OUTCOMES IN ELDERLY PATIENTS ADMITTED WITH SEPSIS IN A TERTIARY CARE HOSPITAL: A FOLLOW UP OBSERVATIONAL STUDY



A dissertation submitted in partial fulfilment of the rules and regulations for MD Geriatrics examination of The Tamil Nadu Dr.M.G.R. Medical University, Chennai to be held in May 2020

Registration number 201726053

DECLARATION

This is to declare that this dissertation titled "Outcomes in elderly patients admitted with sepsis in a tertiary care hospital: A follow-up observational study" is my original work done in partial fulfillment of rules and regulations for MD Geriatrics examination of The Tamil Nadu Dr. M.G.R. Medical University, Chennai to be held in May 2020.

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CERTIFICATE I

This is to certify that this dissertation entitled "Outcomes in elderly adults patients admitted with sepsis in a tertiary care hospital: A follow-up observational study" is a bonafide work of Dr. Stephen Varghese Samuel done towards the partial fulfillment of rules and regulations for MD Geriatrics degree examination of The Tamil Nadu Dr. M.G.R. Medical University, Chennai to be conducted in May 2020.

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CERTIFICATE II

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LIST OF ABBREVIATIONS AND ACRONYMS

CMC	Christian Medical College
ESR	Erythrocyte Sedimentation Rate
CRP	C Reactive Protein
SIRS	Systemic Inflammatory Response Syndrome
q-SOFA	Quick Sequential Organ Failure Assessment
SOFA	Sequential Organ Failure Assessment
AKI	Acute Kidney Injury
COPD	Chronic Obstructive Pulmonary Disease
СТ	Computed Tomogram
CVA	Cerebrovascular Accident
DM	Diabetes Mellitus
CAD	Coronary Artery Disease
BP	Blood Pressure
IHD	Ischemic Heart Disease
ADLs	Activities Of Daily Living
SES	Socioeconomic Status
CKD	Chronic Kidney Disease
CTD	Connective Tissue Disorder
APACHE	Acute Physiology, Age, Chronic Health Evaluation
MAP	Mean Arterial Pressure
INR	International Normalized Ratio
APTT	Activated Prothrombin Time
WBC	White Blood Cells
RBC	Red Blood Cells
AIDS	Acquired Immune Deficiency Syndrome
UTI	Urinary Tract Infection
GI	Gastrointestinal
IQR	Interquartile Range
DAMA	Discharged Against Medical Advice

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ABSTRACT

Purpose: Factors predicting the outcome of sepsis in older patients remains unclear, especially in Indian context. We assessed the outcomes in older adults patients admitted with sepsis in a tertiary care hospital in South India.

Methods: Prospective observational study. Various factors contributing to outcomes in patients admitted with sepsis were documented.

Results: Among 201 hospital admissions with sepsis between March 2018 and September 2019, the overall mortality rate was 36.32% with mean duration of hospital stay of 12.9 days. A higher mortality was noted in patients with a longer duration of ventilation (OR 0.6 CI 0.53-0.87, p value 0.003), longer length of ICU stay (OR 1.1 CI 1.05-1.36, p value 0.006) and in patients on vasoactive supports (OR 26.4, 95% CI 6.13-114.4, p-value <0.001). Higher SOFA and APACHE II scores were not found to be associated with mortality. The Barthel Index worsened after sepsis (<0.001). The most widely used empirically antimicrobial group was the Penicillin group, followed by Carbapenems.

Conclusions: The mortality rate of older patients admitted with sepsis was 36.32%. As SOFA and APACHE II scores did not correlate with increase in mortality, the search for a more robust sepsis severity scoring system in the older person is the need of the hour.

Aim

To determine the outcomes of sepsis in older adults admitted to a tertiary care centre in India.

Objective

- To determine the outcomes of sepsis in older adults admitted to a tertiary care centre in India
- To determine the risk factors in elderly contributing to mortality in patient admitted with sepsis.
- Effect on activities of daily living following sepsis.
- To sensitize doctors about antibiotic stewardship in the elderly.

REVIEW OF LITERATURE

INTRODUCTION

The phenomenon of sepsis was known to man for many centuries. Hippocrates claimed that sepsis ($\sigma\eta'\psi\iota\varsigma$) was the process by which flesh rots, swamps generate foul air, and wounds fester. However, Galen claimed sepsis as a laudable event, necessary for wound healing. Semmelweis noticed an association between puerperal fever and disinfected hands of healthcare professionals. Louis Pasteur isolated pyogenic vibrio as the pathogen responsible for puerperal fever and suggested the use of boric acid to kill these microbes. In 1884 Robert Koch and Friedrick Loeffler postulated germ cell theory –

1. The microorganism must be found in abundance in all organisms suffering from the disease, but should not be found in healthy organisms.

2. The microorganism must be isolated from a diseased organism and grown in pure culture.

3. The cultured microorganism should cause disease when introduced into a healthy organism.

4. The microorganism must be re-isolated from the inoculated, diseased experimental host and identified as being identical to the original specific causative agent.

Even in Koch's time, it was understood that some infectious agents did not fulfil his postulate e.g. viruses. (1). Sepsis was a systemic infection assumed to be due to the invasion of organisms into the blood stream: hence sepsis is often described as "blood poisoning". With the discovery of antibiotics, the germ theory was compromised, as it

did not explain the pathogenesis of sepsis and many succumbed, despite eradication of the inciting pathogen from the blood. After many years of research, it is now clear that the pathogenesis of sepsis is host driven, rather than pathogen driven. Therefore, it has been postulated that sepsis is the response of the host to the pathogen and this causes organ failure. (2) The quality of life after an episode of severe sepsis is an important measurable outcome in older adult patients. Poor quality of life results in poor patient satisfaction and increases health resource utilization.(3) In a landmark study, Quartin et al followed up one thousand five hundred and five patients with sepsis. Among the thirty day survivors, the mean life span was reduced to 4.08 years from a predicted 8.03 years. This showed that sepsis not only resulted in early mortality, but also increased the risk of death up to five years after a sepsis related admission to hospital. (4).

DEFINITION AND ITS LIMITATIONS

Sepsis and septic shock compromise the host's ability to tackle the pathogen resulting in varying degrees of organ failure, which is often described as "multiorgan dysfunction" which may lead to disability or death. The definition of sepsis has undergone numerous changes since early 1990s (5). The International Consensus Panel in 1992 defined sepsis as a "Systemic Inflammatory Response Syndrome" (SIRS), which develops as a response to any infectious cause. The panel proposed the term "severe sepsis" to denote instances in which sepsis is associated with organ failure. "Septic shock" is defined as sepsis complicated by either hypotension that is refractory to fluid administration or the presence of an increase in lactic acid in the blood.(6) A second consensus panel in 2003 described the signs of Systemic Inflammatory Response Syndrome – tachycardia or bradycardia, elevated or reduced total leucocyte count, fever or hypothermia. However,

these findings could be also seen in many infectious and non-infectious diseases, which make them less specific to define sepsis. Acute organ failure was denoted by the terms "severe sepsis" and "sepsis" and these terms were used interchangeably (7). The Systemic Inflammatory Response Syndrome (SIRS) is no longer included in the definition, since it is not always a result of infection.

The Society of Critical Care Medicine and the European Society of Intensive Care Medicine arranged a task force, which included nineteen participants, to revise the definition of sepsis and septic shock.

Based on a consensus, septic shock is defined as "a subset of sepsis in which underlying circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than sepsis alone". Adult patients with septic shock can be identified using the clinical criteria of hypotension requiring vasopressor therapy to maintain mean blood pressure 65 mm Hg or greater and having a serum lactate level greater than 2 mmol/L after adequate fluid resuscitation(8).

The diagnosis of sepsis is fundamentally made at the bedside using clinical suspicion of any underlying infection along with symptoms and signs of organ failure. Furthermore, laboratory, radiological, physiologic and microbiologic data aid in diagnosis of sepsis. It is possible to have sterile cultures and still have sepsis, which is especially true, when partially treated with antibiotics before cultures were obtained.

EPIDEMIOLOGY

It was estimated that 164,000 cases of sepsis occurred in the United States (US) each year from the late 1970s. Discharge data on approximately 750 million hospitalizations in the United States over the 22-year period was reviewed- which identified a total of

10,319,418 cases of sepsis. It was found that sepsis was more common among males than among females with mean annual relative risk of 1.28 [95 percent confidence interval, 1.24 to 1.32] and among non-white persons than among white persons with mean annual relative risk of 1.90 [95 percent confidence interval, 1.81 to 2.00]. Between 1979 and 2000, there was an annual rise in the incidence of sepsis by 8.7 percent, from about 164,000 cases (82.7 per 100,000 population) to nearly 660,000 cases (240.4 per 100,000 population). The rate of sepsis due to fungal organisms increased by 207% and gram-positive bacteria were the predominant pathogens since 1987. The total in-hospital mortality rate fell from 27.8 percent from 1979 through 1984 to 17.9 percent from 1995 through 2000, yet the total number of deaths continued to be high. Mortality was highest among black men. Organ failure contributed cumulatively to mortality, with temporal improvements in survival among patients with fewer than three failing organs (9).

One national database analysis of discharge records from hospitals in the US estimated an annual rate of more than 1,665,000 cases of sepsis between 1979 and 2000 (10).

In another retrospective population-based analysis from 1998 to 2009, populationadjusted rates of septic shock increased from 12.6 cases per 100,000 U.S. adults to 78 cases per 100,000. During this time, age-adjusted hospital mortality associated with septic shock declined from 40.4% to 31.4%. Hospital mortality associated with early central venous catheter insertion significantly decreased from a multivariable-adjusted odds ratio of 1.29 (95% confidence interval 1.14-1.45) prior to 2001 to an adjusted odds ratio of 0.87 (95% confidence interval 0.84-0.90) after 2001 (11).

A retrospective analysis done between 1995 and 2015 from an international database reports a global incidence of 437 per 100,000 person-years for sepsis. This data was

taken from twenty seven studies from seven high-income countries. For these countries, the population incidence rate was 288 (95% confidence interval [CI], 215-386; $\tau = 0.55$) for hospital-treated sepsis cases and 148 (95% CI, 98-226; $\tau = 0.99$) for hospital-treated severe sepsis cases per 100,000 person-years. Hospital mortality was 17% for sepsis and 26% for severe sepsis during this period. However, the limitation in this study was that there were no population-level sepsis incidence estimates from lower-income countries, which limit the prediction of global cases and deaths. When extrapolating data from the available sources of high income countries, estimates of 31.5 million sepsis and 19.4 million severe sepsis cases, with potentially 5.3 million deaths annually were found (12). Increase in incidence of sepsis is attributed to the advancing age of population due to improvement in healthcare practices, immunosuppressive therapy and multidrug resistant infections (13).

The incidence of sepsis varies between the different racial and ethnic groups, but appears to be highest among African-American males (9).

During winter, the incidence of sepsis is higher, probably due to the increased prevalence of respiratory infections.

In a study done using National Hospital Discharge Survey to identify patients with sepsis, severe sepsis, influenza, and viral pneumonia, it was found that the incidence of sepsis increased 16.5% in autumn compared to winter (p value < 0.05). Case-fatality rates due to sepsis were 13% greater during winter compared to summer months (p – value <0.05) (14).

RISK FACTORS

Underlying causes and risk factors in sepsis helps to identify and treat sepsis, as it is considered the fifth leading cause of years of productive life lost due to premature mortality (15).

ADMISSION TO INTENSIVE CARE UNITS AND HIGH DEPENDENCY UNITS:

With the emergence of nosocomial infections, particularly in the intensive care wards, it is roughly estimated that of all infections found in intensive care units, approximately 50% are nosocomial in nature. Patients admitted in intensive care units are at a high risk for nosocomial infection with drug resistant organisms (16).

OLDER ADULTS POPULATION

According to the World Health Organization (WHO) definition, older adults people can be divided into 3 groups – (i) young = less than 65 years of age, (ii) young older adults = 65-85 years of age, (iii) old older adults = above 85 years of age. Amongst this, the old older adults are at the highest risk of accruing infection due to frailty and comorbidities (17).

Over the last decade, the incidence of sepsis among the older adults (>65 years of age) has disproportionately increased. Advancing age has become an independent predictor of mortality due to sepsis. The cause of increased incidence of sepsis among older adults is partly due to advancing healthcare provision extending the life expectancy and

due to aging of immune system. Older patients who succumb to sepsis were found to die early. The older adults who survived were found to have a disability requiring skilled nursing and rehabilitation (18).

In a multicenter prospective cohort study done in Spain among older adults patients above the age of 80 years admitted with blood stream infections, common foci of sepsis was found to be the respiratory tract followed by genitourinary infections. The most common isolate was E.coli (19)(20)(21).

Source	n=120 (%)
Unknown	29 (24)
Urinary tract	31 (26)
Intra-abdominal infection	5 (4)
Biliary	17 (14)
Vascular catheter	14 (12)
Respiratory source	13 (11)
Skin and soft tissue infection	8 (7)
Other source	3 (2)

Table 1. Source of infection in older adults patients

Etiology	n=120 (%)
Escherichia coli	43 (36)
Staphylococcus aureus	11 (9)
Klebsiella pneumoniae	9 (7)
Enterococcus spp	6 (5)
Coagulase-negative staphylococci	25 (21)
Enterobacter spp	2 (2)
Pseudomonas aeruginosa	5 (4)
Streptococcus pneumoniae	2 (2)

[ab]	le 2.	Bacteria	identified	among	olde	er ad	lults
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Older adults patients are also at high risk for infections caused by multidrug-resistant organisms due to increased hospitalizations and an increased early use of broad-spectrum antibiotics, which may select more virulent and resistant strains (20)(21). Though treatment is more or less the same, older adults patients who survive sepsis lead poor quality lives compared to younger patients with similar history(22).

Immunosuppression

Illnesses that depress the defense mechanism of the host to an invading pathogen can increase the risk of infection resulting in sepsis and septic shock. Patients with neoplasms, renal failure, hepatic failure, acquired immunodeficiency syndromes including HIV infection, immunosuppressive therapy, steroids use and asplenism are at a higher risk of developing severe sepsis and death.

DIABETES MELLITUS

Altered immune function is found in patients with diabetes mellitus and is associated with an increased risk of recurrent, nosocomial, and secondary infections leading to sepsis.

OBESITY

Community acquired pneumonia, biliary disease, cutaneous infections and aspiration pneumonia during hospitalization occur at a higher rate in patients with obesity. In the setting of an intensive care unit, obese individuals are at higher risk of ventilatorassociated pneumonia, central venous catheter–related infections, and increased mortality compared to patients who have a normal weight(23).

MALIGNANCY

Malignancy is known to increase the risk of sepsis and septic shock due to various mechanisms. Infection frequently leads to or prolongs hospitalization, and can also lead to acute organ dysfunction (severe sepsis) and eventually death. In a study conducted in cancer hospitals across United States, it was found the in-hospital mortality for cancer patients with severe sepsis was 37.8% and overall, severe sepsis was associated with 8.5% (46,729) of all cancer deaths (24).





The above graph shows that cancer is an independent risk factor for developing severe sepsis at all ages (24).

HISTORY OF PREVIOUS HOSPITALIZATION

An increased risk of sepsis is seen in patients who had been previously hospitalized. This is due to the induction of an altered human microbiome, particularly following the exposure to multiple antibiotics. Ninety days after hospitalization, incidence rate of severe sepsis was 3.3-fold higher. It was also found that the incidence rate was 30% higher after an infection-related hospitalization than in a non-infection-related hospitalization. It was also found that the incidence rate was 70% higher after a hospitalization with infection related to Clostridium difficile compared to infections without Clostridium difficile(25).







(A) Hypothetical timeline for a patient with three exposures and one severe sepsis hospitalization. (B) Hypothetical shifts in microbiome health associated with the patient's clinical history. Microbial diversity is in constant flux, with periods of disruption (dysbiosis) corresponding with hospitalization. (C) Classification of baseline and higher risk periods used to calculate the incidence risk ratios for severe sepsis following each of the three exposures. The baseline risk of sepsis increases over time as patients' age, which is accounted for in the model. CDI = Clostridium difficile infection.(25)

Two study designs were used - the first was a longitudinal design with comparisons done between study subjects in the group and the second was a self-controlled case series design using within-person comparisons of risk factors and comorbidities. (25).

Dysbiosis means disruption to the microbiome – genome of microorganisms in a particular environment which includes body or a part of the body which is associated

with increase in host inflammation and is implicated in the pathogenesis of many chronic illnesses like asthma (26), rheumatoid arthritis(27), obesity(28) and cancer(29).

GENETICS

Genetics has a vital role in studies on sepsis done in both animal model and humans. In some cases, monogenic defects cause specific infection. However, the factors involved in an increased risk of sepsis include genetic polymorphism and defects in antibody production or a lack of T cells, phagocytes, natural killer cells, or complement. In the recent years, genetic studies have shown that impaired recognition of pathogens by innate immunity predisposes to specific infections (30).

OLDER ADULTS AND SEPSIS

In 2017, life expectancy at birth was 78.6 years for the total U.S. population. Life expectancy for men was 76.1 and for women was 81.1 in 2017 according to National Center for Health Statistics 2018. In 2017, life expectancy at age 65 for the total population was 19.5 years, an increase of 0.1 year from 2016. Life expectancy at age 65 for women was 20.6 years and 18.1 years for men. (31)

Older adults patients (> / = 65 years of age) account for 12% of the U.S. population and 64.9% of all cases of sepsis, yielding a relative risk of 13.1 compared with younger patients (95% confidence interval, 12.6-13.6). Older adults patients were more likely to have Gram-negative infections, particularly in association with pneumonia (relative risk, 1.66; 95% confidence interval, 1.63-1.69) and to have co-morbid medical conditions (relative risk, 1.99; 95% confidence interval, 1.92-2.06).

	<65 Yrs of Age (n = 3,654,421)	\geq 65 Yrs of Age (n = 6,767,880)
Cancer	19.2	16.0
Chronic renal failure	13.1	12.1
Congestive heart failure	8.1	23.7
COPD	7.6	13.1
Coronary artery disease	6.3	18.1
Diabetes	17.7	19.1
Hepatic cirrhosis	5.8	2.0
HIV	5.5	0.02
Hypertension	14.0	18.0

Table 3. Comorbidities among sepsis patients stratified by age.

Comorbid conditions among sepsis patients, stratified by age

COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus. Values are percentages. Differences are statistically significant between age groups for each condition at the p < .01 level.

Comorbid conditions among sepsis patients, stratified by age

INDIAN SCENARIO

As per the Report on Medical Certification of Cause of Death 2015 based on Indian

Census report 2011, a total of 1,183,052 medically certified deaths were reported in the

year 2015, of which 31% were men above 65 years of age and 38% were women above

65 years of age.



Figure 3. Distribution of death by age under MCCD – 2015

Figure 4. Percentage distribution of death under MCCD under leading cause.



Percentage distribution of deaths under MCCD by leading cause groups - 2015

The Report on the Medical Certification of Cause of Death 2015 according to Indian census showed deaths due to infectious diseases based on International classification of diseases to be 11%. Diseases of circulatory system remain the most common cause of death in India.



Figure 5. Case-fatality rates increased linearly with age:

Age was an independent predictor of mortality in an adjusted multivariable regression analysis (odds ratio, 2.26; 95% confidence interval, 2.17-2.36). Older adults septic patients died earlier during hospitalization, and older adults survivors were more likely to be discharged to a non-acute health care facility. (18)

IMMUNOSENESCENCE

Older adults are prone to infections due to multiple age related changes which alter defense mechanisms that combat infection. The body is protected from invading pathogens by barriers posed by skin, lungs and the gastrointestinal tract. There is an alteration in these barriers as part of aging, permitting invasion of microbes (32). Due to a decline in cellular and humoral immunity in the older adults, there is a dysfunction in the proliferative capacity of immune cells associated with a decline in specific cytokines and signal transduction.

Immunosenescence affects both innate and adaptive immunity – leading to inverse CD4/CD8 ratio, loss of naïve T-cells, increase in the number of terminally differentiated

T-cells, and a reduction in the function of NK cells. These effects also reduce the older adult response to immunization. (32)

With advancing age, there are more somatic mutations, leading to a decrease in the capacity of cell regeneration, cell repair, and altered functioning of the immune system. The immune dysfunction occurs due to progressive telomere shortening, decreasing the number and capacity for proliferation of immune cells that are normally renewed continuously from hematopoietic stem cells .(32)

The atrophy of thymus due to age, reduces the adaptive cell-mediated immunity – from naïve T-cells to memory T-cells – thereby reducing the production of CD4 and CD8 lymphocytes.(33)

Innate immunity	Decreased function of macrophages (chemotaxis,
	phagocytosis, apopotosis, TLR expression, and cytokine
	production)
	Decreased function of neutrophils (chemotaxis,
	phagocytosis, signal transduction, and apoptosis)
	Decreased function in dendritic cells (antigen presentation,
	chemotaxis, and endocytosis)
	Decreased in phagocytic capacity
	Decreased sensitivity to IFN and growth hormone
	Decreased production of TNF- α and IL-6
	Increased production of IL-10
	Decreased sensitivity to G-CSF
	Decreased expression of TLRs
	Increased number of NK cells
	Decline in NK cell function
	Circulating immature neutrophils

Table 4. A SUMMARY OF IMMUNOSENESCENCE (22)

T-cells	Decreased naïve cells
	Decrease naïve CD4 function
	Decrease naïve CD8 function
	Decreased type 1 cytokine response
	Increased type 2 cytokine response
	Decreased function of mitogen-activated protein kinases
B-cells	Decrease in the number of B-cells
	Reduced antibody affinity
	Decreased response to neoantigens
	Increased level of antibodies
	Hypogammaglobulinemia

TLR, toll-like receptor; *IFN*, interferon; *TNF*, tumor necrosis factor; *IL*, interleukin; *G*-CSF, granulocyte colony-stimulating factor; *NK*, natural killer.

CD4/CD8 ratio is used as a marker of immunosenescence. This ratio increases with age due to CD8 reduction, and 1.6-2.2 is considered the normal range in older adults (34)

Impaired immunity due to aging alongside disease burden is often referred to as immunosenescence. Immunosenescence is seen due to the populating of immune tissues with less functional T cells, and B cells and dendritic cells. The functions of these cells are more of type 2 cytokines (include Interleukin-4, Interleukin -5, Interleukin -6, Interleukin -10, and Interleukin -13) than type 1 cytokines (include interleukin-2, gamma interferon, IL-12 and tumor necrosis factor beta). Older adults with chronic illnesses are more susceptible to common infections(35).

Immunoglobulins: With increasing age, there is an increase in IgG and IgA. The IgG age-related increase was significant only in men, but IgG1 levels showed an age-related

increase both in men and women, whereas IgG3 showed an age-related increase only in men. IgE levels remain unchanged, whereas IgD and IgM serum levels decreased with age; the IgM age-related decrease was significant only in women. In the older adults, the B cell repertoire available to respond to new antigenic challenge is decreased. A lot of memory IgD- B cells are filling immunological space and the amount of naïve IgD+ B cells is decreased. This shift away from a population of predominantly naïve B cells reflects the influences of cumulative exposure to foreign pathogens over time. These age-dependent B cell changes indicate that advanced age is a condition characterized by lack of clonotypic immune response to new extracellular pathogens. In any event, the increase of memory B cells and the loss of naïve B cells, as measured by serum IgD levels, could represent hallmarks of immunosenescence. Impaired immunoglobulin production and specificity of antibody responses are associated with reductions in naïve B cells (40).

Immune function is also compromised by the increasing number of concomitant medical problems that occur with aging. Impaired immunity correlates more with an individual's disease burden than chronologic age. Older adults who have chronic diseases (e.g., diabetes, chronic obstructive pulmonary disease, or heart failure) are more susceptible to common infections and exhibit poorer vaccine responses than those who do not have underlying health issues (35).

The risk of infection is further exacerbated by communal residence or other social institutions for older persons in developed nations, such as daycare programs or senior centers. Institutionalization is a major risk factor, not only for acquiring disease in general, but for acquiring disease due to antibiotic-resistant organisms. Methicillin-

resistant *Staphylococcus aureus* (MRSA), Vancomycin-resistant enterococci (VRE), fluoroquinolone-resistant *Streptococcus pneumoniae*, and multiple-resistant Gramnegative bacilli are more frequent causes of infection among institutionalized older patients than those who are community-dwelling(41)(42)(43). Individuals with indwelling devices, who also had functional disability or wounds, were at greatest risk of MRSA/VRE co-colonization.(44). Antibiotic resistance is fostered in the nursing home setting by debilitated hosts, close proximity of residents, and persistent antibiotic selection pressure. *Antibiotic selection pressure* means an influence exerted by an antibiotic to promote one group of microorganism over another. In the case of antibiotic resistance, antibiotics cause a selective pressure by killing susceptible bacteria and allowing antibiotic resistant bacteria to grow.

A Canadian study showed that a total of 9,373 courses of antibiotics were prescribed for 2,408 patients (66% of all patients in study facilities) over a 12 month period. The incidence of antibiotic prescriptions in the facilities ranged from 2.9 to 13.9 antibiotic courses per 1,000 patient-days. Thirty-six percent of antibiotics were prescribed for respiratory tract infections, 33% for urinary infections, and 13% for skin and soft tissue infections. One third of antibiotic prescriptions for a urinary indication were for asymptomatic bacteriuria. It was also found that 8 to 17 percent of nursing home residents were taking antibiotics at any given time, that 50 to 70 percent were exposed to antibiotics over the course of one year, and that 22 to 89 percent of this antibiotic use was inappropriate (45). Furthermore, in a two-year study of 110,000 nursing home residents in Canada, antibiotic usage was highly variable across nursing homes. The residents of high-use homes are exposed to an increased risk of antibiotic-related harm,

even if they have not directly received these agents. Antibiotic stewardship is needed to improve the safety of all nursing home residents. In this study, the authors predicted that one additional antibiotic-related harm would be generated for every 53 patients admitted to a high rather than low antibiotic-utilizing nursing home (46). Major strategies to enhance antimicrobial stewardship in long-term care include: avoiding treatment of asymptomatic bacteriuria, specifically addressing antibiotics as an intervention that can be avoided in end-of-life discussions and focusing on the shortest, effective duration of therapy for specific syndromes(47).

In aged patients, there are many factors that predispose them to sepsis and place them in the high-risk category. Comorbidities, frailty, malnutrition, and pre-admission status contribute towards the risk factors in this age group. Pre-admission status includes – disuse atrophy resulting from an inactive lifestyle; sarcopenia due to accelerated muscle loss; changes to responsiveness to growth hormones, androgens, and estrogens; neurological alterations; altered cytokine regulation; changes in protein metabolism; and changes in dietary intake (17)(48). Teething issues, mood disorders, and reduced olfactory discrimination caused due to age also leads to reduced appetite – thus, resulting in dietary changes and malnutrition. As pharmacokinetics of drugs alter with age, the potential risk of drug-drug interaction also increases – thus contributing to sepsis (17).

PATHOGENESIS OF SEPSIS

HOST CELL RESPONSE TO PATHOGEN

When host cells encounter pathogen, it initiates activation of innate immunity which consists of macrophages that recognize microbial particles and bind to them causing a cascade of host responses via pattern recognition receptors (PRRs) which lie on the surface of host immune cells. These pattern recognition receptors recognize and bind to the pathogen-associated molecular patterns (PAMPs) that are present in microorganisms (51).

MICROVASCULAR ALTERATIONS IN SEPSIS

In sepsis, blood cells and vascular endothelial cells undergo deleterious effects causing intravascular inflammation. Microvascular alterations frequently occur in sepsis and are due to endothelial dysfunction and interaction of endothelium and circulating cells. Although activation of coagulation system has been extensively shown to occur in sepsis, microthrombosis does not seem to be a major factor. The interplay between coagulation, inflammation and the endothelium seems to cause microvascular dysfunction.

NEUTROPHIL EXTRACELLULAR TRAPS

The trapping function of neutrophil extracellular traps (NETs) conceals the foci of infection and prevent bacterial dissemination. Once containment is lost, bacteria disseminates causing the disease to progress. (55)
SIGNALING CASCADE AND INFLAMMATION

The engagement of Toll like receptors elicits a signaling cascade by activating cytosolic nuclear factorkb (NF-kb). Activated NF-kb moves from the cytoplasm to the nucleus, binds to transcription sites, and induces activation of a large set of genes involved in the host inflammatory response, such as proinflammatory cytokines (tumor necrosis factor alpha, interleukin-1), chemokines (intercellular adhesion molecule-1 [ICAM-1], vascular cell adhesion molecule-1 [VCAM-1]), and nitric oxide. Neutrophils become activated and express adhesion molecules that cause their aggregation and adherence to the margins of the vascular endothelium. Endothelium expresses adherence molecules to attract white blood cells. These neutrophils then go through a series of steps: Rolling, Adhesion, Diapedesis and Chemotaxis. These neutrophils hence migrate to the site of injury (56). The release of mediators by neutrophils at the site of infection causes cardinal signs of local inflammation: rubor (erythema due to local vasodilation and hyperemia), *calor* (warmth), *dolor* (pain), tumor (protein-rich edema due to increased microvascular permeability) and functio laesa (loss of function of the body part affected with inflammation). This process is highly regulated by a mixture of proinflammatory and anti-inflammatory mediators secreted by macrophages in response to microbial invasion (57)(58)(59). The balance of proinflammatory and anti-inflammatory mediators regulates the inflammatory processes, including adherence, chemotaxis, and phagocytosis of invading bacteria, bacterial killing, and phagocytosis of debris from injured tissue (60).

Cytokines are commonly classified in one or the other category.

Table 5. Classification of cytokines

Pro-inflammatory cytokines: (60)) Anti-inflammatory cytokines: (60))
nterleukin-1 (IL-1)	nterleukin-4 (IL4)	
Fumor necrosis factor (TNF)	nterleukin-10 (IL-10)	
Gamma-interferon (IFN-gamma)	nterleukin-13 (IL-13)	
nterleukin-12 (IL-12)	nterferon alpha (IFNa)	
nterleukin-18 (IL-18)	Fransforming Growth Fa	ctor-beta
Granulocyte-macrophage	colony TGFbeta)	
stimulating factor (GM-CSF)		

If the inflammatory mediators balance each other and the initial infectious insult is overcome, homeostasis will be restored. The end result will be tissue repair and healing. (61)

The release of Tumor Necrosis Factor alpha (TNFa) does not need an external stimuli for its production (autocrine secretion), while non-TNF cytokines and mediators (paracrine secretion) increase the levels of other mediators like II-1, IL-2, IL6, IL-8, IL-10, platelet activating factor, interferon, and eicosanoids. The proinflammatory milieu recruits more neutrophils and macrophages. (62)

Cytokines that block the production of Tumor Necrosis Factor alpha and Interleukin-1 are anti-inflammatory cytokines and they suppress the immune system by inhibiting cytokine production by mononuclear cells and monocyte-dependent T helper cells. However, Interleukin-10 and Interleukin-6 increase B cell function (proliferation, immunoglobulin secretion) and encourage the development of cytotoxic T cells (62).

SEPSIS

A 2016 Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM) task force has defined sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection (63)

Sepsis occurs when the release of proinflammatory mediators in response to an infection exceeds the boundaries of the local environment, leading to a more generalized response where anti-inflammatory response leads to recovery from sepsis and pro inflammatory response leads to multiorgan dysfunction. Sepsis can be conceptualized as malignant intravascular inflammation. (62)

COMPLEMENT ACTIVATION

Complements are proteins associated with clearance of pathogens from an organism or host tissue. (68)(69)

Complement activation pathways are of three types: Classical pathway, Mannose-Binding Lectin pathway and the Alternative Pathway. These pathways cleave C3 – common complement of all pathways. The residual molecules of the classical pathway – C1 complex C1q, C1r and C1s binds to antibodies on the surface of a bacterial cell initiating bacterial cell death.

The mannose-binding lectin pathway is commenced when complex of mannose-binding lectin binds to the serine proteases mannose-binding lectin–associated proteases 1 and 2 (MASP1 and MASP2, respectively) to microbial surface and cause microbial

destruction. The alternative pathway is commenced when C3b covalently binds to hydroxyl groups on cell-surface and is activated by low-grade breakdown of C3 in plasma to form C3b complex which binds to C5 to form anaphylatoxin C5a and C5b, which starts microbial destruction by forming membrane-attack complex. (69)(68). There is evidence that inhibition of the complement cascade decreases inflammation and reduces mortality in animal studies. (70)(71).

ROLE OF MICROORGANISMS IN SEPSIS

Bacteria contains certain chemicals: some are found in the cell wall, others in the cytoplasm and organelle of the microbe.

Cell wall also contains: Endotoxin, Peptidoglycan, Muramyl-dipeptide, lipoteichoic acid, Bacterial products, staphylococcal enterotoxin B, toxic shock syndrome toxin-1 (TSST1), Pseudomonas exotoxin A and M protein of beta hemolytic group A streptococci. They contribute to the progression of a local infection to sepsis (79).

ENDOTOXINS IN SEPTIC SHOCK

Endotoxin is a lipopolysaccharide found in the cell wall of gram negative bacteria and is detectable in plasma of septic patients. Elevated serum levels of endotoxins are associated with septic shock and multi-organ dysfunction (MODS).

THE HOST RESPONSE

The host response to sepsis is characterized by both proinflammatory responses and antiinflammatory immunosuppressive responses. The direction, extent, and duration of these reactions are determined by both host factors (e.g., genetic characteristics, age, coexisting illnesses, and medications) and pathogen factors (e.g., microbial load and virulence). Inflammatory responses are initiated by interaction between pathogenassociated molecular patterns expressed by pathogens and pattern recognition receptors expressed by host cells at the cell surface (toll-like receptors [TLRs] and C-type lectin receptors [CLRs]), in the endosome (TLRs), or in the cytoplasm (retinoic acid inducible gene 1-like receptors [RLRs] and nucleotide-binding oligomerization domain-like receptors [NLRs]). The consequence of exaggerated inflammation is collateral tissue damage and necrotic cell death, which results in the release of damage-associated molecular patterns, so-called danger molecules that perpetuate inflammation at least in part by acting on the same pattern-recognition receptors that are triggered by pathogens (84) The molecular link between coagulation and inflammation is created by proteaseactivated receptors (PARs). Protease activated receptor 1is particularly associated with sepsis. Protease activated receptor 1 has cytoprotective effects when stimulated by activated protein C or low-dose thrombin, and disruptive effects on endothelial-cell barrier function when activated by high-dose thrombin (Ruf W. New players in the sepsis-protective activated protein C pathway. J Clin Invest 2010;120:3084-7).

Organ Failure in Severe Sepsis and Dysfunction of the Vascular Endothelium and Mitochondria.

Sepsis is associated with microvascular thrombosis caused by concurrent activation of coagulation (mediated by tissue factor) and impairment of anticoagulant mechanisms as a consequence of reduced activity of endogenous anticoagulant pathways (mediated by activated protein C, antithrombin, and tissue factor pathway inhibitor), plus impaired fibrinolysis owing to enhanced release of plasminogen activator inhibitor type 1 (PAI-1). The capacity to generate activated protein C is impaired at least in part by reduced expression of two endothelial receptors: thrombomodulin (TM) and the endothelial protein C receptor. Thrombus formation is further facilitated by neutrophil extracellular traps (NETs) released from dying neutrophils. Thrombus formation results in tissue hypoperfusion, which is aggravated by vasodilatation, hypotension, and reduced red-cell deformability. Tissue oxygenation is further impaired by the loss of barrier function of the endothelium owing to a loss of function of vascular endothelial (VE) cadherin, alterations in endothelial cell-to-cell tight junctions, high levels of angiopoietin 2, and a disturbed balance between sphingosine-1 phosphate receptor 1 (S1P1) and S1P3 within the vascular wall, which is at least in part due to preferential induction of S1P3 through protease activated receptor 1 (PAR1) as a result of a reduced ratio of activated protein C to thrombin. Oxygen use is impaired at the subcellular level because of damage to mitochondria from oxidative stress (84).

Impaired tissue oxygenation plays a vital role in causing organ dysfunction that is seen in sepsis. Diminished oxygen delivery in septic shock results from hypotension, reduced red-cell deformability, and micro-vascular thrombosis. Inflammation results in dysfunction of vascular endothelium – leading to cell death and loss of barrier integrity resulting in subcutaneous and body-cavity edema (90). Oxidative stress damages mitochondria – that in turn release alarmins.

Alarmins, also known as damage-associated molecular patterns (DAMPs), are normal cell constituents. They are released or secreted from damaged or dead/dying cells and exposed on the cell surface. After binding to plasma membrane or intracellular recognition receptors, alarmins act as danger signals - promoting and exacerbating the inflammatory response. Alarmins differ from exogenous danger signals, also referred to as pathogen-associated molecular patterns (PAMPs), as they stimulate inflammation in the absence of external pathogens. Pathogen-associated molecular patterns alert the immune system of the presence of microbial molecules and external threats.

SEPSIS IN OLDER ADULTS – AN EMERGING CONCERN

Older adults can have severe infection in the absence of typical signs or symptoms This was first documented by Dr.William Osler in 1901 (93). The classical manifestations of SIRS may not be present in the older adults, making sepsis an easily overlooked condition. About 30 to 50 percentage of cases do not exhibit a febrile response, thus the presence of non-specific signs like weakness, malaise, delirium, confusion, loss of appetite, falls, and urinary incontinence should not be ignored (94)

Bacteria are the most likely pathogens implicated, and the most common sites are the respiratory system, urinary tract and soft tissues. Joint infections, infective endocarditis and meningitis can also be the primary source of infection (95). Concomitant pneumonia and influenza constitute the leading infectious cause of death in the older adults. The

presence of concomitant illness and delays in diagnosis contribute significantly to mortality from sepsis in the older adults. Senescence of the immune system seems less important in predisposing to pneumonia than the presence of concomitant illness. Delay in diagnosis is frequently secondary to the atypical presentations of pneumonia in the older adults. The usual symptoms of fever, chills, rigors, and sputum production that are present in young adults may be absent; confusion may be the only presenting symptom. Tachypnea is frequent, but the physical examination, in addition to often being technically difficult, is not sufficiently sensitive in making a diagnosis. Leukocytosis is common, but by no means specific. Chest X-rays frequently show incomplete consolidation and findings are difficult to distinguish from other diseases of the older adults which mimic sepsis, such as congestive heart failure, atelectasis, pulmonary embolism, and malignancy. Therefore, a diagnosis of sepsis requires a high index of suspicion, despite atypical clinical manifestations(96). The reason for poor febrile response in older adults is attributed to impaired thermoregulation which are shivering, vasoconstriction, hypothalamic regulation, and thermogenesis by brown adipose tissue(97).

Baseline body temperature is often lower than 37°C in older adults (98). Since signs of infection are often atypical in the older adult population and the basal body temperature is lower, a rise in temperature from baseline becomes an important indicator of infection (98).Postmenopausal women have lower basal body temperatures than premenopausal women, and the presence of dementia, dependence for activities of daily living, or a low body mass index ($<20 \text{ kg/m}^2$) also increase the risk for developing lower body temperatures (99).

In addition to the frequent absence of fever, infections in older adults may be associated with a nonspecific decline in baseline functional status such as increased confusion, falling, and anorexia. Due to a lack of infection-specific symptoms, these constitutional symptoms commonly trigger diagnostic testing with subsequent antibiotic prescribing.(100)(101)(102).

In the ICU setting, sequential organ failure assessment (SOFA) score is commonly used for the diagnosis of sepsis. Elevated SOFA score is associated with high mortality rate. A quick SOFA score (q-SOFA) includes increased respiratory rate (\geq 22/min), low systolic blood pressure (\leq 100 mmHg), and confusion (GCS <15). It is useful in patients who are at high risk for poor outcomes (63).

Most common sources of sepsis in older adults are – respiratory tract infections, followed by genitourinary tract infections. (22). Multidrug-resistant organisms also have a higher chance of causing infections in the older adults due to immunosenescence and increased number of hospitalizations, leading to early exposure to broad-spectrum antibiotics (20)

SCORES USED IN SEPSIS:

- SOFA score and q-SOFA score
- Acute Physiologic and Chronic Health Evaluation (APACHE) Score
- Simplified Acute Physiologic Score (SAPS)
- Mortality Prediction Model (MPM0)

• SIRS score

SOFA SCORE - SEQUENTIAL ORGAN FAILURE ASSESMENT

SOFA score is a simple measurement of major organ failure which is calculated in the

first 24 hours. (103).

Table 6. Sequential organ failure assessment score

The Sequential Organ I	Failure Assessment (S	OFA) Score*			
·			SOFA Score		
Variables	0	1	2	3	4
Respiratory Pao ₂ /FiO ₂ , mm Hg	>400	≤400	≤300	≤200†	≤100†
Coagulation Platelets ×10³/µL‡	>150	≤150	≤100	≤50	≤20
Liver Bilirubin, mg/dL‡	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular Hypotension	No hypotension	Mean arterial pressure <70 mm Hg	Dop ≤5 or dob (any dose)§	Dop >5, epi ≤0.1, or norepi ≤0.1§	Dop >15, epi >0.1, or norepi >0.1§
Central nervous system Glasgow Coma Score Scale	15	13-14	10-12	6-9	<6
Renal Creatinine, mg/dL or urine output, mL/d∥	<1.2	1.2-1.9	2.0-3.4	3.5-4.9 or <500	>5.0 or <200

*Norepi indicates norepinephrine; Dob, dobutamine; Dop, dopamine; Epi, epinephrine; and FIO2, fraction of inspired oxygen.

Values are with respiratory support. *To convert bilirubin from mg/dL to µmo/L, multiply by 17.1. \$Adrenergic agents administered for at least 1 hour (doses given are in µg/kg per minute). [To convert creatinine from mg/dL to µmo/L, multiply by 88.4.

The initial and highest score of more than 11 or mean score of more than 5 are predictive

of mortality of at least 80%. (103).

Figure 6. Mortality rates in relation to SOFA score (sequential organ failure assessment score) during the first 48 hours of ICU stay- as the SOFA score increases, mortality increases (103)



The SOFA (sequential organ failure assessment score) severity score is based upon the following measurements of organ function:

• Respiratory system – the ratio of arterial oxygen tension to fraction of inspired oxygen

 (PaO_2/FiO_2)

- Cardiovascular system the amount of vasoactive medication necessary to prevent hypotension
- Hepatic system the bilirubin level
- Coagulation system the platelet concentration
- Neurologic system the Glasgow coma score
- Renal system the serum creatinine or urine output

The SOFA score has been endorsed by the Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM) as a tool to facilitate the identification of patients at risk of dying from sepsis (63)(104)(103).

Sepsis is now defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. As an organ dysfunction score, SOFA can be used to identify those whose organ dysfunction is "life-threatening" such that an increase in the SOFA score ≥ 2 is associated with a mortality of ≥ 10 percent. Patients with a SOFA score ≥ 2 who also have vasopressor requirement and elevated а an lactate >2 mmol/L (>18 mg/dL) despite adequate fluid resuscitation have a predicted mortality of 40 percent.

The validity of this score was derived from millions of ICU electronic health record encounters both inside and outside the United States. Among critically ill patients with suspected sepsis, the predictive validity of the SOFA score for in-hospital mortality was superior to that of systemic inflammatory response criteria (SIRS; area under the receiver operating characteristic curve 0.74 versus 0.64) (63). Sensitivity of SOFA score is 70% and specificity is 59%. (105)

Quick SOFA (q-SOFA) score

The quick SOFA (q-SOFA) score has also been proposed by the SCCM/ESICM as a bedside assessment to identify patients with early sepsis outside of the ICU. Q-SOFA includes respiratory rate \geq 22/min, altered mentation, and systolic blood pressure \leq 100 mmHg. Once q-SOFA is more than 2, a clinician must proceed to calculate SOFA score. Similarly, in patients with septic shock, the area under ROC for predicting mortality was greater for q-SOFA score (area under ROC cutoff = 0.89 with 95% CI; 0.85–0.92, sensitivity= 92% and specificity = 85%) when compared to SOFA score (area

under ROC cutoff = 0.63 with 95% CI; 0.55–0.70, Sensitivity = 70%, Specificity = 59%). (105)

Acute Physiologic and Chronic Health Evaluation (APACHE) Score

The APACHE scoring system has four versions from APACHE I to IV which is being used worldwide (106)(107)(108)(109)(110)(111).

In a Prospective study of two four-bed multidisciplinary ICUs of a teaching hospital, data collected over 4 years on 1,721 consecutively admitted patients aged 18 years and above it was found that at the predicted risk of 0.5, sensitivity was 31.6 % and specificity was 97.2 % for APACHE score. However, APACHE score under predicted observed hospital mortality. (108). APACHE IV is the latest version using 129 variables assessed within 24 hours of ICU admission. (111)

Data were generated from over 110,000 patients from 104 ICUs across the United States. Compared with APACHE II and III, APACHE-IV uses a larger set of variables, a new logistical regression equation, and new statistical modeling.

APACHE systems is accurate in discriminating between survivors and non survivors. However, when compared with their discriminatory capacity, APACHE systems, including APACHE-IV, have deteriorating performance over time due to changes in case-mix and new therapies requiring periodical updating. Major drawback of APACHE system is that is was derived only from ICUs within the United States and therefore may not be accurate for patients in other countries or patients admitted with sepsis in wards. There is not major difference within the APACHE system in predicting mortality and APACHE II remains to be popularly used APACHE system (111)

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Simplified Acute Physiologic Score (SAPS)

This scoring system is meant to be used within the first 24 hours of ICU stay. Twenty variables are assigned a specific value depending upon whether or not they are either present or absent and the others are continuous (eg, age). All scores are entered into a mathematical equation, which calculates hospital mortality. The number of variables used is significantly smaller than the APACHE scores.

The latest version is SAPS 3 was validated using data from 20,000 patients admitted to over 300 ICUs in 35 countries and it has good discrimination, but poor calibration when compared to APACHE scoring system (112)(113)(114).

In a Prospective study of two four-bed multidisciplinary ICUs of a teaching hospital, data collected over 4 years on 1,721 consecutively admitted patients aged 18 years and above it was found that at the predicted risk of 0.5, sensitivity was 39.4 % and specificity 95.6 % for SAPS II. Observed hospital mortality of patients with risk of death higher than 60 % was over-predicted by SAPS II. (108).Data extraction for SAPS instruments are easier compared to APACHE. SAPS 3 cannot predict the length of stay unlike APACHE IV (115).

Mortality Prediction Model (MPM)

Mortality prediction model exist in 3 version - MPM₀-I, MPM₀-II, MPM₀-III. It is based on clinical and physiological parameters rather than laboratory data. Variables are assessed at the time of ICU admission – at Zero time and mathematically derived mortality prediction. The MPM₀-II severity score allows to re-measure parameters serially in consecutive days. Among all the scoring system used to predict mortality in patient with sepsis, lowest data extraction burden is for MPM (Mortality prediction model) as it can be completed bedside. MPM cannot predict length of stay and is less accurate in ICUs outside the United States as all the validation were done in United States. (116)(117)(118)(119)

MANAGEMENT OF SEPSIS IN OLDER ADULTS

The management of severe sepsis and septic shock in older adults is performed as per International surviving sepsis guidelines (120).

Resuscitation

Early goal-directed therapy remains the mainstay of the resuscitation bundle in the management of severe sepsis and septic shock in both young adults and older adults patients (121). Focusing on systolic function rather than relying on heart rate remains the most important factor in improving cardiac output while treating older adults patients admitted with septic shock as the heart rate response to sepsis is blunted in the older adults (122). As the systolic function is directly related to left ventricular preload as per Frank starling's law, maintaining an adequate preload remains the goal on increasing cardiac output while treating older adults patients with septic shock (123). Overzealous intravenous crystalloid administration can also be tricky in patients with aging-associated diastolic dysfunction (124). Blood transfusion must be considered when hemoglobin is less than 7 g/dL to maintain a target hemoglobin of 7-9 g/dL (125). Vasopressors like dopamine or norepinephrine can be used to maintain perfusion in the face of life-threatening hypotension after adequate fluid challenges (120)

Source control and antimicrobial therapy

The dosing of antimicrobials should be based on age-related differences in pharmacokinetic and pharmacodynamics parameters as glomerular filtration rate, tubular function, renal blood flow, lean body mass and hepatic blood flow changes with increasing age. (126)(127). There is also an increased incidence of antimicrobial-related adverse effects in the older adults. (126)(127)(128)

Source control of infection and early appropriate empirical antimicrobial therapy remains the goal for treating sepsis and septic shock in the early phase (129)(130)

The early administration of antibiotics has been found to significantly decrease mortality even in older adults sepsis patients. (126). The empirical antimicrobial regimens should be based on patient-factors such as underlying co-morbidities or immune-compromised states, site and severity of infection; environmental factors such as residence in nursing homes, history of repeated hospitalizations and local factors like the expected microbiological organism and the antimicrobial susceptibility patterns (126). Once culture reports and sensitivity patterns are available, targeted therapy must be aimed. (126)

Corticosteroids in sepsis

Adrenal insufficiency is common in patients with septic shock, especially older adults patients (131). The use of steroids for septic shock remains a controversy because of concerns regarding effectiveness of steroids per se, serious adverse effects of steroids like hyperglycemia, immunosuppression (at high doses), poor wound healing, and critical illness related neuropathy (132)(133). However, low dose intravenous

hydrocortisone can be tried in older adults septic shock patients only in such clinical situations where the blood pressure is poorly responsive to fluid resuscitation and vasopressor therapy as recommended by the surviving sepsis guidelines. (120)

Respiratory failure and mechanical ventilation

The need for mechanical ventilation in the older adults is independently associated with increased mortality (134)(135)(136). In the landmark study by the acute respiratory distress syndrome Network, it was found an absolute risk reduction in mortality of 9% (40% *vs* 31%) with a relative risk reduction of 22% in the low tidal volume (6 mL/kg) group, when compared with the conventional tidal volume (12 mL/kg) group (137). On subgroup analysis of the 173 patients aged more than 70 years, ventilation with low tidal volume resulted in an absolute risk reduction of 9.9% in mortality at 28 days (138). Thus, a tidal volume of 6 mL/kg (predicted) body weight in patients with acute lung injury (ALI)/ARDS is recommended even in older adults patients (139).

Glycemic control

The surviving sepsis guidelines recommend the maintenance of blood glucose level < 150 mg/dL with the continuous intravenous infusion of insulin and glucose in patients with severe sepsis following stabilization in the ICU (120).

Other issues

Low-dose unfractionated heparin, low-molecular-weight heparin, or mechanical prophylactic devices should be used for the prophylaxis of deep vein thrombosis, and H₂-receptor blockers or proton pump inhibitors should be used to prevent stress ulcers (120).

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End of life issues

In older adults patients with dismal prognosis, healthcare professionals should be prepared and be equipped to provide quality end-of-life care besides aggressive care. Decisions regarding withholding or withdrawing life-sustaining supports should not be based on the futility of treatment, but should be individualized and centered around patient and family wishes (140)(141)(142). Physicians should discuss the care plan in advance and must clearly communicate the likely outcomes and realistic goals of treatment to the caregivers, family of the patient or sometimes even the patient (143).

PROGNOSIS AND OUTCOME

Hospital mortality rates are also higher in frail than in non-frail patients.

Data regarding subsequent survival and quality of life after severe sepsis are limited, especially in the older adults who usually have a poorer functional outcome. The overall prognosis depends on previous functional status rather than on severity of illness at the time of ICU admission (144)(145)(146)(147).

The baseline physical function and frailty status could aid in prognostication and informed decision-making for very old critically ill patients (148).

Acute severe illness on admission can also influence in-hospital mortality and mortality after discharge in patients aged 80 or over (149)(150)(151)(152)

Studies show that older adults patients have poorer quality of life compared to younger patients, irrespective of admission - whether in ICU or hospital (151)(152).

SETTING

All patients above sixty years of age with suspected or established sepsis as per sepsis 3 definition, admitted in Medical Intensive Care Unit, Medical High Dependency Unit and medical wards in Christian Medical College and Hospital Vellore, Tamil Nadu, India from March 2018 to September 2019 under the departments of Geriatrics, Medicine (Units III, IV and V), Emergency Medicine and Critical Care, receiving standard-of-care treatment were included in the study. Patients were observed and followed-up till discharge. The observations seen in this group were subjected to analysis and comparison.

PARTICIPANTS

All patients above the age of 60 years admitted with suspected or confirmed infection who fulfilled the sepsis 3 definition - Sequential [sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more, or need for organ supports like inotropic requirement to maintain a mean arterial pressure of 65 mmHg or greater,or serum lactate level greater than 2 mmol/L (18 mg/dL) - from March 2018 to September 2019were recruited in the study. Informed consent was taken on the first day of admission either in the ward or in the intensive care unit.

INCLUSION CRITERIA

Patients aged 60 years and above admitted with sepsis in the medical wards and medical intensive care unit in CMC Vellore between March 2018 and September 2019.
Departments involved were Department of Geriatrics, Department of Medicine (Units III, IV and V), Department of Emergency Medicine and Department of Critical Care.

- Patients or their relatives should consent for the study.

EXCLUSION CRITERIA

- Patients or their caregivers who do not agree to give a written consent.
- Patients admitted in surgical wards and surgical intensive care unit.
- Patients diagnosed to have nosocomial infections.

CASE DEFINITION

Older patients, above the age of sixty years, with suspected or confirmed infection with Sequential Organ Failure Assessment score of 2 points or more, or those who need organ supports to maintain a mean arterial pressure of 65 mmHg or greater and serum lactate greater than 2 mmol/L (>18 mg/dl) as per sepsis 3 definition.

DETAILED DIAGRAMMATIC ALGORITHM OF THE PROSPECTIVE

COHORT STUDY



OUTCOMES:

The measured outcomes include - Proportion of sepsis in the older adults patients admitted to a tertiary care centre in India; Factors contributing to sepsis in the older adults like immunosuppression, admission to the Intensive Care Unit, previous hospitalisation, delay in administration of empirical antibiotics, sensitivity of the identified microbe; and Barthel Index before admission and 1week following discharge.

The end points measured include: In-hospital mortality; Length of stay in hospital; Secondary nosocomial infections; Need for organ support such as vasopressor support, ventilation and dialysis; Activities of daily living - Pre-morbid Barthel index and Barthel index at 1 week following discharge.

Older patients with sepsis were included in the study and followed up till death or discharge from the hospital. We analysed the factors that predict mortality in this cohort.

DATA SOURCES/MEASUREMENT:

Demographic variables and Barthel indices were documented after asking the caregiver and data for the laboratory variables were extracted from Clinical Work Station of Christian Medical College, Vellore. SOFA score and APACHE II score were taken from reliable online links (*Attached*).

Variables looked at were:-

Age: 60-69, 70-79, 80 and above; Duration of ICU stay: <5 days >=5 days; Duration of hospital stay: <15 days, >=15 days; Gender: Male or Female; Socioeconomic status: Lower class (<11) or middle and upper class (>=11) (Modified Kuppuswamy scale for socioeconomic status); Pre-morbid Barthel index and Barthel index at 1week after discharge; Temperature: >100 degree Fahrenheit (fever) and <96.8 degree Fahrenheit

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(hypothermia); Heart rate: >=90beats per minute (tachycardia) and <90beats per minute; Glasgow coma scale; CAM score for altered mental status examination: score <4, >=4; mean arterial pressure; SOFA score; APACHE II score: Sum of A (Acute Physiological Score - APS) + B (Age points) + C (Chronic health points) - A: Normal, High abnormal, Low abnormal, B: 55-64 years = 3 points, 65-74 years = 5 points, >=75 years = 6 points, C: if patient has history of severe organ system insufficiency or is immunocompromised - score (a) and score (b). Score (a): for non-operative patients- 5 points (b): for elective postoperative patients- 2 points (Knaus WA, Draper EA, Wagner DP, Zimmerman JE, APACHE II: a severity of disease classification, Critical Care Medicine1985; 13(10):818-829);WBC Count: >12,000/cumm (leucocytosis), <4000/cumm (leukopenia), between 12000 and 4000 (normal); Erythrocyte Sedimentation Rate >20mm/hr, <=20mm/hr; C-Reactive Protein >6, <=6; Procalcitonin: <0.1ng/dl, 0.1-0.24 ng/dl, 0.25-0.5 ng/dl and >0.5 ng/dl; Platelet count: <1,00,000 and >1,00,000; International Normalized Ratio >1.1; Activated Prothrombin Time >42sec; Charlson Comorbidity Index: Scores 1, 2, 3, 4, 5 and 6; Addictions: smoking tobacco in pack years, Present alcohol intake >3 units in men/day and >2 units in women/day (unit of alcohol = 218ml of 4.5%cider, 76 ml of standard 13% wine, 175 ml of 12% red wine, 25ml of standard 40% whiskey and 250 ml 4% standard beer (UK Chief Medical Officers' low risk drinking guidelines Aug 2016); Days of ventilator use: >=5days, <5days; Days of NIV use: >=5days, <5days; Outcomes: Mortality- Dead or Alive. If alive, Barthel index at 1 week after discharge. Outcome will be compared with age (ranging from 60-69, 70-79, 80-89 and above 90 years) and other variables described above.

BIAS:

Only people admitted in a tertiary centre were enrolled. Some patients may not have made it to Emergency Department (ED) or were discharged directly from the Emergency Department due to various reasons. Sterile cultures may be due to the fact that the patients were already started on antibiotics elsewhere.Outcome can vary between patients admitted in ICU and in the ward, and based on both patients' and caregivers' preferences.

SAMPLE SIZE: Assuming an odds ratio of about 2 times with 90% power and 5% level of significance with 40% as the proportion of mortality (proportion of mortality among older adults patients with sepsis varied between 20% to 60%), sample size was calculated to be 260 to show mortality risk among older patients admitted with sepsis.

$$n_{1} = \left[Z_{\alpha} + \exp\left((-\theta^{*2})/4\right) Z_{\beta} \right]^{2} \left(\mathbf{1} + 2\mathbf{P}\delta \right) / \left(P\theta^{*2} \right)$$
$$\delta = \left[1 + \left(1 + \theta^{*2} \right) \exp\left(5\theta^{*2}/4 \right) \right] \left[1 + \exp\left((-\theta^{*2})/4 \right) \right]^{-1}$$

Where,

θ	:	Loge	Odd	ls	Ratio
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P : Overall Proportion (Proportion of Disease)

- α : Significance level
- $1-\beta$: Power

Table 7. Logistic regression for sample size calculation.

Regression methods - Multiple logistic regression

Proportion of disease	0.4	0.5	0.5	0.4	0.4	0.4	0.4	<mark>0.4</mark>
Anticipated odds ratio	2	2	1.5	1.5	1.5	1.6	2	<mark>1.6</mark>

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Power (1- beta) %	80	80	80	80	80	80	90	<mark>90</mark>
Alpha error (%)	5	5	5	5	5	5	5	<mark>5</mark>
1 or 2 sided	2	2	2	2	2	2	2	<mark>2</mark>
Multiple correlation coefficient of the exposure								
variable with the confounders	0.5	0.5	0.5	0.5	0.4	0.3	0.6	<mark>0.3</mark>
Required sample size	131	120	278	309	276	196	200	<mark>260</mark>

CONFOUNDERS:

The potential confounders and effect modifiers were - patients who were admitted to ICU for monitoring where care would be different than that in the ward (given 1:2 nursing care and 24-hour medical cover), and patients who were not willing for ICU care or organ support. This was adjusted for in sensitivity analysis.

STATISTICAL METHODS:

The data entry was performed using Epidata 2.0 software and the analysis by using STATA 15.0 software. The descriptive statistics and frequency tables were used for the description of the data. Graphs such as bar plots, pie charts, histogram plots, etc. were used for data description. The factors predicting mortality were presented using frequency tables and bar plots. The monthly infections (counts) were presented in a time series plot.

To find the significant factors associated with mortality, univariate and multivariate logistic regression analyses were used and risk estimate and its 95% CI were presented. Confounders were adjusted by regression models. Barthel index before and at 1week after discharge were estimated using appropriate descriptive statistics such as mean or

median and the appropriate pre-post-test of significance was used for calculating the p-value. The histogram plot was used for the normality check of the variables. P-value <0.05 was considered as statistically significant.

RESULTS

Two hundred and one patients were recruited to participate in the study. The sample size could not be reached.

BASELINE CHARACTERISTICS OF THE STUDY PATIENTS:

SOCIODEMOGRAPHIC CHARACTERISTICS:

AGE

Two hundred and one patients were enrolled in the study, the median age was 69 years, and majority were in young old group (between 60-69 years).

Table 8. Age distribution

Age group (years)	(n = 201)	%
60-69	107	53.2
70-79	68	33.8
≥80	26	12.9





GENDER

Out of 201 patients studied, 130 (65%) were men and 71 (35%) were women.



Figure 8. Gender distribution in the cohort

SEPSIS SCORES

SOFA AND APACHE II SCORES

Table 9. SOFA score, APACHE II score, median with interquartile range (IQR) in 201 patients

Sepsis scores	Median	n = 201		
		25 th Quartile	75 th Quartile	
SOFA score ≥2	5	3	7	
APACHE II	21	15	26	

In this study, the median SOFA score of ≥ 2 was 5. The median APACHE II score was 21.

DURATION OF HOSPITAL STAY

Table 10. Median duration of stay with interquartile range in 201 patients

The mean duration of hospital stay was 12.9 days, and mean duration of stay in intensive care unit/high dependency unit were 5.63 days

Total duration of stay	All cases	(n = 201)	
	Median	25 th	75 th
Hospital	11	6	17
ICU and HDU	4	0	8

The bar diagram below demonstrates the components of the SOFA score at admission against the number of patients. 114 (56.7%) patients received vasopressors, 108 (53.7%) patients received more than 1 vasopressor, 79 (39.3%) patients received invasive mechanical ventilation, 79 (39.3%) patients received non-invasive mechanical ventilation, 139 (69.1%) patients had serum bilirubin 1.2 mg/d and above, Glasgow coma scale was less than 15 in 117 (58.2%) patients, PaO₂ to FiO₂ ratio was less than 300 in 105 (52.2%) patients, creatinine was \geq 1.2 in 76 (37.8%) patients and mean arterial blood pressure was less than 70 in 75 (37.3%) patients.



Figure 9. Overview of the study population with SOFA score components

SYSTEMIC INFLAMMATORY RESPONSE SYNDROME (SIRS) CRITERIA

SIRS criteria	Frequency	Percentage
Positive	161	80.0
Negative	40	19.9
Total	201	100

Table10: SIRS criteria in the study population





Figure 11. SIRS components and its frequency in the study population



BARTHEL INDEX PRIOR TO ADMISSION AND AT ONE WEEK FOLLOWING DISCHARGE

Table 11. Barthel index prior to admission and at one week following discharge

Activities of daily living	Patients independent with	Patients independent with
	ADLs pre-morbidly	ADLs at 1 week following
	n =201 (%)	discharge
		n =120 (%)
Bowels	199 (99)	114 (95)
Bladder	176 (87.5)	88(73.3)
Grooming	191 (95.0)	82 (68)
Bathing	176 (87.5)	60 (50)
Toilet use	166 (82.5)	54 (45)
Feeding	192 (95.5)	84 (70)
Mobility	143 (71.1)	44 (22)
Transfers	166 (82.5)	48 (40)
Dressing	179 (89)	63(52.5)
Stairs	84 (41.7)	12(10)





In the above figure, the Barthel index at one week following discharge was found to be significantly lower compared to Barthel index prior to admission. Major differences were found in mobility, transfers, bathing, toilet use, dressing and climbing stairs.

ACUTE KIDNEY INJURY (AKI) IN SEPSIS

We observed that majority of the patients had acute kidney injury during their hospital stay.

Table 12. Percentage and number of acute kidney injury in the study population

	n =200	(%)
AKI	120	60
No AKI	79	39.5
Data missing	1	0.5

PATIENTS WITH CHRONIC ILLNESS

We found that 57% of patients admitted with sepsis in the medical wards and intensive care units had at least one chronic illness.

Table 13. Proportion of patients with chronic diseases in the study population

	n =201	%
Chronic illness	116	57.71
No chronic illness	85	42.29

CO MORBIDITIES

The majority of the patients in the cohort had diabetes mellitus (62.1%). Among patients who had diabetes mellitus, the mean HbA1c was found to be 7.58 (CI 6.3, 8.6). This was followed by those with coronary artery disease (31.8%).



Figure 13. Comorbidities in the study population

DELIRIUM

The Confusion Assessment Method was used for patients in the medical wards and medical ICUs within twenty four hours of admission and the majority of the patients with sepsis had delirium (58%). Dementia is a risk factor for delirium. Out of the nineteen patients with dementia (this diagnosis was already made during previous medical encounters), 18 (94.7%) had delirium (P-value <0.003). However, dementia remains an iceberg phenomenon - mostly under-diagnosed and severe depression could have been mislabeled as dementia. Some of the patients with dementia may not have been captured in this cohort.



Figure 14. Proportion of delirium in the study population
ADDICTIONS

In this study, patients who abused tobacco outnumbered patients who abused alcohol.

Substance abuse	n (%)
Tobacco use	66 (32.8)
Present alcohol use	12 (5.9)
Past alcohol use	52 (25.8)

Table 14. Substance abuse in the study population

LABORATORY DATA ANALYSIS OF PATIENTS ADMITTED WITH SEPSIS

In this study of 201 patients admitted with sepsis, we found elevated median serum lactate level, low median serum bicarbonate level and low median serum albumin level. We also found that inflammatory markers like C-reactive protein (CRP), Erythrocyte Sedimentation Rate (ESR) and procalcitonin levels were elevated along with total leucocyte count in a majority of the patients.

Table 15. Laboratory data - median with interquartile range

Laboratory data	n =201		
	Median	25 th Quartile	75 th Quartile
Lactate	2	1.4	3.9
WBC count	12700	9000	17600
ESR	69	38	80
CRP	126	91	175
Procalcitonin	5.9	0.8	23
Serum bicarbonate level	18.8	15	23
Albumin	3	2.5	3.3

MICROBIOLOGICAL DATA IN SEPSIS

ORGANISM IDENTIFIED





Of the 201 patients with sepsis recruited to this study, organisms were isolated from various sources in 87 patients (43%).

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BACTEREMIA

Out of 201 patients admitted with sepsis, 20.9% had microorganisms isolated in blood culture.

SOURCE REDUCTION VIA INVASIVE INTERVENTION

Out of 201 patients recruited, fifteen patients underwent invasive procedures to control the source of infection. Forty percent of them had skin and soft tissue collections requiring drainage, 33.3% had drainage of internal organ abscesses

Source of abscess/collection	n=15	%	Organisms identified	
Osteomyelitis	4	26.6	Pseudomonas (50%),	Fusarium (25%)
			No growth (25%)	
Skin and soft tissue	6	40	Burkholderia (16.6	%), Klebsiella
collections			(16.6%), E. coli (1	6.6%), and No
			growth (50%)	
Internal organ abscess	5	33.3	Empyema thoracic	no growth
			Retropharyngeal	Staphylococcus
			abscess	aureus
			Renal abscess	Enterococci
			Liver abscess	Escherichia coli

Table 16. Source reduction via invasive methods and organisms isolated

ORGAN SUPPORTS:

MECHANICAL VENTILATION

Of the 201 patients admitted with sepsis, 39% required invasive mechanical ventilation and 39% required Noninvasive mechanical ventilation in the first forty eight hours of hospital stay.

HEMODYNAMIC SUPPORT – VASOACTIVE SUPPORT AND CORTICOSTEROID USE

Noradrenaline (52.24%) was the most common inotrope used, in accordance with the present ICU guidelines of the hospital. Around forty percent of the patients were prescribed corticosteroids as part of sepsis protocol.

ANTIBIOTIC STEWARDSHIP

In this study, all 201 patients admitted with sepsis had received the first dose of antibiotics within twenty four hours of admission. A majority of these patients (60%) were antibiotic naïve i.e. they were not prescribed any antibiotics for three months prior to the present admission.





Figure 17: Antibiotic susceptibility



PRIMARY OUTCOME: NUMBER OF OLDER PATIENTS WHO SURVIVED SEPSIS

The mortality rate was 36.32% in this study.



Figure 17. Primary outcome

UNIVARIATE ANALYSIS OF FACTORS ASSOCIATED WITH THE PRIMARY OUTCOME

AGE AND OUTCOME

In the study population, increasing age was not associated with a poor primary outcome. In the subgroup analysis of older patients, we found that the primary outcome did not vary among young old, old old and older old.

Table 17. Age

Age	Non Survivors	Survivors	DAMA
	n (%)	n (%)	n (%)
60-69 (young old)	37 (50.6)	66(55)	4(50)
70-79 (old old)	27(36.9)	38(31.6)	3(37.5)
≥ 80 (older old)	9(12.3)	16(13.3)	1(12.5)
Total	73	120	8

P-value 0.9

DAMA - Discharged Against Medical Advice

GENDER AND PRIMARY OUTCOME

In this study, we also found that gender of the patient did not influence the primary outcome.

Table 18. Gender

Sex	Non Survivors n=73 (%)	Survivors n=120 (%)	DAMA n=8 (%)
Male	48(65.7)	76(63.3)	6 (75)
Female	25(34.2)	44(36.6)	2(25)

P value = 0.77

SOCIOECONOMIC STATUS

Among the seventy three patients who did not survive, the lower socio-economic status was not associated with a poor primary outcome.

Table 19. Socioeconomic status (SES)

Socioeconomic status	Non Survivors	Survivors
	n=73	n=120
	n(%)	n(%)
Class I – Upper (SES score 26-29)	3 (4.11)	11 (9.17)
Class II– Upper middle (SES score 16 - 25)	24 (32.88)	41 (34.17)
Class III– Lower middle (SES score 11-15)	36(49.32)	42 (35.00)
Class IV–Upper lower (SES score 5-10)	10 (13.70)	26(21.67)

P value = 0.18

SOFA SCORE

In this study, we also found that the SOFA scores were higher among non survivors compared to survivors.

Table 20. SOFA Scores

SOFA Score	Non Survivors	Survivors
	n=73 (%)	n=120 (%)
2 to 5	32 (43.84)	79 (65.83)
6 to 10	33 (45.21)	40 (33.33)
≥11	8 (10.96)	1 (0.83)

P value = 0.002

APACHE II SCORE

Table 21. APACHE II score

APACHE 2 Score	Non Survivors	Survivors
	n=73 (%)	n=120 (%)
<20	28 (38.36)	60 (51.72)
≥20	45 (61.64)	56 (48.28)

P value 0.02

In this study, we also found that Acute Physiology Score and Chronic Health Points -

APACHE II scores were higher among non survivors compared to survivors.

SOFA and APACHE II SCORE

In the study population, higher SOFA and APACHE II scores were associated with mortality.

Table 22. SOFA and APACHE II scores

Variable	Not survived		Survived		P value
	mean	SD	mean	SD	
SOFA score	6.41	3.4	4.90	2.3	0.003
APACHE II	22.76	7.9	19.8	6.7	0.008

SYSTEMIC INFLAMMATORY RESPONSE SCORE

In the study population, we did not find any association between non survivors and a positive Systemic Inflammatory Response Score (SIRS).

Table 23. SIRS criteria

II = / J (70)	
58 (79.45)	96 (81.36)
15 (20.55)	22 (18.64)
	10 (70) 58 (79.45) 15 (20.55)

P value 0.84

SOFA SCORE AND SIRS

In the study population, there was no association between a positive SIRS and a higher SOFA score.

Table 24. SOFA score and SIRS

	SIRS	
	SIRS positive	SIRS negative
SOFA Score	n=161 (%)	n=38 (%)
2 to 5	87 (54.04)	24 (63.16)
6 to 10	65 (40.37)	12 (31.58)
≥11	9 (5.59)	2 (5.26)

P value = 0.58

APACHE II AND SIRS

In this study, there was no association between a positive SIRS criteria and a high

APACHE (≥20).

Table 25. APACHE II score and SIRS

APACHE II Score	SIRS positive	SIRS negative
	n = 158	n = 38
	n (%)	n (%)
<20	66 (41.77)	22 (57.89)
≥20	92 (58.23)	16 (42.11)

P value = 0.073

CLINICAL CHARACTERISTICS AND PRIMARY OUTCOME

In this study, a reduced urine output (oliguria), increased heart rate (tachycardia) and

increased respiratory rate (tachypnea) were associated with a higher mortality.

Table 26. Clinical characteristics

Variable	Not survived		Survived		P value
	n=	=73	n=120		
	mean	SD	mean	SD	
Premorbid Barthel index	17.1		17.8		0.2
GCS Score (out of 15)	12.32	3.6	12.8	2.7	0.2
Mean arterial blood pressure (mmHg)	73.24	18.8	78.0	20.8	0.10
Urine output (ml per 24hrs)	1148.6	448.9	1299	472.8	0.03
Temperature (°F)	100	1.5	99.8	1.6	0.2
Respiratory rate (per min)	30.7	9.0	28.4	7.3	0.04

• based on two sample t-test

ACTIVITIES OF DAILY LIVING (BARTHEL INDEX)

In this cohort, the activities of daily living was significantly lower one week following

discharge when compared to the premorbid activities of daily living (P-value <0.001).

Table 27. Barthel Index

Barthel index	Mean	SD
Pre Morbid Barthel index	17.8	3.6
Barthel index at 1week from discharge	13.3	5.2

P value <0.001

Laboratory profile

In the study population, we found that an elevated creatinine, raised ESR, a deranged INR, elevated APTT, low serum albumin and low arterial bicarbonate levels were associated with mortality.

Table 28. Laboratory parameters

Laboratory profile	Not survived n=73		Survived n=120		P-value
	Mean	SD	Mean	SD	
Arterial Bicarbonate level	17.2	5.4	19.9	6.7	0.004
Arterial Lactate	3.46	3.2	2.99	2.6	0.26
HbA1c	8.03	2.1	7.5	1.7	0.27
Serum Sodium	131.6	8.1	133.0	7.1	0.2
Total leucocyte count	13191.7	7578.6	14427.5	7413.5	0.2
ESR	47.28	32.3	67.76	22.7	0.03
CRP	120.8	59.3	143.0	83.6	0.3
Procalcitonin	26.3	47.5	29.4	51.7	0.7
International normalized ratio	1.62	1.7	1.13	0.5	0.009
APTT	42.4	17.8	36	7.8	0.002
Albumin	2.6	0.6	3.1	0.5	<0.001

Table 29. Laboratory parameters in survivors vs. non-survivors

Laboratory profile	Sub groups	Non survivors	Survivors	Р
		n (%)	n (%)	value
S. bilirubin >1.2		27 (36.99)	32 (26.67)	0.01
Creatinine	1.2mg/dl and above	52 (71.23)	78 (65)	
	<1.2mg/dl	21 (28.77)	42 (35.00)	
	Total	73	120	0.64
INR	1.2 and above	30(45.45)	29(29.9)	
(international	<1.2	36 (54.5)	68(70.1)	
normalized ratio)	Total	66	97	0.01
APTT	>42	23 (35.38)	19 (19.59)	
	42 and less	42 (64.62)	78 (80.41)	
	Total	65	97	0.03
Lactate	>2	37 (50.68)	53 (45.3)	
	2 and less	36 (49.32)	64 (54.7)	

	Total	73	117	0.76
Albumin	<3.5	64(88.89)	86(71.67)	
	3.5 and above	8(11.11)	34(28.33)	
	Total	72	120	<0.001

FACTORS AFFECTING OUTCOME

Figure 18. Components of SOFA score and SIRS among survivors and non survivors



DURATION OF HOSPITAL AND ICU STAYS

Variable	Not survived		Survived			P value	
	Median	25 th	75 th	Median	25 th	75 th	0.037
Length of hospital stay	8	4	10	12	8	17	

Table 30. Length of hospital stay

In this study, an increase in the number of days on ventilator and NIV, and inotropes was associated with an increase in mortality. The median (IQR) duration of invasive mechanical ventilation was 3 (1, 5) and median (IQR) duration of noninvasive mechanical ventilation was 2 (1, 3). Since most patients requiring mechanical ventilation were in the intensive care facility, the median (IQR) Intensive care stay was 5.63 (1, 8).

Among admitted patients, we did not find any association between prolonged hospital stay and mortality (P value 0.97). However, we found that length of ICU stay was associated with higher mortality (P value 0.004).

Duration of hospital stay(days)	Non Survivors	Survivors
	n (%)	n (%)
> 15	21(28.77)	34 (28.33)
≥15	52 (71.23)	86(71.67)
Total	73	120

Table 31. Duration of hospital stay

P value = 0.97

Table 32.	Duration	of ICU	stay
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Duration of ICU stay	Non Survivors n (%)	Survivors n (%)
>5 days	40 (54.79)	36 (30.00)
1-5days	19 (26.03)	33 (27.50)
Never admitted in ICU	14 (19.18)	51 (42.50)
Total	73	120

P value = 0.001

Figure 19. Time dependent ROC curve of mortality against duration of ICU stay



The above graph shows that longer the duration of ICU stay was associated with mortality (ROC area is 0.65 with 95% CI 0.57-0.73)

COMORBIDITIES

In older patients admitted with sepsis, we found no statistical difference in comorbidity profile in patients who survived and those who did not survive, except for connective tissue disorders.

Comorbidity	Non Survivors n(%)	Survivors n(%)	P value
Myocardial infarction	12(16.44)	7 (5.83)	0.03
Congestive cardiac failure	16 (21.92)	22 (18.33)	0.09
Peripheral arterial occlusive disease	6 (8.2)	6 (5)	0.36
Cerebrovascular accident	7 (9.5)	16 (13.3)	0.43
Chronic obstructive pulmonary disease	19 (26)	28 (23.3)	0.67
Dementia	5 (6.8)	13 (10.8)	0.35
Connective tissue disorder	9(12.3)	1(0.83)	<0.01
Peptic ulcer disease	5 (6.8)	4(3.3)	0.26
Chronic liver disease	3 (4.1)	8 (6.67)	0.45
Diabetes mellitus	47 (64.3)	72 (60)	0.54
Hemiplegia	3 (4.1)	3 (2.5)	0.60
Chronic kidney disease	15 (20.5)	21 (17.5)	0.65
Solid malignant tumor	5 (6.8)	6(5)	0.64
Leukemia and Lymphoma	2(2.74)	1(0.83)	0.54
AIDS	2(2.7)	0	0.17

Table 33. Comorbidities

CHARLSON COMORBIDITY INDEX AND APACHE II SCORES

In the study population, we found that higher APACHE II scores were associated with higher comorbidity burden, based on Charlson comorbidity index (P value 0.004).

Table 34. Charlsor	comorbidity	index and	APACHE II scor	e
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Charlson comorbidity index	APACHE II <20 n=89(%)	APACHE II >/=20 n=108(%)	TOTAL n=197(%)
<3	65 (73.03)	58 (53.70)	123 (62.44)
≥3	24 (26.97)	50(46.3)	74 (37.56)

P value = 0.004

SMOKING

Smoking was not associated with poor outcome in patients with sepsis. Mean pack years among non-survivors was 11.6 and mean pack years among survivors was 13.9

Table 35. Smoking

	Not survived		Survived		P-value
	n=73	SD	n=120	SD	
Pack years of smoking	11.6	16.4	8.2	13.9	0.12

ORGAN SUPPORTS AND OUTCOME

MECHANICAL VENTILLATION

NON INVASIVE VENTILATION (NIV)

In the study population, 40% patients were put on noninvasive ventilation, which was was associated with a higher mortality.

Table 36. Noninvasive ventilation

NIV	Non survivor	Survivor	Total
	n(%)	n (%)	n(%)
NIV used	21 (28.77)	57 (47.50)	78 (40)
NIV not used	52 (71.23)	63 (52.50)	115 (59.59)
TOTAL	73	120	193

P value = 0.01

INVASIVE VENTILATION

In the study population, 39% patients were put on invasive mechanical ventilation and this was associated with a higher mortality (P value <0.01).

Table 37. Invasive ventilation

Mechanical ventilation	Non survivor	Survivor	Total
	n=13(%)	n=120 (%)	n=193 (%)
Invasive ventilation	49 (67.12)	28 (25.00)	79 (39)
No invasive ventilation	24 (32.88)	92 (76.67)	122 (60.7)

P value = <0.01

DURATION OF USE OF INVASIVE VENTILATION, NON-INVASIVE VENTILATION AND INOTROPES

In the study cohort, we found that a longer duration of invasive ventilation, noninvasive ventilation and duration of inotropic use was associated with an increase in mortality.

Table 38. Duration on ventilator, NIV and inotropes

Duration	Not survived		Survived		P-value
	n=73	SD	n=120	SD	
Ventilator days	6.7	8.2	1.5	3.4	<0.001
NIV days	1	2.2	1.9	2.4	0.012
Number of days on Inotropes	5.7	6.3	2.2	4.0	<0.001

HEMODYNAMIC SUPPORT – INOTROPES AND CORTICOSTEROID USE

Out of the seventy three patients who did not survive, 90.4% used inotropes and 71.2% used more than 1 inotrope.

Table 39. Inotrope use

Inotrope use	Non survivor	Survivor	Total
	n(%)	n(%)	n(%)
Yes	66(90.44)	44(36.67)	110 (56.9)
No	7 (9.59)	76 (63.33)	83 (43.01)
Total	73	120	193

P value = <0.01

Number of	Non survivor	Survivor	Total
inotropes used	n(%)	n(%)	n(%)
1	19 (28.7)	32 (72.7)	51 (46.3)
>1	47 (71.2)	12 (27.2)	59 (53.6)
TOTAL	66	44	110

Table 40.	Number	of inotropes	used

P = < 0.001

CORTICOSTEROIDS IN SEPSIS

In the study population of 201, 78 patients were given corticosteroid therapy to tackle hemodynamic instability. Out of 78 patients in whom corticosteroid therapy was initiated, 47.4% patients survived (P value 0.006).

Corticosteroid	Non survivor	Survivor	Total
therapy	n=73	n=120	n(%)
	n(%)	n(%)	
Yes	35 (44.87)	37 (47.44)	78 (100)
No	38 (30.89)	83 (67.48)	123 (100)

Table 41. Corticosteroid therapy in sepsis

P value 0.006

SOURCE OF INFECTION

The most common source of infection was found to be pulmonary and pleural in origin -47% followed by urinary tract infections (24.8%). In the non survivors, half of the patients had pulmonary and pleural infections followed by urinary tract infections.

		a .		T (1
Source of infection	Non survivors	Survivors	DAMA	Total
	n (%)	n (%)	n (%)	n (%)
Pulmonary and pleural	41 (56 16)	53 (44 17)	1(12.05)	95 (47 26)
I unifoliary and picular	41 (30.10)	33 (77.17)	1(12.03))) (47.20)
I Inin any tract	12 (16 14)	20(24.17)	2(27.5)	44(21.80)
Ormary tract	12 (10.44)	29 (24.17)	3(37.3)	44(21.89)
	0(4.11)	10(0.00)	1 (10 5)	14(6.07)
Skin and soft tissue	3(4.11)	10(8.33)	1(12.5)	14(6.97)
Central nervous system	0	1(0.83)	0	1(0.5)
	-	-(-	-(
Musculoskeletal	3(4 11)	3(25)	1(12.5)	7(3.48)
Właseuloskeletał	5(4.11)	5(2.5)	1(12.3)	7(3.40)
Dana nagal sinus	1(1.27)	0	0	1(0.5)
Para nasai sinus	1(1.57)	0	0	1(0.5)
			-	• (1)
Heart valves	0	2(1.67)	0	2(1)
Gastrointestinal	1(1.37)	10(8.33)	0	11(5.47)
	-()		-	()
Unknown	12(16.44)	12(10)	2(25)	26(12.94)
	12(10.44)	12(10)	2(23)	20(12.74)

Table 42. Foci of sepsis

P value = 0.214

MICROBIOLOGY

ORGANISMS IDENTIFIED

In the study population, 20.9% patients had microorganisms grown in blood cultures.

Micro-organisms were identified in 84 patients from various sites. Fifty percent of

these patients also had a positive blood culture (P value <0.001).

	Organism identified			
	Yes No T			
	n (%)	n (%)		
Organism incubated in blood culture	42 (50)	0	42 (20.9)	
Organism not incubated in blood culture	42(50)	117(100)	159 (79.1)	
	84	117	201	

P value < 0.001

BLOOD CULTURE

Among the patients who did not survive, we found that blood cultures were largely sterile.

Table 44. Blood culture

Blood culture	Non	Survivor	DAMA	Total
	survivor	n (%)	n (%)	
	n (%)			
Organism incubated in blood culture	6(8.22)	34 (28.33)	2 (25)	42(20.9)
Organism not incubated in blood culture	67 (91.78)	86 (71.67)	6(75)	159 (79)
	73	120	8	201

P value 0.002

*DAMA – discharged against medical advice

ORGANISM ISOLATED

In this study, we did not find an association with the isolated organisms and survival.

Table 45. Micro-organisms identified and outcome.

Organisms	Non survivor	Survivor	Total
	n (%)	n (%)	
Gram positive organisms	4(20)	8(13.111)	12(14.12)
Gram negative organisms	12 (60)	49(80.33)	61 (71.7)
Fungi	3 (15)	1 (1.64)	4 (4.5)
Virus	1(5)	3(4.92)	4(4.7)
Total	20	61	81

P value = 0.15

ORGANISM ISOLATED AND DURATION OF HOSPITAL STAY

Of the organisms isolated, 75% were gram negative and 14.1% were gram positive organisms.

Table 46.	Organisms	identified	and duration	of stav	in the	hospital
	Organishis	lacitica		UI JUU		nospitai

Organisms	<15days	15days and	Total
	n (%)	more	
		n (%)	
Gram positive organisms	8 (13.11)	4(16.67)	12 (14.12)
Gram negative organisms	48(78.69)	16(66.67)	64(75.29)
Fungi	1(1.64)	4(16.7)	5(5.88)
Virus	4(6.56)	0	4(4.71)
Total	61	24	85

P value = 0.034

ORGANISMS ISOLATED ON BLOOD CULTURE AND EXPOSURE TO ANTIMICROBIAL AGENTS 3 MONTHS PRIOR TO ADMISSION

We found that out of 84 patients in whom microorganisms were isolated, 20.2% patients were exposed to antimicrobial agents in the past 3 months. We did not find any association between organism identified and exposure to antimicrobials in the past 3 months. Out of 159 blood culture negative cases, 35 (22%) cases were exposed to antimicrobials in the last 3months prior to admission (P value 0.29).

Exposure to antimicrobial agents in	Organism identified		Total
3months prior to admission	Yes	No	
	n=84 (%)	n=117(%)	n=201(%)
Yes	17 (20.24)	23 (19.6)	40 (19.9)
No	67 (79.76)	93 (79.49)	160 (79.6)

Table 47.	Prior exposure	to antimicrob	oials and m	nicrobial i	isolates

P value = 0.695

ANTIMICROBIAL STEWARDSHIP AND OUTCOME

All patients recruited in this study received antibiotics within twenty hours of hospital

admission.

Table 48. Empirical antimicrobial agents and change in antimicrobial agentduring hospital stay

	Empirical	antimicrobia	al agents	Antimicrobials changed		
Antimicrobial	Non	Survivor	P value	Non	Survivor	P value
agents	Survivor $n=73(\%)$	n=120(%)		Survivor $n=73(\%)$	n=12 (%)	
Penicillin	40(54.79)	56 (46.67)	0.19	0	10(8.33)	0.09
Cephalosporin	0	4 (3.33)	0.48	0	6(5)	0.19
Aminoglycosides	1 (1.37)	0	0.65	0	1(0.83)	0.85
Fluoroquinolones	1 (1.37)	2(1.67)	0.93	1 (1.37)	5 (4.17)	0.70
Carbapenems	33 (45.2)	54 (45)	0.18	28 (38.36)	27 (22.5)	0.04
Tetracycline	2 (2.74)	6 (5)	0.50	2(2.74)	1(0.83)	0.51
Macrolides	23 (31.5)	27 (22.5)	0.15	0	0	-
Glycopeptide	4 (5.48)	2 (1.67)	0.48	6 (8.22)	3 (2.5)	0.27
Others	4 (5.48)	11 (9.17)	0.59	15	4(3.33)	0.001

(20.55)			(20.55)	
			(20.55)	

The most widely used empirical antimicrobial agents were from the Penicillin group followed by Carbapenems. This was changed to Carbepenems mainly. However, among the antimicrobials changed, Carbapenems were prescribed to non survivors compared to the survivors (P value 0.04). Also, other antimicrobial agents which included were collistimethate, tigecycline and various other agents like antiviral agents and antifungal agents were prescribed to the non survivors compared to survivors.

CHOICE OF EMPIRICAL ANTIBIOTICS AND DURATION OF HOSPITAL STAY

In this study, patients who received Carbapenems as the initial, empiric antibiotic had a shorter duration of hospital stay, compared to patients who received other antimicrobial agents.

Antimicrobial	Duration of	hospital stay	P value
agents	15days and less	>15days	
	n (%)	n (%)	
Penicillin	74(76.29)	23 (23.71)	0.12
Cephalosporin	4 (2.78)	0	0.12
Aminoglycosides	0	1(1.75)	0.07
Fluoroquinolones	2(1.39)	1(1.75)	0.27
Carbapenems	62 (43.06)	32 (56.14)	0.05
Tetracycline	8(5.56)	0	0.06
Macrolides	37(25.69)	13 (22.8)	0.31

Table 49. Duration of stay with various antimicrobials

Glycopeptide	4(2.78)	2(3.51)	0.086
Others	14 (9.72)	2(3.51)	0.27
Total	144	57	

CHANGE IN EMPIRICAL ANTIMICROBIAL AGENTS

Out of 201 patients recruited in this study, empirical antimicrobial agents were changed in 91 patients.

Table 50. Change in antimicrobial in the hospital

Was empirical antibiotics	Non survivor n=73(%)	Survivor n=120(%)	Total n=201(%)
changed?			
Yes	39 (53.42)	50(41.67)	91 (45.27)
No	34 (30.9)	70(63.3)	110 (54.7)

P value = 0.28

REASONS FOR CHANGING ANTIMICROBIAL AGENTS

The main reason behind changing empirical antimicrobial agent was due to a poor

clinical response (P value < 0.001)

Table 53: Reasons behind change in antimicrobial agents

Reasons behind change in empirical antimicrobials	n=201 (%)
Cost	0
Poor clinical response	57(62.64)
Depending on the microbe incubated and its antimicrobial susceptibility (Targeted therapy)	24 (26.3)
Good clinical response	9 (9.89)
Unknown	1 (1.1)

P value < 0.001

ANTIBIOTIC SUSCEPTIBILITY

Antibiotics	Non Su	irvivors	Survivors		P-value
susceptibility	n=7.	3(%)	n=12	20(%)	
with outcome	Sensitive	Resistant	Sensitive	Resistant	
analysis:					
Penicillin	4(5.48)	4(5.48)	34 (28.57)	15 (12.61)	<0.001
Cephalosporin	5 (6.85)	2(2.74)	23 (19.17)	22 (18.33)	0.001
Aminoglycosides	2(2.74)	3(4.11)	33(27.5)	6 (5)	<0.001
Fluoroquinolones	2(2.74)	4(5.48)	27 (22.5)	16(13.3)	<0.001
Carbapenems	6(8.22)	1(1.37)	39(32.5)	1(0.83)	<0.001
Tetracycline	3(4.11)	0	3(2.5)	1(0.83)	0.017
Macrolides	3(4.11)	1(1.37)	4(3.33)	2(1.67)	0.281
Glycopeptide	2(2.74)	0	5(4.17)	0	0.7
Others	2(2.78)	2(2.78)	5(4.17)	0	0.39

Table 51. Antibiotic susceptibility

COMPLICATIONS DURING HOSPITAL STAY

Sixty three patients (31.5%) developed complications during their in-hospital stay. Forty nine people(24.3%) developed nosocomial infections- 77.5% patients had ventilator acquired infection (p value <0.001). Seventy nine patients(39%) were mechanically ventilated. Of these patients, 49.37% developed ventilator associated pneumonia (p value <0.001).

COMPLICATIONS	n=63	Percentage
Hospital acquired infection	49	77
Myocardial infarction	19	30
Bleed (total)	10	15.8
Gastrointestinal bleed	6	9.5
Hemoptysis	1	1.5
Urogenital bleeding	2	3.1
Other bleeding	1	1.5
Cerebrovascular accident	3	4.7
Venous thromboembolism	1	1.5

Table 52. Complications during hospital stay

Among the 73 patients who did not survive in this study, the majority had complications during their hospital stay (54%, p value <0.001).

Table 53.	Complications	during	hospital	stay
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Complications	Non survivor	Survivor		
during hospital	n=73	n=120		
stay	n (%)	n (%)		
Yes	40 (54.79)	22 (18.33)		
No	33 (45.83)	98 (81.67)		

P value = <0.001

Hospital acquired	Non survivor	Survivor
infection	n=73	n=120
	n (%)	n (%)
Yes	33(45.21)	16 (13.33)
No	40 (54.79)	105 (87.5)

 Table 57: Hospital acquired infections

P value = <0.001

MULTIVARIATE ANALYSIS

Logistic regression was performed to determine the association between the outcome variables - mortality (non-survivors) and the independent variables like age, SOFA score, APACHE II, Respiratory rate, serum albumin, use of invasive mechanical ventilation, duration of invasive mechanical ventilation, intensive care unit stay, vasoactive support, duration of vasoactive support, blood culture and hospital duration. Bivariate and multivariate analyses were done to determine relevant predictors of mortality in older adults admitted with sepsis. On the bivariate analysis, we found that mortality was associated with lower albumin levels (OR=2.9, 95% CI 1.82-2.49, p-value <0.001), need for invasive mechanical ventilation (OR 6.6, 95% CI 3.52-12.6, p-value <0.001), vasoactive support (OR 15.7, 95% CI 6.66-37.03, p-value <0.001) and development of nosocomial infections (OR 5.7, 95% CI 2.87-11.6, pvalue <0.001). On the multivariate analysis, the duration of ventilation (OR 0.6 CI 0.53-0.87, p value 0.003), length of ICU stay (OR 1.1 CI 1.05-1.36, p value 0.006), patients requiring vasoactive supports (OR 26.4, 95% CI 6.13-114.4, p-value <0.001) were associated with mortality. Patients who were on vasoactive supports were much sicker than the other patients, and needed these supports to sustain life.

Higher SOFA and APACHE II scores were not found to be associated with mortality. Hence the need of the hour is to find an appropriate scoring system for the older person in sepsis, in order to recognise and treat him or her early and appropriately, thus decreasing mortality.

Factor	Bivariate analysis			Multivariate analysis		
	OR	95%CI	P-value	OR	95%CI	P-valve
Age	0.9	0.96-1.03	0.9	0.9	0.8-1	0.07
SOFA Score	0.8	0.76-0.93	0.002	1.0	0.88-1.3	0.45
APACHE II	0.9	0.91-0.99	0.02	0.9	0.88-1.04	0.33
Respiratory rate	0.9	0.92-0.99	0.04	1.0	0.95-1.07	0.74
Albumin	2.9	1.82-2.49	<0.001	1.9	0.91-4.11	0.08
Ventilation	6.6	3.52-12.6	<0.001	0.9	0.21-4.2	0.9
Ventilation duration	0.8	0.77-0.89	<0.001	0.6	0.53-0.87	0.003
ICU stay	0.9	0.87-0.96	0.001	1.1	1.05-1.36	0.006
Vasoactive support	15.7	6.66-37.03	<0.001	26.4	6.13-114.4	<0.001
Vasoactive duration	0.8	0.79-0.92	<0.001	1.2	1.06-1.5	0.008
Blood culture	0.2	0.09-0.57	0.002	0.3	0.09-1.1	0.09
Hospital infection	5.7	2.87-11.6	<0.001	2.8	0.79-10.04	0.11

 Table 58: Factors associated with mortality

DISCUSSION

With neither a gold standard test for diagnosis, nor typical presenting signs and symptoms, sepsis is a challenging clinical setting - especially in the older adults - for many physicians. This study highlights the factors contributing to mortality among older patients admitted with sepsis, and is designed to encourage clinicians to provide individualised care.

A total of 201 patients were recruited to participate in the study, of which 64% were men and 35% were women. Females have a longer life expectancy at birth -70.4 years compared to males who have 68 years according to the World Bank data for India 2017. The low proportion of females admitted to this centres could be because sick women are not often brought to hospitals for care - due to financial constraints or social causes which loom large in the Indian context. In this study, we found that the median age of the study population was 69 years. A majority (53%) of the patients were in the age group of 60 to 69 years(young old). In a study done by Martin et al, increasing age was an independent predictor of mortality - however, in a two-sample t-test equal variance analysis, we found that an older age was not a predictor of mortality (P-value 0.8). Among the patients admitted, 36.3% were directly admitted to the Intensive Care Unit and 63.6% were admitted to the wards. Twenty nine percent of the people admitted to the wards were shifted to the ICU, as their condition deteriorated. The overall mortality rate of our cohort was 36.32%, and the mean duration of hospital stay of 12.9 days.

Dr.William Osler documented in 1901 the absence of typical signs or symptoms in older adults with a severe infection which still holds true. We found that the median temperature was 100⁰ Fahrenheit (CI 99.7- 100.5). Median heart rate was 101.2 beats per minute (CI 96.04-106.4). The presence of fever or tachycardia did not predict mortality in older adults. Urine output was 1148 ml/24 hours (CI 1043.1 - 1254.16) among those who did not survive and 1299 ml/24 hours (CI 1212 - 1385.9) among those who survived (P-value 0.03). Mean respiratory rate was 30.7 breaths per minute (CI 28.6 - 32.9) among non-survivors, compared to 28.4 breaths per minute (CI 27.08 - 29.7) among survivors (P-value 0.04). We found 58.33% of patients among the non survivors had a positive CAM score for delirium in the first 24 hours following admission. However, there was no association between CAM score positivity and mortality. Clinically, increased respiratory rate and low urine output were predictors of poor outcome in older adults in this study.

Among laboratory tests done, we found that abnormal arterial lactate level, HbA1c, leucocyte count, CRP and procalcitonin did not predict mortality. However increase in activated partial thromboplastin level and a deranged international normalized ratio, low serum albumin, low serum bicarbonate, and high ESR were associated with mortality.

In a study done among older adults by Iwashyna et al in 2010, many patients with severe sepsis were found to have poor levels of activity as measured by Barthel index

in the period before severe sepsis set in, which worsened after an episode of sepsis. Our study showed that the mean pre-morbid Barthel index of 17.8 (CI 17.18- 18.5) dropped significantly to 13.31 (CI 12.3-14.7) one week after discharge (P value < 0.001).

In the cohort, 32.8% abused tobacco. Tobacco use was not found to be associated with mortality in this study (P-value 0.12).

In a study done in Brazil by Laís et al, it was found that the incidence of acute kidney injury (AKI) in older adults patients admitted with sepsis was 27%. However, o 60% of older adults admitted with sepsis in our study had acute kidney injury (AKI), probably due to sepsis and various other causes.

Many studies show that the presence of previous chronic illnesses and co-morbidities were associated with poor outcomes. In the study by Lemay et al, the average Charlson co-morbidity index was 3.5 (SD 2.6). In our study, we found that out of 73 non-survivors, 43.8% of patients had a Charlson co-morbidity index above 5 and there was no association between Charlson co-morbidity index and mortality (P 0.52). A history of myocardial infarction (P-value 0.03) and connective tissue disorder (P value <0.001) was associated with mortality. The severity of sepsis, based on the SOFA and APACHE II scores, was associated with a high comorbidity burden on Charlson comorbidity index (P value 0.04)

Among the sepsis scores used in the study population, we found that APACHE II and SOFA scores showed a significant association with mortality (SOFA P-value < 0.001, APACHE II P-value 0.03). However, the SIRS did not show any association with mortality (P-value 0.84). On Bivariate analysis, we could not establish that the sepsis scoring system, like SOFA and APACHE II scores, to be of significant in predicting mortality in older adults admitted with sepsis. However, identifying a drop in urine output, tachypnea and identifying patients who might require organ support in the form of vasoactive support early, invasive mechanical ventilation remains the key to decreasing mortality among older adults.

When we compared patients who stayed for more than fifteen days in the hospital with those who stayed for less, we did not find any association with mortality. However, patients who stayed in the Intensive Care Unit for more than five days had a higher mortality (P-value 0.004). The risk of acquiring a nosocomial infection during hospitalization is high, especially in the intensive care unit. One prospective observation study looking at nosocomial infections in patients admitted with sepsis by van Vught et showed that the incidence of nosocomial infection was 13.5% in the older adults. In patients with sepsis, secondary infections were due to indwelling urinary catheters (26%), in hospital acquired pneumonia (25%) and abdominal infections (16%).

In the present study, among survivors, 72.7% of patients were administered one inotrope (P-value < 0.001) and the median number of days on vasoactive support was 2.2 days (CI 1.55 - 3 ; P-value < 0.001), 47.5% of patients used NIV (P-value 0.01),

and 47% of survivors used corticosteroids for hemodynamic instability (P-value 0.006). 67.12% of patients among non-survivors used invasive mechanical ventilation (P-value < 0.001).

In the study done by Martin et al, older patients were more likely to have Gramnegative infections, particularly pneumonia (relative risk 1.66; 95% CI 1.63 - 1.69), and to have co-morbid medical conditions (relative risk 1.99; 95% CI 1.92 - 2.06). In this cohort, we found that 47.26% of patients had pneumonia followed by pyelonephritis (21.8%). There was no association between the foci of infection among survivors and non-survivors (P-value 0.2). Half of the organisms identified were isolated from blood (P-value < 0.001). Among the patients who did not survive, we found that blood cultures were largely sterile (P-value 0.004), probably secondary to the use of antibiotics in the peri-admission window. In this study, all the patients received antibiotics within twenty four hours of admission. The most widely used empirical antimicrobial agent was Penicillin followed by Carbapenems, and the choice of empirical antimicrobial therapy was not associated with a better outcome.

In the study population, patients who developed complications in the hospital succumbed to illness compared to those who had no complications. The most common complications leading to death were nosocomial infection (P-value <0.001), followed by myocardial infarction (P-value 0.01) and gastrointestinal bleed (P-value 0.02) on univariate analysis.

Bivariate analysis showed that mortality was associated with lower albumin (OR=2.9, 95% CI 1.82-2.49, p-value <0.001), requirement of organ supports in the form of

invasive mechanical ventilation (OR 6.6, 95% CI 3.52-12.6, p-value <0.001), and vasoactive support (OR 15.7, 95% CI 6.66-37.03, p-value <0.001), and nosocomial infections during hospital stay (OR 5.7, 95% CI 2.87-11.6, p-value <0.001). In this cohort, the mean duration on ventilator was 6.7days among non survivors compared to 1.5days among survivors (P-value <0.001). Similarly, Mean duration of vasoactive support (inotropic support) was 5.7days among non survivors compared to 2.2days among survivors (P-value <0.001)

On multivariate analysis, patients requiring vasoactive supports had higher mortality. (OR 26.4, 95% CI 6.13-114.4, p-value <0.001) This could probably be due to patients who were on vasoactive support were prone to severe multi-organ dysfunction and could have had poor functional reserves.

LIMITATIONS

- 1. This was done in a tertiary care setting, and hence poor access to medical care may be one of the reasons many other older adults could not reach this facility
- 2. Financial constraints would have robbed others of availing cutting edge medication
- 3. Some others would have gone home from the Emergency Department, as the explained prognosis was poor.
- 4. Other patients would have selected a palliative care approach on the wards due to either poor prognosis, increased age of the patient, or severe financial constraints.
CONCLUSIONS

- The mortality rate in older adults patients admitted with sepsis was 36.32% in the present study
- Factors affecting mortality were a longer duration of ventilation (OR 0.6 CI 0.53-0.87, p value 0.003), longer duration of stay in the ICU stay (OR 1.1 CI 1.05-1.36, p value 0.006) and need of vasoactive supports (OR 26.4, 95% CI 6.13-114.4, p-value <0.001). SOFA and APACHE II scores were not found to be associated with mortality. Hence, an alternative severity scoring system needs to be validated for the older person at the earliest.
- The most common source of sepsis was found to be lung followed by the urinary tract.
- The most common empirical antimicrobials used were from the Penicillin group, followed by Carbapenems. The use of a particular group of antibiotics did not offer mortality benefits. The duration of hospital stay is, however, reduced with the use of initial Carbapenems.
- Nosocomial infections among older patients admitted with sepsis were a major cause of mortality.

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APPENDICES APPENDIX 1 – IRB APPROVAL LETTER



OFFICE OF RESEARCH INSTITUTIONAL REVIEW BOARD (IRB) CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical) Director, Christian Counseling Center, Chairperson, Ethics Committee. Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D., Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM., Deputy Chairperson, Secretary, Ethics Committee, IRB Additional Vice-Principal (Research)

February 13, 2018

Dr. Stephen Varghese Samuel, PG Registrar, Department of Geriatrics, Christian Medical College, Vellore – 632 002.

Sub: Fluid Research Grant: New Proposal:

Outcomes in elderly patients admitted with sepsis in a tertiary care hospital: A follow up observational study".

Dr. Stephen Varghese Samuel, Employment Number: 33869, Postgraduate Registrar, Geriatrics, Dr. Surekha V, Employment Number: 14007, Geriatrics, Dr. Binila Chacko, Medical Intensive Care Unit, Emp No 28471, Dr. Peter John Victor, Emp No 13328), Medical Intensive Care Unit, Dr. Balaji V, Microbiology, Dr. John Antony Jude Prakash, Microbiology, Dr. O.C. Abraham, Medicine unit 4, Dr. Sowmya Sathyendra, General Medicine, Dr. Ramya Iyadurai, Medicine unit 5, Dr. Kuruvilla Prasad Mathews, Geriatrics, Tunny Sebastian, Biostatistics.

Ref: IRB Min. No. 11039 [OBSERVE] dated 04.12.2017

Dear Dr. Stephen Varghese Samuel,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George

Secretary (Ethics Committee) Institutional Review Board Dr. BIJU GEORGE MBS., MD., DM. SECRETARY - (ETHICS COMMITTEE) Institutional Review Board, Christian Medical College, Vellore - 632 002.

Cc: Dr. Surekha V, Dept. of Geriatrics, CMC, Vellore

1 of 4

 Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002

 Tel: 0416 – 2284294, 2284202

 Fax: 0416 – 2262788, 2284481

 E-mail: research@cmcvellore.ac.in

"An took institute and it OFFICE OF RESEARCH. AS A METHOD STREAM TO THE OFFICE OF RESEARCH. A the second sec INSTITUTIONAL REVIEW BOARD (IRB) CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical) Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D., Director, Christian Counseling Center, Chairperson, Research Committee & Principal Chairperson, Ethics Committee. Dr. Biju George, M.B.B.S., MD., DM., Deputy Chairperson, Secretary, Ethics Committee, IRB Additional Vice-Principal (Research) February 13, 2018 Dr. Stephen Varghese Samuel, PG Registrar, Department of Geriatrics, Christian Medical College, Vellore - 632 002. Sub: Fluid Research Grant: New Proposal: Outcomes in elderly patients admitted with sepsis in a tertiary care hospital: A follow up observational study Dr. Stephen Varghese Samuel, Employment Number: 33869, Postgraduate Registrar, Geriatrics, Dr. Surekha V, Employment Number: 14007, Geriatrics, Dr. Binila Chacko, Medical Intensive Care Unit, Emp No 28471, Dr. Peter John Victor, Emp No 13328), Medical Intensive Care Unit, Dr. Balaji V, Microbiology, Dr. John Antony Jude Prakash, Microbiology, Dr. O.C. Abraham, Medicine unit 4, Dr. Sowmya Sathyendra, General Medicine, Dr. Ramya Iyadurai, Medicine unit 5, Dr. Kuruvilla Prasad Mathews, Geriatrics, Tunny Sebastian, Biostatistics. Ref: IRB Min. No. 11039 [OBSERVE] dated 04.12.2017 Dear Dr. Stephen Varghese Samuel, The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Outcomes in elderly patients admitted with sepsis in a tertiary care hospital: A follow up observational study" on December 04th 2017. The Committee reviewed the following documents: 1. IRB application format 2. Case Report Form Information Sheet and Informed Consent Form (Englihs, Tamil, Hindi, 3. Bengali) 4 STROBE checklist 5. cvs of Drs. Stephen Varghese Samuel, Surekha V 6. No. of documents 1-5. The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on December 04th 2017 in the CK Job Hall, Paul Brand Building, Christian Medical College, Vellore 632 004. 2 of 4Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002 Tel: 0416 - 2284294, 2284202 Fax: 0416 - 2262788, 2284481 E-mail: research@cmcvellore.ac.in



OFFICE OF RESEARCH INSTITUTIONAL REVIEW BOARD (IRB) CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical) Director, Christian Counseling Center, Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D., Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM., Deputy Chairperson, Secretary, Ethics Committee, IRB Additional Vice-Principal (Research)

Name	Qualification	Designation	1.0011
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal, Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Affiliation Internal, Clinician
Dr. Anuradha Rose	MBBS, MD, MHSC (Bioethics)	Associate Professor, Community Health, CMC, Vellore	Internal, Clinician
Dr. Thomas V Paul	MBBS, MD, DNB, PhD	Professor, Endocrinology, CMC, Vellore	Internal, Clinician
Dr. RekhaPai	BSc, MSc, PhD	Associate Professor, Pathology, CMC, Vellore	Internal, Basic Medical Scientist
Mr. Samuel Abraham	BSC, BD	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist
Mr. C. Sampath	PGDPM, M. Phil, BL.	Sr. Legal Officer, CMC, Vellore	Internal, Legal Expert
Ms. Grace Rebald	DSC, BL	Advocate, Vellore	External, Legal Expert
Dr Sneha Varkki	M.Sc., (Biostatistics)	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Dr. Soumus	MBBS, DCH, DNB	Professor, Paediatrics, CMC, Vellore	Internal,
athyendra	MBBS, MD (Gen. Medicine)	Professor, Medicine III, CMC, Vellore	Internal,
A. Asha Solomon	MSc Nursing	Associate Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse

IRB Min. No. 11039 [OBSERVE] dated 04.12.2017

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APPENDIX 2 – PATIENTS INFORMATION SHEET

Department of Geriatrics

Christian Medical College Vellore

Patient Information Sheet

"Outcomes in older adults patients admitted with sepsis in a tertiary care hospital:

A follow up observational study".

As we age, we are at an increasing risk to develop very serious infections which may require hospitalization in the Intensive Care Units.

In this study, the risk factors, the outcomes and quality of life in patients who are admitted to this hospital with these serious infections will be studied. Information regarding your/your relative's demographic data, illnesses you have, and results of laboratory and radiological investigations you have had during your in hospital stay will be collected and analyzed.

Participation in this study means that there will not be any additional tests done other than the necessary tests for your/your relative's condition.

You/your relative will receive all the standard treatment for your/ your relative's condition.

Participating in this study is purely voluntary and you/your relative can decide to withdraw from the study at any time. Withdrawal will not have any consequences to further treatment that you/your relative are receiving in this hospital.

The information gathered will be used for research purposes and will be published.

If you have any further queries or doubts, please contact

Dr. Stephen Varghese Samuel

Phone number: 9895246217

IRB number (protocol ID)				Date	DD	MM	YYYY		
IRB no	1	1	0	3	9				
					II				

|--|

Hospital number	
Department:	GERIATRICS / MEDICINE Unit
Date of admission (DD/MM/YYY)	
Date of discharge (DD/MM/YYYY)	
Admitted from	Emergency department 1
	Outpatient department O2
	Others O3
Admitted initially to	ICU/HDU 门
	Ward O2
If admitted in ward, later shifted to ICU?	Yes ()1 No ()2
Readmission to ICU	Yes ()1 No ()2
Informant	Patient Relative others specify-
Information reliable	Yes ()1 No ()2
Financially	Independent Partially dependent
	Dependent

Demography		
Date of birth		Age:
Gender	Male \bigcirc 1 Female \bigcirc 2	
Age in years	60-69 (young old)*	Yes ()1 No ()2
National policy for	70-79 (old old)	Yes ()1 No ()2
older person year 1999,	>80 (older old)*	Yes ()1 No ()2
Ministry of Social Justice		
and empowerment		
SOCIOECONOMIC	Lower class <11 (0-10)	Yes 🗋 1 No 🔵 2
STATUS	(Modified Kuppuswamy socioe	conomic status scale)

- ·			
Drimary	admiccion	diagnoci	· ·
FILLALV	aumission	UIDELIUSE) .
· · · · · · · · · · · · · · · · · · ·			

Premorbid Barthel index (0-20)	
BARTHELS INDEX Collin et al 1988	
Bowels	Mobility
0 = incontinent (or needs to be given	0 = immobile
enemata)	1 = wheelchair independent, including
1 = occasional accident (once/week)	corners
2 = continent	2 = walks with help of one person
	3 = independent (but may use any aid,
Bladder	e.g., stick)
0 = incontinent, or catheterized	
1 = occasional accident (max. once per 24	Transfer
hours)	0 = unable – no sitting balance
2 = continent (for over 7 days)	1 = major neip
Creaming	2 = minor neip (verbai or physical)
Grooming	3 = Independent
0 = needs neip with personal care	Drossing
	0 - dependent
Bathing	1 - needs help, but can do about half
0 = dependent	unaided
1 = independent (or in shower)	2 = independent (including buttons zins
	laces)
Toilet use	
0 = dependent	Stairs
1 = needs some help, but can do	0 = unable
something alone	1 = needs help (verbal, physical, carrying
2 = independent (on and off, dressing,	aid)
wiping)	2 = independent up and down
Feeding	
U = unable	
1 = needs neip cutting, spreading butter,	
2 - independent (food provided within	
reach)	

SOFA SCORE

0	rgan system			0	1	2	3		4	
RE	SPIRATION	Ра	02/FiO2	>400	≤400	≤300	≤2	00	≤100	
	Eye Response		Spontanec	ous eye oper		4 points				
			Opens to v	verbal comm	nand, speed		3 poii	nts		
		Opens to p	oain, not app	olied to face	5		2 poii	nts		
	No eye opening							1 poir	nt	
	Verbal		Alert and o	oriented				5 poii	nts	
	Response		Confused of	conversatio	n, but able t	to answer		4 poii	nts	
			questions							
			Inappropri	ate respons	es, jumbled	d phrases, but		3 poii	nts	
			discernible	e words						
			Incompreh	nensible spe	ech			2 poii	nts	
	• • •		No sounds			<u> </u>		1 poir	nt .	
	Motor		Obeys com	nmands for	movement	fully		6 poi	nts	
	Response		Localizes to				5 poli			
			Abnormal	flovion doc	orticato no		4 poi			
Abnormal f			nexion, dec	corobrato r		2 poi	its atc			
			No respon	esponse, de		Josturing		2 poi	nt	
				1 01 000	50.000-	21				
11/		F IC		0	-	1 00 000	50	,000-	20 000	
				0	1.50.000	2,00,000		,000	20,000	
Н	EPATIC	Bil	irubin	<1.2mg/	1.2-1.9	2.0-5.9	6.0)-	>12	
				dl			11	.9		
C	NS	GC	S	15	13-14	10-12	6-9	9	<6	
CA	ARDIOVASCUL	M	٩P	≥70	<70	Dopa≤5mcg	Do	pa 5-	Dopami	
						/kg/min or	14	.9	ne ≥15	
						Dobut any	or		Or	
				dose	Ep	ineph	Epinep			
					<0	.1	h >0.1			
					NC	orAdr	or			
					<0	.⊥				
P	ΝΛΙ	Cr	atinina	<1 2mg/	1 2_1 0	2_34	2 [5_1 0	>0.1	
				√1.∑IIIR\ ∕1.∑IIIR\	1.2-1.3	23.4	3.5	7-4.3	~J	
		Ur	ine				<5	00ml	<200ml	
Ou		itput/24hr						-200111		

Vicent et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: Results of a multicenter, prospective study. Crit Care Med, 26:1793-1800, 1998.

APACHE II Score:

Critical care Medicine 1985 Oct; 13 (10): 818-29

APACHE II Score: Predicted Mortality:								
Temprature	105.8F	102.2-	101.3-	96.8-	93.2-	89.6	86.0-	<86.0
		1.5.7	102.1	101.2	96.7	-	89.5	F
						93.1		
MAP	>160	130-	110-	70-	50-69	<50		
		159	129	109				
Heart rate	>180	140-	110-	70-	55-69	40-	<40	
		179	139	109		54		
Respiratory rate	>50	35-49	25-34	12-24	10-11	6-9		
Oxygenation	A-	A-a	A-a	A-a	PaO2	PaO	PaO2	PaO2
	a>500	350-	200-	<200	>70	2	55-	<55
	FiO2	499	349	FiO2	FiO2	61-	60	FiO2
	>0.5	FiO2	FiO2	>0.5	<0.5	70	FiO2	<0.5
		>0.5	>0.5			FiO2	<0.5	
						<0.5		
Serum Bicarbonate	>52	41-	32-	22-	18-	15-	<15	
		51.9	40.9	31.9	21.9	17.9		
Arterial pH	>7.7	7.60-	7.50-	7.33-	7.25-	7.15	<7.1	No
		7.69	7.59	7.49	7.32	-	5	ABG
						7.24		data
Serum Sodium	>180	160-	155-	150-	130-	120-	111-	<111
(Na+)		179	159	154	149	129	119	
Serum Potassium	>7	6.0-	5.5-	3.5-	3.0-	2.5-	<2.5	
(K+)		6.9	5.9	5.4	3.4	2.9		
Serum Creatinine	>3.39	1.98-	1.47-	0.62-	<0.62			
		3.38	1.97	1.46				
AKI Yes or No	Yes	No						
Hematocrit	>60%	50-	46-	30.0-	20.0-	<20		
		59.9%	49.9	45.9	29.9			
WBC	>40,00	20,00	16,00	15,00	3000-	1000	<100	
	0	0-	0-	0-	14,90	-	0	
		39,90	19.90	15.90	0	2900		
		0	0	0				
GCS								
Age	>75	65-74	55-64					

History of severe	Yes	No			
organ dysfunction					
or					
Immunocompromi					
sed state					
Post Operative	Yes	No			

Corticosteroid use/immunomodulators use: Yes O1 No O0

Serum lactate _____

HBA1c_____

		Yes (1)
Clinical presentation	Fever >100.9°F	
	Hypothermia	
	<96.8°F	
	Heart rate >90bpm	
	Tachypnea >20/min	
	GCS score<8	
	Altered mental status (CAM score) – score >4	
	Hypotension MAP<65 (Katz ED, Ruoff BE. Commonly Used Formulas and Calculations. In: Roberts: Clinical Procedures in Emergency Medicine. 4th ed. Elsevier Mosby Publishing; 2004:1434.)	
Severity assessment at	SOFA score	
admission	APACHE II Score	

	Leukocytosis		
	W/RC >	•	
	12 000/cum	m	
		cumm	
	ESD>20mm/	hr	
	CDD Scmald	(
	CRP >0mg/d	1	
	Procalciton	<0.1n	
	in level	g/di	
		0.1 - 0.24	
		0.24n	
		g/di	
		0.25 -	
		0.5ng	
		/dl	
		>0.5n	
		g/dl	
	Thrombocyt	openia	
	<100,000/cu	IMM	
	Internationa	1	
	Normalized	r Ratio N	
	1 1		
	Activated		
	Prothrombin	Time	
	>42sec	· · · · · · ·	
	Albumin >3	5mg/dl	
Charlson comorbidity index	,	5 <u>9</u> / 41	
http://www.ncbi.nlm.nih.gov/			
pubmed/3558716			
Plus 1 point for every decade			
Plus I point for every decade			
age 50 years and over,			
maximum 4 points.			
Total score:			1
Addictions	Smoking tob	ассо	
	pack years >	15	
	(http://www	.cance	
	r.gov/diction	nary?C	
	drID=30651	0 Nati	
	onal Cance	r	
	Institute de	finition	

	of pack year)	
	Present Alcohol	
	intake	
	others	
	Other addictions:	
	specify	
	. ,	
SOURCE OF INFECTION	Pulmonary	
	infection	
	Urinary tract	
	Skin	
	Central nervous	
	system	
	, Musculoskeletal	
	Para-nasal sinus	
	infection	
	Genital infection	
	Heart valves	
	GI tract	
	Others: specify:	
	Unknown source of	
	infection	
ANTIBIOTIC STEWARDSHIP	Organism identified	
	Snecify:	
	opeeny)	
	Previous antibiotic	
	exposure	
	Blood culture	
	positive	
Source reduction via invasive m	ethods executed:	Yes
Organism 2 identified:		
COURSE IN THE HOSPITAL	Ventilator	
	Inotropes	-
	- How many	
	davs on	
	inotropes?	
	- Number of	
	inotropes	
	used?	
	Blood products	
	- Blood products	

	used	
	- Number of	
	products used	
	Ventilator days	
	>5days	
	VAP	
	NIV days >5days	
	Dialysis	
Hospital stay	Total hospital stay	
	>15days	
	Total ICU stay	
	>5days	
Hospital bill	Total Expense	
	>60,000Rs	
OUTCOME		
- If survived	BARTHEL INDEX if	
	survived	
	Bowels	
	0 = incontinent (or needs to be	
	given enemata)	
	1 = occasional accident	
	(once/week)	
	2 = continent	
	Bladder	
	0 = incontinent, or catheterized	
	1 = occasional accident (max.	
	once per 24 hours)	
	2 = continent (for over 7 days)	
	Grooming	
	0 = needs help with personal	
	care	
	1 = independent	
	face/hair/teeth/shaving	
	, , , 0	
	Bathing	
	0 = dependent	
	1 = independent (or in shower)	
	Toilet use	
	0 = dependent	

 1 = needs some help, but can do something alone 2 = independent (on and off, dressing, wiping) Feeding 0 = unable 1 = needs help cutting, spreading butter, etc. 2 = independent (food provided within reach) 	
Mobility 0 = immobile 1 = wheelchair independent, including corners 2 = walks with help of one person 3 = independent (but may use any aid, e.g., stick) Transfer 0 = unable – no sitting balance 1 = major help 2 = minor help (verbal or physical) 3 = independent	
Dressing 0 = dependent 1 = needs help, but can do about half unaided 2 = independent (including buttons, zips, laces) Stairs 0 = unable 1 = needs help (verbal, physical, carrying aid) 2 = independent up and down	

Complications in the hospital	No complications	
	Bleedin	GI
	g	
		Hemopty
		sis
		Urogenit
		al
		Others
	CVA	
	Myocard	ial
	infarctior	า
	Hospital a	acquired
	Infection	
	Venous	
	thrombo	embolism
	Others: S	pecify

MODIFIED KUPPUSWAMY SCORE FOR SOCIOECONOMIC SCALE

EDUCATION OF HEAD OF FAMILY	SCORE
PROFESSION OR HONORS	7
GRADUATE	6
POST HIGH SCHOOL DIPLOMA	5
HIGH SCHOOL CERTIFICATE	4
MIDDLE SCHOOL CERTIFICATE	3
PRIMARY SCHOOL CERTIFICATE	2
LITERATE	1
OCCUPATION OF HEAD OF FAMILY	
PROFESSION	10
SEMIPROFESSION	6
CLERICAL OR SELF OWNED SHOP	5
SKILLED WORKER	4
SEMI SKILLED WORKER	3
UNSKILLED WORKER	2
UNEMPLOYED	1
MONTHY INCOME OF FAMILY (2017)	
>41430	12
20715-41429	10
15536-20714	6
10357-15535	4

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6214-10356	3
2092-6213	2
<2091	1
TOTAL SCORE	
26-29 UPPER(I), 16-25 UPPER MIDDLE(II), 11-15 LOWER N	IIDDLE(III), 5-
10 UPPER LOWER(IV), <5 LOWER (V)	

APPENDIX 4 – BARTHEL INDEX

Bowels

- $\overline{0}$ = incontinent (or needs to be given enemata)
- 1 = occasional accident (once/week)
- 2 = continent

Patient's Score	
	_

<u>Bladder</u>

0 = incontinent, or catheterized and unable to manage 1 = occasional accident (max. once per 24 hours)

2 = continent (for over 7 days)

Patient's Score:

Grooming

0 = needs help with personal care 1 = independent face/hair/teeth/shaving (implements provided)

Patient's Score: _____

<u>Toilet use</u>

0 = dependent

1 = needs some help, but can do something alone 2 = independent (on and off, dressing, wiping)

Patient's Score: _

Feeding

0 = unable

- 1 = needs help cutting, spreading butter, etc.
- 2 = independent (food provided within reach)

Patient's Score: _____

Transfer

- 0 = unable no sitting balance
- 1 = major help (one or two people, physical), can sit
- 2 = minor help (verbal or physical)
- 3 = independent

Patient's Score:

Mobility

- 0 = immobile
- 1 = wheelchair independent, including corners, etc.
- 2 = walks with help of one person (verbal or physical)
- 3 = independent (but may use any aid, e.g., stick)

Patient's Score:

Dressing

0 = dependent

1 = needs help, but can do about half unaided

2 = independent (including buttons, zips, laces, etc.)

Patient's Score:

<u>Stairs</u>

- 0 = unable
- 1 = needs help (verbal, physical, carrying aid) 2 = independent up and down

Patient's Score:

Bathing

0 = dependent 1 = independent (or in shower) *Patient's Score:*

Total Score: _____

APPENDIX 5 – CHARLSON COMORBIDITY INDEX

VARIABLE	POINTS
60-69 years of age	2
70-79 years of age	3
80 years and above	4
Myocardial Infarction	1
Congestive Cardiac Failure	1
Peripheral Arterial Occlusive Disease	1
Cerebro-vascular accident	1
Hemiplegia	2
Dementia	1
Chronic Obstructive Pulmonary Disease	1
Connective Tissue Disorder	1
Peptic Ulcer	1
Mild liver disease (without portal hypertension)	1
Liver disease with portal hypertension or cirrhosis	3
Uncomplicated diabetes mellitus	1
Diabetes mellitus with complications	2
Moderate to severe chronic kidney disease (creatinine > 3 or on dialysis)	2
Localised solid tumor	2
Metastatic solid tumor	6
Leukemia	2
Lymphoma	2
HIV-AIDS	6

Source: MD+ CALC

APPENDIX 6 – KUPPUSWAMY SOCIOECONOMIC SCALE

Table 1: Modified Kuppuswamy scale (proposed updating for January 2017).

Education of head of family	Score
Profession or honours	7
Graduate or postgraduate	6
Intermediate or post high school diploma	5
High school certificate	4
Middle school certificate	3
Primary school certificate	2
Literate	1
Occupation of head of family	
Profession	10
Semi-profession	6
Clerical, Shop-owner	5
Skilled worker	4
Semi-skilled worker	3
Unskilled worker	2
Unemployed	1
Monthly income of family	

e nompro y e a				•
Monthly income of fai	mily			
In 1976	In 1998	In 2007	In 2017 (January 2017 CPI)	
>=2000	13408	19844	>41430	12
1000-1999	6704-13407	9922-19843	20715-41429	10
750-999	5028-6703	7441-9921	15536-20714	6
500-749	3352-5027	4961-7440	10357-15535	4
300-499	2011-3351	2976-4960	6214-10356	3
101-299	677-2010	1002-2975	2092-6213	2
<=100	<676	<1001	<2091	1
Socioeconomic class				Total score
Ι	Upper			26-29
II	Upper middle			16-25
III	Lower middle			11-15
IV	Upper lower			5-10
V	Lower			<5

APPENDIX 7 – GLASGOW COMA SCALE

Component	Response	Points
	Eves open spontaneously	+4
	Eye opening to verbal command	+3
Eye	Eye opening to pain	+2
	No eye opening	+1
	Not testable*	NT
	Oriented	+5
Verbal	Confused	+4

	Inappropriate words	+3
	Incomprehensible sounds	+2
	No verbal response	+1
	Not testable*	NT
Motor	Obevs commands	+6
	Localizes pain	+5
	Withdrawal from pain	+4
	Flexion to pain	+3
	Extension to pain	+2
	No motor response	+1
	Not testable*	NT

APPENDIX 8 – SOFA SCORE

Variable	Points			
PaO ₂ /FiO ₂ , mmHg				
≥400	0			
300-399	+1			
200-299	+2			
100-199 and mechanically ventilated	+3			
<100 and mechanically ventilated	+4			

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Platelets, $\times 10^{3}/\mu L$				
≥150	0			
100-150	+1			
50-99	+2			
20-49	+3			
<20	+4			
Glasgow Coma Scale				
15	0			
13–14	+1			
10–12	+2			
6–9	+3			
<6	+4			
Bilirubin, mg/dL (µmol/L)				
<1.2 (<20)	0			
1.2–1.9 (20-32)	+1			
2.0–5.9 (33-101)	+2			
6.0–11.9 (102-204)	+3			
≥12.0 (>204)	+4			
Mean arterial pressure OR administration of vasoactive agents required (listed doses are in units of mcg/kg/min)				
No hypotension	0			
MAP <70 mmHg	+1			
DOPamine ≤5 or DOBUTamine (any dose)	+2			
DOPamine >5, EPINEPHrine ≤ 0.1 , or norEPINEPHrine ≤ 0.1	+3			
DOPamine >15, EPINEPHrine >0.1, or norEPINEPHrine >0.1	+4			
Creatinine, mg/dL (µmol/L) (or urine output)				
<1.2 (<110)	0			
1.2–1.9 (110-170)	+1			
2.0–3.4 (171-299)	+2			
3.5–4.9 (300-440) or UOP <500 mL/day)	+3			
≥5.0 (>440) or UOP <200 mL/day	+4			

SOFA Score	Mortality if initial score	Mortality if highest score
0-1	0.0%	0.0%
2-3	6.4%	1.5%
4-5	20.2%	6.7%
6-7	21.5%	18.2%
8-9	33.3%	26.3%
10-11	50.0%	45.8%
12-14	95.2%	80.0%
>14	95.2%	89.7%
Mean SOFA Score		Mortality
0-1.0		1.2%
1.1-2.0		5.4%
2.1-3.0		20.0%
3.1-4.0		36.1%
4.1-5.0		73.1%
>5.1		84.4%

Source: MD+ CALC
APPENDIX 9 – APACHE SCORE

Criteria	Point values
Age, years	
<u>≤</u> 44	0
45-54	+2
55-64	+3
65-74	+5
>74	+6
History of severe organ insufficiency or immunocomp	omised
Yes, and nonoperative or emergency postoperative patient	+5
Yes, and elective postoperative patient	+2
No	0
Rectal temperature, °C	
≥41	+4
39 to <41	+3
38.5 to <39	+1
36 to < 38.5	0
34 to <36	+1
32 to <34	+2
30 to <32	+3
<30	+4
Mean arterial pressure, mmHg	
>159	+4

>129-159	+3
>109-129	+2
>69-109	0
>49-69	+2
<u>≤</u> 49	+4
Heart rate, beats per minute	
≥180	+4
140 to <180	+3
110 to <140	+2
70 to <110	0
55 to <70	+2
40 to <55	+3
<40	+4
Respiratory rate, breaths per minute	
<u>≥</u> 50	+4
35 to <50	+3
25 to <35	+1
12 to <25	0
10 to <12	+1
6 to <10	+2
<6	+4
Oxygenation (use PaO2 if FiO2 <50%, otherwise use A	-a gradient)
A-a gradient >499	+4
A-a gradient 350-499	+3

A-a gradient 200-349	+2
A-a gradient <200 (if FiO2 over 49%) or pO2 >70 (if FiO2 less than 50%)	0
$PaO_2 = 61-70$	+1
$PaO_2 = 55-60$	+3
PaO ₂ <55	+4
Arterial pH	
≥7.70	+4
7.60 to <7.70	+3
7.50 to <7.60	+1
7.33 to <7.50	0
7.25 to <7.33	+2
7.15 to <7.25	+3
<7.15	+4
Serum sodium, mmol/L	
≥180	+4
160 to <180	+3
155 to <160	+2
150 to <155	+1
130 to <150	0
120 to <130	+2
111 to <120	+3
<111	+4
Serum potassium, mmol/L	

≥7.0	+4
6.0 to <7.0	+3
5.5 to <6.0	+1
3.5 to <5.5	0
3.0 to <3.5	+1
2.5 to <3.0	+2
<2.5	+4
Serum creatinine, mg/100 mL	
≥3.5 and ACUTE renal failure*	+8
2.0 to <3.5 and ACUTE renal failure	+6
\geq 3.5 and CHRONIC renal failure	+4
1.5 to <2.0 and ACUTE renal failure	+4
2.0 to <3.5 and CHRONIC renal failure	+3
1.5 to <2.0 and CHRONIC renal failure	+2
0.6 to <1.5	0
<0.6	+2
Hematocrit, %	
≥60	+4
50 to <60	+2
46 to <50	+1
30 to <46	0
20 to <30	+2
<20	+4
White blood count, total/cubic mm in 1000's	

≥40	+4
20 to <40	+2
15 to <20	+1
3 to <15	0
1 to <3	+2
<1	+4
Glasgow Coma Scale (GCS)	
1 15	15 - [GCS
1 - 15	Score]

APPENDIX 10 – CRITERIA FOR SYSTEMIC INFLAMMATORY RESPONSE SYNDROME (SIRS). ADAPTED FROM MCCLELLAND H AND MOXON A (2014) [9].

Systemic Inflammatory Response Syndrome

Temperature >38.3°C, or <36°C

Heart Rate >90 bmp

Respiratory rate >20 breaths/min

White cell count <4 or >12 g/L

Blood glucose >7.7 mmol/L not diabetic

New altered mental state

APPENDIX 11 – EXCEL SHEET – RAW DATA FROM STUDY

sino	irbno	subjectid	hospho	dent	doa	dod	totdays	admitfror	adminitia	al ward?ici	readmic	financial	979	gender	educat	occup	income	sessoore	class	bowels	bladder	grooming	bathing
1	11039	subjectiu 1	221635h	dept 2	2 ####################################	400 ##########	34	2	auminitia 2	2	2 2	2 3	age 3 6	i3	1 i	2 5	5 6	13	3	2 2	2	grooming 1	batning 1
2	11039	2	183904H	2	2 ########	*****	14	1	2	2	1 2	2 1	1 6	8	2	1 3	3 4	8	4	2	1	1	1
3	11039	3	153512H 353037h	2	L ######### 2 #########	******	21	1	2	2	2 2	2 3	3 b 3 6	5	2	3 6	5 10 5 6	15	3	2	2	1	1
5	11039	5	772833c	2	2 ########	*****	7	1	2	2	1 2	2 8	3 6	8	1 :	2 8	3 3	8	4	2	2	1	1
6	11039 11039	6	577200d 354740h	1	L ######### 2 #########	******	24	1	2	2	2 2	2 3	36 37	3	1 :	2 2	23	8	4	2	2	1	0
8	11039	8	902057A	1	L ########	****	13	1	2	2	2 2	2 3	3 7	6	2	3 4	1 6	13	3	2	1	0	0
9	11039	9	357342H	2	2 ####################################	******	6	1	1	1	2 2	2 1	26	5	1	3 3	3 6	12	3	2	2	1	1
11	11039	11	070900G	1	L #########	*****	16	1	2	2	2 2	2 3	37	1	1 1	3 3	3 3	9	4	2	2	1	1
12	11039	12	121800D	1	L ########	*****	14	1	2	2	2 2	2 2	2 6	1	2	3 4	4	11	3	2	2	1	1
13	11039	13	450734H	2	2 ********	*****	4	2	2	2	1 2	2 3	s 0 3 6	5	1 4	o : 4 4	s 4 1 4	12	3	2	2	1	1
15	11039	15	568804	2	2 ########	****	18	1	1	1 :	2 2	2 2	2 7	2	1 4	4 (5 6	16	2	2	2	1	0
16	11039 11039	16	232274h 031805D	1	L ######### > ##########	******	17	1	2	2	2 1	2 1	1737	2	1 . 2 ·	56	5 3	14	3	2	2	1	1
18	11039	18	019093	1	L #########	*****	3	1	1	1	2 1	2 1	2 8	0	2 !	5 6	5 4	15	3	2	2	1	1
19	11039	19	568377F	2	2 ####################################	******	13	1	1	1	2 2	2 2	27	0	1	5 2	2 10	18	2	2	2	1	1
21	11039	21	495315B	2	2 ########	*****	22	1	1	1	2 2	2 3	3 6	1	1 4	4 4	1 6	10	3	2	2	1	1
22	11039	22	935868A	1	L #########	*****	26	1	2	2	2 2	2 8	3 8	6	2 :	3 2	2 10	15	3	2	1	1	1
23	11039	23	569196H	2	2 ####################################	******	10	1	1	1	2 2	2 3	s / 3 7	0 . 10 :	1 4	4 10) 10	20	1	2	2	1	1
25	11039	25	457164H	1	L ########	*****	15	3	2	2	2 2	2 8	3 8	0	2 .	5 6	5 10	21	2	2	1	1	1
26	11039 11039	26	136474A 229501C	2	L ######### 2 #########	*****	14	2	2	2	2 1	2 3	39 26	9	2	2 3	5 10 3 3	21	2	2	2	1	0
28	11039	28	456841H	2	2 #########	*****	17	1	2	2	1 1	L :	3 6	5	1 :	2 2	2 3	7	4	2	2	1	1
29	11039	29	457294H 585523G	2	2 ####################################	*****	25	1	2	2	1 1	L 1	27	76 : 2	1	3 4	1 4	11	3	2	2	1	1
31	11039	31	231402h	2	2 ########	****	14	1	2	2	1 2	2 3	3 6	9	1 4	4 5	5 4	13	3	2	2	1	1
32	11039	32	561848H	2	2 #########	******	42	1	2	2	1 2	2 3	3 6	6	2.	5 6	5 10	21	2	2	2	1	1
34	11039	34	750378D	2	2 #########	*****	15	1	1	1	2 2	2 3	3 6	9	1 !	5 5	5 6	16	2	2	2	1	1
35	11039	35	680046H	1	L ########	****	6	2	2	2	2 2	2 :	3 7	3	1 4	4 (5 6	16	2	2	2	1	1
36	11039	36	972299G 939942G	2	L ####################################	******	2/	1	2	2	2 1	2 3	3/ 36	7	1	2 2	23	7	4	2	2	1	1
38	11039	38	603388D	2	2 #########	*****	12	1	1	1 :	2 2	2 8	3 6	2	2 :	3 3	3 3	9	4	2	2	1	1
39	11039	39	958029f	2	2 ########## 	******	34	2	2	2	1 1		3 7	2	1 4	4 5	5 10	19	2	2	2	1	1
40	11039	40	105613g	2	2 #########	*****	9	1	2	2	1 1	2 3	3 6	1	1	3 5	5 4	12	3	2	2	1	1
42	11039	42	518715d	2	2 #########	*****	23	1	2	2	1 1	2 8	3 6	1	2 4	4 6	5 10	20	2	2	2	1	0
43	11039	43	072161A 054904	2	2 ########	*****	13	1	2	2	1 2	2 3	s / 2 8	4	1 4	4 5	o 0 5 6	13	3	2	1	1	1
45	11039	45	194556F	2	2 ########	****	3	1	2	2 :	2 2	2 8	3 6	6	1 !	5 10) 10	25	2	2	2	1	1
46	11039	46	186325H 183067H	2	2 ########## 2 ##########	******	3	1	1	2	1 1	2 2	36 27	4	1 4	4 <u>5</u> 2 4	5 4 1 4	13	3	2	2	1	0
48	11039	48	186881H	2	2 ########	*****	24	1	1	1	2 2	2 3	3 7	1	1 4	4 6	5 6	16	2	2	2	1	1
49	11039 11039	49	186732h 297890G	2	2 ######### > #########	******	25	1	1	1	2 2	2 3	3 6	7 2	1	3 3	3 4 3 4	10	4	2	2	1	1
51	11039	51	187824H	2	2 ########	*****	2	1	1	1	2 2	2	3 7	8	2	3 3	3 3	9	4	2	2	1	1
52	11039	52	188400H	2	2 ######### 1 ##########	******	52	1	1	1	2 2	2 3	3 6	6	2	3 4 5 10	1 3 10	10	4	2	2	1	1
54	11039	54	188716H	2	2 ########	*****	5	1	2	2	2 3	3	27	19	1	5 6	5 6	17	2	2	2	1	1
55	11039	55	329636B	2	2 ########	*****	23	1	1	1	2 2	2 3	3 6	7	1 4	4 5	5 4	13	3	2	2	1	1
57	11039	57	035619D	2	2 ####################################	*****	8	1	1	1	2 1	2 3	s 0 3 6	6	1 4	4 5	5 0 5 4	17	3	2	2	1	1
58	11039	58	041511F	1	L ########	****	26	2	2	2	2 2	2 :	3 6	9	1 4	4 5	5 10	19	2	2	2	1	1
59	11039	59 60	189672H 314291H	2	2 ######## 2 #########	******	1/	1	1	1	2 2	2 3	3 6 2 6	2	1 1	3 : 3 4	5 6 1 10	12	3	2	2	1	1
61	11039	61	311158H	2	2 ########	*****	26	1	2	2	1 2	2 3	3 6	9	1 4	4 4	4 4	12	3	2	2	1	1
62	11039 11039	62 63	189848H 350658H	2	2 ######### 7 ##########	******	12	1	2	2	1 2	2 3	36 36	4 2	1	3 5 1 6	5 6 5 6	14	3	2	2	1	1
64	11039	64	550058B	2	2 #########	*****	12	1	1	1	2 1	2 8	3 6	6	1	3 3	8 6	12	3	2	2	1	1
65	11039	65	351063H	2	2 ####################################	******	4	1	2	2	1 2	2 3	8 8	3	1 .	5 6	5 10	21	2	2	2	1	0
67	11039	67	567548	1		******	4	1	2	2	2 2	2 2	- 0 2 7	7	1 3	5 5	. 4 5 10	20	2	2	2	1	1
68	11039	68	351324H	2	2 ########	*****	13	1	2	2	1 3	2 3	3 6	2	2	3 2	2 4	9	4	2	2	1	1
70	11039	70	351525H	2	2 #########	*******	18	1	2	2	1 2	2 3	3 6	0	1	3 3	. 6 3 4	10	4	2	2	1	1
71	11039	71	099410g	2	2 ########	*****	8	1	2	2	2 2	2 3	3 7	1	1	3 4	4	11	3	2	2	1	1
72	11039	72	553849F	2	2 ####################################	******	25	1	1	1	2 1	2 2	, 7 2 6	4	1	3 5	, 3 5 6	9	3	2	2	1	1
74	11039	74	351597H	2	2 #########	****	9	1	1	1	2 2	2 2	2 7	5	1	3	6	12	3	2	2	1	1
75	11039 11039	75	370783D 307463b	2	2 ####################################	******	4	1	1	1	2 2	2 3	37 38	0 4	1	3 5	563	14	3	2	2	1	1
77	11039	77	125583A	1	L #########	*****	26	2	2	2	1 2	2 8	3 7	8	2 (5 (5 10	22	2	2	2	1	0
78	11039	78 79	079084B 352392H	2	2 ######### 	******	12	1	1	1	2 1	2 3	3737	10 : 7 ·	2 4	4 3 5 4	3 4 1 6	11	3	2	2	1	1
80	11039	80	352710H	2	2 ########	*****	4	1	2	2	1 2	2	3 6	3	1	3 2	2 4	9	4	2	2	1	1
81	11039	81	619956	2	2 ########	*****	24	1	2	2	1 2	2 8	3 7	6	2 :	7 10) 12	29	1	2	1	1	0
83	11039	83	353023H	2	2 ##########	*****	19	1	1	1	2 2	2 3	3 6	0	1 (+ . 5 (5 4 5 10	22	2	2	2	1	1
84	11039	85	671702F	2	2 ########	****	8	2	2	2	2 2	2 2	2 6	6	1 4	4 2	2 3	9	4	2	2	1	1
85	11039 11039	85 86	541119F 068410G	2	2 ######### 2 #########	******	9	1	1	2	1 2 2 3	2 3	5 6 3 6	8	1 : 1	2 2	2 4 5 6	14	4	2	2	1	1
87	11039	87	450455H	2	2 ########	*****	5	1	1	1	2 2	2 3	3 7	2	2 .	5 4	1 4	13	3	2	2	1	1
88	11039	88	349028	2	2 ######### ##########	*****	7	2	1	1	2 2	2 3	3 6	ю и	2	5 5	5 10	20	2	2	2	1	1
90	11039	90	353087H	2	2 #########	*******	34	1	2	2	1 2	2 3	3 7	5	2 3	5 5	, 0 5 6	15	2	2	2	1	1
91	11039	91	353990h	2	2 ########	****	2	1	1	1	2 2	2 8	3 6	0	2 4	4 4	4	12	3	2	2	1	1
92	11039 11039	92 93	309965F 354423H	2	2 ######### 2 #########	******	3	1	1	1	2 2	2 3	s 8 3 8	8 6	2 : 1 4	s 5 4 4) 6 1 6	14	3	2	2	1	1
94	11039	94	455423H	2	2 ########	****	8	1	2	2	2 2	2 3	3 7	5	1	5 6	5 10	21	2	2	2	1	1
95	11039	95	074456D	2	2 ######### ###########	******	41	1	1	1	2 1	L 1	2 7	5	1	5 6 5 4	5 10 5 10	22	2	2	2	1	1
97	11039	97	170567B	2	2 #########	****	9	1	1	1	2 2	2 3	3 6	3	2	5 (5 10	20	2	2	2	1	1
98	11039	98	357342H	2	2 ########	****	6	1	2	2	1 2	2 2	2 6	5	1 !	5 (5 10	21	2	2	2	1	1
99	11039	99	287301	2	۳۳#######	*****	12	2	2	4	1 S	4) ŝ	7 וי	2 .	4	+ 3	6	13	3	j 2	2	1	1

100	11039	100 357304H	2 #########		12	1	2	1	2	2 72	1	4	5	10	19	2		2	2	1	1
101	11039	101 357680H	2 #########		15	1	1	2	2	3 71	2	4	4	6	14	3		2	2	1	1
101	11020	102 2621694	2 *******		22	1	2	1	2	2 62	- 1		-	10	20				2	1	1
102	11035	102 5021098	2 ********		22	1	2		2	3 02	1	5	3	10	20	2		2	2	1	1
103	11039	103 1418308	2 #########	*****	30	1	2	1 .	2	3 09	1	4	3	4	11	5	-	2	2	1	1
104	11039	104 450725H	2 #########	*******	3	1	1	2	2	3 63	2	4	5	4	13	3	2	2	2	1	1
105	11039	105 450738H	2 ########	*******	7	1	1	2	2	3 60	1	4	6	6	16	2	2	2	2	1	1
106	11039	106 594234A	2 #########	*****	9	2	2	2	2	3 66	1	3	3	4	10	4	2	2	2	1	1
107	11039	107 451011H	2 #########	*****	8	1	1	2	2	3 74	1	5	6	10	21	2	1	2	2	1	1
108	11039	108 353456H	2 #########	*****	44	1	1	2	1	3 65	1	3	5	6	14	3	1	2	1	0	0
109	11039	109 0210240	2 #########		7	1	1	2	2	1 69	2	3	4	4	11	3		2	2	1	1
110	11029	110 451070b	2 ##########		6	1	1	2	2	2 72	1	2		6	12	2		2	2	1	1
110	11035	111 2070206	2 ****		2	1	1	2	2	3 72	-	2	-	6	14			2	2	1	1
111	11039	111 2070890	2 ******	******	2	1	1 .	2	2	5 70	2	3	5	0	14	3	-	2	2	1	1
112	11039	112 267056c	2 #########	*******	29	1	1	2	2	3 78	1	5	5	10	20	2	2	2	2	1	1
113	11039	113 452450H	2 #########	*****	1	1	1	2	2	3 78	1	3	2	3	8	4	2	2	2	1	1
114	11039	114 338830B	2 #########	*****	6	1	2	1	2	3 61	1	4	5	10	19	2		2	2	1	1
115	11039	115 451525H	2 #########		30	2	2	1	2	3 73	1	3	3	4	10	4		2	2	1	1
115	11030	115 0271904	1		20	2	2	2	2	2 02	2	5	10	10	26	1			1	0	-
110	11039	110 037180A	1 ********	• ••••	5	2	2	2	2	3 82	2	0	10	10	20	1		2	1	U	U
117	11039	117 454128H	2 #########	*****	43	1	1	2	2	3 67	1	5	5	2	12	3		2	2	1	0
118	11039	118 454561H	2 ########	*****	12	1	1	2	2	2 78	1	6	10	10	26	1	2	2	2	1	1
119	11039	119 93515B	2 ########	*****	24	1	2	1	2	3 79	1	6	10	10	26	1	2	2	2	1	1
120	11039	120 621896	2 #########		29	1	2	1	2	3 76	1	2	3	3	8	4		,	2	1	1
121	11029	121 0992790	2 *****		5	1	2	2	2	2 65	-	4	5	6	15			2	2	1	1
121	11035	121 0302700	2		5	1	2	2	2	3 00	2	4	5		15	3	-		2	1	1
122	11039	122 454798H	2 #########	*******	12	1	2	2	2	3 /5	1	3	3	4	10	4		2	2	1	1
123	11039	123 455019H	2 #########	******	10	1	1	2	1	2 75	1	4	5	10	19	2	1	2	2	1	1
124	11039	124 163898G	1 #########	******	32	3	2	2	2	1 78	1	5	3	12	20	2	1	2	2	1	1
125	11039	125 455519H	2 #########	******	13	1	2	1	2	3 62	1	4	4	6	14	3	1	2	2	1	1
126	11039	126 455519H	2 ##########		13	1	2	1	2	3 62	1	5	5	4	14	3		2	2	1	1
127	11020	107 4556700	2			1	1	2	2	2 72		-	-		14			-	2	1	1
127	11035	127 40007011	2			-	-	2	2	3 75	1	-		40	14			2	2		1
128	11022	120 0578948	1 #########	*********	4	3	2	<u> </u>	<u> </u>	2 95	1	/	10	12	29	1	1 3	-	-	1	1
129	11039	129 739475h	1 ########	*****	9	2	2	2	2	1 60	1	6	10	12	28	1	1 1	2	2	1	1
130	11039	130 393936c	2 ########	******	5	1	1	2	2	3 62	2	3	2	6	11	3	2	2	2	1	1
131	11039	131 455922H	2 #########	******	17	1	2	1	2	1 74	1	7	10	12	29	1		2	2	1	1
132	11039	132 589580C	2 #########		12	1	2	1	2	3 66	1	3	3	3	9	4		2	2	1	1
102	11020	122 2160020	1 ********		4	2	2	2	2	2 64	4	3	5	é	10	4	1	2	2	1	1
133	11039	100 210002H	1 *******	*******	4	4	4	4	4	3 04	1	4	5	0	51	3	- · ·	2	4	*	4
134	11039	134 709592c	2 #########	*****	11	1	1	2	2	∠ 86	1	4	5	6	15	3	'	۷	4	1	1
135	11039	135 456841H	2 ########	******	17	1	2	1	2	3 65	1	4	3	4	11	3	3	2	2	1	1
136	11039	136 808265B	2 ########	******	5	1	2	1	2	3 69	2	4	5	6	15	3	1	2	2	1	1
137	11039	137 457470H	2 ########	*****	7	1	1	2	2	3 64	2	4	5	6	15	3		2	2	1	1
138	11039	138 008027	1 ##########		7	2	2	2	2	2 85	1	6	10	10	26	1		2	1	1	1
130	11030	130 40737011	2 *****		11	1	1	2	2	2 74	-	5	10	10	20				2	1	-
155	11055	155 4572758	2 *******	•••••	11	1	1 .	2	2	5 /4	2	5	5	10	20	2	4	2	2	1	1
140	11039	140 012252H	2 #########	*******	14	2	2	1	2	2 66	1	5	6	10	21	2	1	2	2	1	1
141	11039	141 017077C	1 #########	******	8	2	2	2	2	2 68	1	6	6	10	22	2	1	2	2	1	1
142	11039	142 458468H	2 #########	******	13	2	2	1	2	3 60	2	3	3	4	10	4	1	2	2	1	1
143	11039	143 240842	1 #########	*****	7	2	2	2	2	3 75	1	5	5	6	16	2		2	2	1	1
144	11029	144 2294794	1 #####################################		5	1	2	2	2	2 65	2	4	4	10	19	2		2	2	1	1
144	11035	144 22547511	2				2	4	2	2 00	2		-	10	10			2	2		1
145	11039	145 025876G	2 #########	******	10	1	2	1	2	3 63	1	5	6	10	21	2	2	2	2	1	1
146	11039	146 562511F	2 ########	******	9	1	2	1	2	3 66	1	5	5	6	16	2	2	2	2	1	1
147	11039	147 569907H	1 #########	*****	6	1	2	2	2	3 82	2	5	5	10	20	2	2	2	2	1	1
148	11039	148 561422H	2 #########	*****	27	1	1	2	2	3 68	2	5	6	10	21	2		0	0	1	0
149	11039	149 181751H	2 #########		7	1	2	1	2	3 65	2	5	6	10	21	2		2	2	1	1
150	11020	150 561949	2 *****		42	1	2	1	1	2 66	2	6	6	10	22	2		2	2	1	1
150	11035	150 50104011	2 ******		42	1	2	1	2	3 00		5	6	10	22	2		2	2	1	-
151	11039	151 561351H	2 #########	*****	1/	1	2	1	2	2 69	1	5	b	10	21	2		2	2	1	0
152	11039	152 568988H	1 #########	******	1	1	2	2	2	3 76	1	4	5	6	15	3	1	2	1	0	0
153	11039	153 114374B	1 ########	******	14	1	2	2	2	3 66	2	3	5	6	14	3	1 2	2	2	1	1
154	11039	154 185985H	1 #########	******	7	1	2	2	2	2 79	1	5	6	10	21	2	2	2	2	1	1
155	11039	155 480783A	1 #########	******	14	1	2	2	2	3 79	1	5	6	10	21	2	1 2	2	2	1	1
156	11039	156 562786H	2 #########		19	2	1	2	2	3 60	- 1	3	5	6	14	3		2	2	1	1
150	11035	150 50270011	2		15	2	2	2	2	3 00	-	5	3	6	14				2		÷
157	11055	137 4400136	1 ********	•••••	0	2	2	2	2	5 00	2	-	4	0	15	3		2	2	1	1
158	11039	158 2265518	1 ##########	*****	11	2	2	2	2	2 84	2	5	5	10	20	2		2	1	0	0
159	11039	159 511671D	2 #########	******	4	1	1	2	2	3 70	1	5	4	6	15	3	1	2	2	1	1
160	11039	160 238511D	1 #########	*****	10	1	2	2	2	3 76	2	4	3	6	13	3	1	2	2	1	1
161	11039	161 938842G	2 #########	*****	9	2	2	1	2	3 64	1	5	5	6	16	2	1	2	2	1	1
162	11039	162 281601B	1 #########		3	1	2	2	2	3 83	1	5	4	10	19	2		,	2	1	1
163	11039	163 564772H	2 #########		7	1	2	1	2	2 66	- 1	5	6	10	21	2		2	2	1	1
105	11035	103 3047728	2 ******		6	1	2	1	2	2 00	1	5	-	10	21	2	-	2	2		1
104	11039	104 304912H	2 ******	*******	0	1	1	4	2	o 02	2	4	5	0	15	3	1 1	-	4	1	1
165	11039	105 393816D	2 ########	*****	9	1	2	1	2	ه 5	2	4	3	4	11	3	1 3	2	2	1	1
166	11039	166 565203H	2 ########	******	12	1	1	2	2	3 60	2	4	2	3	9	4	1	2	2	1	1
167	11039	167 565222H	2 #########	*****	8	1	2	1	2	3 66	2	4	3	4	11	3	1	2	2	1	1
168	11039	169 771099C	2 ########	*****	13	1	1	2	2	3 61	2	2	2	3	7	4	1	2	2	1	1
169	11039	169 427097A	1 #########		8	1	2	2	2	3 80	1	5	6	10	21	2		2	2	1	1
170	11039	170 565600H	2 #########	*****	10	1	1	2	2	3 64	1	4	5	6	15	-		,	2	1	1
171	11029	171 56/19821	2 ######		6	1	2	1	2	2 65	-	5	6	10	21	3	.	,	2	1	1
1/1	11035	172 5656601	2		2	-	-	-	-	2 00	2	-	0		21				-	-	-
1/2	11039	1/2 202019H	2 ******	*******	3	1	1	4	4	3 03	1	5	4	0	15	3	1 1	-	<u>د</u>	1	1
173	11039	1/3 391539G	1 ########	******	4	1	2	2	2	3 84	1	5	6	10	21	2	1 2	2	2	1	1
174	11039	174 562455H	2 ########	*******	12	1	2	2	2	3 65	2	4	4	6	14	3	1 2	2	2	1	1
175	11039	175 458953F	2 ########	******	13	1	2	1	2	2 71	1	4	5	10	19	2		2	2	1	1
176	11039	176 316355D	1 #########	*****	1	1	2	2	2	3 75	1	3	4	6	13	3	1	2	2	1	1
177	11039	177 566176H	2 #########		10	1	2	2	2	3 60	1	4	4	6	14	3		2	2	1	1
170	11020	179 5664920	2		2	1	2	1	2	2 40		4	2	ě	10		.	2	2	1	1
1/8	11039	170 0004838	2 *******		3	4	-	± .	2 ·	3 08	1	4	3	0	13	3		-	~	-	-
1/9	11039	1/9 20000H	2 #########	******	1/	1	2	2	2	s /2	1	4	3	0	13	3	1 3	4	2	1	1
180	11039	180 543240F	2 ########	******	40	1	1	2	2	3 76	1	4	4	6	14	3	1 2	2	2	1	1
181	11039	181 565856F	2 ########	******	3	1	2	2	2	3 69	2	4	4	6	14	3	2	2	2	1	1
182	11039	182 567550H	2 ########	******	12	1	1	2	2	3 78	2	4	5	6	15	3	3	2	2	1	1
183	11039	183 525779H	1 #########		10	2	2	2	2	2 67	1	5	6	10	21	3		2	2	1	1
104	11020	194 55795011	1		6	2	2	2	2	2 45	1	6	F	10	21	2		2	-	1	1
184	11039	104 JU/80UH	1 ******		10	4	4	2	2	2 00	2	5	0	10	21	2	- · ·	2	2	1	-
185	11039	185 567824H	2 #########	#########	14	1	1	2	2	3 75	1	4	3	4	11	3	3	2	2	1	1
186	11039	186 278095	1 #########	******	5	1	2	2	2	2 72	1	4	4	6	14	3	1	2	2	1	1
187	11039	18 568489H	2 ########	******	10	1	2	1	2	3 60	1	5	6	10	21	2	2	2	2	1	1
188	11039	188 700148A	2 ########	*****	12	1	2	2	2	3 91	2	7	10	12	29	1		2	1	1	1
199	11039	189 2732380	1 ########		18	2	2	2	2	2 71	1	6	10	10	25	1	.	,	2	1	1
107	11035	100 2732300	1		7	1	2	2	2	2 /1	-		20		20				-	1	-
190	11039	190 2/1232H	1 ##########	*******	/	1	2	2	2	5 0/	1	3	2	3	8	4	1 2	2	2	1	1
191	11039	191 257952D	1 #########	******	11	2	2	2	2	3 70	2	6	10	12	28	1	1 3	2	2	1	1
192	11039	192 242912C	1 #########	*******	5	2	2	2	2	2 81	1	6	6	10	22	2	1 3	2	2	1	1
193	11039	193 242753B	1 #########	******	10	1	2	2	2	1 80	1	5	6	10	21	2		2	2	1	1
194	11039	194 212413G	1 #########	*****	4	2	2	2	2	3 89	2	3	3	6	12	3	1	2	0	0	0
195	11039	195 569803H	2 ########		12	1	1	2	2	3 60	1	5	5	6	16	2		2	2	1	1
106	11020	196 6200924	2 #########		1	1	1	2	2	3 64	1	3	2	2				2	2	1	1
190	11039	107 020082H	< ************************************		1	1	2	2	2	. 04	1	3	2	3	ő	4		2	2	1	-
197	11039	197 253257H	1 ##########	******	3	1	2	2	2	3 66	1	3	2	3	8	4	1 2	-	2	1	1
198	11039	198 343254H	1 ########	*****	26	1	2	2	2	3 80	1	4	5	6	15	3	1 2	2	2	1	1
199	11039	199 485029C	1 ########	******	5	2	2	2	2	3 84	2	7	10	12	29	1	1 2	2	1	0	0
200	11039	200 489161B	1 #########	******	4	2	2	2	2	3 77	2	5	6	10	21	2	1	2	2	1	1
200																					

toiloturo	fooding	mobility	transfor	drocsing	stairs	morbidhar	overere	workalror	motorroc		pag2fig2	alatalata	hiliruhin	-	creatining	urincout	tomo	hoartrato	rocorato	corumbic	artorial	lastato	bba1c
2	2 reeding	2 3	transfer	3 2	stairs	2 20	eyerespo 4	5 S	motorres 6	igcsscore 15	380	100000	1.3	map 85	6 creatinine	300	101.3	100	resprate 24	18	7.33	1.4	nbaic
2	2	2		2 2 3 2		0 15 1 19	2	1	5	4	450 376	121000 72000	0.8	88 67	0.8	1300 1300	103	120	30	22	7.5	2.7	
2	2	2 3		3 2	2	2 20	3	4	6	13	380	280000	0.6	55	0.8	1450	101	110	30	22	7.4	1.6	
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2	2	2 3		32 21		2 20 0 11	2	2	5	9	276 180	46000 280000	0.9	40 77	5.6 5.4	200 200	102	112 104	40 40	18	7.28	1.7	
2	2	3		3 2		0 18	4	5	6	15	288	280000	1.8	50	1	1450	102.1	108	40	17	7.33	4.4	
2	2	2 1 2 3		1 1 3 2		D 8 D 17	3	4	6	13	278 360	242000 180000	0.7	50 50	1.9	900 800	102	110 . 100	24	22	7.4	2.1	11.6
2	2	3		3 2		2 19	4	5	6	15	480	200000	1.6	55 50	1.8	800	103	120	18	10	7.34	6.4	6.2
2	2	2 3		3 1		0 15	2	3	5	10	480	200000	0.9	65	2.9	900	102.4	84	24	18	7.49	1.4	6.9
2	2	2		2 2 3 2		0 14 2 20	3	4	5	12	171 456	208000 95000	0.6	50 90	5.6 0.9	100 1200	100 98.6	124 120	20 15	12	7.2	0.9	5.7
2	2	2 3		3 2		2 20	3	4	6	13	325	350000	0.4	60	2	1000	102	112	34	29.7	7.4	1.6	5.7
2	2	2		3 2	2	2 20	3	1	6	10	380	513000	0.8	88	1.3	1600	101	. 68	34	19	7.35	2.7	6.8
2	2	! 3 ! 3		32 32		2 20 2 20	2	2	5	9	98 240	198000 166000	0.5	77 84	3.8 3.6	400 1300	98.6 98.6	83	29 40	6 15	7.43	10.9	7.5
2	2	2		3 2	2	0 16	4	5	6	15	458	147000	0.5	112	1.5	1300	98.6	96	22	24	7.42	1.2	
2	2	! 1 ! 3		1 1 3 2		2 20	4	5	6	15	88 360	153000	3.9	70 80	1.3	1100 1255	98.6 98.6	102	42	20.7	7.31	1.5	
2	2	2 3		2 2	2	0 16	3	2	4	9	86 347	541000 281000	1	73 80	1.2	2500	98.6	90	26	23	7.44	4.3	10
2	2	2		3 2		0 15	3	4	6	13	140	360000	1.1	90	7.3	200	102	. 77	26	16	7.29	1.1	7.3
2	2	23 23		3 2 3 2		2 20 2 20	4	5	6	15	380 222	514000 298000	0.5	60 95	1.8	1520 1380	98.6 100	76 100	18 42	17	7.39	1.6 4.4	6.4 6.2
2	2	2		3 2		0 16	3	4	6	13	487	71000	1.3	92	1.7	1560	102	86	26	12	7.51	1.7	
2	2	2 3 2 3		3 2 3 2		1 19	4	5	6	14	418 502	174000	0.9	60 40	4.1	800	98.6	120	20 40	24	6.94	0.7	4.7
1	2	2		3 2 3 2	<u> </u>	0 16	3	4	5	12	402	49000 280000	4.2	50 50	3.2	1320 100	98.6 98.6	92 i 92	40	19.3	7.4	1.4	7
2	2	. 3		3 2		2 20	4	5	6	15	109	140000	1.5	65	0.8	1800	101	. 130	26	23	7.42	1.5	6.9
2	2	23 23		32 32		2 20 2 20	4	3	5	15	280 162	250000 11100	0.5	40 65	3.2	345 760	101.8	80 . 112	26 29	17	7.39	3.8	6.7 8.3
2	2	2 3		3 2		0 18	3	2	5	10	244	425000	0.3	80	0.6	2100	98.6	80	30	24	7.43	4.5	7.3
0	2	1		1 0) (0 8	4	4	6	14	358	138000	0.9	65	3.7	300	102	. 126	40	21	7.45	1.6	
1	2	2		2 2 1 0		0 15	4	5	6	15	561 223	160000 103000	3.3 1.4	96 65	5.1 5.3	100 1820	101 104.4	. 70	18	4	7.07	10.1	
2	2	2		3 2		0 17	4	5	6	15	100	346000	0.4	112	0.7	1460	98.6	80	28	17	7.33	2.2	7.9
2	2	2		2 2 3 2		14 1 19	3	4	6	14	323	213000 144000	0.7	65 75	0.9	1360	101	102	28	16	7.44	3.8	8.6
2	2	2		2 2	2 1	0 16	4	5	6	15	290 323	263000	0.7	93 26	8.7	1200 950	100.4	84	22	16	7.4	1.3	
2	2	2		3 2	2	0 17	4	5	6	15	282	580000	1.5	73	1.1	500	98.6	132	34	17	7.45	2.6	7.5
2	2	2 3 2 3		32 232		1 19 2 20	4	5	6	15 15	238 385	42000 83000	2.9 4.9	73 107	1.7	1800 1970	100 98.6	100 90	32	19 19	7.38	2	5.8
2	2	2		3 2		0 17	3	4	6	13	390	214000	0.8	90	0.9		98.6	96	30	11	7.35	3.5	
0	1	. 2		0 0		0 4	2	3	5	10	500	334000	0.4	88	0.0	1200	102	100	20	23	7.5	1.1	
2	2	23 3		3 2 3 2		D 18	3	4	6	13	409 340	202000 316000	5.2 0.3	55 66	2.2		100 98.6	110 136	26 40	14	7.46	4.1	
2	2	2 3		3 2		2 20	3	4	5	12	255	326000	0.3	66	0.4		98.6	136	24	23	7.36	13.4	
2	2	2 2		3 2 2 2		2 20 0 16	4	5	6	3	459	20600	0.7	90 75	3.4	1300	98.6	86	20	22	7.35	2.8	
2	2	2 3		3 2		1 19 2 20	4	5	6	15	257 423	78000	0.7	54 57	6.4 1.9	50 300	98.6 100	170 95	42	12	7.3	1.8	
2	2	2		3 2		1 18	3	4	6	13	260	354000	9.3	63	0.8	1600	101.4	162	24	14	7.51	2.5	
2	2	2 3 2 3		3 2 3 2		2 20 2 20	4	5	6	15	352	228000 69000	0.2	40 88	0.9	1300 1200	101	. 118 : 140	20	14	7.4	2.8	
2	2	3		3 2		1 19	2	2	5	9	166 517	245000	0.4	60 73	4.5	1200	100	112	40	8	7.05	16	
2	2	2		3 2		2 20	4	5	6	15	763	57000	0.8	80	1.5	1560	100	110	40	19	7.45	3	
2	2	3		3 2 3 2		2 20 2 20	4	3	6	13 15	226 285	274000 269000	0.4	80 60	1.3 3.3	1500 1200	100 101.8	88 138	30 36	26	7.4	2.6	
2	2	3		3 2		0 18	4	4	6	14	190	58000	1.4	40	1.1	1325	98.6	110	34	18	7.49	1.3	
2	2	2		3 2		10	4	5	6	15	471	224000	0.6	83	2.3	1450	98.6	102	20	16	7.32	6.1	7.6
2	2	2		3 2 3 2	2	2 20 D 16	4	5	6	15	223 125	11700 254000	0.9	80 53	3.1 3.8	1130 1025	101.4	80 120	40 30	19 19	7.29	2	9.4
2	2	2 3		3 2	2	0 18	4	3	6	13	185	167000	1.2	65	5.2	850	98.6	101	40	15	7.29	4.7	
1	2	2		5 2 3 1		0 18	4	3	5	13	352	210000	0.5	75 50	2.4	1650	100	80	40	20	7.4	4.1	
1	2	2		2 2	2 1	0 14	4	4	6	14	495 172	307000	0.4	86 60	1.6	1150 1200	102	86	26 34	17.8	7.48	1.7	6.2
2	2	3		3 2		2 20	3	4	6	13	255	184000	1.7	53	1.7	1350	105	110	34	23	7.4	2	
2	2	23 21		32 222		2 20 0 12	4	4	6	14	219 352	400000 264000	2.6 2.5	98 47	1.3 2.1	2100 1250	102 98.6	118 90	42	17	7.2	5 4.1	
2	2	2		3 2	2	0 17	4	5	6	15	475	175000	0.7	60	4.3	1100	101.2	118	30	17	7.38	1.6	
2	2	. 3		3 2		2 20	4	4	6	14	333	285000	0.7	83	0.9	1050	102	150	20	10	7.50	3.2	
2	2	2 3		3 2 2 2		D 18 D 13	4	5	6	15	297 162	362000 216000	0.6	97 80	0.7	1750 980	98.6 102.4	100	32 44	18	7.47	1.5 2.5	
2	2	3		3 2		2 20	4	5	6	15	228	34000	5.1	90	1	1150	100	132	45	13	7.42	3	
2	2	: 3 ! 1		。2 1 1		2 20 0 11	4	5	6	15 14	120 290	85000 104000	0.4	112 121	3.9 4.7	1020 1200	98.6 98.6	120 86	40 44	18	7.12	1.8	
2	2	2		3 2		0 17	4	5	6	15	414	196000	0.5	80	2.1	1160	98.6	52	32	13	7.22	0.7	
2	2	. 3		3 2		0 18	2	2	4	8	290	156000	0.2	103	2	1560	101	. 82	18	15	7.41	1.3	
2	2	: 3 : 3		3 2 3 2		1 19 2 20	4	4	6	14 13	290 280	411000 160000	0.6 0.8	90 88	1.2	1950 1200	103 98.6	144 80	24 30	15	7.42	1.3	
2	2	. 3		3 2	2		2	1	5	8	182	180000	1.7	77	2.4	1235	101.2	64	40	14	7.5	1.2	
2	2	. 3 ! 3		3 2 3 2	2	. 19 0 18	3	3	6	15	150	230000	0.4	93 43	0.8	880	98.6 98.6	92	40	33	7.56	2.1	
2	2	3		3 2 3 7		2 <u>20</u> 1 19	4	5	6	15	332	326000	1.4	73 105	0.9	1800	98.6 98.6	110 84	32	12	7.41	1.4	
	4	. 3		4			, ,				200	000	0.5	100	0.0	200	50.0		20		1.07		

2	2	3		3 2	1	1 19		3 3	5	11	480	78000	0.6	73	4.9	650	101.8	120	40	15	7.33	0.8	
2	2	2	:	3 2		0 17	4	4 4	6	14	323	227000	0.6	102	1.2	1980	98.6	88	18	13	7.48	1	9.3
2	2	3		3 2		2 20		3 4	6	13	283	251000	1.1	106	1.9	980	102	60	26	20	7.43	1.3	
-		2		- - -		20			6	10	457	24000	2.1	04	0.0	2150	00.6	120	20	26	7 5 6	1.6	6.2
2	2	3		5 2		2 20		• 5	0	15	437	54000	2.1	24	0.5	2150	50.0	120	50	20	7.50	1.0	0.5
2	2	3		3 2		1 19	4	4	6	14	189	30000	4.5	40	4.6	230	100.3	120	40	6.6	6.96	9.6	
2	2	3		3 2		2 20	4	1 5	6	15	288	19000	3.9	76	2.8	1200	100	100	40	16	7.29	8.1	
2	2	3		3 2	(0 18	4	1 5	6	15	414	270000	0.7	65	1.7	1210	98.6	94	24	30	7.53	2.6	
2	2	2		3 2	(0 17	· 2	1 3	6	13	461	44000	0.6	80	0.9	1300	98.6	102	30	28	7.53	5.2	11
1	2	1		1 0	(8 8		1 4	6	14	190	300000	2.7	100	0.3	2100	98.6	104	30	22	7.42	1.6	6.4
2	- 2	- 2		2 2		16		1 5	6	15	01	222000	0.6	60	1	1290	99.6	119	22	11	6.9	10	12.2
2	2	2		2 2		10			6	15	10	223000	0.0	00		1200	50.0	110	32		0.5	10	13.5
2	2	3		3 Z	(18	4	4	0	14	104	290000	0.4	90	0.7	1870	101	88	40	28.0	7.51	1	10.7
2	2	2		3 2	(0 17	4	1 5	6	15	283	449000	0.8	80	1	1300	98.6	80	30	32	7.38	4	
2	2	3		3 2	1	1 19	4	1 5	6	15	115	210000	0.8	15	1.1	1300	103	110	30	36	7.54	2	7
2	2	3		3 2	1	1 19	4	4 4	6	14	224	67000	5.2	54	5.3	900	103	104	40	12	7.12	7	
2	2	3		3 2		2 20		> 4	5	11	272	344000	0.4	90	0.9	2100	102	76	40	28	7.38	1	6.2
2	2	2		2 2		1 19			6	15	20	267000	0.5	20	1.4	1090	102	80	22	10.0	7 21	2	5.4
2		5		J 2		1 15				15	222	175000	0.5	50	1.4	1000	102	00	22	10.0	7.51	2	5.4
U	1	0		1 0	(5		2 1	4	/	323	175000	4.4	22	2.7	080	98.0	98	30	15	7.37	3	5.2
1	2	2		2 2	(0 14	. 4	1 5	6	15	276	48000	0.3	84	4.7	1100	102	110	18	22	7.36	1	
2	2	3		3 2	1	2 20	4	1 5	6	15	371	28000	6.5	73	0.9	1350	98.6	98	34	17	7.42	2	
2	2	3		3 2		0 18		3 4	6	13	194	90000	0.7	73	1.7	1130	98.6	100	32	30	7.14	1	7.5
2	2	3		3 2	(0 18	4	1 5	6	15	290	332000	0.2	78	0.5	1100	98.6	88	20	23	7.48	2	
2	2	3		3 2		2 20		3 4	6	13	371	297000	0.3	53	1.6	1900	98.6	120	18	28	7.37	4	10.5
2	2	3		3 2	1	1 19		2	5	9	335	93000	7.3	54	1.3	1700	98.6	106	16	18	7.34	1	
2	2	2		2 2		1 19			6	15	261	256000	1.1	96	1.2	1200	99.6	77	26	20	7.41	5	0
2	2	2		5 <u>2</u>		1 19			0	15	201	230000	1.1	00	1.5	1500	50.0	//	20	22	7.41	3	0
2	2	3		3 Z	(18	4	+ 5	0	12	300	178000	1.4	12	0.8	2100	100	08	18	22	7.4	12	0.3
2	2	3		3 2		2 20	4	1 5	6	15	113	156000	0.6	83	0.8	1200	99	114	40	25	7.4	2	
2	2	3		3 2	1	2 20	4	1 5	6	15	113	156000	0.6	88	0.8	1500	99	114	40	25	7.4	2	
2	2	2		3 2	1	1 18	4	1 5	6	15	24	207000	0.6	102	0.9	1600	102	98	44	17	7.34	6	
2	2	3		3 2	(18		2 1	5	8		214000	1.8	73	2.4	1100	98.6	104	18				6.8
2	2	3		3 2		2 20		1 5	6	15		264000	0.3	75	3	1225	103	118	20				7.5
2	2	3		2 2		1 10		1 4	6	14	220	307000	0.0	50	0.0	825	100	120	20	15	7.2	2	0.1
2	2				-	19		- 4	5	14	207	307000	0.0	35	0.5	1202	102	120	20	13	7.2	5	0.1
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2	2	3		3 2	1	2 20	4	+ 5	6	15	270	414000	0.4	117	1.7	1380	98.6	90	18	19	7.2	3	6.7
2	2	3		3 2		18	4	1 5	6	15		256000	0.9	50	3.7	950	103	100	24				6.9
2	2	3	-	3 2	1	1 19	4	1 5	6	15	324	366000	0.5	104	5.8	890	98.6	106	36	15	7.2	4	
2	2	3		3 2		2 20	4	1 5	6	15	387	514000	0.5	88	1.8	1300	101	76	28	16.3	7.39	3	6.4
2	2	2		3 7		1 10	-	3 4	6	13	180	329000	0.5	72	19	1125	102	90	3/1		7 2	6	
2	2			2 2		19		. 4	5	10	220	215000	0.3	73	1.7	1200	102	70	34	21	7.2	2	
2	2	3		J 2	-	19	1 8	, 2	<u>с</u>	10	239	212000	0.7	52	1.9	1200	98.0	/8	20	21	7.3	2	
1	2	2		2 2	(0 14	. 4	1 5	6	15	480	140000	2.6	65	1.6	1850	98.6	100	30	26	7.4	2	10
2	2	3		3 2	1	1 19	4	4 4	6	14	593	105000	2.5	90	0.7	2100	98.6	110	24	23	7.5	1.8	
2	2	3		3 2	2	2 20	6	3 3	5	11	420	113000	0.5	80	1.4	1630	98.6	86	18	26	7.4	1.5	
2	2	3		3 2		2 20	1	4	6	14	480	250000	0.7	80	1.8	1160	98.6	80	30	26	7.44	2	6.9
2	2	3		3 2		2 20		2 2	5	11	502	36000	5.1	60	1	1200	100	110	30	30	7.44	0.8	
2	2	3		2		2 20			5	11	302	107000	0.7	60	1	1200	100	110	30	30	7.444	0.0	
2	2	3		3 2		2 20	4	+ 5	0	15	480	197000	0.7	03	1.2	1830	103	/0	20	18	7.4	2	0
2	2	3		3 2	1	2 20	4	1 5	6	15	290	341000	0.7	83	0.8	1200	98.6	140	38	28	7.51	2.4	
2	2	3		3 2	2	2 20	4	1 5	6	15	165	355000	0.4	100	0.6	1025	98.6	120	26	21	7.53	1.9	6.1
2	2	3	1	3 2	2	2 20	4	1 5	6	15	166	66000	1.3	103	4.4	925	98.6	110	32	11	7.28	1.6	8.5
2	2	3		3 2	(18	1	1 3	6	13	390	222000	0.5	83	2.1	1260	102	100	28	15	7.37	3.5	11.5
0	2	1		1 1		n 6		2 2	5	10	268	532000	0.8	112	1	1800	98.6	88	20	21.4	7.12	2.2	71
0	2	1		1 1				2	5	10	200	332000	0.0	112	1	1000	30.0	00	20	21.4	7.12	2.2	7.1
2	2	3		3 2		2 20	4	+ 5	0	15	295	320000	2.9	11	0.9	1240	98.0	120	30	18	7.51	5.7	5.0
2	2	3		3 2		1 19	4	1 5	6	15	300	207000	0.4	33	4	580	101.8	102	40	29	7.49	1.4	
1	2	2		2 2	(0 14	. 4	1 1	5	10	348	139000	0.7	83	2.2	1030	100	92	22	15	7.45	0.9	
1	1	0		0 0		0 5	6	3 3	6	12	70	392000	16.2	63	1.9	350	98.6	118	28	18	7.4	1.3	
2	2	3	3	3 2	(18	4	1 5	6	15	185	454000	0.5	63	1.5	1600	98.6	110	20	18.5	7.44	1.3	
2	2	3		3 2	(18		1 5	6	15	404	162000	12	63	0.7	2400	98.6	104	26	24.3	7 43	0.8	
-	2	2		2 2		20			6	15	200	219000	0.0	112	1.2	1200	00.6	00	20	200	7.52	6.1	07
2	2	-		2		2 20				15	250	210000	0.5	115	1.2	1200	56.0	00	20	23	7.35	0.1	0.7
2	2	3		3 2		2 20	4	1 5	6	15	11	161000	0.7	90	5.6	865	98.6	142	44	19.7	7.29	1	11.6
2	2	3	1	3 2	1	2 20	4	1 5	6	15	233	128000	0.8	83	2.6	1430	98.6	102	26	18	7.3	1.1	9.5
1	1	2		2 1	(0 10	4	1 1	1	6	788	411000	0.2	83	0.5	1240	98.6	86	20	20.4	7.34	3.8	
2	2	3		3 2	1	1 19	4	1 5	1	10	283	129000	2.2	63	1.8	1500	98.6	120	28	13.2	7.33	5	
2	2	2	3	3 2	1	1 18	4	1 5	6	15	289	340000	0.5	73	1.6	1030	100	90	32	19	7.43	1.2	8.9
2	2	3		3 2		2 20		1 5	6	15	302	263000	0.6	87	3.2	1200	102	72	14	21	7 17	2.2	71
2	- 2	-		2 2		2 20			4	2	350	19/000	1.5	110	0.8	1800	102	96	22	18	7.47	1.6	11.2
2	2			2	-	2 20			4		330	154000	1.5	110	0.0	1000	102	50	22	10	7.47	1.0	11.2
2	2	2		3 Z		1/	· ·	4	0	14	429	108000	3.3	57	3.4	930	98.0	04	40	11	7.41	3.3	10.0
2	2	3		3 2		2 20	1	1 1	5	7	377	162000	2.3	43	2	1090	98.6	166	34	5	7.11	13.4	
2	2	3		3 2	1	2 20	4	1 5	6	15	403	219000	1.3	103	1.1	1960	98.6	72	23	11	7.48	2.8	7.5
2	2	3	:	3 2		18	4	1 5	6	15	167	239000	1.6	57	2.7	1200	98.6	129	42	17	7.15	7.2	
2	2	3	1	3 2	1	1 19	4	1 5	6	15	617	198000	0.5	87	2.4	1100	98.6	80	22	24	7.17	1.1	6.6
2	2	3		3 2	1	1 19	1 3	5	3	10	108	217000	0.6	117	4.9	850	101	110	18	16	7.15	3.5	9.7
2	2	2		3 2		2 20		1 5	6	15	367	131000	0.8	63	1.2	1400	98.6	88	32	12	7.45	3.5	6.5
2	2	3		2 2		20		1 0	5	11	227	327000	0.2	107	1 2	1750	92.6	20	20	26	7 44	1.2	0.0
2	2	3		2 2		20		. 3	-	10	167	220000	0.2	70/	1.5	010	00.0	11.4	20	20 0	7.44	1.0	0.1
2	2	3		2	· '	20	+ '		1	-	107	200000	0.0	/3	7.9	010	28.0	114	20	50.8	7.51	1.7	9.1
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2	2	3		3 2	(18	4	4	6	14	257	54000	1.2	87	3.3	1150	98.6	100	20	21	7.43	2.6	5.3
2	2	3		3 2	1	2 20		3 3	5	11	314	158000	0.7	127	2.2	2100	98.6	120	30	21.2	7.43	1.1	4.8
2	2	3	:	3 2	1	2 20	4	1 5	6	15	319	183000	1.4	77	1.4	1300	98.6	138	20	2	7.43	1.6	5.9
2	2	2		3 2	(17		1 5	6	15	385	163000	0.8	93	1.4	1100	102	78	16	18	7.3	1.7	9.4
2	2	2		3 7		2 20		1 6	6	15	446	13000	0.7	82	2.2	1015	98.6	110	30	13.5	7 3/	30	
	2	3		- 2		20	1	. 3	1	2	204	236000	0.7	40	1.2	1200	100	150	30	12.0	7.04	3.5	
1	2	2		<u>د</u> 1	(14	1 1	. 1	1	3	384	220000	0.3	43	1.2	1200	100	128	44	13.9	1.22	4	_
2	2	3	:	ئ 2		2 20	4	• 3	6	13	353	295000	0.4	107	0.8	1200	101.8	104	28	23	7.43	1.4	7.9
2	2	3		3 2	1	2 20	1	l 1	1	3	428	470000	1.3	43	2.9	1350	101.4	108	30	17.5	7.36	3.1	10.3
2	2	3		3 2	(18	1	L 2	5	8	323	57000	0.5	63	0.7	1800	101	140	30	14	7.4	2	
1	2	2		3 2	(0 16		3 3	5	11	248	354000	0.8	90	0.9	1750	98.6	94	32	39	7.39	1.5	7.8
2	2	2		3 2		2 20		1 2	6	13	410	173000	1.5	83	1.6	1400	98.6	86	20	24	7.4	1.5	
2	2	2		2 2		20		. 3	6	10	214	221000	1.5	60	2.0	1200	100	104	20	24	7.4	1.5	
2	2	3		2		20		. 5	0	10	514	221000	0.4	03	2.2	1300	103	104	22	28	7.5	1	
2	2	3		ئ 2		2 20	1 8	s 3	5	11	409	252000	0.7	117	1.8	960	102	120	26	18	7.38	1	7.1
2	2	3		3 2		2 20	4	1 5	6	15	261	365000	0.5	80	0.8	1850	98.6	88	32	26	7.45	1.7	5.5
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128	5.1	1 28 1 32.7	27800	2	2	8	31	1	. 1			7.9	0.9	29 30	1.7	2		2	2	2	2 1	2	2
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118	6	1 37	26600	1	2	5	32	1	. 2			2.4	0.9	29	3.6	2		2	2	2	1 2	2	. 2
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131	4.2	1 30 1 32.4	3600 14800	1	2	2	24	2	1	95	130 111	0.2	0.8	35	2.5	1		2 2	2	2	2 2 2 2	2	2
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133	4.8	1 33.6	10100	2	2	7	23	2	1	70	94	0.6	1.1	39	2.5	1		2	2	2	2 2	2	2
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124	4.4	2 39	6100	2	2	3	14	2	1		101	110.2	0.9	30	4.1	2		2	2	2	2 2	2	2
123	4.4	2 38.1	16300	2	2	3	31 3 13	1	. 2		102	115.2	1	41	3.3	2		2	2	2	1 2	2	2
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130	3.2	1 21.3	24700	1	2	6	5 32	1	. 2	27	76	2.8	0.9	34	3.4	1		2	2	2	2 2	2	2
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5	1	30.0	10500	1	2	4 21	1	1	20				25	3.1	2	4	2	2	2	2	2	2
5.0	2	33.5	10500	1	2	4 20	2	1	50	11	17.4	1	55	2.9	2	1	2	2	2	2	2	2
4.4	2	33.7	7600	1	2	4 1/	1	. 2	38	62		1.3	37	2.2	1	1	2	2	1	2	2	2
3.2	1	21.6	13400	1	2	8 29	1	. 2			24.8	0.9	28	1.7	2	2	2	2	2	2	2	2
4.7	1	31.5	18600	1	2	6 27	1 1	1				0	98	2.7	2	2	2	2	2	2	2	2
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3.8	1	25.5	18900	2	2	13 24	1	1				9	99	1.7	2	2	2	1	2	2	2	2
3.8	1	25.5 30.6	18900 14100	2	2	13 24 2 15	1	1	74	195		9	99 35	1.7	2	2	2	1	2	2	2	2
3.8 3.8 4.2	1	25.5 30.6	18900 14100	2	2	13 24 2 15	1	1	74	195		9	99 35 37	1.7	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	2 2 2 2	2 2 2 2	1 2 2	2 2 2	2 2 2	2 2 2	2 2 2 2 2
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APPENDIX 12 – LIST OF PATIENTS

1	SHYAM JI GUPTA	221635H	98	BACHIAM	131700F
2	RATHINAMMAL	352520J	99	SHANTI DEVI	287301
3	MANOHARAN	153412H	100	BISMAL DAS	357304H
4	ANANDHI	353037H	101	ABIBUNISHA	357680H
5	ANWAR	772833C	102	PHANILAL DAS	362169H
6	LAKSHMANAN G	577200D	103	SHANTHA VS	141830B
7	MAHADEVAN	354740H	104	CHINNAPONNU	450725H
8	HELEN SUNNY	902052A	105	RAGHUPATHY	450738H
	MOHAMMED ALI				
9	ZINNA	357342H	106	MAHALINGAM	594234A
10	SEKHAR	081891C	107	SUBRAMAIYAN P	451011H
11	SEKARAN K	070900G	108	RAMACHANDRAN	353456H
12	SUSHEELA	121800D	109	ADILAKSHMI	021024G
13	JOTHI	351696H	110	NARASIMHAM	451070H
14	SEKHAR M	450734H	111	MOHANA	201089B
15	EKAMBARAM	568804	112	SUBRAMAN	267056C
16	SUBRAMANIAN VK	232274H	113	VENU	452450H
17	VATCHALA	031805D	114	ROBERT	338830B
18	SHANTI DANIEL	19093	115	MURUGESHAN	451525H
19	DAMODARAN	568377F	116	SUSHEELA	037180A
20	SHAFEEQ SHAREEF	974630F	117	KALVIKASUM	454128H
21	ADOLF LOURDU	495315B	118	SRINIVASAN	454561H
22	BEATRICE LINCOLN	935868A	119	DR HENDRY DEVA	093515B
23	KALAMYA DEVI	607374H	120	IRUDAYARAJ	621896
24	SREERAMULU	569196H	121	VIJAYALAKSMI	098278B
25	REETA JEEVANESAN	457164H	122	GOVINDAN	454798H
26	ANBU MANI	136474A	123	CHANDRAN	455019H
27	SALOMI ELIZHABETH	229501C	124	SANGTHUAMA K	163898G
	SUBRAMANYAM				
28	NAIDU R	456841H	125	HYAMANTHI	455459H
29	PANEER SELVAM S	457294H	126	SUBRAMANI	455519H
30	SWAPNA PRAMANIK	585523G	127	VASUDEVAN	455673H
31	ANANDHAN	231402H	128	JOSEPH N P	657894B
				UMESH KUMAR	
32	MANJULA M	561848H	129	SHARMA	739475H
33	GEORGE MS	393554B	130	EZHILARASI	393936C
34	NAGARAJAN	750378D	131	JAYAPALAN	455922H
	UMESH CHANDRA				
35	AMBASTH	680046H	132	MANI	589580C
	VASANTHA				
36	SUBRAMANIAN	972299G	133	ARUMAINATHAN	216002H

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37	SHAMASIVAN	939942G	134	UMAPATH	709592C
38	VENILLA	603388D	135	SUBRAMANI NAIDU	456841H
39	PULLANNA K	958029F	136	KAMONEEZA BEGUM	808265B
40	RAJENDRAN	166761H	137	JESSUVI BEEVI	457470H
41	BABU	105613G	138	PUNITH JHA	457891H
42	LIDIYA MARY	518715D	139	ANNAKUTTY	497279H
43	ZAINA BEE	072161A	140	MALLIGA	812973C
44	JAYARAJ	054904	141	MANIGANAN	154201G
45	ANTONY ROSS	194556F	142	PONGOTHAM	458468H
46	GANESHAN	186325H	143	JONES IMMANUL DOSS	240842
47	KRISHNAN	183067H	144	VASANTHA	229479H
48	VISHWANATHAN	186881H	145	EZEKIEL	025876G
49	SANKARAPPAN	186732H	146	POOBALAN	562511F
50	SARAVANAN	297890G	147	JYOTHI	180156F
51	LAKSHMANAMMAL	187824H	148	VEDANAYAGI S	569907H
52	GUNASUNDAREN	188400H	149	LEYA LAKSHMI	561422H
53	RADHA VENKETESAN	037226A	150	G RANI	181751H
54	SUBBAIAH	188716H	151	SUDHAKARBABU Y	561351H
55	CHINNABABI	329636B	152	NATARAJAN R	568988H
56	JOESPH	566651	153	SHARFUNNISSA	114374B
57	UDIYAN	035619D	154	PADAM SINGH RAI	185985H
58	NARASIMHA REDDY	041511F	155	SIMON.A.K	480783A
59	REDDEPPA	189672H	156	NASAR BASHA	562486H
60	KOCHI BANGAY	314291H	157	PARIMALA S.	446615B
61	SUNDARAMOORTHY	311158H	158	SANTHA.C.S.	226551B
62	DURAI RAJ	189848H	159	RANGANATHAN	511671D
63	LOGANATHAN	350688H	160	VATCHALA S	238511D
64	SYED MUSTAFA	550058B	161	MOHAMMED OMAR	938842G
65	MOSEES B	351063H	162	KRISHNAMOORTHY.A.G	281601B
66	LAKSHMINARAYAN	351142H	163	SUNDARAMOORTHY	564772H
	SARDAR				
67	S.NIZAMUDDIN	527548	164	ABDHA KHATOON	564912H
68	PUSHPA	351324H	165	SUKKUBAI	393816D
69	MANJU CHATERJEE	048597C	166	ANDAMMAL	565203H
70	CHANDRASHEKAR	351525H	167	PUSHPAVATHI	565222H
71	KASIM SHERIF	099410G	168	KANCHA	771099C
72	SAROJA	195734C	169	PANCHARATHNAM	427097A
73	NAGARAJU	553849F	170	THIRUNARAKERASU	565600H
74	RAGUNATHAN REDDY	351597H	171	PREMA	564983H
75	JAMEEL BASHA	370783D	172	ROJA	565619H
76	CHINNARAJ	307463B	173	FRANK DEVANESAN	391539G
77	GLADYS	125583A	174	VASANTHAMMAL	562455H
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78	CHANDRASHEKAR	079084B	175	JAYARAJ	458953F
79	ADHIMULAN F	352392H	176	KARUNAKARAN	316355D
80	VASUDEVAN	352710H	177	VEERAN C	566176H
81	RAJAKUMARI	619956	178	RAJASEKHARAN	566483H
82	JEYARAJ THOMAS	129416	179	ARUMUGAM	566660H
83	PACHUMUTHU	353023H	180	MASTHAN KHAN	543240F
84	BHASKARAN	671702F	181	ADEMTHA	565856F
85	RAJAMMA	541119F	182	RADHAMMA	567550H
86	NAZEER AHMED	068410G	183	RANGANATHAN. M G	525779H
87	SOKKUBAI	450455H	184	JANKI DEVI	294369H
88	MAYARAI	349028H	185	NATESAN G	567824H
89	SUBRAJ	077538H	186	VADIVELU	278095
90	VATCHALA	353087H	187	SIVAGAMI	568489H
91	MURTHI DEVI	353990H	188	SARADA BHAI	700148A
92	ANUSHABAI	309965F	189	PITCHANDI K.	273238C
93	SANKARAN	354423H	190	VARADARAJI	271232H
94	GANESHAN	455423H	191	EILEEN LAKRA	257952D
95	SAHADEVAN	074456D	192	GOVINDASAMY S.	242912C
96	KANAGA BAI	388271G	193	SYED AZAM	242753B
97	GLORY	170567B	194	CHENGAMMAL B.	212413G
195	JAYAPALAN	569803H	195		
196	MANOHARAN	620082H			
197	ARUMUGAM M.	253257H			
	NAGENDRA NATH				
198	DUBEY	343254H			
	MADGE				
199	AMALASINGAM D	485029C			
200	GRACE.T	489161B			
201	SAMUEL S	564879A			