.

In general, raised body temperature or neutrophil leucocytosisare non-specific types of SIRS criteria which for example, can continue to help diagnose infections. Such results adjunct specific infection characteristics(e.g., rash, Lung consolidation, peritonitis, difficult urination) that emphasis focus on the possiblesource and organisms infecting. In sepsis, organ dysfunction is involved, indicating a more complicated pathobiology than infection alongside an inflammatory response alone correlated with it.The priority of the task force on life-threatening organ dysfunction is consistent with the view that cell defects underlying physiological and biochemical anomalies within particular higher levels of regulation and interference were typically at a higher level, including potentialAdmission to critical care or services with high dependency.(1)

Severe sepsis: Hypoperfusion, organ failure, or sepsis due to hypotension; perfusion and hypoperfusion abnormalities can include, but are not limited to, oliguria, lactic acidosis or acute mental illnesses.

Septic shock: Septic shock is characterised as a form of sepsis in which ongoing circulatory and cellular shock is recognised as intense enough metabolic abnormalities to significantly increase mortality. The 2001 Task Force Definitions described septic shock as a condition of acute circulatory failure. In order to differentiate septic shock from cardiovascular dysfunction alone and the importance of recognising cellular disorders, the task force preferred a broader approach.

Markers for sepsis-

Lactate serum
Anion Gap
IL-6,IL-1beta,TNF
Albumin
C-reactive protein (CRP)

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Procalcitonin (PCT)

SERUM LACTATE : Mandatory Biomarker-

Over aerobic conditions, glucose is transformed to pyruvate (glycolysis) in a stepwise manner, and then reaches the mitochondria where this is transformed to acetylCoA. In the citric acid cycle yielding NADH, which acts as an electron (e-) donor, acetylCoA is degraded. These electrons present in the inner mitochondrial membrane, pass through the respiratory complexes I, III and IV, allowing protons (H+) to travel into the space of the intermembrane. Oxygen, finally, serves as an electron acceptor(in complex IV).In complex V, ATP is produced as protons eventually move to the mitochondrial matrix.

The primary defect in type A lactic acidosis is the lack of oxygen, leading the oxidative phosphorylation to stop and hence the accumulation of NADH. Large concentrations of cytosolic NADH change the balance from pyruvate to lactate. The benefit of this approach is that it yields two molecules of ATP and regenerates NAD+. The latter one is of particular importance, since glycolysis needs NAD+. In type B lactic acidosis, either pyruvate or NADH is racked up (non-hypoxic), which switches again the balance towards lactate production.

ANION GAP: utility of anion gap in present day modern medicine-

The total amount of serum chloride and bicarbonate concentration subtracted from the serum sodium concentration is known as the serum anion gap, calculated from the electrolytes estimated in the chemical laboratory. The serum anion gap is used to diagnose and assess acid-base disorders, to test chemical laboratory quality control and to classify disorders such as multiple myeloma, toxicity of bromide, iodide and lithium. Usually, high serum anion gap values suggest metabolic acidosis, but may reflect laboratory error, metabolic alkalosis, paraproteinemia, or hyperphosphatemia. Metabolic acidosis can be split into variants of high anion and normal anion gap that can be observed alone or at the same time.

Acid-base balance disturbances are frequently found in clinical settings and can have a significant effects on the patient's prognosis. In addition, a specific acid-base disturbance identification may give a hint to a disorder. A systematic and analytical approach requires adequate assessment and treatment of acid-base disorders, including:

1)Using the Henderson equation or Henderson-Hasselbalch equation, evaluate the precision of the acid-base values.

2)Thorough physical examination and history taken.

3)Determine the anion gap in the serum.

4)Identify the major acid-base instability and evaluate whether it is a clear or mixed instability.

5)Examine and examine serum electrolytes and additional data from the laboratory.

6)The urine pH and urine electrolytes are determined and the urine anion and osmolar differences are estimated.

CAUSES OF SEPSIS: The most likely source of sepsis is bacterial infections. Fungal, bacterial, or viral infections can also develop sepsis. Any of many locations around the body may be the source of the infection. Prevalent sites of infection and types that may contribute to sepsis include:

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Abdominal System: Infections of the appendix (appendicitis), intestinal problems, infections of the abdominal cavity (peritonitis) and infections of the gallbladder or liver. Central nervous system: Infections of the brain or spinal cord.
Respiratory System: Conditions like pneumonia, for example.
Skin: Through wounds or skin inflammation, or through intravenous (IV) catheter openings, bacteria can reach the skin (tubes inserted into the body to allow or evacuate fluids). Sepsis can also be correlated to conditions such as cellulitis (inflammation of the connective tissue of the skin).
Urinary tract (the kidneys or the bladder): Urinary tract infections are also more prevalent if the patient requires a urinary drainage catheter.

Who is at risk of suffering from sepsis?
Sepsis may impact anybody, but those at particular risk include:
Old age women (more than 65 years of age) or young or pregnant.
Patient with infections or chronic illnesses that are already existing, such as diabetes mellitus,heart diseases, cancer, and kidney disease.
Patients with immune systems that have compromised.
Patients who are already in the hospital facility.
Individuals with severe injuries, such as massive burns or injuries.
Patients who have tubes, catheters(IVs, urinary catheters)or a breathing tube(endotracheal tube).

INVESTIGATIONS IN SEPSIS:
Full blood counts:
Hemoglobin
Total WBC count
Differential Leucocyte count
Platelet count
Blood cultures
Lactate Serum:
Measurement of serum lactate, on a blood gas, to evaluate the extent of the sepsis and to track response to treatment. Lactate is a stress indicator and may be a sign of a worse prognosis (as a reflection of the degree of stress). The risk of tissue hypoperfusion is highlighted by elevated serum lactate and may be present in several cases. After intravenous fluids, lactate can normalise quickly. The category that does worst is patients whose lactate levels fail to normalise after sufficient fluids.
With worse results, serum lactate level more than 4 millimol/L (more than 36 mg/dL) is linked.

Hourly urine output
Kidney Function Test:
Urea
Creatinine
Electrolytes

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Serum Glucose
C-reactive protein
Serum Procalcitonin
Clotting Screen:
Prothrombin time (PT)
Partial thromboplastin time (PTT)
Fibrinogen
ABG:
One of the clinical guidelines for systemic inflammatory response syndrome is $PaCO_2 < 4.3$ kPa (32 mm Hg), which may be hypoxemia or hypercapnia

BACKGROUND/RATIONALE: According to SOFA criteria, sepsis is characterised as fatal Malfunction of an organ caused by a de-regulated reaction of the host to infection. When infection is first suspected, an in-hospital mortality of over ten percent is associated with even a mild degree of organ failure . Sepsis is a fatal Malfunction of the Organ in lay terms that occurs when the body reactsto an septicaemiaand it damagethe tissue and organ itself.reaction to an infection injures its own tissue and organ(1). In such patients, their early diagnosis can alter the prognosis and outcome. In this study serum lactate and anion gap levels estimated in sepsis and they will be tested as to whether they can predict the outcome of sepsis in patients. Only few studies have been done on this subject in Indian setup. In this research serum lactate and anion gap levels estimated in sepsis and they will be studied as to whether they can prognostify the outcome of sepsis in patients.

OBJECTIVES :
1)To evaluate anion gap values in sepsis syndrome.
2)To measure the serum lactate levels in sepsis syndrome.
3) To correlate the anion gap and serum lactate values with outcome of sepsis syndrome.{▪ Severity of sepsis ▪ septic shock ▪ septic shock and death▪ recovery from sepsis}

METHODS:
STUDY DESIGN:
This will be Prospective Observational Study With Control Group- **1**-Uncomplicated sepsis
2-Sepsis with multiorgan failure/shock
3-Death
4-Recovery group

SETTING:
The study will be carried out in Acharya Vinoba Bhave Hospital, Sawangi (Meghe).In this prospective observational study, 160 patients were enrolled and diagnosed on the basis of SOFA criteria Patients were admitted in the Medicine department from October 2020 to January 2022.

INCLUSION CRITERIA: Inclusion of patients as per the SOFA criteria for sepsis.

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EXCLUSION CRITERIA: Patients with either hepatic dysfunction, renal failure, liver cirrhosis with ascites, nephrotic syndrome and burns.

SAMPLE SIZE FORMULA =

$$\frac{Z_{1-\alpha/2}^{2}\, p\,(1-p)}{d^2}$$ where,

$Z_{1-\alpha/2}$ = is standard normal variate (at 5% type I error (P<0.05) it is 1.96 and at 1% type I error (P<0.01) it is 2.58) As in majority of studies P values are considered significant below 0.05 hence 1.96 is used in formula.

p = expected proportion in population based on previous studies or pilot studies.

d = absolute error or precision – has to be decided by researcher.

P = Prevalence of severe sepsis = 28.3%

= 0.283

d = Desired error of margin = 7% = 0.07

$$n = \frac{1.96^{2} * 0.283*(1-0.283)}{0.07^{2}}$$

n = 159.08 = 160 patients needed in the study

STATISTICAL METHODS-

A population parameter is calculated by cross-sectional analysis or cross-sectional tests, such as the prevalence of a disease in a group or the average value within a population of a quantitative variable For the qualitative variable and the variable quantity, the sample size formula is distinct.

EXPECTED OUTCOMES/ RESULTS-

This study aims at prognostify anion gap vis-a-vis serum lactate in sepsis syndrome. The prevalence of severe sepsis in ICU patients is as follows according to previous studies is 28.3.

DISCUSSION:

Su Mi Lee and Won Suk An et al aimed to search a leading incidence of acute mortality is sepsis in hospitals and frequently results in multiple-organ failure which is secondary to positive or negative culture infection. In the Surviving Sepsis Campaign (SSC) Guidelines, Despite appropriate fluid replacement, septic shock is characterised as unrecovered hypotension. Arterial hypotension caused by sepsis is characterised as systolic blood pressure (SBP) below 90 mmHg or mean arterial pressure (MAP) below 70 mmHg or a drop in systolic blood pressure greater than 40 mmHg or less than two standard deviations from baseline. Until recently, three elements, including systemic arterial hypotension, tissue hypoperfusion associated with organ failure, and hyperlactatemia, were thought to consist of septic shock. In accordance with the latest concept of this challenge, under two situations, septic shock may be identified. Persistent hypotension that follows fluid resuscitation is the first state and requires Mean Arterial pressure >65 mmHg to be maintained by vasopressors. Serum lactate level 2 mmol/L is the second state. This very recent concept suggests that

raised serum lactate levels in critically ill patients may designate tissue hypoperfusion linked with signs of organ dysfunction. This study was conducted at Busan, Korea on 2016 Apr 10.This study was conducted on 18,840 patients.(2)

FethiGül et al notesthat, Despite the use of modern antibacterial medications and resuscitation therapies, sepsis remains one of the leading risk factors in critically ill patients. Overall, the outcomes of sepsis have improved, possibly due to an increased emphasis on early detection and other supportive care improvements, but mortality rates remain alarmingly high. Due to the heterogeneity of this disease process, the diagnosis and definition of sepsis is a key concern. While it is clear that much more needs to be done to improve our understanding, it remains difficult to describe sepsis and related terminology. A 1991 consensus conference named sepsis defined the initial principles of systemic inflammatory response syndrome (SIRS) to infection. The concepts of sepsis and septic shock were revised in 2001 in order to incorporate the threshold values for organ damage. The current meanings of sepsis and septic shock changed significantly in early 2016.Sepsis is now defined as a life-fatal failure of the organ caused by the disordered infection response of a host. This research was carried out in Istanbul, Turkey, on 148,907 suspected sepsis patients among 706,399 patients in 165 hospitals on 1 December 2016.(3)

Stephen Trzeciak et al. in order to determine lactate measurements in patients with infection and suspected sepsis, when commonly applied in routine practise, the assessment of mortality risk can have an effect. In particular, the risk of acute-phase death is significantly increased by an initial lactate of more than or equal to 4.0 mmol/l. This study was conducted in 1,177 single patients at One Cooper Plaza, Camden 08103, NJ, USA, with in-hospital mortality of 19 percent as of June 2007.(4)

Mikkelsen et al aimed to assess if the In emergency department(ED) patients with more serious sepsis, the association between the initial serum lactate level and mortality is independent of organ failure and shock. Serum lactate is a potentially useful biomarker for risk-stratifying patients with severe sepsis, but elevated serum lactate may be merely a sign of clinically evident organ dysfunction and/or shock (i.e. refractory hypotension).Mortality independent of clinically evident organ failure and shock in patients admitted to ED with extreme sepsis was associated with initial serum failure and shock. Mortality was separately related to both intermediate and high serum lactate levels. This study was conducted in 830 adults hospitalized with severe sepsis in emergency department of an tertiary centre between 2005-2007(5)

BishalGyawali et al aimed to assess The significant developments over the last three decades in the concept and treatment of sepsis was partly motivated by the changes made in their knowledge of their pathophysiology. There is evidence to suggest that the causes of sepsis can no longer be due exclusively to the infectious agent and its mediated immune response, but rather to major changes in coagulation, immunosuppression and dysfunction of the organ. The implementation of early goal-directed therapy has been a ground-breaking shift in the way they treat sepsis. This involves early identification of at-risk patients and timely

antibiotic treatment, optimization of hemodynamic, and adequate supportive care. This has contributed greatly to the overall improved sepsis outcomes. Research into clinically relevant biomarkers of sepsis is underway and successful findings are yet to be produced. Sequential organ failure assessment and Critical Physiology and Chronic Health Evaluation scoring systems help risk-stratify patients with sepsis. For further scientific studies, advances in targeted therapy approaches and the advancement of therapeutic techniques to mitigate excesses of inflammatory and coagulatory cascades provide possible viable avenues. This analysis summarises the progress made over the past two decades in the diagnosis and treatment of sepsis and explores potential directions for future study. This was multicentre research in New Zealand and Australia that has 101,064 critical patients represents decrease in the trend of sepsis over 12 years(2000-2012)(6). Related studies were reported by Dronamrajuet. al (7), Gupta et. al. (8) and Chiwhaneet. al (9). Fulzeleet. al reported on methods for early detection of postoperative infection (10). Few of the related studies were reviewed (11,12).

Limitations: Financial constraints
Generalizability: this study has been conducted over a small population. Hence it cannot be generalised to community

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