"A COMPARATIVE STUDY OF SOFA, APACHE II, SAPS II, AS A PREDICTOR OF MORTALITY IN PATIENTS OF SEPSIS ADMITTED IN MEDICAL ICU"

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LIST OF ABBREVATIONS

- ACh Acetylcholine
- ACTH Adrenocorticotrophic hormone
- AKI Acute kidney injury
- Ang Angiopoietin
- AP-1 Adaptor protein 1
- APC Activated protein C
- ATF6 Activating transcription factor 6
- AVP Arginine vasopressin
- C3 Complement protein 3
- C5a Complement component 5a
- CAP Cholinergic anti-inflammatory pathway
- CHOP CEBP homologous protein
- CLP Cecal ligation and puncture
- CLRs C-type lectin receptors
- Cpb1 Carboxypeptidase b1
- CRP C-reaction protein
- DAMPs Damage-associated molecular patterns
- DCs Dendritic cells
- DIC Disseminated intravascular coagulation
- ER Endoplasmic reticulum
- ERK1/2 Extracellular signal-regulated kinase 1/2
- ETC Electron transfer chain
- FcγR1 Fc-γ receptor-1
- G-CSF The cytokines granulocyte colony-stimulating factor
- GM-CSF Granulocyte-macrophage colony-stimulating factor
- GRP94 Glucose-regulated protein 94
- HMGB-1 High-mobility group box-1
- HPA Hypothalamic-pituitary-adrenal
- IL-1 Interleukin-1
- iNOS Inducible nitric oxide synthase

- IRAK-M Interleukin-1 receptor-associated kinase-M
- IRE1 Inositol-requiring enzyme 1
- IRF7 Interferon regulatory factor 7
- JNK c-Jun N-terminal kinase
- LODS Logistic Organ Dysfunction Score
- LPS Lipopolysaccharide
- MAPK p38 Mitogen-activated protein kinase
- MCP-1 Monocyte chemoattractant protein-1
- miRNA MicroRNA
- MMPs Matrix metalloproteinases
- NA Noradrenaline
- NF-κB Nuclear factor-κB
- NK cells Natural killer cells
- NLRs NOD-like receptors
- NRF-1 Nuclear respiratory factor-1
- NS Neonatal sepsis
- PAI-1 Plasminogen activator inhibitor-1
- PAMPs Pathogen-associated molecular patterns
- PCT Procalcitonin
- PD-1/PD-L1 Programmed death receptor-1 and programmed death ligand-1
- PERK PKR-like endoplasmic reticulum kinase
- PMX-HP Polymyxin B hemoperfusion
- PRRs Pattern-recognition receptors
- qSOFA Quick Sequential Organ Failure Assessment
- rhAPC Recombinant human APC
- RLRs RIG-I like receptors
- RNS Reactive nitrogen species
- ROS Reactive oxygen species
- rTM Recombinant TM
- SIGIRR Single Ig IL-1R-related molecule
- SIRS Systemic Inflammatory Response Syndrome
- SOCS1 Suppressor of cytokine signaling 1

- SOFA Sequential Organ Failure Assessment
- ST2 Stimulation expressed gene 2
- sTREM-1 Soluble triggering receptor expressed on myeloid cells-1
- TAK-242 Resatorvid
- TFAM Transcriptional activator of mitochondrial transcription factor A
- TLRs Toll-like receptors
- TM Thrombomodulin
- TNF-α Tumor necrosis factor-α
- TOLLIP Toll interacting protein
- t-PA Tissue plasminogen activator
- u-PA Urokinase-type plasminogen activator
- α7nAChR α7 nicotinic ACh receptor

ABSTRACT

Introduction

Sepsis is a life-threatening organ dysfunction with high mortality and morbidity. Various mortality prediction scores are currently in use for prediction of mortality. Although combination of various scores have not been used before. The aim of the study was to compare SOFA, APACHE II, SAPS II, as a predictor of mortality and to access for usefulness of combination of different scores.

Materials and Methods

A one-year hospital based prospective study conducted from 1st January 2020 to 31st December 2020 in KLEs DR Prabhakar Kore hospital& MRC, Belagavi, where 100 patients of sepsis admitted in ICU with evidence of organ dysfunction were included in the study and various scores like SOFA, APACHE II, and SAPS II were calculated at 24 and 48 hours of admission, using laboratory results and clinical examination. and an attempt to access for predictive accuracy of combination of scores was undertaken.

Results

Mortality of 51 % was observed, with maximum admission(37%) and moratilty(39.22%) in age group of 60-79, with higher mortality in female group of (68.63%). Mean SOFA, APACHE II, SAPS II were significantly higher in the mortality group than the recovery group. On comparing individual scores highest sensitivity was seen with APACHE II at 24 as well as 48 hours being 64.10% and 78.79% respectively, highest specificity was seen with SAPS II at 24 and 48 hours being 96.97% and 87.88% respectively. On combining the various scores SAPS II and

SOFA showed highest Youden's index 56.64 at 24 hours

Conclusion

All scores namely SOFA, SAPS II, APACHE II have shown good diagnostic performance in our study with APACHE II showing highest sensitivity at 24 and 48 hours and SAPS II showing highest specificity at 24 and 48 hours. However, on combination of scores SAPS II and SOFA has shown slight better diagnostic performance.

Key words: Acute Physiology and Chronic Health Evaluation (APACHE) III, Simplified Acute Physiology Score (SAPS) II, simplified organ failure assessment (SOFA), Predictor of mortality.

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INTRODUCTION

Infection-induced sepsis is a severe, complex condition with a high fatality rate. However, despite years of research and a huge cost impact on health care systems, sepsis continues to cause high mortality in people.[1]

Appropriate sepsis therapy has been shown to reduce mortality in general critical care patients in recent years.[2,3] Septic patients should be categorised into high-risk and low-risk groups based on main risk scoring systems (e.g., mortality risk).[4]

Sepsis-related organ failure assessment (SOFA) and Acute Physiology and Chronic Health Evaluation scoring system II (APACHE II) are two of the most regularly utilised risk scoring systems. However, there are several drawbacks to using these scales. For example, the APACHE II score has an exaggerated penalty for old age and does not consider malnutrition or cachexia in the chronic health evaluation;[5,6] prognostic biomarkers are thus urgently needed.

Sepsis is hypothesised to be caused by microcirculatory and coagulation abnormalities, which activate coagulation factors and platelets.[7] Severe sepsis can be diagnosed and predicted using laboratory tests for coagulation markers. An important role for activated platelets in sepsis pathogenesis has been revealed by researchers.[8] Immature platelets, referred to as reticulated platelets, are found in the bloodstream. It is the percentage of reticulated platelets (RP percent) that make up the total number of platelets. There is a larger percentage of RP in patients with acute coronary syndromes or stroke than in the general population.[9] There is some indication that RP % can be used as both a normal laboratory test and an affordable daily screening test for bacterial infection in persons with neutrophilia.[10] According to the findings of

another study, it can be used to predict the beginning of sepsis in the emergency room.[11]

In the course of severe sepsis research, reliable prognostic signs have been uncovered. Recent studies on inflammatory imbalance, immunological dysfunction, mitochondrial damage, coagulation disorders, neuroendocrine–immune network anomalies, endoplasmic reticulum stress, and autophagy have substantially increased our understanding of sepsis' aetiology. Many people are still dying from a systemic disease that affects several organs, such as sepsis, even after being admitted to the hospital.

In the past, doctors in intensive care units were able to predict patients' outcomes based on their subjective assessments. This is why it's necessary to anticipate outcomes and evaluate therapy quantitatively for critically sick patients who may undergo physiological distress that could lead to impairment or death in just days, hours, or even minutes. ICU rating methods have thus been developed and widely used. Tachypnea, tachycardia, hypotension, decreased urine output, or altered consciousness are some of the clinical markers used by these systems.

Severity and mortality models make up the two main components of ICU ratings, which are derived using an equation to estimate survival rates in the next several days following hospitalisation.[12] Patients' treatment, triage, or comparative assessments can be compared using these models, which aid in decision-making. It is possible to employ ICU scoring systems in addition to their primary duties in clinical observation of critically-ill patients to monitor the administered treatments and to assess organ dysfunctions during the course of hospitalisation.[13]

Use of scoring methodologies to determine the severity of disease in intensive care units (ICUs) is becoming the norm. APACHE II, Simplified Acute Physiology Score (SAPS) II, and Sequential Organ Failure Assessment (SOFA) are the finest devices for this purpose.[14-15]

The APACHE, SOFA, SAPS, and MPM scoring systems are only a few of the many predictive scoring models available, each with their own set of pros and disadvantages. It's critical to employ a predictive model that's been tested on the target population recently if you want the best results. Other considerations include the system's usability, accessibility, practicality, financial implications, and the evaluation's outcome (e.g. length of hospital stay vs predicted mortality rate).

A good example of this is the APACHE IV model, which is more accurate in predicting mortality than the SAPS model, but it is more difficult and expensive to apply because it requires more variables and requires proprietary software. When employed in intensive care units, the APACHE IV test is more accurate at predicting length of stay than the APACHE II test. Whereas SAPS model is less expensive and easier to use, APACHE IV model is better at predicting length of stay and less susceptible to case-mix effects than the SAPS model.[16]

Hence the present study was done at our tertiary care centre to assess and compare the predictive accuracy for mortality of the three predictive scoring system in the ICU namely SOFA, APACHE II and SAPS II

AIMS AND OBJECTIVES

AIM:

- To assess and compare the predictive accuracy for mortality of the three predictive scoring system in the ICU namely SOFA, APACHE II and SAPS II.

REVIEW OF LITERATURE

Historical Perspectives

The word ‘‘sepsis’’ has its origin in the word ‘‘σ΄ηψις’’, which is the original Greek word for decomposition or putrefaction, and has been used in that context since before Hippocrates.[17-18] Sepsis has been around for more than 2700 years, yet we have only just begun to comprehend the underlying biology of the disease. Even though the name ‘‘sepsis’‘is frequently associated with the modern intensive care unit, the medical idea is far older. Hippocrates (460–370 BC) is credited with coining the term ‘‘sepsis,’‘which refers to the idea that living tissues can be degraded in one of two ways. ‘‘Pepsis’‘ was the term used to describe the process of food digestion or the fermentation of grapes to make wine. It was nutritious, nourishing, and enjoyable. When it comes to ‘‘sepsis,’‘ on the other hand, it was referred to as the rotting of flesh and the decomposition of wounds.[19] Pasteur, Koch, and Lister's observations, which proved the microbial aetiology of the process and dramatically changed the management of infection, predated his views by more than two millennia. Ibn Sina (979–1037 BC) noticed that septicemia (blood putrefaction) and fever occur in the same person. Until the 19th century, classical antiquity's concept of sepsis was used.

There were two major contributions to our understanding of sepsis by Ignaz Semmelweis (1818-1865).[20]

Glasgow Royal Infirmary surgeon Joseph Lister worked there from 1827 to 1912.[21] 50 percent of patients with amputations died of sepsis when he became surgical department chairman. In light of Semmelweis' observations, Pasteur's research findings, and the deaths that occurred at his hospital, Lister formed a connection between the three.

As the medical director at Eppendorf Hospital in Germany, Dr. H. Lennhartz was instrumental in shifting perspectives on sepsis from one of putrefaction to one of bacterial disease. However, it was his student Hugo Schottmüller (1867-1936) who in 1914 established the way for a current description of sepsis: ‘‘Sepsis is present if a focus has developed from which pathogenic bacteria, constantly or periodically, invade the blood stream in such a way that this causes subjective and objective symptoms.”

In 1967, Ashbaugh and colleagues examined patients in intensive care who had difficulty breathing, had poor lung compliance, and had diffuse alveolar infiltration. It was referred to as Adult Respiratory Distress Syndrome (ARDS), a condition that was usually fatal. Severe sepsis patients were rapidly aware of this side effect.

Patients in intensive care units face numerous difficulties due to septic shock and other forms of acute sepsis. Despite the development of critical care medicine, the fatality rate from sepsis ranged from 27% to 55% in different studies.[22-23] There has been an increase in the number of people with sepsis, especially as life expectancy, invasive methods of diagnosis and treatment, multi-drug-resistant bacteria, and cancer and AIDS incidences have increased. Sepsis patients demand a large amount of ICU resources, and the related costs are huge, in addition to their high mortality. When multiple organ failure (MOF) occurs, ICU stay lengthens significantly, which in turn has a negative impact on patient prognosis.[14] Rather than causing organ failure, infection triggers host reactions that damage endothelial cells, increase vascular permeability, activate the intravascular coagulation system, and trigger apoptosis, all of which eventually lead to the development of progressive organ dysfunction. This

new knowledge about sepsis' pathophysiology explains how this happens. Systemic inflammatory response (SIRS) and the concurrent release of pro-inflammatory cytokines have traditionally been blamed for multiple organ failure in sepsis. Researchers now believe sepsis might be categorised as a bimodal illness. Many anti-inflammatory processes are activated during sepsis, including the production and release of cytokine receptor antagonists, as well as anti-inflammatory cytokines.[24]

Terminologies

Terminology	Definition
SIRS	The Systemic Inflammatory Response Syndrome (SIRS) is manifested with two or more of the following criteria: - Fever (Temp > 38.3°C) or hypothermia (Temp < 36°C) - Tachycardia (heart rate >90 beats/min) - Tachypnoea (>20 breaths/min) or $PaCO_2$ < 4.3 kPa (32 mmHg) with Spontaneous Respiration or need for Artificial Respiration - Leukocytosis or leukopenia (WBC > 12,000 or < 4,000/mm^3) or >10% immature forms/ Band cells
Sepsis	Presence of SIRS in response to confirmed or probable source of infection. SIRS is manifested by two or more of the criteria mentioned above.
Severe Sepsis	Severe Sepsis as Sepsis associated with Organ dysfunction, Hypoperfusion, or Hypotension (systolic blood pressure <90 mmHg or a reduction of >40 mmHg from base line in the absence of other causes of hypotension). Hypoperfusion and perfusion abnormalities may include, but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status
Septic Shock	Sepsis with persistent hypotension despite adequate fluid resuscitation. Hypotension is defined as a systolic blood pressure < 90 mmHg or MAP < 65 mmHg or decrease of systolic blood pressure by 40 mmHg or more from the baseline.
Multiple Organ Dysfunction Syndrome (MODS)	Defined as presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention.

Definition of Sepsis

Biological, pathological, and physiologic abnormalities are all hallmarks of sepsis, which is caused by an infection. More than a decade ago, a number of medical investigations defined the term ‘‘sepsis’’ in terms of the various types of infections that can be caused by sepsis.[25] Sepsis' definition and diagnosis have been amended three times by the international academic community in an effort to increase the clinician's understanding of the disease, identify and diagnose sepsis at an early stage, and successfully treat the condition. It was unanimously agreed that ‘‘a life-threatening organ failure’‘ is the third definition of sepsis, which is the result of a host's inadequate response to infection as per the 45th society of critical care medicine.[26] To describe sepsis, one must consider the host's uncontrolled response to infection and life-threatening organ malfunction Severe sepsis might be diagnosed differently depending on whether the patient is in an intensive care unit or not. If the Sequential Organ Failure (SOFA) score is 2 points, then sepsis is diagnosed in patients with an ICU infection or suspected infection; for patients with a non-ICU infection, two qSOFA (systolic blood pressure less than 100 mm Hg, respiratory rate loss greater than 22 times/min, and change in consciousness) or more than two positive sepsis diagnosis are required.

When an infection causes an unstable host response that can lead to death, this new definition underlines the importance of prompt detection, which extends well beyond the risk of infection itself. As a result, the new and improved definition of sepsis 3.0 now incorporates the severe circulatory and metabolic issues caused by sepsis, as well as the significantly increased mortality risk compared to sepsis alone.[27] More than 2 mmol/L of blood lactate in patients with septic shock requires the use of

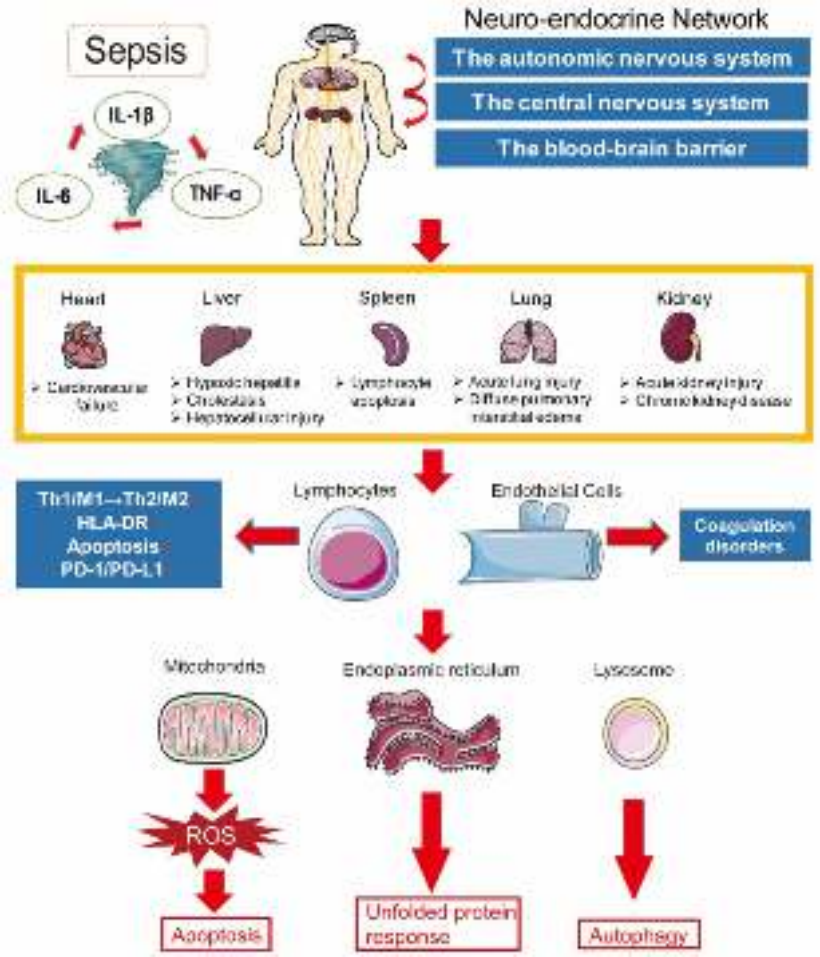
vasopressors to maintain an arterial pressure of 65 or above and a high lactate level i.e., level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia.

However, according to the most recent definition of sepsis, clinical diagnostic criteria such as SOFA, SIRS, Logistic Organ Dysfunction Score, and qSOFA remain ambiguous. A critical care physician at the University of Pittsburgh's Department of Critical Care Medicine, Dr. Seymour, devised an assessment based on the multicenter clinical data collection, suggesting that qSOFA's predictive validity for inpatient mortality was higher than that of SOFA and SIRS among patients suspected of infection. In order to encourage doctors to explore further, begin or escalate treatment, or consider referral to intensive care or increasing the frequency of monitoring, if necessary, the qSOFA standard might be utilised.[28] New diagnostic criteria generated from arduous retrospective investigations were instantly questioned when Sepsis 3.0 was announced. According to the ACCP, qSOFA and SOFA could put patients at risk by delaying the detection of serious infections and delaying treatment.[29] Treating an infection should not be delayed if the qSOFA and SOFA values do not match 2 or more. QSOFA has been the subject of discussion since its first presentation. The qSOFA score is derived from a retrospective analysis of non-ICU patients. It is difficult to obtain clinical information about patients outside of the intensive care unit. This means that the data used in qSOFA assessments may not be comprehensive or objective. There may be a problem with the current qSOFA score because it is too sensitive and specific. If a patient's basic blood pressure is below 100 mmHg and he or she is experiencing discomfort, aggravation, etc., a breathing rate of 22 times per minute may be an indicator of sepsis. It is possible that the qSOFA predictive value may be lower than that of other commonly used scoring systems because qSOFA may be oversensitive. [14,17,18] qSOFA, SOFA, or SIRS cannot be used to define sepsis

alone. The combined use of both of these criteria is necessary while treating patients with sepsis.[30]

Pathogenesis of Sepsis

Severe sepsis isn't just an inflammatory reaction or an immunological illness; rather, it affects several organs and systems in the body. Septic shock's complicated pathophysiology includes an imbalance in the immunological response, immune dysfunction, mitochondrial deterioration, hemorrhagic necrosis and other pathophysiological processes that ultimately contribute to organ malfunction, such as endoplasmic reticulum stress, autophagy, and more.



The complex pathogenesis of sepsis.

Inflammation Imbalance

Sepsis pathogenesis relies heavily on inflammation, which can be produced by a wide range of pathogens, such as bacteria, fungi, parasites and viruses. Intravenous infections often drive macrophages to absorb pathogens and generate pro-inflammatory cytokines, which can trigger cytokine storms and activate innate immune systems. PAMPs and DAMPs can activate pattern recognition receptors (PRRs), which in turn activate a cascade of activation in immune cells that results in the upregulation of inflammatory-related genes. Several types of PRRs, including Toll-like receptors (TLRs), C-type lectin-like receptors (CLRs) and RIG-I like receptors (RLRs), can interact with pathogen components (e.g., LPS) (NLRs).[31] The toll-like receptors (TLRs) are the receptors that receive the greatest attention in research. The TIR domains of TLRs stimulate the myeloid differentiation factor 88-dependent signalling cascade via activating the c-Jun N-terminal kinase (JNK), ERK1/2, mitogen-activated protein kinase (MAPK), and nuclear factor B (NF-B) signalling pathways. In response to these events, toxins such as interleukin (IL)-1, interferon (IFN) regulatory factor 7, and adaptor protein 1 can be generated. So many proteins, both membrane-bound and cytoplasmic-bound, are engaged in these carefully controlled activities, such as the single Ig IL-1R-related molecule (SIGIRR), growth stimulation expressed gene 2 (ST2), and so on [25]. Controlling TLR expression on the cell membrane also has an impact on TLR signalling. Since sepsis patients have elevated amounts of TLR4, TLR2, and mRNA, they are more susceptible to infection.

NLRs, which are soluble cytosolic PRRs, worsen the immunological imbalance caused by sepsis. NOD and LRR domains (similar to TLRs) are present in NLRs. Inflammasomes (also known as inflammatory inflammasomes) are protein complexes that contain a number of NLRs (such as NF-B, IFN-gamma, and AP-1), as well as RICK (also known as RICK). As the caspase-1 precursor is deactivated, it is cleaved into active caspase-1, which in turn deactivates the cytokines IFN-1 and IFN-18.[34]

The CLR family also includes dectins, DC-SIGN, and mannose-binding lectins. But further work is needed on Dectins' control of CLR responses. Despite DC-role SIGN's in the detection of Leishmania, Viruses, and Fungi, greater work is needed into the negative control of CLR responses.[35]

It has been discovered that PPRs, as well as the double-stranded RNA receptors RIG-I, MDA5, and LGP2, are involved in sepsis-induced immune dysfunction.

There are both exogenous and endogenous PAMPs that can stimulate PRRs. Liver cells are reported to release large amounts of HMB-1, which is linked to LPS and transported to cells via RAGE receptors on endothelial and macrophage cells, resulting in cell death (pyroptism) that leads to shock and multiple organ failure and, ultimately, to death in the case of endogenous sepsis.

Immune Dysfunction

Sepsis' pathophysiology is complicated by multiple variables, including the overexpression of cell-associated suppressor receptors, lymphocyte growth inhibitors,

apoptotic-inducing molecules, and anti-inflammatory chemical expression inhibitors.[36-37]

Infections are detected and phagocytized by endothelial cells and neutrophils during sepsis, when they release various substances and proteolytic enzymes that eliminate pathogens. When cytokines (e.g., GM-CSF, TNF-, INF-) or pathogenic microorganisms, chemical mediators, immune complexes, etc., excite mononuclear/ macrophage cells, the activated cells phagocytose and kill various pathogens and present antigens. A considerable amount of active medium is secreted by macrophages after they have been activated by effector T cells that have undergone differentiation, resulting in tissue damage and fibrosis. Septic patients' maturation process of dendritic cells (DCs) in the spleen and lymph nodes has been hindered. Innate immune cells, including as monocytes, natural killer (NK) cells, and granulocytes, are rapidly accumulated as a result of DC activation in sepsis. During the course of sepsis, monocytes play a significant role. Immunosuppression inhibits metabolic processes such as glycolysis, fatty acid oxidation, and oxidative phosphorylation, all of which are impaired in sepsis patients.[38] INF- production by NK cells can be increased, but they lose their ability to stimulate the Th1 immune response necessary for the clearance of bacterial infections.

Immunosuppression following a severe cytokine storm can lead to additional opportunistic infections, a resurgence of potential viruses, and the genesis of new infections. Those who survive may experience immunosuppression. Sepsis-induced immunosuppression affects both adaptive and innate immunity. Because of the stimulation of the TLR signalling pathway and the transition of naive T cells into regulatory T cells induced by cytokines, the immune system is unable to respond

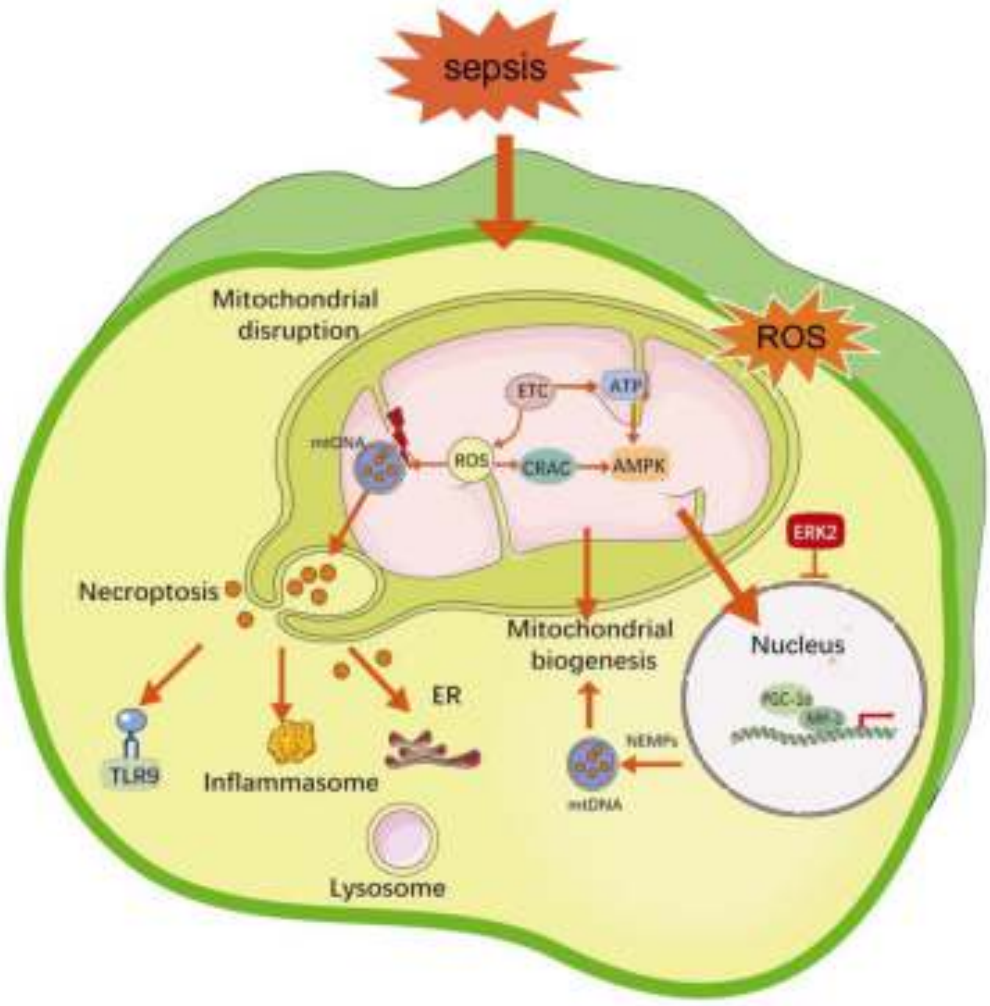
effectively after sepsis, resulting in decreased antigen presentation expression. To date we have identified 26 transcription factors that are linked to (for example IRF4, MUM1).

Mitochondrial Damage

Mitochondria are the primary bacteria for generating energy, synthesising protein, and breaking down trash. Due to mitochondrial damage or dysfunction, the apoptosis of organ cells and immune cells can lead to organ failure and even death as a result of multiple organ failure and oxidative stress, which can be caused by sepsis.

Due to a shortage of oxygen supply and an incomplete oxidative response, sepsis results in a significant increase in free radical production. Antioxidant systems are also impacted by the disease. When leukocytes are subjected to DAMPs or PAMPs that cause inflammation, cytokines are generated that raise the production of the NADPH oxidase enzyme. cytokines stimulate the activity of iNOS, which results in an overproduction of reactive nitrogen species (RNS) and NO. Electron-transfer chain inhibition is prevented when RNS is formed from ROS peroxides (ETC). ROS generation from the mitochondria increases during sepsis because the ETC is faulty. Additionally, mitochondrial damage is caused by decreased ETC activity, intimal injury, and mitochondrial DNA damage. When the mitochondrial matrix expands and ruptures, apoptosis is caused. It has been found that caspase inhibition can increase survival in sepsis, and this is due to the fact that sepsis-related apoptosis occurs in splenic lymphocytes and cells from other organs.[39] There is an increase in hepatocyte NRF-1, an activator of the mitochondrial transcription factor A (TFAM).[40] When damaged mitochondria are eliminated from the body, autophagy is triggered. Although the AMPK/PGC-1/NRF-1/2 signalling system regulates mitochondrial

biogenesis, insufficient ATP generation inhibits the activation of AMPK and the following PGC-1/NRF-1/2 pathway, which results in TFAM expression. Because TFAM is a transcription promoter that moves into the mitochondrial matrix, mitochondrial DNA is produced during mitochondrial biogenesis. There is evidence that mitochondrial density continues to decline following a severe sepsis event.[41] More research is needed to determine the role mitochondrial regulatory mechanisms play in sepsis-induced multiple organ failure and to identify potential therapeutic targets.[42]



The regulation mechanisms of mitochondrial damage during sepsis.

Coagulation Disorders

Sepsis pathophysiology relies heavily on the interaction between inflammation and coagulation. Sepsis activates the coagulation process, which amplifies the inflammatory response, which is triggered by inflammation.[43]

Antithrombotic system, tissue factor pathway inhibitors, and activated protein C (APC) system all control the activation of coagulation in normal settings. In the midst of sepsis, all three channels are thrown into disarray The three coagulation-inhibitor pathways have low levels of sustained protein consumption and breakdown because of poor protein synthesis. It has been shown that thrombomodulin (TM) and endothelial protein C receptor (ECPR) expression is diminished in the inflammatory response. A marked decrease in endogenous fibrinolysis occurs while plasminogen activator (t-PA) and u-PA plasminogen activator (u-PA) are released from vascular endothelial cell storage sites; these plasminogen activators stimulate plasminogen activator stimulation and sub-quantitative production, whereas PAI-1 continues to increase, making this effect diametrically opposite. Meningococcal meningococcal septic shock is more common in those with a PAI-1 polymorphism. When they develop Gram-negative sepsis, patients with the 4G/4G genotype have a greater death rate because of their elevated levels of PAI-1.[44]

Neuroendocrine–Immune Network Abnormalities

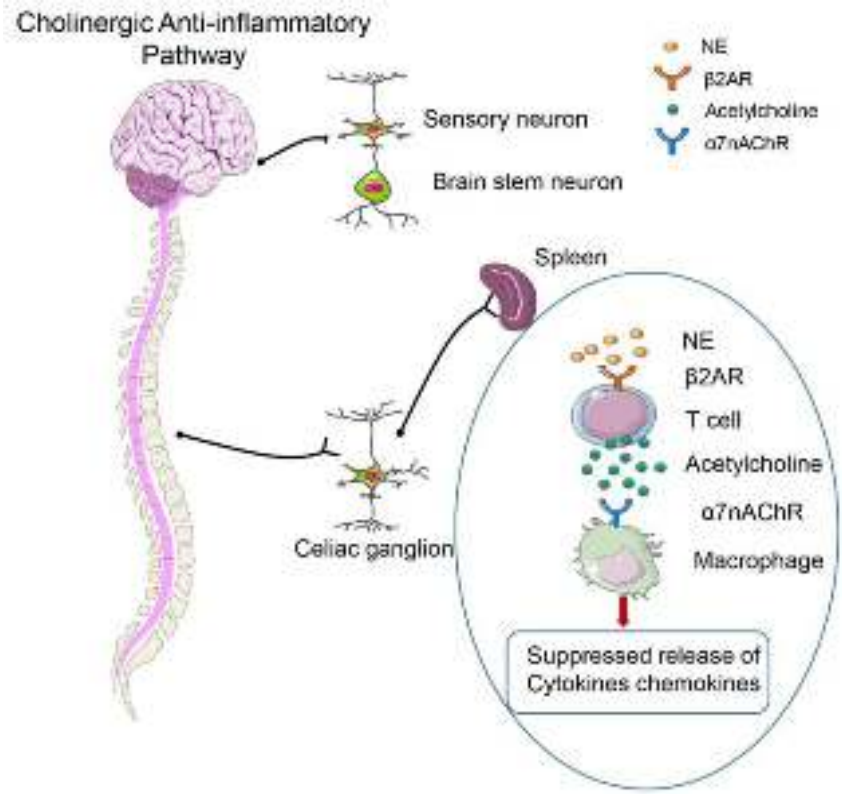
Neuroendocrine–immune system interaction is also considered a significant part of the host response during septic shock. As a result of PAMPs, the central nervous system has three primary mechanisms for dealing with threats: (1) the autonomic nervous system, which includes the vagus and trigeminal nerves; (2)

circulation-based inflammation mediators that are induced by PAMPs in the brain; and (3) activation of the innate immune system.[45]

For example, the vagus nerve and endothelial activity and dysfunction may be seen as “diffuse sensory organs” that deliver messages to the brain via cytokines and neurotoxic mediators.. The HPA axis is activated when the sympathetic and parasympathetic nervous systems are stimulated by efferent impulses from the central nervous system. Affective information While these two hypothalamus nuclei are functioning correctly, they produce corticotropin (CRH) and arginine vasopressin (AV) as a result of their normal activity (AVP). The pituitary gland is able to release more CRH when AVP is administered. As an example, the creation of adrenocorticotrophic hormone (ACTH), which in turn, is responsible for the release of adrenal cortisol, which is important for reducing inflammation and restoring cardiovascular homeostasis, is driven by AVP and CRH in future phases. Due to the decreased levels of CRP, ACTH and adrenal cortisol, the adrenal insufficiency syndrome is formed during sepsis. As a result, the sympathetic branch of the autonomic nervous system influences cytokine production. According to previous research, non-synaptic noradrenaline (NA) release can be activated by LPS, which has been demonstrated to decrease TNF- and IL-12 production and increase the expression of the antiinflammatory cytokine, IL-10. Adrenergic receptors on immune cells, which are linked to cAMP, have been shown to have a role in these findings.[46-47]

Inflammatory reactions are regulated by Ach signalling. A neurotransmitter is a chemical that affects the nervous system. An entirely new method to treating sepsis has been proposed in a study that focuses on the involvement of the vagus nerve in sepsis regulation. While it isn't known for sure, it is likely that activating the Cap can

reduce cytokine production, the differentiation of T cells, and neutrophil killing capacity. There is growing evidence that CAP's anti-inflammatory properties are linked to the vagus nerve, Ach; the Ach's unique 7 nicotinic ACh receptor (nAChR), and related intracellular signal transduction pathways. The 7 nAChR operates as a ‘‘effector”for anti-inflammatory activities by lowering pro-inflammatory molecules, modifying the differentiation and activation of immune cells, and regulating homeostasis when it interacts with ACh. When the vagus nerve is injured, endotoxic shock is more likely. When the nAChR is activated or the vagus nerve is stimulated, it can lessen the body's inflammatory response.[48-49] Cellular types with the 7nAChR also play an important role in anti-inflammatory effects by activating a variety of signalling pathways. For anti-inflammatory actions and cytokine production regulation, nAChRs are hypothesised to have an inhibitory influence on nAChRs.



The function of the cholinergic anti-inflammatory pathway (CAP) in sepsis.

Endoplasmic Reticulum Stress

The endoplasmic reticulum (ER), an intracellular organelle, is involved in the transport, folding, and posttranslational modification of proteins. Sepsis-induced ER stress is caused by the accumulation of proteins that are misfolded or unfolded. This changes the ER's balance and results in oxidative stress and severe calcium abnormalities. There may be an increase in cell mortality in response to ER stress, as signals from the unfolded protein response sensors shift. Finally, activated caspase-12 associated and activated caspase-12 migrating proteins, which are the final steps in the process of apoptosis in the cell. If ER stress (such as glucose-regulated protein 94, CHOP, and caspase-12) is high in various organs, including the heart or liver, then multiple organ failure may be triggered by this elevated ER stress. ER stress induces abnormal apoptosis in septic animals, suggesting that ER stress-mediated apoptosis may be a potential target for therapeutic prevention and therapy of sepsis.[50-51]

Autophagy

As part of the normal process, pathogens and other cytoplasmic compounds are taken up by the autophagosome and subsequently sent to the lysosome for destruction. As a fundamental defence mechanism, autophagy induces and regulates the natural immune-cell inflammatory response, and is a crucial element in the development of sepsis. Severe sepsis can be prevented by the production of anti-inflammatory cytokines, antigen expression, and pathogen clearance through autophagy.[52] T-cell autophagy deficiency in autophagy-deficient mice makes them more susceptible to LPS stimulation, according to a study that genetically ablates the ATG16L1 gene. Restoring cardiac function and mitigating CLP-induced myocardial

damage in a rat model of sepsis can be achieved by activating autophagy with rapamycin.

Biomarkers of Sepsis

To swiftly identify infections and prescribe medicines that are most likely to be effective, to evaluate the effects of medications, and to monitor organ function for prognosis, specific biomarkers associated to sepsis should be employed for clinical diagnosis.

Infection-Related Biomarkers

Procalcitonin (PCT)

PCT contains calcitonin precursors, a thyroid hormone. 73 sepsis patients in intensive care units (ICUs) were retrospectively studied by Pundiche et al. to assess the importance of dynamic procalcitonin (PCT) monitoring in the direction of antibiotic therapy. Antibiotic-resistant infections that could be life-threatening may be predicted by a PCT dynamic assessment, according to the data from the study.[53] Exogenous and endogenous stimuli such as cytokines and LPS can trigger the production of PCT in all organs, and PCT is a blood monocyte chemokine.[54] Patients with bacterial necrosis of the circulation or severe bacterial infections should be tested for PCT, a clinical diagnostic indicator for sepsis. PCT expression elevated dramatically within 2 to 6 hours of sepsis and peaked at 6 to 24 hours. On Day 1, there was a statistically significant difference between survivors (n = 1626) and non-survivors (n = 727), as well as a statistically significant difference on Day 3 (p = 0.002) in the mean PCT levels between the two groups. There was a statistically significant difference (p = 0.62) on Day 1 in a subset of patients with severe sepsis

and shock. PCT has been determined to be the most effective therapeutic option when all biological markers of inflammation are considered. Antibiotics can reduce bacterial resistance and shorten hospital stays when PCT levels fall below 0.5 ng/mL; the relative mortality rate is within 28 days of admission. Antibiotics should be stopped when the serum PCT level falls to 0.25 ng/mL. In the early stages of sepsis, PCT and other blood indicators for sepsis and septic shock can be used to detect the disease.

C-Reactive Protein (CRP)

If you've been infected with pathogens or have been injured by oxidative stress, your body will create CRP, an acute phase protein that's produced by the liver. The most frequently studied indicator of infection and inflammation is C-reactive protein (CRP).[55] There were 495 sepsis patients and 873 healthy subjects included in a meta-analysis to examine the diagnostic accuracy of CRP (CRP) for sepsis. CRP provides a moderate degree of value in the diagnosis of sepsis patients, according to the data.[56] When compared to other acute-phase proteins, the CRP level rises substantially more rapidly. Within 6–8 hours of infection, the CRP level rises and reaches a high within 36–50 hours. CRP has been shown to have a sensitivity range of 68–92 percent and a specificity range of 40–67 percent for detecting bacterial infection. Sepsis patients who have high CRP levels when they are admitted may be able to predict how effectively treatment would work for them if their CRP levels are high within the first 48 hours. As inflammation subsides and antibiotics are administered, CRP levels may reduce as a result of this process. In patients with sepsis, high CRP levels may be associated to the severity of infection and illness progression, but this hasn't been shown definitively.

Cytokines (TNF-α/IL-6)

TNF-α is a pro-inflammatory cytokine that has been widely studied in the pathophysiology of sepsis. Endothelial cells can be activated by TNF- to attract neutrophils. TNF- is released by macrophages within 30 minutes of infection and serves as a mediator and regulator of the body's innate immune response.[57] A sustained rise in TNF- levels is associated with an increase in inflammation and organ damage under the combined action of anti-inflammatory cytokines, resulting in a higher mortality risk in patients with sepsis. TNF- may serve as a significant prognostic marker for sepsis because of this method of action.

In addition to macrophages and lymphocytes (which account for the majority of its synthesis), IL-6 is also released into the body by other cells in response to infection.[58] B and T lymphocyte activation may be influenced by the amount of IL-6 in the blood. A spike in IL-6 levels in burn patients or patients having major surgery has been found to be associated with a wide range of indicators of disease severity. Post-surgical patients with severe sepsis who survive had decreased rates of infection in the first week compared to those who don't, according to current clinical studies. The measurement of IL-6 has been demonstrated to be a straightforward, noninvasive procedure that may be conducted in less than 30 minutes for the diagnosis of neonatal sepsis (NS) in newborns. IL-6, for example, has a sensitivity of 0.79 and a specificity of 0.84 when it comes to predicting necrotizing enterocolitis (NS). In summary receiver operating characteristic curves, the maximum combined sensitivity and specificity (Q value) was 0.82 and the area under the curve was 0.89. Although an overall sensitivity of 80.0 percent and 85.0 percent were found in the meta-analysis for sepsis in the general population, IL-6 exhibited a specificity of 77.0 percent in the

neonatal group.[59-60] As a result, IL-6 appears to be a good predictor of necrotizing enterocolitis (NS) and could be used as a reference for the early diagnosis of sepsis in neonatal intensive care units. In this prospective study, we analysed the clinical diagnostic significance of dynamic serum IL-1, IL-6, IL-8, and TNF- levels in neonatal sepsis, which included 12 patients who had culture-proven sepsis, 21 patients who had culture-negative sepsis, and 17 healthy neonates. The results demonstrate that IL-1, TNF-a, and TNF-b can be used in the diagnosis and evaluation of infant sepsis treatment.

Biomarkers Related to Inflammation Activation and Immune Imbalance

Monocyte Chemoattractant Protein-1 (MCP-1)

The CC chemokine family includes MCP-1, a tiny cytokine. The chemokine/cytokine array and enzyme-linked immunosorbent test were used in a prospective cohort research to find biomarkers for sepsis. Over the course of the study, 143 individuals with sepsis were enrolled and divided into two groups: those who survived (n = 87) and those who didn't (n = 56). Surviving patients had considerably lower plasma levels of MCP-1 compared to non-survivors, which indicates that MCP-1 is a viable biomarker for predicting sepsis outcomes. Chemotactic activation effects of MCP-1 are induced in monocytes/macrophages by monocytes/macrophages in the presence of inflammation. Cell-counting bead arrays were used to analyse the blood of 89 children with acute bacterial infections, including those with community-acquired pneumonia, sepsis, and abscesses. Three different cohorts of patients had significantly lower median plasma MCP-1 levels (24.9 pg/mL on average) than the 20 healthy controls. Another study used LuminexTM analysis to quantify baseline cytokine concentrations, and the results

showed that healthy males and females had serum MCP-1 levels of 62.8 and 55.4 pg/mL, respectively. Serum MCP-1 levels were favourably connected with SOFA ratings in children with meningococcal sepsis (r = 0.68), and in adults who died of sepsis, serum MCP-1 levels were significantly greater than those in survivors.[61-62]

Programmed Death Receptor-1 and Programmed Death Ligand-1 (PD-1/PD-L1)

PD-1 is known to be widely expressed on activated T cells, NK cells, and B cells, and is also expressed in hematopoietic and non-hematopoietic cells. The ability of PD-1 to suppress T-cell activation is dependent on the phosphorylation of the immunoreceptor tyrosine-based switch motif, which leads to the phosphorylation of downstream effector molecules playing a negative regulatory role, and inhibiting T cell proliferation and cytokine production. In the bodies of patients who died of sepsis, spleen cells exhibit severe dysfunction and the lungs also show immunosuppressive effects, which is probably due to the self-programmed death of immune cells caused by the immunosuppression in sepsis. The expression of inhibitory receptors on the surface of T-cells is upregulated due to chronic antigen stimulation, which also suggests the important immunosuppressive mechanism in sepsis.[63] The expression of PD-1 and PD-L1 has been reported to increase in T cells and monocytes of sepsis patients and animal models, respectively. Increasing numbers of studies have demonstrated that PD-1/PD-L1 blockade can be used to treat sepsis. To investigate the significance of dynamic PD-1-related molecules monitoring in evaluating the risk stratification and prognosis of septic patients, the 76 septic shock patients, 59 septic patients, and 29 healthy controls were enrolled to measure the PD-1 and PD-L1 expression on T cell and monocytes by flow cytometry. The results showed that only monocyte PD-L1 was associated with risk stratification and

mortality in 3–4-day septic patients. So far, the effects of PD-1/PD-L1 blockade on sepsis survival have only been tested in animal studies and need to be verified in human patients. Nevertheless, the PD-1/PD-L1 pathway plays a considerable role in sepsis-induced immunosuppression, and the blockade of this pathway may have a therapeutic value.

Soluble Triggering Receptor Expressed on Myeloid Cells-1 (sTREM-1)

sTREM-1 is mainly distributed on the surface of polymorphoonuclear cells and mature monocytes. When TLR2 or TLR4 bind to its ligand, TREM-1 is upregulated.[64] The upregulation of sTREM-1 initiates an intracellular cascade, which gives rise to the increasing expression of TNF-α, IL-8, and IL-1β, as well as increasing neutrophil degranulation. Concurrently, the expression of the anti-inflammatory cytokine IL-10 is downregulated. sTREM-1 is released into the serum by the mechanism of metalloproteinase shedding, and sTREM-1 binds to the ligand TREM-1 and thereby attenuates TREM-1-mediated inflammatory response. To determine the clinical diagnosis value of dynamic sTREM-1 in sepsis, 80 sepsis patients and 80 healthy controls were enrolled with sequencing TREM-1 genetic variation by PCR. The results indicate that the sTREM-1, APACHE II, and rs2234237 polymorphism are risk factors for prognosis by logistic regression. Meanwhile, the biomarkers of sepsis prognosis assessment are the dynamic changes of serum sTREM-1 and rs2234237 polymorphism. As an indicator for sepsis diagnosis, TREM-1 displays a highly favorable diagnostic ability in the identification of Shigella infection and sepsis, with a combined sensitivity of 79% and specificity of 80%. sTREM-1 levels were also dramatically higher in neonates with sepsis than in healthy newborns.[65]

Complement Pathway

Inflammatory cytokine production and caspase-11-dependent cell death are facilitated by the complement mechanism. As part of the phagocytosis process, complement proteins interact with a complement protein 3 (C3) fragment on the surface of microorganisms, which is critical to the bacterial infection and sepsis process. Complement cascade activation releases C5a (a pro-inflammatory peptide), which in turn triggers the release of other components. Complement proteins appear to have a significant role in the inflammation of sepsis patients, and C5a may serve as a critical indicator. Both in mice and in people, severe sepsis alters the levels of C5a.[66-67] Sepsis patients could benefit from C5a testing; however, these are still underutilised for autoimmune inflammatory diagnostics. A new diagnostic marker and therapeutic target for early sepsis is the Cpb1–C3–C3aR pathway. Cpb1 has been identified as a novel mediator of caspase-11 production in macrophages, and it has been shown that Cpb1 mediates caspase-11-dependent cell death. Increases MAPK activity and IFN receptor activation downstream of TLR4 through caspase-11 expression reduces the severity of illness in LPS-induced sepsis or endotoxemic mice.

Neutrophil Surface Receptor (CD64)

As a member of a family of immunoglobulins produced mostly on macrophages and monocytes known as CD64, Fc- receptor-1 (FcR1) is an important immunomodulator in both innate and adaptive immune responses. The expression of FcR1/CD64 on neutrophils in healthy individuals is exceedingly low; nevertheless, this protein is considerably enhanced following inflammation or infection. SIRS and sepsis may be worsened by the presence of FcR1/CD64 on neutrophils. The TLR4 signalling pathway is downregulated by the ablation of FcR1 in septic mice.[68] There

were a total of 1986 patients included in the meta-analysis of CD64 expression in adult sepsis patients in order to examine the diagnostic usefulness of CD64 expression. CD64 was found to be a valuable biomarker for the early detection of sepsis patients in the study outcomes.[69] Consequently, the expression of FcR1/CD64 on neutrophils could be exploited to detect the presence of sepsis.

MicroRNA (miRNA)

Many studies have looked into the role of microRNAs in controlling inflammatory responses. Patients who survived and those who died from sepsis were studied using microarray screenings to examine the expression of serum miR-574-5p, a dynamic serum miRNA. MiR-574-5p was found to be a more accurate predictor of death in sepsis patients than any other single sign. There is a growing body of evidence suggesting the inflammatory response can be inhibited by the actions of the miRNAs miR-9, miR-147, and miR-13299. Evidence suggests that miR-21 is capable of reducing inflammation by suppressing the synthesis of CD4 and NF-B. The expression of miR-21 in NR8383 cells treated with LPS was shown to be reduced. Although the expression of miRNA-218 falls dramatically in rats with acute lung injury, the expression of inflammation-related molecules increases. The activation of RUNX2 and NF-B may be to blame. White blood cell RNA transcripts such as CEACAM4, LAMP1, PLA2G7, and PLAC8 genes are considerably altered in sepsis patients compared to the general population, according to many studies. For sepsis diagnosis, FAIM3:PLAC8 gene expression ratio is more important than PCT.[70]

Plasma Cell-Free DNA

cf-DNA, or cell-free DNA, is extremely rare in normal human plasma; instead, most of the DNA in plasma derives from mitochondrial and nuclear DNA (mtDNA and nucleic acid, respectively). Fragmented, tiny double-stranded molecules (cf-DNA) make up plasma cell-free DNA (nDNA). When a person is suffering from severe sepsis, mtDNA and nDNA are released into the bloodstream, both of which bind to the recognition receptor (PRR), leading in the release of inflammatory cytokines into the bloodstream. The septic shock index can be used to gauge the severity of shock and organ damage, as well as to gauge the prognosis of septic shock. Cf-DNA levels in patients in the intensive care unit (ICU) are higher than those in the general population, according to new research. Patients in the intensive care unit (ICU) have larger concentrations of cf-DNA when they achieve sepsis or death than those of other disease processes and survivors. Cutoff values of 2.35 ng/L in patients with sepsis were shown to be 88 percent sensitive and 94 percent specific. Kung et al. examined plasma mtDNA levels in 68 patients with severe sepsis and 33 healthy patients as controls using real-time quantitative polymerase chain reaction. As a result, the plasma mtDNA concentration in the septic patients was significantly higher than that in healthy control subjects. There was a significant difference between the survival and non-survivor groups when it came to plasma mitochondrial DNA levels on days 1 and 4.[72] On the other hand, the 198 ng/mL receiver operating characteristic (ROC) cutoff value for plasma mitochondrial DNA levels on admission has a sensitivity of 91% and a specificity of 72%. According to research, a 1.0 ng/mL increase in plasma mitochondrial DNA concentration is associated with an increase in mortality rate of 7 percent.[71]

Presepsin (sCD14-ST)

mCD14 and sCD14 are two forms of the cell surface glycoprotein, cluster of differentiation 14 (CD14), which has a glycosylphosphatidylinositol tail (sCD14). A few micrograms of sCD14 can be found in the blood of a healthy person. When mCD14 is detached from the cell membrane, sCD14 can be used to identify apoptotic cells and to transfer other lipid molecules across cells. It can also be used to detect cell death when mCD14 is attached to the cell membrane.

An enzyme known as presepsin, which is also known as protease, breaks down sCD14 in the blood to produce sCD14-ST, which is a 64-amino acid N-terminal fragment. According to recent research on sepsis, the role of sCD14-ST (sCD14-ST) in diagnosing and predicting the disease's severity and mortality is becoming more prevalent. If bacteria and fungi invade a human body, the serum levels of prespsin rise dramatically. This is due to the fact that when the human body is not infected, the levels of prespsin are nearly undetectable. Yaegashi et al. evaluated 75 healthy volunteers, 80 SIRS patients, and 66 sepsis patients. Because of this, the plasma presepsin concentration in sepsis patients was significantly greater than in the control and nonseptic groups.[72] One prospective diagnostic biomarker for adult sepsis, sCD14-ST, can considerably increase within two hours and peak at three hours after infection, according to various studies. For at least five hours following surgery, a rabbit experimental model of sepsis showed a significant increase in the presence of presepsin in the blood of rabbits. A similar capacity to predict sepsis in 100 critically ill persons was demonstrated by PCT prior to sepsis. In research of sepsis and severe sepsis, Sozushima found a connection between the plasma concentration of prespsin and the severity of sepsis.[73] There are numerous studies which show a positive

correlation between the SOFA score and APACHE II and the plasma levels of presepsin. Previous investigations have shown that sepsis patients can benefit from the use of numerous marker controls. In light of these findings, the sCD14-ST diagnostic marker for sepsis has a lot of potential.

Biomarkers Related to Organ Dysfunction

Angiopoietin (Ang)

Neovascularization and the Ang family of proteins are intertwined processes. Vascular endothelial cells are impacted by bacterial endotoxin, which leads in cell migration and the activation of the inflammatory and coagulation pathways. Endothelial cells must remain stable in order to treat sepsis. The Ang–Tie system in the vascular endothelium is activated when sepsis occurs. Both Ang-1 and Ang-2 release endothelial growth factor (EGF), both of which have distinct roles in promoting vascular quiescence. Endothelial cells are stabilised by activating the Tie-2 receptor, while Ang-2 disrupts microvessel integrity by blocking the Tie-2 receptor and hence causes vascular leakage, one of the main mechanisms of organ dysfunction. Both high and low levels or high Ang-2/Ang-1 and low Tie-2 ratios have been connected to poor clinical results, organ dysfunction in sepsis and unsatisfactory outcomes;[74] these studies also imply that Ang-1 may be protective against organ malfunction, which is consistent with the findings of previous studies. It was decided to examine if dynamic Ang-2/Ang-1 ratios in sepsis would be relevant for clinical diagnosis, hence the study included patients with sepsis and healthy blood donors. Patients with a high Ang-2/Ang-1 ratio have a higher risk of complications.

Matrix Metalloproteinases (MMPs)

Following an internal injury, MMP-1 and TIMP-1 are two key regulators of wound healing. Although MMP-9, TIMP-1, and TIMP-2 are all elevated in severe sepsis, their expression levels are not. On the first day of the study, 37 patients with severe sepsis and 37 healthy volunteers were enrolled, and the plasma levels of MMP-2, MMP-9, TIMP-1, TIMP-2, and IL-6 in patients with severe sepsis were examined by ELISA methods to see if they were associated with prognosis. The most sensitive, specific, and positive predictive value (PPV) for sepsis were reported in MMP-9, TIMP-2, and TIMP-1. Another link between TIMP-1 and clinical outcomes in severe sepsis and the development of acute kidney injury (AKI) has been established. TIMP-2 expression increased significantly in mice exposed to CLP and HK-2 cells exposed to LPS. In animal models, TIMP-2 expression is associated with the severity of endotoxin-induced nephrotoxicity, although TIMP-2 silencing reduces CLP-induced cytokine release through blocking the NF-B pathway. Cell death and damage are reduced when TIMP-2 is silenced, and this decrease in cytokine release is most likely due to p-P65, a protein found in the cytoplasm. These findings show that TIMP-2 is a new therapeutic target for sepsis-related acute kidney damage (AKI) because of its harmful role in AKI.

There are numerous indicators that can be utilised to guide treatment in the event of sepsis and risk classification, antibiotic use, severity, and prognosis.[75] Sepsis biomarkers, including PCT, CRP, TNF-/IL-6, MCP-1, miRNA, and more than 170 additional biomarkers, have been identified.

The pathophysiology of sepsis is complicated by the fact that different indicators play diverse roles. Overdiagnosis and overuse of antibiotics can result from

the misuse of specific biomarkers. Many molecular biodiagnostic disciplines, for example, use bacterial DNA in the blood to detect sepsis because of the limited specificity of pathogenic blood cultures. Overdiagnosis of sepsis can be caused by misdiagnosis of bacteremia that has no clinical importance or biological properties using this new method of testing as a result, patients with mild sepsis may be given broad-spectrum antibiotics in an attempt to save their lives. As a side note, there are still a number of pressing scientific questions that must be answered. For instance, what specific biomarkers are used to more effectively distinguish between systemic inflammatory responses caused by sepsis and other critical states? How to combine multiple biomarkers to further improve the accuracy of clinical diagnosis of sepsis? How to rationally select the time of use of antibiotics by monitoring the changes in biomarker levels in patients with confirmed sepsis, and avoid the abuse of antibiotics?

Scoring Systems for Severe Sepsis

‘‘The complexity of modern medicine exceeds the inherent limitations of the unaided human mind.” A study of regularly used systems for assessing the severity of sickness of patients in intensive care illustrates this point. Physiologic variables are used to compute severity of sickness scores. At any given time, millions of data values are captured by bedside monitors, laboratories, and patient-care staff in an Intensive Care Unit (ICU). It is based on this information that severe disease scores can be calculated, as well. In order for scoring systems to be useful, they must be error-free and accurate. When it comes to complicated data collecting and processing, humans have a tendency to make mistakes. Error-free performance by humans is impossible in any system that requires it. Making data collecting and analysis easier for ICU personnel will help them use scoring systems effectively. Because of human

error and data collection efficiency, an automated system that gathers data for severity of sickness classification may be more reliable than an expert who manually enters and analyses data.

In today's health-care setting, it is critical to classify the severity of sickness in order to predict the outcome in the ICU. Researchers can use severity of illness classifications to create cohort groups, evaluate new medicines, and find quality improvement indicators. Based on severity of illness, patients can be classified into groups and allocated precious resources more effectively. Sickness severity scores are routinely used to predict outcomes, quantify illness severity and the level of organ dysfunction, and evaluate resource utilisation in the critical care unit

Examples of scoring systems specific to an organ or disease are the Glasgow Coma Scale (GCS) and the International Classification of Diseases (ICD-10) (ICD). Some of the most commonly used generic scores include Acute Physiology and Chronic Health Evaluation (APACHE), Simple Acute Physiology Score (SAPS), Mortality Probability Model (MPM), and scores that evaluate the presence and severity of organ dysfunction (for example, Multiple Organ Dysfunction Score (MODS), Sequential Organ Failure Assessment (SOFA) (NEMS).

Outcome Prediction Scores

An ICU patient's specific prognosis was not a primary consideration when developing the first outcome prediction scores more than 25 years ago. Because of the rapid advancement of statistical and computational methods as well as patient demographics, sickness prevalence, and intensive care practises, the state of intensive

care has altered considerably since that time. This category's three primary ratings have been updated to reflect the current state of the ICU.

Acute Physiology and Chronic Health Evaluation (APACHE)

One of the most important aspects of the initial APACHE score that was developed in 1981 was its ability to measure the severity of acute illness and to predict the patient's long-term health status prior to admission. 83 Original model was updated and simplified in 1985 to generate the APACHE II score, which is today the most widely used severity of illness score in the world. APACHE II now only measures 12 physiological variables, down from the initial score of 34. As soon as the model was built, a single score was generated based on the impact of age and chronic health conditions. Several factors need to be taken into account when determining a patient's physiological status. The APACHE II score is generated using the 12 physiologic variables, the Glasgow Coma Scale, age, and a chronic health evaluation.

Atrial pH, arterial Pa02, heart rate, temperature, respiratory rate, sodium, potassium, WBC count, hematocrit and bicarbonate are all included in the list of physiological variables. These are all physiologic variables (C). The alveolar-arterial gradient must be calculated when the FiO2 is greater than 0.5. Points are quadrupled for abnormal creatinine levels in the event of acute renal failure. Physical variables are scored from 0 to 4, with a score of four being the most anomalous and zero being the default value for missing results. There is a total score of 0 to 71 in this section. The APACHE II score and the major diagnosis that led to ICU admission are utilised to calculate the expected mortality. Therefore, even when previous health status and the degree of acute physiological dysfunction are comparable, the reason for ICU admission is an important factor in predicting mortality. Furthermore, the

shortcomings of the APACHE II scoring system are well-known and well-documented In large ICU populations, the APACHE II score does not consistently predict individual cases. Performance can suffer from APACHE II's lead-time bias. Admission delays and a variety of referral protocols may result in inaccurate outcomes estimates. Human resources are also required to collect data for all severity of illness assessment systems. A shortage of resources forces many hospitals to not gather severity of illness scores on a regular basis.

As of 1998, APACHE III has been proven and updated. A risk-adjusted ICU length of stay equation was also developed using the APACHE III model. 84 Last year's APACHE IV was built using information from over 100,000 patients treated in 104 ICUs across 45 hospitals in the United States between 2002 and 2003. It is possible to compare the efficiency and use of resources in an intensive care unit using prediction equations (ICU).[77]

Simplified Acute Physiology Score (SAPS)

Uses 13 physiological variables and the patient's age to predict mortality in ICU patients were developed and validated in France in 1984.[78] It took 24 hours for SAPS scores to be calculated after a patient was admitted to an intensive care unit. Le Gall and colleagues,[79] used logistic regression analysis to produce SAPS II, which combines 17 factors: 12 physiological indicators, the patient's age and type of admission, and three variables related to the patient's condition. The SAPS II score was confirmed after 137 consecutive admissions to ICUs in 12 countries. In 2005, SAPS 3 was launched, which was a completely new SAPS model. 16 784 patients from ICUs in 35 countries were mined for data to find and weight variables. Based on patient characteristics prior to admission, ICU admission circumstances, and degree of

physiological derangement within one hour (rather than 24 hours) before or after ICU admission, 20 variables are broken down into three sub-scores. The final score can be achieved between 0 and 217. Seven regions are covered by SAPS 3: Australia; Central and South America; Central and Western Europe (including Eastern Europe); North and North American; Southern European (including Mediterranean) and North American; and Eastern European and North American (including Eastern Europe). It is possible that some of these equations were established with a relatively small sample size, which may have affected their capacity to reliably forecast future results. That the SAPS 3 score can distinguish, calibrate and fit data is supported by substantial evidence. SAPS 3 has used the standardised resource use measure, modified for acute illness severity, to compare resource use between ICUs for the purpose of identifying resource disparities.[80]

Mortality Probability Model (MPM)

There were seven admission factors and seven 24-hour variables that were used in the initial MPM, which was based on data from a single ICU. In 1993, a new MPM II was built using logistic regression techniques on a database of 12,610 ICU patients from 12 different countries. Two scores are available for MPM II, one for patients in for less than 24 hours and the other for those who spend more than 24 hours in the ICU, MPM0 and MPM24. MPM0 has five variables, while MPM24 has eight more variables. Using MPM II, each variable (except for age, which is entered as the actual age in years) is classified as present or absent and given a score of 1 or 0. Regression analysis is used to determine the probability of death in an institution. An index of resource consumption for an ICU was also developed by the authors after the first ICU stay by assigning weights to each day of an ICU stay and a formula for

estimating an ICU's mean WHD-94. In recent years, more than 124,000 patients from 135 intensive care units in North American hospitals (save one in Brazil) were utilised to update the MPM0 database, which was compiled between 2001 and 2004. After one hour of ICU admission, MPM0-III collects 16 factors including three physiological markers to estimate the patient's mortality probability after discharge; consequently, the MPM0 categorization is heavily dependent upon the pre-ICU condition of the patients.

Organ Dysfunction Scores

The primary goal of organ failure ratings is not to predict a patient's prognosis, but rather to describe the severity of organ dysfunction. When it comes to calculating an organ failure score, both time and severity must be taken into account. However, we'll focus on just three organ dysfunction ratings that are commonly used in patients in general intensive care units.

Logistic Organ Dysfunction Score (LODS)

There were 13,152 admissions to 137 ICUs in 12 countries in the LODS database, which was compiled from this extensive data set. Six organ systems were represented by a total of 12 variables using multivariate logistic regression (neurologic, cardiovascular, renal, pulmonary, hematologic, hepatic). During the first 24 hours of admission, all of a patient's vital signs are collected and a score of 0 to 5 is awarded to each system. As with MODS and SOFA, the highest LODS score for respiratory and coagulation is 3, and for the liver, the maximum LODS score is 1; It is possible for the LODS value of 0 to 22. A logistic regression equation can be used to turn the overall LODS into a risk for death, allowing it to fall somewhere in between a

mortality prediction score and an assessment of organ failure. An organ dysfunction score (LODS) of 22 was associated with a 99.997% fatality rate in the study. It was discovered that the LODS accurately described organ dysfunction progression in French ICUs, despite the fact that it had not been properly validated for repeated use.

Multiple Organ Dysfunction Score (MODS)

Based on a review of 30 studies describing organ dysfunction, the MODS was developed. To choose variables for each of the seven organ systems, a set of 'ideal description' criteria were utilised (respiratory, cardiovascular, renal, hepatic, haematological, central nervous system, and gastrointestinal). Since no adequate description of the gastrointestinal system's function could be obtained, it was omitted from the final model. It is based on the first-day characteristics of the six organs, which can range from 0 (normal) to 4 (very abnormal) (most dysfunctional). With 336 surgical ICU admissions and 356 admissions to the same surgical ICU, we developed and validated the score. Even though higher MODS levels are associated with a poorer prognosis, MODS does not predict death in the ICU. As the number of critically sick patients increases, so does the mortality rate in ICUs. A better predictor of outcomes than individual MODS scores is delta MODS.

Sequential Organ Failure Assessment (SOFA) score

Multiple organ failure (MOF) is the major cause of death and serious disease in patients who are extremely ill. As a result of medical advancements in the 1970s, the MOF concept was established. When new treatment options were created to lower the frequency and severity of organ failure, a clearer definition of the severity of organ dysfunction/failure was needed to measure the severity of illness. As a result, a

set of fundamental yet objective criteria for determining the level of organ dysfunction or failure had to be established. The following recommendations for evaluating organ dysfunction were developed as a result of advances in our knowledge of organ dysfunction and failure:

1. Organ dysfunction/failure is a process, not a one-time occurrence. A continuum rather than a one-size-fits-all phenomenon should be considered. Because of this, it is necessary to use a scale when evaluating the candidate.
2. For a variety of reasons, time is critical: (a) The onset and resolution of organ failure can be lengthy processes. The development of organ dysfunction/ failure may not be possible in patients who die too soon. (b) Organ dysfunction/failure can progress in a variety of ways throughout the course of a complicated clinical course. A better knowledge of the illness process can be gained by evaluating the time it takes for the disease to progress naturally or as a result of treatment measures. Thus, the collecting of data should take place on a regular basis.
3. If an organ fails, it should be evaluated using a few simple yet objective criteria that can be assessed easily and routinely in any hospital. There should be no additional effort beyond what is typically done in every ICU to obtain these data. Due to the fact that therapeutic intervention varies between institutions and between patients, it is imperative that the variables employed be as unbiased as feasible.

Ideal variables for Describing Organ Dysfunction / Failure

- Objective
- Simple, easily available, but reliable
- Obtained routinely and regularly in every institution
- Specific for the function of the organ considered
- Continuous variable
- Independent of the type of patients
- Independent of the therapeutic interventions

Severe sepsis-related organ failure assessment (SOFA score) was developed by the European Society of Critical Care Medicine in Paris in October 1994 to describe the level of dysfunction/failure in groups of patients or even in individual patients.[14] Among other things, they decided on the following: To focus on only six organs. For each organ, assign a number from 0 to 4, with 0 being the most normal condition and 4 representing the most abnormal. In order to keep an eye on the day's lowest points. It was found too complicated to include gastrointestinal dysfunction/ failure, which they considered critical, so they dropped it. SoFA (Sequence of Organ Failure Assessment) was later renamed the Score because it is not particular to sepsis. (Table No.4)

The Sequential Organ Failure Assessment (SOFA) score

	0	1	2	3	4
Respiratory: PaO_2/FIO_2(mmHg)	> 400	≤ 400	≤ 300	≤ 200[b]	≤ 100[b]
Renal: Creatinine (mg/dl) or Urine Output	< 1.2	1.2 - 1.9	2.0 - 3.4	3.5 - 4.9 or < 500 ml/d	≥ 5.0 or < 200ml/d
Liver: Bilirubin (mg/dl)	<1.2	1.2 - 1.9	2.0 - 5.9	6.0-11.9	≥ 12.0
Cardiovascular System(CVS): Hypotension	No hypotension	MAP < 70mmHg	Dopamine ≤ 5 or Dobutamine (any dose)[a]	Dopamine > 5 or Epinephrine ≤0.1 or Norepinephrine ≤0.1[a]	Dopamine >15 or Epinephrine >0.1 or Norepinephrine >0.1[a]
Coagulation : Platelet count (x 10^3/mm3)	>150	≤ 150	≤ 100	≤ 50	≤ 20
Central Nervous System(CNS): Glasgow Coma Score	15	13-14	10-12	6-9	< 6

- adrenergic agents administered for at least 1 h(doses given are in μg/kg/min),
- with ventilatory support

J. Marshall et al.23 developed a Multiple Organ Dysfunction Score (MODS) and G. Bernard et al.94 created a Brussels Score.[82] An earlier version of this score was based on a number of factors. The greatest discrepancy between the three scores was in the criteria of cardiovascular dysfunction or failure. Heart rate times right atrial (central venous) pressure divided by mean arterial pressure was used to compute pressure-adjusted heart rate in MODS. Using a score like this made it tough to perform daily bedside calculations. There are many conditions that could produce acidemia in addition to hypotension, such as renal failure or permissive hypercapnorea. Despite the association, cardiovascular dysfunction did not appear to be a reliable predictor of mortality. The need for adrenergic support in the SOFA score was utilised to diagnose cardio-vascular dysfunction or failure. Participants were unable to come up with a better way to explain cardiovascular dysfunction or failure, despite the fact that treatment-related criteria were desirable. It is possible that local protocols may alter, but they were broad enough to have no effect on this review. Even in a clinical setting of any complexity, the formula was easy to calculate.

Though SOFA score was developed primarily to describe morbidity, a retrospective analysis of the relationship between the SOFA score and mortality was obtained, using the European / North American Study of Severity System database which indicated a good correlation of the score with survival. The usefulness of SOFA score was validated in large cohorts of patients by Ferreira et al[83], Moreno et al[84] and in a multi centric prospective study by Vincent et al[85] which revealed excellent correlation with mortality and the SOFA score can be a good prognostic indicator. A comparative study was done for outcome prediction using SOFA score and MODS score by Peres Bota et al in 2001[5] where it was concluded that the SOFA

therapy related Cardiovascular score was a better outcome predictor than the Cardiovascular MODS. Thus the SOFA score is easy to use, gives valuable information about the ongoing organ dysfunction and a reliable outcome predictor.

Severity Assessment Based on Nursing Workload Use

Therapeutic Intervention Scoring System (TISS)

As a way of assessing the severity of sickness and comparing patient care, TISS was first established in 1974. More specialised or time-consuming tasks were given higher values in the initial score, which contained 56 therapeutic activities that could be completed in a 24-hour period. After an update in 1983, the 76-item score was added. A simplified version of TISS-76 was designed in 1996 utilising modern statistical analysis after it was criticised for being excessively time-consuming and complicated. 98 TISS-28 consists of only 28 components, which are organised into seven categories: basic activities, ventilatory support, cardiovascular support, renal support, neurological support, metabolic support, and specialised interventions. The application of a weighted scoring system results in a total score of 78. TISS-28 was examined in 22 Dutch ICUs and 19 Portuguese ICUs and confirmed to be reliable. For every TISS-28 point that a nurse treats, they are entitled to spend 10.6 minutes of their shift time. Utilizing these statistics can help with staffing distribution, evaluating the efficiency of nursing task use, and classifying ICUs based on the quantity (rather than complexity) of patient care they provide.

Nine Equivalents of Nursing Manpower Use Score (NEMS)

It was used to develop NEMS, which was meant to be simpler and more universally applicable, using the TISS-28. An intensive care unit (ICU) nurse is expected to perform a variety of tasks that fall into one of the following categories: basic monitoring; intravenous medications; mechanical ventilation; supplementary ventilation; single and multiple vasoactive medications; dialysis techniques; and a variety of other tasks that fall outside the ICU. Each of these jobs can be completed for a total of 56 points, bringing the total to 56. Safe and effective NEMS use in the ICU has been shown to be practically error-free.[86] Nursing workload efficiency in ICUs may be evaluated using this system to categorise ICUs based on the amount of care (and not just complexity) they provide.

Nursing Activities Score

The Nursing Tasks Score (NAS) is based on TISS-28 and includes additional nursing activities that aren't necessarily related to the severity of the patients' diseases. Members of the group agreed to include these issues on the agenda. During a week-long cross-sectional investigation in 99 ICUs across 15 countries, 100 activities were observed and compared to the TISS-28 items. A total of five new items and 14 subitems are now included in TISS-28 to characterise nurse actions in the intensive care unit (for example, care of family and administrative responsibilities). 60 percent of the average nursing time was spent on new activities; in the development study, 81 percent of the nursing time was spent on NAS activities (versus 43 percent in TISS-28).

Treatment of Severe Sepsis

Fluid Therapy

Septic shock and syphilis-induced cardiomyopathy are only treatable by rehydration. Vasodilatation causes both absolute and relative hypovolemia due to fluid losses (sweating, diarrhoea, fluid transfers to peritoneal cavity) and the mal-distribution of circulation (increased blood flow). Low blood pressure and microcirculatory issues may result from a weakened heart's capacity to pump blood. As far as outcomes go, it appears that resuscitation times, proper amounts of fluid and fluid therapy procedures with clearly defined targets are more significant than the type of fluids.[87]

Type of Fluids

According to meta-analyses, fluid resuscitation in the general ICU population is unaffected by colloids or crystalloids. Patients with severe sepsis should not be given colloids because of the potential for harm, despite the fact that the use of colloids in general has no detrimental effect on patients. HES has a higher risk of acute kidney injury (AKI) than gelatins, which have none. However, the SAFE Study found the use of albumin to be safe compared to the use of ordinary saline solution. Hence use of hyper-oncotic colloids in patients with severe sepsis is controversial.

Fluid Challenge

Patient response to fluids supplied is the basis for the notion of fluid challenge. Fluid challenge can be employed in any patient group with hypovolemia, not just septic patients who are hemodynamically unstable. The fluid challenge protocol should contain the type of fluid, the pace at which it is administered, and the

endpoints and safety limits of the experiment. There is a wide range of options when it comes to the fluid. From 50-200 ml every 10 minutes to 500-1000 ml of crystalloids or colloids every 30 minutes,[88] the proposed rate of fluid administration has changed widely. In the fluid challenge, the primary goal should be to improve the hemodynamics. Fluid challenge and resuscitation end points are not self-evident or widely agreed upon. Cardiac Filling Pressures such as CVP and PCWP have been used as end points. SvO2 or ScvO2 has also been used as an end point. Stroke Volume Variation has been used as an end point. However, ventricular filling pressures have been demonstrated to be a poor predictor of hemodynamic response to fluid challenge in severe sepsis treatment guidelines. At the very least, SVV is ineffective in patients with septic shock who require pressure support breathing. Congestive heart failure and pulmonary oedema can be prevented by using the fluid challenge approach with specific safety limits. In the early stages of treating hemodynamically unstable patients, fluid challenge should be employed, and fluid administration should be reduced once the need for further fluids has passed. In individuals with acute lung damage, excessive fluid intake can be detrimental (ALI). In patients who are restricted in their fluid intake, they are weaned from the ventilator early and spend less time in the ICU.

Vasoactive Treatment

The Target for Vasoactive Treatment

Severe sepsis or septic shock results in hypovolemia, vasodilation, direct myocardial depression, hypotension, anomalies in blood flow distribution, and other indications of cardiovascular dysfunction in the patient. In 85 percent of cases, patients in septic shock need vasoactive support, and fluid resuscitation alone can

only treat minor cardiovascular dysfunction. The Surviving Sepsis Campaign guidelines prescribe a maximum MAP of 65 mmHg. Patients with different pre-existing co-morbidities will have varying MAP target levels, which are unknown. If the MAP is below 65 mmHg, the outcome may be impaired, but if the MAP is greater than 90 with a quick increase in systemic vascular resistance, the mortality rate is also elevated.[89] Norepinephrine, however, did not affect diuresis, splanchnic perfusion, or systemic oxygen metabolism when the MAP was increased from 65 to 85 mm Hg in a small cohort of septic shock patients. Patients in septic shock are at risk for myocardial depression in 44 to 50 percent of cases. Myocardial adrenergic hypo-responsiveness, which is common in septic shock, might linger for many days before resolving in 8-10 days. Survivors usually recover entirely. CO and oxygen delivery should be increased as a goal of inotropic treatment (DO2). SvO2 and ScvO2 can be used as indicators of inadequate oxygen supply in individuals with severe sepsis, but the latter does not correlate well. In critically ill patients, increasing oxygen delivery to abnormally high levels does not reduce mortality.

Vasopressor Drugs

(i) Dopamine

Epinephrine and norepinephrine can be produced from dopamine. Irrespective of dosage, it has an effect on the renal mesentery, coronary arteries, and spleen vessels. In the renal and mesenteric vessels, it activates the vasodilatory dopaminergic DA1 receptors, which results in an increase in heart rate and myocardial contractility, and it causes Vasoconstriction by activating the dopaminergic DA2 receptors, which results in an increase in heart rate and myocardial contractility. In spite of this, dopamine is ineffective in preventing renal failure. Splanchnic blood flow can be

increased, while mucosal flow and hence oxygen delivery can be decreased by dopamine injections. Endocrinological effects of dopamine, such as decreasing prolactin and reducing growth hormone, are possible. Compared to patients who are not given dopamine for septic shock treatment, those given dopamine have a higher fatality rate.[90]

(ii) Norepinephrine (NE)

The adrenergic agonist, norepinephrine (NE), is a neurotransmitter. It is a powerful vasopressor that can be used to treat septic shock that is dopamine resistant. It has been discovered that NE has the same effect on splanchnic blood flow and oxygen delivery as dopamine in moderate septic shock, but epinephrine in severe septic shock is superior. The mucosal pH, a proxy indicator of tissue oxygenation, rises as NE improves oxygen supply to the rest of the body. NE appears to have a favourable effect on splanchnic oxygen supply and utilisation. Systemic blood flow alterations and increased oxygen demand from dopamine or NE in the splanchnic region may lead to splanchnic tissue hypoxia. As first-line vasopressors, SSC guidelines recommend the use of NE and dopamine.

(iii) Epinephrine

There is a wide range of adrenaline-like agonists used in medicine. Spleen blood flow decreases more frequently in patients who receive epinephrine or NE in combination with dobutamine or dobutamine alone than those who receive both medicines. A first-line vasopressor medication, such as epinephrine, should not be utilised for patients with septic shock. Patients with septic shock treated with

epinephrine alone or with NE and dobutamine experienced no difference in mortality rates.[91]

(iv) Arginine Vasopressin (AVP)

The pituitary gland secretes the peptide hormone AVP, which is generated in the hypothalamus. It is a naturally occurring hormone. Direct activation of V1 receptors in vascular smooth muscle cells results in an increase in vascular reactivity to catecholamines. AVP may also inhibit smooth muscle nitric oxide production in the presence of inflammation. The hormone's antidiuretic impact is a result of water resorption and activation of V2 receptors in the renal tubules. The V3 receptors in the pituitary gland have central effects, such as the release of ACTH, in the pituitary gland However, plasma AVP concentrations in septic shock were shown to be insufficient to maintain blood pressure. Even in a state of catecholamine-resistant vasodilatory shock, low dosages of AVP infusion can elevate arterial blood pressure. An infusion rate between 0.01 and 0.04 U/min is advised while utilising vasopressin. Using AVP, a potent vasoconstrictor, may result in decreased CO, cardiac arrest, ischemia of the mesenteric arteries, and ischemic skin lesions, which could be dangerous. As a result of platelet aggregation produced by AVP, thrombocytopenia can develop.

(v) Terlipressin

V1 receptor activity is higher in Terlipressin than AVP, which makes it a long-acting synthetic vasopressin. It has been utilised in septic shock to stabilise haemodynamics by injecting terlipressin. As a result, terlipressin lowers the cardiac index, dissociation, and consumption of oxygen and may pose a risk of long-term

vasoconstriction worldwide and regionally. Maintaining a high cardiac index may necessitate the use of an inotrope such as dobutamine. In adult septic shock, SSC guidelines do not recommend AVP or terlipressin as first line medications.

Inotropic Drugs

(i) Dobutamine

Although dobutamine has a direct effect on the heart's receptors, it has very little effect on the blood vessels. Dobutamine has been demonstrated to be superior than dopamine in the treatment of septic shock in patients with high filling pressures and heart failure. As a result, it has become a common practise in the treatment of patients with severe sepsis and septic shock. As previously indicated, an increase in oxygen dissociation was possible, but this had not been demonstrated to be advantageous. Dobutamine is the first-line inotrope for septic shock.

(ii) Levosimendan

Even though levosimendan, a calcium-sensitizer with inotropic and vasodilatory effects, has not affected mortality compared to dobutamine, it has been proven to be helpful in acute and chronic heart failure. In both experimental sepsis and in individuals with septic shock, levosimendan has been shown to enhance the heart's ability to pump blood. Acute respiratory distress syndrome (ARDS) is associated with septic shock, and levosimendan improves right ventricular dysfunction in these patients (ARDS).[92] 260 Patients with septic shock have showed enhanced stomach mucosal blood flow after receiving levosimendan for treatment of endotoxemia. As of yet, no trials have shown that levosimendan reduces mortality when compared to dobutamine in sepsis-induced cardiac depression treated with the drug.

1. **Early Goal-Directed Therapy**

This notion of early treatment with rigorous set goals was proposed in 2001, about two decades after fluid resuscitation has been the mainstay of haemodynamic treatment for severe sepsis. Goal-directed therapy (EGDT), which took place in the emergency room in the first six hours, with MAP, CVP, urine output, and ScvO2 as target parameters. Fluid resuscitation, vasopressor treatment, dobutamine, and packed red blood cells were employed to achieve preset objectives. When compared to a control group, the goal-directed group observed a 16% decrease in death rates.

Despite the fact that this study was conducted in a single location, it was the first to demonstrate that fundamental haemodynamic parameters reduced mortality significantly. As a result of the introduction of the EGDT concept, death rates have decreased in hospitals.

2. Antimicrobial Treatment

Severe sepsis must be treated with antimicrobials and, if possible, source control because it is an infectious condition. Studies in septic shock reveal that antimicrobial medicines and hemodynamic therapies must be used together to improve outcomes. Blood-borne illnesses have a lower death rate when treated with appropriate empirical antimicrobials. First, broad-spectrum antibiotics should be used, followed by specific antibiotics tailored to the etiological agent. Effectiveness and the timing of antimicrobial treatment must be considered equally significant. Septic shock patients who receive early antimicrobial treatment within an hour of recorded hypotension are more likely to survive than those who receive treatment later in the

course of the illness.In septic shock, a one-hour delay in the introduction of antibiotics diminishes the chance of survival by 12 percent.[93]

3. Source Control

As soon by a patient is diagnosed with severe sepsis, the source of the infection should be ruled out, such as emptying an abscess, debriding necrotic tissue, or removing an infected medical device, or managing a source of persistent bacterial contamination. The advantages and disadvantages of an intervention must be taken into account while deciding on the optimal method of source control. It is preferable to perform abscess drainage using percutaneous means rather than surgical means when the source control goal can be achieved with the least amount of physiologic disturbance. If a focus of infection amenable to source control methods such as an intra-abdominal abscess, a gastrointestinal perforation, cholecystitis, or intestinal ischemia has been detected, source control measures should be performed as soon as possible after first resuscitation. Intravenous access devices can cause septic shock and severe sepsis, which should be discontinued as soon as other vascular access is established.

4. Mechanical Ventilation

74 to 96 percent of patients with severe sepsis have respiratory failure, the most prevalent organ dysfunction. 32 to 83 percent of patients with ALI or ARDS were found to be septic in investigations. Patients who suffered sepsis-related respiratory failure in the ARDS net Research, the first study to indicate a drop in mortality with a particular kind of mechanical ventilation, were more likely to survive. Septic lung injury should not be treated any differently than other lung

injuries at this time, thus patients with severe sepsis receive low-tidal volume treatment.

5. Renal Replacement Therapy

Acute kidney damage (AKI) complicates severe sepsis in up to 42 percent to 53 percent of patients, and as many as 70 percent may require renal replacement therapy. It has been found that high volume haemofiltration can eliminate cytokines, reduce the need for vasopressors, and even reduce mortality in septic shock.[94]

6. Adjuvant Treatment

Glucose Control

Intensive insulin treatment with strict glycemic control was introduced and widely accepted after a study showing a morbidity and mortality reduction in critically ill surgical patients. Heart patients who had recently undergone surgery accounted for 63% of the patients. Mortality rates decreased from 8 percent in patients with blood glucose levels between 4.44-6.1 mmol/l to 4.46 percent in those who had their blood glucose levels lowered. Severe sepsis and multiple organ failure mortality reduction in bloodstream infections and acute renal failure was shockingly significant.

Corticosteroids

High dose corticosteroids (e.g. methylprednisolone 30 mg/kg intravenously) were studied in the treatment of severe sepsis or septic shock in the.[95] Relative adrenal insufficiency in patients with septic shock could lead to vasopressor-resistant hypotension and increased mortality, hence low dosage corticosteroid therapy was

adopted. Low-dose corticosteroids were found to increase survival and improve shock reversal in prospective investigations.

Deep Vein Thrombosis (DVT) Prophylaxis

Deep vein thrombosis is a common consequence in patients with severe sepsis because of the patient's extended immobility, hypercoagulability, and activation of inflammatory and complementing pathways. As a result, these individuals should receive low-dose unfractionated heparin or low-molecular weight heparin for deep vein thrombosis prevention. Septic patients who do not qualify for heparin use (i.e., patients with severe or active coagulopathy, recent intra-cerebral haemorrhage) should use graduated compression stockings or intermittent compression devices as preventative measures (unless contraindicated by the presence of peripheral vascular disease). Patients with severe sepsis with a history of deep vein thrombosis (DVT) are given mechanical and pharmacological therapy.

Stress Ulcer Prophylaxis

Patients with sepsis are more likely to develop a stress ulcer, especially if they have suffered a head injury, have had burns, or have had emergency surgery. Consequently, the surviving sepsis guideline recommends the use of H2 receptor inhibitors or Proton pump inhibitors as stress ulcer prophylaxis. Susralfate is not as effective as H2 receptor inhibitors and is hence not recommended. There has been no direct comparison of proton pump inhibitors with H2 receptor antagonists, hence their relative effectiveness is uncertain. They show equivalence in their ability to raise the pH of the stomach.

Indian ICUs were reviewed in a 2017 prospective study by Palaniappan VK et al.[96] on the efficacy of western-created ICU scoring systems (APACHE II, APACHE IV, and SAPS III). We use a variety of ICU grading systems to assign grades to the patients in our intensive care unit (ICU) (APACHE II, APACHE IV and SAPS III). In order to compile statistics on the patients' demises. determining if Western ICU scoring methods can accurately predict mortality in an Indian ICU by contrasting actual death rates with predictions made by scoring systems (APACHE II, APACHE IV, and SAPS III). The mortality rate in our patient group is 40%, and the authors feel that the scoring systems are valid and may accurately predict death in the Indian context. However, only 33.51 percent, 33.5 percent, and 28.53 percent of patients are projected to die in the course of the study according to APACHE II, APACHE IV, and SAPS III. APACHE II, APACHE IV, and SAPS III scoring systems place an individual patient in our ICU at 1.2, 3.61, and 1.4 times the risk of death anticipated by these scoring systems in terms of mortality. Once the individual patient scores have been acquired, the projected mortality must be multiplied by the aforementioned factor. The SMR for any particular grading system will vary depending on the quality of care offered in each ICU. Therefore, each critical care unit should develop its own SMR based on the scoring methodology. A patient's SAPS III entrance score accurately predicts mortality risk within one hour of ICU admission, unlike other scoring methods. A small sample size prevents substantial inferences from being drawn from this study. There may be a discrepancy between the type of patients we studied and those in the intensive care unit: (ICU). The authors came to the conclusion that there is a linear relationship between the predicted scores and the observed mortality. The observed death rate rises in tandem with the expected score.

The fact that the scoring systems can accurately predict death in an Indian setting suggests that this is the case.

It was determined that Haniffa R et al.[97] were able to identify between those patients admitted to intensive care units (ICUs) who lived and died, as well as their calibration and accuracy, as well as the way missing findings were handled, in a systematic review published in 2018. Researchers observed that 94%, 72.4%, and 25% of the samples were discriminant and calibrated, respectively. It was found in 88.9 percent of cases that good discrimination and calibration could be found, but in 58.3 percent of the cases, it could not be discovered. However, only 10 of these evaluations documented excellent discrimination. Generalizability was hindered by inclusion and exclusion criteria that varied widely, a dearth of post-ICU outcomes, and an inability to properly handle missing value data. When reporting rules were not followed, researchers discovered that robust conclusions concerning prognostic models were compromised. Even with the limitations of calibration, the performance of mortality risk prediction models in LMIC ICUs is at best mediocre. LMIC models including widely available prognostic factors are therefore necessary for developing and validating LMIC models.

Fuchs PA et al.[98] in 2019 studied the diagnostic accuracy of SAPS II, the APACHE II, and SOFA in predicting ICU and post-ICU mortality for patients in a tertiary university ICU. This study's researchers found a baseline SAPS II, APACHE II, and SOFA score of 41.1 20.34, 14.07 8.73, and 6.33 4.12 points. All of the scores were significantly lower when comparing SP versus NSP (p 0.05). Compared to NSP (57.9%), SP (p 0.001) had a significantly lower ICU mortality rate (35.4 percent) (35.3 percent vs. 35.3 percent). It was found that the ROC curve areas under receiver-

operating characteristics (ROC) of SAPS, SOFA and SOFA for the prediction of ICU prognosis (0.826; 0.836; 0.788) were significantly higher than those for the prediction of post-ICU prognosis (0.708; 0.709; and 0.661). APACHE II and SAPS II, on the other hand, are excellent predictors of mortality in the intensive care unit, but they do not, according to the authors, predict survival after discharge. Medical ICU patients and surgeons had better outcomes.

According to a study by Czajka, S. et al.[99] in 2020, three scores, APACHE II and III, as well as the SAPS II, may accurately predict mortality for adult patients in a tertiary intensive care unit both while they are in the hospital and after release. Researchers discovered These scores were 19 (IQR 12–24), 67 (36.5–88) points, and 44 points (IQR 27–56), with corresponding in-hospital mortality ratios of 25.8 percent (IQR 12.2–46.0), 18.5 per cent (IQR 3.8–41.8), and 34.8 per cent (IQR 7.9–59.8), respectively. The percentage of patients who died at the hospital was 35.6%. In addition, the mortality rate for the first 12 months after discharge was 17.4 percent. Each score predicted in-hospital mortality (p 0.05), as well as mortality after hospital discharge (p 0.05), for all three patients: the APACHE II (AUC = 0.71; 95 percent CI (064–0.78), the APACHE III (AUC = 0.72; 95 percent CI (065–0.78), and the SAPS II (AUC = 0.69; 95 per cent CI (062–0.76), with no statistically significant differences. The other two patients: the SAPS II (It was determined by the researchers that all of the scores were reliable indicators of death in the hospital. Post-discharge mortality, their diagnostic accuracy is inferior and of questionable clinical significance in this case In order to produce ratings indicating the long-term prognosis of patients who have been successfully released from the intensive care unit, more research is required.

APACHE II, SIMPLE Acute Physiology Score (SAPS II), and Sequential Organ Failure Assessment (SOFA) were all examined in a 2020 meta-analysis by Ghauri SK et al[100] for their ability to predict death among critically ill patients in intensive care units. It was shown that these three scoring systems had high mortality prediction abilities; their pooled sensitivities were 0.81 (APACHE II), 0.76 (SAPS II), and 0.880. ' (SOFA). Additionally, the authors found that their pooled HSROCs were 0.87 (APACHE II), 0.85 (SAPS II), and 0.880 (APACHE II, respectively) (SOFA). The APACHE II, SAPS II, and SOFA studies all had no evidence of publication bias, but there were significant differences in sensitivity and specificity between the studies (I2=85.21 percent, 84.31 percent; 84.31 percent, 71.67 percent, respectively) between the studies, but no publication bias was found (P=0.689; 0.465; and 0.181, respectively). According to the study's findings, ICU assessments were a good predictor of mortality. When conducting future studies, researchers should employ a combination of generic ICU scores and mortality outcomes. Patients from different nations should also be included.

MATERIAL AND METHODS

A hospital based prospective study was conducted with 100 patients to assess and compare the predictive accuracy for mortality of the three predictive scoring system in the ICU namely SOFA, APACHE II and SAPS II.

Study design: A hospital based prospective study

Study Duration: 1year

Study area: The study was done at our tertiary care centre in the department of general medicine, KLEs DR Prabhakar Kore hospital & MRC, Belagavi on patients admitted in ICU.

Study population: All patients admitted in the ICU of KLES Dr. Prabhakar Kore Hospital, Belgaum of our Tertiary care Hospital who fulfilled the inclusion criteria.

Sample size: 100 patients

Sample size was calculated by using following formula:

$N = (Z^2 \times P \times (1 - P))/d^2$

Z^2= table value of alpha error from Standard Normal Distribution table = 1.96*1.96=3.84

Power (P) = 0.05

(1-P) =0.95

Precision error of estimation (d) = 5%

$d^2 = 0.0025$

$N = (3.84 \times 0.05 \times 0.95)/0.0025 = 92.99$

Hence sample size of 100 patients was selected for the study.

Inclusion criteria

1. Critically ill patients admitted to ICU.
2. Evidence of organ dysfunction.
3. Elevation of SOFA score from baseline by 2 points or more.

Exclusion criteria:

1. Patients who denied consent
2. < 18 years of age
3. Those with documented pregnancy
4. Trauma patients
5. Patients who were discharged for ICU within 24 hours.
6. Patients who died within 24 hours of admission.
7. Patients with primary burns
8. Post CABG surgery

METHODOLOGY

The study was done at our tertiary care centre in the department of general medicine, KLEs DR Prabhakar Kore hospital & MRC, Belagavi after due permission

from the Institutional Ethics Committee and Review Board and after taking Written Informed Consent from the patients.

After approval from the Institutional Ethics Committee a valid informed consent was taken. Once the patients were enrolled for the study, a thorough history and physical examination was done as per proforma. An informed consent was taken in written from patients or patient's attendant.

Patients were subjected to detailed history, examination and necessary investigations were done.

1. Complete blood count
2. Liver function test
3. Renal function test
4. Arterial blood gas
5. Serum procalcitonin
6. Blood cultures
7. Urine culture
8. Chest x ray
9. Ultrasonography SOS
10. Serum lactate SOS

Detailed clinical, and laboratory data were recorded, including arterial blood gas analysis and relevant cultures of blood, urine, sputum, tracheal aspirates, or other samples as indicated.

Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II) and Simplified Acute Physiological Score II (SAPS II) and Sequential Organ Failure Assessment (SOFA) indices were calculated at baseline to assess the severity of illness. The total duration of ICU stay, details mechanical ventilation was also recorded.

Score was calculated within 24 h of admission and repeated after 48h and patients were assessed after 28 days of admission. Scores used as a predictor of mortality were Acute Physiology and Chronic Health Evaluation (APACHE) III, Simplified Acute Physiology Score (SAPS) II, simplified organ failure assessment (SOFA).

For calculating SOFA score, following data was collected-

1. PaO2
2. FiO2
3. Whether patient is on mechanical ventilation.
4. Platelets
5. Glasgow coma scale
6. Bilirubin
7. Mean arterial pressure or administration of vasoactive agents required
8. creatinine

For calculating APACHE-II score, following data was collected-

1. History of severe organ failure or immunocompromise.
2. Age
3. Temperature
4. Mean arterial pressure
5. Ph
6. Pulse rate
7. Respiratory rate
8. Sodium
9. Potassium
10. Creatinine
11. Acute renal failure
12. Hematocrit
13. White blood cell count
14. Glasgow coma scale
15. Fio2

SAPS-II Scoring System was calculated using the following variables-

1. Age
2. Heart rate
3. Systolic blood pressure
4. Temperature
5. Glasgow coma scale
6. PaO2/FiO2
7. Bun or serum urea

8. Urine output
9. Sodium
10. Potassium
11. Bicarbonate
12. Bilirubin
13. Whole blood cell count
14. Chronic disease- metastatic cancer, hematologic malignancy, AIDS
15. Type of admission: sched

Comparison of all three scoring systems was done in terms of sensitivity, specificity, positive predictive value, negative predictive value and Youden's index.

Follow up was conducted telephonically to assess the end point of study in terms of mortality.

STATISTICAL ANALYSIS

We'll utilise SPSS 20.0, a statistical application for social science computers, to perform the statistical study. Mean SD or median will be used for continuous variables that are not normally distributed (IQR). Categorical variables will be represented using frequencies and percentages.

Whitney Mann When comparing normally distributed continuous variables between groups, the U test will be utilized". The chi-squared test, Fisher's exact test, and multivariate analysis are all approaches for comparing nominal categorical data.

The lower the P-value, the more significant the statistical test results are in the majority of cases. Use of visual representations of data was made when necessary. We'll use Microsoft Excel 2010 to create a visual depiction (version 2013).

Use of ROC curve: ROC curves are frequently used to show in a graphical way the corelation between clinical sensitivity and specificity for every possible cut-off for a test or a combination of tests. In addition the area under the ROC curve gives an idea about the benefit of using the test(s) in question.

ROC curves are used to choose the most appropriate cut-off for a test. The best cut-off has the highest true positive rate together with the lowest false positive rate.

As the area under an ROC curve is a measure of the usefulness of a test in general, where a greater area means a more useful test, the areas under ROC curves are used to compare the usefulness of tests.

Yodens index: Youden's index is often used in conjunction with receiver operating characteristic (ROC) analysis. The index is defined for all points of an ROC curve, and the maximum value of the index may be used as a criterion for selecting the optimum cut-off point when a diagnostic test gives a numeric rather than a dichotomous result. The index is represented graphically as the height above the chance line, and it is also equivalent to the area under the curve subtended by a single operating point

OBSERVATIONS AND RESULTS

A hospital based prospective study was conducted with 100 patients to assess and compare the predictive accuracy for mortality of the three predictive scoring system in the ICU namely SOFA, APACHE II and SAPS II.

Distribution of patients according to Age

Majority of the patients (37%) were in the age group of 60-79 years followed by 35% in the age group of 40-59 years, 17% in the age group of 20-39 years, 9% patients in the age group of >80 years and 2% in the age group of 18-20 years. The mean age of the patients was 52.93 ± 20.28 years.

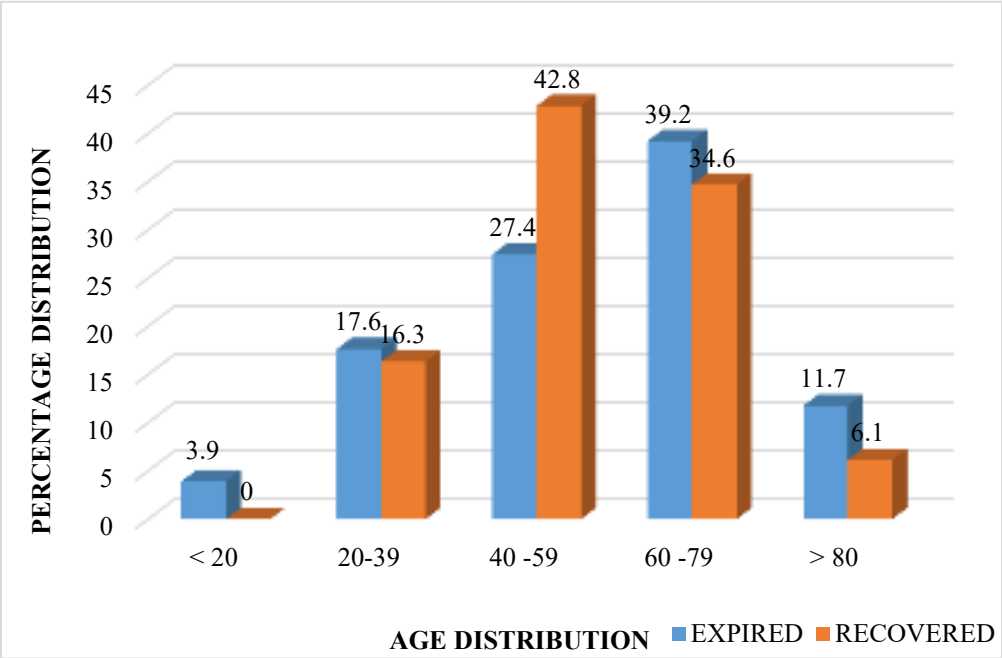
Table 1: Distribution of patients according to age

AGE (YEARS)	NO OF PATIENTS	PERCENTAGE
18-20 years	2	2%
21-39 years	17	17%
40-59 years	35	35%
60-79 years	37	37%
>80 years	9	9%
Total	100	100%
Mean ± SD	52.93 ± 20.28	

Table 2: Distribution of patients according to Age who expired and recovered.

AGE	EXPIRED		RECOVERED		TOTAL
	NUMBER	%	NUMBER	%	
< 20	2	3.92	0	0.00	2
20-39	9	17.65	8	16.33	17
40 -59	14	27.45	21	42.86	35
60 -79	20	39.22	17	34.69	37
> 80	6	11.76	3	6.12	9
TOTAL	51	100.00	49	100.00	100

Graph 1: Graph showing percentage age distribution



Distribution of patients according to Sex

51(51%) patients were males while female patients constituted 49% of the study population.

Table 3: Distribution of patients according to Sex

SEX	NO OF PATIENTS	PERCENTAGE
Male	51	51%
Female	49	49%
Total	100	100%

Graph 2: Graph showing sex distribution

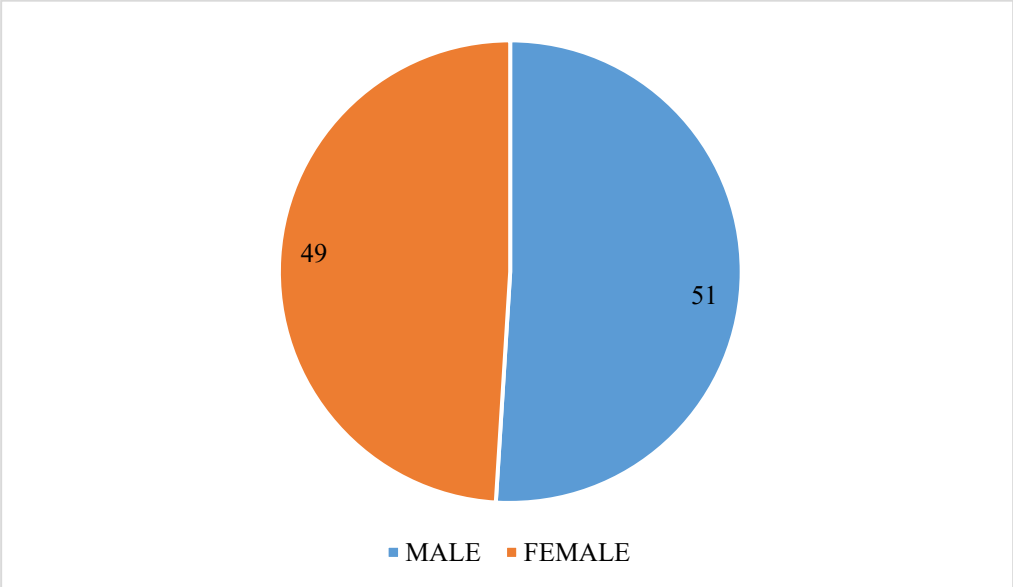
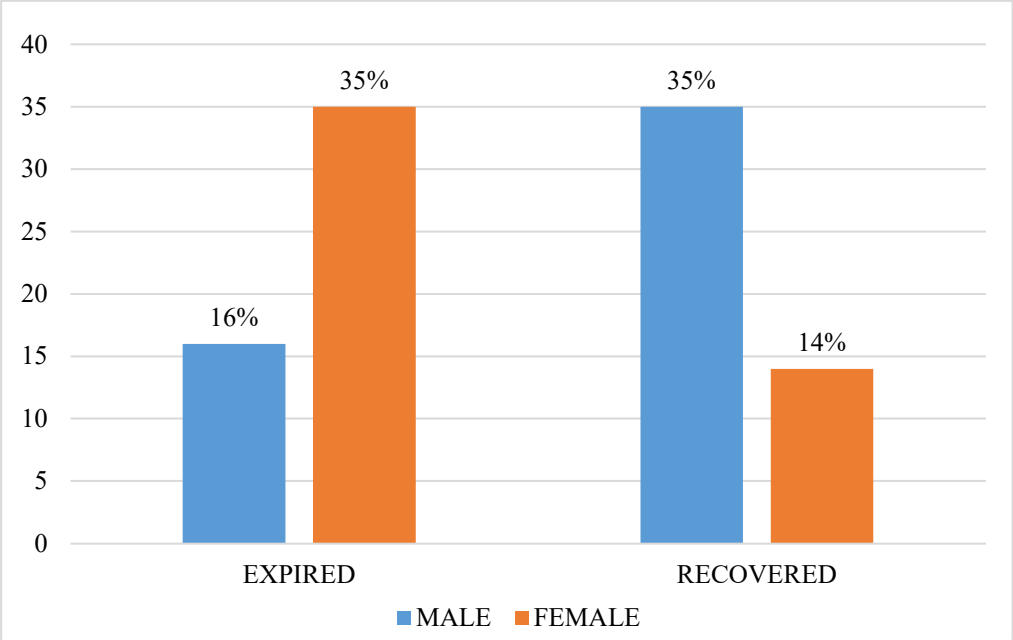


Table 4: Distribution of age according to outcome

GENDER	EXPIRED		RECOVERED		TOTAL
	NUMBER	%	NUMBER	%	
FEMALE	35	68.63	14	28.57	49
MALE	16	31.37	35	71.43	51
TOTAL	51	100.00	49	100.00	100

Graph 3: Percentage distribution of patients according to outcome



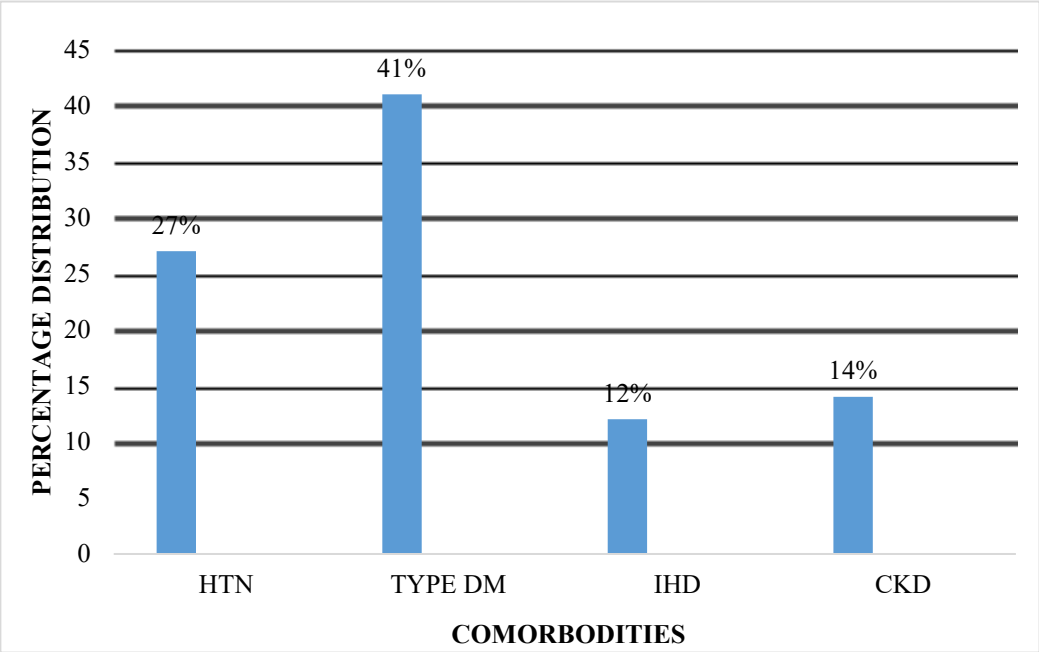
Distribution of patients according to comorbidities

41(41%) patients had diabetes mellitus, 27 (27%) patients had hypertension while 14 (14%) had coronary artery disease (CAD), and 12 (12%) had IHD respectively.

Table 5: Distribution of patients according to comorbidities

COMORBIDITIES	NO OF PATIENTS	PERCENTAGE (%)
Type 2 Diabetes Mellitus (T2DM)	41	41%
Hypertension (HTN)	27	27%
Chronic Kidney Disease (CKD)	14	14%
Ischemic Heart Disease (IHD)	12	12%

Graph 4: Graphical distribution of patients according to comorbidities



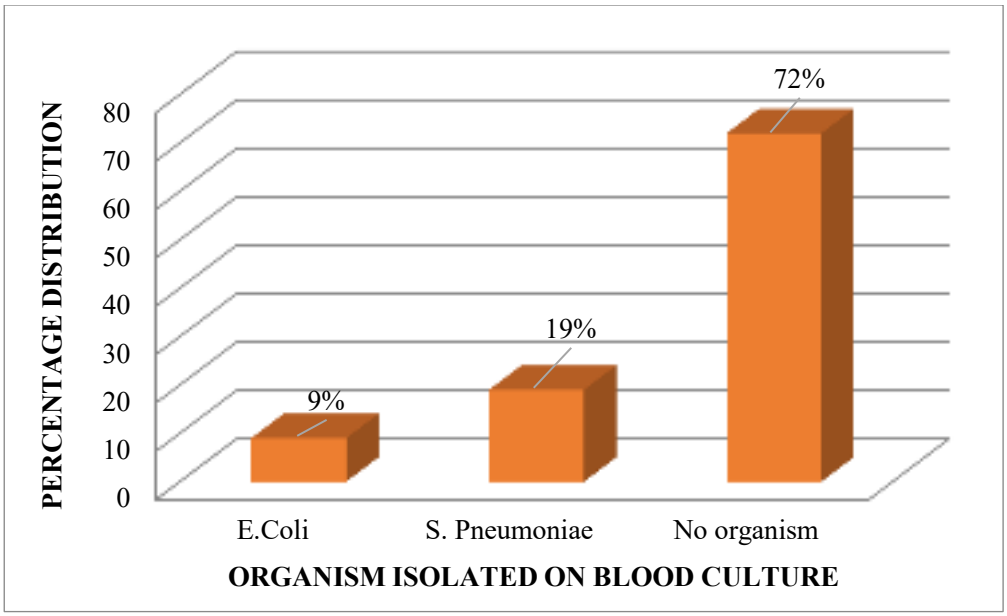
Distribution of patients according to Blood Culture Findings

9 (9%) and 19 (19%) patients had positive blood culture for E.Coli and S. Pneumoniae respectively.

Table 6: Distribution of patients according to organism isolated from Blood Culture

Blood Culture Findings	Number	Percentage
E.Coli	9	9%
S. Pneumoniae	19	19%
No organism	72	72%
Total	100	100%

Graph 5: Distribution of patients according to organism isolated from Blood Culture



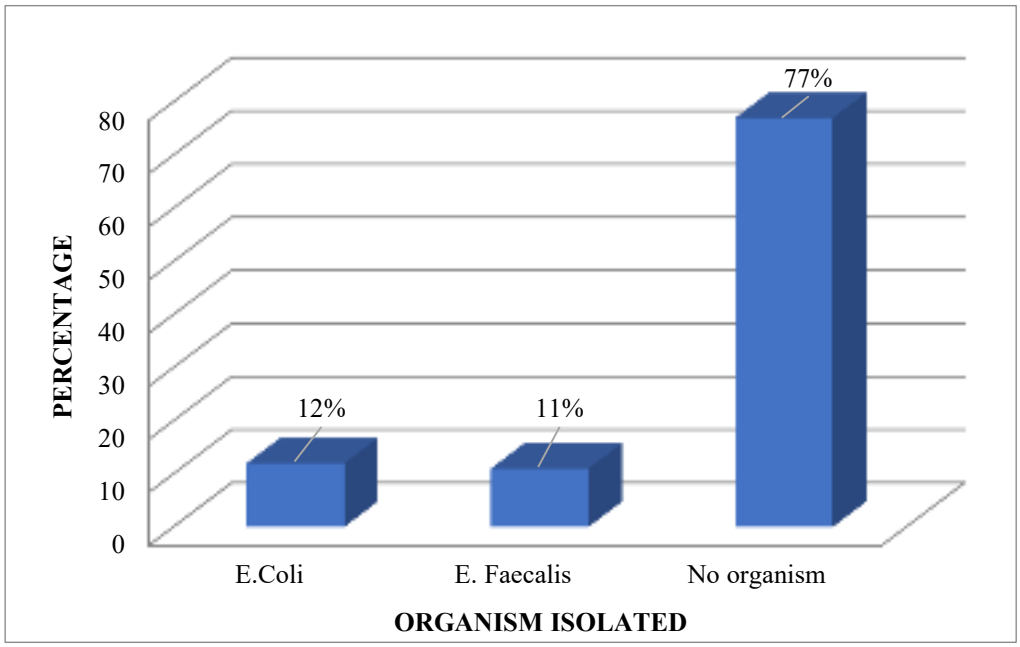
Distribution of patients according to Urine Culture Findings

12 (12%) and 11 (11%) patients had positive urine culture for E.Coli and E. Faecalis respectively.

Table 7: Distribution of patients according to Urine Culture Findings

URINE CULTURE FINDINGS	NO OF PATIENTS	PERCENTAGE (%)
E.Coli	12	12%
E. Faecalis	11	19%
No organism	77	77%
Total	100	100%

Graph 6: Distribution of patients according to Urine Culture Findings



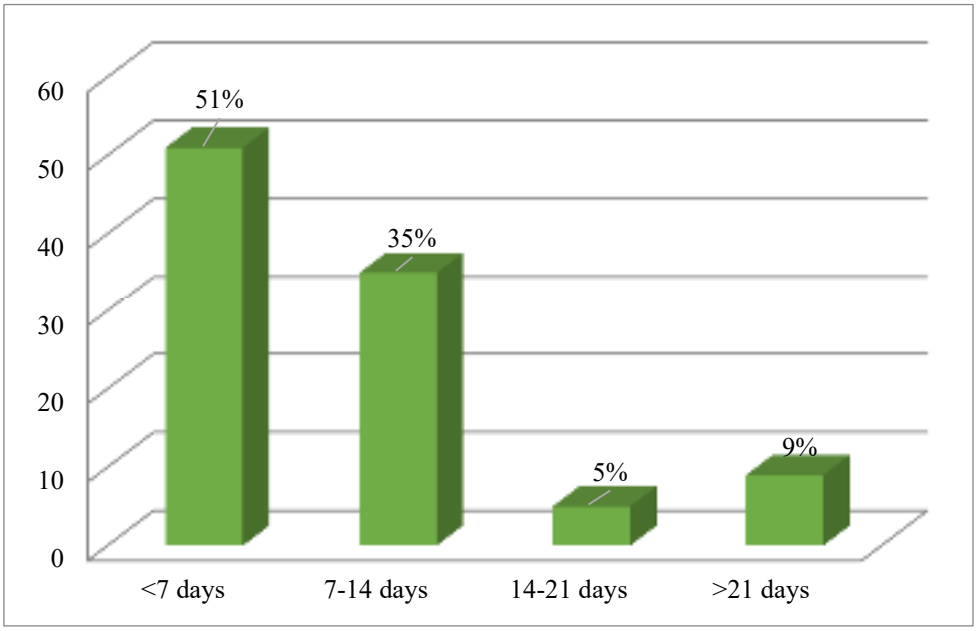
Distribution of patients according to Duration of ICU Stay

The duration of ICU stay for 51 (51%) and 35 (35%) patients was <7 days and 7-14 days respectively while it was 14-21 days and >21 days for 5 (5%) and 9 (9%) patients respectively. The mean duration of ICU stay was 8.51 ± 7.83 days.

Table 8: Distribution of patients according to Duration of ICU Stay

DURATION OF ICU STAY	NO OF PATIENTS	PERCENTAGE
<7 days	51	51%
7-14 days	35	35%
14-21 days	5	5%
>21 days	9	9%
Total	100	100%
Mean ± SD	8.51 ± 7.83	

Graph7: Distribution of patients according to Duration of ICU Stay



Distribution of patients according to Outcome

49 (49%) patients were discharged while 51 (30%) patients expired during ICU stay in our study.

Table 9: Distribution of patients according to Outcome

OUTCOME OF PATIENTS	NO OF PATIENTS	PERCENTAGE
Discharged	49	49%
Mortality	51	51%
Total	100	100%

Table 10: Physiological variables of patients comparison at 24 hours and 48 hours of admission

Parameters	Mean at 24 hours	SD at 24 hours	Mean at 48 hours	SD at 48 hours
GCS	14.48	1.04	14.58	0.82
HR (bpm)	97.83	18.52	102.60	14.97
SBP (mmHg)	111.00	13.37	113.90	16.39
MAP (mmHg)	82.44	14.25	85.97	15.11
RR (breaths per minute)	29.45	5.20	27.56	5.29
Urine Output (ml/kg/hr)	872.30	865.42	1122.00	1098.28
Hematocrit (%)	32.70	2.30	32.14	3.86
WBC (cells/mm^3)*	16.45	10.20	12.92	6.74
Platelet (×10^9/L)**	125.78	73.87	117.19	104.83
BUN (mg/dl)	127.31	68.59	126.86	88.23
Creatinine (mg/dl)	3.64	2.08	3.57	2.34
Sodium (mEq/L)	133.28	8.23	133.32	2.34
Potassium (mEq/L)	4.45	0.95	4.39	0.90

Parameters	Mean at 24 hours	SD at 24 hours	Mean at 48 hours	SD at 48 hours
Bilirubin (mg%)	2.05	1.04	2.04	1.39
Bicarbonate (mEq/L)	14.79	5.16	18.14	6.98
pH	7.35	0.08	7.40	0.07
PaO_2 (mmHg)	99.20	43.94	96.42	52.93
$PaCO_2$ (torr)	28.95	11.88	31.22	11.21
PaO_2/ FiO_2	250.21	90.48	258.22	102.57
A-a gradient (mmHg)	158.31	87.14	132.64	52.13
Lactate (mmol/L)	3.64	3.18	3.05	1.88
PCT (µg/l)	43.28	41.11	44.15	45.47

*Decrease in whole blood count from mean of 16.45 at 24 hours to 12.92 at 48 hours was noticed, which could be attributed to antibiotic use.

**Drop in platelet count was noticed from mean of 125 at 24 hours to 117.19 at 48 hours.

Physiological variables of patients within 24 hours of admission

The mean GCS and HR values of patients within 24 hours of admission were 14.48±1.04 and 97.83±18.52bpm respectively while the mean SBP and MAP values were 111.00±13.37 mmHg and 82.44±14.25 mmHg respectively. The mean RR, Urine Output and Hematocrit values were 29.45±5.20 breaths per minute, 872.30±865.42 ml/kg/hr and 32.70±2.30 % respectively.

The mean WBC and Platelet values of patients within 24 hours of admission were 16.45±10.20 cells/mm^3 and 125.78±73.87 $\times 10^9$/L respectively while the mean BUN and Creatinine values were 127.31±68.59 mg/dl and 3.64±2.08 mg/dl respectively. The mean Sodium, Potassium and Bilirubin values were 133.28±8.23 mEq/L, 4.45±0.95 mEq/L and 2.05±1.04 mg% respectively.

The mean Bicarbonate and pH values of patients within 24 hours of admission were 14.79±5.16 mEq/L and 7.35±0.08 respectively while the mean PaO_2 and $PaCO_2$ values were 99.20±43.94 mmHg and 28.95±11.88 torr respectively. The mean PaO_2/ FiO_2, A-a gradient, Lactate and PCT values were 250.21±90.48, 158.31±87.14 mmHg, 3.64±3.18 mmol/L and 43.28±41.11 µg/l respectively.

Physiological variables of patients within 48 hours of admission

The mean GCS and HR values of patients within 48 hours of admission were 14.58±0.82 and 102.60±14.97bpm respectively while the mean SBP and MAP values were 113.90±16.39 mmHg and 85.97±15.11 mmHg respectively. The mean RR, Urine Output and Hematocrit values were 27.56±5.29 breaths per minute, 1122.00±1098.28 ml/kg/hr and 32.14±3.86 % respectively.

The mean WBC and Platelet values of patients within 48 hours of admission were 12.92±6.74 cells/mm^3 and 117.19±104.83 $\times 10^9$/L respectively while the mean BUN and Creatinine values were 126.86±88.23 mg/dl and 3.57±2.34 mg/dl respectively. The mean Sodium, Potassium and Bilirubin values were 133.32±2.34 mEq/L, 4.39±0.90 mEq/L and 2.04±1.39 mg% respectively.

The mean Bicarbonate and pH values of patients within 48 hours of admission were 18.14±6.98 mEq/L and 7.40±0.07 respectively while the mean PaO_2 and $PaCO_2$ values were 96.42±52.93 mmHg and 31.22±11.21 torr respectively. The mean PaO_2/ FiO_2, A-a gradient, Lactate and PCT values were 258.22±102.57, 132.64±52.13 mmHg, 3.05±1.88 mmol/L and 44.15±45.47 µg/l respectively.

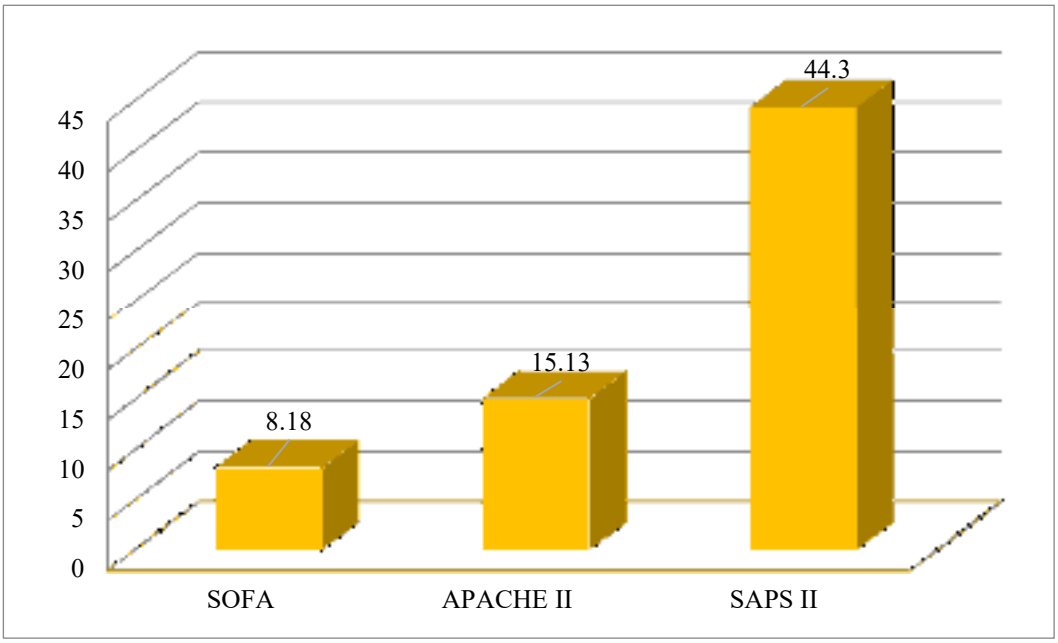
Table 11: SOFA, APACHE II and SAPS II Score of patients within 24 and 48 hours of admission

Parameters	Mean at 24 hours	SD at 24 hours	Mean at 48 hours	SD at 48 hours
SOFA	8.18	2.41	8.31	3.08
APACHE II	15.13	5.02	15.23	4.60
SAPS II	44.30	14.17	43.48	15.62

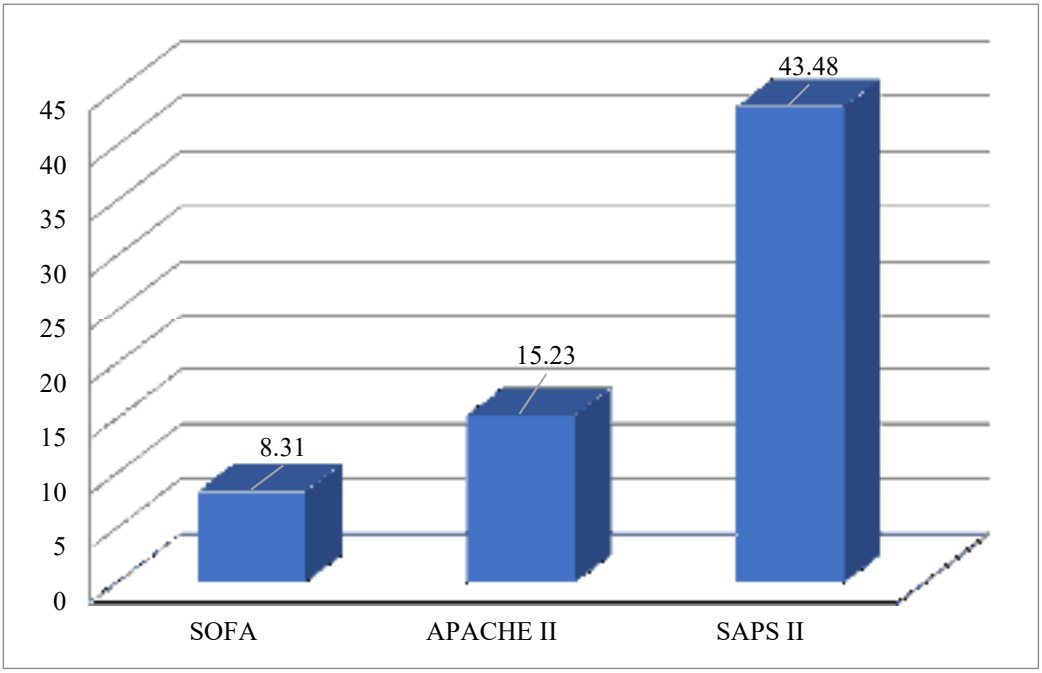
SOFA, APACHE II and SAPS II Score of patients within 24 hours and 48 hours of admission

The mean SOFA score of patients within 24 hours of admission was 8.18±2.41 while the mean APACHE II and SAPS II score were 15.13±5.02 and 44.30±14.17 respectively. The mean SOFA score of patients within 48 hours of admission was 8.31±3.08 while the mean APACHE II and SAPS II score were 15.23±4.60 and 43.48±15.62, respectively.

Graph 8: SOFA, APACHE II and SAPS II Score of patients within 24 hours of admission



Graph 9: SOFA, APACHE II and SAPS II Score of patients within 48 hours of admission



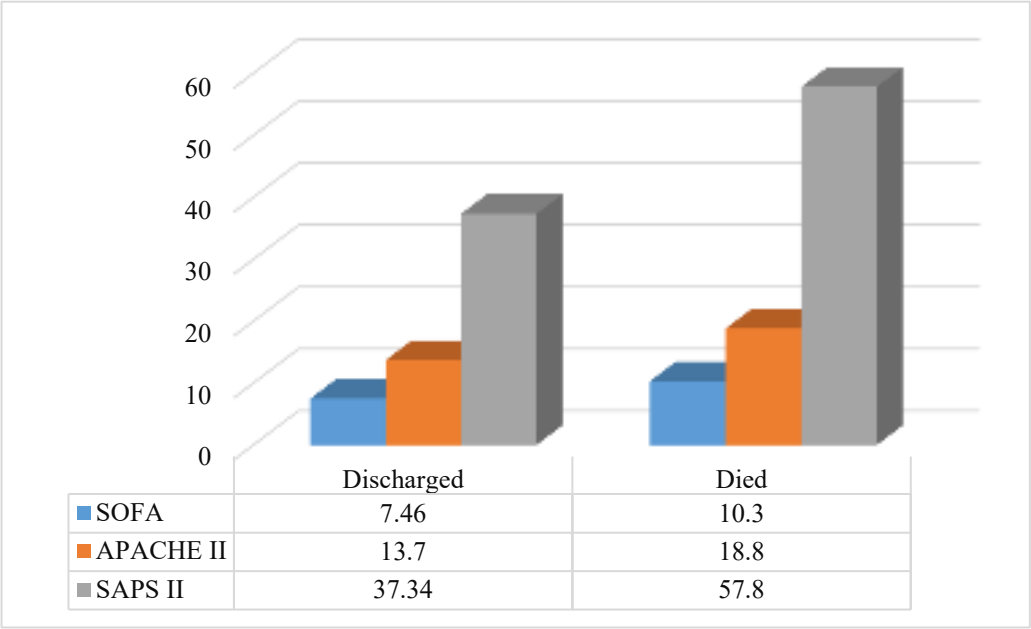
Association of SOFA, APACHE II and SAPS II Score and mortality

The mean SOFA (7.46±2.82 vs. 10.30±2.77), APACHE II (13.70±4.03 vs. 18.80±3.83) and SAPS II (37.34±13.11 vs. 57.80±10.99) score of discharged patients was significantly lower compared to patients who had mortality although as per Student t-test (**p<0.05**) but was statistically not significant.

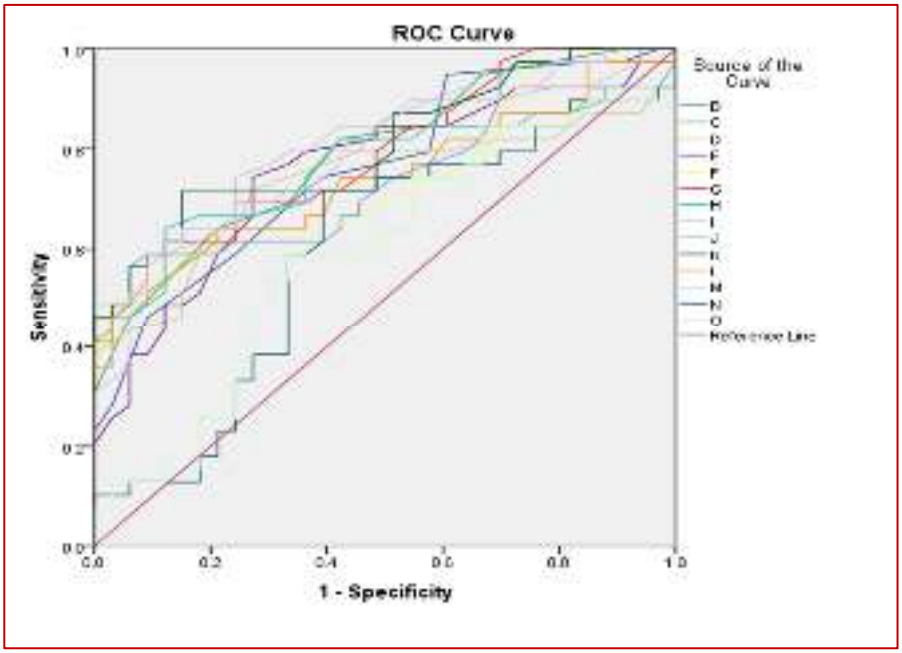
Table 12: Association of SOFA, APACHE II and SAPS II Score and mortality

Parameters	Discharged		Died		p Value
	Mean	SD	Mean	SD	
SOFA	7.46	2.82	10.30	2.77	**<0.05**
APACHE II	13.70	4.03	18.80	3.83	**<0.05**
SAPS II	37.34	13.11	57.80	10.99	**<0.05**

Graph 10: Association of SOFA, APACHE II and SAPS II Score and mortality



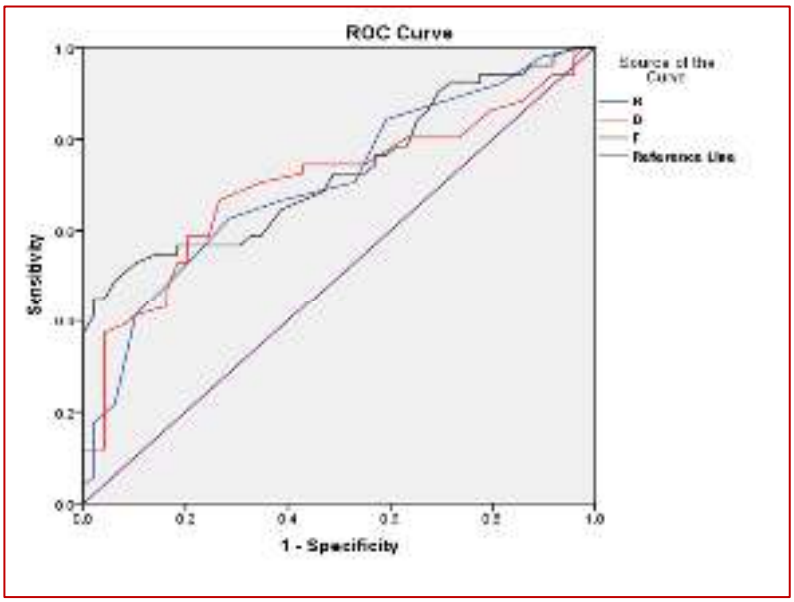
Graph 11: Roc curves of various mortality predicting models



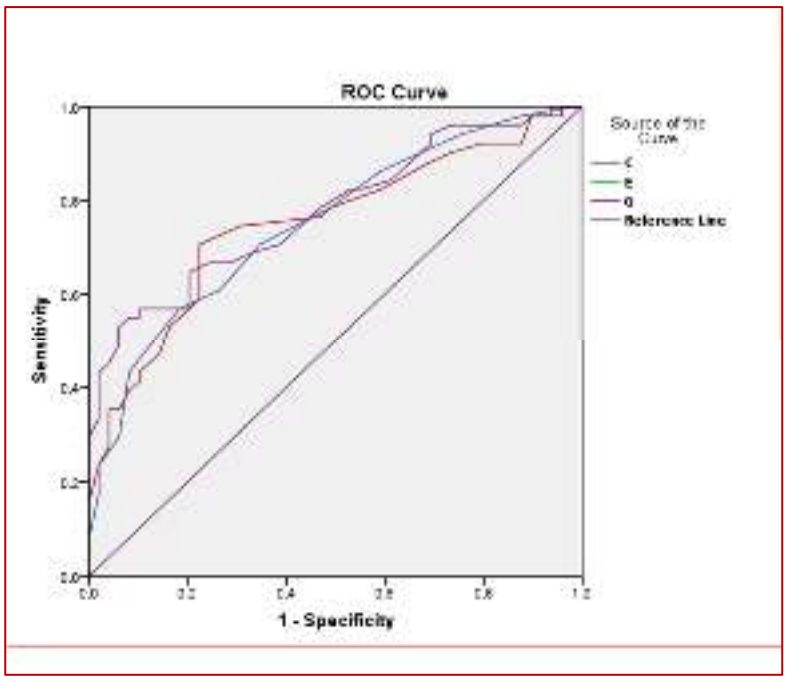
In the above chart:

B	**SOFA**	**24 HR**
C	**SOFA**	**48 HR**
D	**APACHE II**	**24 HR**
E	**APACHE II**	**48 HR**
F	**SAPS II**	**24 HR**
G	**SAPS II**	**48 HR**
H	**SOFA+APA**	24 HR
I	**SOFA+APA**	48 HR
J	**SOFA+SAPS**	24 HR
K	**SOFA+SAPS**	48 HR
L	**APA+SAPS**	24 HR
M	**APA+SAPS**	48 HR
N	**lactate**	**24 HR**
O	**lactate**	**48 HR**

Graph 12: Roc Curve Showing Sensitivity and Specificity For Sofa, Apache II And Saps II At 24 Hrs



Graph 13: Roc Curve Showing Sensitivity and Specificity For Sofa, Apache II And Saps II At 48 Hrs



Area under the curve determines the sensitivity and specificity.

ROC curves of SOFA on prediction of mortality

The area under the ROC curve (AUC) of SOFA on prediction of mortality was 0.759 and 0.7914 respectively at 24 and 48 hours, thus demonstrating statistical significance ($p<0.001$).SOFA score had sensitivity of 46.15% and 64.10%, specificity of 90.91% and 78.79% respectively at 24 and 48 hours, with PPV of 94% and NPV OF 54 %

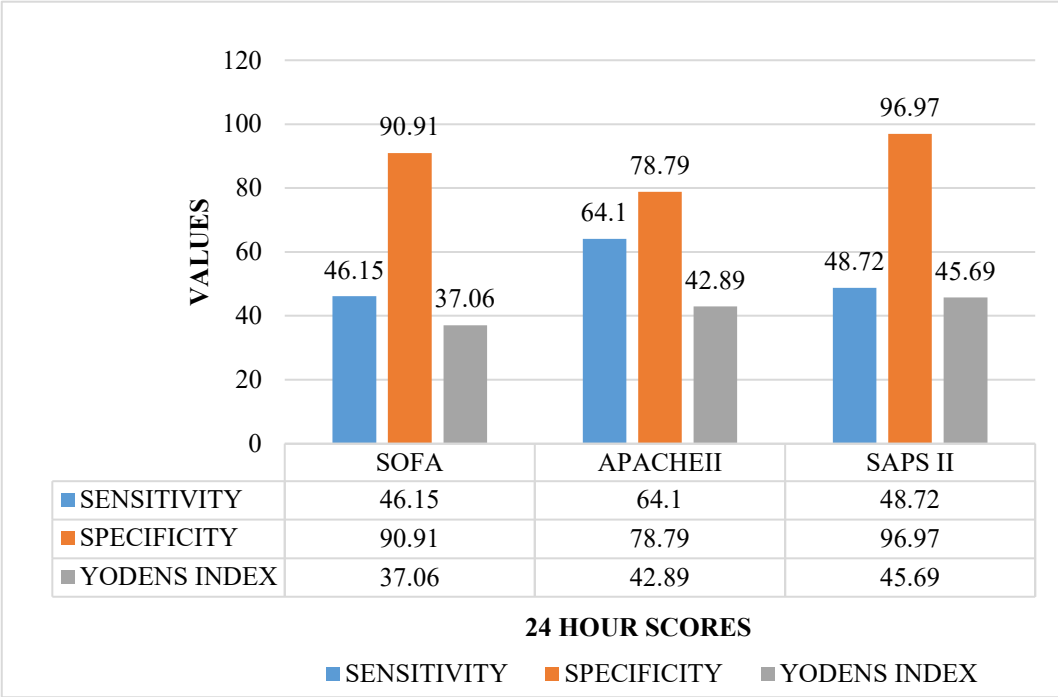
ROC curves of APACHE II on prediction of mortality

The area under the ROC curve (AUC) of APACHE II on prediction of mortality was 0.7319 AND 0.7564 respectively at 24 and 48 hours thus demonstrating statistical significance ($p<0.001$). SOFA score had sensitivity of 64.10% and 78.79% respectively at 24 and 48 hours, with specificity of 78.79% and 72.73% at 24 and 48 hours, 90% PPV and 62% NPV.

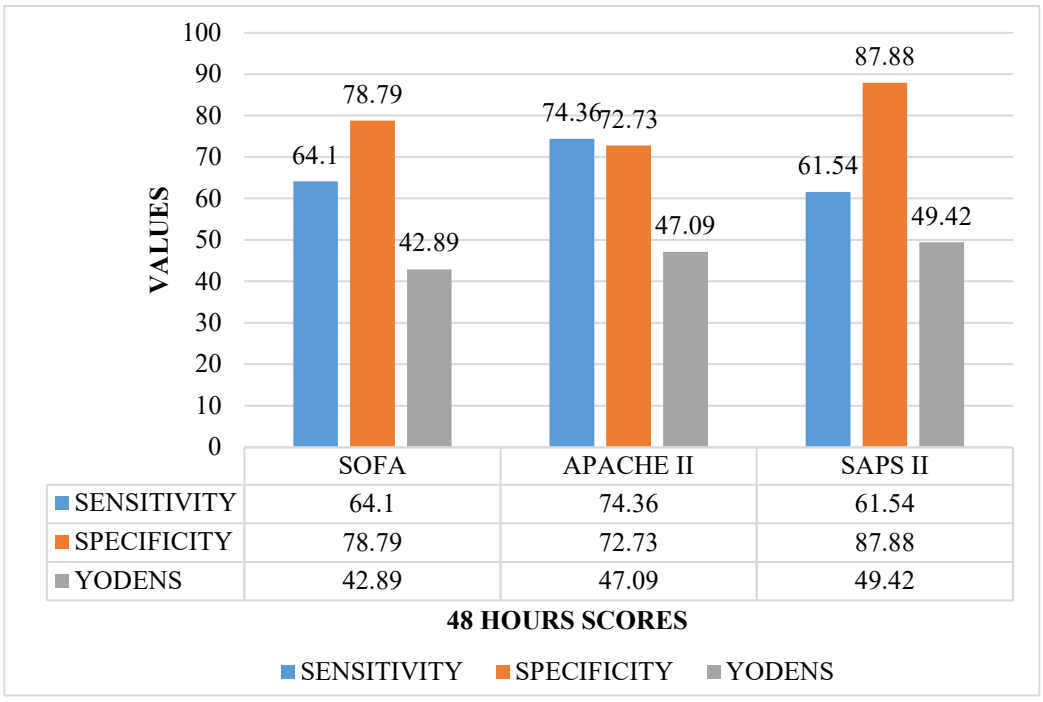
ROC curves of SAPS II on prediction of mortality

The area under the ROC curve (AUC) of SAPS II on prediction of mortality was 0.919 (95% CI: 0.891 - 0.949), thus demonstrating statistical significance ($p<0.001$). SAPS score had sensitivity of 48.72% and 61.54% at 24 and 48 hours, and specificity of 96.97% and 87.88% at 24 and 48 hours, with 96% PPV and 66% NPV.

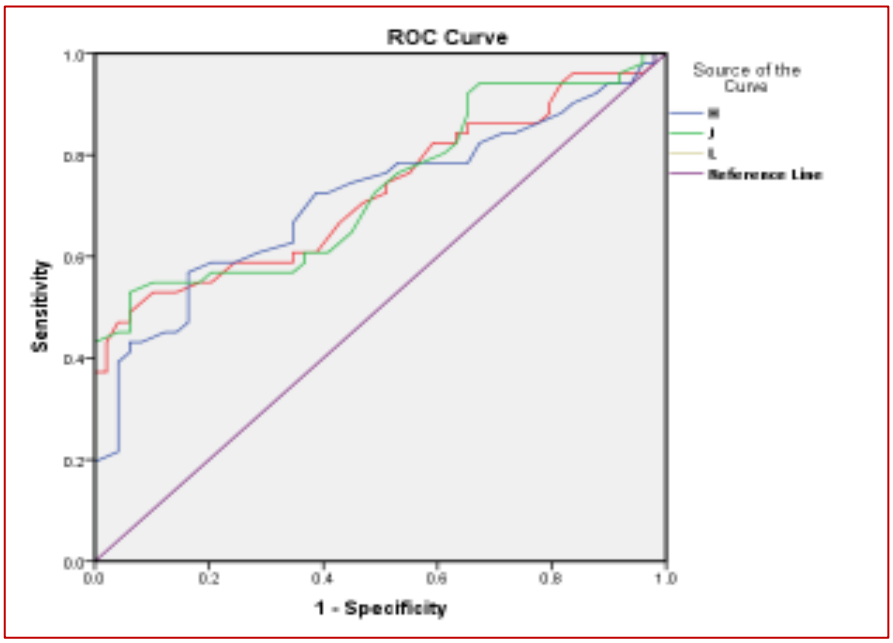
Graph 14: 24 Hour Scores and Respective Indices



Graph 15: 48 Hour Scores and Respective Indices



Graph 16: Roc Curve for Sofa +Apache II 24 Hrs, Sofa+Saps II 24 Hrs, Apache II+Saps II 24 Hrs



Graph 17: Roc Curve for Sofa +Apache II 48 Hrs, Sofa+Saps II 48 Hrs, Apache II+Saps II 48 Hrs

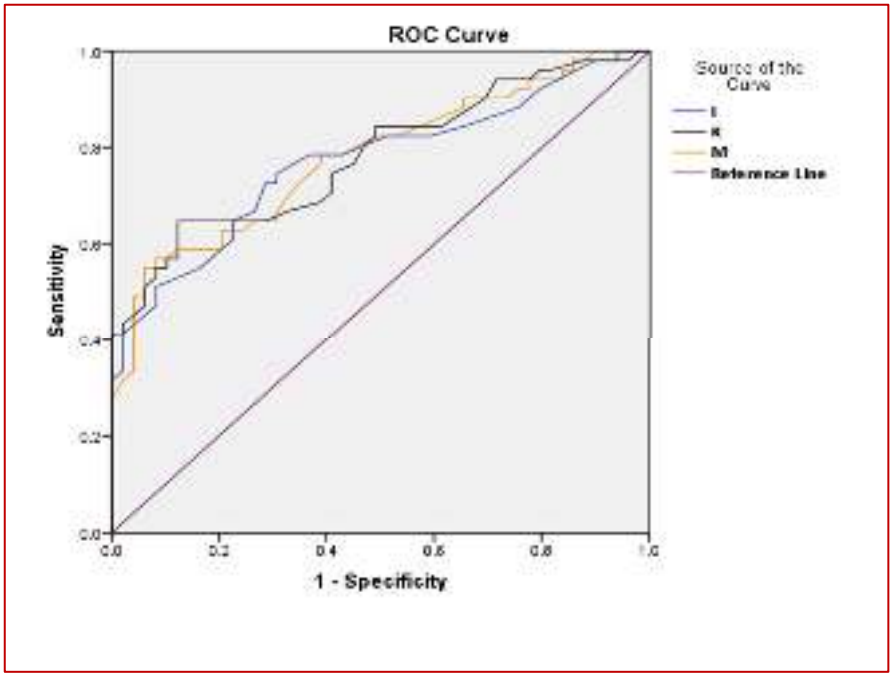


Table 13: Area under curve for combination of different scores at 24 and 48 hours

SOFA+APA	**24 HR**	**0.7638**
SOFA+APA	48 HR	0.8011
SOFA+SAPS	24 HR	0.7529
SOFA+SAPS	48 HR	0.8061
APA+SAPS	24 HR	0.7416
APA+SAPS	48 HR	0.7941

Table 14: Sensitivity, Specificity and Yoden's index for various scores and combination of scores at 24 and 48 hours

VARIABLE		CUT OFF VALUE	SENSITIVITY	SPECIFICITY	*YODEN'S INDEX
SOFA	**24 HR**	9.50	46.15	90.91	37.06
SOFA	**48 HR**	8.50	64.10	78.79	42.89
APACHE II	**24 HR**	19.50	64.10	78.79	42.89
APACHE II	**48 HR**	17.50	74.36	72.73	47.09
SAPS II	**24 HR**	60.00	48.72	96.97	45.69
SAPS II	**48 HR**	51.50	61.54	87.88	49.42
SOFA+APACHE II	**24 HR**	14.75	64.10	87.88	51.98
SOFA+APACHE II	**48 HR**	12.75	74.36	75.76	50.12
SOFA+SAPS	**24 HR**	32.25	56.41	93.94	50.35
SOFA+SAPS	**48 HR**	28.25	71.79	84.85	56.64
APACHE II +SAPS	**24 HR**	34.75	64.10	78.79	42.89
APACHE II +SAPS	**48 HR**	38.25	58.97	90.91	49.88

*YODEN'S INDEX = SENSITIVITY + SPECIFICITY -100. Whichever pair has the highest yoden's index that is considered as the most ideal

In our study maximum sensitivity at 24 hours as well as 48 hours was shown with APACHE II which was 64.10 and 74.36 respectively.

Specificity at 24 as well as 48 hours was maximum with SAPS II being 96.97 and 87.88 respectively.

On combining the scores sensitivity of combination of SOFA and APACHE II score was maximum being 74.36 but still remained comparable to APACHE II score alone. Although specificity for SOFA and SAPS combination score was higher than individual score alone at 24 hours being 93.94.

However, when there are many values of sensitivity and specificity as was in our case, to find out which set gives the best result, yoden's index is used

YODEN'S INDEX= SENSITIVITY+ SPECIFICITY-100

Whichever pair has the highest yoden's index that is considered as the most ideal one in our study yodens index was found to be highest for combination score of SOFA and SAPS at 48 hours being 56.64 and among individual score was highest for SAPS II at 48 hours being 49.42, and was lowest for SOFA score at 24 hours being 37.06.

The above results in our study led to the conclusion that although all the scores described here are individually good predictors of sepsis as well as mortality, however a combination of the scores did show slightly better performance.

DISCUSSION

A hospital based prospective study was conducted with 100 patients to assess and compare the predictive accuracy for mortality of the three predictive scoring system in the ICU namely SOFA, APACHE II and SAPS II.

In our study Majority of the patients (37%) were in the age group of 60-79 years followed by 35% in the age group of 40-59 years, 17% in the age group of 20-39 years, 9% patients in the age group of >80 years and 2% in the age group of 18-20 years. The mean age of the patients was 52.93 ± 20.28 years, these results were similar to the studies of Doerr et al, and when compared with western studies like Dabhi AS et al[103] where the study found majority of patients were in the age group of 21-50 years (64%) here mean age of the study subjects was 40.60 ± 17.24 years and out of 84 study patients, 50 were males and 34 were females. Another prospective observational study conducted by Singh M et al[102] found out of the 120 patients 46 patients were in the age group of 40 to 59 years and 45 patients belonged to 60 to 80 years age group respectively.

The study population had an almost equal male to female representation with 51% male and 49% of female admissions, with a significant higher mortality in the female patients of 68.63% in comparison to only 31.37% mortality in the male patients, in present study recovery rate in the female patients was 28.57%, whereas in male patients was 71.43%, which remained comparable with one of Indian studies conducted by Mohan et al where mortality rate among females was 69.5% and in male population was 38.8% respectively. Another Indian study conducted by Singh M

et al[102] with 71 females and 49 male patients and out of 71 female patients 27 patients i.e. 38% died and out of 49 male patients 16 patients i.e. 32% had died.

In our study 41(41%) patients had diabetes mellitus, 27 (27%) patients had hypertension while 14 (14%) had coronary artery disease (CAD), and 12 (12%) had IHD respectively. Diabetes was most common comorbid condition in our study which is similar to Forecast Study with incidence of diabetes mellitus was 23%, also, Indian study by Singh M et al[102] which is prospective observational study with a sample size of 120, diabetes was found in 64 patients (53.3%), followed by 34 patients with HTN (28.3%), 29 patients had CKD (24%), and 22 patients had COPD (18.3%).

It was observed in our study that the duration of ICU stay was less than 7 days in 51 patients (51%) and 7-14 days in 35 (35%), while about 5 (5%) had a stay for 14-21 days and 9 (9%) patients had stay for >21 days. The mean duration of ICU stay was 8.51 ± 7.83 days in our study which was comparable with Brun-buisson et al where stay in the ICU was for a median of 8.5 days.

In our study when we compared the mean between various variables (namely GCS, heart rate, systolic blood pressure, mean arterial pressure, respiratory rates, urine output, Hematocrit, WBC, platelet, BUN, creatinine, sodium, potassium, bilirubin, bicarbonate, arterial pH, PaO2, PaCO2, PaO2/FiO2, A-a gradient) at 24 hours and at 48 hours didn't show significant difference among the variables, however decrease in whole blood count from mean of 16.45 at 24 hours to 12.92 at 48 hours was noticed, which could be attributed to antibiotic use. Also drop in platelet count was noticed from mean of 125 at 24 hours to 117.19 at 48 hours, but correlation with mortality could not be significantly attributed to these changes,

thrombocytopenia was also seen in study conducted by Awad et al, also leucocytosis was also observed in study by Dabhi AS et al[103]

Among the 100 patients studied 49 (49%) patients were discharged while 51 (51%) patients expired during ICU stay in our study, which when compared with western multicentric studies was much higher such as FORECAST study where total hospital mortality rate was 23.4%, and SOAP study with 27% mortality rate, but remained comparable to Indian studies as with Mohan et al with a mortality rate of 53 %, and Sharma S et al[104] with mortality of 34%.

In our study serum procalcitonin and serum lactate levels were not significant in predicting either the severity or overall mortality of the patients without much significant difference noticed between the levels calibrated at 24 and 48 hours. However, In the FORECAST study increased lactate (67.3%) was associated with organ failure, also PCT was associated with a good prediction for sepsis and bacteremia, along with lactate in Indian studies as well.

In the present study, when we compared discharged group vs mortality group the mean SOFA (7.46±2.82 vs. 10.30±2.77), APACHE II (13.70±4.03 vs. 18.80±3.83) and SAPS II (37.34±13.11 vs. 57.80±10.99) here it was observed that score of discharged patients was significantly lower compared to mortality group as per Student t-test (**$p<0.05$**). Dabhi AS et al[103], Singh M et al[102] and Sharma S et al[104] noted similar observations in their studies.

All the three-scoring system were significant in predicting the mortality of the patients.

Mean score using APACHE II scoring system was 17±7.2 for patients who survived and 25.5±9.1 in mortality group. The difference in mean was 8.5 which was highly significant. The mean score using SAPS II scoring system was 45.7±14.2 for patients who survived and 56.3±19.5 for patients who did not survive and the mean difference between the two groups was 19.6. which is highly significant. The mean score using SOFA scoring system which was 8.1±3.6 for patients who survived and 11.6±4.2 for patients who did not survive and mean difference between the two groups was 3.5 which were highly significant.

Sharma S et al[104] study reported predicted mortality of SAPS 2, APACHE II and SOFA with mean difference in the mortality and recovery group found to be 30 for SAPS 2, 38 for APACHE II and 25 for SOFA score respectively. SAPS2 and SOFA predicted a slightly lower mortality rate than the actual mortality, whereas APACHE II had predicted a higher mortality than the actual mortality.

Dabhi AS et al[103] study reported actual Mortality Rate (AMR) was 60.71%. Mean of Predicted Mortality Rate (PMR) for APACHE-IV was 37.85% and for SAPS-II, it was 72.36% which shows that APACHE-IV had under-predicted overall mortality while SAPS-II had over-predicted overall mortality.

In the present study, the area under the ROC curve (AUC) of SOFA on prediction of mortality was 0.7914 max at 48 hours, thus demonstrating good diagnostic performance. It was statistically significant ($p<0.001$). SOFA score had sensitivity of 46.15% and 64.10%, specificity of 90.91% and 78.79% respectively at 24 and 48 hours, with PPV of 94% and NPV OF 54 %.

Area under the ROC curve (AUC) of APACHE II on prediction of mortality was 0.7564 max at 48 hours, thus demonstrating good diagnostic performance. It was statistically significant ($p<0.001$), sensitivity of 64.10% and 78.79% respectively at 24 and 48 hours, and specificity of 78.79% and 72.73% at 24 and 48 hours, 90% PPV and 62% NPV.

It was observed in the present study that the area under the ROC curve (AUC) of SAPS II on prediction of mortality was 0.7914 max at 48 hours, thus demonstrating good diagnostic performance. It was statistically significant ($p<0.001$). sensitivity of 48.72% and 61.54% at 24 and 48 hours, and specificity of 96.97% and 87.88% at 24 and 48 hours, with 96% PPV and 66% NPV. This is concordant to the studies of Sharma S et al[104] and Singh M et al[102].

Sharma S et al[104] study found SAPS 2 and SOFA had a 100% positive predictive value whereas APACHE II had a PPV of 88%. The NPV was highest in APACHE II score (100%), followed by SAPS 2 (94%) and SOFA (88%). It was also found that SAPS 2 and SOFA had 100% specificity whereas APACHE II had a specificity of 93.9%. However, it was observed that APACHE II had 100% sensitivity as a model for mortality prediction.

Singh M et al[102] prospective observational study showed cut-off point for predicting mortality by SAPS II was taken as 51.5. Mortality falling above this cutoff was taken for comparing the 3 scoring systems. Area under curve for each scoring system with SAPS II having the maximum area of 0.782.

In our study, the ROC analysis shows that the best discrimination was provided by SAPS II score (AUC=0.919) followed by SOFA score (AUC=0.794) and

APACHE II score (AUC=0.7564). APACHE II score has the highest sensitivity (78.79%) and highest specificity for SAPS II (96.97%). Similar observations were noted in the studies of Sharma S et al[104], Singh M et al[102], Nobre G et al[106] and Dabhi AS et al[103].

Sharma S et al[104] study reported best discrimination was provided by SAPS 2 score (AUROC=0.981), followed by APACHE II (AUROC=0.978) and SOFA (AUROC=0.911) on ROC analysis. However, the difference between SAPS 2 and APACHE II score was statistically not significant and the discriminatory powers of SAPS 2 and SOFA scoring showed a statistically significant difference.

Singh M et al[102] prospective observational study reported SAPS II has the highest sensitivity and APACHE II scoring has the highest specificity. When comparing individually, all the 3 scores were significant ($p < 0.05$) in predicting the mortality of the patients, but SAPS II has the most area under the ROC curve with odds ratio of 1.449. SAPS II had higher area of 0.782 compared to APACHE II 0.764 and SOFA 0.733.

Nobre G et al[106] prospective cohort study showed that the most area under the ROC curve was 0.0887 (95% CI 0.743 – 1.032) for the SAPS II, among APACHE II, SAPS II and SOFA scores. The best cutoff value was 39.5 points, and the sensitivity and specificity were 85.7% and 88.9%, respectively. The SAPS 2 mean predicted mortalities for patients with score <39.5 and ≥ 39.5 were $6.31 \pm 0.48\%$ and $48.7 \pm 7.5\%$, respectively.

Dabhi AS et al[103] study showed that the mean of Predicted Mortality Rate (PMR) for APACHE-IV was 37.85% and for SAPS-II, it was 72.36% which shows

that APACHE-IV had under predicted overall mortality while SAPS-II had over-predicted overall mortality of patients with severe sepsis and septic shock. Standardized Mortality Rate for APACHE-IV was 1.60 and for SAPS-II, it was 0.83

A Further attempt was made to determine if the combination of scores had a better predictability than individual scores,

The area under the ROC curve (AUC) of combination score of SOFA and APACHE II on prediction of mortality was 0.7638 at 24 hours and 0.8011 at 48 hours. It was statistically significant ($p<0.001$), with sensitivity of 64.10% and 74.36% at 24 and 48 hours, and specificity of 87.88% and 75.76% at 24 and 48 hours, with Youden's index being 51.98 and 50.12 at 24 and 48 hours thus showing good diagnostic performance.

The area under the ROC curve (AUC) of combination score of APACHE II and SAPS II on prediction of mortality was 0.7416 at 24 hours and 0.7941 at 48 hours. It was statistically significant ($p<0.001$). sensitivity of 64.10% and 58.97% at 24 and 48 hours, and specificity of 78.79% and 90.91% at 24 and 48 hours, with Youden's index being 42.89 and 49.88 at 24 and 48 hours thus showing good diagnostic performance

The area under the ROC curve (AUC) of combination score of SAPS II and SOFA on prediction of mortality was was 0.8061 thus demonstrating good diagnostic performance. It was statistically significant ($p<0.001$). sensitivity of 56.41% and 71.79% at 24 and 48 hours, and specificity of 93.94% and 84.85% at 24 and 48 hours, with highest Youden's index being 56.64 at 48 hours thus showing best diagnostic

performance among all the combination of scores, next best score was seen with SOFA and APACHE II with Youden's index being 51.98 at 24 hours.

Study conducted by Saleh et al also showed similar results although strength of the relation could not be established using sensitivity, specificity or Youden's index.

STRENGTH OF THE STUDY

1. Not just individual scores but an attempt to compare different scores was made in our study.
2. Sensitivity and specificity of various individual scores was established along with combination of scores.
3. Diagnostic performance was established of various scores using Youden's index In Our Study Which Has Not Been Done in the Studies So Far.

LIMITATIONS OF THE STUDY

1. Small size and a single center study.
2. Sequential monitoring of the scores beyond 48 hours was not attempted.
3. Comparison between duration of stay and the severity of the scores was not established in the present study.

CONCLUSION

All the three scores showed good mortality prediction rate but among the scores higher sensitivity was seen with APACHE II score at 24 and 48 hours and higher specificity was seen with SAPS II at 24 and 48 hours. Combination of scores did show a slightly better predictability with combination of SAPS II and SOFA showing maximum Youden's index at 48 hours.

Mortality was comparatively higher among the females and elderly group with most common risk factor being diabetes.

SUMMARY

A hospital based prospective study was conducted with 100 patients to assess and compare the predictive accuracy for mortality of the three predictive scoring system in the ICU namely SOFA, APACHE II and SAPS II. The following observations were noted:

1. Majority of the patients (37%) were in the age group of 60-79 years with maximum mortality in this age group of 39.22 %.
2. Moratlity rate was 51%, with higher mortality in the female group being 68.63%.
3. Diabetes was most common comorbid in our study (41%) and could have been a risk factor for higher mortality in our study.
4. Most common isolate from blood culture was S. pneumoniae (19%), most common isolate from urine culture was E. faecalis (19%)
5. The mean duration of ICU stay was 8.51 ± 7.83 days.
6. No significant difference was observed in the physiological variable over 24 and 48 hours although, decrease in WBC and platelet count was noted at the end of 48 hours.
7. The mean SOFA, APACHE II, SAPS II were significantly higher in the mortality group than the recovery group.
8. All three scores had good diagnostic performance, with max sensitivity at 24 and 48 hours with APACHE II, max specificity at 24 and 48 hours with SAPS II.
9. On further combination of scores, maximum sensitivity was seen with SOFA plus APACHE II at 48 hours, maximum specificity was seen at 24 hours with SOFA plus SAPS II.
10. On application of Youden's index to the combination of scores, best diagnostic performance was seen with SOFA plus SAPS II at 48 hours.

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ANNEXURES

ANNEXURE I- INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed - to-be-University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (India)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http://www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 250 **Date: 24/12/2019**

To.

REG NO: BG0119008
PG student in Medicine,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"COMPARATIVE STUDY OF SOFA, APACHE II, SAPS II, AS A PREDICTOR OF MORTALITY IN PATIENTS OF SEPSIS ADMITTED IN MEDICAL ICU OF KLES PRABHAKAR KORE HOSPITAL "**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Anita Dalal)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

ANNEXURE II- INFORMED CONSENT

Title Of Research Study: COMPARATIVE STUDY OF SOFA, APACHE II, SAPS II, AS A PREDICTOR OF MORTALITY IN PATIENTS OF SEPSIS ADMITTED IN MEDICAL ICU.

Principal Investigator:-

_____

Post Graduate Student,
Department Of General Medicine,
JNMC, Belgaum.

Guide:-

_____

_____

Dept. of Medicine, J. N. Medical College,

Introduction and Purpose:-

In (ICU) intensive care unit patients on admission clinical and laboratory assessment of the severity of illness is an essential component in determining mortality, and morbidity of the patient. Mortality prediction systems have been introduced as tools for assessing the performance of ICUs. Scores mainly used as a predictor of mortality are Acute Physiology and Chronic Health Evaluation (APACHE) III, Simplified Acute Physiology Score (SAPS) II, simplified organ failure assessment (SOFA).

Procedure:

If you agree to be part of the research study, you will be asked the relevant history and will be subjected to relevant clinical examination and investigations. You will also have to give blood and urine samples for the necessary investigations.

Risk and Benefits:

The only risk and possible discomfort you might get is while taking blood from your arm for the investigations. It may cause swelling, pain, redness (rarely happens) at the site from where the blood is drawn.

You may not be benefitted by these investigations but you will be part of this study which is going to be useful to others in the future.

Alternatives:

Taking part in this study is voluntary. You may choose not to take part in this study.

If you decide to take part you can later change your mind and withdraw from the study. Your decision will not change the present or future health care or other services that you receive. The study doctor or sponsor may stop your participation in this study at any time. If you choose not to take part in the study, you will receive the standard treatment for patients with your condition.

Privacy and Confidentiality:

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be confidential in any publication.

Institution / Sponsor's policy:

Does not apply to this research

Financial incentives for participation:

You will not be paid / offered any gifts /incentives for participating in the study.

Authorization to publish the results:

The results of the study would be forwarded to the KLE University, Belgaum as part of requirement towards the completion of MD degree, review and publishing.

In case of the queries during study or in future you may contact following persons,

1) **Dr. Roopa Bellad,** Chairman, JNMC Ethical Committee for Human Research.

CONSENT FORM

I voluntarily agree to take part in this study by signing below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicates that I have read this consent form, or it has Been read to me, this consent form and have had all the questions answered

Signature / Left Thumb print of the Participant or legally authorized representative

Participant's name :……...

Signature / Left thumb impression:……...

of the participant

Name of the legally authorized :……...

representative / guardian

Signature / Left thumb impression :……...

Witness' name :……...

Signature / Left thumb impression :……...

Investigator's name and signature :……...

Date:

Place:

ANNEXURE III

PROFORMA

Patient name: IP number:

Age/Sex: DOA:

Religion: DOD:

Address: Duration of stay:

Occupation:

CHIEF COMPLAINTS:

PAST HISTORY

PERSONAL HISTORY

O/E:

Pulse rate: Blood pressure:

RR TEMP(oral):

Pallor,Icterusetc:

S/E:

Respiratory(any crepts/rhonchi):

CVS:

P/A (hepatosplenomegaly)

CNS:

GCS:

VARIABLES:	**DATE:**	**INFERENCE:**
AGE (YEARS)		
HEART RATE /min		
SYSTOLIC BP (mmHg)		
MAP(mmHg)		
RESPIRATORY RATE/MIN		
URINE OUTPUT(ml/DAY)		
GCS		
VASOPRESSOR		
BUN (mg/dl)		
CREATININE (mg/dl)		
SERUM SODIUM (mEq/L)		
SERUM POTASSIUM (mEq/L)		

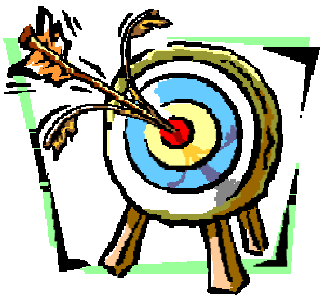
WBC (x 10^3/mm^3)		
PLATELET (x 10^3/ microliters)		
BILIRUBIN (mg/dl)		
PAO2 (mmHg)		
PAO2/FIO2 (mmhg/%)		
A-a GRADIENT		
BICARBONATE (mEq/L)		
PH		
SERUM LACTATE(mg/dl)		
SERUM PROCALCITONIN (microgram/ L)		
BLOOD CULTURE		
CHRONIC DISEASE		
TYPE OF ADMISSION		
EMERGENCY SURGERY		

24 HOURS SCORING SYSTEMS

48 HOURS SCORING SYSTEMS

28 DAYS SCORING SYSTEMS

Introduction



Objectives

Review of Literature

Methodology

Results

Discussion

Conclusion

Summary

Bibliography

Annexure-I

]

Annexure-II

Annexure-III

Annexure-IV

sl no	ip no	age	SEX	duration		gcs	hr	syst bp
1	1034597	60	M	2 DAYS	24HOURS	15	126	90
					48HOURS	15	130	90
2	1033551	56	M	17	24 HOURS	15	76	110
					48HOURS	15	88	120
3	1034925	19	M	2	24 HOURS	15	80	90
					48 HOURS	15	90	80
4	1035300	87	M	5	24 HOURS	15	96	110
					48 HOURS	15	110	120
5	1032205	83	M	13	24 HOURS	15	84	130
					48HOURS	15	90	130
6	1031578	69	M	14	24 HOURS	15	88	130
					48 HOURS	15	94	130
7	1031054	52	M	18	24 HOURS	12	120	120
					48HOURS	13	115	130
8	1031022	58	M	32	24 HOURS	13	114	110
					48 HOURS	13	118	110
9	1032749	63	M	10	24 HOURS	15	110	110
					48 HOURS	15	94	110
10	1029574	83	M	25	24 HOURS	15	75	110
					48 HOURS	15	88	120
11	1029701	53	M	5	24HOURS	10	125	90
					48 HOURS	10	130	100
12	1029044	69	M	8	24 HOURS	15	110	110
					48HOURS	15	98	114
13	1028215	70	M	4	24 HOURS	10	92	110
					48 HOURS	13	98	120
14	1043213	88	M	4	24 HOURS	8	137	110
					48 HOURS	10	114	110
15	1042873	25	M	3	24HOURS	15	130	130
					48HOURS	15	118	130
16	1024773	21	M	3	24 HOURS	14	110	110
					48 HOURS	15	114	114
17	1042853	70	M	10	24 HOURS	15	118	130
					48 HOURS	15	88	120
18	1042803	58	M	6	24 HOURS	15	118	130
					48 HOURS	15	114	140
19	1025247	50	M	16	24 HOURS	15	110	110
					48 HOURS	15	100	114
20	1043380	60	M	3	24 HOURS	12	118	80
					48 HOURS	11	124	100
21	1043386	98	F	3	24HOURS	15	120	130
					48HOURS	15	100	150
22	1043537	70	M		24 HOURS	13	88	130
					48 HOURS	14	94	140
23	1043556	68	M	3	24 HOURS	3	80	90
					48 HOURS	6	145	100

24	1042666	72	M	7	24 HOURS	12	84	140
					48 HOURS	15	88	130
25	1041782	77	M	6	24 HOURS	3	116	100
					48 HOURS	7	124	90
26	1024731	34	M	3	24 HOURS	2	100	80
					48 HOURS	2	110	90
27	1043314	81	M	8	24 HOURS	3	50	110
					48 HOURS	6	86	140
28	1041782	77	M	6	24 HOURS	8	115	60
					48 HOURS	9	124	110
29	1043213	88	M	5	24 HOURS	11	126	70
					48 HOURS	12	110	100
30	1043088	65	F	8	24 HOURS	10	110	130
					48 HOURS	10	114	110
31	1042977	72	M	10	24 HOURS	15	120	110
					48 HOURS	15	110	120
32	1025405	55	M	35	24 HOURS	9	108	160
					48 HOURS	9	110	150
33	1027458	35	M	15	24 HOURS	15	130	130
					48 HOURS	15	140	120
34	1027495	42	F	8	24 HOURS	15	88	90
					48 HOURS	15	90	100
35	1027521	72	M	5	24 HOURS	14	118	100
					48 HOURS	13	110	90
36	1027520	66	F	7	24 HOURS	8	110	100
					48 HOURS	8	114	104
37	1042738	75	F	5	24 HOURS	5	90	90
					48 HOURS	5	84	130
38	1042521	58	M	6	24 HOURS	15	118	200
					48 HOURS	15	90	130
39	1023266	51	M	5	24 HOURS	13	108	110
					48 HOURS	13	110	114
40	1025528	40	M	15	24 HOURS	15	58	110
					48 HOURS	15	48	108
41	1024847	42	F	13	24 HOURS	15	110	150
					48 HOURS	15	100	146
42	1042610	49	M	8	24 HOURS	15	110	90
					48 HOURS	15	108	100
43	1028058	64	M	15	24 HOURS	15	110	90
					48 HOURS	15	98	100
44	1028021	61	F	10	24 HOURS	15	94	100
					48 HOURS	15	96	96
45	1027589	55	F	4	24 HOURS	6	84	130
					48 HOURS	8	90	130
46	1054605	29	F	18	24 HOURS	15	114	130
					48 HOURS	15	110	120
47	1054447	59	M	18	24 HOURS	10	112	120

					48 HOURS	11	120	118
48	105551	56	M	4	24 HOURS	9	116	120
					48 HOURS	10	114	130
49	1055607	70	M	2	24 HOURS	15	130	120
					48 HOURS	15	120	150
50	1055662	35	M	4	24 HOURS	15	108	110
					48 HOURS	15	98	120
51	1054327	41	F	18	24 HOURS	15	108	130
					48 HOURS	15	92	160
52	1054450	34	F	12	24 HOURS	2	104	100
					48 HOURS	2	120	110
53	1054062	53	M	6	24 HOURS	11	130	70
					48 HOURS	2	134	90
54	1053967	27	M	29	24 HOURS	2	120	140
					48 HOURS	2	124	130
55	1053742	60	M	14	24 HOURS	15	80	100
					48 HOURS	15	110	100
56	1053323	68	M	14	24 HOURS	8	120	100
					48 HOURS	7	114	100
57	1053988	27	F	17	24 HOURS	15	110	130
					48 HOURS	13	90	110
58	1051610	46	F	23	24 HOURS	15	120	130
					48 HOURS	15	110	110
59	1053742	60	M	14	24 HOURS	15	80	100
					48 HOURS	15	110	100
60	1055236	36	M	12	24 HOURS	12	118	110
					48 HOURS	12	90	130
61	1053946	48	M	25	24 HOURS	13	120	110
					48 HOURS	13	110	130
62	1053825	72	M	26	24 HOURS	15	87	149
					48 HOURS	15	98	160
63	1053331	48	F	2	24 HOURS	15	100	120
					48 HOURS	15	112	120
64	1055042	53	F	7	24 HOURS	5	118	120
					48 HOURS	5	143	120
65	1053903	43	M	18	24 HOURS	15	84	100
					48 HOURS	15	88	90
66	1052959	62	F	10	24 HOURS	15	108	130
					48 HOURS	15	111	128
67	1057012	24	M	21	24 HOURS	15	120	60
					48 HOURS	15	116	70
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					48 HOURS	15	124	130
69	1054508	31	F	14	24 HOURS	15	120	110
					48 HOURS	15	124	114
70	1054889	70	F	14	24 HOURS	9	100	120
					48 HOURS	8	88	110

71	1056997	20	M	20	24 HOURS	13	130	90
					48 HOURS	12	120	100
72	1059306	38	M	7	24 HOURS	14	100	90
					48 HOURS	13	110	100
73	1056535	75	M	20	24 HOURS	15	110	130
					48 HOURS	15	100	130
74	1059052	18	M	9	24 HOURS	15	130	160
					48 HOURS	15	120	150
75	1057715	30	F	20	24 HOURS	3	109	90
					48 HOURS	3	82	100
76	1058063	21	F	7	24 HOURS	9	102	110
					48 HOURS	3	112	100
77	1057983	48	M	17	24 HOURS	9	110	210
					48 HOURS	9	108	170
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					48 HOURS	15	100	90
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					48 HOURS	11	86	100
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					48HOURS	15	102	130
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82	1057687	39	F	5	24HOURS	12	120	100
					48HOURS	12	130	90
83	1058870	43	M	7	24HOURS	15	110	110
					48HOURS	15	118	100
84	1054020	65	F	26	24HOURS	15	120	110
					48HOURS	15	118	100
85	1057954	56	F	5	24HOURS	13	118	90
					48HOURS	15	100	90
86	1058507	65	M	10	24HOURS	12	98	140
					48HOURS	12	90	130
87	1057008	49	M	15	24HOURS	3	114	90
					48HOURS	3	116	80
88	1057540	67	M	7	24HOURS	15	110	130
					48HOURS	15	114	140
89	1058064	48	F	21	24HOURS	3	112	110
					48HOURS	3	118	114
90	1059503	70	M	9	24HOURS	13	120	90
					48HOURS	12	118	90
91	1060131	80	M	10	24HOURS	11	114	130
					48HOURS	11	116	130
92	1056756	58	M	2	24HOURS	5	118	90
					48HOURS	3	120	80
93	1056730	83	M	2	24 HOURS	12	130	120
					48HOURS	13	120	110
94	1054327	41	F	18	24HOURS	12	110	130

					48 HOURS	13	120	140
95	1058258	40	F	12	24HOURS	15	114	120
					48 HOURS	15	120	130
96	1056538	75	M	21	24 HOURS	15	114	110
					48 HOURS	15	120	120
97	1057704	60	F	19	24 HOURS	15	120	130
					48 HOURS	15	124	120
98	1059858	66	M	4	24HOURS	9	114	130
					48 HOURS	10	120	120
99	1042738	75	F	5	24 HOURS	5	90	90
					48 HOURS	5	84	130
100	1042521	58	M	6	24 HOURS	15	118	200
					48 HOURS	15	90	130

map	resp rate	output	ionotropes	hematocrit	wbc	platelet	bun	creat
65	35	400	3	30.5	32.2	117	173	5.49
65	38	350	3	32	20.9	96	170	6.48
65	28	2400	0	32.5	2.2	48	66	1.4
75	30	1800	0	30.7	2.2	44	61	1.22
63	34	0	2	30	11.1	83	124	5.13
60	30	150	2	42.1	14.2	19	128	3.51
83	35	900	0	37.4	18.6	85	119	1.56
93	30	1000	0	36	23.5	95	110	1.56
103	28	130	0	30.8	7.7	107	135	5.08
103	25	250	0	30.1	5.8	110	127	5.41
103	28	330	0	34.6	14.4	88	212	5.2
103	25	450	0	31.5	13	58	244	5.83
93	35	1300	0	33.2	28.6	278	101	1.1
103	30	2500	0	29.3	16.5	396	31	0.56
83	28	900	1	33	13.5	211	10	0.78
83	25	1100	1	29.6	10	131	15	0.66
83	24	2500	2	35.3	28.7	193	80	4.2
83	20	3700	2	34.1	17.9	190	76	3.54
83	18	0	0	30.1	4.6	34	254	6.51
93	20	200	0	27.5	4.7	28	309	6.45
63	30	100	1	26.5	42.2	67	130	5.21
73	34	150	1	27.5	21.4	24	121	4.37
83	30	350	0	31.3	20.4	274	168	5.4
85	28	350	0	30.3	34.4	186	232	4.86
83	25	1100	0	40.4	12	245	181	5.67
85	24	1300	0	40.4	10.6	170	170	6.03
83	28	0	0	30.7	9.4	52	89	5.15
83	30	150	0	31.3	20.5	35	74	3.34
103	35	1500	0	28	36.6	6.57	35	1.03
103	40	1250	0	25.4	25.2	8.78	26	0.88
73	25	150	0	20.9	11.6	256	287	14.23
75	20	100	0	23.2	11.9	242	82	13.2
103	30	500	0	40.4	17.8	212	62	2.69
93	28	400	0	39	14.5	214	58	2.54
103	30	400	0	42.1	21.9	98	58	3.77
203	28	450	0	41	19	32	68	3.88
83	20	2000	1	19.8	1.9	17	56	0.92
85	22	1900	1	23.7	1.6	26	54	1.02
53	25	160	2	32.9	32.2	171	176	7.56
73	20	1050	2	29.4	46.1	173	170	5.02
103	26	300	0	22	225	646	111	4.4
123	28	400	1	33	192	462	122	4.11
103	28	350	0	23.2	25.2	4.88	158	4.84
103	33	450	0					
63	45	350	2	28.2	28.2	213	100	4.43
83	35	400	1	27.4	26.6	233	114	4.55

107	25	75	0	21.5	10.5	90	131	4.1
103	21	150	0	23.9	10.4	104	68	3.29
73	30	30	3	19.2	64.6	65	149	3.5
63	34	300	2	21.2	65.9	13	173	4.62
63	35	550	2	29.8	52.5	191	153	4.35
73	30	300	3	27.4	45.5	180	160	4.7
83	45	350	0	42	24.2	2.87	68	3.14
103	30	300	0	25.9	20.3	1.94	84	3.35
50	40	NIL	2	15	43.9	57	93	1.64
73	25	300	1	18.5	24.1	42	204	4.89
53	35	150	1	30.7	9.4	52	89	5.15
73	30	250	0					
103	28	600	0	22.6	10.6	150	124	3.2
93	30	500	0	22.6	11.6	154	242	5.36
103	40	900	0	13.5	21.6	135	90	2.52
117	35	1100	0	20.9	17.6	99	127	2.33
113	30	800	0	40.6	14.2	455	47	0.67
110	28	100	0	38.2	10.4	306	36	0.71
103	40	700	0	44	6.6	97	27	1.1
100	44	900	0	37.8	7.4	65	121	0.81
73	25	800	0	37.8	6.5	197	27	1.19
83	20	1100	0	38.9	8.3	26	25	0.71
83	34	600	2	39.8	17	197	103	4.78
60	35	800	2	42	9.6	138	126	4.77
83	28	100	0	22.9	25.9	299	299	3.87
85	20	150	0	32.5	16.7	180	180	3.1
70	24	1140	1	32.7	5.4	90	30	0.81
97	20	1250	1	35.3	5.5	82	23	0.65
230	35	600	0	24.6	19.1	295	154	11.21
97	25	600	0	22	18.2	260	130	11.1
83	20	400	1	36.6	19.7	111	68	3.61
85	21	800	1	37.4	17.1	110	80	3.74
83	20	410	1	20.05	31	133	69	2.51
83	18	350	1	22.4	16.6	68	78	2.09
110	20	400	0	24.9	27.1	636	63	4.09
109	20	300	0	26.3	18.3	513	36	3.11
63	24	600	1	42	12.3	343	42	1.33
73	26	800	0	40	12.3	343	38	1.17
63	20	700	2	42.7	18.6	175	80	2.15
83	24	800	2	40.7	24.1	150	82	2.37
80	24	250	2	26.2	1	271	37	1.32
72	20	300	2	24.2	1.6	300	32	0.6
203	25	800	0	30.4	15.8	327	24	0.33
203	26	900	0	28.2	28.2	352	22	0.57
200	30	900	0	42.3	11.1	239	39	0.57
103	25	1000	0	41	11.3	268	58	0.54
103	30	1000	0	43.2	18.2	523	161	5.37

100	28	900	0	41.4	18.7	418	144	5.24
103	26	1000	0	27	13.5	274	165	5.84
103	24	1100	0	26	23.7	230	170	5.99
103	34	450	0	55.8	40.2	193	54	0.88
110	30	400	0	54	38	130	50	0.9
83	26	600	0	47.8	23	269	50	1.12
103	28	800	0	46	12.2	120	71	2.33
103	32	1410	0	32	7.1	159	18	0.62
120	29	1140	0	34	13.4	297	34	0.35
73	18	0	1	36.9	8.4	192	103	3.01
73	15	0	1	35	14.8	34	123	3.13
53	34	450	2	38.9	15.5	169	106	2.72
63	15	300	2	37.4	12.6	124	124	3.47
83	24	1100	0	40	16.6	290	42	0.78
83	20	900	0	22	7.4	200	99	2.21
73	34	1100	1	38	13.9	480	37	0.64
73	36	1000	1	35	10.8	98	31	0.7
73	28	900	1	41	17.2	153	48	1.63
73	30	800	1	40	18.9	156	56	1.56
103	26	900	0	32.3	22.9	224	163	6.31
83	24	1000	0	32	20.3	180	175	6.12
103	34	1100	0	44	15	240	57	0.81
93	30	1200	0	43	13.1	231	23	0.6
73	34	1100	1	38	13.9	480	37	0.64
73	36	1100	1	35	10.8	98	31	0.7
93	26	1300	0	19.5	7.9	84	34	0.95
103	28	470	0	24	5.3	23	38	0.67
103	34	900	0	44	9.3	250	12	0.38
103	34	1300	0	43	15	283	48	0.81
110	30	1750	0	44	14.1	138	61	0.67
110	28	1950	0	43	24.5	321	23	0.43
110	30	800	0	42	12.4	264	38	0.63
110	32	900	0	41	21	141	40	0.55
110	15	1015	0	36	16.9	182	247	3.99
110	15	485	0	35	11.5	170	257	3.62
73	26	800	0	42	18.4	239	30	0.63
63	28	750	0	44	39.2	261	10	0.84
110	34	350	0	37.7	19.1	298	56	0.9
108	34	550	0	38	15.3	236	25	0.63
53	30	600	2	35	14.14	192	63	0.78
50	34	500	2	36.6	16.59	184	91	1.08
93	34	100	0	30.4	5	32	230	7.7
93	32	50	0	32.4	5.5	37	215	7.7
73	34	800	0	40	14.5	143	26	0.51
75	35	900	0	41	6.7	146	17	0.5
93	28	1000	0	34	13.1	143	108	2.26
83	30	900	0	30	13	269	97	2.04

63	30	50	1	43	23.1	48	106	5.57
73	26	50	0	42	20	41	100	5.3
63	30	900	2	36	15	110	80	1.77
73	28	600	2	37	22.8	83	62	1.54
103	26	900	0	33.4	17.8	291	51	0.85
103	24	1100	0	33	17.5	312	48	0.63
103	30	100	0	20.8	13.1	604	203	4.33
103	34	100	0	20.8	13.5	656	117	2.8
63	15	600	2	34.7	19.1	100	37	0.92
73	15	900	1	32	29.4	182	76	1.32
73	15	1000	0	29.8	13.8	398	14	0.67
63	15	900	1	24.8	13.5	528	12	0.78
150	26	200	0	28.6	14.1	106	129	9.59
130	28	300	0	32.2	10.7	105	105	9.55
73	26	600	1	31.3	17.3	31	42	0.93
63	28	700	1	30.9	9.9	30	38	0.98
73	28	350	0	33.3	27.4	455	228	7.09
63	26	580	0	30	18.8	400	212	7.3
93	30	300	0	32.8	15.9	391	116	4.15
93	30	400	0	27.8	11.8	390	118	4.23
73	20	1000	1	31.8	6.6	259	19	0.54
63	20	900	2	36.2	15.3	234	43	0.79
73	30	1000	0	36	4.1	200	14	0.7
63	34	900	1	37	5.5	215	31	0.45
73	20	1620	2	27.1	2	60	120	5.13
63	24	900	2	28	27.8	94	142	5.37
73	30	750	0	34	16.6	242	145	1.67
63	32	900	0	35	14.6	164	128	1.3
63	34	1400	1	42	9.2	10	24	1.11
63	30	800	1	41	3	32	24	1.04
103	24	1400	0	48.6	12.9	336	112	1.66
103	26	1600	0	47	11	330	122	1.9
63	15	400	2	13.7	10.8	117	191	2.42
53	15	450	2	23.7	17.1	104	212	1.38
110	34	2090	0	34	17.6	119	34	0.81
110	38	1050	0	33.2	10.3	151	28	0.77
73	20	600	1	47.8	21.7	523	20	0.67
75	20	800	2	47.1	18.1	316	86	0.92
63	30	300	2	36.9	31.2	47	134	7.28
63	28	250	2	30.3	17.7	251	130	7
83	25	1100	0	34.8	11.3	508	36	1.8
83	25	1200	0	30.4	10	439	52	1.4
63	34	600	2	44	16.1	261	37	1.04
60	15	500	2	44.1	17.4	150	54	1.98
93	36	900	0	26	6.7	114	115	3.5
73	30	1100	2	28	7.8	90	180	3.74
103	34	1100	0	36	7.1	156	18	0.62

103	32	1200	0	38	13.4	297	24	0.7
83	34	900	0	27.4	12.8	181	43	0.58
93	36	1000	0	30	24.7	224	53	0.61
73	30	1100	0	33.4	17.8	291	51	0.85
83	34	1200	0	34	17.5	312	48	0.63
93	36	900	0	38	29	288	124	1.8
85	34	1000	0	37	13.3	217	86	1.03
93	34	1100	2	28	7.8	90	180	3.74
90	30	1100	0	36	7.1	156	18	0.62
70	24	1140	1	32.7	5.4	90	30	0.81
97	20	1250	1	35.3	5.5	82	23	0.65
230	35	600	0	24.6	19.1	295	154	11.21
97	25	600	0	22	18.2	260	130	11.1

sodium	potassium	bili	bicarb	ph	PAO2	PACO2	PAO2/FIO2	A-a gradient
118	4.01	0.53	8	7.261	213	9.3	426	131.9
118	5.33	0.85	3	7.398	226	12.9	452	114.4
135	4.88	0.82	21	7.44	80.8	27	197	177.8
132	3.83	0.9	19	7.446	63.6	26.8	193	138.2
131	4.55	2.3	10	7.244	66.2	13.2	161	209.6
128	5.47	2.4	16	7.312	68.8	28.4	168	188
136	3.4	2.73	22	7.337	94.7	37.7	126	392.9
137	3.35	4.46	20	7.352	119	38	238	190
125	4.72	2.68	12	7.45	74.3	29.4	354	38.7
135	3.9	0.78	20	7.43	75.3	29.7	359	37.3
138	5.94	3.25	10	7.279	93.9	44.2	233	136
142	5.43	2.22	14.8	7.285	52.2	53.5	131	164.8
136	3.95	3.69	17	7.399	110	41.4	314	87.8
144	3.03	1.39	28	7.514	64.9	30.7	309	46.5
148	2.84	2.24	22	7.455	74.5	36.6	226	115
134	3.8	4.72	27	7.457	93.5	35.8	228	154.1
129	5.89	1.22	15	7.245	81.8	34.3	200	167.7
130	4.23	1.41	18	7.321	58.5	38.9	143	185.2
138	4.51	1.16	12	7.394	75.1	16.6	203	168
135	5.4	1.4	18	7.424	119.2	18.4	322	121.6
137	4.25	0.45	12	7.265	186.9	26.6	234	350.3
134	4.37	0.56	21	7.288	90.9	49.4	152	275.1
123	5.45	0.58	10	7.29	116.4	21.5	284	149.1
135	6.14	0.6	10	7.22	56.9	19.5	139	211.1
165	3.61	0.6	19	7.38	99.5	39.4	474	72
158	3.49	0.64	17	7.36	82.1	34	200	167.7
125	5.22	1.88	12	7.312	151.8	25.6	370	108.5
137	4.2	6.32	15	7.374	88	30.7	196	194.5
137	4.86	0.62	22	7.394	160	39.9	400	75.3
134	5.22	0.64	23	7.453	86.1	31.2	217	160.1
158	3.53	0.24	21	7.24	80	34.6	195	169.1
153	3.62	0.21	13	7.3	92	30.4	227	162.3
133	5.47	0.26	16	7.343	62	345	258	66
137	6.43	6.43	14	7.284	80	37.8	308	58.1
116	6.44	5.42	18	7.385	120	22.4	571	1.7
121	6.29	8.86	14	7.45	71	30.3	338	40.9
137	4.01	5.32	14	7.471	79.8	17.9	380	47.6
133	2.93	8.64	16	7.394	92.6	20.6	441	31.4
132	4.48	1.38	10	7.42	70.4	13.9	156	233.1
134	3.7	2	8.6	7.381	90.6	14.9	238	161.7
143	4.15	0.29	12	7.26	38	32	181	71.7
141	4.42	0.44	12	7.25	46.8	32.5	220	62.3
126	6.18	0.21	10	7.295	100.5	15	497	30.5
146	6.3	0.37	8	7.245	439	23.9	439	244.1
147	6.52	0.29	10	7.232	214	17.8	535	48.9

133	5.47	0.21	19	7.472	62.9	29	300	200
140	4.15	0.28	16	7.458	61.4	21	292	214
142	5.03	0.71	6.2	7.05	152.8	22.9	169	461
141	5.12	0.5	26.2	7.39	55.3	44.3	61	531
132	5.88	26.52	8	7.181	32.7	29.6	65	286.8
134	2.9	19.32	7	7.338	125.4	13.3	157	428.4
134	5.76	0.6	14	7.082	51	47.6	51	602
147	7.12	0.74	20	7.263	85	51.2	100	457
134	4.74	0.71	16	7.05	152	22.9	380	104
140	4.89	0.84	19	7.32	68.9	25.1	76	541.4
125	5.22	1.88	12	7.312	151.8	25.6	523	23
131	5.09	0.17	18.6	7.367	114.1	33.1	278	129.7
123	6.34	0.14	10	7.29	65.6	24.6	312	53.4
135	5.48	1.26	10	7.157	159.1	11.9	636	4.4
137	4.36	2.04	13	7.401	76.7	22.9	153	179.9
133	5.19	0.78	17	7.44	62.7	36.2	89	391.2
131	4.25	0.84	22	7.45	55.3	38	111	253.7
143	3.22	2.3	11	7.33	88	24.7	304	87.8
136	3.88	0.84	14	7.32	61.9	30.6	151	192.2
138	3.47	0.72	19	7.398	94	30	285	103.8
134	3.72	0.84	21	7.41	90	34	273	102.5
117	6.32	0.7	13	7.183	49.7	36.5	124	189.9
130	6.05	0.8	13	7.401	95.3	16.6	238	169.1
139	3.28	11.46	17.2	7.305	131.2	35.3	328	109
132	4.67	12.56	18.3	7.36	124	36.1	310	116.1
145	2.58	0.49	20	7.466	137.8	25.7	274	186.6
143	2.79	0.42	19	7.466	91	26	228	161.7
143	4.55	0.81	17	7.185	74.7	18.3	149	258
149	4.42	0.74	16.7	7.405	278	27.3	556	44.4
127	4.36	0.73	11	7.39	102.1	24.7	486	16.9
143	3.77	0.71	18	7.35	100	27.8	476	15
131	5.75	2.69	11	7.304	44.7	32.3	213	64.7
137	4.66	4.62	17	7.35	96	34.2	457	11
131	4.39	0.71	12	7.393	70.4	19	335	55.6
129	4.46	0.69	17	7.44	73.9	26.4	352	52.1
132	4.69	0.65	17	7.4	59	36.3	250	164
138	4.05	0.7	22	7.4	83.4	37.2	278	166
143	4.34	2.2	17	7.349	71	16.8	245	114.8
143	5.04	2.4	15	7.295	100.5	15	347	87.5
125	3.9	0.72	15	7.46	106	29.4	265	142.4
131	3.3	0.84	16	7.48	111	27.6	278	139.7
137	3.21	0.48	23	7.46	98	32.6	245	237
137	3.07	0.84	25	7.44	137.2	42	343	225.3
144	3.36	0.13	20	7.457	53.9	33.6	54	617.1
140	4.74	0.28	22	7.364	44.5	31.7	74	343.7
131	5.37	0.56	11	7.29	79.2	22.1	377	42.9

134	5.24	0.8	12	7.33	160.3	14.5	403	113.9
141	5.17	0.22	10	7.28	97.7	15.9	465	32.2
146	5.32	0.4	10	7.4	91.5	16.4	436	37.7
140	5.01	1.49	17	7.32	53.6	33.2	89	332.7
142	5.3	1.5	20	7.35	51.6	39.2	52	612
131	7.41	0.5	10	6.9	111	13	271	165.1
132	6.18	0.14	10	7.07	99.2	10.8	472	37
137	4	0.3	23	7.33	94	46.9	157	275.2
139	3.84	0.61	24.7	7.38	77.5	41.9	155	226.6
137	4.74	1.14	17	7.276	61.8	21.7	151	203.4
138	5.43	2.95	13	7.373	359.9	38.1	598	21.2
130	3.74	0.72	16	7.248	462.8	13.8	462	233.8
140	4.08	0.7	20	7.103	170	35.1	340	142.6
133	5.36	0.3	22	7.24	82.4	62	82	553.1
137	5.95	0.3	24	7.238	60.5	77.7	60	555.4
135	4.59	0.42	24	7.4	119.4	31.7	291	133.7
127	3.26	0.5	19	7.45	63.4	29	155	192.7
135	4.19	0.45	18	7.404	62.1	34.8	124	250.9
136	3.88	0.5	20	7.453	94.4	31	230	159.2
130	6.41	2.96	10	7.455	85.5	19.5	407	39.9
131	4.8	4.02	10	7.461	66.6	30	317	45.6
151	4.16	0.48	20	7.46	63.2	28.5	63	614.2
138	5.03	0.73	24	7.41	90.8	30.5	91	584
135	4.59	0.42	24	7.4	119.4	31.7	291	133.7
127	3.26	0.5	19	7.45	63.4	29	155	192.7
134	4.34	1.71	10	7.4	68	24	324	51.7
145	3.02	1.48	15	7.31	78	19	371	48
134	4.18	0.54	29	7.425	40	24.3	50	500
133	3.82	0.84	24	7.358	59	31.7	74	471.8
140	4.35	0.43	18	7.42	84	20	140	318.8
133	3.44	0.5	24	7.45	80	22	133	320.3
146	3.45	0.44	21	7.44	130.9	33.1	218	255.2
150	3.46	0.77	24	7.49	55.7	30.6	101	298.2
169	5.5	0.22	27	7.41	73.3	26.6	147	249.9
177	5	0.24	23	7.46	117	31.4	234	200.3
135	4.51	0.63	23	7.394	131.6	27.9	321	125.9
139	3	0.81	25	7.4	110	30	268	144.8
140	4.38	0.56	18	7.41	71	28.2	118	321.6
134	4.05	1.08	28	7.42	80	25	100	459.1
126	3.17	0.3	11	7.36	106.6	9.4	505	32
128	3.12	0.4	14	7.4	80.3	18	382	46.9
130	4.63	2.21	12	7.35	57.4	21.7	115	272
136	4.26	2.1	14	7.37	91.2	40.9	182	214.2
140	3.64	0.51	26	7.35	65	21	108	336.6
134	4.12	0.61	26	7.45	50	19	71	425.3
140	4.51	0.56	17	7.45	75	30	150	244
148	4.41	0.51	13	7.35	80	28	160	241.5

133	4.69	4.15	10	7.31	84	31	210	169.6
132	3.91	4.36	17	7.31	66.31	13.9	208.6	208
137	3.71	6.58	22	7.3	80	23	381	41
123	2.54	4.96	21	7.28	84	24	400	35.7
137	4.07	0.5	20	7.46	54.4	40.7	259	44.5
134	4.31	0.56	23	7.285	59.3	54.7	282	22.1
127	5.57	0.5	12	7.3	94.5	16.4	236	170
127	4.1	0.5	17	7.35	36.9	32.9	92	207.4
141	4.64	4.19	19	7.43	73.7	31.2	123	315
148	3.53	4.8	23	7.52	128.7	27.5	129	549.9
137	4.65	6.69	20	7.463	71	31.4	178	174.9
146	3.98	7.85	27	7.5	117	29.8	390	59.7
133	3.5	0.95	17	7.401	67.5	33.4	321	40.5
138	3.06	0.94	23	7.304	148.1	22.5	370	109
125	3.71	0.22	23	7.45	88	28	220	162.2
126	3.29	0.3	22	7.35	39.7	51.3	99	181.4
114	3.83	0.19	25	7.4	80	24	381	39.7
119	3.61	0.45	26	7.35	90	26	429	108.2
126	5.79	0.26	13	7.435	60	36.6	150	179.4
129	6.14	0.34	12	7.465	118	33.6	169	338.9
139	4.69	0.3	22	7.3	101	32.2	481	8.5
145	4.61	0.87	20	7.3	141	28.7	202	322
140	2.97	0.22	20	7.45	79.3	30.9	378	31.8
141	3.6	0.42	26	7.23	40.3	55.1	192	40.6
135	4.8	0.84	10	7.228	80.9	18.3	385	46
135	5.37	2.89	11	7.408	47.6	23.8	227	72.4
145	5.07	0.2	14	7.4	118	32	148	412
149	4.97	0.36	29	7.4	115	32	192	272.8
134	4.6	0.66	21	7.4	54	25	257	64.5
135	5.01	0.7	19	7.4	60	26	286	57.2
138	6.04	1	21	7.34	83.5	29	398	30
134	4.5	0.9	20	7.39	73.7	30.7	351	37.7
136	4.64	4.35	16	7.54	171	19.1	244	304
152	2.95	4.91	17	7.414	63.6	17.5	91	413.6
132	4.37	0.95	21	7.44	80.5	26.6	244	121.5
133	3.71	1.4	23	7.44	110.9	31.7	333	84.8
133	6.23	0.39	27	6.87	39.6	44.7	40	617
144	3.95	0.48	29	7.2	71.4	56.9	89	427
124	5.88	0.68	13	7.29	35.9	20.5	171	88.2
129	4.2	0.7	15	7.46	125	11.4	250	217
129	4.31	0.48	11	7.45	80	30	381	32.2
128	4.34	0.5	22	7.4	90	28	429	24.7
135	4.04	0.67	22	7.23	50.4	42.3	50	609.7
135	5.97	0.74	18	7.16	44.4	40	94	569
141	6.29	0.43	13	7.16	31.2	43.4	31	627.5
140	6.1	0.45	12	7.15	46.8	36.8	47	620
137	4	0.3	23	7.33	94	46.9	188	203.9

134	3.84	0.6	25	7.41	69	39.8	99	380.3
132	4.7	0.57	19	7.34	69.9	40.8	100	378.2
144	4.5	0.64	23	7.29	59.7	41.4	85	387.6
137	4.07	0.5	20	7.46	54.4	40.7	78	393.8
134	4.3	0.64	23	7.45	60.4	50.4	86	375.7
145	3.5	0.26	16	7.38	69	33.6	126	281
142	5	0.34	18	7.43	50.3	36.1	91	296.9
140	6.1	0.45	12	7.15	46.8	36.8	47	620
137	4	0.3	23	7.33	94	46.9	188	203.9
145	2.58	0.49	20	7.466	137.8	25.7	274	186.6
143	2.79	0.42	19	7.466	91	26	228	161.7
143	4.55	0.81	17	7.185	74.7	18.3	149	258
149	4.42	0.74	16.7	7.405	278	27.3	556	44.4

lactate	pct	blood culture	urine culture	chronic disease	SOFA	APACHE II	SAPS II
10.64	100	No ORG	e. coli	IHD, T2DM	9	25	68
4.59	100				10	23	71
1.64	0.78	No ORG	NO ORG	NO	6	8	22
2.89	0.41				6	7	25
4.81	61.4	No ORG	NO ORG	NO	13	17	54
7.86	100				14	18	48
2.86	3.54	S. PNEUMONI/	NO ORG	HTN	8	16	44
1.15	3.44				7	14	50
1.34	31.28	No ORG	NO ORG	HTN, IHD, T2DM	8	17	51
2.01	12.42				6	15	45
*1.73	3.58	No ORG	NO ORG	HTN	10	17	54
1.27	6.16				11	20	58
1.17	32.17	S. PNEUMONI/	NO ORG	NO	3	9	33
1.33	27.32				2	13	23
1.74	5.63	No ORG	E. FAECALIS	NO	8	10	26
3.68	1.33				9	10	28
7.61	100	No ORG	NO ORG	NO	8	17	37
3.02	100				9	15	31
2.07	100	E.COLI	NO ORG	CKD, HTN	9	14	51
2.73	100				9	16	51
5.77	46.05	B. CEPACIA	NO ORG	CKD ON MHD, IHD	13	32	65
1.95	30.4				14	27	62
1.95	3.89	No ORG	CANDIDA	T2DM HTN	6	22	56
2	3.52				5	25	51
11.4	0.76	No ORG	NO ORG	IHD, T2DM	5	18	35
15	2.05				7	19	40
1.48	11.43	E.COLI	E.COLI	CKD, IHD	11	33	71
3.72	7.97				10	27	71
1.2	0.64	No ORG	NO ORG	NO	0	9	23
1.08	1.58				2	9	18
7.6	100	No ORG	K.PNEUMONIAE	CKD	8	22	33
5.4	32.81				7	18	39
	0.25	NO ORG	NO ORG	CKD, T2DM, HTN,	4	16	41
	0.25				3	17	51
59.9	91.76	E.COLI	NO ORG	HTN, T2DM	8	22	52
	100				11	20	57
0.95*	8.07	No ORG	E.COLI	RVD POSITIVE	9	13	47
1.54	20.44				8	13	55
1.37*	100	No ORG	NO ORG	CLD	11	26	58
2.79	100				10	28	46
25.8	1.92	No ORG	NO ORG	T2DM	6	36	73
50.3	1.47				6	34	58
2.24*	2.94	No ORG	NO ORG	T2DM HTN IHD	4	27	65
2.14*	4.16	No ORG	NO ORG	CA LUNG	10	42	98
2.09	9.85				9	38	89

	4.51	No ORG	NO ORG	CKD ON MHD, IHD	10	25	53
	8.54				6	19	45
149	36.5	No ORG	NO ORG	MDS	15	46	105
30.1	49.58				17	42	92
4.08*	4.21	No ORG	CANDIDA SPECIES	CLD	18	42	90
3.71	6.35				17	39	88
5.8	0.22	No ORG	NO ORG	CKD	10	41	96
2.07	10.17				8	35	74
149.5	30	No ORG	NO ORG	IHD, T2DM	10	34	90
30.1	49.58				15	35	71
	11.43	NO ORG	NO ORG	CKD/ HTN	9	29	68
1.55*	100	No ORG	NO ORG	CKD/T2DM	7	18	51
5.46	100				7	26	66
*17.23	0.65	No ORG	NO ORG	IHD, T2DM	4	25	57
6.2	0.95				9	19	46
	0.06	No ORG	MIXED FLORA	T2DM	7	13	48
	0.04				6	14	39
	26.24	A. BAUMANI	MIXED FLORA	T2DM	5	6	26
	19				4	12	30
	1.11	NO ORG	CANDIDA SPECIES	NO	3	2	31
	0.62				5	0	19
	46.71	S.EPIDERMIDI	NO ORG	T2DM	9	31	58
	56.02				10	28	55
	7.46	E.COLI	E.CLOACAE	T2DM	10	30	70
	16.03				10	22	70
	18.73	No ORG	NO ORG	T2DM	10	30	73
	12.73				10	30	66
	17.06	No ORG	NO ORG	CKD/ HTN	7	35	41
	40.72				4	15	37
18	100	COAG NEG ST/	E.COLI	NO	6	13	40
22	100				6	13	30
27.4	61.27	No ORG	NO ORG	CLD	9	19	48
12.2	16.371				8	12	39
1.68*	2.82	No ORG	CANDIDA SPECIES	T2DM	4	16	43
1.39	2.8				4	13	37
	0.55	No ORG	NO ORG	NO	6	7	31
	0.65				1	4	28
23.7	15.71	No ORG	NO ORG	HTN	6	11	35
29.7	0.26				8	10	41
17.2	14.28	NO ORG	NO ORG	CA COLON	6	10	46
23.5	4.3				5	8	51
	0.15	S. EPIDERMIDI	NO ORG	NO	5	15	42
	0.84				4	18	42
1.2	0.03	No ORG	K.PNEUMONIAE	NO	4	14	27
1.97	0.06				4	7	27
	45	No ORG	S. HAEMOLYTICUS	CKD/HTN/ T2DM/	7	27	43

	99.76				7	24	43
	7.61	COAG NEG ST/	C. FREUNDI COMP	CKD/T2DM	7	20	39
	5.5				6	18	43
	1.9	S.HEMOLYTICU	NO ORG	T2DM	3	18	66
	2				6	18	63
10.6	1.94	No ORG	NO ORG	T2DM	2	12	32
	3.77				3	15	29
	16.27	No ORG	NO ORG	NO	2	1	19
	12.04				2	5	23
2.76	26.79	NO ORG	NO ORG	NO	12	24	65
5.6	40.74				14	20	68
1.6	40.65	E.COLI	ENTEROBACTER	T2DM/HTN	8	23	57
1.98	61.99				12	28	75
0.8	0.1	No ORG	NO ORG	NO	8	22	56
1.8	0.68				10	27	64
0.8	0.09	No ORG	NO ORG	NO	5	4	35
0.72	1.42				7	12	41
1.01	1.84	ACINETOBACT	NO ORG	T2DM/HTN/ PARK	9	20	58
0.44	14.09				9	18	48
3.62	59.81	No ORG	NO ORG	NO	6	12	38
3.35	33.92				8	9	44
	0.12	No ORG	NO ORG	NO	4	11	31
	0.04				4	9	24
0.8	0.09	No ORG	NO ORG	NO	5	4	35
0.72	1.42				7	12	41
	0.19	No ORG	NO ORG	CLD	5	16	23
	0.12				6	15	36
5.51	3.17	No ORG	NO ORG	NO	5	13	29
0.92	4.18				5	11	35
	0.23	No ORG	NO ORG	NO	4	10	43
	0.14				3	15	43
	0.13	No ORG	E. COLI	NO	2	8	34
	0.59				3	13	40
1.21	50	E. FAECALIS	C. FREUNDI COMP	T2DM/ HTN/ PSOI	10	31	62
1.28	60.4				9	30	67
3.04	100	No ORG	NO ORG	NO	2	2	27
5	100				3	6	31
	0.52	No ORG	NO ORG	NO	3	9	44
	0.18				3	10	37
72	1.38	NO ORG	NO ORG	nephrotic syndron	4	10	43
45	6.35				5	11	39
	66.15	E. COLI	E.COLI	NO	11	16	44
	38.14				11	16	44
	0.04	No ORG	E.COLI	NO	4	7	23
	0.08				6	8	25
	0.04	E. FAECIUM	NO ORG	T2DM/HTN/IHD/P	3	11	43
	0.06				2	11	51

	100	No ORG	NO ORG	NO	14	19	54
	100				14	19	54
5.04	0.13	No ORG	NO ORG	NO	9	10	30
5.74	6.15				9	15	36
1.03	0.22	No ORG	NO ORG	T2DM	2	14	42
0.87	0.27				2	12	38
3.4	5.3	No ORG	NO ORG	NO	5	20	40
5.4	4.2				4	17	34
3.22	1.87	CANDIDA ALBI	NO ORG	NO	13	17	67
11.18	2.52				14	19	68
3.91	0.6	No ORG	NO ORG	NO	9	8	37
5.84	0.43				9	19	58
1.93	0.76	S. EPIDERMIDI	NO ORG	NO	9	25	44
1	0.81				9	21	41
4.77	0.89	COAG NEG ST/	MIXED FLORA	NO	7	38	32
5.4	0.72				8	43	32
2.5	2.41	NO ORG	NO ORG	CKD/T2DM/HTN	8	21	53
1.5	2.9				7	22	43
1.21	0.61	No ORG	NO ORG	HTN/T2DM	5	18	46
0.82	100				5	21	52
3.7	0.6	No ORG	NO ORG	PULMONARY TB	6	18	42
1.58	0.78				9	20	57
2.7	0.04	No ORG	NO ORG	NO	4	6	29
1.51	0.05				6	17	34
5	100	NO ORG	E.COLI	T2DM	10	13	34
2.74	100				14	16	44
	0.06	NO ORG	NO ORG	T2DM/HTN	4	14	60
	0.51				5	12	42
5.09	0.86	S.HEMOLYTICU	K.PNEUMONIAE	RHD	9	14	29
5.35	0.55				7	9	31
1.53	0.04	No ORG	NO ORG	T2DM	4	14	36
2	0.05				4	12	33
4.15	3.31	DIPHTHEROID	NO ORG	HTN	14	31	78
2.15	6.75				16	25	87
1.04	4.8	No ORG	NO ORG	T2DM	3	9	28
0.97	11.9				3	10	28
7.7	0.27	E.FAECALIS	NO ORG	T2DM	10	30	66
2.35	9				11	24	64
1.75	100	E.COLI	E.COLI	T2DM/HTN/COPD	12	32	82
2.74	100				11	25	61
32	0.35	No ORG	NO ORG	T2DM/HTN	4	17	45
31.7	0.19				3	15	39
5.4	0.56	No ORG	NO ORG	HTN/IHD	11	26	69
5.7	1.3				13	30	79
7.34	5.67	S.HEMOLYTICU	NO ORG	HTN/T2DM/IHD	10	31	67
10.4	6.4				13	27	63
5.37	16.27	NO ORG	NO ORG	NO	5	8	33

7.37	12.04				5	8	35
	0.13	No ORG	NO ORG	NO	4	10	44
	2.31				4	12	46
	0.22	No ORG	NO ORG	T2DM	4	13	43
	0.27				4	13	47
	0.79	No ORG	NO ORG	T2DM	3	13	25
	41.62				2	13	22
10.4	6.4				13	27	63
5.37	16.27	NO ORG	NO ORG	NO	5	8	33
	18.73	No ORG	NO ORG	T2DM	10	30	73
	12.73				10	30	66
	17.06	No ORG	NO ORG	CKD/ HTN	7	35	41
	40.72				4	15	37

mortality
M AT DAY 2

R

M AT DAY 2

M AT DAY 5

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ANNEXURE IV – MASTER CHART

					gcs		hr		syst bp		map		resp rate		output		ionotropes		hematocrit		wbc		platelet		bun		creat		sodium		potassium		bili		bicarb		ph		PAO2		PACO2		PAO2/FIO2		A-a gradient		lactate		pct				SOFA		APACHE II		SAPS II	
sl no	ip no	age	Sex	duration	24 HR	48 HR			24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	blood culture	urine culture	chronic disease	24 HR	48 HR	24 HR	48 HR	24 HR	48 HR	mortality
1	1034597	60	M	2	15	15	126	130	90	90	65	65	35	38	400	350	3	3	30.5	32	32.2	20.9	117	96	173	170	5.49	6.48	118	118	4.01	5.33	0.53	0.85	8	3	7.26	7.398	213	226	9.3	12.9	426	452	131.9	114.4	10.64	4.59	100	100	No ORG	e. coli	IHD, T2DM	9	10	25	23	68	71	M AT DAY 2
2	1033551	56	M	17	15	15	76	88	110	120	65	75	28	30	2400	1800	0	0	32.5	30.7	2.2	2.2	48	44	66	61	1.4	1.22	135	132	4.88	3.83	0.82	0.9	21	19	7.44	7.446	80.8	63.6	27	26.8	197	193	177.8	138.2	1.64	2.89	0.78	0.41	No ORG	NO ORG	NO	6	6	8	7	22	25	R
3	1034925	19	M	2	15	15	80	90	90	80	63	60	34	30	0	150	2	2	30	42.1	11.1	14.2	83	19	124	128	5.13	3.51	131	128	4.55	5.47	2.3	2.4	10	16	7.24	7.312	66.2	68.8	13.2	28.4	161	168	209.6	188	4.81	7.86	61.4	100	No ORG	NO ORG	NO	13	14	17	18	54	48	M AT DAY 2
4	1035300	87	M	5	15	15	96	110	110	120	83	93	35	30	900	1000	0	0	37.4	36	18.6	23.5	85	95	119	110	1.56	1.56	136	137	3.4	3.35	2.73	4.46	22	20	7.34	7.352	94.7	119	37.7	38	126	238	392.9	190	2.86	1.15	3.54	3.44	S. PNEUMONIAE	NO ORG	HTN	8	7	16	14	44	50	M AT DAY 5
5	1032205	83	M	13	15	15	84	90	130	130	103	103	28	25	130	250	0	0	30.8	30.1	7.7	5.8	107	110	135	127	5.08	5.41	125	135	4.72	3.9	2.68	0.78	12	20	7.45	7.43	74.3	75.3	29.4	29.7	354	359	38.7	37.3	1.34	2.01	31.28	12.42	No ORG	NO ORG	HTN, IHD, T2DM	8	6	17	15	51	45	R
6	1031578	69	M	14	15	15	88	94	130	130	103	103	28	25	330	450	0	0	34.6	31.5	14.4	13	88	58	212	244	5.2	5.83	138	142	5.94	5.43	3.25	2.22	10	15	7.28	7.285	93.9	52.2	44.2	53.5	233	131	136	164.8	1.73	1.27	3.58	6.16	No ORG	NO ORG	HTN	10	11	17	20	54	58	R
7	1031054	52	M	18	12	13	120	115	120	130	93	103	35	30	1300	2500	0	0	33.2	29.3	28.6	16.5	278	396	101	31	1.1	0.56	136	144	3.95	3.03	3.69	1.39	17	28	7.4	7.514	110	64.9	41.4	30.7	314	309	87.8	46.5	1.17	1.33	32.17	27.32	S. PNEUMONIAE	NO ORG	NO	3	2	9	13	33	23	R
8	1031022	58	M	32	13	13	114	118	110	110	83	83	28	25	900	1100	1	1	33	29.6	13.5	10	211	131	10	15	0.78	0.66	148	134	2.84	3.8	2.24	4.72	22	27	7.46	7.457	74.5	93.5	36.6	35.8	226	228	115	154.1	1.74	3.68	5.63	1.33	No ORG	E. FAECALIS	NO	8	9	10	10	26	28	R
9	1032749	63	M	10	15	15	110	94	110	110	83	83	24	20	2500	3700	2	2	35.3	34.1	28.7	17.9	193	190	80	76	4.2	3.54	129	130	5.89	4.23	1.22	1.41	15	18	7.25	7.321	81.8	58.5	34.3	38.9	200	143	167.7	185.2	7.61	3.02	100	100	No ORG	NO ORG	NO	8	9	17	15	37	31	R
10	1029574	83	M	25	15	15	75	88	110	120	83	93	18	20	0	200	0	0	30.1	27.5	4.6	4.7	34	28	254	309	6.51	6.45	138	135	4.51	5.4	1.16	1.4	12	18	7.39	7.424	75.1	119.2	16.6	18.4	203	322	168	121.6	2.07	2.73	100	100	E.COLI	NO ORG	CKD, HTN	9	9	14	16	51	51	R
11	1029701	53	M	5	10	10	125	130	90	100	63	73	30	34	100	150	1	1	26.5	27.5	42.2	21.4	67	24	130	121	5.21	4.37	137	134	4.25	4.37	0.45	0.56	12	21	7.27	7.288	186.9	90.9	26.6	49.4	234	152	350.3	275.1	5.77	1.95	46.05	30.4	B. CEPACIA	NO ORG	CKD ON MHD, IHD, T2DM, HTN	13	14	32	27	65	62	M
12	1029044	69	M	8	15	15	110	98	110	114	83	85	30	28	350	350	0	0	31.3	30.3	20.4	34.4	274	186	168	232	5.4	4.86	123	135	5.45	6.14	0.58	0.6	10	10	7.29	7.22	116.4	56.9	21.5	19.5	284	139	149.1	211.1	1.95	2	3.89	3.52	No ORG	CANDIDA	T2DM HTN	6	5	22	25	56	51	R
13	1028215	70	M	4	10	13	92	98	110	120	83	85	25	24	1100	1300	0	0	40.4	40.4	12	10.6	245	170	181	170	5.67	6.03	165	158	3.61	3.49	0.6	0.64	19	17	7.38	7.36	99.5	82.1	39.4	34	474	200	72	167.7	11.4	15	0.76	2.05	No ORG	NO ORG	IHD, T2DM	5	7	18	19	35	40	M
14	1043213	88	M	4	8	10	137	114	110	110	83	83	28	30	0	150	0	0	30.7	31.3	9.4	20.5	52	35	89	74	5.15	3.34	125	137	5.22	4.2	1.88	6.32	12	15	7.31	7.374	151.8	88	25.6	30.7	370	196	108.5	194.5	1.48	3.72	11.43	7.97	E.COLI	E.COLI	CKD, IHD	11	10	33	27	71	71	M
15	1042873	25	M	3	15	15	130	118	130	130	103	103	35	40	1500	1250	0	0	28	25.4	36.6	25.2	6.6	8.8	35	26	1.03	0.88	137	134	4.86	5.22	0.62	0.64	22	23	7.39	7.453	160	86.1	39.9	31.2	400	217	75.3	160.1	1.2	1.08	0.64	1.58	No ORG	NO ORG	NO	0	2	9	9	23	18	R
16	1024773	21	M	3	14	15	110	114	110	114	73	75	25	20	150	100	0	0	20.9	23.2	11.6	11.9	256	242	287	82	14.23	13.2	158	153	3.53	3.62	0.24	0.21	21	13	7.24	7.3	80	92	34.6	30.4	195	227	169.1	162.3	7.6	5.4	100	32.81	No ORG	K.PNEUMONIAE	CKD	8	7	22	18	33	39	M
17	1042853	70	M	10	15	15	118	88	130	120	103	93	30	28	500	400	0	0	40.4	39	17.8	14.5	212	214	62	58	2.69	2.54	133	137	5.47	6.43	0.26	6.43	16	14	7.34	7.284	62	80	345	37.8	258	308	66	58.2	5.1	6.4	0.25	3.9	NO ORG	NO ORG	CKD, T2DM, HTN, COPD	4	3	16	17	41	51	R
18	1042803	58	M	6	15	15	118	114	130	140	103	203	30	28	400	450	0	0	42.1	41	21.9	19	98	32	58	68	3.77	3.88	116	121	6.44	6.29	5.42	8.86	18	14	7.39	7.45	120	71	22.4	30.3	571	338	1.7	40.9	59.9	64	91.76	100	E.COLI	NO ORG	HTN, T2DM	8	11	22	20	52	57	M
19	1025247	50	M	16	15	15	110	100	110	114	83	85	20	22	2000	1900	1	1	19.8	23.7	1.9	1.6	17	26	56	54	0.92	1.02	137	133	4.01	2.93	5.32	8.64	14	16	7.47	7.394	79.8	92.6	17.9	20.6	380	441	47.6	31.4	0.95	1.54	8.07	20.44	No ORG	E.COLI	RVD POSITIVE	9	8	13	13	47	55	R
20	1043380	60	M	3	12	11	118	124	80	100	53	73	25	20	160	1050	2	2	32.9	29.4	32.2	46.1	171	173	176	170	7.56	5.02	132	134	4.48	3.7	1.38	2	10	8.6	7.42	7.381	70.4	90.6	13.9	14.9	156	238	233.1	161.7	1.37	2.79	100	100	No ORG	NO ORG	CLD	11	10	26	28	58	46	R
21	1043386	98	F	3	15	15	120	100	130	150	103	123	26	28	300	400	0	1	22	33	225	192	646	462	111	122	4.4	4.11	143	141	4.15	4.42	0.29	0.44	12	12	7.26	7.25	38	46.8	32	32.5	181	220	71.7	62.3	25.8	50.3	1.92	1.47	No ORG	NO ORG	T2DM	6	6	36	34	73	58	M
22	1043537	70	M		13	14	88	94	130	140	103	103	28	33	350	450	0	0	23.2	27	25.2	28	4.9	5.1	158	155	4.84	4.3	126	121	6.18	6.1	0.21	0.31	10	11	7.3	7.31	100.5	100	15	14	497	490	30.5	31	2.24	2.5	2.94	3.1	No ORG	NO ORG	T2DM HTN IHD	4	4	27	30	65	61	R
23	1043556	68	M	3	3	6	80	145	90	100	63	83	45	35	350	400	2	1	28.2	27.4	28.2	26.6	213	233	100	114	4.43	4.55	146	147	6.3	6.52	0.37	0.29	8	10	7.25	7.232	439	214	23.9	17.8	439	535	244.1	48.9	2.14	2.09	4.16	9.85	No ORG	NO ORG	CA LUNG	10	9	42	38	98	89	M
24	1042666	72	M	7	12	15	84	88	140	130	107	103	25	21	75	150	0	0	21.5	23.9	10.5	10.4	90	104	131	68	4.1	3.29	133	140	5.47	4.15	0.21	0.28	19	16	7.47	7.458	62.9	61.4	29	21	300	292	200	214	3.4	3.9	4.51	5.1	No ORG	NO ORG	CKD ON MHD, IHD, T2DM, HTN	10	6	25	19	53	45	R
25	1041782	77	M	6	3	7	116	124	100	90	73	63	30	34	30	300	3	2	19.2	21.2	64.6	65.9	65	13	149	173	3.5	4.62	142	141	5.03	5.12	0.71	0.5	6.2	26	7.05	7.39	152.8	55.3	22.9	44.3	169	61	461	531	149	30.1	36.5	49.58	No ORG	NO ORG	MDS	15	17	46	42	105	92	M
26	1024731	34	M	3	2	2	100	110	80	90	63	73	35	30	550	300	2	3	29.8	27.4	52.5	45.5	191	180	153	160	4.35	4.7	132	134	5.88	2.9	26.52	19.3	8	7	7.18	7.338	32.7	125.4	29.6	13.3	65	157	286.8	428.4	4.08	3.71	4.21	6.35	No ORG	CANDIDA SPECIES	CLD	18	17	42	39	90	88	M
27	1043314	81	M	8	3	6	50	86	110	140	83	103	45	30	350	300	0	0	42	25.9	24.2	20.3	2.9	1.9	68	84	3.14	3.35	134	147	5.76	7.12	0.6	0.74	14	20	7.08	7.263	51	85	47.6	51.2	51	100	602	457	5.8	2.07	0.22	10.17	No ORG	NO ORG	CKD	10	8	41	35	96	74	M
28	1041782	77	M	6	8	9	115	124	60	110	50	73	40	25	0	300	2	1	15	18.5	43.9	24.1	57	42	93	204	1.64	4.89	134	140	4.74	4.89	0.71	0.84	16	19	7.05	7.32	152	68.9	22.9	25.1	380	76	104	541.4	149.5	30.1	30	49.58	No ORG	NO ORG	IHD, T2DM	10	15	34	35	90	71	M
29	1043213	88	M	5	11	12	126	110	70	100	53	73	35	30	150	250	1	0	30.7	31.7	9.4	10	52	56	89	90	5.15	6.1	125	121	5.22	5.1	1.88	2.1	12	16	7.31	7.354	151.8	150	25.6	24	523	515	23	24	1.5	5.46	11.43	20	NO ORG	NO ORG	CKD/ HTN	9	9	29	31	68	70	M
30	1043088	65	F	8	10	10	110	114	130	110	103	93	28	30	600	500	0	0	22.6	22.6	10.6	11.6	150	154	124	242	3.2	5.36	131	123	5.09	6.34	0.17	0.14	19	10	7.37	7.29	114.1	65.6	33.1	24.6	278	312	129.7	53.4	1.55	5.46	100	100	No ORG	NO ORG	CKD/T2DM	7	7	18	26	51	66	R
31	1042977	72	M	10	15	15	120	110	110	120	103	117	40	35	900	1100	0	0	13.5	20.9	21.6	17.6	135	99	90	127	2.52	2.33	135	137	5.48	4.36	1.26	2.04	10	13	7.16	7.401	159.1	76.7	11.9	22.9	636	153	4.4	179.9	17.23	6.2	0.65	0.95	No ORG	NO ORG	IHD, T2DM	4	9	25	19	57	46	R
32	1025405	55	M	35	9	9	108	110	160	150	113	110	30	28	800	100	0	0	40.6	38.2	14.2	10.4	455	306	47	36	0.67	0.71	133	131	5.19	4.25	0.78	0.84	17	22	7.44	7.45	62.7	55.3	36.2	38	89	111	391.2	253.7			0.06	0.04	No ORG	MIXED FLORA	T2DM	7	6	13	14	48	39	R
33	1027458	35	M	15	15	15	130	140	130	120	103	100	40	44	700	900	0	0	44	37.8	6.6	7.4	97	65	27	121	1.1	0.81	143	136	3.22	3.88	2.3	0.84	11	14	7.33	7.32	88	61.9	24.7	30.6	304	151	87.8	192.2			26.24	19	A. BAUMANI	MIXED FLORA	T2DM	5	4	6	12	26	30	R
34	1027495	42	F	8	15	15	88	90	90	100	73	83	25	20	800	1100	0	0	37.8	38.9	6.5	8.3	197	26	27	25	1.19	0.71	138	134	3.47	3.72	0.72	0.84	19	21	7.4	7.41	94	90	30	34	285	273	103.8	102.5			1.11	0.62	NO ORG	CANDIDA SPECIES	NO	3	5	2	0	31	19	R
35	1027521	72	M	5	14	13	118	110	100	90	83	60	34	35	600	800	2	2	39.8	42	17	9.6	197	138	103	126	4.78	4.77	117	130	6.32	6.05	0.7	0.8	13	13	7.18	7.401	49.7	95.3	36.5	16.6	124	238	189.9	169.1			46.71	56.02	S.EPIDERMIDIS	NO ORG	T2DM	9	10	31	28	58	55	M
36	1027520	66	F	7	8	8	110	114	100	104	83	85	28	20	100	150	0	0	22.9	32.5	25.9	16.7	299	180	299	180	3.87	3.1	139	132	3.28	4.67	11.46	12.6	17	18	7.31	7.36	131.2	124	35.3	36.1	328	310	109	116.1			7.46	16.03	E.COLI	E.CLOACAE	T2DM	10	10	30	22	70	70	M
37	1042738	75	F	5	5	5	90	84	90	130	70	97	24	20	1140	1250	1	1	32.7	35.1	5.4	5.5	90	82	30	23	0.81	0.65	145	143	2.58	2.79	0.49	0.42	20	19	7.47	7.466	137.8	91	25.7	26	274	228	186.6	161.7			18.73	12.73	No ORG	NO ORG	T2DM	10	10	30	30	73	66	M

38	1042521	58	M	6	15	15	118	90	200	130	230	97	35	25	600	600	0	0	24.6	22	19.1	18.2	295	260	154	130	11.21	11.1	143	149	4.55	4.42	0.81	0.74	17	17	7.19	7.405	74.7	278	18.3	27.3	149	556	258	44.4			17.06	40.72	No ORG	NO ORG	CKD/ HTN	7	4	35	15	41	37	R
39	1023266	51	M	5	13	13	108	110	110	114	83	85	20	21	400	800	1	1	36.6	37.4	19.7	17.1	111	110	68	80	3.61	3.74	127	143	4.36	3.77	0.73	0.71	11	18	7.39	7.35	102.1	100	24.7	27.8	486	476	16.9	15	18	22	100	100	COAG NEG STAPH	E.COLI	NO	6	6	13	13	40	30	R
40	1025528	40	M	15	15	15	58	48	110	108	83	83	20	18	410	350	1	1	20.1	22.4	31	16.6	133	68	69	78	2.51	2.09	131	137	5.75	4.66	2.69	4.62	11	17	7.3	7.35	44.7	96	32.3	34.2	213	457	64.7	11	27.4	12.2	61.27	16.371	No ORG	NO ORG	CLD	9	8	19	12	48	39	R
41	1024847	42	F	13	15	15	110	100	150	146	110	109	20	20	400	300	0	0	24.9	26.3	27.1	18.3	636	513	63	36	4.09	3.11	131	129	4.39	4.46	0.71	0.69	12	17	7.39	7.44	70.4	73.9	19	26.4	335	352	55.6	52.1	1.68	1.39	2.82	2.8	No ORG	CANDIDA SPECIES	T2DM	4	4	16	13	43	37	R
42	1042610	49	M	8	15	15	110	108	90	100	63	73	24	26	600	800	1	0	42	40	12.3	12.3	343	343	42	38	1.33	1.17	132	138	4.69	4.05	0.65	0.7	17	22	7.4	7.4	59	83.4	36.3	37.2	250	278	164	166			0.55	0.65	No ORG	NO ORG	NO	6	1	7	4	31	28	R
43	1028058	64	M	15	15	15	110	98	90	100	63	83	20	24	700	800	2	2	42.7	40.7	18.6	24.1	175	150	80	82	2.15	2.37	143	143	4.34	5.04	2.2	2.4	17	15	7.35	7.295	71	100.5	16.8	15	245	347	114.8	87.5	23.7	29.7	15.71	0.26	No ORG	NO ORG	HTN	6	8	11	10	35	41	R
44	1028021	61	F	10	15	15	94	96	100	96	80	72	24	20	250	300	2	2	26.2	24.2	1	1.6	271	300	37	32	1.32	0.6	125	131	3.9	3.3	0.72	0.84	15	16	7.46	7.48	106	111	29.4	27.6	265	278	142.4	139.7	17.2	23.5	14.28	4.3	NO ORG	NO ORG	CA COLON	6	5	10	8	46	51	R
45	1027589	55	F	4	6	8	84	90	130	130	203	203	25	26	800	900	0	0	30.4	28.2	15.8	28.2	327	352	24	22	0.33	0.57	137	137	3.21	3.07	0.48	0.84	23	25	7.46	7.44	98	137.2	32.6	42	245	343	237	225.3			0.15	0.84	S. EPIDERMIDIS	NO ORG	NO	5	4	15	18	42	42	M
46	1054605	29	F	18	15	15	114	110	130	120	200	103	30	25	900	1000	0	0	42.3	41	11.1	11.3	239	268	39	58	0.57	0.54	144	140	3.36	4.74	0.13	0.28	20	22	7.46	7.364	53.9	44.5	33.6	31.7	54	74	617.1	343.7	1.2	1.97	0.03	0.06	No ORG	K.PNEUMONIAE	NO	4	4	14	7	27	27	R
47	1054447	59	M	18	10	11	112	120	120	118	103	100	30	28	1000	900	0	0	43.2	41.4	18.2	18.7	523	418	161	144	5.37	5.24	131	134	5.37	5.24	0.56	0.8	11	12	7.29	7.33	79.2	160.3	22.1	14.5	377	403	42.9	113.9			45	99.76	No ORG	S. HAEMOLYTICUS	CKD/HTN/ T2DM/	7	7	27	24	43	43	R
48	105551	56	M	4	9	10	116	114	120	130	103	103	26	24	1000	1100	0	0	27	26	13.5	23.7	274	230	165	170	5.84	5.99	141	146	5.17	5.32	0.22	0.4	10	10	7.28	7.4	97.7	91.5	15.9	16.4	465	436	32.2	37.7			7.61	5.5	COAG NEG STAPH	C. FREUNDI COMPLEX	CKD/T2DM	7	6	20	18	39	43	M
49	1055607	70	M	2	15	15	130	120	120	150	103	110	34	30	450	400	0	0	55.8	54	40.2	38	193	130	54	50	0.88	0.9	140	142	5.01	5.3	1.49	1.5	17	20	7.32	7.35	53.6	51.6	33.2	39.2	89	52	332.7	612			1.9	2	S.HEMOLYTICUS	NO ORG	T2DM	3	6	18	18	66	63	M
50	1055662	35	M	4	15	15	108	98	110	120	83	103	26	28	600	800	0	0	47.8	46	23	12.2	269	120	50	71	1.12	2.33	131	132	7.41	6.18	0.5	0.14	10	10	6.9	7.07	111	99.2	13	10.8	271	472	165.1	37	10.6	14	1.94	3.77	No ORG	NO ORG	T2DM	2	3	12	15	32	29	R
51	1054327	41	F	18	15	15	108	92	130	160	103	120	32	29	1410	1140	0	0	32	34	7.1	13.4	159	297	18	34	0.62	0.35	137	139	4	3.84	0.3	0.61	23	25	7.33	7.38	94	77.5	46.9	41.9	157	155	275.2	226.6			16.27	12.04	No ORG	NO ORG	NO	2	2	1	5	19	23	R
52	1054450	34	F	12	2	2	104	120	100	110	73	73	18	15	0	0	1	1	36.9	35	8.4	14.8	192	34	103	123	3.01	3.13	137	138	4.74	5.43	1.14	2.95	17	13	7.28	7.373	61.8	359.9	21.7	38.1	151	598	203.4	21.2	2.76	5.6	26.79	40.74	NO ORG	NO ORG	NO	12	14	24	20	65	68	M
53	1054062	53	M	6	11	2	130	134	70	90	53	63	34	15	450	300	2	2	38.9	37.4	15.5	12.6	169	124	106	124	2.72	3.47	130	140	3.74	4.08	0.72	0.7	16	20	7.25	7.103	462.8	170	13.8	35.1	462	340	233.8	142.6	1.6	1.98	40.65	61.99	E.COLI	ENTEROBACTER	T2DM/HTN	8	12	23	28	57	75	M
54	1053967	27	M	29	2	2	120	124	140	130	83	83	24	20	1100	900	0	0	40	22	16.6	7.4	290	200	42	99	0.78	2.21	133	137	5.36	5.95	0.3	0.3	22	24	7.24	7.238	82.4	60.5	62	77.7	82	60	553.1	55.4	0.8	1.8	0.1	0.68	No ORG	NO ORG	NO	8	10	22	27	56	64	M
55	1053742	60	M	14	15	15	80	110	100	100	73	73	34	36	1100	1000	1	1	38	35	13.9	10.8	480	98	37	31	0.64	0.7	135	127	4.59	3.26	0.42	0.5	24	19	7.4	7.45	119.4	63.4	31.7	29	291	155	133.7	192.7	0.8	0.72	0.09	1.42	No ORG	NO ORG	NO	5	7	4	12	35	41	M
56	1053323	68	M	14	8	7	120	114	100	100	73	73	28	30	900	800	1	1	41	40	17.2	18.9	153	156	48	56	1.63	1.56	135	136	4.19	3.88	0.45	0.5	18	20	7.4	7.453	62.1	94.4	34.8	31	124	230	250.9	159.2	1.01	0.44	1.84	14.09	ACINETOBACTER BAUMANI	NO ORG	T2DM/HTN/ PARKINSONS	9	9	20	18	58	48	M
57	1053988	27	F	17	15	13	110	90	130	110	103	83	26	24	900	1000	0	0	32.3	32	22.9	20.3	224	180	163	175	6.31	6.12	130	131	6.41	4.8	2.96	4.02	10	10	7.46	7.461	85.5	66.1	19.5	30	407	317	39.9	45.6	3.62	3.35	59.81	33.92	No ORG	NO ORG	NO	6	8	12	9	38	44	R
58	1051610	46	F	23	15	15	120	110	130	110	103	93	34	30	1100	1200	0	0	44	43	15	13.1	240	231	57	23	0.81	0.6	151	138	4.16	5.03	0.48	0.73	20	24	7.46	7.41	63.2	90.8	28.5	30.5	63	91	614.2	584			0.12	0.04	No ORG	NO ORG	NO	4	4	11	9	31	24	R
59	1053742	60	M	14	15	15	80	110	100	100	73	73	34	36	1100	1100	1	1	38	35	13.9	10.8	480	98	37	31	0.64	0.7	135	127	4.59	3.26	0.42	0.5	24	19	7.4	7.45	119.4	63.4	31.7	29	291	155	133.7	192.7	0.8	0.72	0.09	1.42	No ORG	NO ORG	NO	5	7	4	12	35	41	M
60	1055236	36	M	12	12	12	118	90	110	130	93	103	26	28	1300	470	0	0	19.5	24	7.9	5.3	84	23	34	38	0.95	0.67	134	145	4.34	3.02	1.71	1.48	10	15	7.4	7.31	68	78	24	19	324	371	51.7	48			0.19	0.12	No ORG	NO ORG	CLD	5	6	16	15	23	36	R
61	1053946	48	M	25	13	13	120	110	110	130	103	103	34	34	900	1300	0	0	44	43	9.3	15	250	283	12	48	0.38	0.81	134	133	4.18	3.82	0.54	0.84	29	24	7.43	7.358	40	59	24.3	31.7	50	74	500	471.8	5.51	0.92	3.17	4.18	No ORG	NO ORG	NO	5	5	13	11	29	35	R
62	1053825	72	M	26	15	15	87	98	149	160	110	110	30	28	1750	1950	0	0	44	43	14.1	24.5	138	321	61	23	0.67	0.43	140	133	4.35	3.44	0.43	0.5	18	24	7.42	7.45	84	80	20	22	140	133	318.8	320.3			0.23	0.14	No ORG	NO ORG	NO	4	3	10	15	43	43	R
63	1053331	48	F	2	15	15	100	112	120	120	110	110	30	32	800	900	0	0	42	41	12.4	21	264	141	38	40	0.63	0.55	146	150	3.45	3.46	0.44	0.77	21	24	7.44	7.49	130.9	55.7	33.1	30.6	218	101	255.2	298.2			0.13	0.59	No ORG	E. COLI	NO	2	3	8	13	34	40	R
64	1055042	53	F	7	5	5	118	143	120	120	110	110	15	15	1015	485	0	0	36	35	16.9	11.5	182	170	247	257	3.99	3.62	169	177	5.5	5	0.22	0.24	27	23	7.41	7.46	73.3	117	26.6	31.4	147	234	249.9	200.3	1.21	1.28	50	60.4	E. FAECALIS	C. FREUNDI COMPLEX	T2DM/ HTN/ PSORIASIS	10	9	31	30	62	67	M
65	1053903	43	M	18	15	15	84	88	100	90	73	63	26	28	800	750	0	0	42	44	18.4	39.2	239	261	30	10	0.63	0.84	135	139	4.51	3	0.63	0.81	23	25	7.39	7.4	131.6	110	27.9	30	321	268	125.9	144.8	3.04	5	100	100	No ORG	NO ORG	NO	2	3	2	6	27	31	M
66	1052959	62	F	10	15	15	108	111	130	128	110	108	34	34	350	550	0	0	37.7	38	19.1	15.3	298	236	56	25	0.9	0.63	140	134	4.38	4.05	0.56	1.08	18	28	7.41	7.42	71	80	28.2	25	118	100	321.6	459.1			0.52	0.18	No ORG	NO ORG	NO	3	3	9	10	44	37	M
67	1057012	24	M	21	15	15	120	116	60	70	53	50	30	34	600	500	2	2	35	36.6	14.1	16.6	192	184	63	91	0.78	1.08	126	128	3.17	3.12	0.3	0.4	11	14	7.36	7.4	106.6	80.3	9.4	18	505	382	32	46.9	72	45	1.38	6.35	NO ORG	NO ORG	nephrotic syndrome, TB	4	5	10	11	43	39	M
68	1056531	58	M	20	15	15	130	124	130	130	93	93	34	32	100	50	0	0	30.4	32.4	5	5.5	32	37	230	215	7.7	7.7	130	136	4.63	4.26	2.21	2.1	12	14	7.35	7.37	57.4	91.2	21.7	40.9	115	182	272	214.2			66.15	38.14	E. COLI	E.COLI	NO	11	11	16	16	44	44	R
69	1054508	31	F	14	15	15	120	124	110	114	73	75	34	35	800	900	0	0	40	41	14.5	6.7	143	146	26	17	0.51	0.5	140	134	3.64	4.12	0.51	0.61	26	26	7.35	7.45	65	50	21	19	108	71	336.6	425.3			0.04	0.08	No ORG	E.COLI	NO	4	6	7	8	23	25	M
70	1054889	70	F	14	9	8	100	88	120	110	93	83	28	30	1000	900	0	0	34	30	13.1	13	143	269	108	97	2.26	2.04	140	148	4.51	4.41	0.56	0.51	17	13	7.45	7.35	75	80	30	28	150	160	244	241.5			0.04	0.06	E. FAECIUM	NO ORG	T2DM/HTN/IHD/PTCA	3	2	11	11	43	51	R
71	1056997	20	M	20	13	12	130	130	90	100	63	73	30	26	50	50	1	0	43	42	23.1	20	48	41	106	100	5.57	5.3	133	132	4.69	3.91	4.15	4.36	10	17	7.31	7.31	84	66.31	31	13.9	210	208.6	169.6	208			100	100	No ORG	NO ORG	NO	14	14	19	19	54	54	R
72	1059306	38	M	7	14	13	100	110	90	100	63	73	30	28	900	600	2	2	36	37	15	22.8	110	83	80	62	1.77	1.54	137	123	3.71	2.54	6.58	4.96	22	21	7.3	7.28	80	84	23	24	381	400	41	35.7	5.04	5.74	0.13	6.15	No ORG	NO ORG	NO	9	9	10	15	30	36	M
73	1056535	75	M	20	15	15	110	100	130	130	103	103	26	24	900	1100	0	0	33.4	33	17.8	17.5	291	312	51	48	0.85	0.63	137	134	4.07	4.31	0.5	0.56	20	23	7.46	7.285	54.4	59.3	40.7	54.7	259	282	44.5	22.1	1.03	0.87	0.22	0.27	No ORG	NO ORG	T2DM	2	2	14	12	42	38	R
74	1059052	18	M	9	15	15	130	120	160	150	103	103	30	34	100	100	0	0	20.8	20.8	13.1	13.5	604	656	203	117	4.33	2.8	127	127	5.57	4.1	0.5	0.5	12	17	7.3	7.35	94.5	36.9	16.4	32.9	236	92	170	207.4	3.4	5.4	5.3	4.2	No ORG	NO ORG	NO	5	4	20	17	40	34	M
75	1057715	30	F	20	3	3	109	82	90	100	63	73	15	15	600	900	2	1	34.7	32	19.1	29.4	100	182	37	76	0.92	1.32	141	148	4.64	3.53	4.19	4.8	19	23	7.43	7.52	73.7	128.7	31.2	27.5	123	129	315	549.9	3.22	11.18	1.87	2.52	CANDIDA ALBICANS	NO ORG	NO	13	14	17	19	67	68	M
76	1058063	21	F	7	9	3	102	112	110	100	73	63	15	15	1000	900	0	1	29.8	24.8	13.8	13.5	398	528	14	12	0.67	0.78	137	146	4.65	3.98	6.69	7.85	20	27	7.46	7.5	71	117	31.4	29.8	178	390	174.9	59.7	3.91	5.84	0.6	0.43	No ORG	NO ORG	NO	9	9	8	19	37	58	M
77	1057983	48	M	17	9	9	110	108	210	170	150	130	26	28	200	300	0	0	28.6	32.2	14.1	10.7	106	105	129	105	9.59	9.55	133	138	3.5	3.06	0.95	0.94	17	23	7.4	7.304	67.5	148.1	33.4	22.5	321	370	40.5	109	1.93	1	0.76	0.81	S. EPIDERMIDIS	NO ORG	NO	9	9	25	21	44	41	R
78	1060074	63	M	8	15	15	118	100	100	90	73	63	26	28	600	700	1	1	31.3	30.9	17.3	9.9	31	30	42	38	0.93	0.98	125	126	3.71	3.29	0.22	0.3	23	22	7.45	7.35	88	39.7	28	51.3	220	99	162.2	181.4	4.77	5.4	0.89	0.72	COAG NEG STAPH	MIXED FLORA	NO	7	8	38	43	32	32	M
79	1060691	56	F	7	11	11	88	86	110	100	73	63	28	26	350	580	0	0	33.3	30	27.4	18.8	455	400	228	212	7.09	7..3	114	119	3.83	3.61	0.19	0.45	25	26	7.4	7.35	80	90	24	26	381	429	39.7	108.2	2.5	1.5	2.41	2.9	NO ORG	NO ORG	CKD/T2DM/ HTN	8	7	21	22	53	43	R
80	1059106	56	M	17	15	15	114	102	130	130	93	93	30	30	300	400	0	0	32.8	27.8	15.9	11.8	391	390	116	118	4.15	4.23	126	129	5.79	6.14	0.26	0.34	13	12	7.44	7.465	60	118	36.6	33.6	150	169	179.4	338.9	1.21	0.82	0.61	100	No ORG	NO ORG	HTN/T2DM	5	5	18	21	46	52	M
81	1057164	67	F	7	8	7	118	120	110	110	73	63	20	20	1000	900	1	2	31.8	36.2	6.6	15.3	259	234	19	43	0.54	0.79	139	145	4.69	4.61	0.3	0.87	22	20	7.3	7.3	101	141	32.2	28.7	481	202	8.5	322	3.7	1.58	0.6	0.78	No ORG	NO ORG	PULMONARY TB	6	9	18	20	42	57	M
82	1057687	39	F	5	12	12	120	130	100	90	73	63	30	34	1000	900	0	1	36	37	4.1	5.5	200	215	14	31	0.7	0.45	140	141	2.97	3.6	0.22	0.42	20	26	7.45	7.23	79.3	40.3	30.9	55.1	378	192	31.8	40.6	2.7	1.51	0.04	0.05	No ORG	NO ORG	NO	4	6	6	17	29	34	R

83	1058870	43	M	7	15	15	110	118	110	100	73	63	20	24	1620	900	2	2	27.1	28	2	27.8	60	94	120	142	5.13	5,37	135	135	4.8	5.37	0.84	2.89	10	11	7.23	7.408	80.9	47.6	18.3	23.8	385	227	46	72.4	5	2.74	100	100	NO ORG	E.COLI	T2DM	10	14	13	16	34	44	M
84	1054020	65	F	26	15	15	120	118	110	100	73	63	30	32	750	900	0	0	34	35	16.6	14.6	242	164	145	128	1.67	1.3	145	149	5.07	4.97	0.2	0.36	14	29	7.4	7.4	118	115	32	32	148	192	412	272.8			0.06	0.51	NO ORG	NO ORG	T2DM/HTN	4	5	14	12	60	42	R
85	1057954	56	F	5	13	15	118	100	90	90	63	63	34	30	1400	800	1	1	42	41	9.2	3	10	32	24	24	1.11	1.04	134	135	4.6	5.01	0.66	0.7	21	19	7.4	7.4	54	60	25	26	257	286	64.5	57.2	5.09	5.35	0.86	0.55	S.HEMOLYTICUS	K.PNEUMONIAE	RHD	9	7	14	9	29	31	R
86	1058507	65	M	10	12	12	98	90	140	130	103	103	24	26	1400	1600	0	0	48.6	47	12.9	11	336	330	112	122	1.66	1.9	138	134	6.04	4.5	1	0.9	21	20	7.34	7.39	83.5	73.7	29	30.7	398	351	30	37.7	1.53	2	0.04	0.05	No ORG	NO ORG	T2DM	4	4	14	12	36	33	R
87	1057008	49	M	15	3	3	114	116	90	80	63	53	15	15	400	450	2	2	13.7	23.7	10.8	17.1	117	104	191	212	2.42	1.38	136	152	4.64	2.95	4.35	4.91	16	17	7.54	7.414	171	63.6	19.1	17.5	244	91	304	413.6	4.15	2.15	3.31	6.75	DIPHTHEROID SPECIES	NO ORG	HTN	14	16	31	25	78	87	M
88	1057540	67	M	7	15	15	110	114	130	140	110	110	34	38	2090	1050	0	0	34	33.2	17.6	10.3	119	151	34	28	0.81	0.77	132	133	4.37	3.71	0.95	1.4	21	23	7.44	7.44	80.5	110.9	26.6	31.7	244	333	121.5	84.8	1.04	0.97	4.8	11.9	No ORG	NO ORG	T2DM	3	3	9	10	28	28	R
89	1058064	48	F	21	3	3	112	118	110	114	73	75	20	20	600	800	1	2	47.8	47.1	21.7	18.1	523	316	20	86	0.67	0.92	133	144	6.23	3.95	0.39	0.48	27	29	6.87	7.2	39.6	71.4	44.7	56.9	40	89	617	427	7.7	2.35	0.27	9	E.FAECALIS	NO ORG	T2DM	10	11	30	24	66	64	M
90	1059503	70	M	9	13	12	120	118	90	90	63	63	30	28	300	250	2	2	36.9	30.3	31.2	17.7	47	251	134	130	7.28	7	124	129	5.88	4.2	0.68	0.7	13	15	7.29	7.46	35.9	125	20.5	11.4	171	250	88.2	217	1.75	2.74	100	100	E.COLI	E.COLI	T2DM/HTN/COPD	12	11	32	25	82	61	M
91	1060131	80	M	10	11	11	114	116	130	130	83	83	25	25	1100	1200	0	0	34.8	30.4	11.3	10	508	439	36	52	1.8	1.4	129	128	4.31	4.34	0.48	0.5	11	22	7.45	7.4	80	90	30	28	381	429	32.2	24.7	32	31.7	0.35	0.19	No ORG	NO ORG	T2DM/HTN	4	3	17	15	45	39	R
92	1056756	58	M	2	5	3	118	120	90	80	63	60	34	15	600	500	2	2	44	44.1	16.1	17.4	261	150	37	54	1.04	1.98	135	135	4.04	5.97	0.67	0.74	22	18	7.23	7.16	50.4	44.4	42.3	40	50	94	609.7	569	5.4	5.7	0.56	1.3	No ORG	NO ORG	HTN/IHD	11	13	26	30	69	79	M
93	1056730	83	M	2	12	13	130	120	120	110	93	73	36	30	900	1100	0	2	26	28	6.7	7.8	114	90	115	180	3.5	3.74	141	140	6.29	6.1	0.43	0.45	13	12	7.16	7.15	31.2	46.8	43.4	36.8	31	47	627.5	620	7.34	10.4	5.67	6.4	S.HEMOLYTICUS	NO ORG	HTN/T2DM/IHD	10	13	31	27	67	63	M
94	1054327	41	F	18	12	13	110	120	130	140	103	103	34	32	1100	1200	0	0	36	38	7.1	13.4	156	297	18	24	0.62	0.7	137	134	4	3.84	0.3	0.6	23	25	7.33	7.41	94	69	46.9	39.8	188	99	203.9	380.3	5.37	7.37	16.27	12.04	NO ORG	NO ORG	NO	5	5	8	8	33	35	M
95	1058258	40	F	12	15	15	114	120	120	130	83	93	34	36	900	1000	0	0	27.4	30	12.8	24.7	181	224	43	53	0.58	0.61	132	144	4.7	4.5	0.57	0.64	19	23	7.34	7.29	69.9	59.7	40.8	41.4	100	85	378.2	387.6			0.13	2.31	No ORG	NO ORG	NO	4	4	10	12	44	46	M
96	1056538	75	M	21	15	15	114	120	110	120	73	83	30	34	1100	1200	0	0	33.4	34	17.8	17.5	291	312	51	48	0.85	0.63	137	134	4.07	4.3	0.5	0.64	20	23	7.46	7.45	54.4	60.4	40.7	50.4	78	86	393.8	375.7			0.22	0.27	No ORG	NO ORG	T2DM	4	4	13	13	43	47	M
97	1057704	60	F	19	15	15	120	124	130	120	93	85	36	34	900	1000	0	0	38	37	29	13.3	288	217	124	86	1.8	1.03	145	145	3.5	5	0.26	0.34	16	18	7.38	7.43	69	50.3	33.6	36.1	126	91	281	296.9			0.79	41.62	No ORG	NO ORG	T2DM	3	2	13	13	25	22	M
98	1059858	66	M	4	9	10	114	120	130	120	93	90	34	30	1100	1100	2	0	28	36	7.8	7.1	90	156	180	18	3.74	0.62	140	137	6.1	4	0.45	0.3	12	23	7.15	7.33	46.8	94	36.8	46.9	47	188	620	203.9	10.4	5.37	6.4	16.27	NO ORG	NO ORG	NO	13	5	27	8	63	33	M
99	1042738	75	F	5	5	5	90	84	90	130	70	97	24	20	1140	1250	1	1	32.7	35.3	5.4	5.5	90	82	30	23	0.81	0.65	145	143	2.58	2.79	0.49	0.42	20	19	7.47	7.466	137.8	91	25.7	26	274	228	186.6	161.7			18.73	12.73	No ORG	NO ORG	T2DM	10	10	30	30	73	66	M
100	1042521	58	M	6	15	15	118	90	200	130	230	97	35	25	600	600	0	0	24.6	22	19.1	18.2	295	260	154	130	11.21	11.1	143	149	4.55	4.42	0.81	0.74	17	17	7.19	7.405	74.7	278	18.3	27.3	149	556	258	44.4			17.06	40.72	No ORG	NO ORG	CKD/ HTN	7	4	35	15	41	37	R