"SEQUENTIAL ORGAN FAILURE ASSESSMENT SCORE(SOFA) AS A PROGNOSTIC MARKER IN PATIENTS WITH SEPSIS IN AN INTENSIVE CARE UNIT OF A TERTIARY HOSPITAL." – A ONE YEAR HOSPITAL BASED CROSS-SECTIONAL STUDY."

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ENDORSEMENT

This is to certify that the dissertation entitled **"SEQUENTIAL ORGAN FAILURE ASSESSMENT SCORE (SOFA) AS A PROGNOSTIC MARKER IN PATIENTS WITH SEPSIS IN AN INTENSIVE CARE UNIT OF A TERTIARY HOSPITAL." – A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"** is a bonafide research work done by **REG NO. BG0115001.**

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ABBREVITION:

%	Percentage
ARDS	Acute respiratory distress syndrome
BP	Blood pressure
BPM	Beats per minute
CKD	Chronic kidney disease
CLD	Chronic liver disease
COPD	Chronic obstructive pulmonary disease
CVA	Cerebrerovascular accident
DM	Diabetes mellitus
FIO2	Fraction of inspired oxygen
GCS	Glasgow coma scale
HTN	Hypertension
IHD	Ischemic heart disease
hr	Hour
MAP	Mean arterial pressure
MHD	Maintenance hemodialysis
OPP	Organophosphorus poisoning
PAO2	Partial pressure of oxygen
RR	Respiratory rate
SBP	Spontaneous bacterial peritonitis

SOFA	Sequential organ failure assessment score
TB	Tuberculosis
TEMP	Temperature
WBC	Whole blood count

ABSTRACT

Background and objectives

Sepsis with multiple organ dysfunction syndrome (MODS) is a common cause of Intensive Care Unit (ICU) mortality and morbidity. Early start of appropriate effective antimicrobial therapy is important for a favourable outcome in the patient with sepsis. Cultures and serology are available only after 24 to 48 hours. In the crucial hours the physician has to depend on clinical symptoms and laboratory parameters to aid in diagnosis and management. An efficient predictor of prognosis of sepsis is required to assess morbidity and mortality of this condition.

There are many scoring systems to determine and predict the mortality of sepsis, Such as **GLASGOW COMA SCALE, SAPS II, APACHE, SOFA** score. Currently available outcome prediction models such as the APACHE [Acute Physiology and Chronic Health Evaluation], SAPS [simplified acute physiology score], and MPM [mortality probability model's systems) calculate a prediction on values taken within the first 24 hours of an ICU stay.

In SOFA score, daily scoring of individual and composite scoring is possible. Higher sofa score is associated with worst outcome and also response of organ dysfunction to therapy can be followed over time. The Sequential Organ Failure Assessment score (SOFA score) is used to track a patient's status during the stay in an intensive care unit (ICU). The SOFA score is a scoring system to determine the extent of a person's organ dysfunction or rate of failure.[93] This score is based on six different parameters, one each for the respiratory, cardiovascular, hepatic, coagulation, renal and neurological systems.

The objectives of present study were to assess the predictive value of sofa score at 0 and 48 hours with outcome in sepsis patients with multiorgan dysfunction.

Methods

The present cross-sectional study was conducted on patients with Sepsis admitted in Intensive care unit of KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Belagavi from Jan 2016 to Dec 2016. Relevant data was collected by a detailed interview with patient or the attender, clinical examination, lab reports. Patient were enrolled as sepsis based on: Inflammatory response syndrome, and severe sepsis criteria as per American college of chest physicians and society of critical care medicine. They were then scored according to the SOFA score at admission and after 48 hours. These findings were noted on a predesigned and pretested proforma.The comparison of categorical data was done using Chi-square test or Fisher's exact test. Continuous data was compared using independent sample't' test. In case of more than two means one-way ANOVA was used to compare the data. ROC analysis was also done to predict the sensitivity and specificity of score. A probability value ('p' value) of less than or equal to 0.05 was considered as statistically significant.

Results:

We enrolled 130 subjects in our study, out of which 86 were males and 44 were females. We observed that 40% subjects in our study were in the age group of 40-59 years. Diabetes (60%) and hypertension (40.77%) were the most common co morbidity and pneumonia (26.15%) and urosepsis (19.23%) were the leading cause of sepsis in our study group. We also observed in our study that, the mean sofa score for 0 hours (admission) for survivors was 5.39 and non-survivor was 10.85 whereas at 48 hours the mean sofa score for survivor was 4.16 and non-survivor was 12.83 respectively.

We also observed that patient with mean sofa score at admission of 2.95 had a stay of less than 7 days, with 5.69 had a stay of 8-15 days and those with 7.5 had a stay of above 15 days. At a mean score of 10 there was eventual mortality, while a mean score of 14.8 had worst outcome in the form of mortality within 24 hours of admission., Similarly cases with mean sofa score of 1.26 at 48 hours had a stay of less than 7 days, with 4.69 had a stay of 8-15 days and those above 8.20 had a stay of above 15 days. Patients with a score of 12.83 had mortality.

On plotting ROC curve, we observed that the optimum cut off value for SOFA score for predicting mortality both at 0 and 48 hours was 7.5. The sensitivity and specificity to predict mortality at 0 hours was 87.8% and 75.3% respectively while at 48 hours sensitivity was 100% and specificity was 83.1%. The AUC obtained for ROC curve was 0.920 and 0.971 at admission and 48 hours respectively, suggesting SOFA score at 48 hours as a better predictive index for outcome.

Conclusion

In our study population, Diabetes and hypertension were the most common co morbidity, pneumonia and urosepsis were the leading cause of sepsis.There was a higher percentage of mortality and longer duration of stay with increasing SOFA scores.

Through statistical analysis we reached to a cut off value of 7.5 for predicting the outcome of patients. The sensitivity and specificity of score at 0 hours was found 87.8% and 75.3% while for 48 hours was 100% and specificity was 83.1%, thus 48 hours score was more specific and sensitive for prediction of outcome. Similarly, we found that AUC for 0 hours and 48 hours was 0.920 and 0.971 respectively, thus score at 48 hours was better predictor as compared to score at admission.

Keywords: SEPSIS, SOFA SCORE, MORTALITY, APACHE, SAPSII, ICU.

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INTRODUCTION

Sepsis is a syndrome clinically defined as the body's systemic inflammatory response to infection.[1] severe sepsis and septic shock are the end results of the body's maladaptive and inappropriate response to pathogenic microbes, resulting in organ dysfunction, tissue hypo perfusion and dysoxia, and ultimately death.[2]The concept of sepsis syndrome originated during the time of Hippocrates. But it was not until the nineteenth century when Sir William Osler recognized that "except on few occasions, the patient appears to die from the body's response to infection rather than to the infection" (Hodgkin, 2008). During a long period of time great confusion existed as to the description of systemic inflammatory response to infection, and several terms were used interchangeably: septicemia, sepsis, sepsis syndrome and septic shock. In clinical practice sepsis is the most confusing term used to describe the body's systemic response to infection, and to many clinicians' sepsis implies a life-threatening state. Finally, in 1992, the American College of Chest Physicians and the Society of Critical Care Medicine Consensus Conference outlined definitions of Systemic Inflammatory Response Syndrome (SIRS), sepsis, severe sepsis and septic shock in an effort to standardize the classification of host responses to infection.[3]

Despite continued advances in medicine and technology, the incidence of sepsis is increasing. The incidence of severe sepsis and septic shock has increased over past 30 years and annual number of cases now is greater than 7, 50,000(~ 3 per 1000 population). Severe sepsis is a contributing factor in >200,000 deaths per year in the United States, approximately two thirds of the cases occur in patients with significant underlying illness. Sepsis is the leading cause of death in U.S. hospitals.[4]62% of people hospitalized with sepsis are re-hospitalized within 30

days.[5]As many as 92% of sepsis cases originate in the community[6]. Mortality from sepsis increases 8% for every hour that treatment is delayed[7]. As many as 80% of sepsis deaths could be prevented with rapid diagnosis and treatment[8]. Sepsis affects over 26 million people worldwide each year and is the largest killer of children – more than 5 million each year. [9] • More than 1.6 million people in the U.S. are diagnosed with sepsis each year – one every 20 seconds and the incidence is rising 8% every year. [10,11] • 258,000 people die from sepsis every year in the U.S. – one every 2 minutes; more than from prostate cancer, breast cancer and AIDS combined. [12,13] • More than 42,000 children develop severe sepsis each year and 4,400 of these children die, more than from pediatric cancers. [14] • Sepsis causes at least 75,000 maternal deaths every year worldwide and is driving rise in pregnancy-related deaths in the U.S.[14,15] • Every day, 38 sepsis patients require amputations[16] • Sepsis survivors have a shortened life expectancy, are more likely to suffer from an impaired quality of life, and are 42% more likely to commit suicide. [17,18]

The incidence of sepsis is found to be greater at the extremes of age, occurring in 5.3/1000 patients under 12 months of age and 26.2/1000 patients aged 65 years or older.[19] Age-related alterations in the host immune system affect an individual's response to an infectious challenge.[20]Older individuals have been found to exhibit dysregulation in Toll-like receptor (TLR) trafficking, deficits in dendritic cell function secondary to decreased numbers and/or decreased receptor signaling, an increased proportion of naive B cells, signaling deficits in the T-cell receptor CD3 complex, increased numbers of inhibitory receptors and changes in cytokine signaling.[21]

Tissue dysoxia, is defined as limited metabolic energy production due to a lack of oxygen supply or utilization, which clinically manifests as shock.[22] In the background of sepsis, this form of shock is typically distributive in nature, and results in a relative hypovolemia secondary to systemic vascular dilation and increased capillary permeability and leakage. This further leads to a decrease in oxygen uptake and utilization and results in organ failure, tissue necrosis, and lacticacidosis.[23] Alterations in cardiac output (CO), oxygen carrying capacity (i.e.: anemia), and oxyhemoglobin saturation (i.e.: hypoxemia) together leads to decrease oxygen uptake in the tissue.[24]

Sepsis is a complex syndrome that is difficult to define, diagnose and treat. From clinical studies sepsis can be seen as a continuum of severity that begins with an infection, followed in some cases by sepsis, severe sepsis – with organ dysfunction – and septic shock. There has been a substantial increase in the incidence of sepsis during the last decades, and it appears to be rising over time, with an increasing number of deaths occurring despite a decline in overall in-hospital mortality (Bone, 1992)[25]. Advanced age, underlying co morbidities and number of organ dysfunction are factors which are consistently associated with higher mortality in severe sepsis and septic shock. This makes sepsis as a major cause of mortality and morbidity throughout the world. Mortality rates with severe sepsis and septic shock range from 25% to over 75%, with higher rates of death in patients with multi–organ dysfunction and prolonged hypoperfusion.[1] Severe sepsis and septic shock account for greater than 17% of all in hospital deaths and is the eleventh leading cause of death in the United States.[26]

The management of sepsis is closely related to the availability of relevant equipment and efficacy of clinical and serological indices, and ICU based scoring systems which is used as a guide for the prognostication and effective treatment goals. The development of cost effective and easily attainable clinical parameters that would effectively prognosticate the outcome of sepsis patients would be invaluable within an emergency department setting. Availability of such parameters would result in optimized triaging, risk stratification and also contribute to accurate identification of intensive care unit candidates amongst severely ill patients, at a fraction of the cost.

Lack of clinical diagnostic criteria, high cost, and no availability of isolation techniques result in misdiagnosis, treatment failure, and improper utilization of resources.[27]Etiology remains unestablished during the first crucial 24-48 h. Various scoring systems such as Glasgow scale, APACHE II and III and sequential organ failure assessment (SOFA) scoring have been validated and are being used in predicting prognosis of patients admitted in intensive care unit (ICU).

The European Society of Intensive Care Medicine organized a consensus meeting in Paris in October 1994 to create a so-called Sepsis-related Organ Failure Assessment (SOFA) score,[27] to describe quantitatively and as objectively as possible the degree of organ dysfunction over time in groups of patients or even in individual patients. Six organ dysfunctions were assessed using initial SOFA score and graded from 0 to 4. There are two major applications of such a SOFA score: To improve our understanding of the natural history of organ dysfunction and to assess the effects of new therapies on the course of organ dysfunction. This could be used to characterize patients at entry or to evaluate the effects of treatment.[27]

Simplified Acute Physiology Score (SAPS) was introduced in France in 1984 which included 13 variables and age. Later in 1993, it was modified to SAPS II[28] which was calculated as the sum of points assigned to each of the 17 variables (12 physiological variables, age, type of admission, and three underlying diseases). Previously used scores such as SAPS, Acute Physiology Age Chronic Health Evaluation (APACHE)[29] did not focus on the severity of MOD. They could only estimate prognosis and compare results among Intensive Care Units (ICU's). The physiological parameters in these scores were affected by treatment. These scores did not guide decisions regarding therapeutic interventions. Serial evaluation of therapy-related improvement could not be done using these scores.

The evaluation of organ dysfunction should be based on a limited number of simple but objective variables that are easily and routinely measured in every institution. The collection of this information should not impose any intervention beyond what is routinely performed in every ICU. This prompted us to study the prognostic value of sequential organ failure assessment score at admission and after 48 hours of admission and also to correlate the value of mean sofa score with the outcome in critically ill patients in icu care of our tertiary hospital.

OBJECTIVE

To assess the prognosis in patients with sepsis and multi organ dysfunction at presentation and after 48 hours using sequential organ failure assessment score.

REVIEW OF LITERATURE

Historical note

Sepsis has been a condition which is hard to recognize and diagnose. Marcus Terentius Varro the ancient Roman scholar and writer (116 BC–27 BC), was quoted as noting that "small creatures, invisible to the eye, fill the atmosphere and when breathed through the nose cause dangerous diseases". Perhaps the most perceptive description of sepsis was by the historian, philosopher, humanist and Renaissance author Niccolo Machiavelli (1469–1527), as reported in his treatise, *The Prince*, in 1513 Early in the book, he very articulately stated that, "hectic fever, at its inception, is difficult to recognize but easy to treat; left unattended it becomes simple to recognize and difficult to treat." [30] Though hectic fever is not the term by which we know sepsis currently, the description of an ailment that is difficult to identify in its beginning stages, at a time when the condition may be responsive to treatment, and more difficult to treat in its later more apparent phases is a distinct depiction of the more severe forms of sepsis.[30]

A wide variety of definitions for sepsis were made trying to comprehend sepsis. Among the first ideas was to think of sepsis as a systemic host response to an infection[31]

In fact, it was classically described by the eminent American physician William Osler (1849–1919) in his pivotal observation that "the patient appears to die from the body's response to an infection rather than from the infection itself".[30] Closer to the modern era, in 1972 this concept was fortified in a medical review, noting that "it is our response that makes the disease".[31]

The broad idea has long been considered a form of poisoning, often termed as blood poisoning, but moreover suggesting the presence of pathogenic organisms or their toxins in the tissues or blood. It was the non-success of these medical definitions, and multiple futile attempts towards developing diagnostic tools and assays to recognize sepsis, that led to a consensus for conference, focusing on a way to clinically define sepsis.[31]

Definition

In 1992, the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) jointly published the consensus definitions of sepsis.[3]In 2001, an International Sepsis Definition Conference[32] was sponsored by the Society of Critical Care Medicine (SCCM), the European Society of Intensive Care Medicine (ESICM), the American College of Chest Physicians (ACCP), the American Thoracic Society (ATS), and the Surgical Infection Society (SIS) to revisit the 1992 sepsis guidelines.[3] Based on this conference a consensus document was developed, concluding that there was not enough evidence to support a change to the previous definitions.[32]

<u>"Systemic inflammatory response syndrome</u>

- Body temperature < 36°C or > 38°C
- Heart rate > 90 beats per minute
- Respiratory rate
    - > 20 breaths per minute or,
    - An arterial partial pressure of carbon dioxide <4.3 kPa (32 mmHg)

- White blood cell count
    - < 4000 cells/mm^3 (4 x 109 cells/L) or
    - > 12,000 cells/mm^3 (12 x 109 cells/L), or
    - The presence of > 10% immature neutrophil band forms..."

"Sepsis

- SIRS that has a proven or suspected microbial etiology

Severe sepsis

- Fulfilling at least ≥ 2 of SIRS criteria.
- Associated or suspected source of infection
- One or more of the following
    - Evidence of end organ damage
        - Elevated creatinine levels, > 120 μmol/L or
        - Altered mental status, GCS < 14
        - Platelet count <80,000/L or 50% decrease in platelet count from highest value recorded over previous 3 days
    - Serum lactate levels of ≥ 4mg/dL
    - Episode of hypotension (<90/60 mmHg), which responds to initial fluid resuscitation.

Septic shock

- Fulfilling at least ≥ 2 or more of SIRS criteria
- Associated or suspected source of infection
- Persistent hypotension (<90/60 mmHg) which does not respond to adequate fluid resuscitation."[3]

MODS[32]

- "Dysfunction of more than one organ, requiring intervention to maintain homeostasis."
- These are among the most frequently quoted definitions in critical care and they have become second nature to many critical care physicians (intensivists) and other intensive care providers all over the world. Their novel explanation of the SIRS criteria and specific definitions for sepsis, severe sepsis, septic shock and multiple organ dysfunction syndrome were all critical developments in the field of sepsis.[30]
- Since these consensus definitions had limitations in clinical use, they were revisited in 2001[3,30]

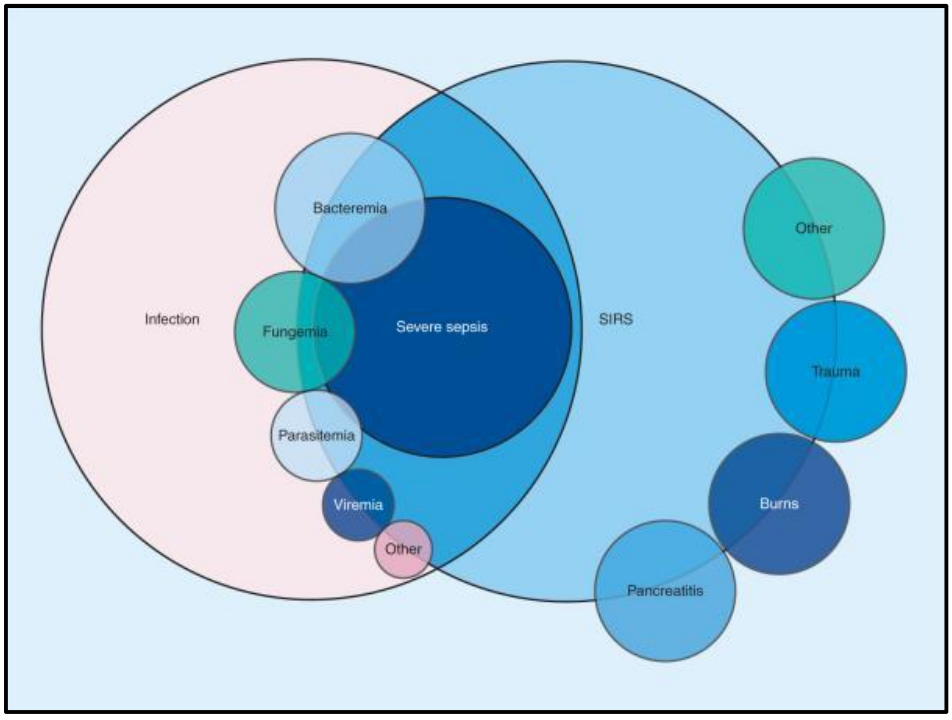


Figure 1.SIRS: Systemic inflammatory response syndrome[30]

Even though there were many fallacies recognized of the current definitions, there was no better alternative identified. There was considerable consideration to expanding the foundational `systemic inflammatory response syndrome' criteria to include other parameters that may be associated with sepsis. However, these represented an enhancement of the potential diagnostic criteria that would, if anything, make the sepsis definition less specific than it was previously. In addition, some of the criteria coincided with the definitions developed for identifying organ dysfunction, which is a critical component of distinguishing severe sepsis and septic shock. Perhaps the most important result from the 2001 Consensus Conference was the proposal for a `Predisposition, Infection, Response and Organ dysfunction' (PIRO) system for staging sepsis. The concept of PIRO was similar to staging cancer or other medical conditions, and it appears that these criteria do allow for differentiating groups of patients with sepsis.[33]

Epidemiology

Worldwide

The worldwide stated prevalence of severe sepsis in hospital per 100 admissions during the previous decade was between 2.6 to 12.4. The prevalence of severe sepsis in ICUs per 100 ICU admissions ranges between 11 to as high as 30.[34]

A two-decade study of US hospitalizations recognized an increase in the incidence of sepsis among hospitalized patients by 8.7% per year.[27] at present, it is evaluated that there are more than 1,000,000 cases of sepsis among hospitalized patients each year in the USA. Numerous reports have shown the incidence of sepsis

and severe sepsis risings in additional of the growth of the population. Similar reports exist from the UK, Australia and from Croatia.[30]

The incidences of sepsis, severe sepsis and septic shock are less well-described in the developing world.[40] There are more data obtainable on the incidence of infectious diseases, which remains a constant battle for which there are many high incidence conditions. As infectious diseases are certainly the cause of sepsis, sepsis presumably is of parallel or even greater significance in these areas of the world than in the most developed nations. The responsible organisms for sepsis are more likely to be Gram-negative enteric pathogens and atypical pathogens.[41]

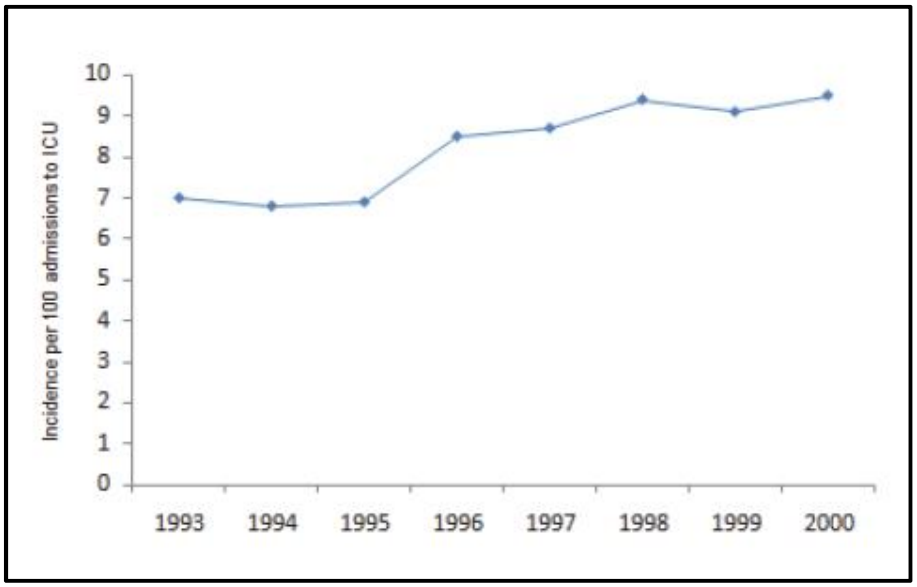


Figure 2. Incidence of septic shock. Data collected over an 8-year period from 22 hospitals[35]

Annual incidence of sepsis is stated to be 20-300/100,000 population with a mortality rate ranging between 30% and 80%.[36, 37]

The incidence of sepsis is affected by multiple patient-specific factors. It has been long accepted that age is an important component of someone's risk for

developing sepsis. The incidence of sepsis is greatest at the extremes of age, occurring in 5.3/1000 patients under 12 months of age and 26.2/1000 patients aged 65 years or older[20]

More recently it has been acknowledged that race, ethnicity and gender may also contribute to the differential risk for developing sepsis.[30]

The risk factors also include variety of co morbid medical conditions. Most obvious are conditions like HIV, cancer, diabetes and in patients on steroids, each of which may modify the immune system. These conditions result in a significantly elevated risk for developing sepsis, and may also increase the risk of nosocomial sepsis given these individuals recurrent interactions with healthcare systems.[41]

Indian scenario

No conclusive data on the incidence of sepsis in India is available.[7] Though, a multicenter, prospective, observational study was organized in four intensive therapy units (ITUs) in India from June 2006 to June 2009 to determine the incidence of severe sepsis among 5,478 ITU admissions. SIRS with organ dysfunction was found in 1,385 (25%) patients, of which 731 (52.77%) were due to sepsis. The incidence of severe sepsis was 16.45% of all admissions. Mean age of the study population was 58.17 years (SD 18.66), of which 57.71% were male.[42]

Clinical features

The clinical manifestations of sepsis are exceedingly variable, depending on the initial site of infection, the causative organism, the pattern of acute organ dysfunction, the underlying health status of the patient, and the interval before start of the treatment. The signs of both infection and organ dysfunction may be elusive, and

thus the most recent international consensus guidelines provide a long list of warning signs of incipient sepsis.

Acute organ dysfunction most commonly affects the respiratory and cardiovascular systems. Respiratory derangement is classically manifested as the acute respiratory distress syndrome (ARDS), which is defined as hypoxemia with bilateral infiltrates of no cardiac origin.[43, 44] cardiovascular compromises is manifested primarily as hypotension or a raised serum lactate level. After adequate volume expansion, hypotension frequently persists, requiring the use of vasopressors[1]

The brain and kidneys are also often affected. Central nervous system dysfunction is classically manifested as obtundation or delirium. Imaging studies generally show no focal lesions, and findings on electroencephalography are usually consistent with non-focal encephalopathy. Critical illness polyneuropathy and myopathy are also common, especially in patients with a continued ICU stay. Acute kidney injury is manifested as decreasing urine output and an increasing serum creatinine level and frequently requires treatment with renal-replacement therapy. Paralytic ileus, elevated aminotransferase levels, altered glycemic control, thrombocytopenia and disseminated intravascular coagulation, adrenal dysfunction, and the euthyroid sick syndrome are all common in patients with severe sepsis[43]

Pathophysiology

Host Response

As the concept of the host theory emerged, it was first expected that the clinical features of sepsis were the result of overly exuberant inflammation. Later, Bone et al.[35] advanced the idea that the initial inflammatory response gave way to a subsequent "compensatory anti-inflammatory response syndrome." However, it has become clear that infection triggers a much more complex, variable, and prolonged

host response, in which both proinflammatory and anti-inflammatory mechanisms can add to clearance of infection and tissue recovery on the one hand, and organ injury and secondary infections on the other[45]

The specific response in any patient rest on the causative pathogen (load and virulence) and the host (genetic characteristics and coexisting illnesses), with differential responses at local, regional, and systemic levels. The composition and direction of the host response possibly change over time in parallel with the clinical course. In general, proinflammatory reactions (directed at eliminating invading pathogens) are thought to be accountable for collateral tissue damage in severe sepsis, whereas anti-inflammatory responses (important for limiting local and systemic tissue injury) are implicated in the greater susceptibility to secondary infections.

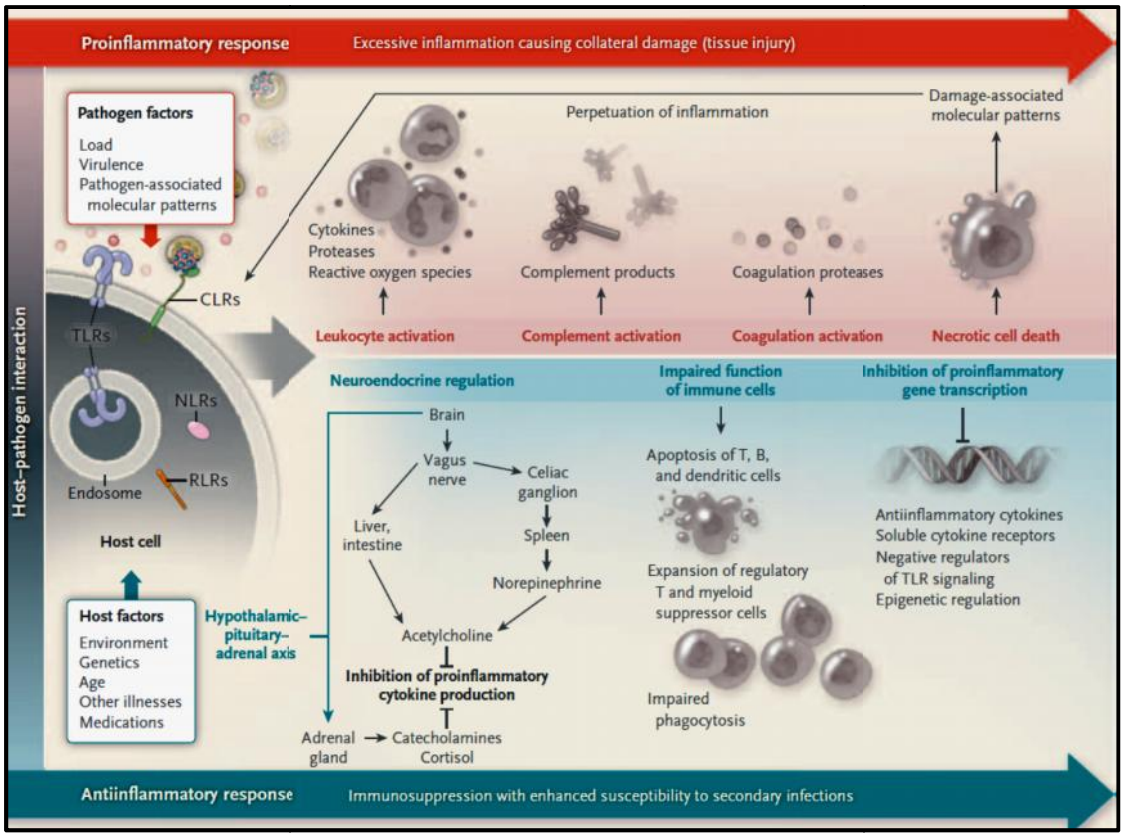


Figure 3. The Host Response in Severe Sepsis[43]

Innate Immunity

Knowledge of pathogen recognition has increased enormously in the past decade. Pathogens activate immune cells through a communication with pattern-recognition receptors, of which four main classes — toll-like receptors, C-type lectin receptors, retinoic acid inducible gene 1–like receptors, and nucleotide-binding oligomerization domain–like receptors — have been recognized, with the last group partially acting in protein complexes called inflammasomes.[37]

These receptors recognize structures that are preserved among microbial species, so-called pathogen-associated molecular patterns, resulting in the up-regulation of inflammatory gene transcription and beginning of innate immunity. The same receptors also sense endogenous molecules freed from injured cells, so-called damage-associated molecular patterns, or alarmins, such as high-mobility group protein B1, S100 proteins, and extracellular RNA, DNA, and histones. Alarmins are also released during sterile injury such as trauma, giving upsurge to the concept that the pathogenesis of multiple organ failure in sepsis is not essentially different from that in noninfectious critical illness.[46]

Coagulation Abnormalities

Severe sepsis is almost invariably associated with different coagulation, frequently leading to disseminated intravascular coagulation.[47] Excess fibrin deposition is driven by coagulation through the action of tissue factor, a transmembrane glycoprotein expressed by various cell types, by impaired anticoagulant mechanisms, including the protein C system and ant thrombin and by negotiated fibrin removal owing to depression of the fibrinolytic system.

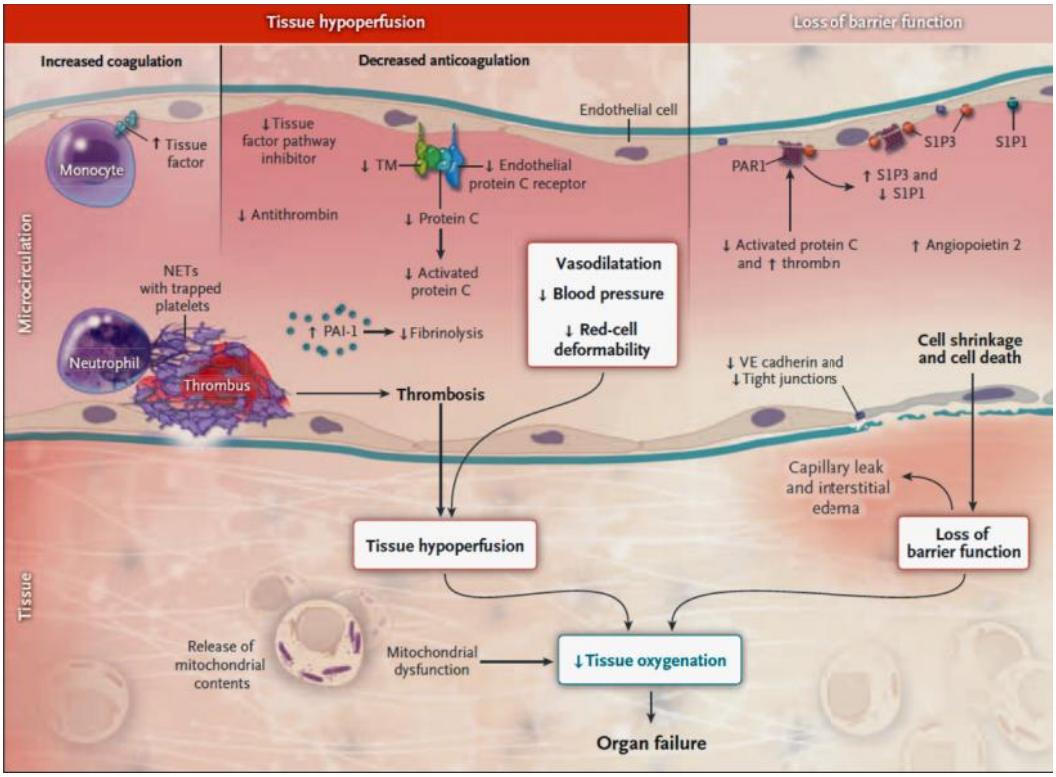


Figure 4. Organ Failure in Severe Sepsis and Dysfunction of the Vascular Endothelium and Mitochondria[47]

Protease-activated receptors (PARs) form the molecular link between coagulation and inflammation. Among the four subtypes that have been known, PAR1 in particular is associated in sepsis.[47] PAR1 exerts cyto-protective effects when stimulated by activated protein C or low-dose thrombin but applies disruptive effects on endothelial-cell barrier function when activated by high-dose thrombin. The protective effect of activated protein C in animal models of sepsis is reliant on its capacity to activate PAR1 and not on its anticoagulant properties.[48]

Anti-inflammatory Mechanisms and Immunosuppression

The immune system harbors humoral, cellular, and neural mechanisms that attenuate the potentially injurious effects of the proinflammatory response.[45]

Phagocytes can switch to an anti-inflammatory phenotype that promotes tissue repair, and regulatory T cells and myeloid-derived suppressor cells additionally reduce inflammation. In addition, neural mechanisms can inhibit inflammation.[49]

In the so-called neuroinflammatory reflex, sensory input is transmitted through the afferent vagus nerve to the brain stem, from which the efferent vagus nerve activates the splenic nerve in the celiac plexus, give rise to norepinephrine release in the spleen and acetylcholine secretion by a subset of CD4+ T cells. The acetylcholine release targets α7 cholinergic receptors on macrophages, suppressing the release of proinflammatory cytokines.[50]

In animal models of sepsis,[49] disruption of this neural-based system by vagotomy surges susceptibility to endotoxin shock, whereas stimulation of the efferent vagus nerve or α7 cholinergic receptors attenuates systemic inflammation.

Patients who survive early sepsis but remain dependent on intensive care have evidence of immunosuppression, in part reflected by decreased expression of HLA-DR on myeloid cells. These patients often have ongoing infectious foci, despite antimicrobial therapy, or reactivation of latent viral infection.[43]

Multiple studies have documented reduced responsiveness of blood leukocytes to pathogens in patients with sepsis,[45] findings that were recently verified by postmortem studies revealing strong functional impairments of splenocytes found from patients who had died of sepsis in the ICU. Besides the spleen, the lungs also showed evidence of immunosuppression; both organs had enhanced expression of ligands for T-cell inhibitory receptors on parenchymal cells.[51] Enhanced apoptosis, especially of B cells, CD4+ T cells, and follicular dendritic cells, has been involved in

sepsis-associated immunosuppression and death. Epigenetic regulation of gene expression may also contribute to sepsis-associated immunosuppression.[43]

Organ Dysfunctions

Although the mechanisms that trigger organ failure in sepsis have been only partially elucidated, impaired tissue oxygenation plays a key role. Several factors — including hypotension, reduced red-cell deformability and microvascular thrombosis — contribute to reduced oxygen delivery in septic shock. Inflammation can cause dysfunction of the vascular endothelium, along with cell death and loss of barrier integrity, leading to subcutaneous as well as body-cavity edema. In addition, mitochondrial damage caused by oxidative stress and other mechanisms impairs cellular oxygen use. Moreover, injured mitochondria release alarmins into the extracellular environment, including mitochondrial DNA and formyl peptides, which can activate neutrophils and cause further tissue injury.[43]

Evolution of pathogens

The causative organisms for sepsis have evolved over many years. Originally sepsis was termed, and strongly considered to be, a disease specifically related to Gram-negative bacteria.[52] this is because sepsis was considered to be a response to endotoxin – a molecule that was thought to be relatively specific for Gram-negative bacteria. In fact, some of the original studies of sepsis prove that Gram-negative bacteria were among the most common causes of sepsis.[53]

This resulted in a number of trials that focused on Gram-negative therapies, and even highly specific therapies for endotoxin, which were felt to be potentially useful treatments for sepsis. We now identify that sepsis may occur from any bacteria,

as well as from fungal and viral organisms. More recent epidemiology studies reveal that Gram-positive bacteria have become the most common cause of sepsis in the past 25 years.[39]

Large epidemiologic studies show Gram-positive organisms overriding Gram-negatives in the early- to mid-1980s as the most common cause of sepsis in the USA. According to the most recent estimates in sepsis, there are approximately 200,000 cases of Gram-positive sepsis each year, equated with approximately 150,000 cases of Gram-negative sepsis.[39]

While bacterial causes of sepsis have increased with the general increases in incidence, fungal causes of sepsis have grown at an even more rapid pace.[39] This may characterized general increase in nosocomial cases of sepsis, or it may reflect our effective treatment of bacterial infections, thus upholding fungal infections to a more leading role. While there has been a general increase in the number of fungal nosocomial infections, we have also detected shifts away from the most common *Candida albicans* organism to the more recalcitrant *torulopsis, glabrata* and *krusei* subspecies.[30]

Sepsis tends to occur from specific and consistent sources. Respiratory infections are always the most common cause of sepsis, severe sepsis and septic shock.[30]

Overall, respiratory infections account for around half of all cases of sepsis. The next most common causes are genitourinary and abdominal sources of infection with primary bacteremia and unknown sources being the next most common causes. The occurrence of acute organ dysfunction (i.e., severe sepsis) is linked to the source

of infection, as in patients with respiratory infections who are at higher risk for developing respiratory organ dysfunction.[30]

Regardless of the era and the organisms, the treatment of infection is the keystone of antisepsis therapy. There are two particular constituents of antimicrobial therapy that are important. The first is early antimicrobial therapy, with initiation of antibiotics in a suitable time interval reliant on the location of the patient. There are particular data from patients with pneumonia, and from those with septic shock, that show that delays in antimicrobial therapy lead to a suggestively increased risk of dying. Especially critical for septic shock, the risk of dying increases by approximately 10% for every hour of delay in receiving antibiotics.[30]

The other important component of antimicrobial therapy is correctness of the antimicrobial regimen. It may be instinctive that coverage of the appropriate organisms is critical, as failure to cover the appropriate organisms is equal with delays of antimicrobial therapy. A variety of studies of infected and septic patients show that inappropriate antimicrobial therapy is a reliable predictor of poor outcomes.[30]

With a view point of clinical perspective, this means that the antimicrobial therapy must always be empiric. The choice of antibiotics, and the timing of their administration, cannot wait for isolation and identification of the causative organism and determination of the organism's sensitivity to various antibiotics. These principles lie behind the observation that combination antimicrobial therapy may be superior to monotherapy.[54]

In addition, in certain circumstances antibiotic therapy alone is not sufficient to treat the infection causing sepsis, in which case source control is also essential to eradicate the infection.[30]

Treatment

The Surviving Sepsis Campaign, an international consortium of professional societies involved in critical care, treatment of infectious diseases, and emergency medicine, recently published the third iteration of clinical guidelines for the management of severe sepsis and septic shock.

Guidelines for the Treatment of Severe Sepsis and Septic Shock from the Surviving Sepsis Campaign.[1]

Element of Care Grade

"Resuscitation

- Begin goal-directed resuscitation during first 6 hr. after diagnosis
- Begin initial fluid resuscitation with crystalloid and consider the addition of albumin.
- Consider the addition of albumin when substantial amounts of crystalloid are required to maintain adequate arterial pressure.
- Avoid hetastarch formulations.
- Begin initial fluid challenge in patients with tissue hypo perfusion and suspected hypovolemia, to achieve ≥30 ml of crystalloids per kilogram of body weight.
- Continue fluid-challenge technique as long as there is hemodynamic improvement.

- Use norepinephrine as the first-choice vasopressor to maintain a mean arterial pressure of ≥65 mm Hg.
- Use epinephrine when an additional agent is needed to maintain adequate blood pressure.
- Add vasopressin (at a dose of 0.03 units/min) with weaning of norepinephrine, if tolerated.
- Avoid the use of dopamine except in carefully selected patients (e.g., patients with a low risk of arrhythmias and either known marked left ventricular systolic dysfunction or low heart rate).
- Infuse dobutamine or add it to vasopressor therapy in the presence of myocardial dysfunction (e.g., elevated cardiac filling pressures or low cardiac output) or ongoing hypoperfusion despite adequate intravascular volume and mean arterial pressure.
- Avoid the use of intravenous hydrocortisone if adequate fluid resuscitation and vasopressor therapy restore hemodynamic stability; if hydrocortisone is used, administer at a dose of 200 mg/day.
- Target a hemoglobin level of 7 to 9 g/dl in patients without hypoperfusion, critical coronary artery disease or myocardial ischemia, or acute hemorrhage.

Infection control

- Obtain blood cultures before antibiotic therapy is administered.
- Perform imaging studies promptly to confirm source of infection.
- Administer broad-spectrum antibiotic therapy within 1 hr after diagnosis of either severe sepsis or septic shock.
- Reassess antibiotic therapy daily for de-escalation when appropriate.

- Perform source control with attention to risks and benefits of the chosen method within 12 hr after diagnosis.

Respiratory support

- Use a low tidal volume and limitation of inspiratory-plateau-pressure strategy for ARDS.
- Apply a minimal amount of positive end-expiratory pressure in ARDS.
- Administer higher rather than lower positive end-expiratory pressure for patients with sepsis-induced ARDS.
- Use recruitment maneuvers in patients with severe refractory hypoxemia due to ARDS.
- Use prone positioning in patients with sepsis-induced ARDS and a ratio of the partial pressure of arterial oxygen (mm Hg) to the fraction of inspired oxygen of <100, in facilities that have experience with such practice.
- Elevate the head end of the bed in patients undergoing mechanical ventilation, unless contraindicated.
- Use a conservative fluid strategy for established acute lung injury or ARDS with no evidence of tissue hypo perfusion.
- Use weaning protocols.

Central nervous system support

- Use sedation protocols, targeting specific dose-escalation end points.
- Avoid neuromuscular blockers if possible in patients without ARDS.
- Administer a short course of a neuromuscular blocker (<48 hr) for patients with early, severe ARDS.

General supportive care

- Use a protocol-specified approach to blood glucose management, with the initiation of insulin after two consecutive blood glucose levels of >180 mg/dl (10 mmol/ liter), targeting a blood glucose level of <180 mg/dl.
- Use the equivalent of continuous venovenous hemofiltration or intermittent hemodialysis as needed for renal failure or fluid overload.
- Administer prophylaxis for deep-vein thrombosis.
- Administer stress-ulcer prophylaxis to prevent upper gastrointestinal bleeding.
- Administer oral or enteral feedings, as tolerated, rather than either complete fasting or provision of only intravenous glucose within the first 48 hr after a diagnosis of severe sepsis or septic shock.
- Address goals of care, including treatment plans and end-of-life planning as appropriate".[1]

"The most important elements of the guidelines are planned into two "bundles" of care: an initial management bundle to be accomplished within 6 hours after the patient's presentation and a management bundle to be accomplished in the ICU".[1] Implementation of the bundles is associated with an improved outcome.[43]

"The principles of the initial management bundle are to provide cardiorespiratory resuscitation and mitigate the immediate threats of uncontrolled infection. Resuscitation requires the use of intravenous fluids and vasopressors, with oxygen therapy and mechanical ventilation provided as necessary. The exact constituents required optimizing resuscitation, such as the choice and amounting of fluids, appropriate type and intensity of hemodynamic monitoring, and role of adjunctive vasoactive agents, all remain the subject of ongoing debate and clinical

trials; many of these issues will be enclosed in this series. Nonetheless, some form of resuscitation is considered essential, and a standardized approach has been advocated to ensure prompt, effective management".[1]

"The initial management of infection requires forming a possible diagnosis, obtaining cultures, and initiating appropriate and timely empirical antimicrobial therapy and source control (i.e., draining pus, if appropriate)".[43]

The choice of empirical therapy depends on the suspected site of infection, the setting in which the infection developed (i.e., home, nursing home, or hospital), medical history, and local microbial-susceptibility patterns. Inappropriate or delayed antibiotic treatment is associated with increased mortality. Thus, intravenous antibiotic therapy should be started as promptly as possible and should cover all likely pathogens. It has not been determined whether combination antimicrobial therapy produces better outcomes than adequate single-agent antibiotic therapy in patients with severe sepsis.[43] Current guidelines recommend combination antimicrobial therapy only for neutropenic sepsis and sepsis caused by pseudomonas species. Empirical antifungal therapy should be used only in patients at high risk for invasive candidiasis.[55]

The patient should also be relocated to an appropriate setting, such as an ICU, for ongoing care. After the first 6 hours, attention directs on monitoring and support of organ function, avoidance of complications, and scaling down of care when possible. De-escalation of initial broad-spectrum therapy may prevent the emergence of resistant organisms, diminish the risk of drug toxicity, and reduce costs, and evidence from observational studies specifies that such an approach is safe.[56]

The only immunomodulatory therapy that is currently advocated is a short course of hydrocortisone (200 to 300 mg per day for up to 7 days or until vasopressor support is no longer required) for patients with refractory septic shock.[1] This reference is supported by a meta-analysis,[57] but the two largest studies had contradictoryresults,[50,51] and other clinical trials are ongoing.[60,61]

Clinical outcomes

Patients with sepsis are typically considered to be patients who have a high risk of morbid complications and death. This is in large part due to the organ dysfunction caused by sepsis, and the attendant complications of treating the organ dysfunction. Septic patients tend to be high resource consumers in the hospital and in the ICUs, and their existence affects the outcomes of those ICUs overall. For example, ICUs with a higher percentage of patients with sepsis also inevitably have higher average mortality rates.[38]

In addition, the costs of sepsis are quite extensive. There are estimates from around the world that consistently report cases of sepsis to cost from US$25,000 to $50,000 per episode.[30]

There are various ways to foresee the risk of mortality in patients with sepsis. The most simplistic approach may be to accurately classify the patient according to their stage of sepsis. Subjecting the consensus conference definition, near about estimates of fatality rates (the percentage of patients who die) is as follows:

- Sepsis: 10–20%
- Severe sepsis: 20–50%
- Septic shock: 40–80%

The PIRO system is attractive for its possible ability to group sepsis patients according to specific factors that may produce more homogeneous groups, such as comorbidities, type or source of infection and dysfunctional organ systems, among others. So far, whether PIRO staging is adding to this simple prediction scheme is still to be determined.

Perhaps more important than these crude mortality assessments are that the risk of dying with sepsis has been falling over the past three decades. From data extending back to 1979, the risk of dying with sepsis was near 30% in the early years, and since the year 2000 the risk has been under 20%.[27] Similar results have also been detected when analyzing temporal changes in mortality from clinical trials of sepsis therapies.[62]

Unfortunately, despite an obvious reduction in patient's risk of dying, owing to the increasing incidence of sepsis, the total number of people dying with the condition each year continues to rise. In fact, the number of people dying from sepsis each year (estimated to exceed 200,000) is similar to the number of people dying with acute myocardial infarction, and far outdoes those who die from HIV, breast cancer or stroke. In the USA, sepsis is the tenth leading cause of death overall.[30]

Markers for prediction of mortality

Sepsis is diagnosed by history and physical findings, validated by laboratory data such as circulating leukocyte count, body fluid examination and culture.

Detecting the syndrome in hospitalized patients is predominantly important, as nosocomial sepsis is associated with longer lengths of stay and higher mortality rates compared with community-acquired sepsis.[63,64] Most patients will meet at least three

SIRS criteria at intensive care unit (ICU) admission.[65] Fever occurs in approximately 60% of patients at admission but may be repressed in those with advanced age, renal failure or patients taking anti-inflammatory medications. Hypothermia, though uncommon, is an ominous finding associated with mortality rates of up to 60%. The lethality of hypothermia likely is not a result of the temperature itself but rather the relationship of hypothermia with underlying chronic diseases, shock and an amplified inflammatory response. Tachypnea is present in up to 80% of ICU patients. Although possible, the diagnosis should be questioned in patients lacking tachypnea or gas exchange abnormalities. Hypoxia is common in septic patients; more than 90% of patients will develop sufficient hypoxemia that involves supplemental oxygen, generally correlating with a PaO2/FiO2 ratio less than 300. Tachycardia is nearly universal and is an important sign of sepsis, unless patients have intrinsic cardiac disease or is consuming nodal blocking treatment .Abnormalities in circulating leukocyte count (more than 12,000 cells/mm3 or fewer than 4000 cells/mm3) are numerous enough to be considered important diagnostic criteria.[63]

Several serum biomarkers are claimed to have diagnostic and/or prognostic value, but none have established acceptable sensitivity and specificity for routine clinical use.

The serum lactate level is suggested to be a marker of global hypo-perfusion and tissue hypoxia in sepsis. According to the theory, even before patients develop blunt hypotension, tissue perfusion is impaired by myocardial depression, relative hypovolemia from a leaky endothelium, amplified metabolic demands and impaired vasoregulatory mechanisms. Consequently, oxygen demand surpasses supply and

anaerobic production of lactate ensues. Not all agreed that lactate production was a reliable marker of global hypoxia in sepsis.[66]

Animal models of polymicrobial sepsis indicated that certain organs, especially the liver and small intestine, may be more sensitive to impaired oxygen delivery. Regardless of its exact mechanism of production, patients admitted with a sepsis-related diagnosis and elevated serum lactate levels (greater than 4 mmol/L) had a bigger mortality rate. It is also seen that mortality rates have come down in septic patients with higher lactate clearance rates after 6 hours of therapy. Serum lactate is a constituent of prognostic models in severe sepsis and septic shock and concentrations increased in this patients.[63]

Procalcitonin and C-reactive protein (CRP), both markers of inflammation, have been reviewed as potential diagnostic tests in sepsis. The reported sensitivities and specificities of these tests vary, hence neither has achieved widespreadapproval.[63]

Most prognostic models assess survival using data collected at admission or within the first 24 hours in ED. There are two types including general models and disease-specific models.[63]

The main categories of general prognostic models contain the models for evaluating the severity of illness that is, APACHE II and III, Simplified Acute Physiology Score (SAPS) II, Mortality Prediction Model (MPM) II and the models for quantifying organ dysfunction and failure that is, Logistic Organ Dysfunction System, Multiple Organ Dysfunction Score, Organ System Failure (OSF), Sequential Organ Failure Assessment (SOFA).[63]

The organ dysfunction that results from sepsis is central to the pathogenesis of the disease.

A 3000-parient ED-based study established that organ dysfunction with septic shock signified increasingly worse outcomes. Patients with suspected infection alone had a mortality rate of 2.1%, while the existence of SIRS criteria and suspected infection had a mortality rate of only 1.3%.[59] However, the mortality rate was 9% for those patients with severe sepsis (sepsis plus organ dysfunction) and 28% for those with septic shock.[60]

The cardiovascular insufficiency is the most significant events in severe sepsis leading to morbidity and mortality categorized by global tissue hypoxia, decreased contractility and ventricular dilatation.[55]

Echocardiography findings demonstrated that in 40-50% of patients with severe sepsis progressed to myocardial depression and changes in cardiac performances. The responsible mechanisms for this organ dysfunction are possibly mitochondrial dysfunction, myocardial cell death; however, the cardiac function is fully reversible in the survived patients.[55]

Hematologic manifestation of organ dysfunction is well-recognized in severe sepsis. The most common deviations include leukocytosis, anemia, thrombocytopenia, abnormal PT and aPTT and DIC.[55]

Patients with sepsis often display neurologic impairments displayed by altered mental status and lethargy, commonly referred as septic encephalopathy. The incidence has been stated between 10 and 70%. The mortality rate in patients with

septic encephalopathy is higher than that in septic patients without substantial neurologic involvement.[55]

The lung is an early target of the inflammatory response to sepsis. These effects are seemingly irrespective of the primary infection that causes sepsis. Significant right-to-left shunting, arterial hypoxemia and intractable hypoxemia occur. The consequential morbidity is high and is a common endpoint to sepsis-related deaths. Sepsis produces a highly catabolic state and places substantial demands on the respiratory system. In the same time span, airway resistance increases and muscle function is disrupted. Irrespective of whether pneumonia is the cause of sepsis, the common pulmonary endpoint is acute respiratory distress syndrome (ARDS). The development of ARDS occurs 4 to 24 hours after radiographic abnormalitiesadvances.[55]

An absolute or relative adrenal insufficiency is common in sepsis. Depending on the balance of circulating cytokines, augmentation or suppression of the hypothalamic-pituitary axis is possible. Interleukin (IL) 1 and IL-6 both stimulate the hypothalamic-pituitary-adrenal axis. TNF-and corticostatin depress pituitary function. Other factors added to adrenal insufficiency in sepsis include decreased blood flow to the adrenal cortex, decreased pituitary function and pituitary secretion of adrenocorticotropic hormone due to severe stress.[55]

However, despite the infinite resources available patient with septic shock have a high mortality, as yet there is no predictive scoring system which gives accurate predictions of outcome for individual patient. Survival from an episode of septic shock is reliant on patient's age, number of failed organs, previous health and

the time delay before the onset of medical intervention, as well as the correctness and quality of medical care.[61]

The time required to order, draw, analyze, and report laboratory tests is substantial, mainly when these are used to fulfill criteria for diagnosis or to make clinical decisions. On the one hand, protocol-driven laboratory draws, screen low-risk patients, potentially generating many false positives. On the other hand, relying on laboratory information to outline treatment strategies causes delays in care. Hence non-laboratory instant bedside "red flags" for sepsis may alert providers to initial assessment of those at risk for severe sepsis, like shock index. Correspondingly, a clinical basis to re-prioritize those with more benign parameters on presentation would direct resources appropriately.

The severe sepsis is defined as the presence of sepsis and related organ dysfunction. Clinical trials and observational studies usually use a scoring system for the assessment of the severity of organ function impairment. Most popular among them are Sequential Organ Failure Assessment (SOFA) score [27], Logistic Organ Dysfunction System (LODS) [68], and Multiple Organ Dysfunction Score (MODS) [69]. All of these systems rely on the number and degree of organ dysfunction. Similar feature for all systems is the measurement of the type and severity of physiologic function derangement by summing the points of dysfunction from six key organ systems: cardiovascular, respiratory, neurological, renal, hepatic, and coagulation. The assessment of the impact of each organ dysfunction to the outcome of the patients admitted to the ICU with a diagnosis of severe sepsis was undertaken in this study applying a set of reliable statistical methods. The choice of the SOFA system was made because it was created to describe a sequence of complications in septic patients

[27]. Some multicenter and multinational studies using SOFA system showed different prognostic value of each organ dysfunction and unequal contribution to outcome in general ICU population [27, 70, 71]. Similar investigations in septic patients are lacking. The objectives of the study were to evaluate the impact of organ dysfunction in severe sepsis and to determine the effectiveness of organ dysfunction scores to discriminate outcome after admission to the ICU.

HISTORY OF DEVELOPMENT OF SOFA SCORE:

The ESICM organized a consensus meeting in Paris in October 1994 to create a so-called sepsis-related organ failure assessment (SOFA) score, to describe quantitatively and as objectively as possible the degree of organ dysfunction/failure over time in groups of patients or even in individual patients

There are two major applications of such a SOFA score:

1. To enhance our Understanding of the natural course of organ dysfunction/failure and the association between the failure of the various organs.
2. To assess the effects of new therapies on the course of organ dysfunction/failure. This could be used to characterize patients at entry (and even serve within the entry criteria) or to evaluate the effects of treatment.

Severity indices have been designed primarily to evaluate a risk of death from an initial evaluation [72], even though there has been a recent tendency to evaluate severity indexes repeatedly to evaluate the time course of the disease [73]. Most importantly, the existing severity indices do not allow evaluation of the individual function of each organ separately.

The participants decided: (1) to limit the number of organs studied to 6. As an example, attempting to include dysfunction/failure of the gut was felt to be very important, but also too complex and was therefore abandoned. (2) To use a score from 0 (normal) to 4 (most abnormal) for each organ. (3) To record the worst values on each day.

Since the mortality rate is directly related to the degree of organ dysfunction, it is evident that it must also be related to the SOFA score for each organ system.

The relation between the SOFA score on ICU admission and the mortality rate was studied in 1643 patients with sepsis by the European/North American Study of Severity System (ENAS). Such a retrospective analysis has several problems. First, the ENAS data base was not created to study sepsis and septic shock specifically, so that the identification of sepsis was accomplished retrospectively. Second, it was not always possible to separate the patients in the ENAS data base for all value limits used in the SOFA. This was true for the cardiovascular status (only three groups) and for the coagulation system (only two groups). Finally, patient prognosis was only related to the SOFA on ICU admission. Nevertheless, two aspects of the data are encouraging. First, they generally show an increasing mortality rate with a greater SOFA score for each organ. Second, they show a good distribution of patient numbers among the different scores.

A "Multiple Organ Dysfunction Score" was developed by J. Marshall et al. [74] and a so-called "Brussels Score" [75] was developed by G. Bernard et al. at the time of the round table conference on clinical trials in sepsis [76]. A major difference among the three scores is based on the criteria of cardiovascular dysfunction/failure. In the "Multiple Organ Dysfunction Score~' it is based on the complex calculation of the

pressure adjusted heart rate, defined as the" product of heart rate times the right atrial (central venous) pressure divided by the mean arterial pressure". Such a score, calculated a number of times over any 24 h period, can only be computed, so that it removes the simplicity of the score. In the "Brussels Score;' it is based on hypotension and acidemia, but acidemia can be caused by factors other than circulatory failure, including renal failure or (permissive) hypercapnia. Thus, even if it is significantly related to mortality, it does not reflect the degree of cardiovascular dysfunction. In SOFA score, cardiovascular dysfunction/failure is defined on the basis of requirements for adrenergic support. Even though it is preferable to avoid treatment-related criteria, the participants found no better way to describe cardiovascular dysfunction/failure. Although the type of adrenergic support may differ from one institution to another, the categories were broad enough to avoid a major impact of local protocols on this assessment.

Table 2 Differences between commonly used scoring systems and the SOFA score

Scoring systems	SOFA score
Evaluate risk of mortality	Evaluate morbidity
Aim = prediction	Aim = description
Often complex	Simple, easily calculated
Does not individualize the degree of dysfunction/failure of each organ usually obtained early after admission	Does individualize the degree of dysfunction/failure of each organ obtained daily

In developing a scoring system, such as SOFA, for assessing and monitoring organ dysfunction, several important features need to be considered. Organ failure is, is a continuum of alterations in organ function from normal function, through varying degrees of dysfunction, to organ failure. Second, the description of organ dysfunction needs to be based on simple, easily repeatable variables specific to the organ in

question and readily available in all institutions. Third, organ dysfunction is not static. It will change over a course of time, and a scoring system requires being able to take this time factor into account. In using the SOFA for outcome prediction, the ability to perform serial SOFA scores allow a more effective representation of the dynamics of illness including the effects of therapy compared with traditional outcome prediction models at the time of ICU admission. Although some investigators have used the APACHE II score over time, [77, 78, 79] this process has never been validated. Derived measures from the APACHE III system have also been proposed for use on a daily basis, [80] but APACHE III is not available in the public domain, and its daily use has again not been validated.

The SOFA score is a useful tool to stratify and compare patients in clinical trials.[81, 82] Moreno et al[83] recently demonstrated that the initial SOFA score can be used to quantify the degree of organ dysfunction or failure present on admission, that the Δ-SOFA score can demonstrate the degree of dysfunction or failure developing during an ICU stay, and that the total highest SOFA score can represent the cumulative organ dysfunction occurred in that patient. They also demonstrated a strong correlation of all these parameters with mortality outcome.

METHODOLOGY

The present study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi from January 2016 to December 2016.

Study design and duration

The study design was a hospital based cross sectional study.

Study period

The present study was done for the period of one year from January 2016 to December 2016.

Place

The present study was carried out in the Intensive care unit at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi a tertiary care teaching hospital attached to Jawaharlal Nehru Medical College, Belagavi.

Source of Data

Patients presenting with sepsis in the Intensive care unit at KLES Dr Prabhakar Kore Hospital and MRC, Belagavi

Sample size:

UNIVERSAL SAMPLE SIZE

All the patients with sepsis in intensive care unit at KLES Dr Prabhakar Kore Hospital and MRC, Belagavi were enrolled during the study period

Sampling procedure

All the patients with sepsis in intensive care unit at KLES Dr Prabhakar Kore Hospital and MRC, Belagavi were enrolled during the study period

Hence it was a universal sample size.

Selection criteria

Inclusion Criteria:

1. Patients aged 18 and above.
2. Patients who are in severe sepsis or systemic inflammatory response syndrome.

Exclusion Criteria:

Patients less than 18 years of age.

Ethical clearance

Prior to the beginning, the study was approved by the Institutional Ethics Committee, Jawaharlal Nehru Medical College, Belagavi.

Informed consent

The patients who fulfilled the selection criteria were informed about the nature of study and a written informed consent was obtained (Annexure–I).

Data Collection

PATIENTS WERE ENROLLED AS SEPSIS BASED ON:

INFLAMATORY RESPONSE SYNDROME AND SEVERE SEPSIS CRITERIA AS PER AMERICAN COLLEGE OF CHEST PHYSICIANS AND SOCIETY OF CRITICAL CARE MEDICINE.

"Systemic inflammatory response syndrome

i. Body temperature less than 36°C or greater than 38°C
ii. Heart rate greater than 90 beats per minute
iii. Respiratory rate greater than 20 breaths per minute or, an arterial partial pressure of carbon dioxide less than 4.3kPa (32 mmHg)
iv. White blood cell count less than 4000 cells/mm^3(4 x 109 cells/L) or greater than 12,000 cells/mm^3 (12 x 109 cells/L), or the presence of greater than 10% immature neutrophil band forms.

Requirements for severe sepsis patients:

i. Fulfilling at least 2 or more of SIRS criteria
ii. Has an associated or suspected source of infection

Has one or more of the following

a) Evidence of end organ damage (eg. Elevated creatinine levels > 120 µmol/L , altered mental status or GCS <14, renal output <0.5 ml/kg/hr despite adequate fluid resuscitation, pao2/fio2 <250, or if lung is the only dysfunctional organ)
b) Platelet count less than 80,000 or decrease in 50% platelet count from highest value recorded in previous three days.

c) Episode of hypotension (<90/60 mmHg), which responds to initial fluid resuscitation.

d) Unexplained metabolic acidosis, PH less than or equal to 7.30 or a base deficit of 5.0meq/l and a plasma lactate level>1.5 times than the upper lab reporting value".[3]

At the Emergency Department, the demographic data of the patients was noted along with the history of presenting illness and other comorbid conditions. Further these patients underwent clinical examination followed by systemic examination. Patients were evaluated for the following parameters on admission.

- Body temperature was measured by a medical thermometer.
- Blood pressure was measured by a sphygmomanometer on right upper arm at arrival at the emergency department.
- Heart rate was measured by palpatory method, first at arrival at emergency department.
- Respiratory rate.
- Glasgow coma scale

Collection of sample: Blood samples were collected from the subjects with all aseptic precautions. 10 ml of venous blood was collected from median cubital vein by disposable plastic syringe. The needle was detached from the nozzle and blood transferred immediately in to a dry, clean, ionized, graduated, screw capped plastic test tube with a gentle push to avoid haemolysis.

SOFA score calculated on the basis of these criteria at 0 hours and at 48 hours.

Table 1: SOFA score

Organ system	Score				
	0	1	2	3	4
Respiratory: PaO_2/FiO_2	>400	≤400	≤300	≤200	≤100
Renal: Creatinine (mg/dl)	<1.2	1.2-1.9	2.0-3.4	3.5-4.9; urine output ≤500 ml/day	>5.0; urine output <200 ml/day
Hepatic: Bilirubin (mg/dl)	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular: Hypotension	No hypotension	MAP < 70 mmHg	Dopamine ≤ 5[a], dobutamine (any dose)	Dopamine > 5[a] or epinephrine ≤ 0.1[a] or norepinephrine ≤ 0.1[a]	Dopamine > 15[a] or epinephrine > 0.1[a] or norepinephrine > 0.1[a]
Hematologic: Platelet count (10^3/mcL)	>150	≤150	≤100	≤50	≤20
Neurologic: Glasgow coma scale score	15	13-14	10-12	6-9	<6

[a]Adrenergic agents administered for at least 1 h (doses given are in µg/kg/min). FiO_2=Fractional inspired oxygen, MAP=Mean arterial pressure, PaO_2=Arterial oxygen tension, SOFA=Sequential organ failure assessment

Investigations:

Patients were subjected to following investigations.

- Complete blood count
- Platelet count
- White blood cell count
- Differential cell count
- Random blood sugar levels
- Serum electrolytes
- Serum lactate levels
- Serum urea levels
- Serum creatinine levels
- Liver function test
- Chest X-ray
- Arterial blood gas study
- Blood culture and sensitivity

Statistical Methods

The data obtained was coded and entered into Microsoft excel spreadsheet and data was analyzed using SPSS version 23 and MedCalc software. The categorical data was expressed in terms of rates, ratios and percentages and the continuous data was expressed in terms of mean ± standard deviation. The comparison of categorical data was done using Chi-square test or Fisher's exact test. Continuous data was compared using independent sample't' test. In case of more than two means one-way ANOVA was used to compare the data. A probability value ('p' value) of less than or equal to 0.05 was considered as statistically significant.

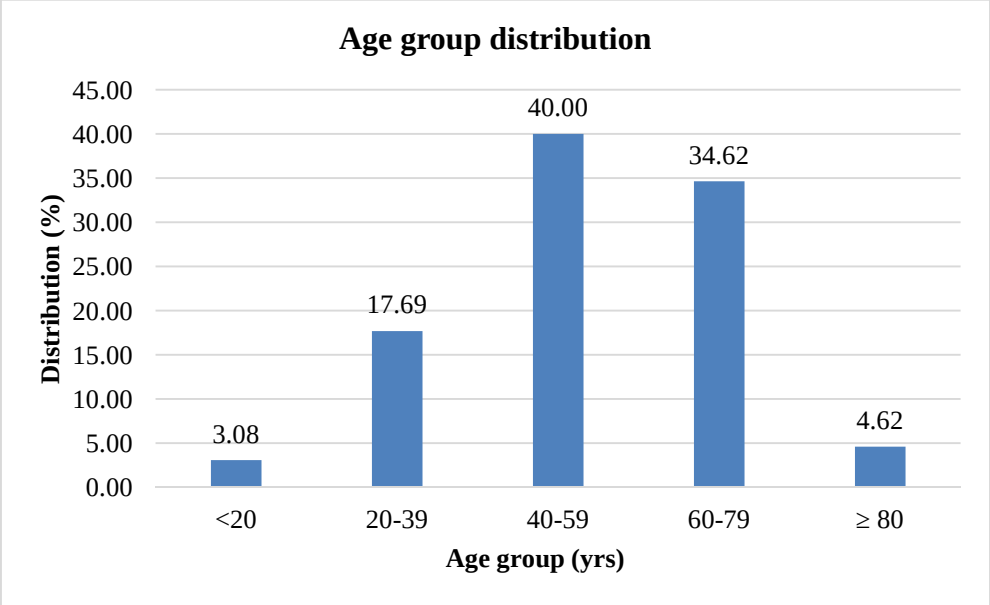
RESULTS

This one-year hospital based cross sectional study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2016 to December 2016. A total of 130 patients admitted with sepsis in the intensive care unit were studied.

The data obtained was coded and entered into the excel spreadsheet. The data was analyzed and the final results and observations were tabulated as below.

Table 1. Age distribution:

Age	Number	Percentage
<20	4	3.08
20-39	23	17.69
40-59	52	40.00
60-79	45	34.62
≥ 80	6	4.62
TOTAL	130	100



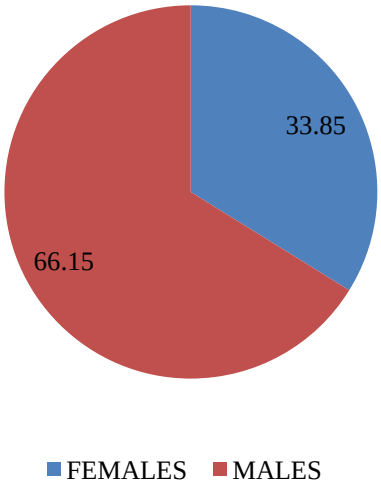
Graph 1: Bar chart of Age Group distribution in study population (N=130)

In the present study, maximum numbers of patients were in the age group of 40-59 years followed by 60-79 years that is 40% and 34.62% respectively. The youngest patient was of 18 years and the oldest was 84 years.

Table 2.Sex Distribution

SEX	NUMBER	PERCENTAGE
FEMALES	44	33.85
MALES	86	66.15
TOTAL	130	100

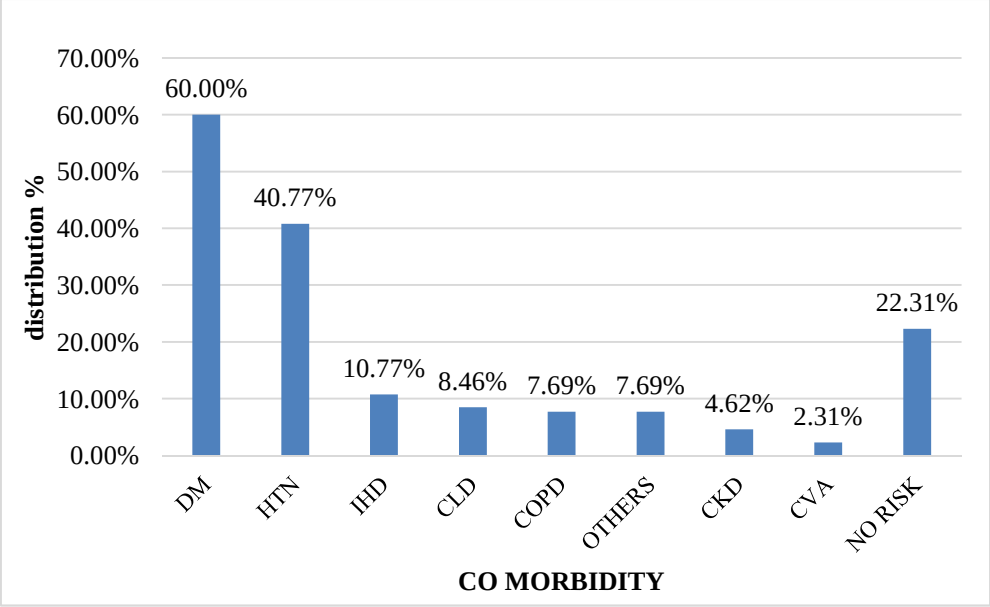
Graph 2: Pie Chart Of Gender Distribution In Study Population



In the present study, out of 130 cases 86(66.15%) were males and 44 (33.85%) were females. Male preponderance was seen with Male to Female ratio of 1.95:1.

Table 3. Descriptive analysis of risk factor in study population (n=130)

Risk factor	Number	Percentage
DM	78	60.00%
HTN	53	40.77%
IHD	14	10.77%
CLD	11	8.46%
COPD	10	7.69%
OTHERS	10	7.69%
CKD	6	4.62%
CVA	3	2.31%
NO RISK	29	22.31%



Graph 3: Bar chart of Risk Factors distribution in study population (N=130)

In the present study, most of the patients had Diabetes (60%) followed by HTN (40.77%). The other comorbid conditions are shown as above. Other condition as stated above included retroviral disease positive status, pulmonary Koch's, Bed sore, BPH, hypothyroidism, seizure disorder.

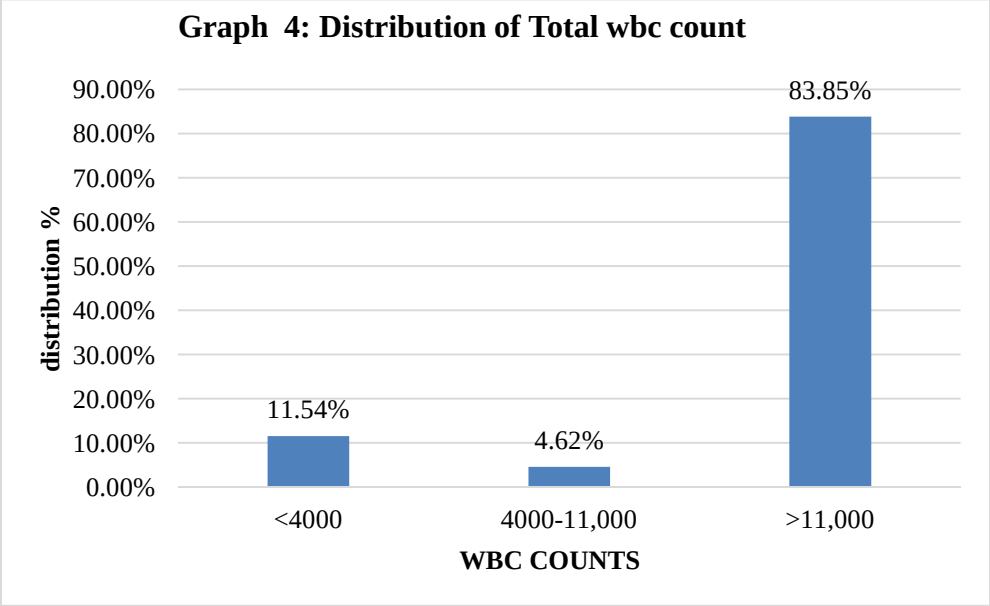
Table4: Summary of Vital Parameter in study population (N=130)

Parameter	Number	Percent
Pulse rate		
80-100	17	13.08%
>100	113	86.92%
Blood pressure		
<90/60mmhg	65	50%
>90/60mmhg	65	50%
Respiratory rate		
<20	7	5.38%
>20	123	94.62%
Temperature		
<96.8	--	
96.9-100.3	61	46.92%
>100.4	69	53.08%

In the present study, 86.92% of cases presented with pulse rate of above 100bpm. 65 cases (50%) had blood pressure > 90/60 mmhg and <90/60mmhg each. 53.08% cases were found to have a temperature of above 100.4 ^{0}F. 94.62% cases presented with respiratory rate above 20.

Table 5: Descriptive analysis of WBC in study population (N=130)

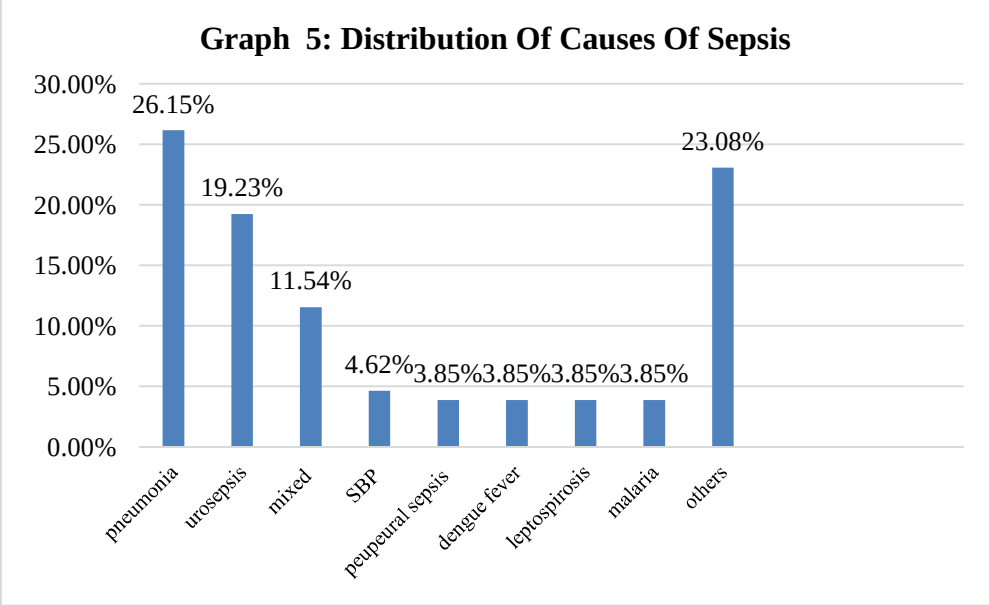
WBC	NO.	%
<4000	15	11.54%
4000-11,000	6	4.62%
>11,000	109	83.85%



Among the study population, the WBC was <4000 in 15 cases (11.54%), 4000-11,000 in 6 cases (4.62%) and >11,000 in 109 cases (83.85%).

Table 6. Diagnosis distribution among patients with sepsis:

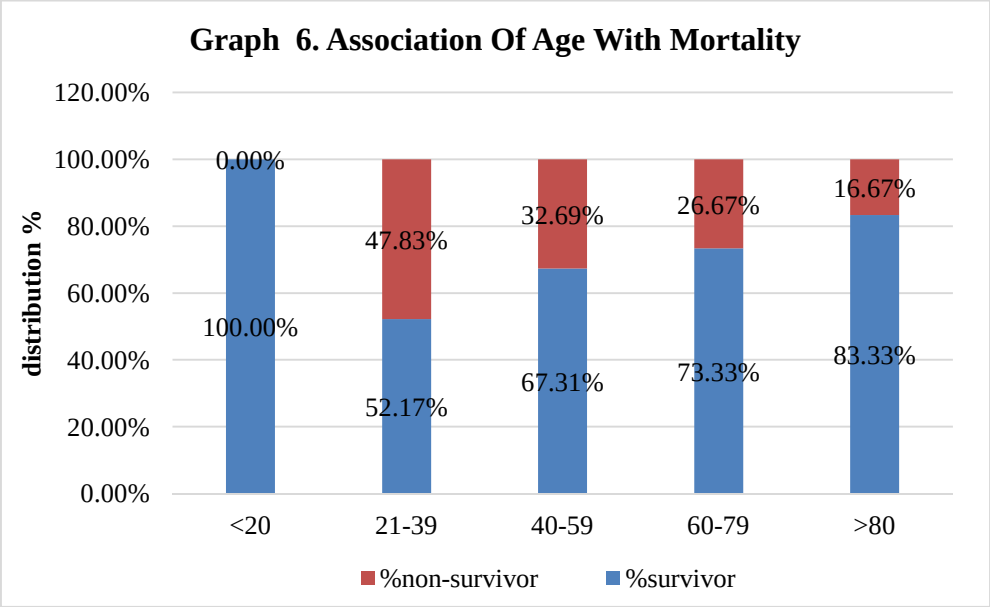
Etiology	Cases	%
Pneumonia	34	26.15%
Urosepsis	25	19.23%
Mixed	15	11.54%
Sbp	6	4.62%
Puerperal sepsis	5	3.85%
Dengue fever	5	3.85%
Leptospirosis	5	3.85%
Malaria	5	3.85%
Others	30	23.08%
Total	130	



In present study, it was observed that maximum cases of sepsis were due to pneumonia (26.15%) followed by urosepsis (19.23%). The rest causes are mentioned as above. The mixed infections were cases with two or more sources of infection such as bedsore with pneumonia, pneumonia with SBP, urosepsis with lower limb cellulitis, OPP with aspirational pneumonia. Other causes included cellulitis, meningitis, bronchiectasis, mucormycosis, Ludwig's angina, parotid abscess, choleycystitis, abdominal tuberculosis, intestinal obstruction, lung abscess, and empyema

Table.7.Association of Age with Mortality:

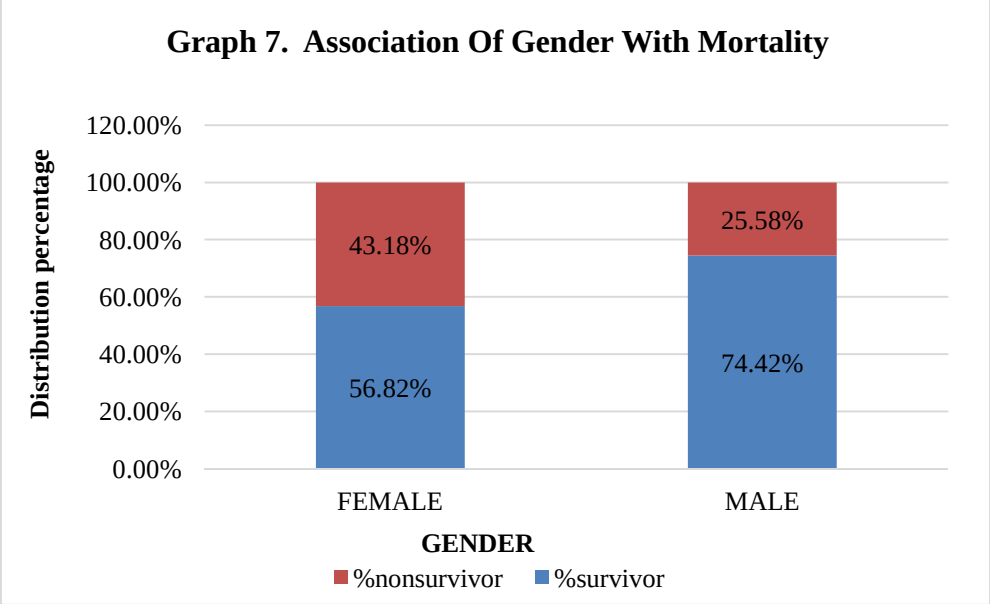
Age	Survivors	Non-survivors	total	%survivor	%non-survivor
<20	4	0	4	100.00%	0.00%
21-39	12	11	23	52.17%	47.83%
40-59	35	17	52	67.31%	32.69%
60-79	33	12	45	73.33%	26.67%
>80	5	1	6	83.33%	16.67%
Total	89	41	130		



In present study, the age group with maximum mortality was in the range of 40-59 (17 cases) followed by age group between 60-79 years (12 cases). The MEAN age for survivor is 53.25 and non-survivor is 49.

Table 8.Sex Distribution with Mortality:

SEX	Survivors	Non-survivors	Total	%survivor	%no survivor
FEMALE	25	19	44	56.82%	43.18%
MALE	64	22	86	74.42%	25.58%



In the present study, we found that mortality was more in number of female cases as compared to males which was 43.18% and 25.58% respectively.

Table 9. Causes of mortality in cases with sepsis:

Causes of mortality	Number	Percentage
Pneumonia	10	24.39
Spontaneous bacterial peritonitis	6	14.63
Puerperal sepsis	4	9.76
Urosepsis	4	9.76
Lower limb cellulitis, urosepsis	2	4.88
Abdominal tb	1	2.44
Acute gastroenteritis	1	2.44
Ards	1	2.44
Intestinal obstruction	1	2.44
Leptospirosis	1	2.44
Lung abscess	1	2.44
Meningitis, pneumonia	1	2.44
Mucormycosis	1	2.44
Opp, bedsore	1	2.44
Opp, bedsore, pneumonia, upper limb cellulitis	1	2.44
Peritonitis	1	2.44
Pneumonia, cholecystitis	1	2.44
Pulmonary koch's	1	2.44
Viral hepatitis	1	2.44
Wound infection	1	2.44
Total	41	100.00

In present study, it was found that maximum cases of mortality had pneumonia (24.39%) followed by SBP (14.63%) followed by puerperal sepsis and urosepsis with 9.76 % each. Other causes of mortality are mentioned as above.

TABLE 10. Descriptive analysis of number of cases with individual organ dysfunction:

a. At 0 hr

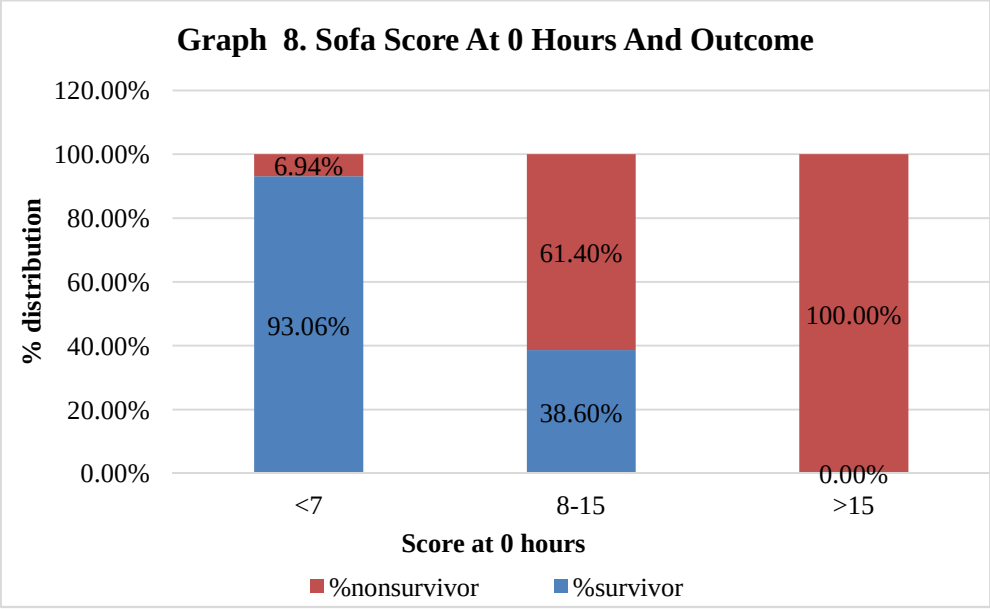
Score	Number of patients involved in organ dysfunction at admission					
	Pao2/fio2	**Platelet**	**Bilirubin**	**Gcs**	**Map**	**Creatinine**
0	39	23	55	56	33	31
1	62	49	41	41	4	51
2	25	41	25	6	87	23
3	4	12	4	23	6	13
4	nil	5	5	4	0	12
Total	130	130	130	130	130	130

b. At 48 hrs

Score	Number of patients involved in organ dysfunction at 48 hours					
	PAO2/FIO2	**Platelet**	**Bilirubin**	**GCS**	**MAP**	**Creatinine**
0	54	22	58	63	69	30
1	32	39	42	26	1	44
2	29	37	15	16	38	26
3	10	23	7	19	17	11
4	nil	4	3	1	0	14
Total	125	125	125	125	125	125

Table 11. Sofa score at presentation:

Sofa score	Number	No survivors	Survivors	%survivor	%no survivor
≤7	72	5	67	93.06%	6.94%
8-15	57	35	22	38.60%	61.40%
>15	1	1	0	0.00%	100.00%
Total	130	41	**89**		

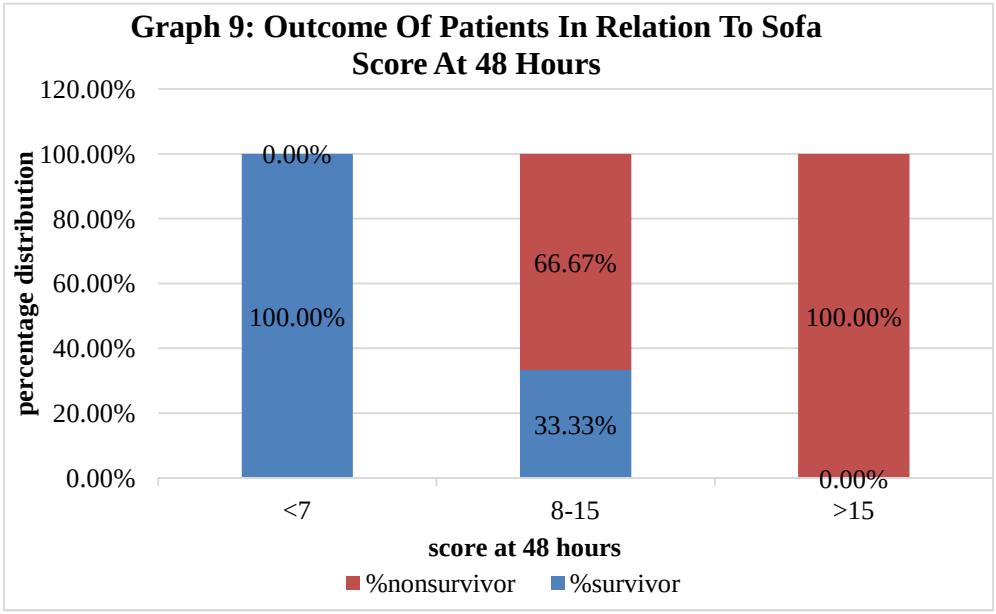


	Survivors		**Non-survivors**			
	Mean	S.D.	Mean	S.D.	P value	Inference
SCORE AT 0 HR	5.39	2.73	10.85	2.71	<0.0001	HS

In present study, we observed that for sofa scores at admission above 15 had 100% mortality and for scores between 8-15 there was a mortality of 61.40% followed by 6.94% mortality below the score of 7. The mean value of Sofa score in survivors was 5.39 with SD 2.73 and mean value of Sofa score for non survivors was 10.85 respectively. The p value (<0.0001) was significant for association of mean sofa score with outcome. There were **5 cases** of mortality within 24 hours.

Table 12. Sofa score at 48 hours:

Score	Number	Survivor	Non-survivor	%survivor	%no survivor
<7	74	74	0	100.00%	0.00%
8-15	45	15	30	33.33%	66.67%
>15	6	0	6	0.00%	100.00%
Total	125	89	36		



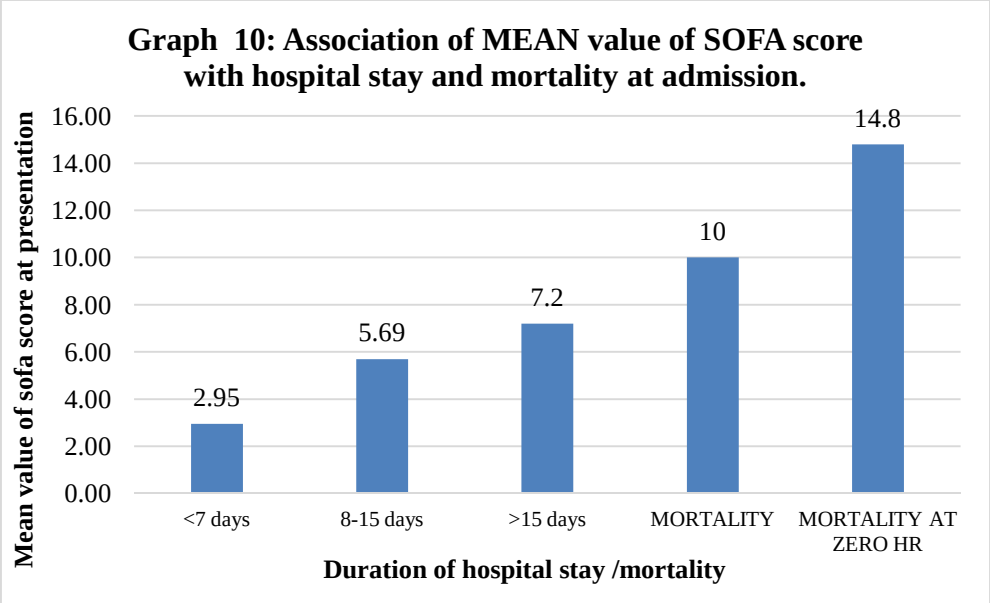
	Survivors		Non-survivors			
	Mean	**S.D.**	**Mean**	**S.D.**	**P value**	**Inference**
SCORE AT 48 HR	4.16	3.24	12.83	3.68	<0.0001	HS

In present study, we observed that for sofa scores at admission above 15 had 100% mortality and for scores between 8-15 there was a mortality of 66.67% followed by no mortality below the score of 7.The mean sofa score for survivors was 4.16 and non survivors was 12.83 respectively. The p value (<0.0001) was significant for prediction of outcome based on mean sofa score.

TABLE 13. Analysis of mean value of SOFA score at 0 hrs (admission) and its association to hospital stay and mortality

MEAN AND S.D. FOR TOTAL SCORE AT O HOUR

Duration of hospital stay	Mean	S.D.
<7 days	2.95	1.90
8-15 days	5.69	2.60
>15 days	7.2	3.42
MORTALITY	10	2.94
MORTALITY AT ZERO HR	14.8	1.10
p VALUE	<0.0001	HS
p VALUE IS OBTAINED USING ONE WAY ANOVA		

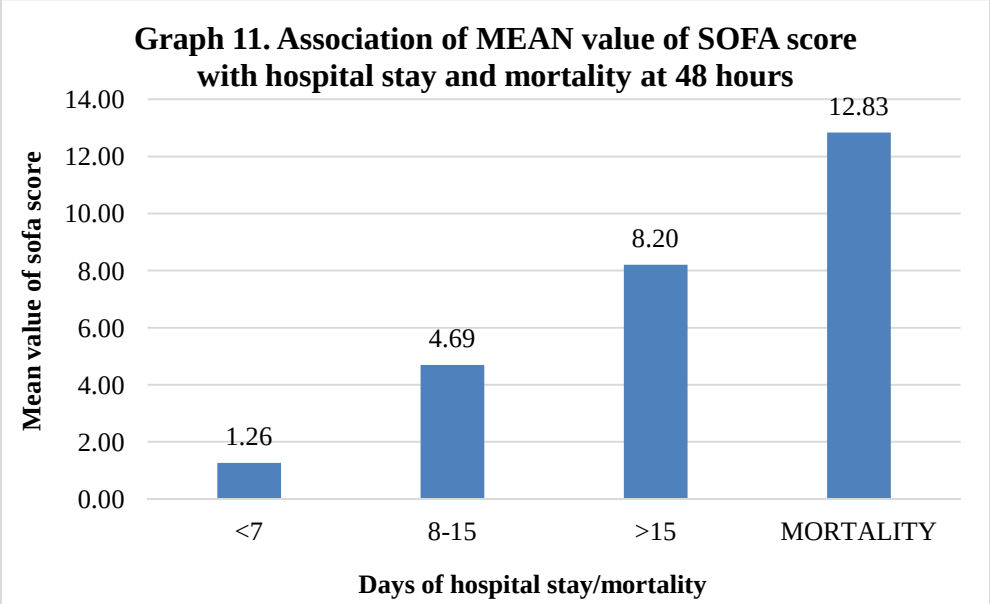


In present study, it was observed that patients with mean value of sofa score at admission of 2.95 had a stay of less than 7 days, while those with 5.69 had a stay of 8-15 days and those with 7.2 had a stay of above 15 days. It was also observed that with a score of 10 there was higher mortality eventually, while score of 14.8 had worst outcome in the form of mortality within 24 hours of admission. The p value for predicting the outcome and hospital stay with mean sofa score was significant.

TABLE 14. Analysis of mean value of SOFA scores at 48 hrs and its association to hospital stay and mortality.

MEAN AND S.D. FOR TOTAL SCORE AT 48 HOURS

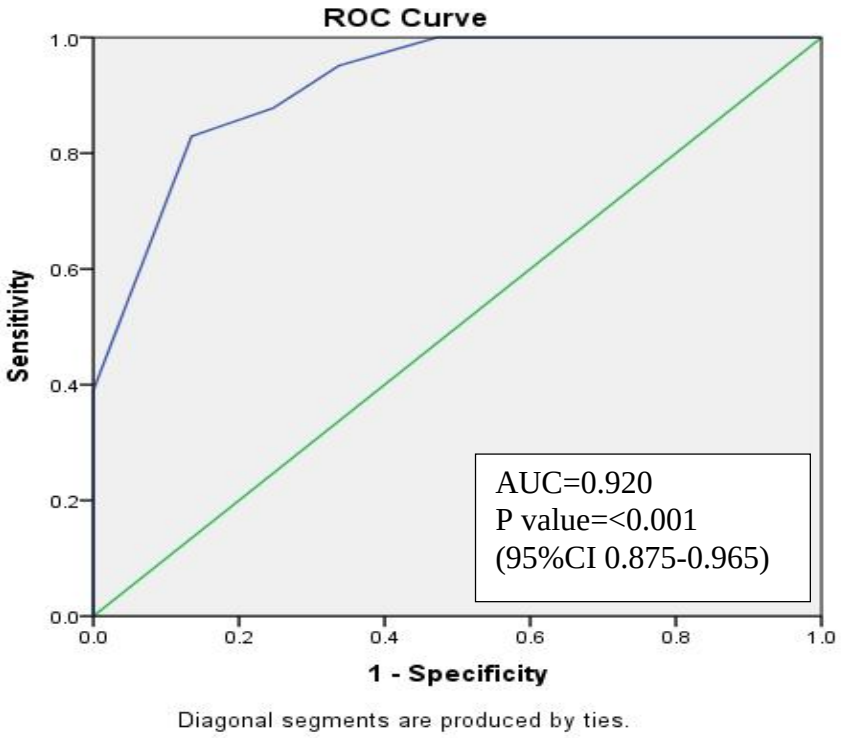
Duration of hospital stay	Mean	S.D.
<7	1.26	1.24
8-15	4.69	2.99
>15	8.20	4.09
MORTALITY	12.83	3.68
p VALUE	<0.001	VS
p VALUE IS OBTAINED USING ONE WAY ANOVA		



In present study, it was observed that patients with mean value of sofa score at 48 hours of 1.26 had a stay of less than 7 days, while those with 4.69 had a stay of 8-15 days and those with 8.20 had a stay of above 15 days. It was also observed that with a score of 12.83 there was mortality. The p value at 48 hours for predicting the outcome and hospital stay with MEAN SOFA score was significant.

ROC ANALYSIS

Graph 12: Predictive validity of sofa score admission in predicting mortality (N=130)



Basing on the ROC analysis the best cut off point for SOFA score at admission which yields best possible combination of sensitivity and specificity was identified as 7.5. Hence it was categorized as < 7.5, 7.5 and above and its validity in predicting mortality was analyzed

Table 15: Association of Overall mortality with Sofa score at 0 in study population (N=130)

Sofa score at 0	Overall mortality		Chi square	P-value
	Mortality	Survival		
7.5 and above (N=58)	36 (62.07%)	22 (37.93%)	45.208	**<0.001**
upto7.49 (N=72)	5 (6.94%)	67 (93.06%)		

Out of 58 people with 7.5 and above sofa score at 0 hrs, 36 (62.07%) had Overall mortality. Out of 72 people with upto7.49 sofa score at 0 hrs, only 5 (6.94%) had Overall mortality the difference between Sofa score at 0 hrs with Overall mortality was statistically significant (P value <0.001)

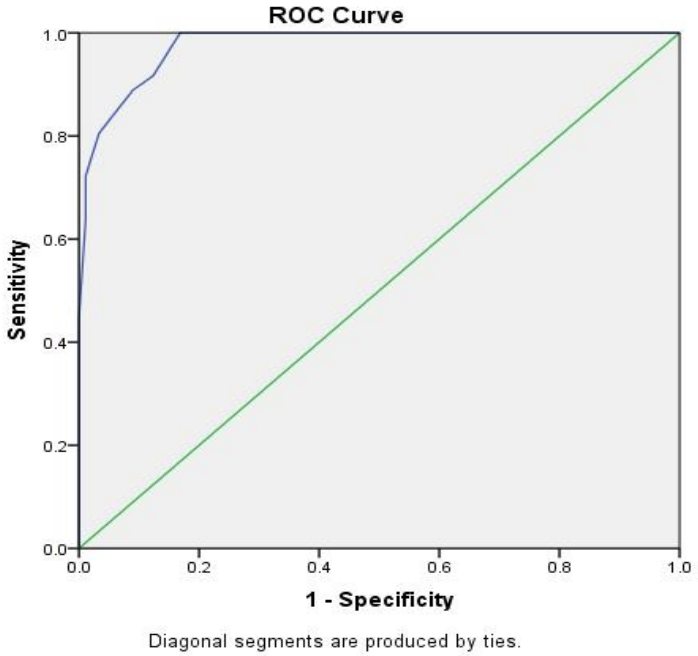
Table 16: predictive validity of Sofa Score at 0 hours in predicting overall mortality (N=130)

Parameter	Value	95% CI	
		Lower	Upper
Sensitivity	87.8%	77.79%	97.8%
Specificity	75.3%	66.32%	84.2%
False positive rate	24.7%	15.76%	33.7%
False negative rate	12.2%	2.18%	22.2%
Positive predictive value	62.1%	49.58%	74.6%
Negative predictive value	93.1%	87.18%	98.9%
Diagnostic accuracy	79.2%	72.26%	86.2%

Sensitivity of Sofa Score at 0 hrs in predicting overall Mortalitywas87.8% (95 CI 77.9%- 97.8%),

Specificity of Sofa Score at 0 hrs in predicting overall Mortality was75.3% (95 CI 66.32%-84.2%), False positive rate of Sofa Score at 0 hrs in predicting overall Mortality was 24.7% (95 CI 15.76%-33.7%), False negative rate of Sofa Score at 0 hrs in predicting overall Mortality was 12.2% (95 CI 2.18%-22.2%), Positive predictive value of Sofa Score at 0 hrs in predicting overall Mortality was 62.1% (95 CI 49.58%-74.6%), Negative predictive value of Sofa Score at 0 hrs in predicting overall Mortality was93.1% (95 CI 87.18%-98.9%),and the total diagnostic accuracy of Sofa Score at 0 hrs in predicting overall Mortality was79.2% (95 CI 72.26%-86.2%).

Graph 13: Predictive validity of sofa score at 48 hours in predicting subsequent mortality (N=125)



Basing on the ROC analysis the best cut off point for SOFA score at 48 hours, which yields best possible combination of sensitivity and specificity was identified as 7.5. Hence it was categorized as < 7.5, 7.5 and above and its validity in predicting mortality was analyzed.

Table 17: Association of Mortality after 48 hours with sofa score in study population (N=125)

Sofa score at 48	Mortality after 48 hours	
	Mortality	**Survival**
7.5 and above (N=51)	36 (70.59%)	15 (29.41%)
upto7.49 (N=74)	0 (0%)	74 (100%)

Out of 51 people with 7.5 and above sofa score at 48 hrs, 36 (70.59%) had Mortality. Out of 74 people with upto7.49 sofa score at 48 hrs, 0 (0%) had Mortality. No statistical test could be done due to "0" number of subjects in one of the cells.

Table 18: Predictive validity of Sofa Score in predicting Mortality at 48 hours (N=120)

Parameter	Value	95% CI	
		Lower	**Upper**
Sensitivity	100.0%	100.00%	100.0%
Specificity	83.1%	75.37%	90.9%
False positive rate	16.9%	9.08%	24.6%
False negative rate	0.0%	0.00%	0.0%
Positive predictive value	70.6%	58.08%	83.1%
Negative predictive value	100.0%	100.00%	100.0%
Diagnostic accuracy	88.0%	82.30%	93.7%

Sensitivity of Sofa Score in predicting Mortality after 48 hours was 100%(95 CI 100%- 100%),Specificity of Sofa Score at 48 hours in predicting Mortality was 83.1%(95 CI 75.37%- 90.9%),False positive rate of Sofa Score in predicting Mortality after 48 hours was 16.9%(95 CI 9.08%- 24.6%),False negative rate of Sofa Score in predicting Mortality after 48 hours was 0%(95 CI 0.00%- 0.00%),Positive predictive value of Sofa Score in predicting Mortality after 48 hours was 70.6%(95 CI 58.08%-83.1%),Negative predictive value of Sofa Score in predicting Mortality after 48 hours was 100%(95 CI 100%- 100%),and the total diagnostic accuracy of Sofa in predicting Mortality after 48 hours was 88% (95 CI 82.03%-93.7%).

Table 19: Comparison of predictive validities of SOFA scores at admission and at 48 hours.

Parameter	AUC(Area under the curve)	95% CI	P value
SOFA at admission	0.920	(0.875-0.965)	<0.001
SOFA at 48 hours	0.976	(0.955-0.997)	<0.001

The Area under the curve of ROC curve for SOFA score at Admission in predicting Mortality was 0.920(95% CI 0.875-0.965), which was statistically significant. The Area under the curve of ROC curve for SOFA score at 48 hrs in predicting Mortality was 0.976 (95% CI 0.955-0.997), which was statistically significant.

DISCUSSION

In this cross-sectional study of 130 patients with sepsis, demographic factors, comorbid conditions, clinical presentation and laboratory parameters were evaluated. SOFA score was applied to the cases under study at admission and after 48 hours.

In our study population, there were 130 cases of sepsis, out of which there were 89 survivors and 41 non-survivors and out of those 41 non-survivors, 5 patients had mortality within first 24 hours of admission.

In the present study, it was observed that maximum number of patients with sepsis were in the age group 40-59 years which had 52 cases(40%) followed by 60-79yrs with 45 pts (34. 62%).The youngest patient was 18yrs old and the oldest was 85yrs. This is comparable to the study done by Martin GS et al and Mayr et al.[84, 85]

In our study 86 (66.15%) patients were males and 44 (33.85%) patients were females. Male preponderance was seen with Male: Female ratio of 1.95:1.This finding is consistent with a study done by Sakry et al.[86]

Diabetes was the most common co morbid condition 78 (60%) found among patients in our study followed by hypertension that is 53 patients (40.77%) followed by IHD-14 patients (10.77%), CLD-11 patients (8.46%), COPD-10 patients (7.69%), others were 10 patients (7.69%) which includes bed sore, seizure disorder, BPH, RVD positive status, pulmonary Koch's, CKD-6 patients (4.62%), CVA-3 patients (2.31%) and cases with no risk were -29(22.31%). This was in concordance with the study done by Abhinandan et al.[87]

In our study we observed distribution of patients according to vital parameters, and observed that maximum patients presented with tachycardia which were 113 cases (86.92%).65 cases (50%) presented with blood pressure below 90/60mmhg and 65 cases (50%) presented with a blood pressure of above 90/60mmhg , 123 cases (94.32%) presented with tachypnoea , 69 cases(53.08%) presented with a temperature of above 100.4^0F, 61 cases(46.92%) had temperature of $96.9\text{-}100.3^0$F. our findings were comparable to the study done by Zohreh Aminzadeh et al.[88]

We observed that the most common cause of sepsis in our study population was pneumonia - 34 cases (26.15%), followed by urosepsis (19.23%) followed by mixed infection 11.54% which includes patients with bedsore with pneumonia, lower limb cellulitis with pneumonia, OPP with pneumonia, SBP with pneumonia, followed by SBP, 4.62%, puerperal sepsis 3.85%, dengue fever 3.85%, leptospirosis 3.85%, malaria 3.85%, and others- 23.08% which include cellulitis, meningitis, bronchiectasis, mucormycosis, cholecystitis, Ludwig's angina, parotid gland abscess, intestinal obstruction, abdominal tuberculosis. Similar observation was found in the study by Alberti et al.[89]

We observed that maximum mortality was in the age group of 40 -59 that is total of 17 patients followed by 60-79yrs where there was a mortality of 12 patients. The mean age for non-survivor was 49yrs and survivors 53.25yrs. Our observation is not consistent with other studies, maybe due to difference in the sample size

Similarly, when we compared sex with mortality, we observed females had a higher percentage of non-survivors (43.18%) when compared to males (25.58%). This is comparable to the study by Jones et al.[90]

On comparing etiology of sepsis with mortality, we found highest mortality was seen in pneumonia patients (24.39%), followed by spontaneous bacterial peritonitis in chronic liver disease patients (14.63%). This observation is similar to that by Mayr et al.[85]

In our study, we observed that for a score ≤7, 5 patients (6.94%) had mortality, score of 8-15 had a mortality of 35 cases (61.4%) and score >15 had 1 patient who had mortality (100%). We also observed the mean score SOFA score at admission (o hour) for survivor was 5.39 and mean SOFA score for non-survivor was 10.85, this was statistically significant. In the study done by Bale et al, it was observed there were 56 % mortality among those with SOFA ≤7, 70% mortality for score between 8-15.[91]They also noted that the mean sofa score for survivors 4.5 and non survivor was 6.63 respectively. The discrepancy between studies can be due to the difference in sample size.

Similarly, we observed after 48 hours patients with sofa score <7 had 0 mortality, score of 8-15 had a mortality of 30 cases (66.67%) and above 15 had 6 non-survivors (100%). The mean SOFA score at 48 hours for survivor was 4.16 and mean SOFA score for non-survivor was 12.83, this also was statistically significant. Though Bale et al in their study observed that <7 there were 52% non-survivor and between the score of 8-15 there was 88% non-survivors.[91] The mean score for survivors was 2.5 and for non-survivors was 6.96,respectively.

In the present study, it was observed that patients with mean value of sofa score at admission of 2.95 had a stay of less than 7 days, with 5.69 had a stay of 8-15 days and those with 7.2 had a stay of above 15 days. It was also observed that with a score of 10 there was higher mortality eventually, while score of 14.8 had worst

outcome in the form of mortality within 24 hours of admission. The p value for predicting the outcome and hospital stay with mean sofa score was significant. Similarly, we observed, patients with mean sofa score at 48 hours of 1.26 had a stay of less than 7 days, with 4.69 had a stay of 8-15 days and those with 8.20 had a stay of above 15 days. It was also observed that with a score of 12.83 there was mortality. The p value for predicting the outcome and hospital stay with MEAN SOFA score at 48hours was significant.

On plotting ROC curve for sofa score at 0 hours and 48 hours we observed the following. SOFA score of 7.5 was the optimum cut off for both 0 and 48 hours. At 0 hours above the score of 7.5 there was 62.07 % mortality and for a score below 7.5 mortality was 6.94% which was statistically significant, whereas at 48hours for a score above 7.5 there was a mortality of 70.59% and below 7.5 there was no mortality.

With the cutoff of 7.5, the sensitivity and specificity of SOFA score at 0 hours was 87.8% and 75.3% respectively. While at 48 hours the sensitivity was 100% and specificity was 83.1%.

The AUC obtained from the ROC curve at 0 hours and 48 hours was 0.920 and 0.971 respectively which shows SOFA score at 48 hours was a better predictor of outcome. Study by Abrar et al[92] showed a similar optimal cut of 7.5 which had a corresponding sensitivity and specificity of 77.4% and 74.4%.[92] A study by Jones et al demonstrated AUC of 0.75 at 0 hours and AUC of 0.84 at 72 hours.[90]

CONCLUSION

In our study, we enrolled 130 cases of sepsis:

- We observed that maximum of cases of sepsis were in the age group of 40-59 years (40%).
- Male cases (66.15%) outnumbered females (33.85%) with a male to female ratio of 1.95:1.
- Diabetes (60%) and Hypertension (40.77%) were the most common co morbidity seen in our study.
- The most common etiology for sepsis was pneumonia (26.15%) and urosepsis (19.23%).
- 84.92% cases presented with tachycardia and 94.62% presented with tachypnea. 53.08% and 50% cases had high grade fever and hypotension respectively.
- There was higher mortality in the age group of 40-59 years which was 32.69%.
- We observed that females had higher mortality (43.18%) as compared to males (25.58%).
- The mean sofa score for 0 hours (admission) for survivors was 5.39 and non-survivor was 10.85 whereas at 48 hours the mean sofa score for survivor was 4.16 and 12.83 for non-survivor respectively.
- In our study, we observed that patient with mean sofa score at admission of 2.95 had a stay of less than 7 days, with 5.69 had a stay of 8-15 days and those with 7.5 had a stay of above 15 days. At a mean score of 10 there was eventual

mortality, while a mean score of 14.8 had worst outcome in the form of mortality within 24 hours of admission.

- Similarly, cases with mean sofa score of 1.26 at 48 hours had a stay of less than 7 days, with 4.69 had a stay of 8-15 days and those with 8.20 had a stay of above 15 days. Patients with a score of 12.83 had mortality.
- On plotting ROC curve, we observed that the optimum cut off value for SOFA score for predicting mortality both at 0 and 48 hours was 7.5.
- The sensitivity and specificity to predict mortality at 0 hours was 87.8% and 75.3% respectively while at 48 hours sensitivity was 100% and specificity was 83.1%
- The AUC obtained for ROC curve was 0.920 and 0.971 at admission and 48 hours respectively, suggesting SOFA score at 48 hours as a better predictive index for outcome.

SUMMARY

This one-year hospital based cross sectional study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum from January 2016 to December 2016. A total of 130 patients admitted with sepsis in the intensive care unit were studied to find out the predictive value for sequential organ failure assessment score in outcome of sepsis patients.

We observed, Diabetes and hypertension were the most common co morbidity, Pneumonia and urosepsis were the most common causes of sepsis.

There was a higher percentage of mortality and longer duration of stay with increasing SOFA scores at both 0 and 48 hours.

Through statistical analysis we reached to a cut off value of 7.5 for predicting the outcome of patients. The sensitivity and specificity of score at 0 hours was found 87.8% and 75.3% while for 48 hours Sensitivity was 100% and specificity was 83.1%, hence 48 hours score was more specific and sensitive for prediction of outcome. Similarly, we found that AUC for 0 hours and 48 hours was 0.920 and 0.971 respectively, thus SOFA score at 48 hours was a better predictor as compared to score at admission.

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ANNEXURE I

CONSENT FOR PARTICIPATION IN RESEARCH

Mr. /Mrs._____ we are requesting you to enroll yourself in study titled **"SEQUENTIAL ORGAN FAILURE ASSESSMENT SCORE (SOFA) AS A PROGNOSTIC MARKER IN PATIENTS WITH SEPSIS IN AN INTENSIVE CARE UNIT OF A TERTIARY HOSPITAL." – A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY".-**

You have been requested to participate in research because your profile matches with the study group. All the patients admitted with SEPSIS can become participants of study. During the study you will be asked some questions and you are supposed to answer to the best of your knowledge.

Your participation in the research is absolutely voluntary. Your decision to participate in the study or otherwise will not affect your relationship with J.N.M.C. If you decide not participate you are free to withdraw at any time.

The purpose of research is to assess the severity and outcome of patients of sepsis with multi organ dysfunction at presentation and after 48 hours using sequential organ failure assessment score

Procedure involved

A detailed history, clinical examination, blood investigations to be conducted for the patients.

Risks and benefits

There are no risks involved and benefits are many. The study helps to identify the predictive value of sofa score in the outcome of patients with sepsis with multiorgan dysfunction in ICU care.

Alternatives

Even if you decline to participate, there will not be any change in the line of your management or the relationship with your doctor. You will be told about all the new information that may affect your decision to participate in the study.

Withdrawing/removal from study

You can withdraw any time from the study as you wish. You will not be penalized for such a decision.

Privacy and confidentiality

The only people to know that you are a research subject are the members of research team. No information about you or provided by you during the research will be disclosed to others without your written permission except:

In case of emergency to protect your rights and welfare if required by law.

Financial incentives for participation

You will not be paid any monetary benefits or free gifts for participation in the research. You will not be reimbursed for expenses.

Authorization to publish results

When the results of the research are published or discussed in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

CONSENT STATEMENT

I, the undersigned, have been explained in my own vernacular language about the study and my participation in the study is voluntary. If I want I can withdraw at any time. Also I have been given enough time to clear my doubts about the study and my rights as a study participant.

In case you have any questions about your rights as a study participant you can contact Dr. Ganga Pilli (09448868866).

Signature or the left thumb impression of the participant or legally authorized representative.

Participant's name: _____Signature: _____

Witness name: _____ Signature: _____

Experimenter's name: _____ Signature: _____

Guardian's name: _____ Signature: _____

Place: _____

Date: _____

ANNEXURE-II

PROFORMA

Case No:

NAME:

AGE/SEX:

IP No.

ADDRESS:

OCCUPATION:

COMPLAINTS AT PRESENTATION:

RISK FACTORS

EXISTING DIAGNOSIS:

ADMISSION DIAGNOSIS:

1)

2)

3)

PHYSICAL EXAMINATION:

GENERAL CONDITION:

Pallor: Yes/No

Icterus: Yes/No

Lymphadenopathy: Yes/No

Cyanosis: Yes/No

Clubbing: Yes/No

Edema: Yes/No

VITALS:

Temperature:

Pulse:

Respiratory rate:

Blood pressure:

SYSTEMIC EXAMINATION:

R. S.:

C.V.S.:

P.A.:

C.N.S.:

Investigations:

TOTAL COUNT:

PLATETLET COUNT:

SOURCE OF INFECTION IF KNOWN:

OTHERS:

Organ System	**SCORE**					**total**
	0	1	2	3	4	
Respiration PaO_2/FiO_2, mmhg	□ >53.3	□ 40-53.3	□ 0-39.9	□ 0-25.2	□ 0-13.3	
	□ >400	□ ≤400	□ ≤300	□ ≤200	□ ≤100	
Coagulation,Haematol. Platelets , x10E9/L *	□ >150	□ 101-150	□ 51-100	□ 21-50	□ 0-20	
Hepatic Bilirubin, µmol/l mg/dL	□ 0-19 <1.2	□ 20-32 1.2-1.9	□ 33-101 2.0-5.9	□ 102-204 6.0-11.9	□ >204 >12.0	
CNS Glasgow Coma Score	□ 15	□ 13-14	□ 10-12	□ 6-9	□ <6	
Circulation, Cardiovasc. MAP, mmHg	□ >70	□ 0-70	□ Dopamine ≤5.0 or dobutamine (any dose) [a]	□ Dopamine 5-14,9 or epi ≤0.1 or norepi ≤0.1 [a]	□ Dopamine ≥15 or epi >0.1 or norepi >0.1 [a]	
Renal s-creatinine, µmol/l mg/dL	□ <110 <1.2	□ 110-170 1.2-1.9	171-299 2.0-3.4	□ 300-440 3.5-4.9	□ >440 or dialysis >5.0	
Or urine output				Or <500 mL/24h	Or <200 mL/24h	

SOFA SCORE AT 0 HOURS:

SOFA SCORE AT 48 HOURS:

Organ System	**SCORE**					**total**
	0	1	2	3	4	
Respiration PaO_2/FiO_2,mmhg	□ >53.3	□ 40-53.3	□ 0-39.9	□ 0-25.2	□ 0-13.3	
	□ >400	□ ≤400	□ ≤300	□ ≤200	□ ≤100	
Coagulation,Haematol. Platelets , x10E9/L *	□ >150	□ 101-150	□ 51-100	□ 21-50	□ 0-20	
Hepatic Bilirubin, µmol/l mg/dL	□ 0-19 <1.2	□ 20-32 1.2-1.9	□ 33-101 2.0-5.9	□ 102-204 6.0-11.9	□ >204 >12.0	
CNS Glasgow Coma Score	□ 15	□ 13-14	□ 10-12	□ 6-9	□ <6	
Circulation, Cardiovasc. MAP, mmHg	□ >70	□ 0-70	□ Dopamine ≤5.0 or dobutamine (any dose) [a]	□ Dopamine 5-14,9 or epi ≤0.1 or norepi ≤0.1 [a]	□ Dopamine ≥15 or epi >0.1 or norepi >0.1 [a]	
Renal s-creatinine, µmol/l mg/dL	□ <110 <1.2	□ 110-170 1.2-1.9	171-299 2.0-3.4	□ 300-440 3.5-4.9	□ >440 or dialysis >5.0	
Or urine output				Or <500 mL/24h	Or <200 mL/24h	

Serial no.	I.P NO.	AGE	SEX	Risk factor	Vitals				INVESTIGATION			0 HOURS) for organ dysfunction							SCORE AT 48 HOURS OF ADMISSION							primary diagnosis	outcome at 0 hours	hospital stay in days / expired after 48 hours.
					BP	PR	TEMP (^{0}F)	RR	WBC	source of infection (if known)	OTHERS	PAO2/FIO2	PLATELET	bilirubin	GCS	MAP(mmhg)	creatinine	total score	FAO2/FIO2	platelet	bilirubin	GCS	MAP	creatinine	total score			
1	751781	24	F	NIL	70systolic	140 bpm	102.0	44	18,000	urine-sheets of pus 1		1	2	1	1	2	1	8	3	3	2	3	3	1	15	sepsis with MODS secondary to pyleonephritis		mortality
2	769372	28	M	NIL	110/70mmhg	134 bpm	101.0	28	15,600	-		1	0	0	0	0	0	1	1	0	0	0	0	0	1	sepsis secondary to pneumonia		8
3	779236	21	F	NIL	90/60mmhg	116 bpm	101.0	38	14,500			0	1	0	0	0	0	1	0	0	0	0	0	0	0	pneumnia,sepsis with shock		10
4	798563	54	F	HTN,DM	80/60mmhg	138 bpm	99.6	40	46,000	peritonitis		1	1	0	0	0	0	2	0	2	0	0	0	0	2	peritonitis.sepsis in shock		18
5	769993	43	F	HTN,DM	80 systolic	118bpm	99.0	26	14,700			0	1	2	1	2	0	6	1	2	2	1	0	0	6	sepsis secondary to acute cholecystitis,DM,HTN		12
6	796702	48	M	DM	90/60mmhg	120bpm	104.0	30	3,600	urine- c/s		0	0	0	0	0	0	0	0	0	0	0	0	0	0	urosepsis		4
7	775114	45	m	DM,HTN,	70 systolic	124bpm	99.8	42	19,600			1	2	4	2	2	0	11	2	2	4	2	2	1	13	choleycystitis,aspirationn pneumonia sepsis		mortality
8	777997	55	F	DM	80 systolic	114bpm	102.0	34	25,600			1	1	0	1	2	0	5	0	1	0	0	0	0	1	pleural effusion,pnemunia,sepsis		10
9	769513	84	F	DM,HTN,	80 systolic	142 bpm	101.0	40	28,500			1	1	0	1	2	1	6	1	0	0	0	0	0	1	urosepsis,pneumonia		8
10	746926	45	F	-	70 systolic	126bpm	101.0	38	2400			1	2	1	1	2	4	11	1	2	2	2	2	4	14	leptospirosis,ARF sec to sepsis		mortality
11	743909	54	M	DM	70 systolic	124bpm	99.8	36	1,75,000	urine- c/s	E.COLI	1	2	0	2	2	4	11	2	2	1	2	3	4	14	urosepsis,sepsis with shock		mortality
12	744958	70	M	BPH,DM,HTN	100/70	90bpm	98.5	28	21,300			0	2	1	0	0	2	4	0	1	0	0	0	2	3	Rt pyelonephritis with sepsis		7
13	740054	70	M	Post CABG,DM,HTN, COPD	90/60	108BPM	98.5	40	3,400	sputum c/s	Staph.aureus	1	2	0	0	2	1	6	0	1	0	0	0	1	2	Rt lower lobe pneumonia wih sepsis		14
14	739823	19	M	-	80 systolic	136bpm	103.0	29	2000			0	2	0	0	2	1	5	0	3	0	0	0	0	3	DENGUE FEVER WITH SEPSIS AND MODS		7
15	763458	23	M	MVP	90/60	128bpm	104.0	34	15,300			0	1	0	0	0	1	0	0	0	0	0	0	0	0	Lt sided pneumonia with sepsis		6
16	753225	63	M	-	90/70	104bpm	102.0	28	14,000	blood c/s	S.Paratyphi	0	S	2	0	0	1	4	0	1	3	0	0	0	4	ENTERIC FEVER WITH SESPIS		6
17	751446	80	M	IHD,DM,HTN	100/70	124bpm	100.0	19	17,800			0	0	0	0	0	0	0	0	0	0	0	0	0	0	Acute Gastroenteritis with sepsis ,MODS		5
18	751496	40	M	HTN	80systolic	114bpm	102.0	42	49,000			2	3	1	3	2	1	12	3	2	1	3	3	2	14	Viral pnemonia with sepsis		mortality
19	784241	61	M	Old CVA,DM	90/60	136bpm	101.0	40	38,900			1	1	0	1	0	1	4	1	1	0	1	0	1	4	DKA ,Lt sided pneumonua,Sepsis		15
20	746346	68	F	Old CVA,DM,HTN,POST CABG	80 systolic	124 bpm	100.0	46	14,500			1	0	0	2	2	1	6	1	1	0	2	0	1	5	Aspiration pneumonia with sepsis		12
21	714691	64	M	k/c/o chronic liver disease	80/60 mmhg		102.0	38	32.4	Ascitic fluid cells-4000		1	2	2	2	2	1	10	2	3	3	3	3	1	15	SBP with sepsis.CLD,DM		mortality
22	714380	40	M		80 systolic	126 bpm	99.8	34	48,000			2	1	6	2	2	1	9	1	3	1	3	2	1	11	Aspiration pneumonia with sepsis, Organophosphorus compound posioning		15
23	714136	65	M	HTN, IHD, DM	80 systolic	136 bpm	103.0	36	3,200			1	2	1	0	2	1	7	2	3	1	1	2	1	10	Leptospirosis, Sepsis with MODS, Grade 3 Bedsore		15
24	701489	27	M		80/50 mmhg	136 bpm	100.0	44	1,01,200	Pus C/S- Staph.aureus		2	4	1	2	2	2	13	2	4	2	2	3	3	16	Sepsis secondary to wound infection, S/P # left tibia		mortality
25	708045	54	M	DM	90/60 mmhg	98 bpm	101.0	36	16,900			1	2	0	0	2	1	6	2	2	1	1	2	2	10	Lung Abcess in sepsis, DM		20
26	701507	42	M	DM	100/70 mmhg	114 bpm	99.8	26	3,600			1	1	0	1	0	1	4	2	1	0	0	2	1	6	Obstructive uropathy with Sepsis, DM		9
27	712118	60	F	IHD,DM, Hypothyroid	70 systolic	114 bpm	100.0	32	38,000			1	1	1	2	1	1	7	2	1	1	1	2	1	8	Pneumonia with Sepsis, IHD, DM, Hyperthyroidism		mortality
28	716561	65	F	DM, HTN	90 systolic	112 bpm	101.0	36	22,600			1	0	0	0	2	0	3	0	0	0	0	0	0	0	Malaria, Sepsis with MODS		8
29	716501	76	M	Chronic Alcoholism	90/60 mmhg	134 bpm	100.0	34	42,000			1	1	1	0	0	0	3	0	1	2	0	0	0	3	Alcoholic Pancreatitis, Sepsis with MODS		10
30	712532	62	M	DM,HTN,Old CVA	80 systolic	132 bpm	102.0	36	42,000			2	1	1	2	2	1	9	2	2	1	3	3	2	13	Dengue Fever, Sepsis with Grade 3 Bedsore, Old CVA, DM, Hypertension		18
31	753124	38	M		80/60 mmhg	124 bpm	100.0	38	24,600			0	1	0	0	2	1	4	0	1	0	0	0	0	1	Acute Gastroenteritis, ARF secondary to sepsis		6
32	746573	59	F	DM,HTN, Hypothyroid, Post CABG	90/60 mmhg	120 bpm	102.0	28	2300			0	1	1	0	0	1	3	2	3	1	1	1	2	10	sepsis secondary to osteoyleitis Lt knee,post CABG,HTN,DM,HYPOTHYROIDISM		14
33	764212	37	M	OPP with intermediate syndrome	90/60 mmhg	124 bpm	104.0	38	49,000			2	1	3	3	2	4	15								OPP with imtermediate syndrome, Sepsis secondary to bedsore	mortality	
34	767237	45	M	DM,HTN, Post CABG	90/60 mmhg	106 bpm	101.0	24	13,400			1	1	0	0	0	1	3	0	0	0	0	0	1	1	Malaria with Sepsis with MODS, DM, HTN, Post CABG,		4
35	778132	64	M	COPD, Myasthenia Gravis	80 systolic	126 bpm	103.0	40	26000			3	1	1	3	3	3	14	1	1	0	3	3	2	10	Sepsis secondary to right sided pneumonia, Grade 2 Bedsore		mortality
36	748976	62	M	DM	90/60 mmhg	124 bpm	101.0	40	3,600			1	2	1	0	0	0	4	0	2	1	0	0	0	3	Sepsis secondary to hepatic abcess		12
37	754922	81	F	Old CVA, Seizure Disorder	70 systolic	136 bpm	102.0	40	18,400	ET Tube, C/S- Acinetobacter Baumanni		2	2	1	2	2	0	9	1	2	0	2	2	1	8	Sepsis secondary to aspiration pneumonia, Old CVA, Seizure Disorder		mortality
38	748818	62	M	DM,HTN	80 systolic	128 bpm	98.0	36	19,600	Pus C/S- Coagulase -ve Staph.aureus		0	0	0	0	2	1	3	0	1	0	0	0	1	2	Sepsis secondary to left lower limb cellulitis, DM, HTN		10
39	749317	58	F	Post MVR, HTN, DM	90/60 mmhg	106 bpm	101.0	28	32000			0	1	0	0	0	1	2	0	1	0	0	0	0	1	Sepsis secondary to Pneumonia, Post MVR, DM, HTN		7
40	747733	46	M	DM, HTN	70 systolic	126 bpm	102.0	48	1,200			2	3	2	1	0	1	9	1	1	1	2	2	1	8	Sepsis secondary to Pneumonia,DM, HTN		14
41	768375	24	M		90/60 mmhg	114 bpm	102.0	36	25,800	Urosepsis, Leptospirosis		2	1	1	1	0	1	6	1	1	0	0	0	1	3	Urosepsis		7
42	760859	71	M	DM,HTN	80/60 mmhg	98 bpm	102.0	26	25,600			0	0	2	0	2	4	8	1	1	1	0	0	4	7	Urosepsis, Acute on Chronic Kidney Disease		10
43	759884	45	M	Chronic Alcoholism	80 systolic	124 bpm	102.0	40	21,600			1	2	2	1	2	3	11	1	3	3	3	0	2	12	ARF secondary to Hepatorenal syndrome, Sepsis secondary to SBP		mortality
44	761756	68	M	DM	90 systolic	94 bpm	99.0	26	15,300			0	2	2	0	2	1	7	0	2	1	0	0	1	4	Malaria, Dengue, Sepsis,DM		12
45	743030	46	M	DM, HTN	70 systolic	112 bpm	99.0	42	22,000	Urine C/S- E.Coli		1	2	1	1	2	4	11	0	1	0	0	0	4	5	ARF secondary to urosepsis, DM		9
46	743490	50	F	DM, HTN	110/70 mmhg	114 bpm	99.0	27	17,300			0	0	0	0	2	1	3	0	1	0	0	0	2	3	Sepsis secondary to lt lower limb cellulilits, Malaria, DM		7
47	759071	47	M		80 systolic	62 bpm	100.0	28	2,800	Blood c/s- Chrysobacterium Meningosepticum		2	2	3	3	3	2	15								Sepsis secondary to aspiration pneumonia, Menengitis	mortality	
48	778626	58	M	Chronic Alcoholism, HTN, DM	90/60 mmhg	112 bpm	100.0	18	15,600			1	3	3	1	0	0	8	2	3	3	1	2	0	11	Sepsis secondary to acute hepatitis, HTN, DM		9
49	698417	82	M	HTN, DM	100/70 mmhg	134 bpm	99.8	22	11,600			0	1	0	0	0	0	1	0	0	0	0	0	0	0	Dengue, HTN, DM		6
50	766176	22	F		80/60 mmhg	124 bpm	100.0	32	28,100			2	4	2	2	2	3	15	2	4	2	2	3	2	15	Peurpeural Sepsis, aspiration Pneumonia		mortality
51	7848280	61	M	fracture acetabulam	90/60mmhg	112bpm	98.6	28	52,100			2	1	1	2	0	2	8	2	2	0	1	2	2	9	Aspiration pneumonia ,AKI secondary to sepsis ,fracture acetabulam		16
52	784146	64	M		70 systolic	126 bpm	103.0	34	18,600			1	4	2	2	2	1	12	2	4	2	2	2	1	13	viral hepatitis with sespis		mortality

Serial no.	I.P NO.	AGE	SEX	Risk factor	Vitals				INVESTIGATION			0 HOURS) for organ dysfunction							SCORE AT 48 HOURS OF ADMISSION							primary diagnosis	outcome at 0 hours	hospital stay in days / expired after 48 hours.
					BP	PR	TEMP (°F)	RR	WBC	source of infection (if known)	OTHERS	PAO2/FIO2	PLATELET	bilirubin	GCS	MAP(mmhg)	creatinine	total score	FAO2/FIO2	platelet	bilirubin	GCS	MAP	creatinine	total score			
53	718295	53	F	DM	70 systolic	102bpm	98.5	26	41,300			0	2	1	1	2	3	9	1	3	1	1	3	3	12	urosepsis		mortality
54	710946	25	M		90/60mmhg	94bpm	102.0	28	4,200			1	1	1	2	2	1	8	0	1	0	1	0	1	3	sepsis secondary to right lower lobe pneumonia		10
55	799166	49	F	DM,HTN	130/70mmhg	112bpm	99.0	28	1,100			2	3	0	2	0	4	11	3	4	1	3	3	4	18	ARF SECONDARY TO SEPSIS,PLELONEPHRITIS		mortality
56	799906	65	M	COPD, HTN,DM	80/60mmhg	114bpm	102.0	30	21,300			2	0	0	0	2	0	4	2	0	0	0	0	0	2	Rt sided pneumonia with sepsis,COPD,HTN,DM		14
57	799731	80	F	DM,HTN	90/60mmhg	110bpm	102.0	28	17,800			1	1	0	1	2	2	7	0	2	0	0	0	1	3	sepsis secpndary to b/l lower lobe pneumonia,DM,HTN		9
58	799076	75	M	OSA,Bed sore grade ii,DM,HTN	100/70mmhg	118bpm	99.4	36	19,100			1	1	0	1	2	1	6	1	2	1	1	0	1	6	Urosepsis,OSA,DM,HTN,Bed Sore grade ii		12
59	799989	70	M	Alcoholism,HTN,DM	80/60mmhg	114bpm	98.4	28	16,500			0	0	1	0	2	1	4	1	1	1	0	0	1	4	Acute on Chronic Pancreatitis.SEPSIS WITH MODS		10
60	799890	56	M	COPD,HTN,smoker	90/60mmhg	124bpm	102.0	36	18,100			3	0	1	0	2	1	7	2	0	0	0	0	1	3	B/L lower lobe pneumonia with sepsis,COPD,HTN		8
61	799272	76	F	HTN,DM	70 systolic	126bpm	99.8	32	16,300			1	3	0	2	2	1	9	1	2	1	3	2	2	11	Small bowel obstruction ,Sepsis secondary to Lt sided pneumonia,HTN,DM		mortality
62	799522	25	M		80/60mmhg	110bpm	99.4	30	19,100			0	3	0	0	2	1	6	0	2	2	0	0	3	7	Leptospirosis,SEPSIS with MODS		12
63	799733	62	M	CKD,HTN	90/60mmhg	114bpm	99.6	34	17,700			1	1	0	0	2	4	8	0	1	0	0	0	4	5	Urosepsis ,Acute on Chronic kidney disease,HTN		8
64	800704	70	F	COPD,CKD,HTN	110/70mmhg	118bpm	102.0	32	24,700			1	1	0	0	2	4	8	1	0	0	0	0	4	5	Lt sided pneumonia with sepsis,Acute on chronic renal failure,HTN,COPD		12
65	801084	48	F	HTN,RA,CKD	80/50mmhg	102bpm	99.5	29	34,000			1	2	1	0	2	3	9	1	2	0	0	0	2	5	Rt sided pneumonia with sepsis,acute on chronic kidney disease,HTN,RA10		10
66	800884	84	M	COPD,DM,SEIZURE DISORDER	80/60mmhg	114bpm	103.0	30	17,300			1	1	1	1	2	1	7	2	2	1	1	2	1	9	Rt sided pneumonia with sepsis ,COPD,DM		12
67	800250	79	M	DM,HTN,COPD	80systolic	114bpm	102.0	34	17,100			1	0	1	0	2	1	5	2	1	1	1	2	3	10	Urosepsis,COPD,DM,HTN		15
68	740053	50	M	DM,HTN,Chronic smoker	90/60mmhg	92bpm	99.2	18	13,200	Urine C/S- klebsiella		0	1	0	0	2	1	4	1	2	0	0	2	2	7	Cystitis ,Sepsis with MODS		8
69	739825	23	M		120/70mmhg	84bpm	101.0	18	14,400			0	1	1	0	0	0	2	0	0	1	0	0	0	1	Lt sided pneumonia		6
70	740016	18	F		90/60mmhg	88bpm	102.0	19	4,200			0	2	1	0	0	0	3	0	1	0	0	0	0	1	Dengue fever,Sepsis with MODS		7
71	782615	65	M	COPD	80systolic	120bpm	101.0	40	17,500			3	2	2	2	2	2	13	3	3	1	3	2	2	14	B/l pneumonia with sepsis,COPD		mortality
72	783204	67	M	HTN,Chronic bronchitis	100/70mmhg	98bpm	98.6	32	15,600			2	0	1	1	0	1	5	1	1	1	0	0	1	4	Lt sided pneumonia with sepsis ,Chronic bronchitis,HTN		10
73	669387	46	F	DM	80/60mmhg	128bpm	102.0	42	24,900			3	2	2	2	2	2	13	3	3	4	4	3	3	20	Severe sepsis,ARDS,Acute GE		mortality
74	718959	25	F		70systolic	120bpm	101.0	24	23,000			1	3	2	3	2	3	14	3	3	2	3	3	4	18	Acute Gastroenteritis with sepsis ,MODS		mortality
75	801082	28	F		110/70mmhg	124bpm	98.6	34	21,500			2	2	4	3	3	2	16								Puepeural sepsis with MODS	mortality	
76	801657	48	M	Chronic liver disease(alcoholic)	90/60mmhg	118bpm	102.0	32	19,100			1	3	4	2	3	1	14	3	3	4	3	3	3	19	ALD with portal hypertension in encephalopathy,sepsis sec to SBP mortality		mortality
77	802117	62	M	CKD,DM	90/60mmhg	98bpm	99.4	42	19,600			1	0	0	0	2	4	7	2	0	0	0	0	4	6	Rt sided pneumonia with sepsis ,CKD,DM		10
78	801980	62	M	DM,HTN	110/70mmhg	110bpm	98.0	26	14,200			2	0	0	1	3	4	10	2	2	1	3	3	4	15	Sepsis sec to Rt lower limb cellulitis,Urosepsis,HTN,DM		mortality
79	801471	52	F	DM	90/60mmhg	118bpm	103.0	28	3,800			2	1	0	1	2	0	6	1	0	0	0	0	1	2	Lt sided pneumonia with sepsis		8
80	801906	53	M	DM	100/40mmhg	98bpm	98.6	24	49,000			1	2	1	1	2	2	9	0	1	0	1	2	2	6	Urosepsis9emphysematous pyelonephritis),DM		12
81	802445	73	M	HTN,DM,IHD	80systolic	118bpm	98.6	34	11,400			1	2	1	2	2	3	11	0	1	1	1	0	3	6	obstructive uropathy,ARF sec to Sepsis,HTN,DM,IHD		14
82	802390	55	F	DM	90/60mmhg	106bpm	99.4	23	19,000			1	2	0	0	2	2	7	1	3	0	1	2	3	10	Lt sided pneumonia wih sepsis,DM		mortality
83	801285	49	F		100/70mmhg	114bpm	99.0	17	23,700			1	2	1	1	2	1	8	0	1	1	1	3	2	8	Urosepsis		10
84	802713	35	M	OPP with intermediate syndrome	100/70mmhg	130bpm	102.0	34	23,700			2	2	1	2	2	0	9	2	3	0	3	3	1	12	OPP with imtermediate syndrome, Sepsis secondary to Lt sided pneumonia,Rt hand cellulitis		mortality
85	802976	48	M	DM	100/80mmhg	126bpm	98.3	32	29,800			0	1	0	0	2	2	5	0	0	0	0	2	2	4	Urosepsis,DM		8
86	693563	60	M	DM,Alcoholic	80/60mmhg	123bpm	99.6	30	26,400			1	3	0	1	2	2	9	0	3	1	1	2	2	9	Acute on chronic pancreatitis ,sepsis,DM,CLD		14
87	692115	75	M	DM,HTN,IHD	80systolic	114bpm	102.0	28	37,700			0	0	2	1	2	3	8	0	1	1	0	2	2	6	Sepsis sec to Lt diabetic foot,HTN,DM,IHD		12
88	693219	44	M	DM	90/60mmhg	102bpm	99.4	32	2,600			0	2	0	0	2	1	5	1	1	1	0	0	0	3	Malaria with sepsis with MODS		8
89	697646	66	F	DM,COPD	80/60mmhg	98bpm	99.2	28	17,000			1	2	2	1	2	2	10	0	2	1	0	0	1	4	UTI,DKA with sepsis,COPD,DM		10
90	698336	50	F	DM	90/60mmhg	124bpm	100.0	24	3,200			0	2	2	0	0	1	5	0	2	2	1	0	0	5	Viral hepatitis with sepsis		12
91	708040	43	M	ALD,HTN	100/70mmhg	106bpm	100.0	26	21,600			0	2	2	1	0	1	6	0	3	3	1	2	1	10	Sepsis secondary to SBP,ALD with portal hypertension		mortality
92	698402	72	M	DM,HTN,IHD	100/70mmhg	114bpm	102.0	28	13,600			1	1	0	0	2	2	6	0	1	0	0	2	3	6	urosepsis,IHD,HTN.DM		8
93	768632	42	M	DM	90/60mmhg	112bpm	101.0	26	21,600			0	0	0	0	2	1	3	0	0	0	0	0	1	1	sepsis sec to Rt lower limb cellulitis,DM		7
94	695853	56	M	HTN,DM,CKD on MHD	70 systolic	114bpm	101.0	34	20,400			2	1	1	2	2	4	12	2	2	1	3	2	4	14	Acute on chronic kidney disease,aspiration pneumonia with sepsis,HTN,DM		mortality
95	721628	65	F	old pulmonarykochs,DM,HTN	90/60mmhg	114bpm	102.0	28	42,300			2	1	1	1	2	2	9	3	3	1	3	2	2	14	bronchiectasis,old kochs,sepsis with MODS,DM,HTN		mortality
96	733432	43	F	NAFLD,DM	90/60mmhg	98bpm	100.0	30	18,000			0	3	2	1	2	1	9	0	3	2	2	2	2	11	sepsis sec to SBP,NAFLD with portal hypertension,DM		mortality
97	726962	49	F	DM,k/c/o RVD	70 systolic	124bpm	102.0	27	41,000			1	2	2	1	2	2	10	2	3	3	3	3	2	16	abdominal tuberculosis,RVD,aSepsis ,DM		mortality
98	730020	60	F	DM	90/60 mmhg	108bpm	101.0	28	26,200			1	1	0	1	0	2	5	2	2	1	1	0	1	7	pulmonary kochs with sepsis ,DM		14
99	729775	48	M	DM	90/60mmhg	126bpm	100.0	26	13,000			0	1	0	0	0	2	3	0	0	0	0	0	0	1	urosepsis,DM		7
100	729631	50	F	DM,HTN	90/60mmhg	106bpm	102.0	30	19,800			0	1	2	1	2	1	7	1	2	2	2	2	1	10	sepsis sec to cholecystitis ,DM,HTN		14
101	721807	68	M	old pulmonary kochs,DM	70 systolic	107bpm	101.0	38	41,000			2	2	1	1	2	1	9	1	3	2	3	2	2	13	Sepsis secondary to lung abcess,Old pulmonary kochs,DM		mortality
102	721673	45	M	DM	100/70mmhg	120bpm	102.0	28	16,100			1	0	0	0	0	0	1	0	0	0	0	0	0	0	pulmonary kochs with sepsis ,DM		6
103	734244	55	M	HTN	100/70mmhg	116bpm	100.0	28	14,300			2	1	0	2	2	4	11	1	1	0	1	0	4	7	Lt foot cellulitis with sepsis,ARF sec to sepsis ,HTN		16
104	726906	73	M	DM,IHD	80 systolic	114bpm	102.0	36	21,300			1	1	0	1	2	0	5	0	1	0	0	0	0	1	Lt sided pneumonia with sepsis ,DM,HTN		10

Serial no.	I.P NO.	AGE	SEX	Risk factor	Vitals				INVESTIGATION			0 HOURS) for organ dysfunction							SCORE AT 48 HOURS OF ADMISSION							primary diagnosis	outcome at 0 hours	hospital stay in days / expired after 48 hours.
					BP	PR	TEMP (°F)	RR	WBC	source of infection (if known)	OTHERS	PAO2/FIO2	PLATELET	bilirubin	GCS	MAP(mmhg)	creatinine	total score	PAO2/FIO2	platelet	bilirubin	GCS	MAP	creatinine	total score			
105	732342	18	M		80/60mmhg	94bpm	101.0	23	3,200			0	4	1	0	2	0	7	0	2	0	0	0	0	2	dengue fever WITH SEPSIS AND MODS		6
106	757821	42	M	HTN	90/60mmhg	124bpm	102.0	34	4,100			1	3	2	1	2	2	11	0	2	1	0	0	1	4	malaria with sepsis		10
107	737002	51	F	DM	80/60mmhg	114bpm	101.0	30	31,300			0	1	0	0	2	3	6	0	2	0	0	0	4	6	urosepsis,Acute on chronic kidney disease,DM		12
108	738150	30	F		90/60mmhg	116bpm	104.0	34	30,800			1	4	2	1	2	3	13	3	3	1	3	2	1	13	puerpueral sepsis ,DIC		mortality
109	734574	53	F	DM	80/60mmhg	118bpm	102.0	26	17,700			0	1	0	0	0	0	1	0	0	0	0	0	1	1	leptospirosis with sepsis ,DM		8
110	690695	18	M		90/60mmhg	102bpm	99.0	18	11,800			0	1	0	0	0	1	2	0	1	0	0	0	2	3	Rt pyelonephritis with sepsis		8
111	782981	33	M	Chronic liver diease	80/50mmhg	108bpm	99.0	30	21,400			1	2	4	2	3	3	15								pneumonia left sided ,Chronic liver disease with portal hypertension	mortality	
112	782696	75	M	Chronic liver disease(hepatitis b)	80 systolic	114bpm	101.0	30	14,600			1	0	2	1	2	1	7	2	2	2	2	2	1	11	Sepsis secondary to SBP,CLD 9HEPATITIS B)		mortality
113	782916	70	M	DM,HTN,CKD ON MHD,IHD	80 systolic	128bpm	102.0	28	14,700			2	0	1	1	2	3	9	2	2	1	2	2	4	13	B/L lower lobe pneumonia with sepsis,DM,HTN,IHD,CKD ON MHD		mortality
114	690853	54	M		90/60mmhg	124bpm	102.0	36	24,000			1	1	0	0	0	0	2	0	0	0	0	0	0	0	ludwigs angina ,sepsis with MODS		8
115	694596	55	M	DM,HTN	80/60mmhg	114bpm	100.0	32	1,43,000			1	2	1	2	2	2	10	1	2	1	1	0	3	8	Aspiration pneumonia with sepsis ,AKI secondary to sepsis ,Rt sided pyelonephritis		14
116	758344	21	M	CML	70systolic	130bpm	101.0	30	18,000			1	3	1	1	2	0	8	1	2	1	2	2	1	9	Mucormycosis with sepsis,CML		mortality
117	749686	62	M	DM,HTN,	90/60mmhg	118bpm	99.6	28	40,800	Pus c/s-Serratia odonfera 1		1	1	1	0	2	0	5	0	1	0	0	0	1	2	Lt sided pyelonephritis with sepsis ,HTN,DM		10
118	687501	24	M		80 systolic	108bpm	101.0	40	22,600			2	0	0	0	2	0	4	2	0	0	0	0	0	2	Viral pneumonia with sepsis		7
119	688622	40	F	DM	70 systolic	91bpm	99.0	28	15,800			1	2	0	1	2	0	6	1	2	1	1	2	1	8	Rt lower limb cellulitis with sepsis,DM		mortality
120	691298	55	F	DM,HTN	90/60mmhg	126bpm	99.4	30	17,200			1	2	0	0	2	0	5	0	2	1	0	0	1	4	Parotid gland abcess with Sepsis		10
121	690912	30	F		80/60mmhg	120bpm	102.0	28	28,000			1	0	1	0	2	1	5	0	1	1	1	2	1	6	Peupeural sepsis		10
122	689708	65	M	DM,HTN,IHD	80/60mmhg	98bpm	99.0	34	28,600			0	2	0	2	2	2	8	0	1	0	1	0	2	4	Rt sided pyelonephritis with sepsis,HTN,DM,IHD		10
123	690856	22	F		90/60mmhg	114bpm	102.0	32	2,500			0	2	0	0	2	0	4	0	1	0	0	0	0	1	Cerebral malaria with sepsis		8
124	763454	23	M		90/60mmhg	128bpm	101.0	34	13,300			0	1	0	0	0	1	2	0	1	0	0	0	1	2	leptospirosis with sepsis		10
125	801083	25	F		80 systolic	120bpm	102.0	40	28,700			1	2	4	2	2	2	13								peupeural sepsis	mortality	
126	814293	52	F	HTN,DM	90 systolic	110bpm	101.0	36	17,000			2	0	3	1	2	2	11	3	2	3	2	2	1	13	viral pneumona with sepsis ,DM,HTN		mortality
127	819120	46	M	DM,K/C/O CKD on MHD	80 systolic	116bpm	99.0	28	10,600			1	1	2	1	2	3	8	1	1	1	0	2	3	8	Lt sided pneumonia with sepsis,CKD on MHD,DM		12
128	815894	78	M	DM.IHD,HTN	90 systolic	114bpm	100.0	26	12,600			1	2	2	2	1	1	9	2	3	2	2	2	2	13	Intestinal obstruction with sepis,IHD,HTN,DM		mortality
129	816658	63	M	DM,HTN	90/60 mmhg	123bpm	99.0	24	11,300			0	1	1	1	1	1	5	2	1	0	0	0	1	4	urosepsis ,DM,HTN		8
130	816872	64	M	DM,HTN,IHD	90/60mmhg	110bpm	99.0	28	10,500			1	1	2	0	1	1	6	1	2	1	0	0	1	5	Lt sided pneumonia with sepsis,HTN,DM,IHD		12

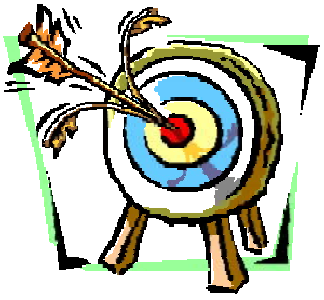
ANNEXURE-IV

KEY TO MASTER CHART:

BP	-	Blood Pressure
BPM	-	Beats Per Minute
CABG	-	Coronary Artery Bypass Surgery
CKD	-	Chronic Kidney Disease
CLD	-	Chronic Liver Disease
CML	-	Chronic Myeloid Leukemia
COPD	-	Chronic Obstructive Pulmonary Disease
C/S	-	Culture Sensitivity
CVA	-	Cereberovascular Accident
DIC	-	Disseminated Intravascular Coagulation
DKA	-	Diabetic Ketoacidosis
DM	-	Diabetes Mellitus
E.COLI	-	Escheresia Coli
ET	-	Endotracheal Tube
FIO2	-	Fraction Of Inspired Air
GCS	-	Glasgow Coma Scale
HTN	-	Hypertension
IHD	-	Ischemic Heart Disease
LT.	-	Left
MAP	-	Mean Arterial Pressure
MHD	-	Maintenance Haemodialysis
NAFLD	-	Non Alcoholic Fatty Disease
OPP	-	Organophosphorus Compound Poisoning

PAO2	-	Partial Pressure Of Oxygen
PR	-	Pulse Rate
RR	-	Respiratory Rate
RT	-	Right
RVD	-	Retroviral Disease
SBP	-	Spontaneous Bacterial Peritonitis
STAPH.AUREUS	-	Staphylococuccus Aureus.
TEMP `	-	Temperature

Introduction



Objectives

Review of Literature

Methodology

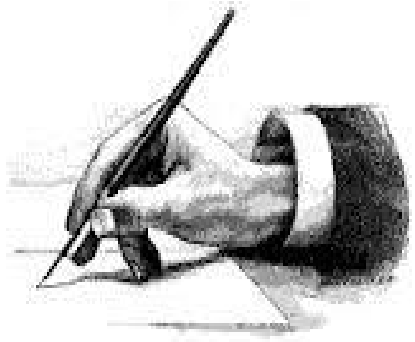
Results

Discussion

Conclusion

Summary

Bibliography



Annexure-I

Annexure-II

Annexure-III

Annexure-IV