A DISSERTATION ON

"SHOCK INDEX AS PREDICTOR OF OUTCOME IN PATIENTS WITH SEPSIS IN CHENGALPATTU MEDICAL COLLEGE HOSPITAL"

Dissertation submitted to

THE TAMILNADU Dr. M.G.R MEDICALUNIVERSITY,

CHENNAI-600 032

In partial fulfilment of the regulations

For the award of the degree of

M.D (GENERAL MEDICINE)

BRANCH-1

REG.NO: 200120103008

GOVT. CHENGALPATTU MEDICAL COLLEGE & HOSPITAL,

CHENGALPATTU-603001

MAY 2023

CERTIFICATE

This is to certify that the dissertation titled " **SHOCK INDEX AS PREDICTOR OF OUTCOME IN PATIENTS WITH SEPSIS IN CHENGALPATTU MEDICAL COLLEGE HOSPITAL** " is the bonafide original work of **Dr.LOKESH R**,in partial fulfilment of the requirements for M.D. Branch-1 (General Medicine) Examination of the Tamil Nadu Dr. M.G.R. Medical University to be held in May 2023. The period of study was from April 2021 to March 2022.

Dr.R.NARMADHA LAKSHMI,M.D.,DCH

HOD & Professor
Department of General Medicine Govt.
Chengalpattu Medical College
Chengalpattu

PROFESSOR AND HOD
DEPT OF GENERAL MEDICINE
CHENGALPATTU MEDICAL COLLEGE
CHENGALPATTU

PLACE: CHENGALPATTU

DATE: 13.12.2022

Dr. K. NARAYANASAMY MD., DM

DEAN,
Govt. Chengalpattu Medical College
Chengalpattu

DEAN
Chengalpattu Medical College
Chengalpattu

BONAFIDE CERTIFICATE

This is to certify that dissertation "**SHOCK INDEX AS PREDICTOR OF OUTCOME IN PATIENTS WITH SEPSIS IN CHENGALPATTU MEDICAL COLLEGE HOSPITAL**"is a bonafide work performed by **Dr LOKESH R**, postgraduate student of General medicine, Chengalpattu medical college, Chengalpattu, under my guidance and supervision in fulfilment of regulations of The Tamil Nadu Dr. M.G.R Medical University for the award of M.D. Degree during the Academic period 2020-2023.

Rnarmee 13.12.22

Dr.R.NARMADHA LAKSHMI,M.D.,DCH
HOD & Professor
Department of General Medicine Govt.
Chengalpattu Medical College
Chengalpattu

PROFESSOR AND HOD
DEPT OF GENERAL MEDICINE
CHENGALPATTU MEDICAL COLLEGE
CHENGALPATTU

Place: CHENGALPATTU

Date: 13.12.2022

DECLARATION

I, **Dr. LOKESH R** , solemnly declare that dissertation titled "**SHOCK INDEX AS PREDICTOR OF OUTCOME IN PATIENTS WITH SEPSIS IN CHENGALPATTU MEDICAL COLLEGE HOSPITAL**"is a bonafide record of work done by me in the Department of Internal Medicine, Government Chengalpattu Medical College and Hospital during April 2021 to March 2022 under the guidance of **Prof. Dr. R. NARMADHA LAKSHMI, M.D, DCH**, Professor of General Medicine, Government Chengalpattu Medical College and Hospital, Chengalpattu. This dissertation is submitted to Tamil Nadu Dr. M.G.R. Medical University, in partial fulfilment of the University regulations for the award of M.D. Degree (Branch 1) General Medicine- May 2023.

SIGNATURE OF THE CANDIDATE

Place: CHENGALPATTU

Date: 13.12.2022

ACKNOWLEDGEMENT

I would like to thank our beloved Dean, Govt. Chengalpattu Medical College and Hospital, **DR.K.NARAYANASAMY M.D.,D.M.,** for permitting me to utilize the hospital facilities for this dissertation.

I extend my sincere thanks to **Prof. Dr. R. NARMADHA LAKSHMI, M.D, DCH,** Professor and Head of the Department of Medicine, Govt.Chengalpattu Medical College and Hospital for her guidance during the study.

I am immensely greatful to my professor **Dr. JAYALAKSHMI M.D.,** senior associate professor of general medicine, Govt.Chengalpattu Medical College and Hospital for her constant and valuable guidance throught the course and during the study. I owe my sincere thanks to my co-guide **Dr. SUDHA M.D.,** Assistant Professor for his guidance and support throughout the conduct of the study and also during my post graduate course.

I owe my sincere thanks to **DR.NAMASHIVAYAM., M.D.,** my senior Associate Professor of general medicine for his valuable advice and appropriate suggestions. I also extend my thanks to the Statistician and all the laboratory technicians for their valuable support throughout my dissertation work.

I extend my thanks to God almighty, my parents , my postgraduates colleagues who stood by me during my times of need. Their help and support have been invaluable to the study.Last but not the least, with sincere gratitude; I thank all the patients who contributed so much to this study without whom this study would not have been possible.

PLAGIARISM CERTIFICATE

This is to certify that this dissertation work titled "**SHOCK INDEX AS PREDICTOR OF OUTCOME IN PATIENTS WITH SEPSIS IN CHENGALPATTU MEDICAL COLLEGE HOSPITAL**" of the candidate , **Dr. LOKESH R** , with the Registration Number **200120103008** for the award of degree of M.D **in the branch of GENERAL MEDICINE-BRANCH-I**. I personally verified the urkund.com website for the plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows percentage of 13% plagiarism in the dissertation.

13.12.22

Dr.R.NARMADHA LAKSHMI,M.D.,DCH
HOD & Professor
Department of General Medicine Govt.
Chengalpattu Medical College
Chengalpattu

PROFESSOR AND HOD
DEPT OF GENERAL MEDICINE
CHENGALPATTU MEDICAL COLLEGE
CHENGALPATTU

Place: Chengalpattu

Date: 13.12.2022

Ouriginal
by Turnitin

Document Information

Analyzed document	thesis final.docx (D152770998)
Submitted	12/9/2022 12:58:00 PM
Submitted by	Lokesh R
Submitter email	lokeshrd6@gmail.com
Similarity	13%
Analysis address	lokeshrd6.tnmg@analysis.urkund.com

Institutional Ethics Committee
Chengalpattu Medical College
Registration No: ECR/774/Inst/TN/2015
IEC Approval Letter – Amended 11.01.2021

No. IEC-CMC/Approval/19/2021 **Dated: 30.03.2021**

Principal Investigator:
Dr. R. Lokesh
1st Year PG,
Dept. of General Medicine,
Chengalpattu Medical College
Chengalpattu

Co-Investigators:
Dr. R.Narmadha Lakshmi, M.D., D,Ch. Professor & HOD ,
Dept. of General Medicine, Chengalpattu Medical College
Dr. S. Sudha, M.D., Assistant Professor,
Dept. of General Medicine, Chengalpattu Medical College

Ref.No.: CMCH – 21 – PR – 240
Title of Work: Shock index as predictor of outcome in patients with sepsis in Chengalpattu Medical College Hospital.
The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC e-meeting held as per ICH-GCP guidelines, New Drug and clinical trials Rule March 2019 requirements & ICMR – EC Guidance during COVID – 19 Pandemic on 25.03.2021 at the Medical Education Unit, Chengalpattu Government Medical College, Chengalpattu at 11.00 AM for the IEC-Chengalpattu Medical College members.

The Members of the committee, the Secretary and the Chairperson are pleased to inform you that your proposed project mentioned above is **Approved** in its presented form.

1. This approval is valid for three years or the duration of the project whichever is less.
2. Should inform the IEC in case of any changes in study procedure, methodology, sample size investigation, investigator or guide or any other changes.
3. Should not deviate from the area of work for which you had applied for ethical clearance.
4. Should inform the IEC immediately, in case of any adverse events or serious adverse reactions, if encountered during from study seven days.
5. Should abide to the rules and regulations of the institution(s).
6. Should complete the work within the specific period and if any extension is required, you should apply for the permission again for extension period.
7. A yearly progress report of the project has to be submitted to the IEC for review.
8. Should submit a copy of the trial work to the ethical committee on completion of the study.

(Dr.A.Anitha)
Member Secretary Ethics Committee

Member Secretary
Institutional ethics Committee
Chengalpattu Medical College & Hospital
Chengalpattu - 603 001

S No:	TABLE OF CONTENTS
1	INTRODUCTION
2	AIM
3	OBJECTIVES
4	LITERATURE REVIEW
	4.1 GLOBAL SCENARIO
	4.2 INDIAN SCENARIO
	4.3 RISK FACTORS
	4.4 IMPORTANCE OF EARLY RECOGNITION
	4.5 NEED FOR SCORING SYSTEMS
	4.6 SOFA SCORE
	4.7 q SOFA SCRE
	4.8 LACTATE LEVEL
	4.9 SHOCK INDEX
	4.8 JUSTIFICATION OF THE STUDY
5	METHODOLOGY
	5.1 STUDYSETTING
	5.2 STUDY DESIGN
	5.3 PARTICIPANTS

ABBREVIATIONS

DAMA: Discharge against medical advice

ED: Emergency department

ICU: Intensive care unit

SI: Shock index

SOFA : Sequential organ Failure Assessment

q SOFA : quick SOFA

SIRS: Systemic Inflammatory response syndrome

GCS: Glasgow Coma Scale

MSSA: Methicillin Sensitive Staphylococcal Aureus

MRSA: Methicillin Resistant Staphylococcal Aureus

NFGNB: Non Fermenting Gram Negative Bacilli

CSF: Cerebrospinal Fluid

ABSTRACT

BACKGROUND : The importance of early recognition of sepsis with initiation of treatment and its effects on survival outcome have long been recognized. Due to this non- availability of easy diagnostic scores and criteria, multiple attempts are being made to develop scores which can identify sepsis early.

AIM : To assess whether in patients with suspected sepsis at chengalpattu medical College hospital ,shock index is a good predictor of clinical outcome .

MATERIALS AND METHODS :

After getting approval of Institutional Ethical committee ,100 patients with suspected infection above 18 years of age, who are admitted in the Intensive medical Care Units (IMCU) of Govt. Chengalpattu medical college are selected for this study. The disease spectrum and the outcomes are studied. Shock index at initial presentation to the emergency medicine department (ED) was compared to the traditional mortality predictors like SOFA score and the newly designed q SOFA score.

RESULTS :

Among the 100 patients, 78 (78 %) had a suspected sepsis Initial shock index was less than 0r = 1 in 28 (28 %) patients and 72 (72%) had shock index values greater than 1.0 at presentation .

CONCLUSION :

Shock index perfomed as a good indicator of in-hospital mortality, and its performance was comparable to other established indices like q SOFA scores, SOFA score .Shock index greater than or equal to 1.0 at initial assessement is associated with greater rates of ICU admission, inotropic requirement and ventilator support. Usefullness of shock index as a mortality predictor was comparable over all the etiologiesof sepsis

SHOCK INDEX AS PREDICTOR OF OUTCOME IN PATIENTS WITH SEPSIS IN CHENGALPATTU MEDICAL COLLEGE HOSPITAL

Introduction

Since 700 BC, humans have been reported as having sepsis. Greeks used the word "sepsis" to describe decay or decomposition. It made reference to an infection-related disease that is highly lethal and life-threatening. Sepsis continues to be a sickness that is challenging to describe and diagnose, leading to significant morbidity and mortality even in the current day with the availability of sophisticated modalities for organ support in critical care units.

One of the main factors contributing to medical and surgical patients' in-hospital mortality and morbidity is sepsis. Sepsis, severe sepsis, and septic shock are all included in the sepsis spectrum. One in five admissions to ICUs are due to severe sepsis, which is also the main cause of death in non-coronary ICUs[1]. Despite this, there is little available information on early predicting indicators. According to data from western nations, sepsis incidence ranges from 10% to 30% overall, and death ranges from 10% to 56%[2]. According to data from India, the overall fatality rate for sepsis patients is around 14%, while the mortality rate for just severe sepsis is higher than 50%[3]. Early sepsis diagnosis and application of evidence-based treatments have been shown to enhance outcomes and lower death from sepsis[4]. It is believed that one of the key factors in lowering mortality from sepsis-related multiple organ failure is shortening the time it takes to diagnose severe sepsis[5]. Sepsis bundle start is significantly hampered by a lack of early identification. The use of sepsis screening techniques has been linked to a reduction in sepsis-related mortality, and they have been created to monitor ICU patients[6].

Sepsis early detection with treatment beginning and its implications on survival outcome have long been understood. Numerous attempts are being made to produce scores that can detect sepsis early due to the lack of simple diagnostic scores and criteria.

In the assessment and treatment of acutely unwell and injured patients, prediction tools and risk stratification algorithms are crucial. Vital signs frequently begin in the compensatory phase of shock within normal ranges. One such measure that has been researched in many patient populations is the shock index (SI), which is calculated as the ratio of heart rate (HR) to systolic blood pressure (SBP). In addition to traditional vital indicators, SI also approximated hemodynamic state when it was first introduced in 1967. Although some data suggests that up to 0.9 is acceptable[7], the normal range for this unitless measure is currently recognised to be 0.5-0.7. Values that are close to 1.0 are a sign of shock and worsening hemodynamic condition. Even when HR and SBP are within normal ranges, elevation in SI has been linked to decreased left ventricular end-diastolic pressure and circulatory volume[7,8]. In an ongoing effort to increase the predictive usefulness of SI, age SI (age SI) and modified SI (MSI) [HR/mean arterial pressure (MAP)] have also been proposed. As DBP is also used to assess clinical severity of illness[9], MSI was created to include the MAP rather than just SBP. The paediatric adjusted shock index (SIPA), which was created for paediatric populations, has proved to be more accurate than the conventional adult cutoffs[10]. Age SI has been shown to be more suggestive of death in senior patients. Despite these developments, there is disagreement on the circumstances under which, and whether or not, SI should be used in emergency rooms (ED).

The shock index (SI) is calculated by dividing the heart rate by the systolic blood pressure. In healthy adults, the typical range is between 0.5 and 0.7. Shock index is a straightforward bedside technique that even non-medical staff can utilise. Peripheral vasodilatation reduces systemic vascular resistance in sepsis patients (SVR). As a compensatory strategy, the heart rate rises in an effort to keep the blood pressure stable. Thus, the blood pressure may be normal in the early stages of sepsis. Consequently, blood pressure may not be a good indicator of a patient with early sepsis on its own. The tachycardia would, however, cause the shock index to rise, and this can help detect early sepsis.

Sepsis emerges as a variety of clinical signs and is characterised as organ dysfunction brought on by the body's reaction to infection. Sepsis has complicated pathogenic pathways and sometimes involves several organs, thus a variety of things can affect how well it will turn out. The prognosis for septic infections can be affected by a wide range of circumstances. For instance, when it comes to the host, abnormalities in the inflammatory response of the host may point to a higher risk of fatal illness[11].

Poor results have been linked, for instance, to the failure to develop a fever (or hypothermia), the emergence of leukopenia, thrombocytopenia, hyperchloremia, a patient's comorbidities, age, hyperglycemia, hypocoagulability, and the failure of procalcitonin to fall[12].

Site of infection: The location of the infection in sepsis patients may have a significant impact on the course of their illness, with sepsis from a urinary tract infection typically having the lowest fatality rates. The prognosis of patients with sepsis has been predicted using a number of grading systems[13].

For the diagnosis of sepsis[14], the Sequential Organ Failure Assessment (SOFA), a scoring instrument to evaluate organ function, was developed. The Quick SOFA (qSOFA), a condensed form of the SOFA, was recommended as an auxiliary tool for the rapid detection of sepsis in high-risk patients[15] in 2016 updated recommendations on sepsis and septic shock. Since 1996, organ function in critically ill patients has also been evaluated using the Logistic Organ Dysfunction System (LODS), a grading system for organ dysfunction developed by Le Gall et al. The scoring indices SOFA score and qSOFA score suggested by sepsis-3 to aid in sepsis diagnosis have a strong link with the outcome of sepsis. Organ failure affects LODS scores in different ways. In contrast to SIRS criteria or the qSOFA score, Raith observed that among persons with suspected infections admitted to an ICU, a rise in SOFA score of 2 or more had a stronger predictive accuracy for in-hospital death[16].

Aims and Objectives

PRIMARY OBJECTIVE:

- To assess whether in patients with suspected sepsis at chengalpattu medical college hospital, shock index is a good predictor of clinical outcome.

SECONDARY OBJECTIVES:

- Role of shock index in predicting ICU requirement.
- Shock index in predicting need for hemodynamic support.
- Shock index in predicting ventilatory requirement.
- Shock index and its relation to duration of hospital stay.
- Correlation of shock index with other mortality predictors (initial SOFA score and q SOFA score).
- Usefulness of shock index across the various etiologies for sepsis.

Review of Literature

Background:

The heart rate (HR) divided by systolic blood pressure is known as the shock index (SI). It has been studied in patients either at risk of or experiencing shock from a variety of causes: trauma, hemorrhage, myocardial infarction, pulmonary embolism, sepsis, and ruptured ectopic pregnancy. While HR and SBP have traditionally been used to characterise shock in these patients, they often appear normal in the compensatory phase of shock and can be confounded by factors such as medications (eg, antihypertensives, betaagonists). SI >1.0 has been widely found to predict increased risk of mortality and other markers of morbidity, such as need for massive transfusion protocol activation and admission to intensive care units. Recent research has aimed to study the use of SI in patients immediately on arrival to the emergency department (ED). In this review, we summarise the literature pertaining to use of SI across a variety of settings in the management of ED patients, in order to provide context for use of this measure in the triage and management of critically ill patients.

Sepsis:

Sepsis is a medical emergency that describes the body's systemic immunological response to an infectious process that can lead to end-stage organ dysfunction and death. Despite significant advancements in the understanding of the pathophysiology of this clinical syndrome, advancements in hemodynamic monitoring tools, and resuscitation measures, sepsis remains one of the major causes of morbidity and mortality in critically ill patients[17]. The annual incidence of severe sepsis and septic shock in the United States is up to 300 cases per 100,000 people. Sepsis is also the most expensive healthcare problem in the United States, accounting for more than $20 million (about 5.2% of the total hospital cost) in 2011 alone[18]. The global epidemiological burden of sepsis is, however, difficult to ascertain. It is estimated that more than 30 million people are affected by sepsis every year worldwide, resulting in potentially 6 million deaths annually. Mortality rates from sepsis, as per the data from the Surviving Sepsis Campaign 2012, were approximately 41% in Europe versus approximately 28.3% in the United States[19]. This difference

however disappeared when adjusted for disease severity[19]. This implies that the mortality in sepsis varies according to patient characteristics as well. A multicenter study in Australia and New Zealand that included 101,064 critical patients showed that the mortality rate in sepsis has decreased over the years from around 35% in 2000 to about 20% in 2012[17].

Definition:

Over the years, our understanding of the complex pathophysiology of sepsis has improved, and so has our ability to define sepsis. The word sepsis is derived from the Greek word for "decomposition" or "decay," and its first documented use was about 2700 years ago in Homer's poems. It was subsequently used in the works of Hippocrates and Galen in later centuries[20]. In the 1800s, the "Germ theory" of disease was conceived and there was some recognition that sepsis originated from harmful microorganisms. The first modern definition was attempted in 1914 by Hugo Schottmüller who wrote that "sepsis is present if a focus has developed from which pathogenic bacteria, constantly or periodically, invade the blood stream in such a way that this causes subjective and objective symptoms[21]." Over the course of the 20th century, numerous experimental and clinical trials were able to demonstrate the importance of the host immune response to the manifestations of sepsis. However, due to heterogeneity of the disease process, it posed serious difficulties in recognizing, treating, and studying sepsis. Finally, at an SCCM-ACCP conference in 1991, Roger Bone and his colleagues laid the foundation for the first consensus definition of sepsis. There have been significant advances in the pathobiology of sepsis in the last two decades. We have a better understanding of cell biology, biochemistry, immunology, and morphology, as well as changes in circulation and organ function. This understanding has led to the changes in the definition of sepsis. This has also contributed to better management of sepsis leading to changes in the epidemiology of the sepsis.

Risk factors

Anyone affected by an infection, severe injury, or serious non-communicable disease can progress to sepsis but vulnerable populations are at higher risk including:

- Older persons,
- Pregnant or recently pregnant women,
- Neonates,
- Hospitalized patients,
- Patients in intensive care units,
- People with HIV/AIDS,
- People with liver cirrhosis,
- People with cancer,
- People with kidney disease,
- People with autoimmune diseases,
- And people with no spleen.

Common Causes

In 2017, the largest contributors to sepsis cases and sepsis-related mortality across all ages were diarrhoeal diseases (9.2 to 15 million annual cases) and lower respiratory infections (1.8-2.8 million annually)[22]. However, non-communicable diseases are on the rise; one-third of sepsis cases and nearly half of all sepsis-related deaths in 2017 were due to an underlying injury or chronic disease[22]. Maternal disorders were the most common non-communicable disease complicated by sepsis. Among children, the most common causes of sepsis-related deaths were neonatal disorders, lower respiratory infections, and diarrhoeal diseases[22]. Group B streptococcus is the leading cause of both neonatal and maternal sepsis, though Escherichia coli is an emerging threat[23]. Both of these pathogens have displayed considerable resistance to treatment and are considered priority pathogens for research and development (R&D) of new antibiotics.

Pathophysiology of sepsis:

There has been a marked evolution in our understanding of the molecular pathobiology and immunology of sepsis. Previously it was felt that hemodynamic manifestations of sepsis were primarily related to the hyperimmune host response to a particular pathogen[14]. However, a large body of work on the molecular basis of sepsis has revealed a far more nuanced and complex interplay between the infectious agent and host that together produce the heterogeneous manifestations of sepsis.

Innate immunity and inflammatory mediators

The first step in the initiation of the host response to the pathogen is the activation of innate immune cells, constituted primarily by macrophages, monocytes, neutrophils, and natural killer cells. This occurs via the binding of pathogen-associated molecular patterns (PAMPs), such as bacterial endotoxins and fungal β-glucans to specific pattern recognition receptors, on these cells. Another source of such interaction are damage-associated molecular patterns (DAMPs) that may be intracellular material or molecules released from dead or damaged host cells, such as ATP and mitochondrial DNA. These bind to specific receptors on monocytes and macrophages such as toll-like receptors (TLRs), C-type leptin receptors, NOD-like receptors (nucleotide-binding oligomerization domain) and RIG-1 like receptors (retinoic acid inducible gene 1). This results in the activation of intracellular signal transduction pathways that cause the transcription and release of proinflammatory cytokines like TNFα, IL-1, and IL-6. In addition, some of the pattern recognition receptors, such as the NOD-like receptor group, can aggregate into larger protein complexes called inflammasomes that are involved in the production of crucial cytokines, such as IL-1β and IL-18 as well as caspases, which are involved in programmed cell death. Proinflammatory cytokines cause activation and proliferation of leukocytes, activation of the complement system, upregulation of endothelial adhesion molecules and chemokine expression, tissue factor production, and induction of hepatic acute phase reactants. In sepsis, there is an exaggeration of the above immune response resulting in collateral damage and death of host cells and tissues.

Dysregulation of hemostasis

In sepsis, there is an intersection between the inflammatory and hemostatic pathways, with the simultaneous activation of both the inflammatory and the coagulation cascades. The spectrum of this interaction can vary from mild thrombocytopenia to fulminant disseminated intravascular coagulation (DIC). The aetiology of the dysregulation of coagulation in sepsis is multifactorial. The hypercoagulability of sepsis is thought to be driven by the release of tissue factor from disrupted endothelial cells (other sources include monocytes and polymorphonuclear cells)[24]. In fact, in vitro experimental models of endotoxemia and bacteremia have shown a complete inhibition of inflammation-induced thrombin production with the blockade of tissue factor[25]. Tissue factor then causes the systemic activation of the coagulation cascade resulting in the production of thrombin, activation of platelets, and formation of platelet– fibrin clots. These microthrombi can cause local perfusion defects resulting in tissue hypoxia and organ dysfunction. In addition to the procoagulant effect described above, there is a depression of the anticoagulant effects of protein C and antithrombin that would normally temper the coagulation cascade. Protein C is converted to its active form (activated protein C) by thrombomodulin which itself is activated by thrombin. Activated protein C then exerts an anticoagulant effect by degradation of factors Va and VIIIa acting in concert with activated protein S. It is also known to have potent anti-inflammatory effects via the inhibition of TNFα, IL-1β, and IL-6 and limiting of neutrophil and monocyte adhesion to endothelium. In patients with severe systemic inflammation, such as in sepsis, there are decreased plasma levels of protein C, downregulation of thrombomodulin, and low levels of protein S thus allowing for the unregulated propagation of the coagulation cascade[26]. In addition to the hypercoagulability described above, a reduction of fibrinolysis is also observed as a result of sepsis. As TNFα and IL-1β levels increase, tissue plasminogen activators are released from vascular endothelial cells. The resultant increase in activation of plasmin is blunted by the sustained increase in plasminogen activator inhibitor type 1 (PAI-1). The net effect is diminished fibrinolysis and fibrin removal, which contributes to the perpetuation of microvascular thrombosis.

Immunosuppression

Interestingly, the initial proinflammatory state of sepsis is often superseded by a prolonged state of immunosuppression. There is a decrease in the number of T cells (helper and cytotoxic) as a result of apoptosis and a decreased response to inflammatory cytokines. Postmortem studies of ICU patients who died of sepsis demonstrated a global depletion of CD4+ and CD8+ T cells, most notably found in the lymphoid organs such as the spleen. Studies have also demonstrated decreased production of crucial cytokines such as IL-6 and TNF in response to endotoxin[27]. In septic patients, neutrophils were found to have expressed fewer chemokine receptors, and there was diminished chemotaxis in response to IL-8[28]. The above findings suggest that the immune system in a septic individual is unable to stage an effective immune response to secondary bacterial, viral, or fungal infections. Based on a study that showed that a low lymphocyte count early in sepsis (day 4 of diagnosis) is predictive of both 28-day and 1-year mortality, it has been postulated that early lymphopenia can serve as a biomarker for immunosuppression in sepsis[29].

Cellular, tissue, and organ dysfunction

The underlying mechanism behind tissue and organ dysfunction in sepsis is the decreased delivery to and utilisation of oxygen by cells as a result of hypoperfusion. Hypoperfusion occurs due to the cardiovascular dysfunction that is seen in sepsis[30]. The incidence of septic cardiomyopathy varies from 18% to 60% in various studies. It is thought to be related to circulating cytokines, such as TNFα and IL-1β among others, which can cause depression of cardiac myocytes and an interference with their mitochondrial function. The most important feature of septic cardiomyopathy is that it is acute in onset and reversible. Second, the low left ventricular ejection fraction is accompanied by normal or low left ventricular filling pressures (unlike in cardiogenic shock) with increased left ventricular compliance[31]. Multiple studies have shown both systolic and diastolic dysfunction with decreased stroke volumes and increased end-diastolic and end-systolic volumes in sepsis.

A definite effect on mortality as a result of myocardial depression, however, has not yet been established. In addition, because of the arterial and venous dilation

(induced by inflammatory mediators) and consequent reduced venous return, a state of hypotension and distributive shock is produced by sepsis. There is dilation of all three components of the microvasculature—arterioles, venules, and capillaries. This is exacerbated by the leakage of intravascular fluid into the interstitial space as a result of loss of endothelial barrier function induced by alterations in endothelial cadherin and tight junctions. All the above changes in the body's hemodynamics in conjunction with microvascular thrombosis (described earlier) can result in hypoperfusion of tissues and organs. Consequently, there is increased anaerobic glycolysis in cells resulting in the production of lactic acid.

In addition, the reactive oxygen species (ROS) produced by the inflammatory response cause dysfunction of mitochondria and a drop in ATP levels. These mechanisms cause damage at the cellular level. The broader alterations described below that occur in the tissue and organs collectively and cumulatively contribute to much of the morbidity and mortality of sepsis. There are significant alterations to the endothelium with disruption of its barrier function, vasodilation, increased leukocyte adhesion, and the creation of a procoagulant state. This results in accumulation of edoema fluid in the interstitial spaces, body cavities, and subcutaneous tissue. In the lungs, there is disruption of the alveolar–endothelial barrier with accumulation of protein-rich fluid in the interstitial lung spaces and alveoli. This can cause a ventilation–perfusion mismatch, hypoxia, and decreased lung compliance producing acute respiratory distress syndrome (ARDS) in extreme cases.

In the kidneys, a combination of reduced renal perfusion, acute tubular necrosis, and more subtle defects in the microvasculature and tubules together produce varying degrees of acute kidney injury. In the gastrointestinal tract, the increased permeability of the mucosal lining results both in bacterial translocation across the bowel well and autodigestion of the bowel by luminal enzymes.

In the liver, there is a suppression of bilirubin clearance producing cholestasis. Altered mentation is commonly noted in sepsis and is indicative of CNS dysfunction. The endothelial changes described above undermine the blood–brain barrier, causing the entry of toxins, inflammatory cells, and cytokines.

The ensuing changes of cerebral edema, neurotransmitter disruption, oxidative stress, and white matter damage give rise to a clinical spectrum of septic encephalopathy that varies from mild confusion to delirium and coma. Sepsis is known to produce a catabolic state. There is a rapid and significant breakdown of muscle to produce amino acids for gluconeogenesis that will fuel the immune cells. In addition, increased insulin resistance can result in a state of hyperglycemia.

Signs and symptoms

Sepsis is a medical emergency and can present with various signs and symptoms at different times. Warning signs and symptoms include:

- Fever or low temperature and shivering,
- Altered mental status,
- Difficulty breathing/rapid breathing,
- Increased heart rate,
- Weak pulse/low blood pressure,
- Low urine output,
- Cyanotic or mottled skin,
- Cold extremities,
- And extreme body pain or discomfort[32-34].

Suspecting sepsis is a first major step towards early recognition and diagnosis.

Indicators for early prediction of outcome in sepsis[35]

Still a significant contributor to postoperative morbidity and mortality is sepsis. Numerous biochemical markers have undergone evaluations to determine how well they might be able to predict sepsis patient prognosis. In general, one must distinguish between markers that are used to identify patients at risk for lethal sepsis before to surgery and those that are used to anticipate lethal outcomes of septic complications early on. In the first, interleukin (IL)-12 synthesis by mononuclear phagocytes is analysed. Higher lethality was linked to lower IL-12 levels. As they were linked to a worse prognosis in sepsis, cytokine-associated gene polymorphisms

such the loss of monocyte HLA-DR expression and homozygotism for the tumour necrosis factor B2 allele have a place in preoperative risk assessment. Decreased L-selectin and raised IL-18, IL-6, and PCT plasma concentrations are some of the most crucial biochemical markers for early prediction of deadly outcome in sepsis. Unfavorable prognosis was linked to increased plasma concentrations of calcitonin gene-related protein and increased nuclear factor kappaB activity in mononuclear phagocytes.

Prediction of survival of patients with sepsis.

The search for biomarkers in clinical settings has now spanned several decades, with studies dating back to the early 1970s still being relevant today[36]. Medical literature is replete with general purpose articles on sepsis. The initial focus of the research was on clinical trials to find therapeutic characteristics that might serve as new or repurposed medication targets. The key shift in direction took place in the early 2000s, when extensive epidemiological data started to become available to the public and gave rise to the development of sizable retrospective studies[37]. Indeed, this new data influx has led to a continual stream of computer and medical studies where researchers have employed different data science methodologies to identify correlations between clinical parameters and sepsis outcomes, with patient survival being among the most significant. The practitioners' community began introducing various early warning scores, such as physiological monitoring methods for detecting critically deteriorating patients[38], which contributed to the landscape. A select few scores—APACHE[39], SAPS[40], SOFA[41], and qSOFA score10—quickly became common in clinical settings and de facto benchmarks for benchmarking research. In addition to these long-standing community shared scores, other formulas using alternative variables have been defined in the literature[42]. These include the dynamic pulse pressure and vasopressor (DPV), the delta pulse pressure (-PP), and the sepsis hospital mortality score (-SHMS)[44]. Even though early warning ratings have gained widespread acceptance, there isn't much proof that they actually enhance patient outcomes[38]. Since the early years[24] to the present day[45], algorithms based on multivariate (Cox) regression on clinical variables have been an important component

of all statistical methods[44]. Intriguingly, these methods' features are not just restricted to clinical variables; over the past few years, a number of teams have experimented with additional components from cutting-edge omics technologies like metabolomics[46], SNPs genomics[47], circulating microRNA[48], blood metabolites[49], or lymphocyte apoptosis[50], frequently in combination with more traditional biomarkers and compared the results with various scores. Unfortunately, these statistically based approaches performed relatively poorly, with only a very small percentage of research obtaining a satisfactory degree of efficacy[51]. In fact, Gwarri-Sridhar and colleagues asserted decision trees to be better to regression techniques in 2010.

Prediction of outcome in case of sepsis by using various tools

In the assessment and treatment of acutely unwell and injured patients, prediction tools and risk stratification algorithms are crucial. Vital signs frequently begin in the compensatory phase of shock within normal ranges.

Shock Index:

One such metric that has been explored in numerous patient populations is the shock index (SI), which is the ratio of heart rate (HR) to systolic blood pressure (SBP). First established in 1967, SI provides an approximation of hemodynamic condition in addition to conventional vital signs. Though some data suggests that values up to 0.9 are acceptable[52], the usual range for this unitless metric is now considered as 0.5-0.7. Values that are close to 1.0 are a sign of shock and worsening hemodynamic condition.

Even when HR and SBP are within normal ranges, elevation in SI has been linked to decreased left ventricular end-diastolic pressure and circulatory volume8. In addition to SI, age SI (age SI) and modified SI (MSI) [HR/mean arterial pressure (MAP)] have also been suggested in an effort to increase the predictive value. As DBP is also used to assess clinical severity of illness[9], MSI was created to include the MAP rather than just SBP. It has been demonstrated that age-SI is a better predictor of death in geriatric patients. When compared to the typical adult cutoffs, the paediatric adjusted shock index (SIPA), which was created for paediatric populations,

has shown to be more reliable. Despite these developments, there is disagreement on the circumstances under which, and whether or not, SI should be used in emergency rooms (ED)[52,53].

Table: Variations of Shock Index

Shock index (SI) name variation	Equation	Notes
SI	HR/SBP	
Modified SI (MSI)	HR/MAP	• MAP substituted for SBP
Age SI	Age × (HR/SBP)	• SI multiplied by patient's age
Shock Index Pediatric Adjusted (SIPA)	(HR/SBP)	• Formula for SI is the same. Cutoffs are different for each age group: o Ages 4–6: >1.22 o Ages 7–12: >1.0 o Ages 13–16: >0.9

HR, heart rate; MAP, mean arterial pressure; SBP, systolic bood pressure

Shock index in sepsis

The Third International Consensus Definitions Task Force changed the definition of sepsis in 2016 from SIRS criteria to a life-threatening organ dysfunction caused by a dysregulated host response to infection, as measured by the use of Sequential Organ Failure Assessment (SOFA) and qSOFA ("quick" SOFA; (“quick” SOFA; ≥2 of the following: respiratory rate ≥22/minute, SBP ≤100 mm Hg or altered mentation) were recommended to identify sepsis in the hospital and ED settings, respectively[54]. SI has not been compared to or added to SOFA or qSOFA, despite being considered as an additional metric to identify patients who fit SIRS criteria and need prompt attention. When the SI was >0.7, subjects had a 3 times higher likelihood of hyperlactatemia when compared to those with SI 0.8 for at least 80% of ED vital sign measurements required vasopressors within 72 hours of admission, compared to only 11.6% of patients without a sustained elevation in SI[55]. A retrospective cohort of 2524 adult patients compared SI with 2 SIRS criteria and modified SIRS (SIRS

excluding white blood count) to predict serum lactate 4 m This study evaluated trends over time rather than using a single SI value (i.e. triage of vital signs).

The use of SI at the beginning of sepsis therapy did not predict the use of vasopressors or mortality. Similar to other vital signs, EMS-based trends of SI over time may help doctors spot individuals who are in septic shock. The use of SI to forecast the hemodynamic response to volume increase has also been studied. A prospective observational study[33] examined central venous pressure (CVP), SI, and volume responsiveness in 25 patients with septic shock who received 34 volume expansions (10 mL/kg over 20 min). The primary outcome was an increase in cardiac index (CI) measured by echocardiography of about 15% after expansion. With an NPV of 93% (95% CI 71-100%), patients with a CVP 8 mm Hg and SI 1 were unlikely to react to volume augmentation (13 nonresponders and 1 responder). Patients were more likely to respond to fluids if their SI was greater than 1.

This suggests that when determining whether a patient may respond to more fluid boluses, a high CVP and a relatively low SI work better together than either one alone. This may help prevent fluid overload in critically ill patients. It is uncertain how SI would compare to SOFA and qSOFA, which have better test features than SIRS and have been compared to SIRS for outcomes in sepsis. Additionally, combining the enhanced specificity of SI >1 with the higher sensitivity of SIRS criteria may result in a more precise method of identifying septic patients in need of urgent treatment. More research is required to identify the groups that will benefit the most and the precise cut points in SI that will produce the best test characteristics, but it looks that SI >1 may be utilised to help direct fluid resuscitation and the use of vasopressors[56].

The SOFA score:

Since its creation in the early 1990s, the SOFA score has been included into a variety of critical care elements, and it is currently often used in the daily monitoring of acute morbidity in critical care units. The SOFA score was created to offer population-level insights on the acute morbidity of ICU patients, but in recent years, its scope of use has significantly expanded. It is now utilised as a crucial criterion in

the diagnosis of the sepsis syndrome on a patient-by-patient basis following the creation of new definitions. With the adoption of organ dysfunction scores as an endpoint in exploratory trials for sepsis by the European Medicines Agency (EMA) and others, it is also increasingly utilised to assess the efficacy of potential treatment medicines in phase II trials[57].

The development of the SOFA score

Following a consensus meeting in 1994, the SOFA (Sequential Organ Failure Assessment) score was created with the stated goal of creating a score "to describe quantitively and as objectively as possible the degree of organ dysfunction/failure over time in groups of patients or even individual patients." Although the authors accepted that any functional morbidity score must also be connected with mortality, the score was created to describe a series of consequences of critical illness rather than to forecast the outcome. The score was initially referred to as the sepsisrelated organ failure assessment, but early on it was realised that it could also be used to assess acute morbidity in a variety of critical illnesses, so the name was changed. Six distinct values, one for each of the respiratory, cardiovascular, hepatic, coagulation, renal, and neurological systems, were used to calculate the SOFA. Each score ranged from 0 to 4, with a higher score indicating progressive organ dysfunction. The development team proposed its use as an alternative to other assessments of multiple organ dysfunction that had been developed in the early 1990s after retroactively demonstrating that the score detected differences in illness severity. After the score's initial validation, prospective analysis of the score's usefulness in 16 nations was conducted. The study demonstrated that a few subscores and the overall score were related to survival. In their analysis of the effects of the maximum SOFA score in the same population, Moreno et al. found a strong correlation between rising score and mortality. As a discriminator of survival status at ICU discharge, the score performed well. In addition to looking at the maximum SOFA score, the correlation between ICU mortality and the change in score, or delta SOFA (total maximum SOFA score minus admission total SOFA score), was also very strong. The SOFA score, its highest value during an ICU stay, and the change in SOFA over time have all been

verified as valid methods for the measurement of morbidity in critical illness[58]. The score is now a standard component of observational study reporting.

Table: The parameters used to evaluate the Sequential Organ Failure Assessment (SOFA) result

Respiratory system	
PaO_2/FiO_2 (mmHg)	SOFA score
> 400	0
< 400	1
< 300	2
< 200 with respiratory support	3
< 100 with respiratory support	4
Nervous system	
Glasgow Coma Scale	SOFA score
15	0
13–14	1
10–12	2
6–9	3
< 6	4
Cardiovascular system	
Mean arterial pressure (MAP) OR administration of vasopressors required	SOFA score
MAP > 70 mmHg	0
MAP < 70 mm/Hg	1
Dopamine ≤ 5 µg/kg/min or dobutamine (any dose)	2
Dopamine > 5 µg/kg/min OR epinephrine ≤ 0.1 µg/kg/min OR norepinephrine ≤ 0.1 µg/kg/min	3
Dopamine > 15 µh/kg/min OR epinephrine > 0.1 µg/kg/min OR norepinephrine > 0.1 µg/kg/min	4
Liver	
Bilirubin (mg/dl) [µmol/L]	SOFA score
< 1.2 (< 20)	0
1.2–1.9 [20–32]	1
2.0–5.9 [33–101]	2
6.0–11.9 [102–204]	3
> 12.0 [> 204]	4
Coagulation	
Platelets $\times 10^3$/ml	SOFA score
> 150	0
< 150	1
< 100	2
< 50	3
< 20	4
Kidneys	
Creatinine (mg/dl) [µmol/L]; urine output	SOFA score
< 1.2 [< 110]	0
1.2–1.9 [110–170]	1
2.0–3.4 [171–299]	2
3.5–4.9 [300–440] (or urine output < 500 ml/day)	3
> 5.0 [> 440]; urine output < 200 ml/day	4

Modified from Vincent et al. [5]

Calculation of the SOFA score standard approach

Traditionally, the SOFA score may be determined at ICU admission and at each 24-hour interval that follows. The instrument uses six criteria (respiratory, cardiovascular, renal, neurological, hepatic, and haematological) that represent how an organ system functions and assigns a score from 0 to 4 as explained below. Zero points are awarded when the physiological parameters do not match any row. When more than one row matches the physiological characteristics, the row with the highest score is chosen.

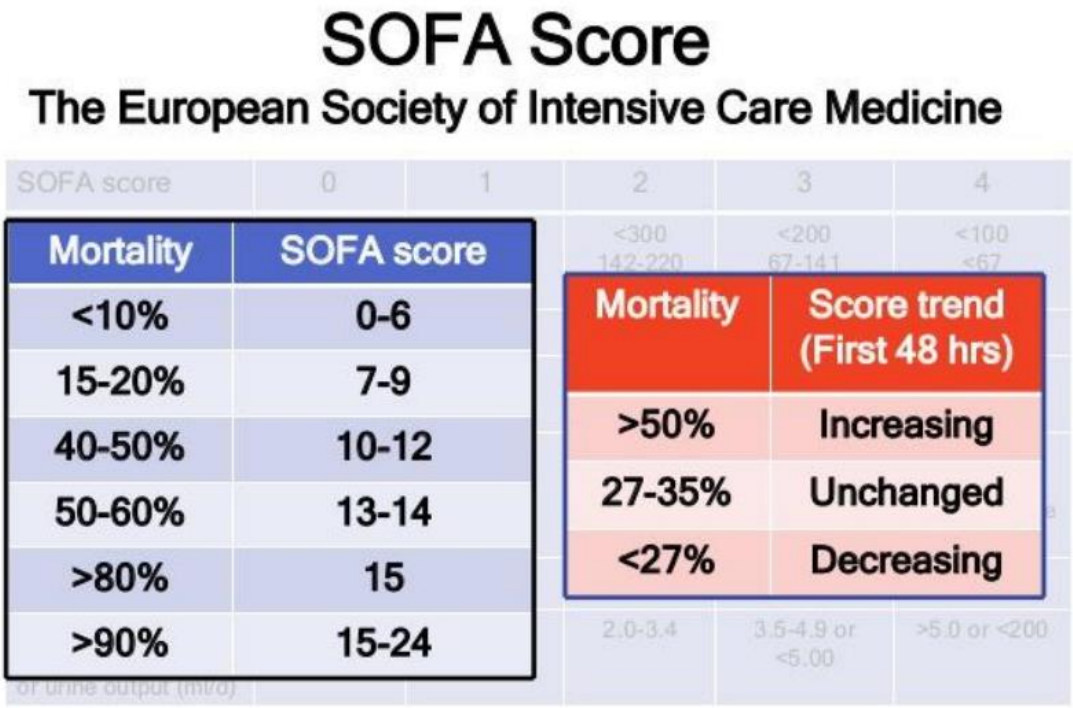


FIG: SOFA score and mortality

SOFA score terminology

The SOFA score has been applied in a range of applications with some variation in the terminology employed. A number of terms are commonly used and are associated with the following definitions:

Admission SOFA: The admission SOFA score is calculated based on the most severe value for each sub-score in the 24 h preceding admission to ICU[58].

Daily Maximum SOFA score: The daily maximum SOFA score is equivalent to the daily SOFA score as when calculated for each 24 h assessment; the most severe value of each sub-score for that time period should be calculated in the assessment of the SOFA score.

Maximum SOFA score: The maximum SOFA score describes the highest daily SOFA score over the course of the study period.

Delta SOFA score: The delta SOFA is calculated as the change in total SOFA score (or that of an individual sub-score) between a defined time point and the baseline value. The baseline value may be the admission SOFA or a defined study day.

Mean SOFA: The mean SOFA score is calculated for an individual patient over the course of a defined study period based on the total SOFA score for each study day

Extending the application of SOFA scoring

Since the initial consensus criteria for sepsis were created in the early 1990s, defining the syndrome has proven to be difficult. Expert opinion served as the foundation for the definitions of sepsis and septic shock. The term "life-threatening organ failure caused by a dysregulated host response to infection" was redefined in 2016 using an innovative technique and data-driven analysis. The team showed that the SOFA score was a more effective discriminant than the conventional SIRS and comparable to the more sophisticated Logistic Organ Dysfunction System (LODS). As a result, organ dysfunction was defined as a change in SOFA score of two or more points as a result of infection, which was associated with a 10% mortality rate. The authors realised that although the SOFA score can frequently be regarded as zero in patients who were previously healthy, the existence of persistent organ dysfunction prevents the use of an absolute value to determine the presence of infection. For doctors and researchers in critical care, this shift from observing to identifying a syndrome is extremely relevant.

Using SOFA as an outcome in clinical trials

Many researchers have suggested SOFA or delta SOFA as a potentially reliable surrogate in clinical trials because to the relationship between SOFA score upon admission and during ICU stay and long-term outcomes. This method has the benefit of requiring shorter durations of follow-up to assess efficacy, but this is only true if a change in SOFA is a clinically meaningful result or if it truly serves as a surrogate for a later critical outcome. This strategy will be more reliable if study teams publish the subscores that make up the SOFA along with the trial data, as they do with all composite outcomes. Changes in the CVS SOFA score, which showed a significant improvement during the study period in patients treated with angiotensin II, were a crucial secondary end point in the ATHOS-3 trial59. It's interesting that the study neglected to determine the vasopressor dose equivalency in the angiotensin II intervention group. This is a flaw that vasopressor studies should take into account fixing in the future. In contrast, the primary outcome measure in patients with septic shock and a noradrenaline requirement of 0.1 g/kg/min in the upcoming STRESS-L study of the effect of treatment with the beta blocker Landiolol will be "the mean SOFA score over the first 14 days from entry to the trial and whilst in ICU." With this method, no patients are eliminated from the end point analysis in the event that a patient dies before the study's end and the mean SOFA score across the period stays comparable across all patients regardless of survival duration. In 87 research, de Grooth et al.[60] examined the use of SOFA and its relationship to mortality. They investigated the relationship between using a fixed-day SOFA at a specific time point in the study, which enables comparisons of acute morbidity at that time point between study groups, and delta SOFA (defined as the change in SOFA score from baseline/maximum to a defined time point). They showed that employing delta SOFA was substantially connected with decreased heterogeneous mortality. The endpoint of a fixed day SOFA was not consistently linked to death.

qSOFA SCORE

After an international task force revised the clinical standards for sepsis and created the Third International Consensus Definitions for Sepsis and Septic Shock in 2016, the quick SOFA (qSOFA) score gained notoriety (Sepsis-3).

q SOFA is a surrogate for SOFA in those settings in which all components of SOFA are not routinely measured. It has 3 components:

Respiratory rate >21 breaths/min

Systolic arterial blood pressure ≤100 mm Hg

Altered mental status (Glasgow Coma Scale<15

LACTATE LEVEL

Humans cannot survive if lactate is not produced because it is an essential source of energy, especially during times of starvation. Lactate is converted to lactic acid, which contributes to an acidic environment, and it can also be converted to bicarbonate, which is a major source of alkalemia under normal physiological conditions (cardiac and skeletal muscle). The overproduction of lactate in sepsis patients is assumed to be caused by tissue hypoxia, which causes an increase in anaerobic glycolysis and a rise in serum lactate levels (30). decreased lactate clearance as a result of acute renal damage and liver dysfunction. Usually, lactate generation outpaces lactate clearance, and this might get worse when someone is seriously ill. According to numerous studies, patients with higher serum lactate levels than those with lower serum lactate levels had a significantly higher rate of acute hospital mortality. As a result, lactate level has been employed as a prognostic marker for mortality. Particularly, individuals with initial serum lactate levels greater than or equal to 4.0 mmol/L were at higher mortality risk, and an elevated initial lactate level significantly raised the risk of dying. Lactate levels greater than or equal to 4.0 mmol/L were 55% (95% CI 41% to 68%) sensitive and 91% (95% CI 90% to 93%) specific for acute mortality (death within 3 days), while they were 36% (95% confidence interval [CI] 27% to 45%) sensitive and 92% (95% CI 90% to 93%)

specific for any death. Deaths in the acute period and in hospitals rose linearly with lactate levels. Initial lactate levels below 4 mmol/l had minimal effect on the likelihood of death, whereas those above 4.0 mmol/l were associated with a sixfold increased risk of acute-phase death.

Sepsis Prevention

There are two main steps to preventing sepsis:

- Prevention of microbial transmission and infection
- Prevention of an infection evolving into sepsis

Effective hygiene practises, like hand washing, safe food preparation, improved sanitation and water quality and availability, providing access to vaccines, particularly for those at high risk, and appropriate nutrition, including breastfeeding for newborns, are all necessary for infection prevention in the community.

In order to effectively prevent infection in healthcare institutions, infection prevention and control (IPC) teams and programmes must be in operation. In addition, a clean, functional environment and equipment are also essential.

The right antibiotic treatment of infection, including optimization, rapid medical attention seeking, and early diagnosis of sepsis signs and symptoms, is necessary to prevent the evolution to sepsis in both community and health care facilities.

Diagnosis and Clinical Management

The above-mentioned signs and symptoms, as well as the identification of particular biomarkers (such as procalcitonin and C reactive protein), are essential for the early diagnosis of sepsis and the prompt implementation of its proper clinical care. In order to direct targeted antimicrobial treatment after early recognition, diagnostics to help identify a cause pathogen of infection leading to sepsis are important. Once the infection's origin has been identified, source management measures including

abscess drainage are crucial. AMR poses a risk to the therapeutic management of sepsis since it frequently necessitates the use of empirical antibiotic therapy. In the early stages of sepsis care, early fluid resuscitation to improve volume status is also crucial. Vasopressors may also be needed to maintain and improve tissue perfusion. Exams and evaluations conducted repeatedly, along with the observation of vital signs, direct the right care of sepsis throughout time.

Early treatment in usual resuscitation patients

	PROCESS	ARISE	ProMISe
Hours to Identification	1.5 (+/−0.75)	1.3[a] (0.5–2.4)	1.7 (+/−1.4)
Identification by lactate alone[b]	45%	30%	45%
Hours to antibiotic[a] administration	76.1% less than 3 hours[c]	1.12 (.63–1.8)	1.3 α (0.6–2.4)
Fluids prior to randomization (liters)	2.1 (+/−1.4)	2.6 (+/−1.3)	2.0 (+/−1.1)
Hours to randomization[a]	3.0 (+/−1.6)	2.7 (2.0–3.9)	2.5 (1.8–3.5)
Fluids 0–6 h (liters)[a]	2.8	1.7	2.0
Central venous catheter	58%	62%	51%
Vasopressor use	48%	58%	47%
ED LOS[a] (h)	NR	2.0 (1.0–3.8)	1.3 (.4–2.9)

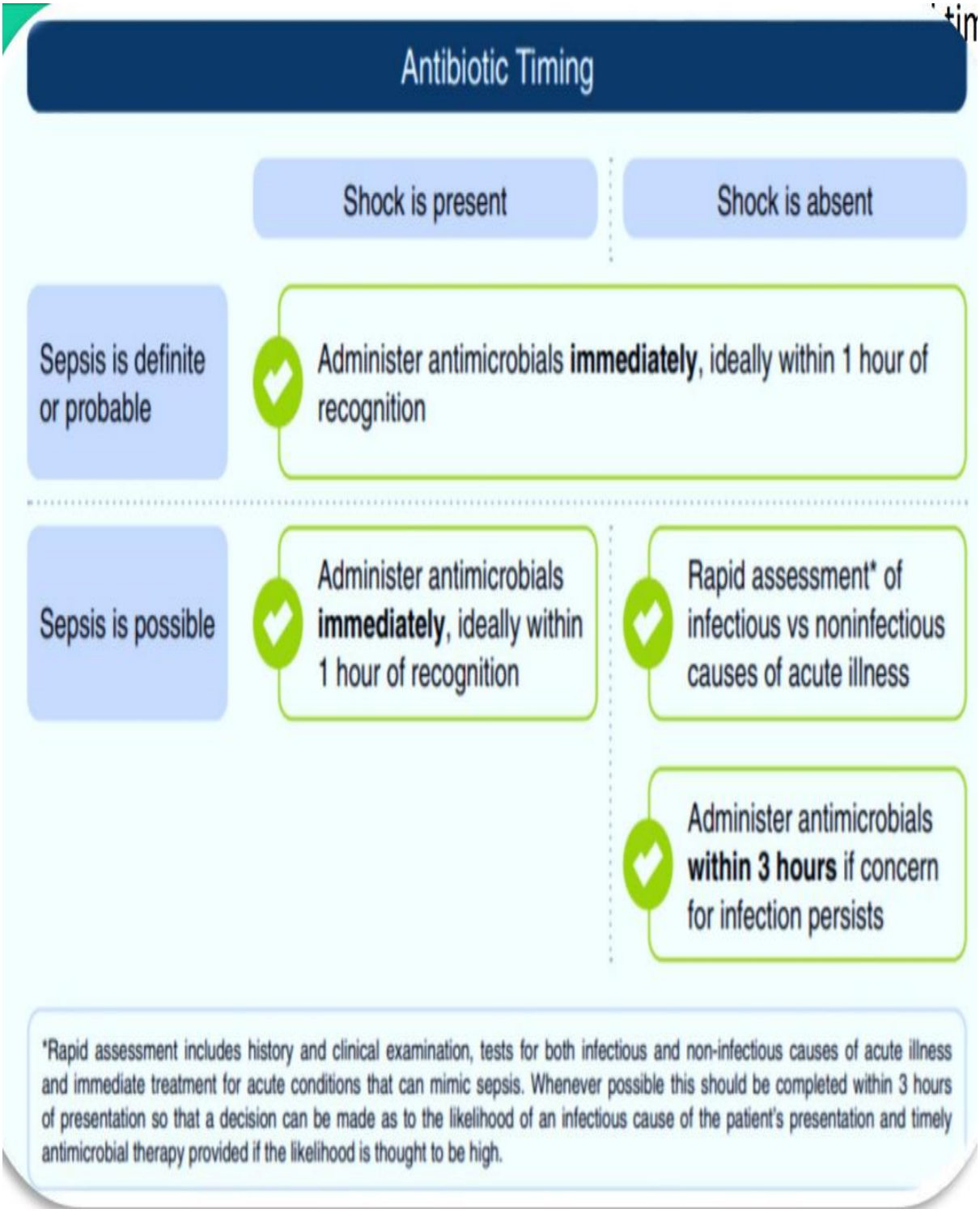
(+/−) denote means with standard deviation; α point at which all inclusion criteria met in ProMISe include antibiotic initiation.

Abbreviation: NR, Not Reported.

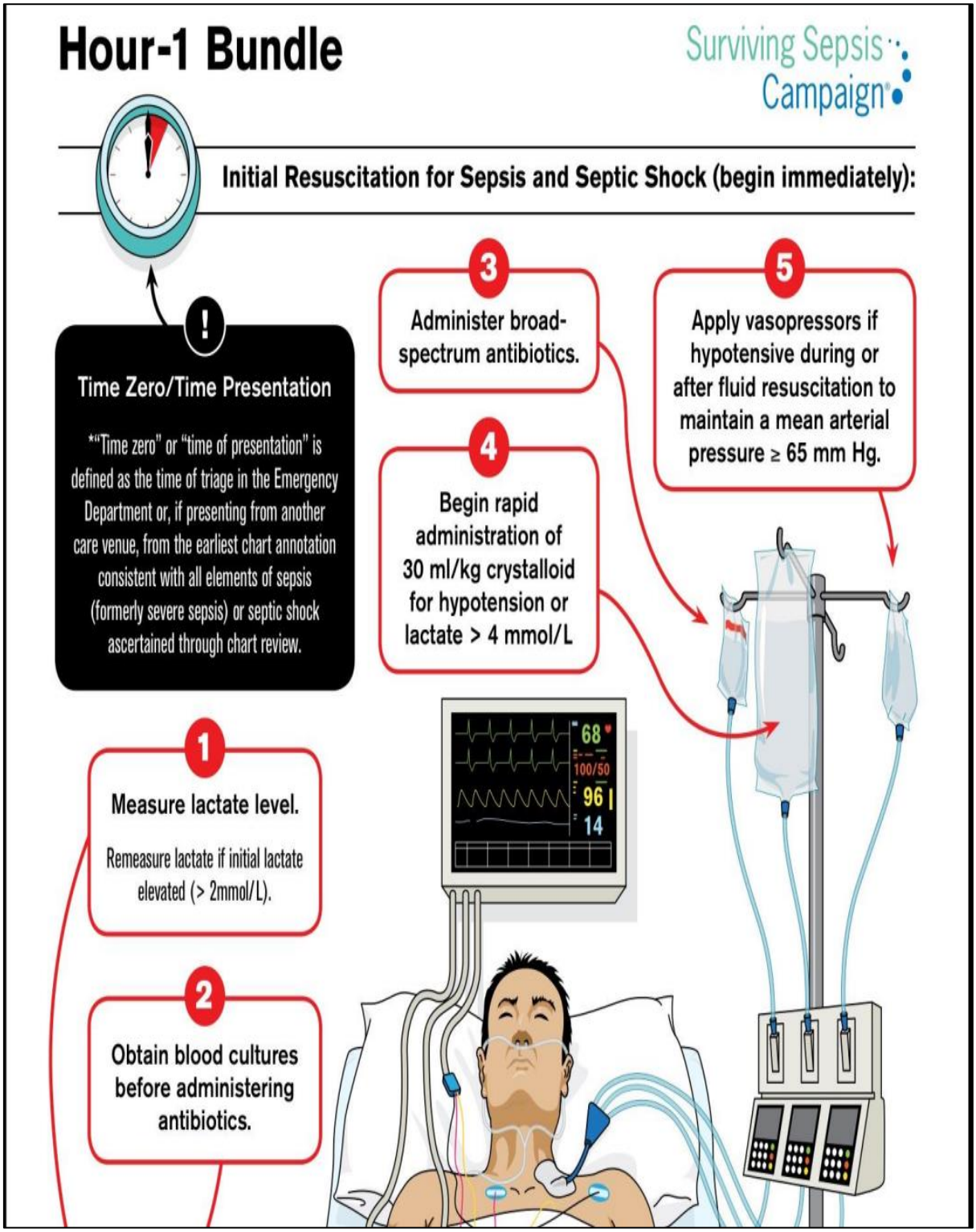
[a] Median (IQR) unless otherwise noted.

[b] Percent of normotensive, usual resuscitation patients identified by lactate ≥4 mmol/l alone.

[c] Related to randomization time.


Antibiotic Timing
Shock is present
Shock is absent
Sepsis is definite or probable
Administer antimicrobials immediately, ideally within 1 hour of recognition
Sepsis is possible
Administer antimicrobials immediately, ideally within 1 hour of recognition
Rapid assessment* of infectious vs noninfectious causes of acute illness
Administer antimicrobials within 3 hours if concern for infection persists
*Rapid assessment includes history and clinical examination, tests for both infectious and non-infectious causes of acute illness and immediate treatment for acute conditions that can mimic sepsis. Whenever possible this should be completed within 3 hours of presentation so that a decision can be made as to the likelihood of an infectious cause of the patient's presentation and timely antimicrobial therapy provided if the likelihood is thought to be high.

Surviving Sepsis Campaign



Review of Studies:

50 patients who were diagnosed with severe sepsis or septic shock and were hospitalised to the University of Malaya Medical Centre between June 2009 and June 2010 were the subjects of a retrospective observational study that Yussof S J M et al. did in 2012. Retrospective patient identification was done using information from the resuscitation room's registration book. For this pilot trial, 50 patients were chosen. 19 males (38%) and 31 females (62%) made up the population. Age range (minimum, maximum): 54.5 (17.0, 84.0). There were 31 cases of severe sepsis (62%) and 19 cases of septic shock (38%) respectively. There were 12 (24%) cases of other infections, 8 (16%) cases of gastro-intestinal tract infections, 13 (26%) cases of urological sepsis, and 17 (34%) cases of pneumonia. There were a total of 23 (46%) survivors and 27 (54%) deaths. The value of the shock index is defined as systolic blood pressure divided by heart rate was calculated. After two hours of resuscitation in the ED and the Shock Index upon presentation to the ED (SI 1) (SI 2). Mann-Whitney U and Chi Square analysis were used to test the median, minimum, and maximum variables. Re-evaluations of the significant parameters' sensitivity, specificity, and cut-off points were performed. To evaluate the prognostic value of these factors for outcome, ROC curves and AUC values were created. Two of the seven factors evaluated were found to be significantly different (p 0.05). The best predictor for mortality according to the sensitivity, specificity, and ROC analyses was (SI 2), which had a sensitivity of 80.8%, specificity of 79.2%, and AUC value of 0.8894 [CI95 0.8052, 0.9736] at a cut-off point of 1.0. According to the study's findings, (SI 2) may be used as a potentially accurate predictor of death in patients who present to an emergency room with septic shock and severe sepsis. To ascertain this parameter's validity, a bigger prospective investigation should be conducted[61].

A retrospective single-center investigation was carried out in the ICU of a tertiary hospital in 2015 by Biney I et al. Included were patients who had been admitted to the ICU with sepsis. From admission till ICU discharge, vital signs were taken every four hours, and the SI was determined for each set of measurements. A persistent SI elevation was characterised as having a SI over 0.7 for at least 50% of

the measurements. A total of 66 patients were examined, and of those, 45 (or 68%) had a prolonged SI elevation. The mean age of the group, 48% men and 86% African Americans, was 6115 years. Patients with a prolonged SI elevation were younger (58-16 vs. 68-11 years; p=0.04) than those without one. A total of 16 (24.2%) people passed away. Patients with a prolonged SI elevation had a greater rate of ICU mortality (33% vs. 4.8%; p=0.013) than patients without a sustained SI elevation. The sustained SI elevation group had a larger mean number of organ failures (52.3 vs. 3.52.2; p=0.022) than the non-sustained SI elevation group. The mean APACHE II score was the same for both groups (21.50 7.37 vs. 20.38 5.47; p=0.567). Additionally, there was no difference between the two groups in the frequency of new-onset arrhythmias (46.6% vs. 28.6; p=0.16) or the use of negative chronotropic treatment (47.6% vs. 47.6%; p=1). In patients admitted to the ICU with severe sepsis, a prolonged elevation of the SI is linked to higher morbidity and mortality, according to this study's findings[62].

In order to manage patients with sepsis and predict negative outcomes in these patients, Tseng J et al. (2015) conducted a review of the literature. To find English-language articles on the SI in humans, the PubMed, Scopus, Web of Science, and Google Scholar databases were searched for relevant information in the medical literature. These studies showed that the SI could assess the efficacy of fluid resuscitation and the likelihood of a response to additional fluid. It can predict the presence of lactic acidosis. The SI also helps predict the development of organ failure and mortality. Consequently, this easily available bedside measurement has utility in the identification, management and prediction of prognosis in patients with sepsis[63].

In 2015, Mann et al conducted a single-center retrospective review between June 2013 and September 2014 comprised of patients presenting to a public academic hospital ED. Subjects were identified by a computerised algorithm to detect the following: at least 2 SIRS criteria, suspected infection, and either hypotension or lactate > 4 after 2L of IV fluid resuscitation. Cases with blatantly incorrect diagnosis were disqualified. Following the administration of 2 litres of IV fluid, vital signs were monitored and utilised to determine the shock index. The use of vasopressor treatment

within 24 hours and in-hospital mortality were the primary outcomes that were examined using chi-squared testing and multivariate logistic regression. 217 cases met the criteria for inclusion. They separated the shock index into three groups that were predetermined: normal (n=31), 0.8 to 1.2 (n=102), and >1.2 (n=84). 19%, 24%, and 33% of each group died, respectively (p=0.20). Compared to patients in the normal group, there was no statistically significant increase in the odds of mortality for patients in the intermediate (OR 1.37, CI 0.48 - 3.90) or highest (OR 2.24, CI 0.79 - 6.38) categories of shock index. Within 24 hours, 52%, 57%, and 73% of each group used vasopressor therapy; this difference was statistically significant (p=0.04). This study found that a higher shock index of > 1.2 was substantially linked with increased usage of vasopressor medication in the first 24 hours in patients who arrived to the ED with symptoms suggestive of sepsis. Insufficient power was used in our investigation to identify a difference in mortality[64].

For eligible studies published up to December 23, 2016, Zhang et al. conducted a systematic search of PubMed, Embase, and the Cochrane Library in 2017. They used a variety of keyword combinations, including "shock index," "shock-index," "acute myocardial infarction," "ST elevation myocardial infarction," "non-ST segment elevation myocardial infarction," "STEMI," "NSTEMI," "AMI," and "MI." All-cause in-hospital mortality, short-term negative outcomes, and long-term negative outcomes were the 3 main outcomes for this analysis. Results: 226 citations were found through database searches. In the end, an analysis of 8 studies involving 20,404 patients was conducted. High SI was linked to an increased risk of dying while in the hospital (pooled RR=10.96, 95% CI: 2.00-59.94, P=.01). Adverse outcomes were significantly higher in the high SI group compared to the low SI group (pooled RR=1.93, 95% CI: 1.10–3.39, P=.02; I 2=95%). Individuals with high SI had an increased risk of long-term adverse outcomes (pooled RR=2.31, 95% CI: 1.90–2.81, P< .001) compared to low SI. This study concluded that high SI may increase the in-hospital mortality, short-term, and long-term adverse outcomes in AMI patients[65].

In 2018, Johns, Tracy J conducted a cohort study of patients with suspected and/or confirmed infection fulfilling atleast 2 SIRS criteria who presented to the

emergency department and were subsequently admitted in the medical wards or in the medical ICU. This was a single centre study done at Christian Medical College, Vellore, a tertiary care hospital primarily catering to the middle and low income group patients from all over India, predominantly the south Indian and the north eastern states. From the initial emergency department documentation of the heart rate and systolic blood pressure, shock index was calculated. Similarly SOFA score, q SOFA scores were calculated and the first lactate levels were observed. Usefullness of shock index in predicting the in-hospital mortality was investigated and this was compared with other outcome predictors like SOFA score, q SOFA score and lactate. The study enrolled 575 patients who met the inclusion criteria between January 1st, 2016, and June 30th, 2017. As a significant risk factor, diabetes was found to be present in 34.6% of patients. Majority of culture verified illnesses were caused by gramme negative bacteria. The most prevalent gramme positive and gramme negative bacteria, respectively, were staphylococcus aureus and E. coli. Lungs (15.8%) and the urinary tract (24.7%) were the main causes of sepsis. The majority of infections with negative cultures were due to scrub typhus (16.1%) and H1N1 (7.3%). At the time of presentation to the emergency room, 70.6% of the study cohort had shock index values greater than 1.0. In-hospital deaths were higher in patients with higher shock indices at the time of admission (shock indices greater than or equal to 1.0) than in patients with lower shock indices (7.69%), with an absolute difference of 29.99% and a p value less than 0.001. No matter what the cause of the infection was, the shock index had a negative impact on mortality. Similar to the previous finding, shock index values above 1.0 were linked to higher rates of ICU admission (48.0% versus 11.6%), more inotropic use (51.47% versus 1.77%), and higher rates of ventilator support (58.37% versus 19.52%) during the first 48 hours of hospitalisation. Performance of shock index was comparable with that of SOFA, q SOFA and lactate. This study concluded that higher shock index (more than 1.0) values at the time of presentation was related with higher fatality rates, higher rates of ICU admission and greater requirement for ventilator and inotropic support. Additionally, it performed well as a predictor of death for all infectious etiologies. As a result, it can be utilised as a triage tool for septic patients, especially in settings with limited resources[66].

In 2019, Ravi K et al conducted studies among patients fulfilling the Surviving Sepsis Campaign 2012 guidelines criteria for sepsis within the ICU were included over two years. On the first day of admission, APACHE II, SAPS II, and SOFA scores were calculated in addition to baseline haematological, biochemical, and metabolic parameters. Patients were monitored up to their passing or ICU release. Receiver operating curve analysis, the chi-square test, and the student t-test were performed. Results: During the course of the study, 100 patients were enrolled. 35 percent of people died altogether (68.6% of men and 31.4% of women). Patients with septic shock and severe sepsis had mortality rates of 88.6% and 11.4%, compared to none in the sepsis group. On multivariate analysis, APACHE II score greater than 27, SAPS II score greater than 43, and SOFA score greater than 11 on the day of admission were significant predictors of mortality. According to ROC analysis, SAPS II had the highest specificity (82.9%), whereas APACHE II had the highest sensitivity (92.3%). Additionally, this study came to the conclusion that all three ratings did a good job of predicting death. Overall, APACHE II was the best predictor of mortality in critically ill patients because it had the highest sensitivity. The SAPS II model exhibited the highest specificity, making it a stronger predictor of improvement than mortality. The sensitivity and specificity of SOFA were in the middle[67].F

From conception to March 26, 2019, Middleton D. J. et al. conducted an electronic search of the following databases: MEDLINE, EMBASE, Allie and Complementary Medicine Database (AMED), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Open Grey, ClinicalTrials.gov, and the WHO International Clinical Trials Registry Platform (WHO ITRP). Studies had to evaluate the shock index's prognostic accuracy or any changes to it for outcomes of mortality or the need for organ support in either sepsis or pneumonia. The Downs and Black checklist was used to conduct the methodological evaluation. Due to heterogeneity, the evidence was compiled using a narrative methodology. 15 studies (8697 patients) were included in this review out of 759 records that were screened. With high specificity and low sensitivity, shock index 1 at the time of hospital admission was a moderately accurate predictor of mortality in patients with sepsis or community-acquired pneumonia. Results relating to organ support were only reported in one

study. This review came to the conclusion that an elevated shock index at the time of hospital admission accurately predicts sepsis-related mortality. Due to its simplicity, shock index may have advantages over current sepsis scoring systems[68].

In 2019, S.M. From January 2016 to December 2017, all adult febrile patients who were triaged and had a temperature of 38°C or higher were included, according to Althunayyan et al. We calculate the SI with cut-off levels of 0.7 and 1 and the MSI with cut-off levels of 1 and 1.3 based on the triage vital sign. We provide information on the predictors' Relative Risk, Sensitivity, Specificity, Positive and Negative Predictive Values. outcomes associated with sepsis, including hyperlactatemia, ICU hospitalisation, and 28-day mortality Patient sample size is 274. Our inclusion/exclusion criteria were met by 274 patients. Out of the 274 patients, 252 (92%) were septic, 62 (22%) had hyperlactatemia, 20 were admitted to the intensive care unit, and 5 (within 28 days) passed away. An MSI of 1 had a sensitivity of 90% for predicting sepsis, 85% for admittance to the ICU, and 100% for mortality within 28 days. For all the non-significant statistical trends of increased accuracy of MSI over SI, MSI of 1.3 demonstrated a specificity (59%-100%). MSI and SI were revealed to be potential indicators in this study's triage of feverish patients. However, it was discovered that no single MSI or SI cut-off value had the best accuracy for predicting sepsis and outcomes related to sepsis. To evaluate the inclusion of MSI in a multi-item scale system for the prediction of sepsis and its associated effects, more research is necessary[69].

Ospina-Tascón, G.A. et al. discovered in 2020 that the risk of death increased over time with increasing levels of Pre-VPs/DSI or VPs/DSI (One-way ANOVA, p 0.001). Only when DSI simultaneously rose were progressive DAP declines or HR increases linked to increasing mortality risks. Pre-VPs/DSI, SOFA, and early lactate all had similar areas under the ROC curves, however mean arterial pressure and systolic shock index performed poorly as predictors of mortality. DSI*NE and DSI time course. (Repeated-measures ANOVA, p 0.001) The dose was considerably higher in non-survivors from both populations. This study came to the conclusion that DSI at pre-vasopressor and vasopressor start points can represent a very early

identifier of patients at high risk of death. Very early start of vasopressors displayed an evident benefit in higher Pre-VPs/DSI quintile. DAP or HR values on their own cannot clearly identify this risk. Future research need to investigate the usefulness of DSI to initiate or guide therapeutic measures in the early resuscitation of septic shock[70].

In January through December of 2021, a prospective observational study was carried out in a teaching hospital for tertiary care by Devendra Prasad K et al. The quick sequential organ failure assessment (qSOFA) and systemic inflammatory response syndrome criteria were used to classify patients with sepsis. MSI was taken into account as a predictor variable, co-morbidities as an explanatory variable, and the need for mechanical ventilation and step down from the intensive care unit as outcome variables. According to the area under the curve of 0.749 (95% CI: 0.600-0.897; p-value = 0.002) and a sensitivity of 68.75% in predicting mechanical ventilation after 24 hours (MSI 1.59), the MSI value on arrival to the emergency department among patients with co-morbidities had fair predictive validity in predicting the need for mechanical ventilation after 24 hours. Among people without co-morbidities, the MSI value on arrival to the emergency department had fair predictive validity in predicting the need for mechanical ventilation after 24 hours, as indicated by the area under the curve of 0.879 (95% CI: 0.770-0.988; p-value < 0.001) and a sensitivity of 83.33% in predicting the need for mechanical ventilation after 24 hours (MSI ≥ 1.67). This study also came to the conclusion that MSI can be used as an indicator to forecast how sepsis patients will fare in the emergency room. Patients with and without co-morbidities can be told whether they need mechanical breathing and to leave the intensive care unit after 24 hours using a straightforward MSI calculation done at the bedside[71].

1350 citations were reviewed in 2022 by Vang, M., et al., with a 0.90 inter-rater reliability. There were 38 cohort studies total, of which 14 reported the main result. Adult trauma patients with a SI 1 had a significantly higher in-hospital mortality rate than those with a SI 1, according to all studies. The meta-analysis includes 12 trials with 348,687 people altogether. The pooled risk ratio (RR) of in-

hospital mortality was 4.15 (95% CI 2.96–5.83). The overall quality of evidence was low. In-hospital mortality was found to be four times more likely in adult trauma patients with an initial SI of 1 in the ER or trauma center, according to this systematic review[72].

Materials and Methods

STUDY DESIGN: COHORT STUDY

STUDY POPULATION:

Patients with suspected infection above 18 years of age, who are admitted in the Intensive medical Care Units (IMCU) of Govt. Chengalpattu medical college are selected for this study. The disease spectrum and the outcomes are studied. Shock index at initial presentation to the emergency medicine department (ED) was compared to the traditional mortality predictors like SOFA score and the newly designed q SOFA score.

SAMPLE SIZE :100

STUDY DURATION: one year

INCLUSION CRITERIA:

Adults more than 18 years.

Suspected infection with fulfillment of two of the four criteria (mentioned below) below for systemic inflammatory response syndrome.

Temperature >38 or <36

Heart rate >90 beats per minute.

Respiratory rate >20 breaths per minute or $PaCO_2$ <32 mm Hg

WBC count >12,000/cumm, <4000/cumm, or >10% immature form

EXCLUSION CRITERIA:

Age less than 18 years

Presence of acute cerebrovascular event

Acute coronary syndrome

Acute pulmonary edema

Status asthmaticus

Cardiac dysrhythmias (as primary diagnosis)

Contraindication to central venous catheterization

Acute gastrointestinal haemorrhage

Seizure disorder

Drug overdose

Burn injury

Trauma

Requirement for immediate surgery

Immunosuppression (because of organ transplantation)

All the patients meeting the required criteria are enrolled into the study thus minimizing the chances of any selection bias.

Methodology:

Routine blood investigations

Urine analysis and urine culture, sensitivity

Blood culture and sensitivity

Serology (Malaria, Scrub Typhus, Leptospirosis, Dengue)

Sputum analysis for AFB stain, gram stain, culture and sensitivity

Arterial blood gas analysis

Chest X-ray PA views and lateral view

Ascitic fluid analysis for cell count, AFB, gram stain, culture and sensitivity is done

CSF analysis for cell count, AFB, gram stain, culture and sensitivity is done

Pleural fluid analysis for cell count, AFB, gram stain, culture and sensitivity is done

SOFA score:

SOFA score	0	1	2	3	4
Respirationa PaO_2/FIO_2 (mm Hg) SaO_2/FIO_2	>400	<400 221–301	<300 142–220	<200 67–141	<100 <67
Coagulation Platelets $10^3/mm^3$	>150	<150	<100	<50	<20
Liver Bilirubin (mg/dL)	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12.0
Cardiovascular[b] Hypotension	No hypotension	MAP <70	Dopamine </=5 or dobutamine (any)	Dopamine >5 or norepinephrine </=0.1	Dopamine >15 or norepinephrine >0.1
CNS Glasgow Coma Score	15	13–14	10–12	6–9	<6
Renal Creatinine (mg/dL) or urine output (mL/d)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9 or <500	>5.0 or <200

q-SOFA score:

Temperature >38 or <36

Heart rate >90 beats per minute.

Respiratory rate >20 breaths per minute or PaCO2 <32 mm Hg

WBC count >12,000/cumm, <4000/cumm, or >10% immature form

DATA ANALYSIS:

The data will be entered in Microsoft excel and will be analysed by using SPSS software. Appropriate tests of significance will be done.

Table: Descriptive analysis of age in study population (N=100)

Parameter	**Mean ± SD**	**Median**	**Minimum**	**Maximum**
Age	53 ± 8.98	54.50	30.00	66.00

Table : Descriptive analysis of sex in the study population (N=100)

Sex	**Frequency**	**Percentages**
Female	36	36.00%
Male	64	64.00%

Figure : Pie chart of sex in the study population (N=100)

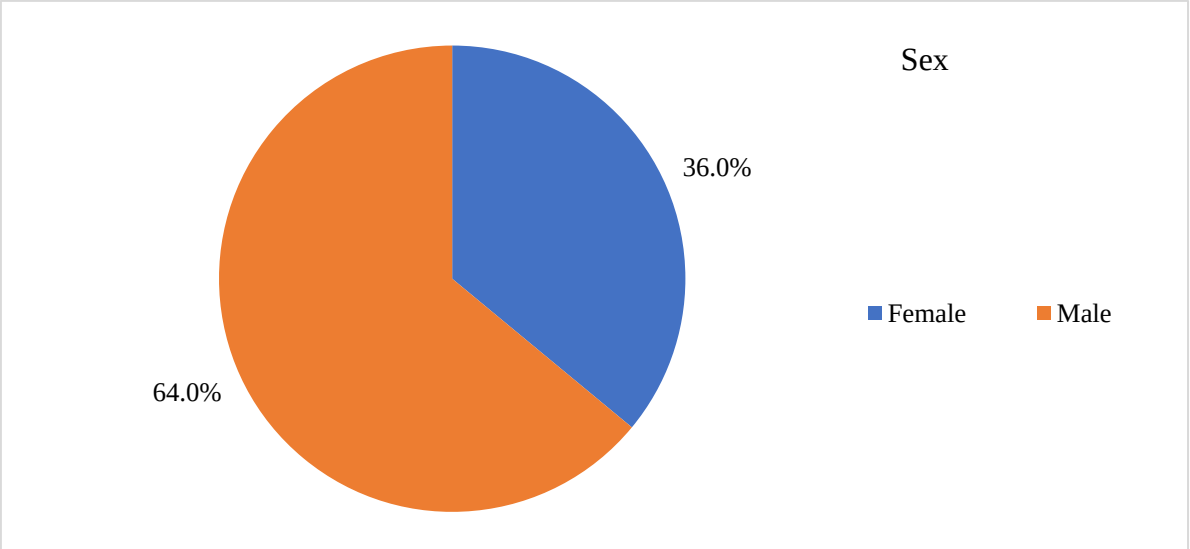


Table: Descriptive analysis of fever in the study population (N=100)

Fever	Frequency	Percentages
No	2	2.00%
Yes	98	98.00%
Difficulty Breathing	Frequency	Percentages
No	34	34.00%
Yes	66	66.00%
Altered Sensorium	Frequency	Percentages
No	44	44.00%
Yes	56	56.00%
Decreased Urine	Frequency	Percentages
No	50	50.00%
Yes	50	50.00%
Smoking	Frequency	Percentages
No	50	50.00%
Yes	50	50.00%
Dm	Frequency	Percentages
No	66	66.00%
Yes	34	34.00%
Htn	Frequency	Percentages
No	84	84.00%
Yes	16	16.00%
Ckd	Frequency	Percentages
No	72	72.00%
Yes	28	28.00%
Heart Failure	Frequency	Percentages
No	70	70.00%
Yes	30	30.00%

BASELINE	NUMBER (%)
Age (years)	53 ± 8.98
Males	64 (64%)
Diabetics	66 (66 %)
Confirmed infection (culture/ X ray/)	78 (78%)
Culture positive	22 (22%)
X ray positive	56(56%)
Serology positive	15(15%)

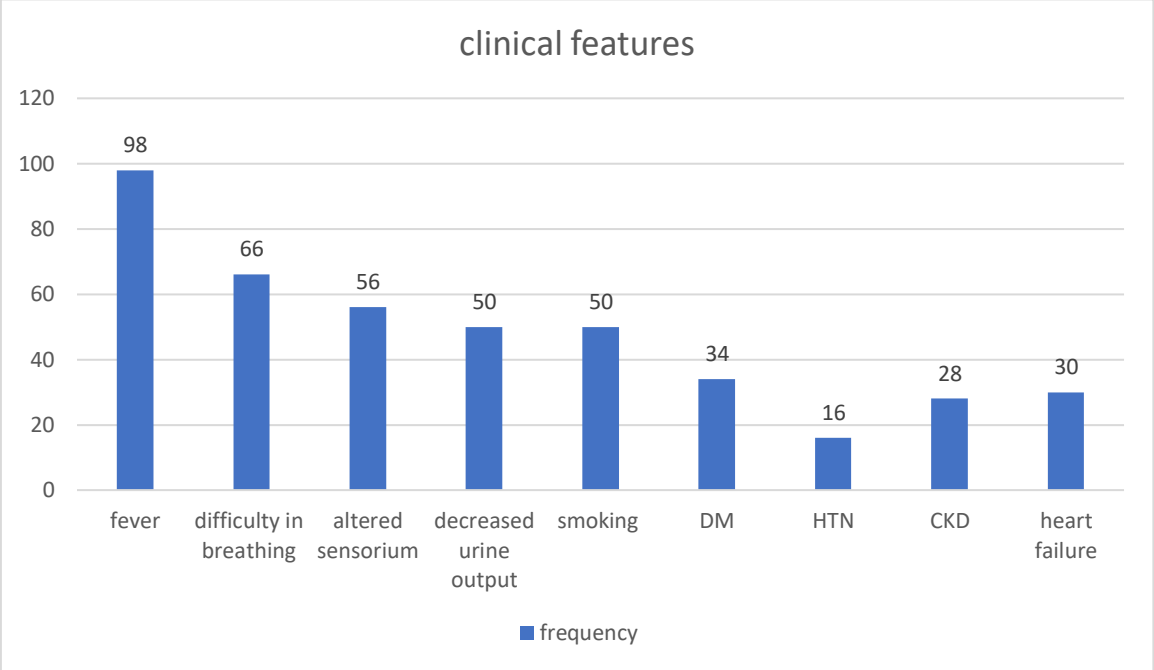


Table: Descriptive analysis of shock index and SOFA scores in study population (N=100)

Parameter	Mean ± SD	Median	Minimum	Maximum
Shock Index	1.48 ± 0.72	1.30	0.58	3.50
Q- Sofa	2.68 ± 0.47	3.00	2.00	3.00
Sofa	9.08 ± 1.92	9.00	6.00	14.00

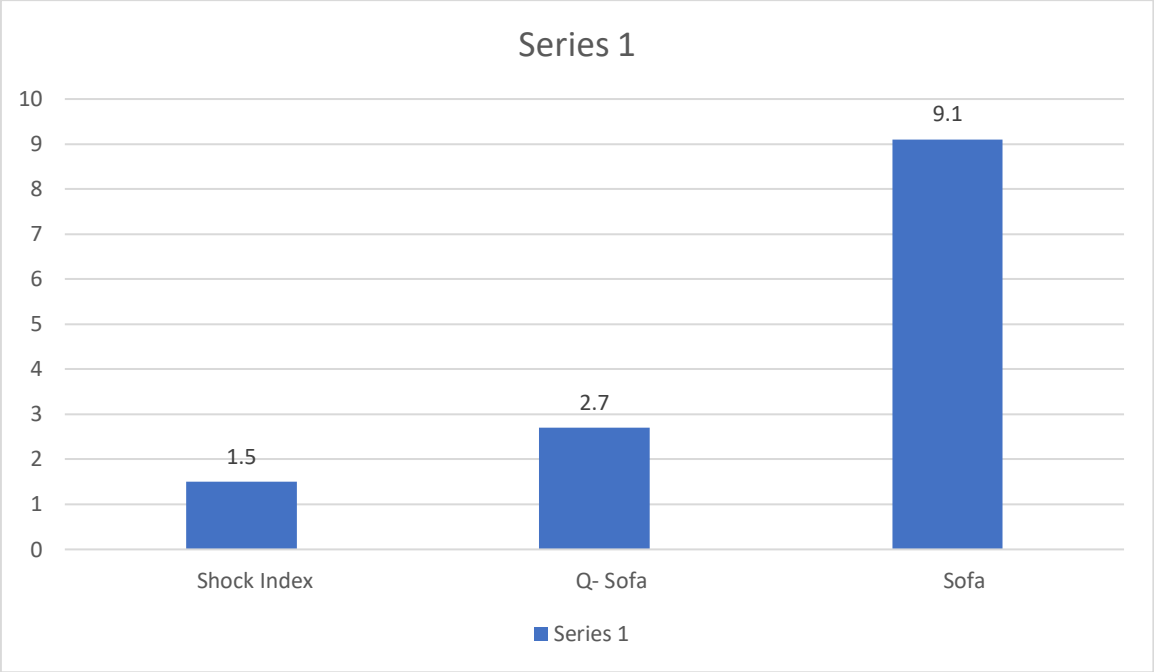


Table: Descriptive analysis of PARAMETER in study population (N=100)

Parameter	Mean ± SD	Median	Minimum	Maximum
Platelets	36.04 ± 42.89	1.90	0.90	99.00
Total Bilirubin	1.56 ± 0.32	1.50	1.10	2.20
Hb	10.75 ± 2.11	10.15	6.70	14.10
Na +	130.6 ± 2.74	132.00	122.00	135.00
K+	4.16 ± 0.49	4.20	3.60	5.30
Wbc	20.07 ± 5.71	21.00	3.80	33.00
Creatinine	2.2 ± 1.04	1.90	1.20	6.50

INFECTION : Among the 100 patients, 78 (78 %) had a confirmed infection (culture

/ X ray positive). 22 (22%) had positive culture reports. Chest

X ray was suggestive of pneumonia in 56 (11.4 %) ,serology was

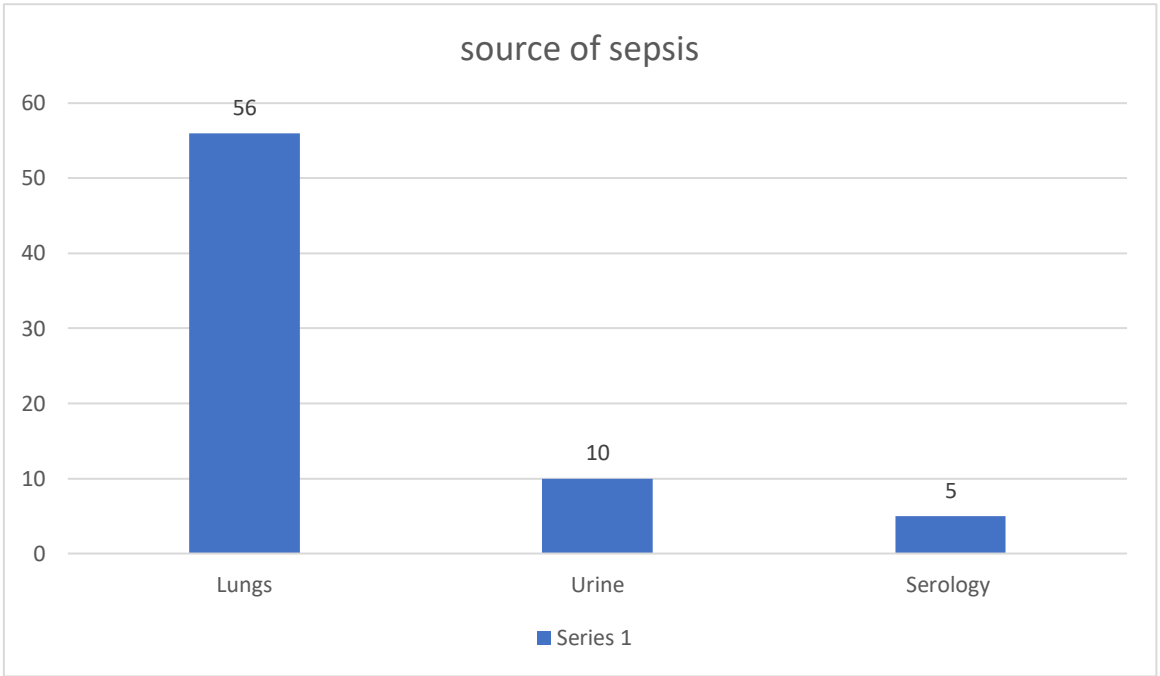
positive in 15(15%) of patients.

SHOCK INDEX: Initial shock index was less than 0r = 1 in 28 (28 %) patients and 72 (72%)

had shock index values greater than 1.0 at presentation .

SOURCE OF SEPSIS (CULTURE + X RAY POSITIVE)

	N= 100	%
Lungs	56	56
Urine	10	10
Serology	5	5



ETIOLOGY OF CULTURE POSITIVE SEPSIS

CULTURE POSITIVE	NUMBER (%)
E . coli	9 (40 %)
Klebsiella	6 (27%)
Pseudomonas	5 (22%)
Acinetobacter	2 (9%)
TOTAL	22

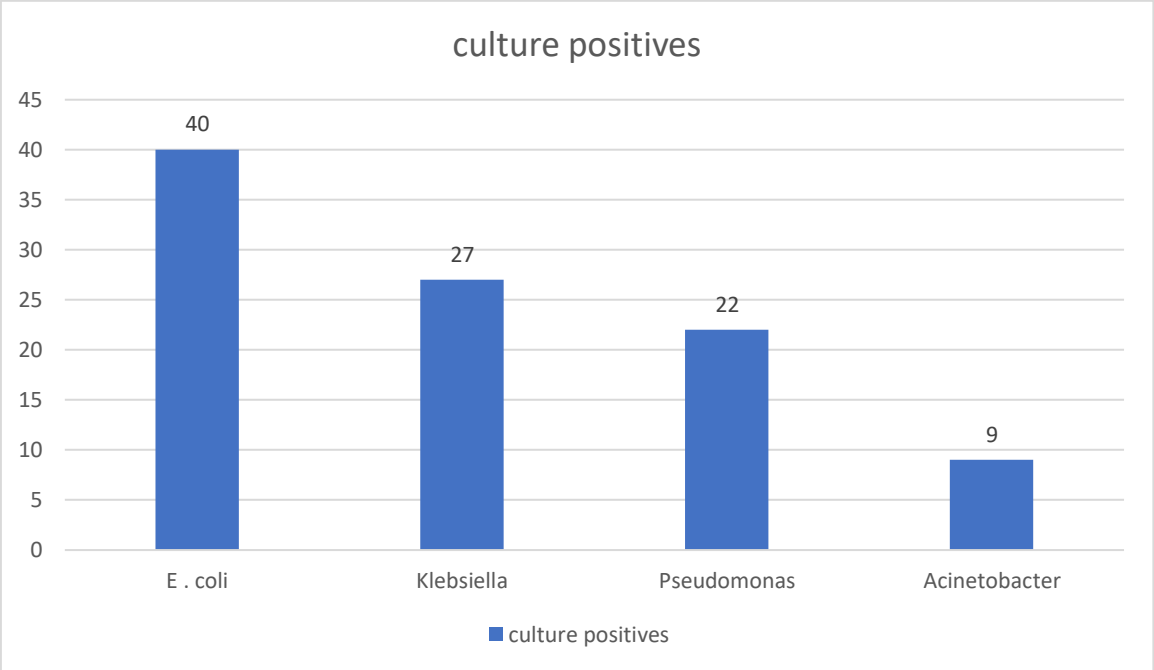
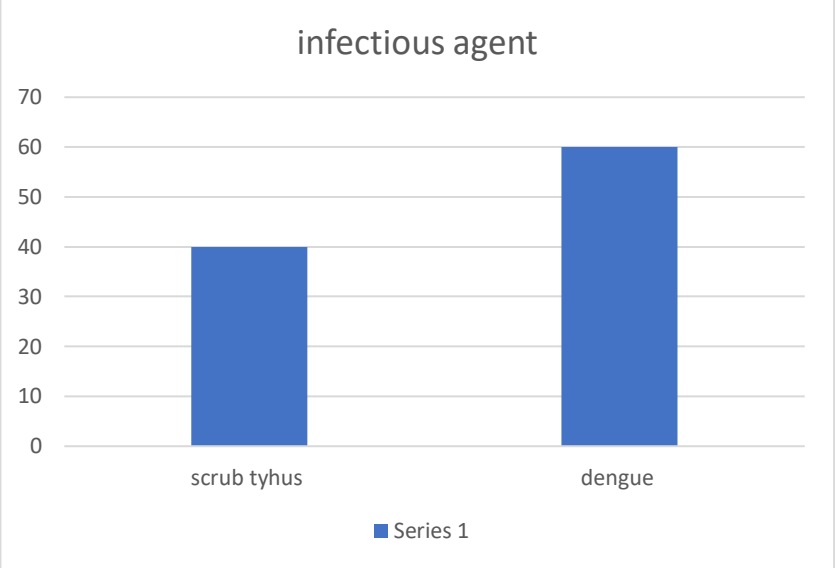


Table 7: Etiology of serology positive cases

SEROLOGY POSITIVE SEPSIS

INFECTIOUS AGENT	NUMBER (%)
Scrub typhus	2 (40 %)
Dengue	3 (60%)
TOTAL	5



PRIMARY OUTCOME:

OUTCOME AT DISCHARGE

The primary outcome studied was the clinical condition at discharge.

Among the 100 patients included in the study, 68 (68.7 %) improved and were discharged. 24 (24%) patients died during the hospital stay and 8 (8 %) patients liked to go to another institution .

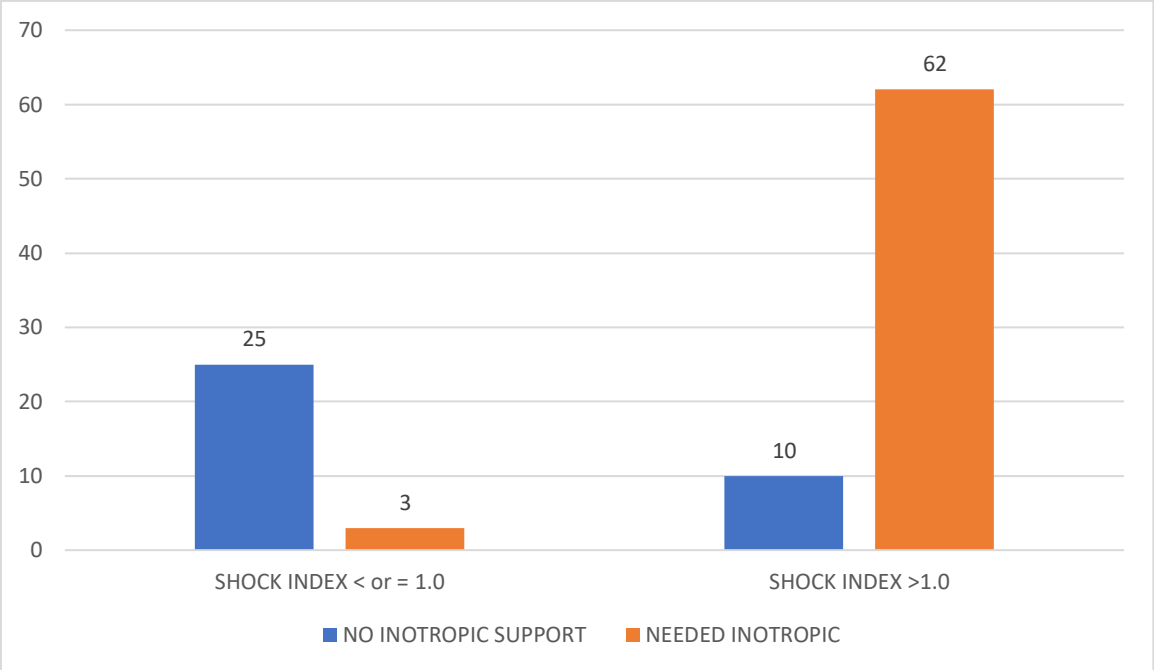
In the group with shock index less than or = 1, 24 (85 %) patients improved and 4 (15 %) patients died. In the group with shock index of more than 1 at presentation, 48 (72%) patients improved and 24 (28%) died.

INOTROPIC REQUIREMENT WITHIN INITIAL 48 HOURS

Among the total cohort of patients 100 , 65 required inotropic support within 48 hours of hospital admission

SHOCK INDEX AND INOTROPIC REQUIREMENT

	NO INOTROPIC SUPPORT	NEEDED INOTROPIC SUPPORT
SHOCK INDEX < or = 1.0	25	3
SHOCK INDEX >1.0	10	62



In the group with shock index < or =1 , 3 (12 %) people out of 28 needed inotropes. In the group with shock index more than 1.0 62 (86%) patients needed inotropes in the initial 48 hours.

VENTILATORY SUPPORT DURING THE INITIAL 48 HOURS

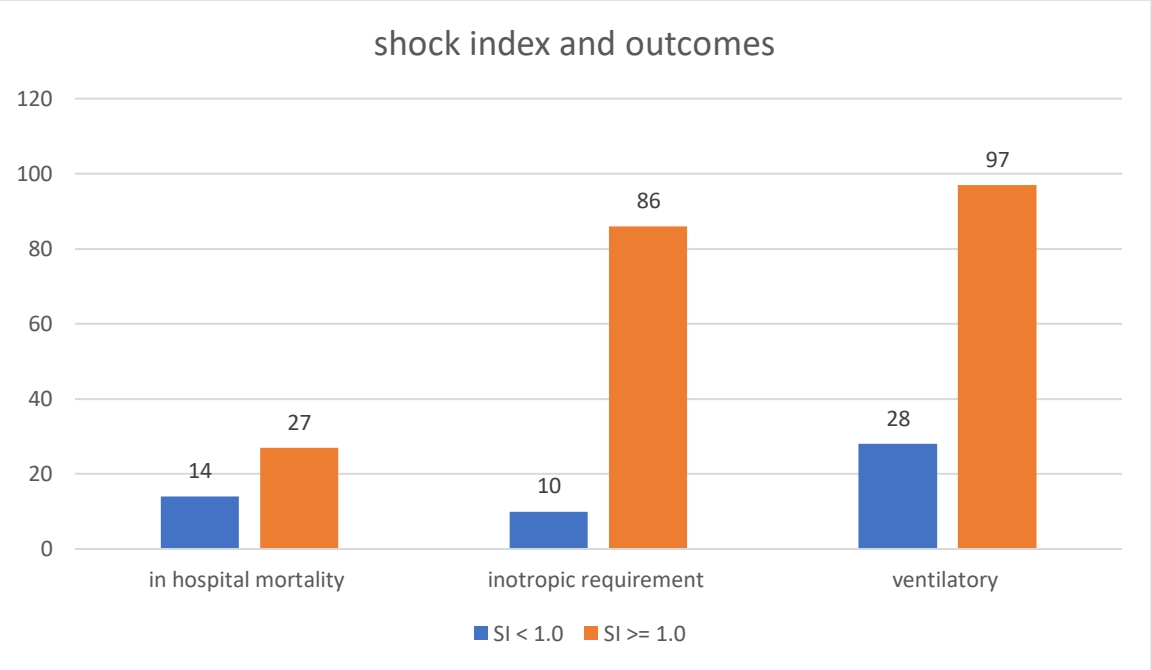
22 (22 %) patients did not require any form of ventilator assistance . 51(41 %)patients had to be managed with non invasive ventilation (NIV) and 27 (19 %) required invasive ventilation.

SHOCK INDEX AND VENTILATORY REQUIREMENT

In the cohort with shock index < or = 1 , 6 (26%) required NIV and 2 (15 %) required invasive ventilation. In the group with shock index more than 1.0, 47 (74 %) required NIV support and 23 (85 %) required invasive ventilatory support.

SCORING SYSTEMS IN PREDICTING OUTCOMES SHOCK INDEX AND OUTCOMES

		SI < 1.0 N = 28	SI >= 1.0 N= 72	Absolute Difference %	P value
PRIMARY OUTCOME					
	In- hospital mortality	4 (14 %)	20 (27%)	13	<0.001
SECONDARY OUTCOMES					
1	Inotropic requirement during initial48 hours	3(10 %)	62 (86%)	80	<0.001
3	Ventilatory requirement during initial 48 hours	8 (28)	70 (97%)	69	<0.001



SHOCK INDEX AS PREDICTOR OF OUTCOME IN PATIENTS WITH SEPSIS IN CHENGALPATTU MEDICAL COLLEGE HOSPITAL

Discussion:

The shock index (SI) is calculated by dividing the heart rate by the systolic blood pressure. The usual range in healthy persons is 0.5 to 0.7. Even non-medical employees can use the simple bedside method known as shock index. In individuals with sepsis, peripheral vasodilatation lowers systemic vascular resistance (SVR). The heart rate increases as a coping mechanism in an effort to maintain the blood pressure's stability. Thus, in the early stages of sepsis, the blood pressure could be normal. As a result, blood pressure alone may not be a reliable predictor of a patient with early sepsis. However, the tachycardia would raise the shock index, which can aid in early sepsis detection. With sepsis from a urinary tract infection often having the lowest fatality rates, the site of the infection in sepsis patients may have a substantial impact on the course of their illness. Several grading systems have been used to predict the prognosis of sepsis patients.[73] The Sequential Organ Failure Assessment (SOFA), a scoring tool to assess organ function, was created for the diagnosis of sepsis. In 2016 updated recommendations on sepsis and septic shock, the Quick SOFA (qSOFA), a simplified version of the SOFA, was suggested as an additional tool for the quick diagnosis of sepsis in high-risk patients.[74] This is a Cohort study conducted among the 100 adult patients who were suspected for infection with fulfillment of two of the four criteria (mentioned below) below for systemic inflammatory response syndrome; Temperature >38 or <36 , Heart rate >90 beats per minute, Respiratory rate >20 breaths per minute or PaCO2 <32 mm Hg, WBC count >12,000/cumm, <4000/cumm, or >10% immature form . This study was conducted

to assess whether shock index is a good predictor of clinical outcome in patients with suspected sepsis at Chengalpattu Medical College Hospital.

The mean age of the participants was found to be 53 ± 8.98 years. Nasa etal found that the mean of the patients with the sepsis was around 63 years.[75] This slight indifference was due to a fact that difference distribution of age was involved in our study. There are obvious distinctions in how each sex and gender reacts to infection and septic shock. Estrogens sometimes boost immunological response to the point of triggering autoimmune illness. Testosterone inhibits immunological response, which might occasionally increase the effects of trauma. Studies are being done on treatments utilising sex hormones to lessen autoimmune disease flare-ups and enhance outcomes following sepsis and hemorrhagic shock.[76] In our study we found that there was a male predominance with participation.

We found that nearly half of the study population were smokers. However, a study was conducted by Alroumi etal to find the impact of smoking on patient outcomes in severe sepsis and septic shock. They addressed that only 18% of the study subjects were smokers. This difference was due to the eligibility criteria restriction with the study samples.[77] Nearly all (98%) of the participants had fever. A typical sign of sepsis, fever, is frequently thought to indicate a better prognosis for survival. Elevating body temperature may inhibit microbial development and improve host immune responses, according to experimental evidence. But in sepsis patients, the high energy expenditure of fever may make the situation even more lethal. In the ICU, fever control is frequently used, mostly with patients who have infections.[78]

Hammon etal noticed that Renal illness was the most typical main diagnosis, and diabetes (44.0%) and chronic renal failure (11.6%) were typical comorbidities. However, we found that heart failure was the most common co-morbidity (30%). Severe and sometimes fatal, sepsis is characterised by widespread organ failure brought on by individuals' abnormal responses to infection. The combination of heart failure and sepsis has a complex pathophysiological mechanism, high mortality, and a high likelihood of ICU admission (ICU).[79]

This was followed by chronic kidney disease (CKD-34%) and diabetes (28%). Hypertension was observed only in 16% of the subjects. [80] As the prevalence of diabetic mellitus (DM) has rapidly increased worldwide, sepsis has become more common in DM patients. These two serious illnesses underscore the need to learn more about the critical components of the immune response that are relevant to both ailments and pose a global public health risk. In this respect, it is well known that diabetes patients have impaired function of the cells involved in the innate and adaptive immune responses. These modified reactions encourage the growth of microorganisms, a process that aids in the development of sepsis.[81]

Studies have shown that those with chronic renal illness have a higher chance of developing sepsis. The severity of sepsis is exacerbated by advancing CKD in part because less cytokines are cleared by the kidneys. Both HMGB1 release and splenic apoptosis brought on by CKD may play a significant role as shared mediators of CKD and sepsis.[82]

Middleton DJ etal found that mean elevated shock index at the time of hospital admission accurately predicts mortality in sepsis. Due to its simplicity, the shock

index may have advantages over current sepsis scoring systems.[83] Althunayyan etal highlighted that an MSI of ≥ 1 had a sensitivity of 90% for predicting sepsis, 85% for admittance to the ICU, and 100% for mortality within 28 days. A specificity range of 59% to 100% for all the outcomes of interest was shown by an MSI of ≥ 1.3. statistically insignificant tendencies that MSI is more accurate than SI. In our study the mean Shock Index was 1.48 ± 0.72. The most numerous circulating cells are red blood cells, also known as erythrocytes, which are created in the bone marrow through a complicated and multi-step process called erythropoiesis that starts with the differentiation of multipotent hematopoietic stem cells into erythroid-committed precursors. Reticulocytes, which complete the maturation process into erythrocytes, are produced and released into the bloodstream in the last stage. Reduced RBC count is a hallmark of sepsis, which may result from a variety of causes relating to altered RBC generation or survival.[85] In our study the mean hemoglobin level was lesser in patients with sepsis.

The activation of platelets occurs during sepsis as a result of a number of events, including the pathogen's direct contact with DAMP receptors expressed on the platelet surface, activation of the coagulation system, an inflammatory response, and endothelial tissue damage. When activated, platelets perform a variety of tasks. The surface of activated platelets expresses a number of receptors that either boost their ability to combine with other surrounding platelets and leukocytes or that bind and sequester external pathogens. A typical observation in septic patients is a decrease in platelet count, or thrombocytopenia, with incidence rates ranging from 20 to 70%

in various studies.[86] We also observed the similar findings in our study with respect to the platelets.

Agnello etal highlighted that WBC count may be low or even normal in some sepsis patients. As a result, the specificity of total WBC as a biomarker of sepsis is low.[87] We similarly found the result lining with the previous reference. As a sign of liver damage, admission serum bilirubin levels have been added into severity of disease rating systems in critical illness. Patel [88] etal found that mean bilirubin was greater than 1 in their study. Similarly, we found that the mean bilirubin was 1.56 ± 0.32 mg/dl.

The Q-SOFA was developed by Sepsis-3 to help identify patients with suspected infections who are at high risk for a poor outcome (defined as in-hospital mortality or an ICU stay of 3 days) outside of the ICU. The SOFA is a validated intensive care unit (ICU) mortality prediction score.[89] The mean Q-SOFA and SOFA score of the subjects were found to be 2.68 ± 0.47 and 9.08 ± 1.92 respectively. This was augmented by the study conducted by Li etal who found the near results relative to our study findings.[90]

CONCLUSIONS

The conclusion of the study are as follows:

The study described the spectrum of septic patients presenting to a tertiary care hospitalin south India.

Shock index perfomed as a good indicator of in-hospital mortality, and its performance was comparable to other established indices like q SOFA scores, SOFA score .

Shock index greater than or equal to 1.0 at initial assessement is associated with greaterrates of ICU admission, inotropic requirement and ventilator support.

Usefullness of shock index as a mortality predictor was comparable over all the etiologiesof sepsis.

LIMITATIONS

This study was done in a single centre tertiary care hospital, the disease representation may not reflect the actual populations disease spectrum in the community due to referral bias.

References

1. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome and associated costs of care. Critical Care Med. 2001;29(7):1303-10.d
2. Moss M. Epidemiology of sepsis: race, sex, and chronic alcohol abuse. Clin Inf Dis. 2005;41:490-7.
3. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med. 2013;39(2):165-228.
4. Levy MM, Dellinger RP, Townsend SR, LindeZwirble WT, Marshall JC, Bion J, et al. The surviving sepsis campaign: results of an international guideline-based performance improvement program targeting severe sepsis. Intensive Care Med. 2010 Feb 1;36(2):222-31.
5. Jones AE, Shapiro NI, Trzeciak S, Arnold RC, Claremont HA, Kline JA. Emergency Medicine Shock Research Network (EMShockNet) Investigators. Lactate clearance vs central venous oxygen saturation as goals of early sepsis therapy: a randomized clinical trial. JAMA. 2010;303:739-46.
6. Evaluation for severe sepsis screening tool, institute for healthcare improvement Ihi.org, 2018. Available at:http://www.ihi.org/IHI/Topics/CriticalCare/Sepsis /Tools/EvaluationforSevereSepsisScreeningTool.ht ml. Accessed 19 November 2018
7. Rousseaux J, Grandbastien B, Dorkenoo A, Lampin M, Leteurtre S, Leclerc F. Prognostic value of shock index in children with septic shock. Pediatr Emerg Care. 2013;29(10):1055–1059. doi:10.1097/ PEC.0b013e3182a5c99c
8. Zarzaur BL, Croce MA, Fischer PE, Magnotti LJ, Fabian TC. New vitals after injury: shock index for the young and age × shock index for the old. J Surg Res. 2008;147(2):229–236. doi:10.1016/j.jss.2008.03.025

9. Torabi M, Moeinaddini S, Mirafzal A, Rastegari A, Sadeghkhani N. Shock index, modified shock index, and age shock index for prediction of mortality in emergency severity index level 3. Am J Emerg Med. 2016;34(11):2079–2083. doi:10.1016/j.ajem.2016.07.017
10. Acker SN, Bredbeck B, Partrick DA, Kulungowski AM, Barnett CC, Bensard DD. Shock index, pediatric age-adjusted (SIPA) is more accurate than age-adjusted hypotension for trauma team activation. Surgery. 2017;161(3):803–807. doi:10.1016/j.surg.2016.08.050
11. Xia WF, Li BY, Lin WS, et al. Progress in Diagnosis and Treatment of Sepsis. Medical Recapitulate 2019,25:2169-73.
12. Schuetz P, Birkhahn R, Sherwin R, et al. Serial Procalcitonin Predicts Mortality in Severe Sepsis Patients: Results From the Multicenter Procalcitonin MOnitoring SEpsis (MOSES) Study. Crit Care Med 2017;45:781-9
13. Huang SW, Guan XD, Chen J, et al. Comparison of four intensive care score modes in the patients with severe sepsis. Chinese Journal of Critical Care Medicine 2005;11:802-3.
14. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:801-10.
15. Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:762-74.
16. Raith EP, Udy AA, Bailey M, et al. Prognostic Accuracy of the SOFA Score, SIRS Criteria, and qSOFA Score for In-Hospital Mortality Among Adults With Suspected Infection Admitted to the Intensive Care Unit. JAMA 2017;317:290-300
17. Kaukonen K, Bailey M, Suzuki S, et al. Mortality related to severe sepsis and septic shock among critically Ill patients in Australia and New Zealand, 2000–2012. JAMA 2014; 311(13): 1308–1316.

18. Torio CM and Andrews RM. National inpatient hospital costs: the most expensive conditions by payer, 2011. Statistical Brief #160. August, 2013. Rockville, MD: Agency for Healthcare Research and Quality.
19. Levy MM, Artigas A, Phillips GS, et al. Outcomes of the surviving sepsis campaign in intensive care units in the USA and Europe: a prospective cohort study. Lancet Infect Dis 2012; 12(12): 919–924.
20. Funk DJ, Parrillo JE and Kumar A. Sepsis and septic shock: a history. Crit Care Clin 2009; 125(1): 83–101.
21. Gül F, Arslantaş MK, Cinel I, et al. Changing definitions of sepsis. Turk J Anaesthesiol Reanim 2017; 45(3): 129–138.
22. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. Lancet (London, England). 2020;395(10219):200-11.
23. Lawn JE, Bianchi-Jassir F, Russell NJ, Kohli-Lynch M, Tann CJ, Hall J, et al. Group B Streptococcal Disease Worldwide for Pregnant Women, Stillbirths, and Children: Why, What, and How to Undertake Estimates? Clin Infect Dis. 2017;65(suppl_2):S89-S99.
24. Remick DG. Pathophysiology of sepsis. Am J Pathol 2007; 170(5): 1435–1444.
25. van der Poll T and Opal SM. Host–pathogen interactions in sepsis. Lancet Infect Dis 2008; 8(1): 32–43.
26. Esmon CT. The interactions between inflammation and coagulation. Br J Haematol 2005; 131(4): 417–430
27. Hotchkiss RS, Tinsley KW, Swanson PE, et al. Sepsis-induced apoptosis causes progressive profound depletion of B and CD4+ T lymphocytes in humans. J Immunol 2001; 166(11): 6952–6963.
28. Heagy W, Hansen C, Nieman K, et al. Impaired ex vivo lipopolysaccharide-stimulated whole blood tumor necrosis factor production may identify “septic” intensive care unit patients. Shock 2000; 14(3): 271–276.

29. Heagy W, Nieman K, Hansen C, et al. Lower levels of whole blood LPS-stimulated cytokine release are associated with poorer clinical outcomes in surgical ICU patients. Surg Infect 2003; 4(2): 171–180.
30. Jones AE and Puskarich MA. Sepsis-induced tissue hypoperfusion. Crit Care Nurs Clin North Am 2011; 23(1): 115–125.
31. Vieillard-Baron A. Septic cardiomyopathy. Ann Intensive Care 2011; 1(1): 6
32. United States Centers for Disease Control and Prevention. Healthcare Professional (HCP) Resources : Sepsis. Updated August 27, 2019. T06:23:15Z. https://www.cdc.gov/sepsis/get-ahead-of-sepsis/hcp-resources.html (accessed 25 February 2020).
33. Global Sepsis Alliance. Toolkits. https://www.world-sepsis-day.org/toolkits/ (accessed 25 February 2020).
34. UK Sepsis Trust. Education. 2018. https://sepsistrust.org/education/ (accessed 25 February 2020).
35. Novotny A, Emmanuel K, Bartels H, Siewert JR, Holzmann B. Parameter der frühen Prädiktion des Sepsisverlaufs [Indicators for early prediction of outcome in sepsis]. Chirurg. 2005 Sep;76(9):837-44. German. doi: 10.1007/s00104-005-1077-z. PMID: 16094522.
36. Tao, T. et al. Te top cited clinical research articles on sepsis: a bibliometric analysis. Crit. Care 16, R110. https://doi.org/10.1186/ cc11401 (2012).
37. Kempker, J. A. & Martin, G. S. A global accounting of sepsis. Lancet 395, 168–170 (2020).
38. McLymont, N. & Glover, G. W. Scoring systems for the characterization of sepsis and associated outcomes. Ann. Transl. Med. 4, 527–527. https://doi.org/10.21037/atm.2016.12.53 (2016)
39. Georgescu, A.-M., Szederjesi, J., Copotoiu, S.-M. & Azamfrei, L. Predicting scores correlations in patients with septic shock: a cohort study. Rom. J. Anaesth. Intensive Care 21, 95–98 (2014).
40. Dabhi, A. S., Khedekar, S. S. & Mehalingam, V. A prospective study of comparison of APACHE-IV & SAPS-II scoring systems and calculation of

standardised mortality rate in severe sepsis and septic shock patients. J. Clin. Diagn. Res. 8, MC09-MC13 (2014).

41. Lambden, S., Laterre, P. F., Levy, M. M. & Francois, B. Te SOFA score - development, utility and challenges of accurate assessment in clinical trials. Crit. Care 23, 374. https://doi.org/10.1186/s13054-019-2663-7 (2019).
42. Fang, W.-F. et al. Application of dynamic pulse pressure and vasopressor tools for predicting outcomes in patients with sepsis in intensive care units. J. Crit. Care 52, 156–162. https://doi.org/10.1016/j.jcrc.2019.05.003 (2019).
43. Li, W., Wang, M., Zhu, B., Zhu, Y. & Xi, X. Prediction of median survival time in sepsis patients by the SOFA score combined with diferent predictors. Burns Traumahttps://doi.org/10.1093/burnst/tkz006 (2020).
44. Roh, J. et al. Factors predicting long-term survival of patients with sepsis on arrival at the emergency department. Medicine 98, e16871. https://doi.org/10.1097/md.0000000000016871 (2019).
45. Mochizuki, K. et al. Benefcial efect modifcation on survival outcome of sepsis between ART-123 and polymyxin B-immobilised haemoperfusion: a nationwide Japanese registry study. Ann. Intensive Care 10, 57 (2020).
46. Ferrario, M. et al. Mortality prediction in patients with severe septic shock: a pilot study using a target metabolomics approach. Sci. Rep. 6, 20391 (2016).
47. Mewes, C. et al. CTLA-4 genetic variants predict survival in patients with sepsis. J. Clin. Med. 8, 70. https://www.who.int/sepsi s/en/3 (2019).
48. Roderburg, C. et al. Circulating MicroRNA-150 serum levels predict survival in patients with critical illness and sepsis. PLoS ONE 8, e54612 (2013).
49. Wang, J., Sun, Y., Teng, S. & Li, K. Prediction of sepsis mortality using metabolite biomarkers in the blood: a meta-analysis of death-related pathways and prospective validation. BMC Med. 18, 83 (2020).
50. Jiang, W. et al. Evaluation of a combination “lymphocyte apoptosis model” to predict survival of sepsis patients in an intensive care unit. BMC Anesthesiol. 18, 89 (2018).

51. Luhr, R., Cao, Y., Söderquist, B. & Cajander, S. Trends in sepsis mortality over time in randomised sepsis trials: a systematic literature review and meta-analysis of mortality in the control arm, 2002–2016. Crit. Care 23, 241 (2019)
52. Acker SN, Ross JT, Partrick DA, Tong S, Bensard DD. Pediatric specific shock index accurately identifies severely injured children. J Pediatr Surg. 2015;50(2):331–334. doi:10.1016/j.jpedsurg.2014.08.009
53. Berger T, Green J, Horeczko T, et al. Shock index and early recognition of sepsis in the emergency department: pilot study. West J Emerg Med. 2013;14(2):168–174. doi:10.5811/westjem. 2012.8.11546
54. Imhoff BF, Thompson NJ, Hastings MA, Nazir N, Moncure M, Cannon CM. Rapid emergency medicine score (REMS) in the trauma population: a retrospective study. BMJ Open. 2014;4(5):e004738. doi:10.1136/bmjopen-2013-004738
55. Wira C, Francis M, Bhat S, Ehrman R, Conner D, Siegel M. The shock index as a predictor of vasopressor use in emergency department patients with severe sepsis. West J Emerg Med. 2014;15(1):60– 66. doi:10.5811/westjem.2013.7.18472
56. 3. Singer M, Deutschman CS, Seymour C, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). JAMA. 2016;315(8):801–10.
57. Guideline on clinical investigation of medicinal products for the treatment of sepsis. Edited by European Medicine Agency. CHMP/EWP/4713/03 2006.
58. Ferreira FL, Bota DP, Bross A, Melot C, Vincent JL. Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA. 2001; 286(14):1754–8.
59. Khanna A, English SW, Wang XS, Ham K, Tumlin J, Szerlip H, et al. Angiotensin II for the treatment of vasodilatory shock. N Engl J Med. 2017; 377(5):419–30
60. de Grooth H-J, Geenen IL, Girbes AR, Vincent J-L, Parienti J-J, Oudemans-van Straaten HM. SOFA and mortality endpoints in randomized controlled

trials: a systematic review and meta-regression analysis. Crit Care. 2017;21(1):38.

61. Yussof SJ, Zakaria MI, Mohamed FL, Bujang MA, Lakshmanan S, Asaari AH. Value of Shock Index in prognosticating the short-term outcome of death for patients presenting with severe sepsis and septic shock in the emergency department. Med J Malaysia. 2012 Aug;67(4):406-11. PMID: 23082451.
62. Biney, Isaac & Shepherd, April & Thomas, Joylene & Mehari, Alem. (2015). Shock Index and Outcomes in Patients Admitted to the ICU With Sepsis. CHEST Journal. 148. 337A. 10.1378/chest.2281151.
63. Tseng J, Nugent K. Utility of the shock index in patients with sepsis. Am J Med Sci. 2015 Jun;349(6):531-5. doi: 10.1097/MAJ.0000000000000444. PMID: 25782337
64. Mann, Blake & Hough, Catherine & Carlbom, David. (2015). Shock Index as a Predictor of Hospital Outcomes in Patients With Sepsis. CHEST Journal. 148. 350A. 10.1378/chest.2265483.
65. Zhang X, Wang Z, Wang Z, Fang M, Shu Z. The prognostic value of shock index for the outcomes of acute myocardial infarction patients: A systematic review and meta-analysis. Medicine (Baltimore). 2017 Sep;96(38):e8014. doi: 10.1097/MD.0000000000008014. PMID: 28930837; PMCID: PMC5617704.
66. Johns, Tracy J.. "Shock index as predictor of outcome in patients with sepsis: A cohort study." (2018).
67. Ravi K., Vinay K., Rao AK. Study of spectrum of sepsis and prediction of its outcome in patients admitted to ICU using different scoring systems. Int J Adv Med 2019;6:155-9
68. Middleton DJ, Smith TO, Bedford R, Neilly M, Myint PK. Shock Index Predicts Outcome in Patients with Suspected Sepsis or Community-Acquired Pneumonia: A Systematic Review. J Clin Med. 2019 Jul 31;8(8):1144. doi: 10.3390/jcm8081144. PMID: 31370356; PMCID: PMC6723191.
69. Althunayyan SM, Alsofayan YM, Khan AA. Shock index and modified shock index as triage screening tools for sepsis. J Infect Public Health. 2019 Nov-

Dec;12(6):822-826. doi: 10.1016/j.jiph.2019.05.002. Epub 2019 May 18. PMID: 31113741.

70. Ospina-Tascón, G.A., Teboul, JL., Hernandez, G. *et al.* Diastolic shock index and clinical outcomes in patients with septic shock. *Ann. Intensive Care* **10**, 41 (2020).
71. Devendra Prasad K, Abhinov T, Himabindu K, et al. (December 08, 2021) Modified Shock Index as an Indicator for Prognosis Among Sepsis Patients With and Without Comorbidities Presenting to the Emergency Department. Cureus 13(12): e20283. DOI 10.7759/cureus.20283
72. Vang, M., Østberg, M., Steinmetz, J. *et al.* Shock index as a predictor for mortality in trauma patients: a systematic review and meta-analysis. *Eur J Trauma Emerg Surg* **48**, 2559–2566 (2022).
73. Huang SW, Guan XD, Chen J, et al. Comparison of four intensive care score modes in the patients with severe sepsis. Chinese Journal of Critical Care Medicine 2005;11:802-3.
74. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:801-10.
75. Nasa P, Juneja D, Singh O. Severe sepsis and septic shock in the elderly: An overview. World J Crit Care Med. 2012 Feb 4;1(1):23-30. doi: 10.5492/wjccm.v1.i1.23. PMID: 24701398; PMCID: PMC3956061.
76. Beery TA. Sex differences in infection and sepsis. Crit Care Nurs Clin North Am. 2003 Mar;15(1):55-62. doi: 10.1016/s0899-5885(02)00028-x. PMID: 12597040.
77. Alroumi F, Abdul Azim A, Kergo R, Lei Y, Dargin J. The impact of smoking on patient outcomes in severe sepsis and septic shock. J Intensive Care. 2018 Jul 28;6:42. doi: 10.1186/s40560-018-0312-x. PMID: 30065844; PMCID: PMC6064183.
78. Zhang, B., Guo, S., Fu, Z. et al. Association between fluid balance and mortality for heart failure and sepsis: a propensity score-matching analysis.

BMC Anesthesiol 22, 324 (2022). https://doi.org/10.1186/s12871-022-01865-5

79. Schortgen F. Fever in sepsis. Minerva Anestesiol. 2012 Nov;78(11):1254-64. Epub 2012 Jul 6. PMID: 22772856.
80. Hammond NE, Kumar A, Kaur P, Tirupakuzhi Vijayaraghavan BK, Ghosh A, Grattan S, Jha V, Mathai D, Venkatesh B; Sepsis in India Prevalence Study (SIPS) Investigator Network. Estimates of Sepsis Prevalence and Outcomes in Adult Patients in the ICU in India: A Cross-sectional Study. Chest. 2022 Jun;161(6):1543-1554. doi: 10.1016/j.chest.2021.12.673. Epub 2022 Jan 31. PMID: 35092747.
81. Trevelin SC, Carlos D, Beretta M, da Silva JS, Cunha FQ. Diabetes Mellitus and Sepsis: A Challenging Association. Shock. 2017 Mar;47(3):276-287. doi: 10.1097/SHK.0000000000000778. PMID: 27787406.
82. Leelahavanichkul A, Huang Y, Hu X, Zhou H, Tsuji T, Chen R, Kopp JB, Schnermann J, Yuen PS, Star RA. Chronic kidney disease worsens sepsis and sepsis-induced acute kidney injury by releasing High Mobility Group Box Protein-1. Kidney Int. 2011 Dec;80(11):1198-211. doi: 10.1038/ki.2011.261. Epub 2011 Aug 10. PMID: 21832986; PMCID: PMC3491658.
83. Middleton DJ, Smith TO, Bedford R, Neilly M, Myint PK. Shock Index Predicts Outcome in Patients with Suspected Sepsis or Community-Acquired Pneumonia: A Systematic Review. J Clin Med. 2019 Jul 31;8(8):1144. doi: 10.3390/jcm8081144. PMID: 31370356; PMCID: PMC6723191.
84. Althunayyan SM, Alsofayan YM, Khan AA. Shock index and modified shock index as triage screening tools for sepsis. J Infect Public Health. 2019 Nov-Dec;12(6):822-826. doi: 10.1016/j.jiph.2019.05.002. Epub 2019 May 18. PMID: 31113741.
85. Effenberger-Neidnicht K., Hartmann M. Mechanisms of Hemolysis During Sepsis. Inflammation. 2018;41:1569–1581. doi: 10.1007/s10753-018-0810-. [PubMed] [CrossRef] [Google Scholar] [Ref list]

86. Levi M. Platelets in Critical Illness. Semin. Thromb. Hemost. 2016;42:252–257. doi: 10.1055/s-0035-1570080. [PubMed] [CrossRef] [Google Scholar] [Ref list]
87. Agnello L, Giglio RV, Bivona G, Scazzone C, Gambino CM, Iacona A, Ciaccio AM, Lo Sasso B, Ciaccio M. The Value of a Complete Blood Count (CBC) for Sepsis Diagnosis and Prognosis. Diagnostics (Basel). 2021 Oct 12;11(10):1881. doi: 10.3390/diagnostics11101881. PMID: 34679578; PMCID: PMC8534992.
88. Patel JJ, Taneja A, Niccum D, Kumar G, Jacobs E, Nanchal R. The association of serum bilirubin levels on the outcomes of severe sepsis. J Intensive Care Med. 2015 Jan;30(1):23-9. doi: 10.1177/0885066613488739. Epub 2013 May 22. PMID: 23753252.
89. Seymour CW, Liu VX, Iwashyna TJ, et al. Assessment of clinical criteria for sepsis: for the third International Consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016;315(8):762-774. DOI: https://doi.org/10.1001/jama.2016.0288
90. Liu C, Suo S, Luo L, Chen X, Ling C, Cao S. SOFA Score in relation to Sepsis: Clinical Implications in Diagnosis, Treatment, and Prognostic Assessment. Comput Math Methods Med. 2022 Aug 10;2022:7870434. doi: 10.1155/2022/7870434. PMID: 35991153; PMCID: PMC9385349.

APPENDIX I: PERFORMA FOR DATA COLLECTION

STUDY TITLE: **SHOCK INDEX AS PREDICTOR OF OUTCOME IN PATIENTS WITH SEPSIS IN**

CHENGALPATTU MEDICAL COLLEGE HOSPITAL

DEMOGRAPHIC DATA

Name

Hospital number :Age : Gender:

CLINICAL PARAMETERS

Heart rate (beats /min):Systolic BP (mmHg): Diastolic BP (mmHg):

Mean arterial pressure (mmHg):Respiratory rate (breath/min):

Temperature (degree F)

Glasgow coma scaleLAB PARAMETERS

Lactate levels:

Arterial pH:

Serum HCO3 (mmol/L):P/F ratio:

Sodium (meq/L): Potassium (meq/L): Creatinine (mg/dl): Bilirubin (mg/dl): Hemoglobin (gm%):

WBC count (per cubic mm): Platelet count (per cubic mm):

MICROBIOLOGY

Blood culture- positive / negative/not done. Urine culture - positive /

negative/not done. Sputum culture- positive / negative/not done.CSF culture-positive / negative/not done.

Ascitic fluid - positive / negative/not done. Dengue serology- positive / negative/not done. Scrub serology- positive / negative/not done.

Chest Xray- suggestive / not suggestive. Identified bacteria:

COURSE IN HOSPITAL

Direct ICU admission (yes/no)Ward stay alone (yes/no)

Transfer to ICU from ward within 48 hours (yes/no)Duration of total hospital stay (in days)

Inotropes requirement – yes/ no

Ventilatory requirements (invasive/ non invasive)- yes/no.

CONDITION AT DISCHARGE

1.Improved2.Death

3.Discharge against medical advise.

CALCULATED INDICES

SOFA score qSOFA score SHOCK INDEX

APPENDIX II : INFORMATION SHEET

INFORMATION SHEET

INFORMATION SHEET

Study Title- Shock index as predictor of outcome in paients with septic shock in Chengalpattu Medical College Hospital .

Study title for lay public- The usefulness of shock index in predicting death or survival inpatients with fever and low blood pressure.

Purpose- Fever associated with low blood pressure is a leading cause of death. There are warning signs like high heart rate and some blood tests which can indicate severity of thecondition. If these warning signs are identified early, death could be prevented.

Procedure- blood pressure and heart rate will be recorded. Blood tests necessary toidentify the cause of fever will be done.

Benefit to subject- It will be ensured that necessary tests for diagnosis of fever will becarried out at the appropriate time.

Benefit to others- Fever with low blood pressure is a leading cause of death. Byidentifying the risk factors early, adverse outcome (death) could be prevented.

Confidentiality- Patients personal details will e kept confidential and wil not be revealedat any time except by law to share any

such information.

Participation- It is your decision whether to take part in the study or not. There is no compulsion. A decision not to take part in the study will not affect the standard of care.No money or additional tests have to be done as part of study.

Results and publication- The results of the study will be analysed and submitted as part of my thesis and if approved, will be published for the interest of medical fraternity.

The results of the study will be published in a medical journal,but you will not be identified by name in any publication.

For any further details feel free to contact the principal investigator:

APPENDIX III : CONSENT FORM

சுயஒப்புதல் படிவம்

ஆய்வுசெய்யப்படும் தலைப்பு: " செங்கல்பட்டு மருத்துவக் கல்லூரி மற்றும் மருத்துவமனையில் கல்லீரல் இழைநார் வளர்ச்சியில் மேல் இரைப்பை உணவுக்குழாய் உள்நோக்கல் மூலம் உறுதி செய்யப்படும் உணவுக்குழாய் மாறுபாடுகளின் முன்கணிப்பபாளர்களை குறித்த ஆய்வு"

ஆய்வுசெய்யப்படும் இடம்:

பங்குபெறுபவரின் பெயர்:

பங்குபெறுபவரின் வயது:

பங்குபெறுபவரின் எண் :

மேலேகுறிப்பிட்டுள்ள மருத்துவஆய்வின் விவரங்கள் எனக்கு விளக்கபட்டுள்ளது. நான் இவ்வாய்வில் தன்னிச்சையாக பங்கேற்கின்றேன். எந்தகாரணத்தினாலோ, எந்த சட்டசிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக்கொள்ளலாம் என்றும் அறிந்துகொண்டேன்.

இந்த ஆய்வு சம்பந்தமாகவோ, இதைசார்ந்து மேலும் ஆய்வுமேற்கொள்ளும்போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர், என்னுடைய மருத்துவஅறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவை இல்லை என அறிந்துகொள்கிறேன். இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ,முடிவையோ பயன்படுத்திக் கொள்ள மறுக்கமாட்டேன்.

இந்த ஆய்வில் பங்குகொள்ள ஒப்புக்கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம்:

சாட்சியாளரின் கையொப்பம்:

இடம்:

தேதி:

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்:

ஆய்வாளரின் கையொப்பம் :

இடம்: **தேதி:**

APPENDIX IV -ABSTRACT BACKGROUND

Severe sepsis has substantial clinical and financial, challenges. Previous studies have shown that early identification of sepsis is associated with better outcome. However limited resources are a major obstacle in early identification of sepsis patients. This is also complicated by the various etiologies responsible for sepsis and the heterogenecitypresentations. Shock index gains significance in this context as it is an easily calculablescore which can even be measured by non-medical personnel.

AIM

To study the disease spectrum of patients with suspected sepsis and assess the usefulnessof shock index in predicting the clinical outcome .

OBJECTIVES PRIMARY OBJECTIVE:

To assess whether in patients with suspected sepsis, shock index is a good predictor ofclinical outcome.

SECONDARY OBJECTIVES:

Role of shock index in predicting ICU requirement.
Shock index in predicting hemodynamic support. Shock index in predicting ventilatory requirement. Shock index and its relation to duration of hospital stay.

Correlation of shock index with other mortality predictors (lactate levels, initial SOFA score and q SOFA score).

Usefullness of shock index across the various etiologies for sepsis.METHODS

We conducted a observational study of patients with suspected and/or confirmed infection fulfilling atleast 2 SIRS criteria who presented to the emergency department and were subsequently admitted in the medical wards or in the medical ICU. This was a single center study done at Chengalpattu Medical College, a tertiary care hospital primarilycatering to the middle and low income group patients from all over India, predominantly the south Indian and the north eastern states. From the initial emergency department documentation of the heart rate and systolic blood pressure, shock index was calculated. Similarly SOFA score, q SOFA scores were calculated and the initial lactate levels were noted. Usefullness of shock index in predicting the in-hospital mortality was assessed and this was compared with other outcome predictors like SOFA score, q SOFA score .

FINDINGS

Between April 2021 and March 2022, 100 patients fulfilling the inclusion criteria were enrolled into the study. 70.6% of the study population had shock index values greaterthan equal to 1.0 at the time of presentation to the emergency department. Patients with higher shock index at the time of admission (shock index greater than or equal to 1.0), had higher in-hospital deaths (37.68%) than patients with shock index less than 1.0 (7.69%), with an absolute difference of 29.99% and p value less than 0.001. This effect of shock index on mortality was irrespective of the etiology of infection. Similarly shock index values greater than 1.0 was also associated with higher rates of ICU admission (48.0% versus 11.6%) , greater need of inotropic (51.47% versus 1.77%) and ventilator support (58.37% versus 19.52%) during the

initial 48 hours of hospital stay. Performance of shock index was comparable with that of SOFA, q SOFA .

CONCLUSION

Higher shock index (greater than 1.0) values at the time of presentation was associated with higher mortality rates, higher rates of ICU admission and greater need for ventilatorand inotropic support. Hence it can be used as a triaging tool for septic patients, especially in the resource poor settings.

MASTER CHART

S LNO	NAME	AGE	SEX	Fever	Difficulty breathing	Altered sensorium	Decreased urine	SMOKING	DM	HTN	CKD	HEART FAILURE	SBP	DBP	HR	SHOCKINDEX	RR	TEMP	GCS	CREAT	PLATELETS	TOTAL BILIRUBIN	Hb	PaO2/FiO2	Na+	K+	WBC	N/L	CXR pneumonia	UrineC/S SVD	BloodC/S	Mode:venti (MV)//o2/CPAP	q-SOFA	SOFA
1	valli	35	F	y		y	y						90	60	110	1.2	18	102	12	1.7	90	2.11	9.2	<400	133	3.6	22	80/10	y			O2	3	6
2	Panchavarnum	49	F	y	y	y				y	y		150	90	108	0.72	22	101	13	1.3	92	1.41	9.8	<300	132	4.9	3.8	88/9				O2	2	7
3	Pitchai	65	M	y	y	y	y	y	y			y	60	40	121	2.01	24	100	7	2.1	93	1.1	10.1	<100	131	3.6	17	92/6	y			M.V	3	12
4	Dhesingu	59	M	y		y	y	y					80	60	132	1.65	28	101	13	1.5	1.5	1.8	13	<300	132	4.2	18	70/18				O2	3	7
5	Ramalakshmi	38	F	y	y	y	y		y		y		40	?	140	3.5	25	100	8	6.5	1.8	1.21	9.2	<100	133	3.9	21	78/12	y	+		M.V	2	14
6	Sarasu	45	F				y				y		70	30	110	1.57	28	100	14	2.8	0.9	1.3	8.8	<400	129	4.2	22	80/8				O2	3	7
7	Malliga	47	F	y		y							80	50	112	1.4	18	100	13	2.7	1.1	1.2	8.2	<200	1281	3.6	29	88/10			+	O2	2	7
8	Thirunavukarasu	48	M	y	y								60	?	122	2.03	18	101	9	3.3	1.3	2.2	14	<100	134	5.0	27	88/8				M.V	3	9
9	Arokiaraj	65	M	y	y	y	y	y	y	y	y	y	170	100	99	0.58	29	99	12	2.6	1.1	2.2	9	<200	122	4.9	16	80/9	y			CPAP	3	10
10	Muthu	46	M	y				y					60	40	101	1.68	33	99	1	1.9	90	2.1	6.7	<300	129	4.2	18	70/7	y			O2	3	11
11	Pandi	63	M	y	y	y	y	y	y			y	130	60	92	0.69	32	99	14	2.8	1.2	1.9	8.8	<400	133	3.6	22	78/9	y				3	9
12	Boominathan	54	M	y				y					70	50	112	1.6	16	100	15	1.9	90	1.8	9.2	<400	132	4.2	24	77/9	y			O2	3	10
13	John peter	50	M	y	y		y						110	70	121	1.1	16	102	15	2.3	1.3	1.7	6.8	<400	129	4.9	26	88/3		+			3	9
14	Baskar	56	M	y		y		y			y		100	60	131	1.3	20	101	14	2.2	1.7	1.5	9.4	<400	130	4.2	22	82/9					3	6
15	Sanjeevi	60	M	y					y			y	90	50	122	1.35	19	101	14	1.9	1.57	1.4	11	<200	132	3.9	21	80/10	y			O2	2	8
16	Vasantha	62	M	y	y		y		y		y	y	70	40	110	1.57	222	1001	13	1.6	1.9	1.21	14	<400	129	3.6	20	82/10	y		+		2	8
17	Mathialagan	53	M	y	y	y				y			80	60	98	1.22	24	100	141	1.7	1.68	1.4	14	<300	129	4.0	18	85/5				O2	3	10
18	Loganathan	63	M	y			y		y			y	110	70	92	0.83	18	101	14	1.4	90	1.61	12	<300	133	4.2	22	80/5	y			O2	2	11
19	Jeyaraman	52	M	y	y								120	80	94	0.78	26	100	14	1.5	2.8	1.5	9.6	<400	133	4.2	21	72/10					2	7
20	Raji	45	M	y		y		y					90	60	112	1.24	20	101	13	1.3	2.2	1.8	9.3	<200	133	4.3	33	77/10	y	+		CPAP	2	10
21	Saravanakumar	30	M	y			y	y					100	70	110	1.1	16	101	14	1.2	68	1.4	13	<400	132	3.6	17	68/18					3	6
22	Karuppiah	62	M	y	y	y		y	y		y	y	40	?	122	3.05	18	99	12	3.8	55	1.41	10.1	<400	129	5.3	12	77/10	y			M.V	3	11
23	Sunderrajan	52	M	y	y	y	y	y		y			40	?	110	2.75	22	100	14	2.2	1.1	1.31	13.2	<100	130	3.9	16	72/10	y			M.V	3	12
24	Dhanasekharan	57	M	y				y					90	60	99	1.1	17	99	14	1.5	99	1.2	14.1	<300	132	4.1	22	88/10					3	10
25	Arumugam	58	M	y		y		y	y			y	100	70	99	0.99	15	101	14	1.3	88	1.21	13	<400	1321	3.6	12	92/05		+			3	9
26	Thomas	43	M	y	y	y	y	y					90	70	110	1.22	Y	101	13	1.5	90	1.5	12.8	<400	133	4.0	16	90/06				O2	3	8
27	Pitchaiammal	63	F	y	y	y	y						90	60	120	0.8	18	100	12	1.5	98	1.6	10.2	<400	135	3.6	18	90/10	y			O2	3	7
28	Marimuthu	38	M	y	y	y				y	y		140	90	108	0.72	22	101	14	1.3	92	1.2	8.8	<300	132	4.9	3.8	88/9				O2	2	9

29	Athilekshmi	65	F	y	y	y	y	y	y			y	70	40	122	2.01	24	100	8	2.2	93	1.1	10.6	<100	127	3.6	17	92/6	y		+	M.V	3	11
30	Omprakash	56	M	y	y	y	y	y					80	60	132	1.65	28	101	13	1.5	1.5	1.8	13	<300	132	4.2	18	70/18				O2	3	8
31	Vishalakshi	55	F	y	y	y	y		y		y		40	?	138	3.5	25	100	8	5.5	1.8	1.3	9.2	<100	129	3.9	21	78/12	y	+		M.V	2	14
32	Jehangirkhan	54	M	y	y		y				y		80	30	110	1.57	26	100	14	3.8	0.9	1.3	12.3	<400	129	4.2	22	80/8				O2	3	8
33	Padmamani	53	M	y	y	y							80	50	112	1.4	18	100	12	2.7	1.1	1.2	8.2	<200	124	3.6	29	88/10				O2	2	8
34	Subbulakshmi	43	F	y	y								50	?	122	2.03	18	101	9	3.8	1.3	2.2	14	<100	134	5	27	88/8				M.V	3	9
35	Murugan	40	M	y	y	y	y	y	y	y	y	y	160	100	99	0.58	30	99	13	2.8	1.2	2.2	9	<300	122	4.9	16	80/9	y	+		CPAP	3	10
36	Anantham	48	F	y	y			y					60	40	110	1.68	28	99	14	1.9	90	2.1	10.2	<300	129	4.2	18	70/7	y			O2	3	11
37	Puspham	65	F	y	y	y	y	y	y			y	120	60	92	0.69	32	99	14	2.8	1.3	1.9	8.8	<400	133	3.6	22	78/9	y				3	9
38	Nadarajan	66	M	y	y			y					70	50	121	1.6	16	100	15	1.9	90	1.8	9.2	<400	132	4.2	24	77/9	y			O2	3	10
39	Murugeswari	45	F	y	y		y						110	70	101	1.1	16	102	15	2.1	1.3	1.7	7.8	<300	129	4.9	26	88/5		+			3	9
40	Kuttiyammal	54	F	y		y		y			y		100	60	121	1.3	20	101	14	2.3	1.7	1.5	9.4	<400	130	4.2	22	90/10					3	6
41	Vellaisamy	55	M	y	y				y			y	90	50	122	1.35	19	101	14	1.9	1.6	1.4	11	<200	132	3.9	21	90/10	y			O2	2	8
42	Agal ya	60	F	y	y		y		y		y	y	80	40	110	1.57	22	101	13	1.8	1.9	1.21	14	<400	129	3.6	20	82/10	y		+		2	8
43	Murugan	57	M	y	y	y				y			80	60	98	1.22	24	100	14	1.7	1.5	1.4	14	<300	129	4	18	85/5				O2	3	10
44	Arunachalam	55	M	y			y		y			y	110	70	92	0.83	18	101	14	1.4	90	1.4	12	<300	133	4.2	22	80/5	y			O2	2	11
45	Nagammal	60	F	y	y								120	80	94	0.78	26	100	14	1.5	2.8	1.5	9.6	<400	133	4.2	21	72/10					2	7
46	Jeyalekshmi	65	F	y	y	y		y					90	60	108	1.24	20	101	13	1.4	2.2	1.9	9.8	<200	130	4.3	33	77/10	y	+		CPAP	2	10
47	Sekhar	50	M	y			y	y					100	70	110	1.1	18	101	14	1.2	90	1.5	13	<200	132	3.6	17	78/20					3	7
48	Arumugam	55	M	y	y	y		y	y		y	y	40	?	132	3.05	18	99	12	2.8	79	1.4	10.2	<400	129	5.3	12	77/10	y	+		M.V	3	10
49	Rani	35	F	y	y	y	y	y		y			40	?	110	2.75	22	100	14	2.2	1.5	1.3	12.2	<100	130	3.9	16	88/10	y		+	M.V	3	11
50	Jarina begum	56	F	y				y					70	60	99	1.1	20	99	14	1.5	88	1.5	12.8	<300	132	4.1	22	78/20					3	9
51	Ramayi	35	F	y		y	y						90	60	110	1.2	18	102	12	1.7	90	2.11	9.2	<400	133	3.6	22	80/10	y			O2	3	6
52	Pancha va rnum	49	F	y	y	y				y	y		150	90	108	0.72	22	101	13	1.3	92	1.41	9.8	<300	132	4.9	3.8	88/9				O2	2	7
53	Pitchai	65	M	y	y	y	y	y	y			y	60	40	121	2.01	24	100	7	2.1	93	1.1	10.1	<100	131	3.6	17	92/6	y			M.V	3	12
54	Rajusundaram	59	M	y		y	y	y					80	60	132	1.65	28	101	13	1.5	1.5	1.8	13	<300	132	4.2	18	70/18				O2	3	7
55	Ramalakshmi	38	F	y	y	y	y		y		y		40	?	140	3.5	25	100	8	6.5	1.8	1.21	9.2	<100	133	3.9	21	78/12	y	+		M.V	2	14
56	Sarasu	45	F				y				y		70	30	110	1.57	28	100	14	2.8	0.9	1.3	8.8	<400	129	4.2	22	80/8				O2	3	7
57	Malliga	47	F	y		y							80	50	112	1.4	18	100	13	2.7	1.1	1.2	8.2	<200	1281	3.6	29	88/10			+	O2	2	7
58	Thiru	48	M	y	y								60	?	122	2.03	18	101	9	3.3	1.3	2.2	14	<100	134	5	27	88/8				M.V	3	9
59	Arasu	65	M	y	y	y	y	y	y	y	y	y	170	100	99	0.58	29	99	12	2.6	1.1	2.2	9	<200	122	4.9	16	80/9	y			CPAP	3	10
60	Muthukrishnan	46	M	y				y					60	40	101	1.68	33	99	1	1.9	90	2.1	6.7	<300	129	4.2	18	70/7	y			O2	3	11
61	Pandirajan	63	M	y	y	y	y	y	y			y	130	60	92	0.69	32	99	14	2.8	1.2	1.9	8.8	<400	133	3.6	22	78/9	y				3	9
62	prakash	54	M	y				y					70	50	112	1.6	16	100	15	1.9	90	1.8	9.2	<400		4.2	24	77/9	y			O2	3	10
63	John peter	50	M	y	y		y						110	70	121	1.1	16	102	15	2.3	1.3	1.7	6.8	<400	129	4.9	26	88/3		+			3	9
64	Baskar	56	M	y		y		y			y		100	60	131	1.3	20	101	14	2.2	1.7	1.5	9.4	<400	130	4.2	22	82/9					3	6
65	Sanjeevi	60	M	y					y			y	90	50	122	1.35	19	101	14	1.9	1.57	1.4	11	<200	132	3.9	21	80/10	y			O2	2	8

66	Vasantha	62	M	y	y		y		y		y	y	70	40	110	1.57	222	1001	13	1.6	1.9	1.21	14	<400	129	3.6	20	82/10	y		+		2	8
67	Mathialagan	53	M	y	y	y				y			80	60	98	1.22	24	100	141	1.7	1.68	1.4	14	<300	129	4	18	85/5				O2	3	10
68	Loganathan	63	M	y			y		y			y	110	70	92	0.83	18	101	14	1.4	90	1.61	12	<300	133	4.2	22	80/5	y			O2	2	11
69	Jeya raman	52	M	y	y								120	80	94	0.78	26	100	14	1.5	2.8	1.5	9.6	<400	133	4.2	21	72/10					2	7
70	Raji	45	M	y		y		y					90	60	112	1.24	20	101	13	1.3	2.2	1.8	9.3	<200	133	4.3	33	77/10	y	+		CPAP	2	10
71	Sara va nakumar	30	M	y			y	y					100	70	110	1.1	16	101	14	1.2	68	1.4	13	<400	132	3.6	17	68/18					3	6
72	kumar	62	M	y	y	y		y	y		y	y	40	?	122	3.05	18	99	12	3.8	55	1.41	10.1	<400	129	5.3	12	77/10	y			M.V	3	11
73	Sunderrajan	52	M	y	y	y	y	y		y			40	?	110	2.75	22	100	14	2.2	1.1	1.31	13.2	<100	130	3.9	16	72/10	y			M.V	3	12
74	Dhanasekharan	57	M	y				y					90	60	99	1.1	17	99	14	1.5	99	1.2	14.1	<300	132	4.1	22	88/10					3	10
75	Arumugam	58	M	y		y		y	y			y	100	70	99	0.99	15	101	14	1.3	88	1.21	13	<400	1321	3.6	12	92/05		+			3	9
76	Raman	43	M	y	y	y	y	y					90	70	110	1.22	Y	101	13	1.5	90	1.5	12.8	<400	133	4	16	90/06				O2	3	8
77	Saroja	63	F	y	y	y	y						90	60	120	0.8	18	100	12	1.5	98	1.6	10.2	<400	135	3.6	18	90/10	y			O2	3	7
78	Marimuthu	38	M	y	y	y				y	y		140	90	108	0.72	22	101	14	1.3	92	1.2	8.8	<300	132	4.9	3.8	88/9				O2	2	9
79	Saraswathi	65	F	y	y	y	y	y	y			y	70	40	122	2.01	24	100	8	2.2	93	1.1	10.6	<100	127	3.6	17	92/6	y		+	M.V	3	11
80	Omprakash	56	M	y	y	y	y	y					80	60	132	1.65	28	101	13	1.5	1.5	1.8	13	<300	132	4.2	18	70/18				O2	3	8
81	Vishalakshi	55	F	y	y	y	y		y		y		40	?	138	3.5	25	100	8	5.5	1.8	1.3	9.2	<100	129	3.9	21	78/12	y	+		M.V	2	14
82	Senthil	54	M	y	y		y				y		80	30	110	1.57	26	100	14	3.8	0.9	1.3	12.3	<400	129	4.2	22	80/8				O2	3	8
83	Padmamani	53	M	y	y	y							80	50	112	1.4	18	100	12	2.7	1.1	1.2	8.2	<200	124	3.6	29	88/10				O2	2	8
84	Subbulakshmi	43	F	y	y								50	?	122	2.03	18	101	9	3.8	1.3	2.2	14	<100	134	5	27	88/8				M.V	3	9
85	Murugan	40	M	y	y	y	y	y	y	y	y	y	160	100	99	0.58	30	99	13	2.8	1.2	2.2	9	<300	122	4.9	16	80/9	y	+		CPAP	3	10
86	Anantham	48	F	y	y			y					60	40	110	1.68	28	99	14	1.9	90	2.1	10.2	<300	129	4.2	18	70/7	y			O2	3	11
87	Puspham	65	F	y	y	y	y	y	y			y	120	60	92	0.69	32	99	14	2.8	1.3	1.9	8.8	<400	133	3.6	22	78/9	y				3	9
88	Nagarajan	66	M	y	y								70	50	121	1.6	16	100	15	1.9	90	1.8	9.2	<400	132	4.2	24	77/9	y			O2	3	10
89	Murugeswari	45	F	y	y		y						110	70	101	1.1	16	102	15	2.1	1.3	1.7	7.8	<300	129	4.9	26	88/5		+			3	9
90	Kuttiyammal	54	F	y		y		y			y		100	60	121	1.3	20	101	14	2.3	1.7	1.5	9.4	<400	130	4.2	22	90/10					3	6
91	Vellaisamy	55	M	y	y				y			y	90	50	122	1.35	19	101	14	1.9	1.6	1.4	11	<200	132	3.9	21	90/10	y			O2	2	8
92	Agal ya	60	F	y	y		y		y		y	y	80	40	110	1.57	22	101	13	1.8	1.9	1.21	14	<400	129	3.6	20	82/10	y		+		2	8
93	Murugan	57	M	y	y	y				y			80	60	98	1.22	24	100	14	1.7	1.5	1.4	14	<300	129	4	18	85/5				O2	3	10
94	perumal	55	M	y			y		y			y	110	70	92	0.83	18	101	14	1.4	90	1.4	12	<300	133	4.2	22	80/5	y			O2	2	11
95	vadivu	60	F	y	y								120	80	94	0.78	26	100	14	1.5	2.8	1.5	9.6	<400	133	4.2	21	72/10					2	7
96	Jaya	65	F	y	y	y		y					90	60	108	1.24	20	101	13	1.4	2.2	1.9	9.8	<200	130	4.3	33	77/10	y	+		CPAP	2	10
97	Senthilkumaran	50	M	y			y	y					100	70	110	1.1	18	101	14	1.2	90	1.5	13	<200	132	3.6	17	78/20					3	7
98	Arun	55	M	y	y	y		y	y		y	y	40	?	132	3.05	18	99	12	2.8	79	1.4	10.2	<400	129	5.3	12	77/10	y	+		M.V	3	10
100	kaniga	35	F	y	y	y	y	y		y			40	?	110	2.75	22	100	14	2.2	1.5	1.3	12.2	<100	130	3.9	16	88/10	y		+	M.V	3	11