SERIAL SERUM ALBUMIN &OTHER LIVER PARAMETERS MONITORING AS A PROGNOSTIC MARKER IN PATIENTS WITH SEPSIS.

Dissertation submitted in partial fulfillment of the Requirement for the award of the Degree of

DOCTOR OF MEDICINE

BRANCH I - GENERAL MEDICINE

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THE TAMILNADU

DR.M.G.R.MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

CERTIFICATE FROM THE DEAN

This is to certify that the dissertation entitled "**SERIAL SERUM ALBUMIN &OTHER LIVER PARAMETERS MONITORING AS A PROGNOSTIC MARKER IN PATIENTS WITH SEPSIS** " is the bonafide work of **Dr. JAI GANESH.K** in partial fulfillment of the university regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, for **M.D General Medicine Branch I** examination to be held in May 2020.

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DECLARATION

I, **Dr.JAI GANESH.K** declare that, I carried out this work on "**SERIAL SERUM ALBUMIN &OTHER LIVER PARAMETERS MONITORING AS A PROGNOSTIC MARKER IN PATIENTS WITH SEPSIS**" at the Department of General Medicine, Government Rajaji Hospital, Madurai under the guidance of **Dr.DAVID PRADEEP KUMAR, M.D(GM)., DGM.,MRCP.,** Professor, Department of General Medicine, Madurai medical college, Madurai.

I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree, Diploma to any other University, Board either in India or abroad.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the award of **Doctor of Medicine (M.D.), General Medicine Branch-I**, examination to be held in **May 2020.**

Place: Madurai
Date:

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Introduction

INTRODUCTION

Sepsis is a common and deadly disease. HIPPOCRATES said that sepsis was characterized by festering wounds and rotten flesh. Several centuries later, GALEN described sepsis as laudable event required for wound healing. Once the germ theory was proposed by SEMMELWEIS, PASTEUR, and others in the 19th century, sepsis was redefined as a systemic infection referred to as "BLOOD POISONING" and was thought to be due to pathogen invasion and spread in the bloodstream of the host. However, germ theory didnot fully explain sepsis: many septic patients died despite successful removal of the inciting pathogen.

BONE AND COLLEGUES defined sepsis as a **systemic inflammatory response** to Infection. Yet sepsis arose in response to many different pathogens, and septicemia was neither a necessary condition nor a helpful term.

Thus, these investigator instead proposed the term ***severe sepsis*** to describe cases where sepsis was complicated by Acute organ dysfunction and the term ***septic shock*** for a subset of sepsis patients that were complicated by hypotension despite adequate fluid resuscitation along with perfusion abnormalities.

In the past 2 decades, research has revealed that many patients develop acute multi organ dysfunction in response to infection but without

a measurable inflammatory markers (i.e., without the systemic inflammatory response syndrome [SIRS]).

Sepsis Definitions Task Force ,2016 proposed **the 3rd International Consensus Definitions denoting that *sepsis* is a dysregulated host response to infection that leads to acute multiorgan dysfunction**. Numerous ICU scoring systems are used to predict mortality are in current use like APACHE II and SAPS II score. These scoring systems are cumbersome and are done a first 24 hours of admission during which precious time is lost in administering therapy.Hence serum Albumin a Negative acute phase reactant decreases and other liver parameters increases after an acute inflammatory insult such as sepsis . It is a common finding in critically ill patients,where it has shown promise not only as a predictor of organ failure and ionotropes requirement but of mortality,morbidity and hospital stays.

This study is an attempt to understand the usefulness of serial serum Albumin and other liver parameters monitoring in predicting the mortality ,morbidity,ventilator support and ionotropes requirements in sepsis patients.

Objective of Study

AIMS AND OBJECTIVES OF THE STUDY

1) To study the correlation between the serial serum Albumin monitoring and other liver parameters and mortality, morbidity, ionotropes, ventilator requirement and hospital stay of sepsis patients.
2) To develop a simple, inexpensive and dynamic marker of critical Illness.

Review of Literature

REVIEW OF LITERATURE

Definition

Septicaemias:

The term septicaemia implies active replication of bacteria in the blood stream associated with systemic manifestations. 'Bacteraemia' means the presence of bacteria in the blood which may be transient and without subjective symptoms.

Septic shock :septic shock is characterized by hypotension (systolic BP less than 90 mmHg), hypoxia, increased sr.lactic acid levels, high-anion-gap metabolic acidosis, and oliguria with a urine output of less than 30 ml/h.

Multiple organ dysfunction which may also include disseminated intravascular coagulation leads to a mortality of up to 50%. Sepsis has very high morbidity and mortality, which leads to major healthcare burden in the world. Though there is far advancement in the therapeutic options, the mortality rate remains high due to the delay in the diagnosis because of lack of availability of reliable diagnostic methods. There is significant improvement in the outcome of the patients in early goal directed therapy in severe sepsis and septic shock.

Definition Changes in 2016

- A task force of 19 leaders in the field of sepsis was convened by SCCM and the European Society of Intensive Care Medicine (ESICM)
- *Sepsis:* A life-threatening organ dysfunction caused by a dysregulated host response to infection.
- The new diagnostic tool for sepsis : quickSOFA(qSOFA), 2 of 3 indicators below:
    1) An alteration in mental status.
    2) A decrease in systolic blood pressure of <100 mmHg
    3) A respiration rate >22 breaths/min
- *Septic Shock:*
    1) A subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.
    2) Persisting hypotension requiring vasopressors to maintain MAP ≥65 mm Hg.
    3) Blood lactate >2 mmol/L despite adequate volume resuscitation.

DEFINITION CONSOLIDATION

	OLD	NEW
SEPSIS	suspected infection + SIRS	suspected infection + 2 ≥ qSOFA or rise in SOFA score by ≥ 2
SEVERE SEPSIS	sepsis + hypotension, hypoxia, elevated lactate or other lab markers of end organ dysfunction	(category removed)
SEPTIC SHOCK	sepsis + hypotension after adequate fluid resuscitation	sepsis + vasopressors + lactate > 2

OLD AND NEW CRITERIAS FOR SEPSIS AND SEPTIC SHOCK

CONDITION	DEFINITION	COMMON CLINICAL FEATURES	CRITERIA IN 1991/2003 ("SEPSIS-1"/"SEPSIS-2")	CRITERIA IN 2016 ("SEPSIS-3")
Sepsis	A life-threatening organ dysfunction caused by a dysregulated host response to infection	Include signs of infection, with organ dysfunction, plus altered mentation; tachypnea; hypotension; hepatic, renal, or hematologic dysfunction	Suspected (or documented) infection plus ≥2 systemic inflammatory response syndrome (SIRS) criteria[a]	Suspected (or documented) infection and an acute increase in ≥2 sepsis-related organ failure assessment (SOFA) points[b]
Septic shock	A subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities lead to substantially increased mortality risk	Signs of infection, plus altered mentation, oliguria, cool peripheries, hyperlactemia	Suspected (or documented) infection plus persistent arterial hypotension (systolic arterial pressure, <90 mmHg; mean arterial pressure, <60 mmHg; or change in systolic by >40 mmHg from baseline	Suspected (or documented) infection plus vasopressor therapy needed to maintain mean arterial pressure at ≥65 mmHg and serum lactate >2.0 mmol/L despite adequate fluid resuscitation

PATHOGENESIS

1) For many years, the clinical features of sepsis were considered the result of an excessive inflammatory host response (SIRS).
2) More recently, it has become apparent that infection triggers a much more complex, variable, and prolonged host response than was previously thought. The specific response of each patient depends on the pathogen(load and virulence) and the host (genetic composition and comorbidity),with different responses at local and systemic levels.
3) Generally,pro-inflammatory reactions (directed at eliminating pathogens) are responsible for "collateral" tissue damage in sepsis, whereas anti-inflammatory responses are implicated in the enhanced susceptibility to secondary infections that occurs later in the course. These mechanisms can be characterized as an interplay between two "fitness costs"direct damage to organs by the pathogen and damage to organs stemming from the host's immune response.
4) The host's ability to resist as well as tolerate both direct and immunopathologic damage will determine whether uncomplicated infection becomes sepsis.

Microbial factors

1) Bacterial load
2) Endotoxin (Gram -ve), teichoic acid (Gram +ve)
3) Activation of complement cascade.

Host factors

1. Systemic inflammatory response syndrome (SIRS)
2. Release of immune mediators (IL-1 and TNF - a)
3. Endothelial damage.
4. Activation of coagulation cascade
5. Myocardial function.

TABLE 89-2 MICROORGANISMS COMMONLY IDENTIFIED IN SEPTIC PATIENTS BASED ON HOST FACTORS

HOST FACTOR	ORGANISMS TO CONSIDER
Asplenia	Encapsulated organisms, particularly *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis*, *Capnocytophaga canimorsus*
Cirrhosis	*Vibrio*, *Salmonella*, and *Yersinia* species; encapsulated organisms, other gram-negative rods
Alcohol abuse	*Klebsiella* species, *S. pneumoniae*
Diabetes	Mucormycosis, *Pseudomonas* species, *Escherichia coli*, group B streptococci
Neutropenia	Enteric gram-negative rods, *Pseudomonas*, *Aspergillus*, *Candida*, *Mucor* species, *Staphylococcus aureus*, streptococcal species
T-cell dysfunction	*Listeria*, *Salmonella*, and *Mycobacterium* species, herpesviruses (including herpes simplex, cytomegalovirus, varicella-zoster virus)
Acquired immunodeficiency syndrome	*Salmonella* species, *S. aureus*, *Mycobacterium avium* complex, *S. pneumoniae*, group B streptococci

ROUTE OF INFECTIONS IN HOSPITALISED PATIENTS

Clinical problem	Usual pathogen(s)
Urinary catheter	*Escherichia coli*, *Klebsiella* spp., *Proteus* spp., *Serratia* spp., *Pseudomonas* spp.
Intravenous catheter	*Staphylococcus aureus*, *Staph. epidermidis*, *Klebsiella* spp., *Pseudomonas* spp., *Candida albicans*
Post-surgery:	
Wound infection	*Staph. aureus*, *E. coli*, anaerobes (depending on site)
Deep infection	Depends on anatomical location
Burns	Gram-positive cocci, *Pseudomonas* spp., *Candida albicans*
Immunocompromised patients	Any of the above

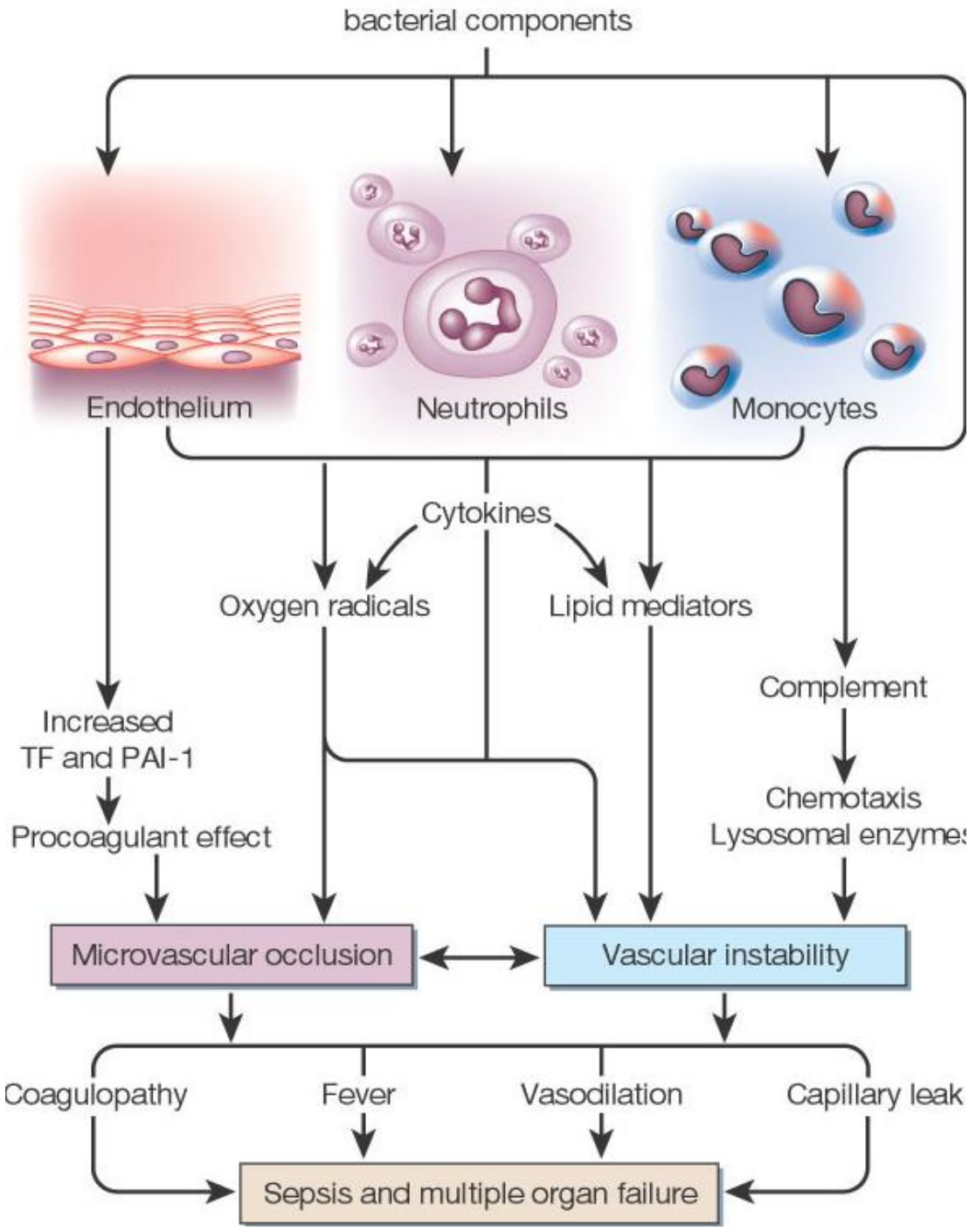
8.24 Sites of infection in critically ill patients

Sites of infection	Investigations and comments
Major	
Intravenous lines (particularly central)	If the patient develops sepsis, replace any lines that have not been changed for > 4 days
Lungs	High risk of nosocomial pneumonia in intubated patients. After ICU stay > 3–4 days, particularly if antibiotics are given, the nasopharynx becomes colonised with Gram-negative bacteria, which migrate to the lower respiratory tract. Prophylaxis with parenteral and enteral antibiotics (selective decontamination of the digestive tract) reduces the incidence of nosocomial pneumonia
Abdomen	Consider intra-abdominal abscess or necrotic gut in patients who have had abdominal surgery Pancreatitis, acute cholecystitis or perforated peptic ulcer may develop as a complication of critical illness. Ultrasound, CT, aspiration of collections of fluid/pus and laparotomy may be required
Urinary tract	Urine culture (but this is a relatively unusual source in unexplained sepsis)
Other	
Heart valves	Transthoracic or transoesophageal echocardiogram
Meninges	Lumbar puncture after checking coagulation and platelet count
Joints and bones	X-ray, gallium or technetium white cell scan
Nasal sinuses, ears, retropharyngeal space	Clinical examination, plain X-ray, CT
Genitourinary tract (particularly post-partum)	PV examination, ultrasound
Gastrointestinal tract	PR examination, stool culture, *Clostridium difficile* toxin, sigmoidoscopy

T-cell receptor or immunoglobulins.

- The innate immune system is activated by cell wall components and secreted proteins which are produced by the microorganisms.
- Gram negative cell walls contain bacterial endotoxin and lipopolysaccharide.
- There are two components in endotoxin . Lipid A is a component of endotoxin which plays a major role in immunostimulation.
- The humans are more susceptible to the immunostimulation of sepsis.

LPS and BACTERIAL COMPONENTS

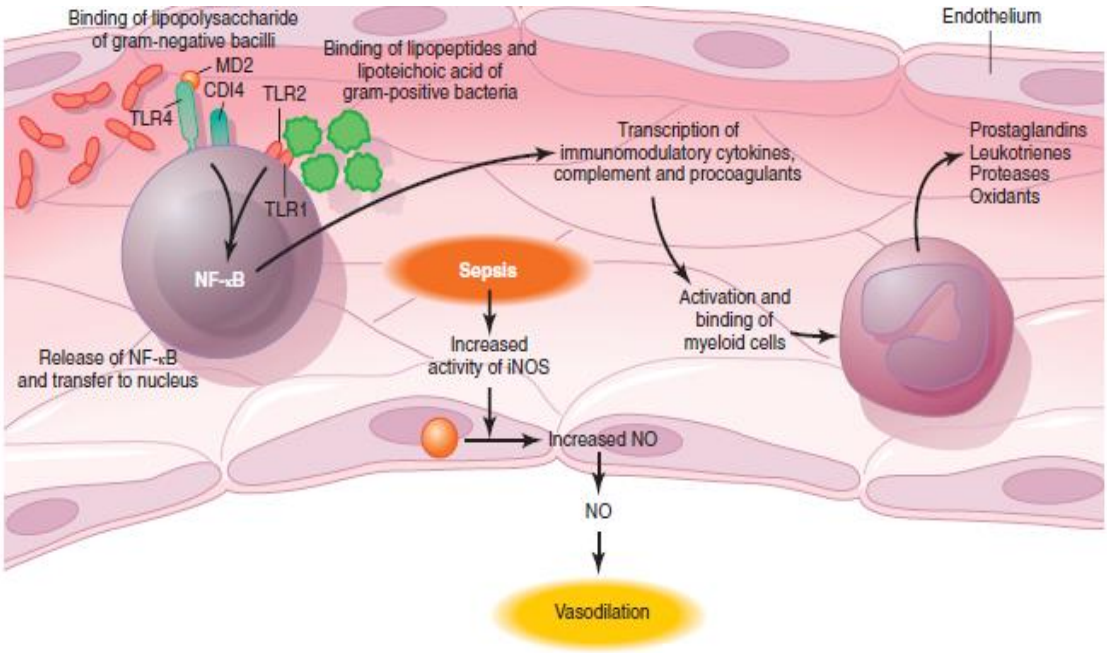


Lipopolysacharide

- LPB is the binding protein for lipopolysaccharide. After binding to LPB , it is transferred to CD 14 expressed by leukocytes.
- Bactericidal increasing protein is produced by polymorphonuclear cells and it causes modulation of the activity of LPS prevents LPS from binding to LPB. Binding of LPS to LPB results in induction of signal transduction, resulting in toll-like Receptors (TLRs)activation , Which is mediated by CD14.Toll like receptors.
- TLRs are present even in invertebrates and plants. It causes regulation of defense against the microorganisms. Ten TLRs have been discovered .
- The ligand specificity of TLR is of wide range like lipoproteins,peptidoglycan, lipopolysaccharide, and lipoteichoic acid from various pathogens . TLR4 is the lipopolysaccharide receptor, Gram + cell wall components are predominantly recognized by TLR2, while flagellin is recognized by TLR5 and bacterial DNA is recognized by TLR9.
- The role of toll like receptors are studies in the mice having mutations in the gene of toll like reptors.Mice with mutations in toll like receptor 4 gene did not have any response to lipopolysaccharide

and were resistant to toxic shock but mice with mutations in toll like receptor gene were susceptible.

- Sepsis itself has been demonstrated to up-regulate expression of TLR2 and TLR4 .In experimental models, immunomodulators that decrease expression or activation of TLRs decrease lethality. It has therefore been proposed that the exaggerated proinflammatory response characteristic of the acute respiratory distress syndrome (ARDS), SIRS, and severe sepsis may be due to overexpression of TLRs or the consequent excess activation of NF-kappaB and other nuclear transcription factor.



- Other than TLRs several other pathway by which recognition of microorganism is possible by the cells have been discovered .
    1. Peptidoglycan-recognition protein(PGRPs). Different PGRPs can distinguish between Gram positive and Gram-negative bacteria.
    2. TREM-1 and MDL-1 cause activation of monocytes.

- There is a severe activation of innate immune system following initial interaction with microorganism which causes coordination of cellular and humoral components of immunity. Monocytes and lymphocytes release proinflammatory molecules Interleukin-1, Interleukin-6, and tumor necrosis factor-alpha, but in addition to it Interleukin-8, Interleukin-12, Interleukin- 15,and Interleukin-18.
- In addition antiinflammatory mediators (IL-4, IL-10, IL-ra) are produced to balance the proinflammatory mediators in an attemptto eliminate the foreign antigen. Pro inflammatory and antiinflammatory pathways are tightly regulated. These pathways are closely connected to other pathways involved in homeostasis.

To name a few;

- Lipid mediators
- Neutrophil-endothelial cell activation
- Coagulation/fibrinolytic system

- Nitric oxide production
- Oxidant/antioxidant pathway
- Acute phase proteins
- Hypothalamic-pituitary-adrenal axis
- Cell apoptosis
- Heat-shock proteins:

- All these pathways are liked with the feedback loops in a very complexed manner. Severe sepsis and septic shock occurs due to dyregulated homeostatic mechanisms.
- TNF-alpha is the first proinflammatory cytokine to be released in sepsis, followed by interleukin-1, interleukin-6, and interleukin-8. TNF and interleukin-1 are synergistic as well as similar in action.Second messengers are generated after they bind to the receptors the second messengers are phospholipase C and A2 , G-proteins, oxygen free radicals and cAMP
- In addition, a number molecule production are induced such as:

  1. ELAM
  2. Tissue factor
  3. ICAM-1
  4. Cyclooxygenase
  5. Fibrinolytic proteins

6. Plasminogen activator inhibitor-1
7. Clotting proteins
8. Plasminogen activator
9. Phospholipase A2 (PLA2)
10. Nitric oxide synthetase.

The anti-inflammatory cytokine are interleukin-4, interleukin-10,interleukin-13, and TGF-beta2. Switching of TH1 to TH2 activation is done by anti-inflammatory cytokines. Interleukin-1 and TNF-alpha are suppressed by them.

ANNEXIN -1

- Annexin-1 (ANXA-1), previously named lipocortin-1, is a 37kd protein produced by mononuclear cells during the resolution phase of sepsis that has potent antiinflammatory properties and protects against LPS lethality.
- ANXA-1 inhibits PLA2, inducible nitric oxide synthetase (iNOS), and cyclooxygenase-2 (COX- 2) while it increases interleukin-10 release by macrophages. ANXA-1 prevents neutrophil adhesion to activated endothelium and inhibits neutrophil migration.

- The anti-inflammatory cytokines is to keeps the inflammation under control.Homeostasis is achieved by a balanced pro and anti-inflammatory
- mediators. SIRS and MODS occurs when this homeostasis is \ affected.
- Excessive anti-inflammatory cytokines will cause anergy resulting in a state more prone for infections.

COAGULATION SYSTEM ACTIVATION:

Procoagulant pathways is activated in sepsis due to imbalance in hemostasis.This imbalance is the main cause of organ dysfunction in sepsis. coagulopathy occurs because of activation of coagulant pathway.This results in DIC,which is characterised by intravascular thrombosis.

The extrinsic pathway of coagulation system is mainly involved in the pathogenesis of sepsis. Intrinsic pathway can also be activated in sepsis by the endotoxin .Tissue factor is highly thrombogenic.

- Tumor necrosis factor-alpha, interleukin 1, and plasminogen activating factor complement increased tissue factor expression.The main source of tissue factor in sepsis is the granulocytes and monocytes.

- Antibodies against tissue factor has been studied in experiment models.They have demonstrated the suppression of coagulation cascade.

Tissue factor pathway inhibitor (TFPI),Thrombomodulin pathway and ATIII suppress the tissue factor mechanism.

Anti-Inflammatory Mechanisms

The immune system contains humoral, cellular, and neural mechanisms that may exacerbate the potentially harmful effects of the pro-inflammatory response.

Phagocytes can switch to an anti-inflammatory phenotype that promotes tissue repair, while regulatory T cells and myeloid-derived suppressor cells further reduce inflammation. The so-called neuroinflammatory reflex may also contribute: sensory input is relayed through the afferent vagus nerve to the brainstem, from which the efferent vagus nerve activates the splenic nerve in the celiac plexus, with consequent norepinephrine release in the spleen and acetylcholine secretion by a subset of CD4+ T cells.

The acetylcholine release targets cholinergic Receptors on macrophages, reducing proinflammatory cytokine release.

Disruption of this neural-based system by vagotomy renders animals more vulnerable to endotoxin shock, while stimulation of the efferent

vagus nerve or cholinergic receptors attenuates systemic inflammation in experimental sepsis.

Immune Suppression:

Patients who survive early sepsis but remain dependent on intensive medical care occasionally demonstrate evidence of a suppressed immune system.

These patients may have ongoing infectious foci despite antimicrobial therapy or may experience the reactivation of latent viruses.

Multiple investigations have documented reduced responsiveness of blood leukocytes to pathogens in patient with sepsis; these findings were recently corroborated by post-mortem studies revealing strong functional impairments of splenocytes harvested from ICU patients who died of sepsis.

Immune suppression was evident in the lungs as well as the spleen; in both organs, the expression of ligands for T cell–inhibitory receptors on parenchymal cells was increased.

Enhanced apoptotic cell death, especially of B cells, CD4+T cells, and follicular dendritic cells, has been implicated in sepsis associated immune suppression and death. In a cohort of >1000 ICU admissions for sepsis, secondary infections developed in 14% of patients, and the associated genomic response at the time of infection was consistent with

immune suppression, including impaired glycolysis and cellular gluconeogenesis.

The most common secondary infections like catheter-related bloodstream infections, ventilator-associated infections, and abdominal infections.

It is unknown whether the dysfunctional immune system is driving multi organ dysfunction and secondary infections or whether the immune system itself is just another dysfunctional organ.

Organ Dysfunction:

Although the mechanisms that underlie organ failure in sepsis are only partially known, impaired tissue oxygenation plays a key role.

Several factors contribute to reduced oxygen delivery in sepsis and septic shock, including hypotension, reduced red-cell deformability, and microvascular thrombosis.

Inflammation can cause dysfunction of the vascular endothelium, accompanied by cell death and loss of barrier integrity, giving rise to subcutaneous and body-cavity edema. An excessive and uncontrolled release of nitric oxide causes vasomotor collapse, opening of arteriovenous shunts and pathologic shunting of oxygenated blood from susceptible tissues.

In addition, mitochondrial damage due to oxidative stress and other mechanisms impairs cellular oxygen utilization. The slowing of oxidative metabolism, in parallel with impaired oxygen delivery, reduces cellular O2 extraction.

Yet energy (i.e., ATP) is still needed to support basal, vital cellular function, which derives from glycolysis and fermentation and thus yields H+andlactate.

With severe or prolonged insult, ATP levels fall beneath a critical threshold, bioenergetic failure ensues, toxic reactive oxygen species are released, and apoptosis leads to irreversible cell death and organ failure.

Generally,organs such as the lung undergo extensive microscopic changes, while other organs may undergo rather few histologic changes. In fact, some organs (e.g., the kidney) may lack significant structural damage while still having significant tubular-cell changes that impair function.

Glucocorticoid in sepsis

- Whether critically ill patients are commonly have adrenal failure is difficult to dispute. Eventhough a randomly taken total serum cortisol or a total cortisol Level following 250 microgram of corticotropin is commonly used to diagnose adrenal insufficiency,this investigation has a number of drawbacks.

- Cortisol binding globulin level decreases during infection and the affinity of the hormone to bind is also decreased during acute illness, resulting in an increase in the free biologically active form of the hormone.
- Moreover, due to alterations in

GLUCOCORTICOIDS RECEPTOR number and/or function neither the total nor free cortisol reflects actual tissue glucocorticoid activity.

Nevertheless, despite these limitations, a random total cortisol of <15 μg / dL or a level <20 μg / dL after 250μg corticotropin in patient with severe sepsis is generally regarded as diagnostic of CRITICAL ILLNESS RELATED INSUFFICIENCY(CIRCI).

OVERVIEW OF SPECTRUM OF ILLNESS AND SEPSIS

PATHOPHYSIOLOGY

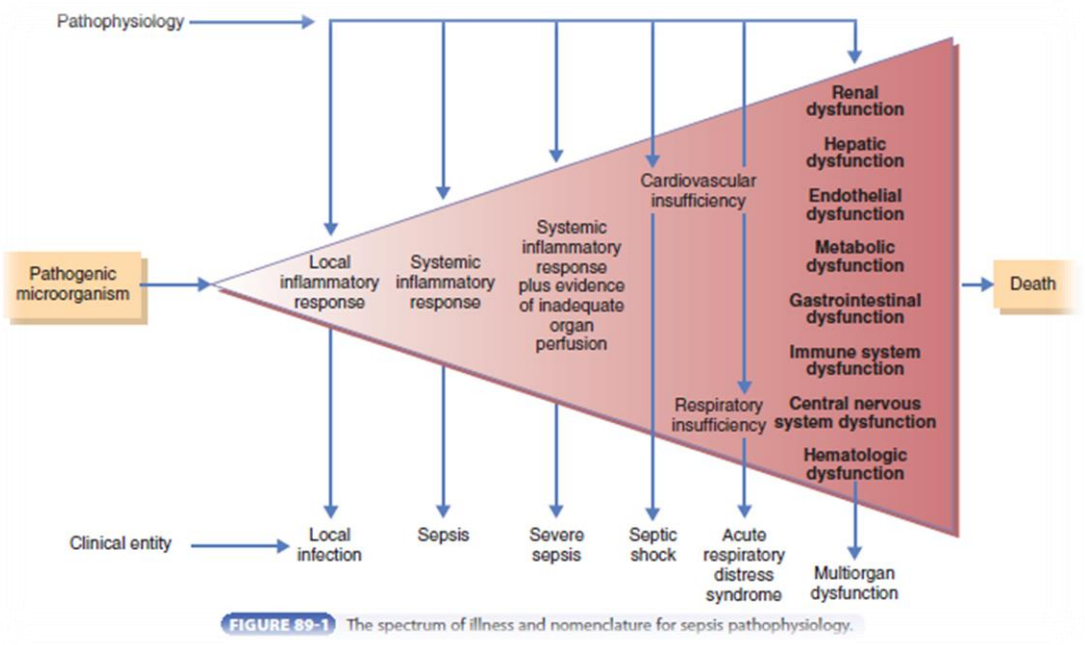


FIGURE 89-1 The spectrum of illness and nomenclature for sepsis pathophysiology.

CLINICAL FEATURES:

GENERAL CLINICAL FEATURES:

- Fever or hypothermia
- Tachypnoea
- Tachycardia
- Bounding pulse
- Cold extremities.
- Jaundice.
- Petechia,purpura.

1. CENTRAL NERVOUS SYSTEM:

- coma
- Delirium
- Septic encephalopathy
- Critical illness related polyneuropathy and myopathy.

2. CARDIOVASCULAR SYSTEM:

- Hypotension
- cold extremities.

3. RESPIRATORY SYSTEM:

- Acute Respiratory Distress syndrome.

4. RENAL DYSFUNCTION:

- Azotemia
- Oliguria
- Acute kidney injury.

5. METABOLISMS:

LIPID METABOLISM:

- Increased Triglycerides and VLDL
- Decreased HDL and LDL and Serum Cholesterol.

GLUCOSE METABOLISM: Hypoglycemia.

6. **COAGULANT DYSFUNCTION:**
    - DIC
7. **IMMUNE DYSFUNCTION REACTIVATION**
8. **HEPATIC DYSFUCTION:**
    - Jaundice
    - Hypoprotenaemia induced peripheral edema.
9. **CUTANEOUS MANIFESTATIONS:**
    - Erythroderma gangreonosum
    - pustular lesions.
    - cellulitis and Gangrene.
10. **AUTONOMIC DYSFUNCTION.**

DIAGNOSIS:

1.COMPLETE BLOOD COUNT:

- Leucocytosis or sometimes leucopenia
- Thrombocytopenia-DIC
- Anaemia

2.COAGULATION STUDY:

- Elevated prothrombin time.
- Decreased fibrinogen -DIC
- Increased D-dimer-DIC

3.LIVER FUNCTION TEST:

- Elevated bilirubin,aminotransferase levels
- Decreased serum proteins.

4.RENAL FUNCTION TEST:

- Elevated serum creatinine and Blood urea level.

5.BLOOD CULTURE:

- 3 sets of blood cultures taken from three different sites before administration of antibiotics.

6.URINE ROUTINE AND CULTURE

7.BACTERIAL CULTURES-Tip of IV

Catheter,secreation of endotracheal tube.

8.**Gram staining of peripheral blood.**

9.SERUM PROCALCITONIN LEVEL

10.SERUM ELECTOLYTES.

IMAGING MODALITIES:

1.Chest X ray.(R/O PNEUMONIA OR INFILTRATES)

2.Ultrasound abdomen and pelvis.(R/O BILIARY OBSTRUCTION)

3.CT ABDOMEN AND PELVIS. SUSPECTED CASE OF ACUTE

MYOCARDIAL INFARCTION:

1.Cardiac enzymes.

2.ECG.

INVASIVE PROCEDURES:

1.Lumbar puncture.

2.THORACOCENTESIS(PLEURAL EFFUSION)

3.PARACENTESIS(In case of Ascites)

4.SWAN GANZ

CATHETERISATION(Assess volume status)

DIAGNOSTIC CRITERIA:

General variables

- Fever (core temperature >38.3°C)
- Hypothermia (core temperature <36°C)
- Heart rate >90/min or >2 SD above the normal value for age
- Tachypnoea
- Altered mental status
- Significant oedema or positive fluid balance (>20 mL/kg over 24 hours)
- Hyperglycaemia (plasma glucose >120 mg/dL) in the absence of diabetes

Inflammatory variables

- Leukocytosis (WBC count >12,000 /mL)
- Leukopaenia (WBC count <4000/mL)
- Normal WBC count with >10% immature forms
- Plasma C-reactive protein >2 SD above the normal value
- Plasma procalcitonin >2 SD above the normal value

Haemodynamic variables

- Arterial hypotension (SBP <90 mmHg, MAP <70, or an SBP decrease >40 mmHg) or <2 SD below normal for age)
- SvO_2 >70%
- Cardiac index >3.5 L/min/m^2

Organ dysfunction variables

- Arterial hypoxaemia (PaO_2/FiO_2 <300)
- Acute oliguria (urine output <0.5 mL/kg/h for at least 2 hours)
- Creatinine increase >0.5 mg/dL
- Coagulation abnormalities (INR >1.5 or aPTT >60 sec)
- Ileus (absent bowel sounds)
- Thrombocytopaenia (platelet count <100,000/µL)
- Hyperbilirubinaemia (plasma total bilirubin >4 mg/dL)

Tissue perfusion variables

- Hyperlactatemia (>1 mmol/L)
- Decreased capillary refill or mottling

DIFFERENTIAL DIAGNOSIS:

*ADRENAL INSUFFICIECY

*BURNS

*TRAUMA

*ACUTE PANCREATITIS

*PULMONARY EMBOLISM

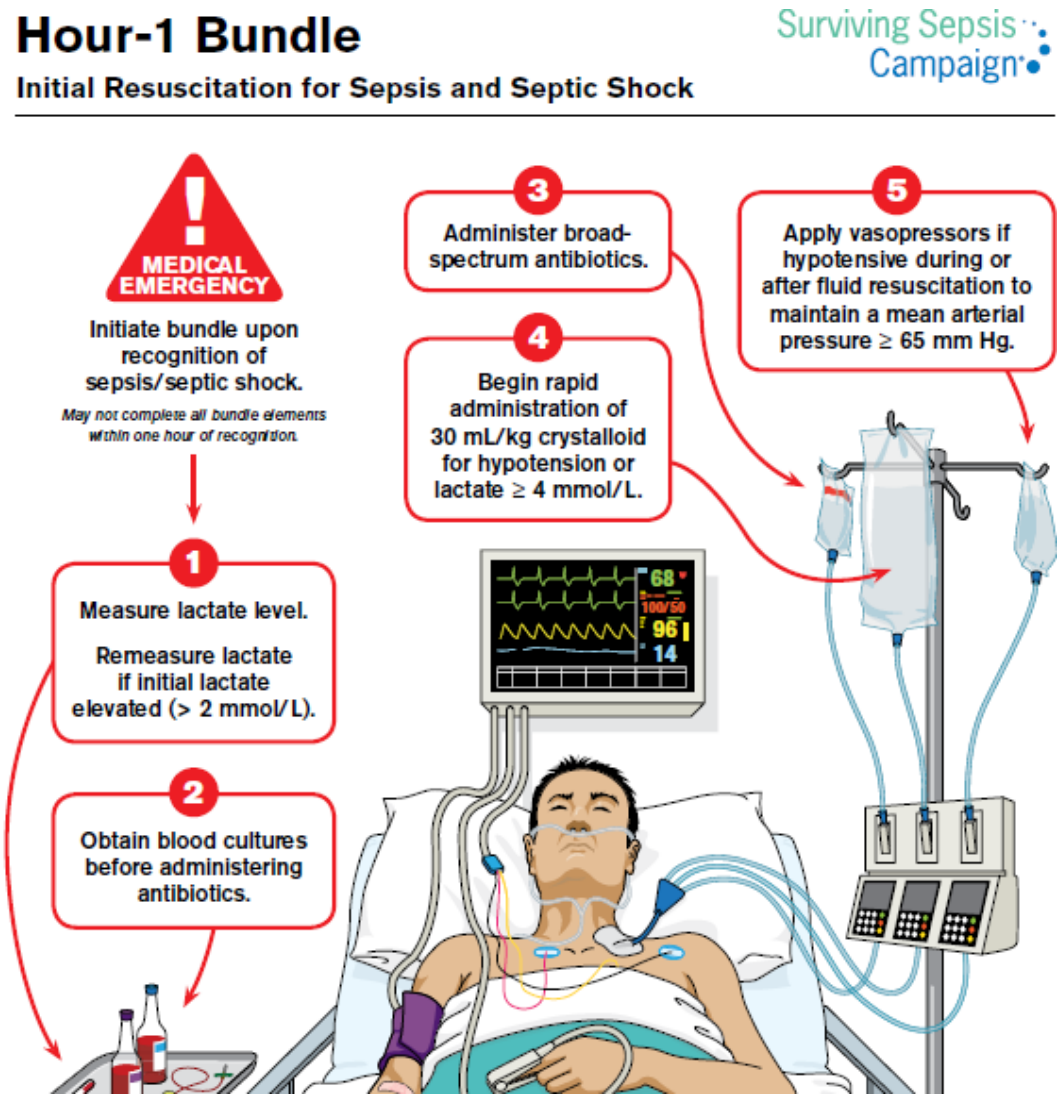
*AORTIC DISSECTION

*ACUTE MYOCARDIAL INFARCTION

*CARDIAC TAMPONADE.

Above mentioned conditions mimics SEPSIS in the form of HYPOTENSION and ORGAN FAILURE.

MANAGEMENT OF SEPSIS:



INITIAL RESUSCITATION

Protocolized, quantitative resuscitation of patients with sepsis-induced tissue hypoperfusion (defined in this document as hypotension persisting after initial fluid challenge or blood lactate concentration ≥ 4 mmol/L). Goals during the first 6 hrs of resuscitation:

a) Central venous pressure (CVP) 8–12 mm Hg

b) Mean arterial pressure (MAP) ≥ 65 mm Hg

c) Urine output ≥ 0.5 mL/kg/hr

d) Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively.

° In patients with elevated lactate levels targeting resuscitation to normalize lactate.

ANTIMICROBIAL THERAPY:

Administration of effective intravenous antimicrobials within the first hour of recognition of septic shock and severe sepsis without septic shock as the goal of therapy.

a) Initial empiric anti-infective therapy of one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into tissues presumed to be the source of sepsis.

b) Antimicrobial regimen should be reassessed daily for potential de-escalation.

° Use of low procalcitonin levels or similar biomarkers to assist the clinician in the discontinuation of empiric antibiotics in patients who initially appeared septic, but have no subsequent evidence of infection.

Combination empirical therapy for neutropenic patients with severe sepsis and for patients with difficult-to-treat, multidrug-resistant bacterial pathogens such as Acinetobacter and Pseudomonas spp. For patients with severe infections associated with respiratory failure and septic shock, combination therapy with an extended spectrum beta-lactam and either an aminoglycoside or a fluoroquinolone is for P. aeruginosa bacteremia. A combination of beta-lactam and macrolide for patients with septic shock from bacteremic Streptococcus pneumoniae infections.

b) Empiric combination therapy should not be administered for more than 3–5 days. De-escalation to the most appropriate single therapy should be performed as soon as the susceptibility profile is known.

Duration of therapy typically 7–10 days; longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteremia with *S. aureus*; some fungal and viral infections or immunologic deficiencies, including neutropenia.

Antiviral therapy initiated as early as possible in patients with severe sepsis or septic shock of viral origin. Antimicrobial agents should not be used in patients with severe inflammatory states determined to be of noninfectious cause.

TABLE 297-3 Initial Antimicrobial Therapy for Severe Sepsis with No Obvious Source in Adults with Normal Renal Function

CLINICAL CONDITION	ANTIMICROBIAL REGIMENS[a]
Septic shock (immunocompetent adult)	The many acceptable regimens include (1) piperacillin-tazobactam (3.375–4.5 g q6h), (2) cefepime (2 g q12h), or (3) meropenem (1 g q8h) or imipenem-cilastatin (0.5 g q6h). If the patient is allergic to β-lactam antibiotics, use (1) aztreonam (2 g q8h) or (2) ciprofloxacin (400 mg q12h) or levofloxacin (750 mg q24h). Add vancomycin (loading dose of 25–30 mg/kg, then 15–20 mg/kg q8–12h) to each of the above regimens.
Neutropenia (<500 neutrophils/μL)	Regimens include (1) cefepime (2 g q8h), (2) meropenem (1 g q8h) or imipenem-cilastatin (0.5 g q6h) or doripenem (500 mg q8h), or (3) piperacillin-tazobactam (3.375 g q4h). Add vancomycin (as above) if the patient has a suspected central line–associated bloodstream infection, severe mucositis, skin/soft tissue infection, or hypotension. Add tobramycin (5–7 mg/kg q24h) plus vancomycin (as above) plus caspofungin (one dose of 70 mg, then 50 mg q24h) if the patient has severe sepsis/septic shock.
Splenectomy	Use ceftriaxone (2 g q24h, or—in meningitis—2 g q12h). If the local prevalence of cephalosporin-resistant pneumococci is high, add vancomycin (as above). If the patient is allergic to β-lactam antibiotics, use levofloxacin (750 mg q24h) or moxifloxacin (400 mg q24h) plus vancomycin (as above).

SOURCE CONTROL:

A specific anatomical diagnosis of infection requiring consideration for emergent source control be sought and diagnosed or excluded as rapidly as possible, and intervention be undertaken for source control within the first 12 hr after the diagnosis is made, if feasible.

When infected peripancreatic necrosis is identified as a potential source of infection, definitive intervention is best delayed until adequate demarcation of viable and nonviable tissues has occurred.

When source control in a severely septic patient is required, the effective intervention associated with the least physiologic insult should be used (eg, percutaneous rather than surgical drainage of an abscess). If intravascular access devices are a possible source of severe sepsis or septic shock, they should be removed promptly after other vascular access has been established.

INFECTIONS CONTROL:

a) Selective oral decontamination and selective digestive decontamination should be introduced and investigated as a method to reduce the incidence of ventilator-associated pneumonia; this infection control measure can then be instituted in health care settings and regions where this methodology is found to be effective.

b) Oral chlorhexidine gluconate be used as a form of oropharyngeal decontamination to reduce the risk of ventilator-associated pneumonia in ICU patients with severe sepsis.

HEMODYNAMIC SUPPORT AND ADJUNCTIVE THERAPY

FLUID THERAPY OF SEVERE SEPSIS:

- Crystalloids as the initial fluid of choice in the resuscitation of severe sepsis and septic shock.
- Against the use of hydroxyethyl starches for fluid resuscitation of severe sepsis and septic shock.

- Albumin in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids.

- Initial fluid challenge in patients with sepsis-induced tissue hypoperfusion with suspicion of hypovolemia to achieve a minimum of 30 mL/kg of crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid may be needed in some patients.Fluid challenge technique be applied wherein fluid administration is continued as long as there is hemodynamic improvement either based on dynamic (eg, change in pulse pressure, stroke volume variation) or static (eg, arterial pressure, heart rate) variables.

VASOPRESSORS:

- Vasopressor therapy initially to target a mean arterial pressure (MAP) of 65 mm Hg.

- Norepinephrine as the first choice vasopressor.

    - Epinephrine (added to and potentially substituted for norepinephrine) when an additional agent is needed to maintain adequate blood pressure.

Vasopressin 0.03 units/minute can be added to norepinephrine (NE) with intent of either raising MAP or decreasing NE dosage (UG).

Low dose vasopressin is not recommended as the single initial vasopressor for treatment of sepsis-induced hypotension and vasopressin doses higher than 0.03-0.04 units/minute should be reserved for salvage therapy (failure to achieve adequate MAP with other vasopressor agents).

° Dopamine as an alternative vasopressor agent to norepinephrine only in highly selected patients (eg, patients with low risk of tachyarrhythmias and absolute or relative bradycardia).

• Phenylephrine is not recommended in the treatment of septic shock except in circumstances where

(a) norepinephrine is associated with serious arrhythmias,

(b) cardiac output is known to be high and blood pressure persistently low or

(c) as salvage therapy when combined inotrope/vasopressor drugs and low dose vasopressin have failed to achieve MAP target.

Other Supportive Therapy of Severe Sepsis Blood Product Administration

- Once tissue hypoperfusion has resolved and in the absence of extenuating circumstances, such as myocardial ischemia, severe hypoxemia, acute hemorrhage, or ischemic heart disease, we recommend that red blood cell transfusion occur only when hemoglobin concentration decreases to <7.0 g/dLto target a hemoglobin concentration of 7.0 –9.0 g/dL in adults.

- Not using erythropoietin as a specific treatment of anemia associated with severe sepsis.
    - Fresh frozen plasma not be used to correct laboratory clotting abnormalities in the absence of bleeding or planned invasive procedures.
- Not using antithrombin for the treatment of severe sepsis and septic shock.
- Low dose dopamine should not be used for renal protection.

IONOTROPICS THERAPY:

- A trial of dobutamine infusion up to 20 micrograms/kg/minbe administered or added to vasopressor (if in use) in the presence of
    (a) myocardial dysfunction as suggested by elevated cardiac filling pressures and low cardiac output, or

b) ongoing signs of hypoperfusion, despite achieving adequate intravascular volume and adequate MAP.

- Not using a strategy to increase cardiac index to predetermined supranormal levels.

CORTICOSTEROIDS THERAPY:

- ° Not using intravenous hydrocortisone to treat adult septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (see goals for Initial Resuscitation). In case this is not achievable, we suggest intravenous hydrocortisone alone at a dose of 200 mg per day.
- ° Not using the ACTH stimulation test to identify adults with septic shock who should receive hydrocortisone.
- ° In treated patients hydrocortisone tapered when vasopressors are no longer required.
- Corticosteroids not be administered for the treatment of sepsis in the absence of shock.
- ° When hydrocortisone is given, use continuous flow .

BLOOD PRODUCTS ADMINISTRATIONS:

- Once tissue hypoperfusion has resolved and in the absence of extenuating circumstances, such hemorrhage, or ischemic heart disease, we recommend that red blood cell transfusion occur only when

hemoglobin concentration decreases to <7.0 g/dLto target a hemoglobin concentration of 7.0 –9.0 g/dL in adults.

- Not using erythropoietin as a specific treatment of anemia associated with severe sepsis.
- Fresh frozen plasma not be used to correct laboratory clotting abnormalities in the absence of bleeding or planned invasive procedures .
- Not using antithrombin for the treatment of severe sepsis and septic shock.
- In patients with severe sepsis, administer platelets prophylactically when counts are <10,000/mm3 (10 x 109/L) in the absence of apparent bleeding. We suggest prophylactic platelet transfusion when counts are <20,000/mm3 (20 x 109/L) if the patient has a significant risk of bleeding. Higher platelet counts (≥50,000/mm3 [50 x 109/L]) are advised for active bleeding, surgery, or invasive procedures.

MECHANICAL VENTILATIONS IN SEPSIS INDUCED ARDS:

- Target a tidal volume of 6 mL/kg predicted body weight in patients with sepsis-induced ARDS.

- Plateau pressures be measured in patients with ARDS and initial upper limit goal for plateau pressures in a passively inflated lung be ≤30 cm H2O .
- Positive end-expiratory pressure (PEEP) be applied to avoid alveolar collapse at end expiration (atelectotrauma).
  - Strategies based on higher rather than lower levels of PEEP be used for patients with sepsis- induced moderate or severe ARDS
  - Recruitment maneuvers be used in sepsis patients with severe refractory hypoxemia.
  - Prone positioning be used in sepsis-induced ARDS patients with a Pao2/Fio2 ratio ≤ 100 mm Hg in facilities that have experience with such practices .
- That mechanically ventilated sepsis patients be maintained with the head of the bed elevated to 30-45 degrees to limit aspiration risk and to prevent the development of ventilator-associated pneumonia.
  - That noninvasive mask ventilation (NIV) be used in that minority of sepsis-induced ARDS patients in whom the benefits of NIV have been carefully considered and are thought to outweigh the risks.
- That a weaning protocol be in place and that mechanically ventilated patients with severe sepsis undergo spontaneous breathing trials regularly to evaluate the ability to discontinue mechanical ventilation when they satisfy the following criteria:

a) arousable;

b) hemodynamically stable (without vasopressor agents);

c) no new potentially serious conditions;

d) low ventilatory and end-expiratory pressure requirements; and

e) low Fio2 requirements which can be met safely delivered with a face mask or nasal cannula. If the spontaneous breathing trial is successful, consideration should be given for extubation.

- Against the routine use of the pulmonary artery catheter for patients with sepsis-induced ARDS.
- A conservative rather than liberal fluid strategy for patients with established sepsis-induced ARDS who do not have evidence of tissue hypoperfusion.
- In the absence of specific indications such as bronchospasm, not using beta 2-agonists for treatment of sepsis-induced ARDS.

SEDATION,ANALGESIC AND NEUROMUSCULAR BLOCADE IN SEPSIS:

- Continuous or intermittent sedation be minimized in mechanically ventilated sepsis patients, targeting specific titration endpoints.

- Neuromuscular blocking agents (NMBAs) be avoided if possible in the septic patient without

ARDS due to the risk of prolonged neuromuscular blockade following discontinuation. If NMBAs must be maintained, either intermittent bolus as required or continuous infusion with train-of-four monitoring of the depth of blockade should be used.

° A short course of NMBA of not greater than 48 hours for patients with early sepsis-induced ARDS and a Pao2/Fio2 < 150 mm Hg.

BLOOD GLUCOSE CONTROL:

- A protocolized approach to blood glucose management in ICU patients with severe sepsis commencing insulin dosing when 2 consecutive blood glucose levels are >180 mg/dL. This protocolized approach should target an upper blood glucose ≤180 mg/dL rather than an upper target blood glucose ≤ 110 mg/dL.

- Blood glucose values be monitored every 1–2hrs until glucose values and insulin infusion rates are stable and then every 4 hrs thereafter. Glucose levels obtained with point-of-care testing of capillary blood be interpreted with caution, as such measurements may not accurately estimate arterial blood or plasma glucose values.

RENAL REPLACEMENT AND SODIUM BICARBANOTE THERAPY:

- Continuous renal replacement therapies and intermittent hemodialysis are equivalent in patients with severe sepsis and acute renal failure.
- Use continuous therapies to facilitate management of fluid balance in hemodynamically unstable septic patients.
- Not using sodium bicarbonate therapy for the purpose of improving hemodynamics or reducing vasopressor requirements in patients with hypoperfusion-induced lactic acidemia with pH ≥7.15.

DEEP VEIN THROMBOSIS PROPHYLAXIS:

- Patients with severe sepsis receive daily pharmacoprophylaxis against venous thromboembolism (VTE). This should be accomplished with daily subcutaneous low-molecular weight heparin (LMWH) (versus twice daily UFH, grade 2C versus three times daily UFH). If creatinine clearance is <30 mL/min, use dalteparin (grade 1A) or another form of LMWH that has a low degree of renal metabolism or UFH.

- Patients with severe sepsis be treated with a combination of pharmacologic therapy and intermittent pneumatic compression devices whenever possible.
- Septic patients who have a contraindication for heparin use (eg, thrombocytopenia, severe coagulopathy, active bleeding, recent intracerebral hemorrhage) not receive pharmacoprophylaxis, but receive mechanical prophylactic treatment, such as graduated compression stockings or intermittent compression devices, unless contraindicated. When the risk decreases start pharmacoprophylaxis.

STRESS INDUCED ULCER PROPHYLAXIS:

- Stress ulcer prophylaxis using H2 blocker or proton pump inhibitor be given to patients with severe sepsis/septic shock who have bleeding risk factors.
- When stress ulcer prophylaxis is used, proton pump inhibitors rather than H2RA.

NUTRITIONS:

- Administer oral or enteral (if necessary) feedings, as tolerated, rather than either complete fasting or provision of only intravenous glucose within the first 48 hours after a diagnosis of severe sepsis/septic shock.

- Avoid mandatory full caloric feeding in the first week but rather suggest low dose feeding (eg, up to 500 calories per day), advancing only as tolerated.

- Use intravenous glucose and enteral nutrition rather than total parenteral nutrition (TPN) alone or parenteral nutrition in conjunction with enteral feeding in the first 7 days after a diagnosis of severe sepsis/septic shock.
- Use nutrition with no specific immunomodulating supplementation rather than nutrition providing specific immunomodulating supplementation in patients with severe sepsis.

SETTING GOALS OF CARE:

- Discuss goals of care and prognosis with patients and families.
- Incorporate goals of care into treatment and end-of-life care planning, utilizing palliative care principles where appropriate.
- Address goals of care as early as feasible, but no later than within 72 hours of ICU admission.

SCORES:

APACHE II	APACHE II was designed to provide a morbidity score for a patient. It is useful to decide what kind of treatment or medicine is given. Methods exist to derive a predicted mortality from this score, but these methods are not too well defined and rather imprecise. APACHE II is an updated version.
SAPS II	SAPS II was designed to provide a predicted mortality, that does not reflect the expected mortality for a particular patient, but is good for benchmarking. In a rather simple way, it makes it possible to provide a single number that describes the morbidity of a number of patients.
SAPS III	SAPS III was designed to provide a realistic predicted mortality for a particular patient or a particular group of patients. It does this by calibrating against known mortalities on an existing set of patients, for a specific definition of mortality
SOFA	SOFA-Sequential Organ Failure Assessment was designed to provide a simple daily score that indicates how the status of the patient evolves over time.

PIRO BASED APPROACH IN SEPSIS

	P Predisposition	I Infection	R Response	O Organ dysfunction
Available	Age Comorbidities Chronic conditions Baseline severity Source of admission	Pathogen Susceptibility Bacteremia Bacterial load Site of infection Nosocomial or community-acquired infection	Clinical Resolution Hypoxemia Hypotension Immune Response	ARDS Shock Acute renal failure MODS SOFA
Future	Genetics Polymorphisms of toll-like receptor, tumor necrosis factor, IL-1 and CD14	Genotyping Assay of microbial products (LPS), mannan and bacterial DNA Detection of virulence factors	Biomarkers Nonspecific markers of activated inflammation (PCT or IL-6) or impaired host responsiveness (HLA-DR)	Mithocondrial dysfunction Endothelial damage and activation

ARDS - Acute Respiratory Distress Syndrome; MODS - Multiple Organ Dysfunction Syndrome; SOFA - Sequential Organ Failure Assessment; PCT – procalcitonin; IL-1 – interleukin 1, IL-6 – interleukin 6; LPS – lipopolissacaride; DNA – dexoxiribonucleic acid; HLA-DR – D related human leukocyte antigens.

ALBUMIN IS THE MOST ABUNDANT PROTEIN IN HUMAN PLASMA

The liver synthesizes approximately 12 g of albumin per day, epresenting about 25% of total hepatic protein synthesis and half its secreted protein. About 40% of the body's albumin circulates in the plasma, where it accounts for roughly three-fifths of total plasma protein by weight (3.4-4.7g/dL). The remainder resides in the extracellular space. Because of its relatively low molecular mass (about 69 kDa) and high concentration,albumin is thought to contribute 75 to 80% of the **osmotic pressure** of human plasma. Like most other secreted proteins, albumin is initially synthesized as a **preproprotein**. Its **signal peptide** is removed as it passes into the cisternae of the rough endoplasmic reticulum. A second

hexapeptide is cleaved from the new N-terminus farther along the secretory pathway.

Mature human albumin consists of a single polypeptide chain, 585amino acids in length, that is organized into three functional domains. Its ellipsoidal conformation is stabilized by a total of 17 intrachain disulphide bonds. A major role of albumin is to bind to and transport numerous **ligands**. These include free fatty acids (FFA), calcium, certain steroid hormones, bilirubin, copper, and tryptophan. A variety of drugs, including sulfonamides, penicillin G, dicumarol, and aspirin, also bind to albumin; a finding with important pharmacologic implications. Preparations of human albumin have been widely used in the treatment of burns and of hemorrhagic shock.

Some humans suffer from genetic mutations that impair their ability to synthesize albumin. Individuals whose plasma is completely devoid of albumin are said to exhibit **analbuminemia**. Surprisingly, persons suffering from an albuminemia display only moderate edema. Depressed synthesis of albumin also occurs in a variety of diseases, particularly those of the liver. The plasma of patients with **liver disease** often shows a decrease in the ratio of albumin to globulins (decreased albumin-globulin ratio). The synthesis of albumin decreases relatively early in conditions of protein malnutrition, such as **kwashiorkor**.

ALBUMIN

i. The name is derived from the white precipitate formed when egg is boiled (Latin, albus =white). Albumin constitutes the major part of plasma proteins.

ii. **ii.** It has one polypeptide chain with 585 aminoacids. It has a molecular weight of 69,000 D. It is elliptical in shape.

iii. It is synthesized by hepatocytes; therefore estimation of albumin is a **liver function test**. Albumin is synthesized as a precursor, and the signal peptide is removed as it passes through endoplasmic reticulum.

iv. Albumin can come out of vascular compartment. So albumin is present in CSF and interstitial fluid.

v. Half-life of albumin is about 20 days. Liver produces about 12 g of albumin per day, representing about 25% of total hepatic protein synthesis.

Functions of Albumin

1. Colloid osmotic pressure of plasma

i. The total osmolality of serum is 278-305 m osmol/kg (about 5000 mm of Hg). But this is produced mainly by salts, which can pass easily from intravascular to extravascular space. Therefore, the osmotic pressure exerted by electrolytes inside and outside the vascular compartments will cancel each other. But proteins cannot

easily escape out of blood vessels, and therefore, proteins exert the **'effective osmotic pressure'.** It is about 25mm Hg, and 80% of it is contributed by albumin. The maintenance of blood volume is dependent on this effective osmotic pressure.

ii. According to **Starling's hypothesis**, at the capillary end the blood pressure (BP) or hydrostatic pressure expels water out, and effective osmotic pressure (EOP) takes water into the vascular compartment.

iii. At arterial end of the capillary, BP is 35 mm Hg and EOP is 25 mm; thus water is expelled by a pressure of 10 mm Hg. At the venous end of the capillary, EOP is 25 mm and BP is 15 mm, and therefore water is imbibed with a pressure of 10 mm. Thus the number of water molecules escaping out at arterial side will be exactly equal to those returned at the venous side and therefore blood volume remains the same.

iv. If protein concentration in serum is reduced, the EOP is correspondingly decreased. Then return of water into blood vessels is diminished, leading to **accumulation of water in tissues**. This is called **edema**.

v. Edema is seen in conditions where albumin level in blood is less than 2g/dl.

2. Transport Function

Albumin is the carrier of various hydrophobic substances in the blood. Being a watery medium, blood cannot solubilize lipid components.

i. **Bilirubin** and **nonesterified fatty acids** are specifically transported by albumin.

ii. **Drugs** (sulpha, aspirin, salicylate, dicoumarol, phenytoin),

iii. **Hormones:** steroid hormones, thyroxine

iv. **Metals:** Albumin transports copper. Calcium and heavy metals are non-specifically carried by albumin. Only the unbound fraction of drugs is biologically active.

3. Buffering action

All proteins have buffering capacity. Because of its high concentration in blood, albumin has maximum buffering capacity. Albumin has a total of 16 histidine residues which contribute to this buffering action.

4. Nutritional function

All tissue cells can take up albumin by pinocytosis. It is then broken down to amino acid level. So albumin may be considered as the transport form of essential amino acids from liver to extrahepatic cells. Human albumin is clinically useful in treatment of liver diseases, hemorrhage, shock and burns.

Clinical Applications

1. Blood brain barrier

Albumin–fatty acid complex cannot cross blood–brain barrier and hence fatty acids cannot be taken up by brain. The **bilirubin from albumin may be competitively replaced by drugs like aspirin**.Being lipophilic, unconjugated bilirubin can cross the blood brain barrier and get deposited in brain. The brains of young children are susceptible; free bilirubin deposited in brain leads to **kernicterus** and mental retardation.

2. Drug interactions

When two drugs having high affinity to albumin are administered together, there may be competition for the available sites, with consequent displacement of one drug. Such an effect may lead to clinically significant drug interactions, e.g. phenytoin –dicoumarol interaction.

3. Protein-bound calcium

Calcium level in blood is lowered in hypoalbuminemia.Thus, even though total calcium level in blood is lowered, ionized calcium level may be normal, and so tetany may not occur.

Calcium is lowered by 0.8 mg/dl for a fall of 1 g/dl of Albumin.

4. Therapeutic use

Human albumin is therapeutically useful to treat burns, hemorrhage and shock.

5. Edema

Hypo-albuminemia will result in **tissue edema** (seeStarling's law).

5a. **Malnutrition**, where albumin synthesis is depressed (*generalized edema*)

5b. **Nephrotic** syndrome, where albumin is lost through urine (*facial edema*)

5c. **Cirrhosis** of liver (mainly *ascites*), where albumin synthesis is less and it escapes into ascitic fluid.

5d. **Chronic congestive cardiac failure:** Venouscongestion will cause increased hydrostatic pressure and decreased return of water into capillaries and so *pitting edema* of feet may result.

6. **Normal value**Normal level of Albumin is 3.5–5 g/dl. Lowered levelof albumin (hypo-albuminemia) has important clinical significance.

7. Hypo-albuminemia

7a. **Cirrhosis of liver:** Synthesis is decreased.

7b. **Malnutrition:** Availability of amino acids is reduced and albumin synthesis is affected.

7c. **Nephrotic syndrome:** Permeability of kidney glomerular membrane is defective, so that albumin is excreted in large quantities.

7d. Albuminuria: Presence of albumin in urine is called albuminuria. It is always pathological. Large quantities (a few grams per day) of albumin are lost in urine in nephrotic syndrome. Small quantities are lost in urine in acute nephritis, and other inflammatory conditions of urinary tract. Detection of albumin in urine is done by heat and acetic acid test. In **micro-albuminuria** or minimal albuminuria or pauci-albuminuria, small quantity of albumin (30-300 mg/d) is seen in urine (Paucity = small in quantity).

7e. Protein losing enteropathy: Large quantities of albumin is lost from intestinal tract.

7f. Analbuminemia is a very rare condition, where defective mutation in the gene is responsible for absence of synthesis.

Albumin-Globulin Ratio

In hypo-albuminemia, there will be a compensatory increase in globulins which are synthesized by the reticulo-endothelial system. Albumin-globulin ratio (A/G ratio) is thus altered or even reversed. This again leads to edema.

Hypoproteinemia

Since albumin is the major protein present in the blood, any condition causing lowering of albumin will lead to reduced total proteins in blood (hypoproteinemia).

Hyper-gamma-globulinemias

1. **Low albumin level**
2. When **albumin level is decreased**, body tries to compensate by increasing the production of globulins from reticulo-endothelial system.

2. Chronic infections

Gamma globulins are increased, but the increase is smooth and wide based.

3. Multiple myeloma

Drastic increase in globulins is seen in *paraproteinemias*, when a sharp spike is noted in electrophoresis. This is termed as **M-band** because of the monoclonal origin of immunoglobulins. The monoclonal origin of immunoglobulins is seen in multiple **n**myeloma. Monoclonal gammopathies are characterized by the presence of a monoclonal protein which can be detected by serum protein electrophoresis and typed by immunofixation electrophoresis.The light chains are produced in excess which is excreted in urine as Bence Jones proteins(BJP)when their serum level increases.Multiple myeloma is the most common type of monoclonal gammopathy. Free light chain assay along with kappa and lambda ratio in serum and urine is found to be very useful in early diagnosis, monitoring the response to treatment and prediction of prognosis.

Materials and Methods

METHODOLOGY

STUDY:SERIAL SERUM ALBUMIN &OTHER LIVER PARAMETERS MONITORING AS A PROGNOSTIC MARKER IN PATIENTS WITH SEPSIS.

SOURCE OF DATA:

The study was conducted on patients admitted to medical ICU/Medical emergency ward, GOVT.RAJAJI HOSPITAL,MADURAI after getting ethical committee approval.

METHOD OF STUDY:

- Studydesign:Prospective,Observational study.
- Sample size: 100
- Sample method:Simple random sampling.
- Duration of study: 10 months.
- Method of collection of specimens and processing:

Patients blood samples was collected on day of admission and serum was separated by centrifugation, and then serum Albumin, SGOT,SGPT,TOTAL BILIRUBIN,PT,INR were monitored serially on day 1,3,5,7.by using BROMOCRESOL GREEN method on auto-analyser for Albumin, LFT by DIAZO methods.

INCLUSION CRITERIA:

All sepsis patients with age >13years.

EXCLUSION CRITERIA:

- Patients who denied formal consent.
- Chronic malnutritions
- Chronic liver disease.
- Nephrotic syndrome.
- Protein losing enteropathy.

ETHICAL CLEARANCE: Applied for

CONSENT: Individual written and informed consent.

ANALYSIS: Statistical analysis performed using appropriate tests as required according to data.

CONFLICT OF INTEREST: NIL

FINANCIAL SUPPORT: SELF

INVESTIGATIONS:

- Complete blood count.
- Blood urea
- serum creatinine
- Serum electrolytes
- Random blood sugar
- Liver function test.PT,INR.
- Fasting blood sugar

- post prandial blood sugar
- Urine culture sensitivity
- Blood culture sensitivity
- Sputum culture sensitivity(if needed)
- Arterial blood gas analysis
- Chest X ray
- ECG/USG KUB/Abdomen(if needed)
- CSF analysis(in suspected meningitis)

Data was collected using a pre tested proforma meeting the objectives of the study. Detailed history, physical examination and necessary investigation was undertaken. The purpose of the study was explained to the patient and informed consent obtained. Patient was followed up during the course of the hospital stay and the outcome of the patient (i.e.death/survival) is recorded.

STATISTICAL ANALYSIS:

Statistical analysis were performed with IBM SPSS version 16(SPSS Inc., Chicago, IL). Descriptive statistics was computed ; data were tested for normality using Shapiro wilks normality test. Since the data levels were normally distributed, hence serial LFT and serum albumin among survivors and non survivors were compared using independent student t-test . The confidence interval was set at 95%. Chi square test or Fisher's Exact Test was used to compare categorical variables.

Bivariate logistic regression model were used to identify independent predictors of mortality and to examine the relation between serum albumin, LFT and mortality.

The predictive values of serial serum albumin, LFT were compared by calculating the area under curve (AUC) of the receiver operating characteristic curve (ROC).

Results and Interpretation

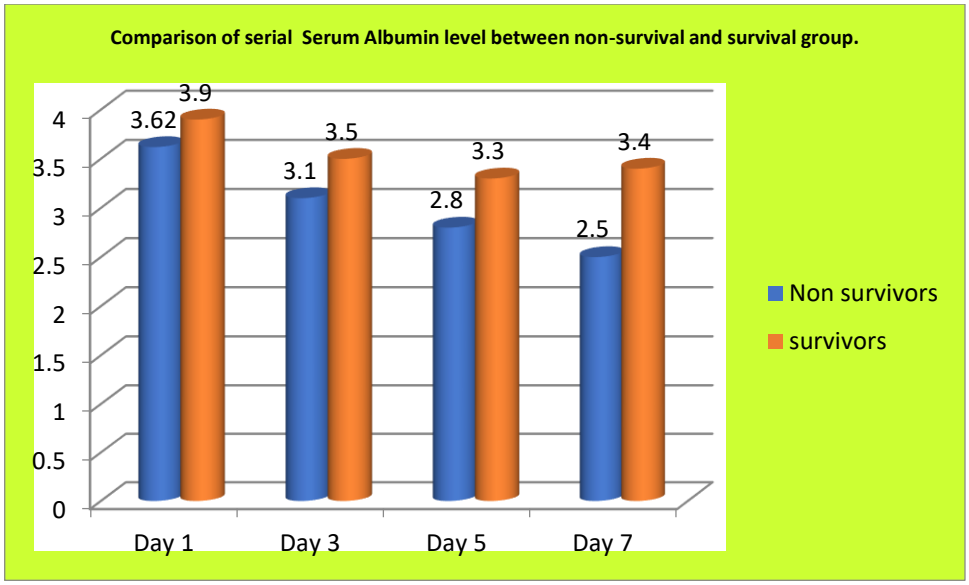
RESULTS

Descriptive statistics (N=100)				
	Mean	Std. Deviation	Minimum	**Maximum**
Age in yrs	53.81	13.26779	18	87
Serum albumin (g/dl)				
Day 1	3.82	0.55	2.8	5.5
Day 3	3.4	0.49	2.3	4.7
Day 5	3.20	0.51	2.2	4.7
Day 7	3.1	0.67	2	4.9
SGOT				
Day 1	41.11	13.26	22	76
Day 3	46.41	13.28	28	82
Day 5	49.66	14.92	30	98
Day 7	52.79	16.20	32	100
SGPT				
Day 1	42.69	12.38	21	88
Day 3	48.02	12.87	30	90
Day 5	51.9	14.76	30	97
Day 7	55.39	17.84	30	105
Total bilirubin				
Day 1	1.124	0.23	0.7	1.9
Day 3	1.30	0.32	0.6	2.2
Day 5	1.42	0.41	0.7	2.4
Day 7	1.56	0.55	0.8	3

INR				
Day 1	1.2	0.34	0.7	2.6
Day 3	1.4	0.4	0.8	2.8
Day 5	1.5	0.50	0.9	3.2
Day 7	1.6	0.63	0.9	3.5

Comparison of Serial Serum Albumin level between non-survival and survival group.							
Parameters	**Non survivors N=32**			**Survivors N=68**			
	Mean	**Std. Deviation**	**Std. Error Mean**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**p value**
Age	55.59	12.349	2.183	52.97	13.686	1.66	0.359
Serum albumin							
Day 1	3.628125	0.422156	0.074627	3.910588	0.586041	0.071068	0.016*
Day 3	3.18125	0.417703	0.07384	3.538235	0.490212	0.059447	0.001*
Day 5	2.859375	0.34721	0.061379	3.372059	0.49801	0.060393	0.001*
Day 7	2.565625	0.351595	0.062154	3.479412	0.593135	0.071928	0.001*

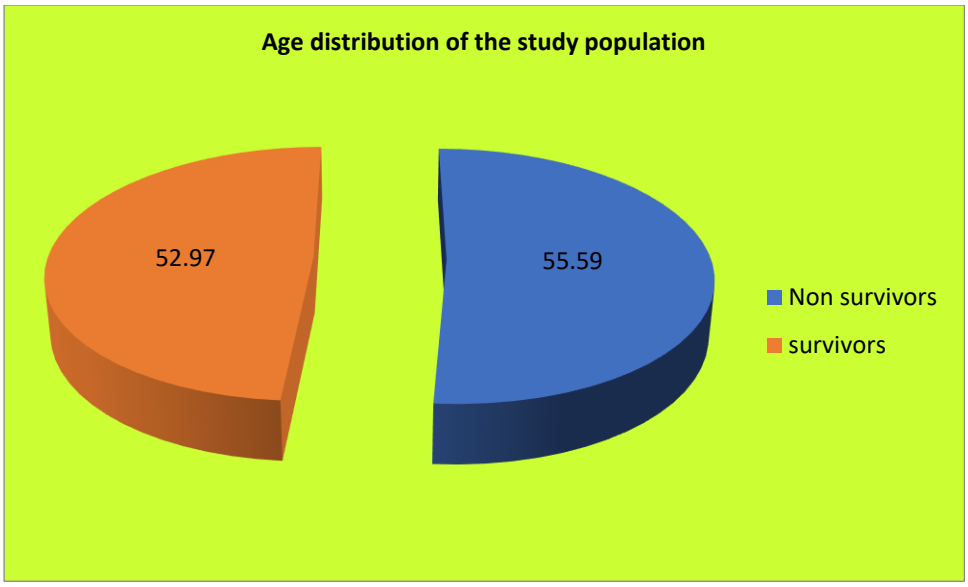
Unpaired student t test ; (* $p < 0.05$ shows statistically significant)



The serial serum albumin monitoring in a ICU patients with SEPSIS gives a significant prognostic values for early intervention and monitoring,correlate significantly with survivors rate,out of 100 patients 68 were survived and 32 were not survived.serial serum Albumin on day 1 mean value 3.91,day 3 mean value 3.53,day 5 with mean value 3.37,day 7 with mean value 3.47 except day 1 all other serial monitoring albumin value statistically significant shows p value <0.05.

In a study by NIRMALA et al marginally higher serum Albumin was found in survivor Vs Nonsurvivor on Day 1(3.46 Vs 3.44),but the difference was statistically not significant.

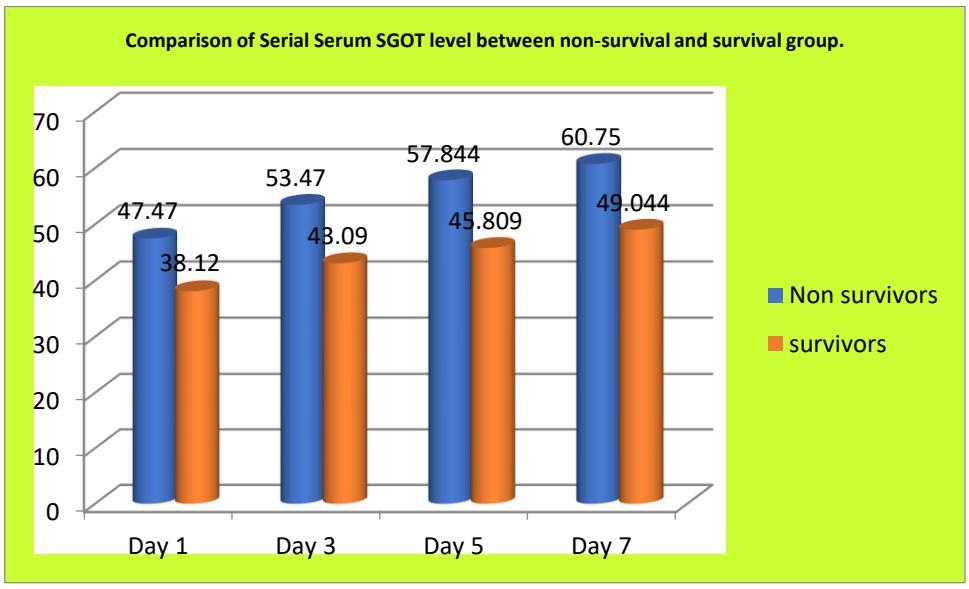
MEAN AGE DISTRIBUTION OF STUDY POPULATIONS



Out of 100 patients 68 patients(mean value 55.59) were survived and 32(mean value 52.97) patients were Nonsurvived. Age wise distribution is not correlate statistically significant(p value 0.359).

Comparison of Serial Serum SGOT level between non-survival and survival group.

	Non survivors N=32			Survivors N=68			
SGOT	**Mean**	**Std. Deviation**	**Std. Error Mean**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**p value**
Day 1	47.47	14.458	2.556	38.12	11.619	1.409	0.001*
Day 3	53.47	15.005	2.653	43.09	11.023	1.337	0.001*
Day 5	57.844	17.0561	3.0151	45.809	12.1474	1.4731	0.001*
Day 7	60.75	17.1727	3.0357	49.044	14.3864	1.7446	0.001*

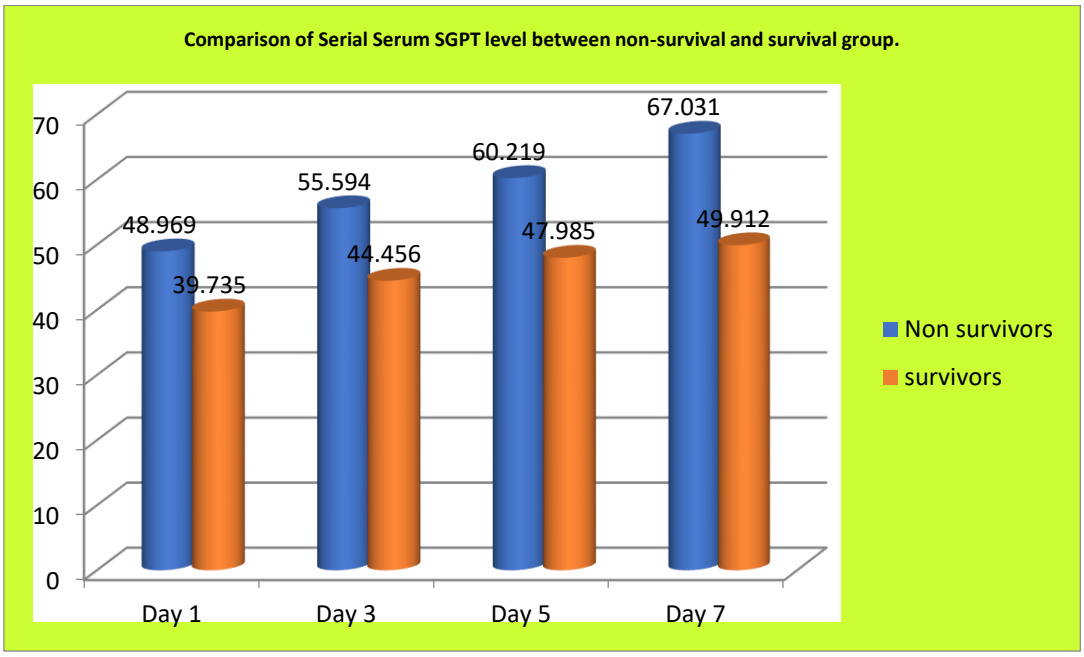


Serial SGOT comparison is correlate well with the SURVIVOR populations and positive prediction of NON SURVIVOR and it was correlate statistically significant with p value <0.05.

Comparison of Serial Serum SGPT level between non-survival and survival group.

	Non survivors N=32			Survivors N=68			
SGPT	**Mean**	**Std. Deviation**	**Std. Error Mean**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**p value**
Day 1	48.969	12.757	2.2551	39.735	11.1135	1.3477	0.001*
Day 3	55.594	13.476	2.3823	44.456	10.9836	1.332	0.001*
Day 5	60.219	15.3302	2.71	47.985	12.8278	1.5556	0.001*
Day 7	67.031	18.9064	3.3422	49.912	14.4973	1.7581	0.001*

Unpaired student t test; (* p< 0.05 shows statistically significant)

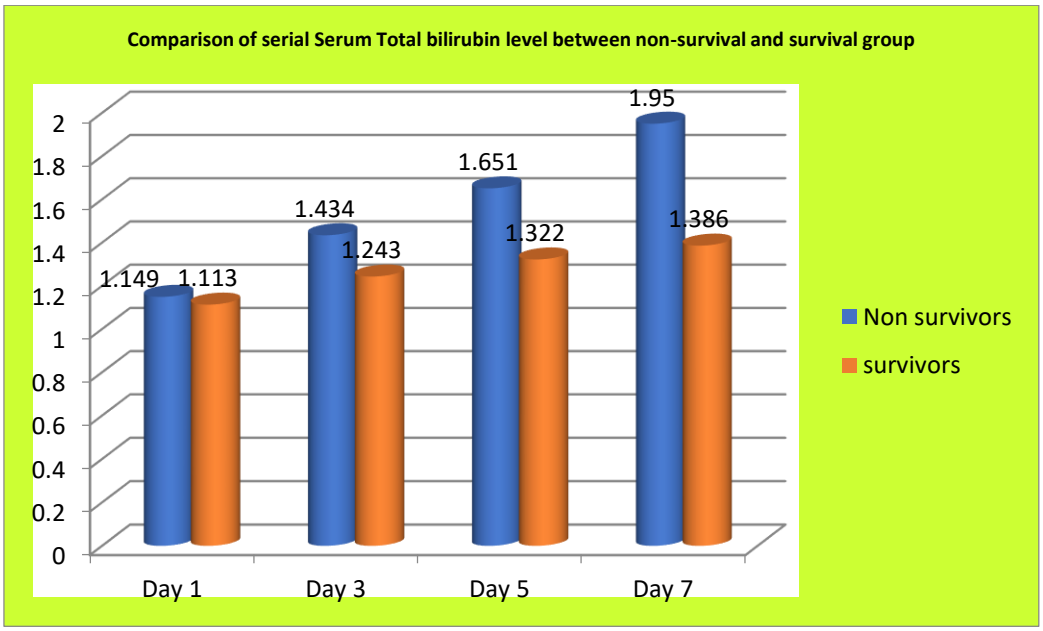


Serial SGPT comparison is correlate well with the SURVIVOR populations and positive prediction of NON SURVIVOR and it was correlate statistically significant with p value <0.05.

Comparison of Serial Serum Total bilirubin level between non-survival and survival group.

	Non survivors N=32			Survivors N=68			
Total bilirubin	**Mean**	**Std. Deviation**	**Std. Error Mean**	**Mean**	**Std. Deviation**	**Std. Error Mean**	**p value**
Day 1	1.149	0.2173	0.0384	1.113	0.2418	0.0293	0.477
Day 3	1.434	0.3454	0.0611	1.243	0.2952	0.0358	0.005*
Day 5	1.651	0.4225	0.0747	1.322	0.3622	0.0439	0.001*
Day 7	1.95	0.5417	0.0958	1.386	0.4606	0.0559	0.001*

Unpaired student t test; (* p< 0.05 shows statistically significant)

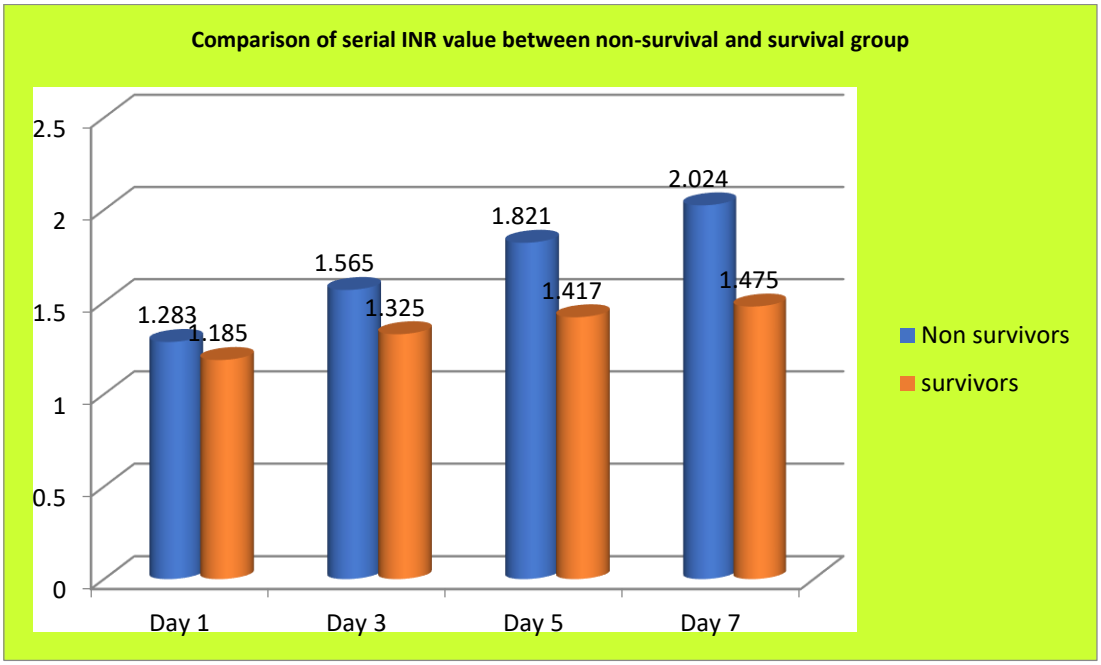


Total bilirubin monitoring on Day 1 is not correlate statistically significant but further serial monitoring of Bilirubin on Day 3,5,7 correlate statistically significant with p value<0.05.

Comparison of INR value between non-survival and survival group.

INR	Non survivors N=32			Survivors N=68			p value
	Mean	Std. Deviation	Std. Error Mean	Mean	Std. Deviation	Std. Error Mean	
Day 1	1.283	0.3825	0.0676	1.185	0.3314	0.0402	0.192
Day 3	1.565	0.3828	0.0677	1.325	0.4109	0.0498	0.006*
Day 5	1.821	0.4236	0.0749	1.417	0.491	0.0595	0.001*
Day 7	2.024	0.5128	0.0907	1.475	0.6122	0.0742	0.001*

Unpaired student t test; (* p< 0.05 shows statistically significant)



INR monitoring on Day 1 is not correlate statistically significant but further serial monitoring of INR on Day 3,5,7 correlate statistically significant with p value<0.05.

Comparison of categorical variables among Non survivors and survivors group

variables	Non survivors N(%)	Survivors N(%)	p value
Male	18 (53.1%)	33 (48.5%)	
Female	15 (46.8%)	31 (45.6%)	0.482
Hospital stay (< 7 days)	4 (12.5%)	35 (51.4%)	0.001*
Hospital stay (>7 days)	28 (87.5%)	31 (45.6%)	
No Ionotropes	0 (0%)	36 (52.9%)	
Ionotropes	32 (100%)	32 (47.1%)	0.001*
Not ventilated	12 (37.5%)	63 (92.6%)	
Mechanical ventilation	20 (62.5%)	5 (7.4%)	0.001*

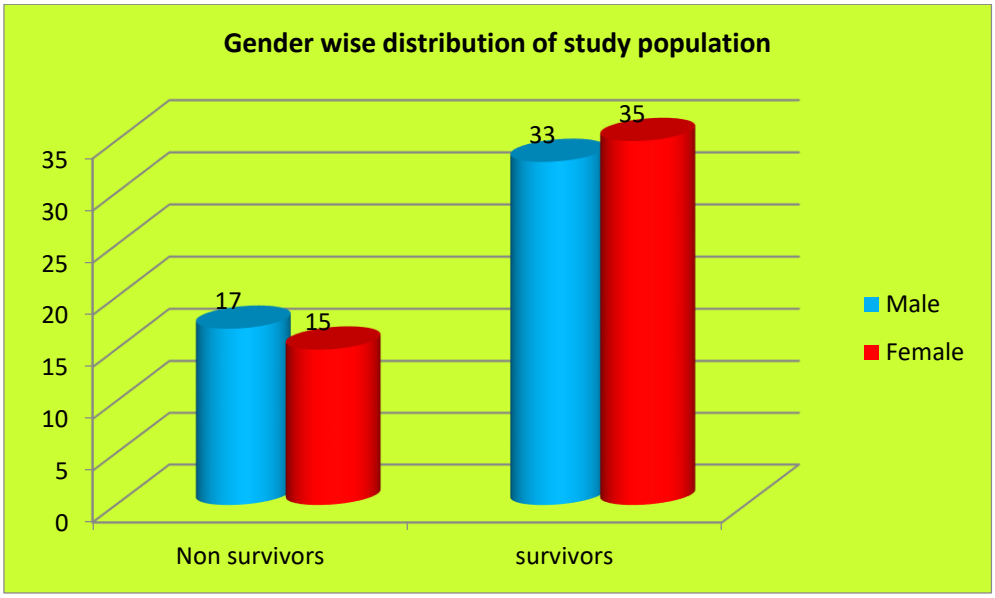
Fisher's Exact Test; (* p< 0.05 shows statistically significant)

Sex wise distribution is not significantly correlated,but Duration of hospital,Ionotropes support,Mechanical ventilation needed all are stastistically correlate with serial monitoring of SERUM ALBUMIN&OTHER LIVER PARAMETERS.

In a study by Santhosh et al,Serum Albumin in survivor having complication and with prolonged hospital stay>21days was significantly low ($p<0.05$)

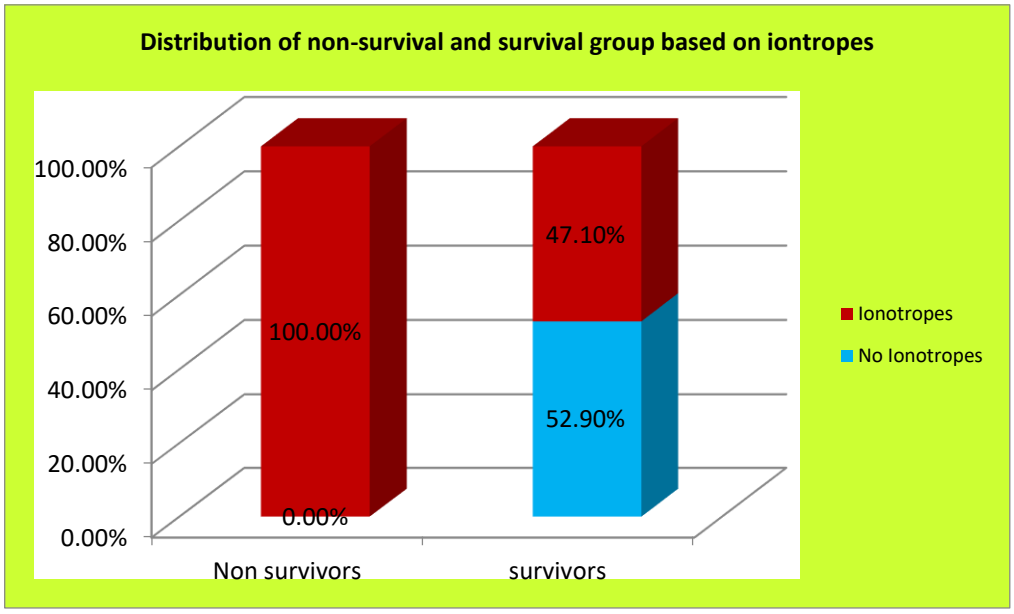
Dubois et al cocluded that hypoalbuminemia was a potent dose dependent.,independent predictor of poor outcomes in term of mortality,morbidity.,and duration of hospital stay.

Santosh et al.,reported that serum Albumin in survivor with ventilator requirement was significantly very low.



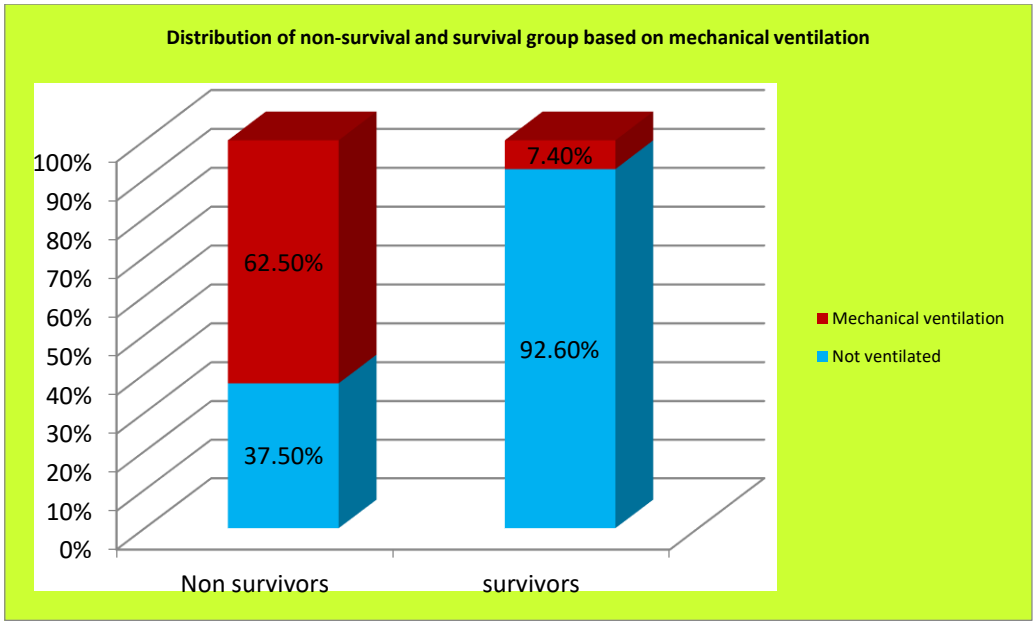
Out of 100 population among NON SURVIVOR 15 are female,17 are male and in SURVIVOR 35 were female,33 were male.

DISTRIBUTION OF STUDY POPULATIONS BASED ON IONOTROPES REQUIREMENT.



100% of NON SURVIVORS required ionotropes,among SURVIVOR 52.90% not required ionotropes,47.10% required ionotropes support.

DISTRIBUTION OF STUDY POPULATIONS BASED ON MECHANICAL VENTILATION REQUIREMENT.



DISTRIBUTION OF STUDY POPULATIONS BASED ON CO-MORBIDITY

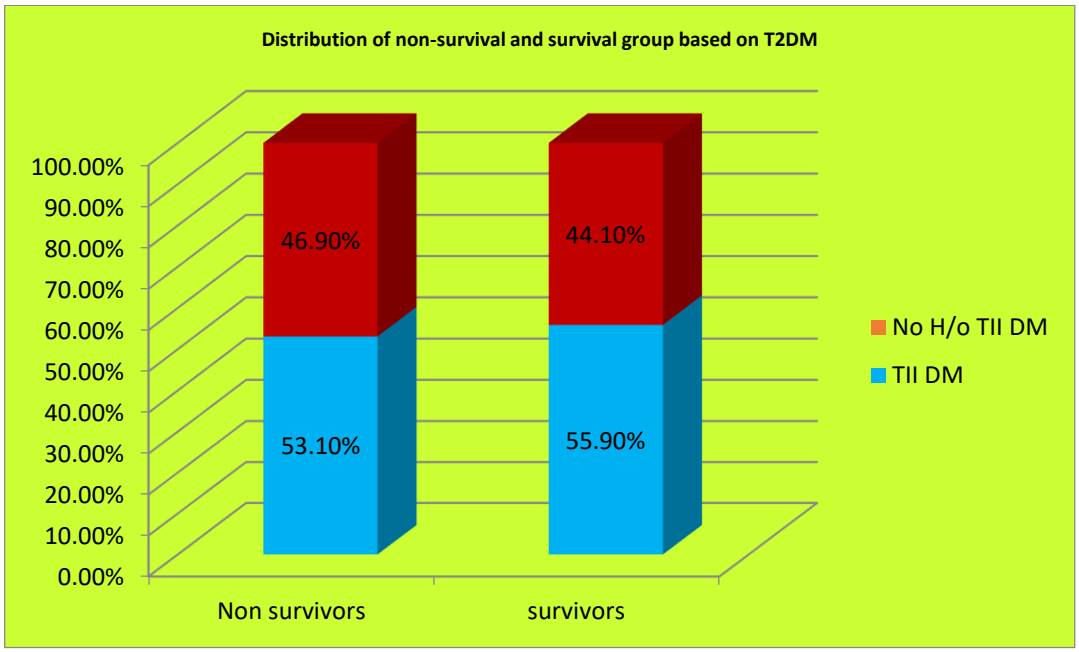


Table showing the need of mechanical ventilator support and serial serum albumin

	Mechanical Ventilation not required (N=75)		Mechanical Ventilation required (N= 25)		
	Mean	**Std. Deviation**	**Mean**	**Std. Deviation**	**p value**
Serum albumin					
Day 1	3.8736	0.55891	3.66	0.512348	0.095
Day 3	3.502667	0.473621	3.188	0.492714	0.008*
Day 5	3.309333	0.504084	2.904	0.417812	0.001*
Day 7	3.356	0.620863	2.68	0.594418	0.001*

Unpaired student t test ; (* p< 0.05 shows statistically significant)

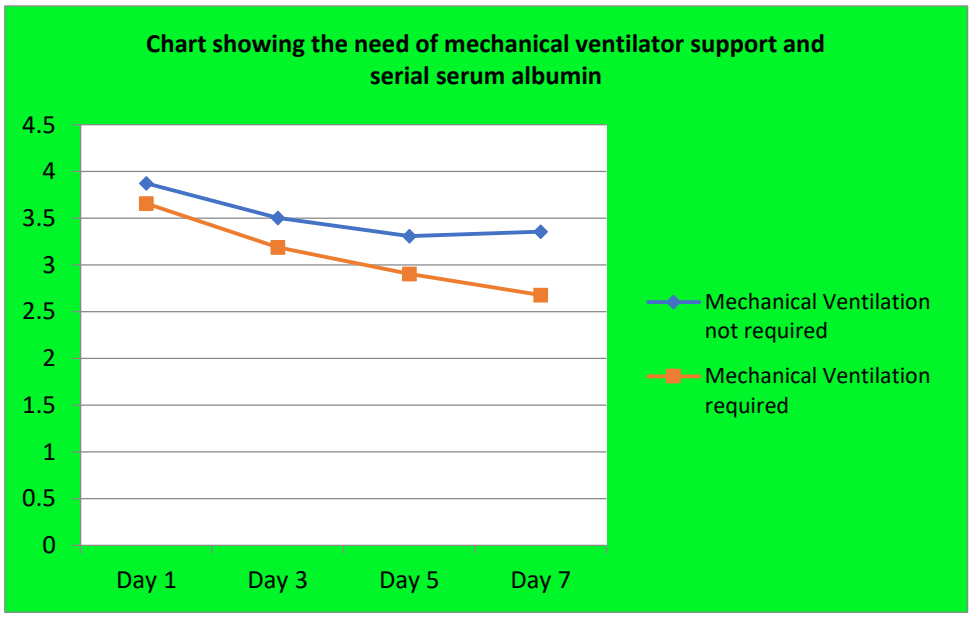


Table showing the need of mechanical ventilator support and serial serum SGOT

SGOT	Mechanical Ventilation not required (N=75)		Mechanical Ventilation required (N= 25)		
	Mean	Std. Deviation	Mean	Std. Deviation	p value
Day 1	38.18667	11.71935	49.88	13.995	0.001*
Day 3	43.56	11.65986	54.96	14.38888	0.001*
Day 5	46.48	12.68683	59.2	17.21434	0.002*
Day 7	49.12	13.61335	63.8	18.52476	0.001*

Unpaired student t test ; (* $p < 0.05$ shows statistically significant)

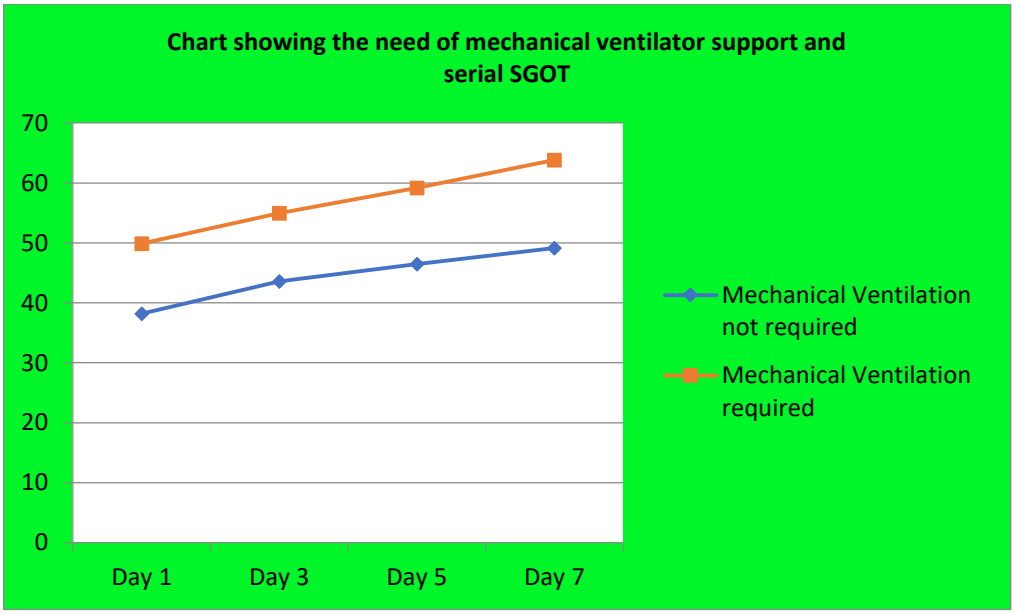


Table showing the need of mechanical ventilator support and serial SGPT

SGPT	Mechanical Ventilation not required (N=75)		Mechanical Ventilation required (N= 25)		
	Mean	Std. Deviation	Mean	Std. Deviation	p value
Day 1	39.56	10.25254	52.08	13.62877	0.001*
Day 3	44.89333	10.19085	57.4	15.53759	0.001*
Day 5	48.70667	12.04583	61.48	17.99333	0.002*
Day 7	51.70667	15.39197	66.44	20.3492	0.001*

Unpaired student t test ; (* p< 0.05 shows statistically significant)

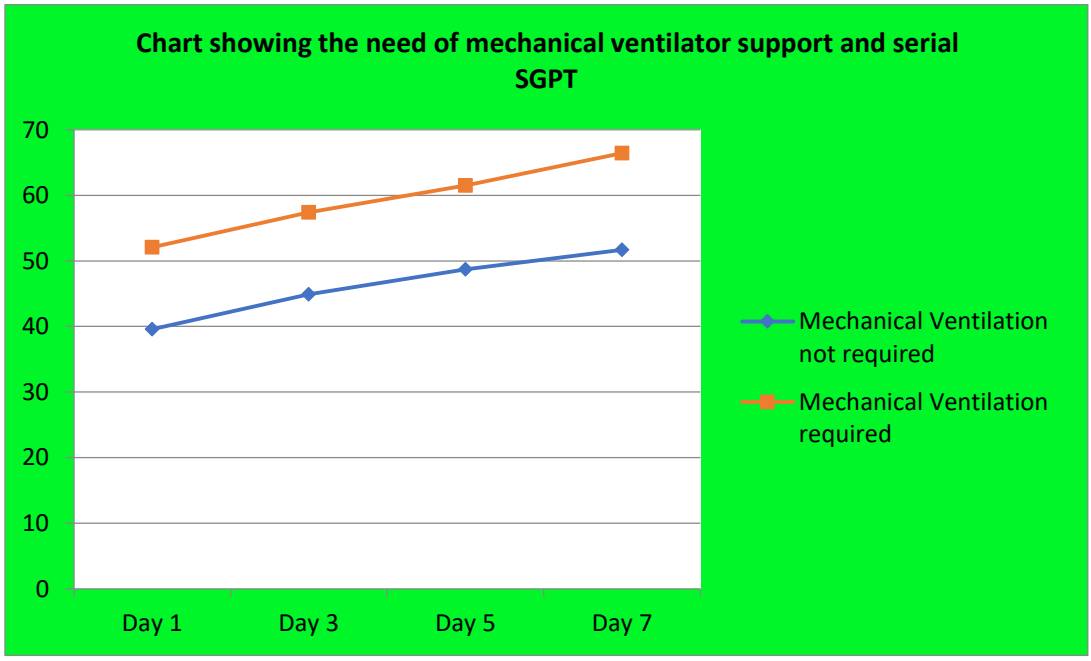


Table showing the need of mechanical ventilator support and serial total bilirubin

Total bilirubin	Mechanical Ventilation not required (N=75)		Mechanical Ventilation required (N= 25)		
	Mean	Std. Deviation	Mean	Std. Deviation	p value
Day 1	1.102667	0.225397	1.1908	0.250398	0.103
Day 3	1.2588	0.285581	1.44	0.391578	0.041
Day 5	1.3716	0.361394	1.5928	0.503947	0.051
Day 7	1.4556	0.488891	1.8996	0.606771	0.002*

Unpaired student t test ; (* p< 0.05 shows statistically significant)

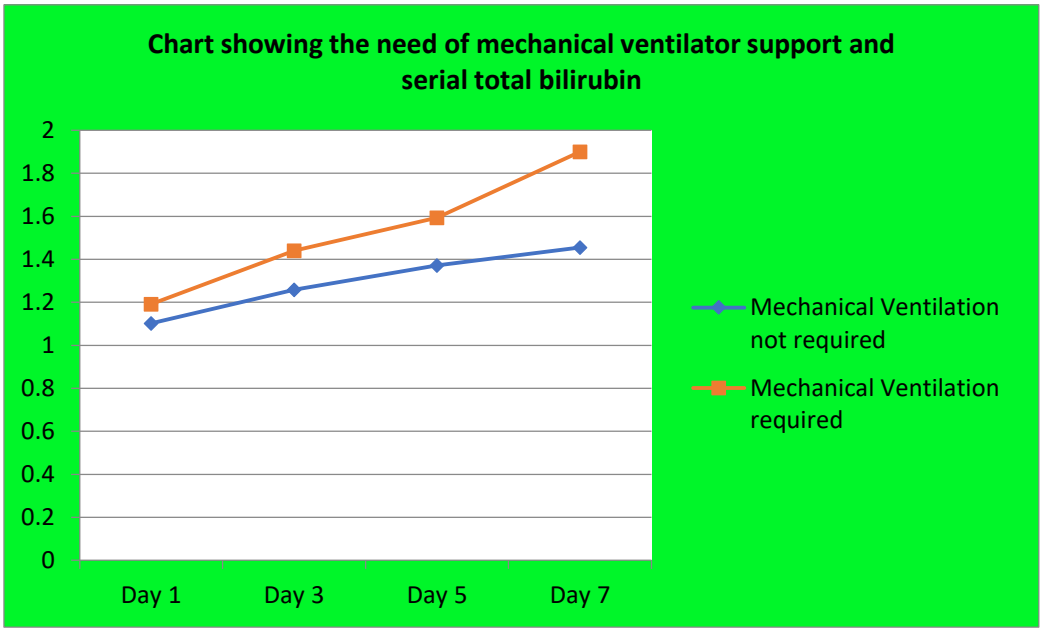
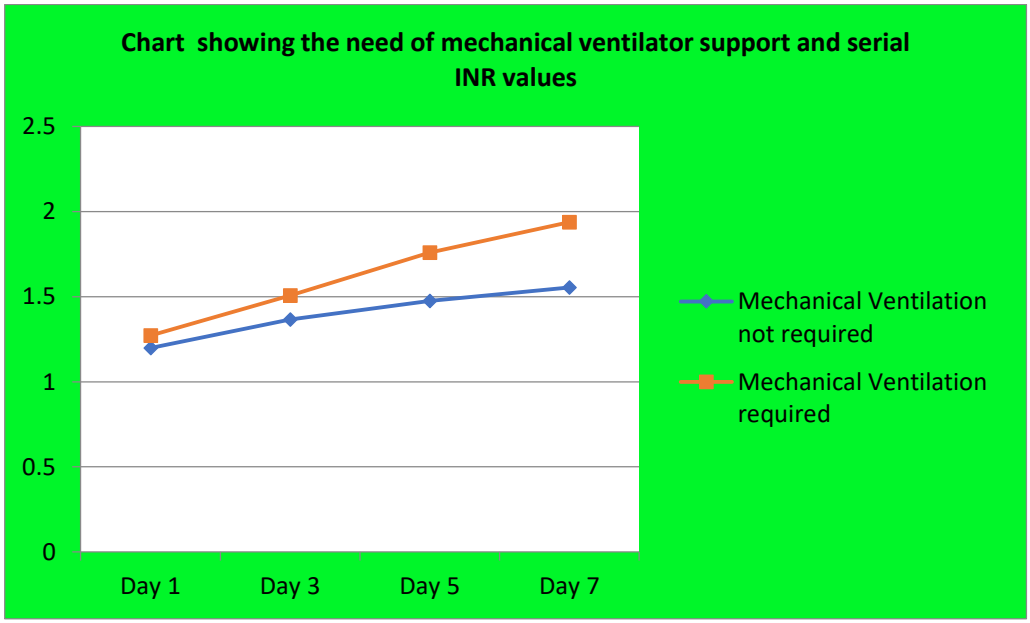


Table showing the need of mechanical ventilator support and serial INR values

INR	Mechanical Ventilation not required (N=75)		Mechanical Ventilation required (N= 25)		
	Mean	Std. Deviation	Mean	Std. Deviation	p value
Day 1	1.198	0.31862	1.2716	0.432557	0.365
Day 3	1.366267	0.395791	1.5076	0.463081	0.142
Day 5	1.475067	0.478738	1.7592	0.532454	0.014*
Day 7	1.554933	0.614398	1.9392	0.616238	0.008*

Unpaired student t test ; (* p< 0.05 shows statistically significant)



Logistic regression for independent factor in mortality

Variable	Beta coefficient	S.E.	Wald	Odds ratio	95.0% C.I.for odds ratio		P value
					Lower	Upper	
Serum albumin	4.01	1.487	7.272	55.123	2.99	101.6	0.007*
SGOT	0.084	0.045	3.544	1.088	0.997	1.187	0.06*
SGPT	-0.111	0.047	5.479	0.895	0.816	0.982	0.019*
Total bilirubin	-0.741	1.217	0.37	0.477	0.044	5.182	0.543
INR	1.318	1.278	1.065	3.738	0.306	45.725	0.302
Mechanical Ventilation	-3.014	1.038	8.436	0.049	0.006	0.375	0.004*

CI=confidence intervals. p<0.1 significant on univariate analysis were included in the model. *P<0.05 significant on binomial logistic regression

Table shows results of univariate and bivariate logistic regression analyses comparing patients for predictor factor in mortality. The overall logistic regression model was statistically significant (x^2 = 84.5, p = 0.001*), indicating that the predictor variables included in the model together differentiate between subjects in a reliable manner regarding mortality.

Discussion

DISCUSSION

1. MORTALITY

Serial serum Albumin and other liver parameters like SGOT,SGPT,INR,TOTAL BILIRUBIN monitoring on Day 1,3,5,7 significantely correlate with the mortality of study population .initial fall in above mentioned parameters with gradual increase in value have a statisticaly significant correlation.meanwhile gradual fall in above mentioned parameters values have a worst prognosis.out of 100 study populations 68 were SURVIVED and 32 were NON-SURVIVED.

2. IONOTROPES REQUIREMENTS:

Out of 100 study populations 32(47.1%) survivor required ionotropes support and 32(100%) Non-survivor required ionotropes support.so,it is clear cut showing that serial Albumin and other liver paramaters monitoring have a strong clinically significant correlation with the requirement of ionotropes.

3. HOSPITAL STAY:

Out of 100 study populations 31(45.6%) survivor ,28(87.5%)Non-survivor are stayed more than 7days.so,with reduced Albumin level and increased OT,PT,INR,TOTAL BILIRUBIN levels having more hospital stays.

In a study by SANTOSH et al.,serum Albumin in survivor having complications and with prolonged stay(>21days)was significantely low.

DUBOIS et al .,concluded that hypoalbuminaemia was potent dose dependent predictor of poor outcomes in terms of mortality,morbidityand prolongation of hospital stay.

4. VENTILATOR REQUIREMENT:

Out of 100 study populations 5(7.4%)of survivor ,20(62.5%)of Non-survivor were required ventilator support.its implied that that serial Albumin and other liver paramaters monitoring have a strong clinically and statisticaly significant correlation with the requirement of mechanical ventilator.

SUMMARY

Sepsis has very high morbidity and mortality, which leads to major healthcare burden in the worldwide.Though there is far advancement in the intensive therapeutic options, the mortality rate remains high due to the delay in the diagnosis because of lack of availability of reliable diagnostic methods. There is significant improvement in the outcome of the patients in early goal directed therapy in severe sepsis and septic shock.Serum albumin is a NEGATIVE ACUTE PHASE REACTANT its concentrations changes in response to inflammation.liver parameters also influenced by sepsis by many direct and indirect mechanisms as we discussed in detailed in review of literature.Hence,Serial monitoring of serum Albumin and other liver parameters have a significant outcome with assessing sepsis patients mortality,morbidity,durations of hospital stay,ionotropes requirement,mechanical ventilations requirements.

This study was conducted at GOVT.RAJAJI MEDICAL COLLEGE,MADURAI.,to highlight that Serial Serum Albumin and other Liver parameters monitoring as a prognostic marker in patient with sepsis. After getting approval from ethical committee 100 patients who are presented with features of SIRS and suspicious of infections which leads to sepsis were selected after fulfilling the exclusion criteria.Serum sample

collected from the patient on Day 1,3,5,7 for measuring SERUM ALBUMIN,SGOT,SGPT,TOTAL BILIRUBIN,INR.

1) Totally 100 patients were included in the study the mean age group of patients were 53.81+SD13.26.
2) Out of 100 patients 52 patients were male and 46 patients were females.
3) Mortality in this study was 32 patients out of 100 study populations.mortality was more among female patients in this study than male patients and age was an independent predictors of mortality.
4) Mean Serum albumin value on Day 1,3,5,7 are 3.82,3.4,3.2,3.1 respectively.
5) SGOT mean values on Day 1,3,5,7 are41.11,46.41,49.66,52.79 respectively.
6) SGPT mean values on Day 1,3,5,7 are 42.69,48.02,51.90,55.39 respectively.
7) Total Bilirubin mean values on Day 1,3,5,7 are 1.12,1.30.1.42,1.56 respectively.
8) INR mean values on Day 1,3,5,7 are 1.2,1.4,1.5,1.6 respectively.

Limitation

LIMITATIONS OF STUDY

- Need more informations about durations of hospital stay,mechanical ventilator support,ionotropes support.
- Immunocompromised state like PLHA,CANCER patients on chemotherapy are not excluded.

Conclusion

CONCLUSION

- Serial Albumin level and other Liver parameters estimations might be one of the major factor determining the outcomes of Sepsis.
- Serum albumin measured in all sepsis patients but serial monitoring provides idea in the prognosis of the patients.
- Sepsis patients have high mortality rates.Early recognition of such patients can prompt more aggressive management to improve their survival.
- Mortality, morbidity, durations of hospital stay, mechanical ventilation,ionotropes requirements are statistically significant with serial monitoring of Serum Albumin and other liver parameters levels.
- In resource limited settings as ours a good,efficient and cost effective indicators are required to predicts the risk of mortality and morbidity.In such clinical situations simple serum Albumin and other liver parameters are serves as an indicator of overall clinical status in patients with sepsis.

Annexure

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PROFORMA

Name:

Age / Sex:

Occupation:

Presenting complaints:

Past History:

H/o DM, HT, CKD, CVD, DRUG INTAKE, Thyroid disorders, Alcohol intake

Clinical Examination:

General Examination:

Consciousness

Orientation

Pallor

Clubbing

Lymphadenopathy

Hydration status

Febrile

Signs of External Markers of Tuberculosis

Vitals:

PR

BP

RR

SpO2

Temperature

Systemic examination:

CVS:

RS:

ABDOMEN:

CNS:

Laboratory investigations:

Complete Blood count and ESR

Serial Liver function Test

Renal function Test

Serial serum Albumin

Blood c&s

Urine c&s

Chest X ray

Electrocardiogram

ஆராய்ச்சி ஒப்புதல் படிவம்

பெயர்: தேதி:

வயது: நோயாளி எண்:

ஆராய்ச்சி சேர்க்கை எண்:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு விளக்கபட்டது.

எனக்கு விளக்கபட்ட விஷயங்களை நான் புரிந்து கொண்டு எனது முழுமனதுடன் சம்மதிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில்தான் பங்குபெறுகிறேன் மற்றும் நான் இந்த ஆராய்ச்சியில் இருந்து எந்த நேரமும் பின்வாங்கலாம் என்றும் அதனால் எந்தபாதிப்பும் எனக்கு ஏற்படாது என்பதையும் புரிந்து கொண்டேன்.

நான் என்னுடைய சுயநினைவுடன் மற்றும் முழு சுதந்திரத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் பங்குகொள்ள சம்மதிக்கிறேன்.

Anti Plagiarism Certificate

CERTIFICATE - II

This is to certify that this dissertation work titled **"SERIAL SERUM ALBUMIN &OTHER LIVER PARAMETERS MONITORING AS A PROGNOSTIC MARKER IN PATIENTS WITH SEPSIS"** of the candidate **Dr.JAI GANESH K** with registration Number **201711107** for the award of **M.D.,** in the branch of **GENERAL MEDICINE.** I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **8** percentage of plagiarism in the dissertation.

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Ethical Committee Approval Letter

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Name of the Candidate	:	Dr.K.Jai Ganesh
Course	:	PG in MD., General Medicine
Course of Study	:	2017-2020
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	Serial serum albumin & other liver parameters monitoring as a prognostic marker in patient with sepsis.
Ethical Committee as on	:	29.10.2018

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

Member Secretary Chairman Dean / Convenor

Prof Dr V Nagaraajan
M.D., MNAMS, D.M., Dsc.,(Neuro), Dsc (Hon)
CHAIRMAN
Madurai Medical College
Madurai

DEAN
Madurai Medical College
Madurai-20

31 OCT 2018

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AGE	SEX	Sr.ALBUMIN DAY 1	DAY 3	DAY 5	DAY 7	OT 1	3	5	7	PT DAY 1	3	5	7	TB DAY 1	3	5	7	INR DAY 1	3	5	7	T2DM	MECHANICAL VENTILATION	IONOTROPES	SURVIVOR/ NONSURVIVOR	HOSPITAL STAY <7 (Or)>7 DAYS
32	M	3.2	3	2.8	3.1	32	36	31	36	43	45	46	48	0.8	0.6	0.7	0.8	1	1.1	1.3	1.1	Y	N	N	S	<7
44	M	4.1	3.1	2.6	2.2	50	52	41	40	58	52	42	46	1.3	1.1	1	0.9	1.6	1.4	1.2	1.1	Y	Y	Y	NS	>7
47	M	5	4.6	4.2	4.4	44	42	48	46	50	44	42	41	1.1	1	0.9	1.2	1.2	1.4	1.6	1.2	N	Y	N	S	>
38	F	3.6	2.3	2.5	2	69	66	50	52	51	59	66	60	1.5	1.4	1.6	2	1.9	1.8	2	1.8	N	Y	Y	NS	>
46	M	3.8	3.1	3	2.8	42	41	40	46	58	54	60	66	1	0.9	1.1	1.6	1.4	1.6	1.8	2	N	Y	Y	NS	<
51	F	3.6	3.2	3	2.6	60	64	70	72	68	78	88	80	1.6	1.6	2	2.2	2.2	2.8	3.2	3.5	N	Y	Y	S	>
52	F	2.8	2.6	2.6	2.4	68	64	62	60	58	52	54	54	1.2	1.4	1.2	1.6	2.6	2.4	2.8	2	Y	Y	Y	NS	>
48	F	3.6	2.4	2.8	3	62	64	70	74	64	66	70	80	1.6	1.4	1.6	2	2.1	2.3	2.6	2.8	N	N	N	S	>
55	M	4	3.6	3.4	3.2	68	64	54	48	48	42	44	40	1.2	1.4	1.6	1.4	1.8	2	2.4	2.6	N	N	Y	S	>
48	M	3.8	3.6	3.2	3	42	49	55	56	41	46	50	58	1	1.1	1.6	1.7	1.7	1.9	2	2	N	N	Y	S	>
41	M	3.6	3.2	2.6	2	59	63	66	70	52	60	64	68	0.8	1.2	1.4	2	1.4	1.7	1.8	2.3	N	Y	Y	NS	>
52	M	3	2.8	2.9	2.6	44	42	48	49	41	42	46	47	1	1	1.1	1.2	1.01	1.2	1.6	2	Y	Y	Y	NS	<
55	M	3.4	3.2	3	2.8	50	52	54	58	50	58	64	66	1	1.3	1.6	1.8	1.4	1.8	2	2.4	N	N	Y	NS	<
60	M	4.12	4	3.8	3.6	42	44	46	48	50	52	54	60	1.2	1.1	1.6	1.8	1.04	1.08	1.2	1.6	Y	N	N	S	<
57	F	3.6	3	2.9	2.8	56	66	68	73	60	64	62	70	1	1.3	1.6	2	1.6	1.8	2	2.2	N	N	Y	NS	<
61	M	5	4.2	4.4	4.8	52	48	42	44	56	54	54	52	1	0.8	0.7	0.9	1.04	1.05	1.04	1.02	N	N	N	S	<
70	M	3.7	3.4	3.6	4	44	43	40	39	41	41	40	42	0.9	0.8	0.8	0.9	1.01	1.04	1.06	1.08	Y	N	Y	S	<
62	M	3.9	3.4	3.2	4	38	39	38	42	39	39	41	42	0.9	0.9	0.7	1	1	0.9	1.01	1	N	Y	N	S	>
18	M	4	3.5	3.01	3.04	52	55	59	60	54	54	57	59	1.1	1.2	1	1.2	1.01	1	1.01	1	Y	Y	Y	S	>
29	M	3.8	3.6	3	2.9	48	53	56	60	58	68	69	77	1.07	2	2.02	2.09	1.08	2	2.06	2.08	Y	Y	Y	NS	>
39	F	3.2	2.6	2.4	2.9	65	73	88	96	60	63	88	100	1.9	2.02	2.04	2	2.04	2.01	2.08	3	Y	N	Y	S	>
49	F	4	3.5	3	2.8	33	32	47	48	38	47	54	65	1	1.09	1.4	1.6	1.09	2	2.02	2.06	N	N	Y	NS	>
62	F	3.5	3.5	3.3	2.9	67	76	78	98	43	65	76	87	1.2	1.4	1.6	1.7	2.4	2.6	2.8	3	N	N	Y	S	<
46	F	4.3	4	3.8	3.4	34	38	43	48	39	38	42	49	0.9	1	0.8	1	0.9	0.8	1	1	Y	N	N	S	<
60	F	3.2	3.1	2.7	2.5	42	48	51	52	36	39	40	41	0.9	1	1.04	1.07	1	1.04	1.05	1.1	Y	N	Y	S	>

57	F	3.8	3.4	3.4	3.7	49	46	42	40	55	54	50	47	0.8	1	1.09	1.1	1	1.03	1.04	1.9	N	N	Y	S	<
55	M	3.2	3	3.2	3.6	65	66	58	52	68	61	58	54	1	1.1	1	1	0.9	1	1.09	1.08	N	N	N	S	<
53	M	3.8	3.6	3.6	3.9	40	48	46	42	50	52	47	44	0.7	0.9	1	0.8	0.7	0.9	1	0.9	N	N	N	S	<
52	M	4.2	4	3.6	3	48	52	55	60	40	46	54	66	0.9	1	1.1	1.4	0.9	1	1.4	1.6	Y	N	Y	NS	>
52	M	3.8	3.6	2.8	2.4	59	72	76	88	50	66	76	98	1.3	1.6	1.8	2	1.8	2	2.2	2.4	N	N	Y	NS	>
56	F	3.6	3.3	3	2.8	46	56	66	78	41	49	52	59	1	1.2	1.3	1.7	1	1.4	1.9	2	Y	Y	Y	NS	>
60	F	3.4	2.9	2.7	2.5	75	80	98	43	56	60	66	79	1	1.2	1.4	2	1.8	2	2.5	3	Y	N	Y	NS	>
61	F	3.7	3.2	3.1	3.6	49	53	54	47	47	58	56	46	1.1	1.6	1.2	1	1.04	1.2	1.5	1.05	Y	N	N	S	<
62	M	3.9	3.6	3.1	2.9	48	59	60	68	46	78	90	100	1.1	1.6	2.2	2.8	1.09	2	2.4	3.03	N	N	Y	NS	>
66	M	4	3.4	3	2.9	60	76	88	92	74	82	89	100	1.4	2	2.4	3	1.4	2	2.1	2.6	N	Y	Y	NS	>
50	M	3	2.7	2.2	2	76	82	90	94	88	90	95	105	1.2	1.9	2.2	2.6	1.09	1.5	2	2.6	Y	Y	Y	NS	>
53	F	3.4	3.1	2.7	2.3	55	59	64	70	51	59	64	68	1.1	1.5	1.9	2.1	1	1.09	1.2	1.6	N	Y	Y	NS	>
49	F	3.8	3.2	2.8	3.3	44	49	54	60	38	46	53	47	1.4	1.2	1.1	1	1	1.1	1	1.3	N	N	N	S	<
40	F	3.6	3.8	4	3.8	22	28	30	32	29	36	39	41	0.8	1	0.9	1.1	1	1.02	1.05	1.2	Y	N	N	S	<
39	F	5	4.2	3.6	3	36	53	69	80	41	59	67	89	1.1	1.8	2.1	2.6	1	1.2	1.6	2	Y	Y	Y	NS	>
39	F	5.2	4.6	4	3.4	29	33	41	60	33	49	59	60	1	1.6	1.8	2	1.1	1.5	1.9	2	Y	N	Y	S	>
37	M	5.4	4.2	3.6	3	29	39	48	52	37	49	59	72	1.1	1.4	2	2.4	1.3	1.8	2	2.4	Y	N	Y	S	>
43	F	4.8	4	3.8	3.6	34	49	55	69	32	42	49	58	1.2	1.4	1.9	2	1.1	1.5	1.8	2	N	N	N	S	>
42	F	4.2	3.6	3.1	2.9	29	38	41	60	34	40	52	59	1	1.4	1.6	2.2	1.4	1.9	2	2.1	Y	N	Y	S	>
45	M	4.9	3.6	3.2	3,4	39	42	54	60	48	52	59	62	1.1	1.6	1.8	2	1.1	1.4	1.6	1.8	N	N	N	S	>
56	F	4	3.4	3	2.9	41	44	49	52	59	60	66	72	1.2	1.4	1.9	2.1	1.5	1.9	2	2.1	N	N	Y	NS	>
82	M	3.4	3	2.8	2.4	69	74	88	98	70	88	97	102	1.5	1.9	2	2.2	1.3	1.7	2	2.5	Y	Y	N	S	>
80	F	3.3	3	2.8	2.4	70	82	94	100	62	77	87	98	1.8	2.2	2.4	2.8	1.5	2	2.3	2.7	Y	Y	Y	NS	>
73	F	3.4	3.9	4.1	4.9	28	38	49	44	21	31	43	55	1.3	1.5	1.7	2.1	1.6	1.9	2	2.1	N	N	N	S	<
18	M	4.6	4.2	4	4.4	32	42	44	47	33	42	52	60	1.5	1.9	1.1	1	1.7	2	2.2	2.5	Y	N	N	S	<
52	M	3.4	3.2	2.8	3.3	22	34	41	59	29	34	45	54	0.9	1.1	1.6	1.8	0.9	1	1.1	1.3	N	N	Y	S	<
58	F	3.2	2.8	2.2	2	29	39	41	49	30	40	54	60	1.4	1.9	2	2.4	1	1.3	1.8	2.1	N	N	Y	NS	>
58	F	3.6	3.1	2.8	2.4	30	48	52	62	40	54	60	72	1	1.6	2	2.8	0.8	1.4	2	2.3	Y	Y	Y	NS	>
53	F	4.2	3.6	3.1	3.7	40	52	41	39	51	52	40	38	1.2	1.6	1.1	0.9	0.9	1.2	1.1	1	N	N	Y	S	>

57	M	4	3.3	3	3.8	29	34	48	58	38	42	50	41	0.8	1	1.2	1.6	0.9	1	1	1	N	N	Y	S	<
59	M	3.8	3.2	3	3.6	30	38	42	48	36	40	46	38	1	1.1	1.6	1	1	1.1	1.2	1	Y	N	N	S	<
60	M	4.2	3.6	3.2	3.8	32	38	40	40	32	38	42	49	1	1	1.2	1	1	1	1	1	N	N	N	S	<
61	F	3.6	3.2	3	3.4	30	49	40	36	34	46	50	40	1.2	1.4	1.6	1.8	1.2	1.5	1.5	1	Y	N	Y	S	<
62	F	3.8	3.5	3.2	2.8	28	35	40	38	37	40	42	42	1.3	1.5	2	1.8	1.3	1.5	1.8	1.5	Y	N	Y	NS	>
64	F	3.5	3.4	2.8	2.5	40	46	50	48	40	38	48	45	1.4	1.8	2	2.4	1.2	1.4	1.6	2	Y	N	Y	S	>
51	F	3.6	3.5	3.2	3	42	36	30	45	48	49	50	52	0.8	1.2	1.8	2	1.5	1.8	2	2	N	N	Y	S	>
53	F	3.2	2.8	2.5	2.2	40	48	50	52	48	50	50	48	1	1.5	1.6	1.8	1.4	1.8	2	2.2	Y	N	Y	NS	>
49	F	3	2.8	2.4	2	42	48	50	58	50	52	54	60	0.7	1.2	1.3	1.5	1.2	1.5	1.8	2	Y	N	Y	S	>
47	M	3.3	2.8	2.5	2.2	48	49	50	52	48	46	50	52	0.8	1.2	1.6	2	0.8	1.2	1.6	2	Y	Y	Y	NS	>
51	M	3.5	2.5	2.2	2	44	50	46	54	46	48	54	56	1.3	1.1	1.4	1.5	1.4	1.3	1.5	2.1	N	Y	Y	NS	>
61	M	3.4	2.6	2.5	2.8	36	46	52	54	48	44	56	48	1.2	1.4	1.6	1.6	1.2	1.4	1.8	2	Y	N	Y	S	>
67	M	3.2	3.6	3.8	4	22	34	44	46	28	32	34	40	1.2	1.4	1.4	1.6	1	1.1	1.2	1.4	N	N	N	S	<
81	F	3.2	3	2.8	2.6	29	37	43	46	30	38	41	46	1.2	1.1	1.4	1.5	1	1.2	1.2	1	Y	N	Y	S	>
80	M	3.3	3	2.9	2.5	52	62	69	72	54	59	62	72	1.4	1.9	2	2.4	1.2	1.5	2	2.2	N	Y	Y	NS	>
78	M	3.4	3.1	3	3.3	48	54	58	64	44	56	60	68	1.6	1.8	2	2.4	1.4	1.5	1.5	1.8	Y	N	Y	S	>
67	M	5	4.5	4.7	4.9	42	40	43	42	38	40	42	44	1.1	1.1	1	1	1	1	1	1	Y	N	N	S	<
66	F	4	3.6	3.4	3.9	32	43	38	38	29	34	30	30	1.2	1.1	1.1	0.9	1	1.2	1.2	1	N	N	Y	S	<
61	F	3.4	3	3.1	3.3	34	36	38	40	24	38	37	40	0.8	1	1.1	1	1.5	1.2	1	1	Y	N	N	S	>
60	F	3.3	3	2.9	3	28	30	32	40	42	54	38	48	0.9	1	1.2	1.1	1.2	1.4	1.2	1.4	N	N	Y	S	>
52	M	4.5	3.7	3.4	3.6	30	32	36	40	32	36	40	42	0.9	1	1.1	1.2	1.3	1.4	1.5	1.5	N	N	Y	S	>
22	F	5.5	4.7	4.2	4	28	32	36	35	27	30	34	38	0.9	1	1	1.1	1	1	1	1	Y	N	N	S	<
49	F	4.7	4.3	4	3.9	30	38	40	44	32	39	40	42	1.1	1.2	1.1	1.1	1.1	1.3	1.3	1	Y	N	Y	S	<
51	M	3.8	3.6	3.6	3.7	36	38	40	42	42	44	46	48	1.2	1.1	1.3	1	1.2	1.2	1	1	N	N	N	S	<
27	M	5	4.7	4.3	4.7	33	36	38	40	41	42	48	42	1.1	1.2	1.2	1.2	1.4	1.5	1.5	1.5	Y	N	N	S	<
54	F	4	3.7	3.6	3.4	31	35	36	38	29	32	33	36	1.3	1.4	1.4	1.3	1.2	1.2	1	1	N	N	Y	S	>
52	F	4.1	3.8	4	4.2	28	34	36	38	29	33	36	38	1.2	1.1	1.2	1.3	1.2	1.1	1.1	1.5	Y	N	N	S	<
50	M	3.8	3.7	3.6	3.9	28	30	30	33	29	31	35	37	1.1	1.2	1.2	1.1	1	1.3	1.3	1.1	Y	N	N	S	<
32	M	3.8	3.2	3	2.9	37	42	55	65	30	42	49	54	1.3	1.7	1.8	2	1.2	1.5	1.5	1.6	Y	N	Y	S	>

56	F	3.6	3.4	3.3	3.5	34	37	39	34	28	35	39	34	1.4	1.4	1.6	1.2	1.1	1.2	1	1.2	N	N	N	S	<
55	F	3.6	3.4	3.5	3.6	28	30	32	36	30	32	34	38	1.2	1.4	1.4	1.6	1.2	1.2	1.5	1.2	Y	N	N	S	<
54	F	3.8	3.6	3.6	3.6	36	38	42	44	36	38	36	36	1.4	1.4	1.3	1.2	1	1.1	1.2	1.3	Y	N	N	S	<
30	F	4	3.8	4	4.2	38	42	44	46	38	40	44	42	1.3	1.1	1.1	1.2	1.1	1	1	1	Y	N	N	S	<
58	M	4.2	3.8	3.8	3.8	33	39	42	44	29	38	41	44	0.9	1	1.1	0.9	1	1	1.2	1.2	N	N	N	S	<
57	M	4	3.5	3.2	2.8	28	32	36	38	32	38	37	42	1	1.1	1	1	1.1	1.1	1	0.9	Y	N	Y	NS	>
59	M	3.8	3.6	3.4	3.2	24	28	32	36	30	37	40	41	0.8	0.9	1	1	0.9	0.9	1	0.9	N	N	Y	S	>
63	M	3.4	3.2	3	2.9	32	43	44	48	38	40	42	43	0.9	0.9	1	1	0.8	0.8	1	1	Y	N	Y	S	>
42	F	3.6	3.4	3.3	3	28	32	36	34	40	42	44	41	0.9	0.9	1	1	0.9	1	0.9	1	Y	N	N	S	>
62	F	3.4	3.3	3.2	3.4	30	32	33	34	42	44	42	44	1	1.1	1.1	1.2	1	1	1	1.2	Y	N	N	S	<
63	M	4	3.8	3.6	3.8	28	32	34	39	29	32	40	42	1.1	1.2	1.2	1.4	0.9	1	1.2	1.1	Y	N	N	S	<
65	M	3.7	3.5	3.2	3	28	32	40	44	30	32	39	48	1.2	1.4	1.6	1.8	0.9	1	1.3	1.4	Y	Y	Y	NS	>
72	F	3.6	3.3	3	2.8	31	40	52	64	40	54	60	68	1.4	1.6	1.9	2	1	1.2	1.4	1.5	N	Y	Y	NS	>
37	F	4	3.6	3.4	3.2	37	42	46	39	43	50	55	63	1.2	1.4	1.1	1	1.1	1.2	1.4	1	Y	N	Y	S	>
78	F	3.3	3.1	3	3.3	43	47	49	44	38	37	34	34	1.4	1.6	1.4	1.3	1	1.2	1.3	1	Y	N	Y	S	<
56	M	3.9	3.6	3.4	3.2	40	48	48	59	22	36	43	48	1.1	1.2	1.2	1.1	1.2	1.5	1.5	1.3	N	N	N	S	<
87	M	3.6	3.4	3.2	3	28	30	34	38	30	36	32	32	1	1	1	1	1	1	1	1	Y	Y	Y	NS	>