# CLINICAL PROFILE AND OUTCOME OF PATIENT WITH ACUTE RESPIRATORY DISTRESS SYNDROME IN INTENSIVE CARE UNIT-A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"

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# Endorsement by the HOD, Principal/Head of the Institution

This is to certify that the dissertation entitled "**CLINICAL PROFILE AND OUTCOME OF PATIENT WITH ACUTE RESPIRATORY DISTRESS SYNDROME IN INTENSIVE CARE UNIT-A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY**" is a bonafide research work done by **REG. NO. BG0116003.**


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# ABSTRACT

**INTRODUCTION:**

Acute respiratory distress syndrome (ARDS) can be associated with significant morbidity and mortality among hospitalized patients. Although ARDS represents a complex syndrome with considerable morbidity and mortality, recent advances in clinical care have improved outcomes. Identification of subjects at high risk of developing mortality may aid the clinicians in efficient management of high risk cases and may reduce significant amount of mortality. Various risk scoring systems have been available for this purpose. There are retrospective studies on clinical course and outcome and only a few prospective studies in Indian literature. This study was a cross sectional prospective study where an attempt was made to study the clinical profile, and outcome of patients with ARDS admitted in ICU and the predictive validity of various scoring systems (SOFA, APACHE II AND APACHE III, qSOFA) in predicting mortality.

**MATERIALS AND METHODS**

This study was a cross sectional prospective study, conducted in the Intensive Care Unit (ICU), at KLE**S** Dr.Prabhakar Kore Hospital and MRC Belagavi. All the eligible patients above 18 years admitted to the Intensive care unit and confirmed cases of ARDS based on the Berlin definition of ARDS were considered as study population. Patients with clinical or investigative procedures suggestive or left sided cardiac dysfunction and people with significant underlying lung disease were excluded from the study. All the patients have undergone appropriate imaging, biochemical and serological investigation to identify the etiology of ARDS. All the study participants were also evaluated at admission by APACHE II, APACHE III, SOFA, qSOFA score

were computed for all. The utility of APACHE II& III in predicting outcome (improved Vs expired) was assessed by Receiver Operative curve (ROC) analysis. area under the ROC curve along with it's 95% CI and p value are presented. P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

**RESULTS:**

A total of 60 subjects were included in the final analysis. The mean age of study population was 41.4 ± 14.51 with the ranged between 18 to 77 years. Among the study participants,34(56.7%) participants were males and remaining 26(43.3%) were females. Among the study population, 17(28.3%) participants had pneumonia. The number of OP poisoning, abdominal sepsis, dengue, H1N1, undiagnosed fever, pancreatitis, sepsis-chronic liver diseases, sepsis-intra uterine death, snake bite, UTI, leptospirosis, paraquat poisoning, acute fulminant viral hepatitis, malaria and scrub typhus was 6(10%), 3(5%), 5(8.3%), 5(8.3%), 4(6.7%), 3(5%), 4(6.7%), 2(3.3%), 2(3.3%), 2(3.3%), 1(1.7%), 1(1.7%) and 1(1.7%) respectively.

The mean APACHE II score of study population was 16.9 ± 7.09 with the ranged between 2 to 35. The mean APACHE III score of study population was 71.58 ± 28.63 with the ranged between 10 to 139.The median SOFA score in the study population was 7.5(IQR:5,9)Out of 60 people, 18(30%) participants were intubated.Among the study population, 29(48.33%) participants had qSOFA score of 1, 27(45%) had q SOFA of 2 and 4 (6.67%) had qSOFA score of 3.In the study 75% study population was in sepsis. The mean mechanical ventilation days of study population was 5.08 ± 2.76 with the ranged between 2 to 14 days. The mean stay in hospital days of study

population was 8.43 ± 4.06 with the range between 3 to 18. Days. The mean ICU stay of study population was 6.48 ± 3.04 with the ranged between 2 to 17 days.

Among the study population 31(51.7%) participants had improved and 29(48.3%) participants had expired. The APACHE II score had excellent predictive validity in predicting mortality, as indicated by area under the curve of 0.933 (95% CI 0.857 to 1, P value <0.001). The APACHE III score had poor predictive validity in predicting expired, as indicated by area under the curve of 0.696 (95% CI 0.559 to 834, P value 0.010).The SOFA score had good predictive validity in predicting expired, as indicated by area under the curve of 0.871 (95% CI 0.779 to 963, P value <0.001)

**CONCLUSIONS:**

The study had concluded that APACHE II score had best predictive validity in predicting adverse outcome in patients with ARDS, followed by SOFA score. APACHE-III had poor predictive validity and q SOFA score may not be useful prediction tool.

# ABBREVIATIONS

| Glossary | Abbreviations |
|---|---|
| AECC | American-European Consensus Conference |
| ALI | Acute Lung Injury |
| ALVEOLI | Assessment of Low tidal Volume and Elevatedend expiratory pressure to Obviate Lung Injury |
| APACHE | Acute Physiology and Chronic Health Evaluation |
| ARDS | Acute respiratory distress syndrome |
| CI | Confidence Interval |
| CPAP | Continuous positive airway pressure |
| ECCO2R | Extracorporeal CO2 removal |
| ECMO | Extracorporeal membrane oxygenation |
| FIO2 | Fraction of inspired oxygen |
| GC | Glucocorticoid |
| Gra | Glucocorticoid receptor alpha |
| HFOV | High-frequency oscillatory ventilation |
| HFV | High frequency ventilation |
| ICU | intensive care unit |
| iNO | Inhaled nitric oxide |
| MOF | Multiple Organ Failure |
| NF-kB | Interaction between nuclear factor-kappa B |
| NMBA | Neuromuscular blocking agents |
| OI | oxygenation index |
| OR | Odds ratio |

| | |
|---|---|
| PEEP | Positive end expiratory pressure |
| PH | Pulmonary hypertension |
| RCTs | Randomized controlled trials |
| ROC | Receiver Operative curve |
| RR | Relative risk |
| TNF | Tumor Necrosis Factor |
| TRALI | Transfusions or transfusion associated acute lung injury |

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# INTRODUCTION

**Definition of ARDS (Berlin definition):**

Acute respiratory distress syndrome (ARDS) is defined as "distress occurring within 1 week of a known clinical insult or new insult or worsening respiratory symptoms with chest imaging showing bilateral opacities – not fully explained by effusions, lobar/lung collage, or nodules and the origin of oedema leading to respiratory failure not fully explained by cardiac failure of fluid overload." There is a need for objective assessment (e.g. echocardiography) to exclude hydrostatic oedema if no risk factor present.

The definition categorises ARDS based on the degree of hypoxemia as mild (200 mm Hg < $PaO_2/FIO_2$ ≤ 300 mm Hg or CPAP >5cm$H_2O$), moderate (100 mm Hg < $PaO_2/FIO_2$ ≤ 200 mm Hg or CPAP >5cm$H_2O$), and severe ($PaO_2/FIO_2$ ≤ 100 mm Hg or CPAP >5cm$H_2O$).[1]

**The burden of adult ARDS global and India:**

Cross-sectional studies have demonstrated that patients with ARDS represent approximately 5% of hospitalised, mechanically ventilated patients.[2] Most studies have shown that rates of mild ARDS represent only 25% of patients with ARDS, with approximately 75% of patients having moderate or severe ARDS.[3, 4] However, approximately one-third of patients with initially mild ARDS are reported to progress to moderate or severe disease.

The incidence of ARDS varies widely across the globe. The differences in the clinical definitions used is one of the important contributing factors for this variation, apart from existing true differences in the burden of the disease in the various population. ARDS affects close to 200,000 patients annually in the United States, and

despite an overall improvement in the disease, the mortality remains a highly lethal condition. [4, 5] Majority of the prospective US cohort studies have used AECC definition and the reported incidence have ranged from 64.2 [6] to 78.9 [4] cases/100,000 person-years. Whereas estimates from Northern Europe (17 cases/100,000),[7] Spain (7.2 cases/100,000),[8] and Australia/New Zealand (34 cases/100,000)[9] have shown substantially lower rates. Reasons for the large variation in ARDS incidence are unclear and may include major differences in demographics and healthcare delivery systems.[8] The true incidence ARDS in Indian hospitalized patients is lacking, as there is no large-scaledata available to aid this assessment. Almost all the studies conducted on ARDS in India are limited to profiling studies of patients who had developed ARDS. Studies assessing the incidence of ARDS are often limited to a particular disease entity like trauma or respiratory infection etc.[10] Hence, the studies do not provide any incidence estimate.[11] However, in one of the studies have assessed the mortality rates in the North Indian and Western Indian population that were 47.8% [12] and 57%, respectively.

**Common etiologies of ARDS**

The etiology of ARDS can be divided into pulmonary (direct) and extra-pulmonary (indirect) causes. Infective and aspiration pneumonia are the commonest pulmonary causes of ARDS, whereas systemic sepsis is the predominant extra-pulmonary cause of acute lung injury.[12] Both medical and surgical conditions can contribute towards ARDS. Medically, a significant proportion of cases in tropical climates are caused by infections such as malaria, scrub typhus, enteric fever, and leptospirosis or injuries gained by poisoning, near hanging, and near-drowning.[12]

**Treatment outcome following ARDS (mortality, need for mechanical ventilation, duration of ICU stays, cost of the treatment and long term sequel)**

**Mortality** - ARDS is associated with a hospital mortality of approximately 40%.[4, 8] Mortality varies according to the severity of oxygenation deficit. In the Berlin definition clinical study cohort, mortality was 27% in patients with mild ARDS, 32% in those with moderate ARDS and 45% in patients with severe ARDS.[3] Although worsening oxygenation is a risk factor for ARDS mortality, patients generally die from multisystem organ failure or progressive underlying illness; only a minority of ARDS patients (13% to 19%) die from refractory respiratory failure.[8, 13] Although mortality has declined since last two decades [14] initial progress in reducing ARDS mortality is likely due to increased implementation of a low tidal–volume mechanical ventilation strategy that reduces further lung injury, systemic inflammation, and subsequent multisystem organ failure. However, among patients who receive low tidal–volume ventilation, mortality rates remain unchanged. Thus, additional treatments for ARDS are sorely needed.[15, 16]

Because of the high mortality and substantial variability in outcomes in patients with ARDS, identification of risk factors for mortality are important to determine prognosis and guide clinical decision-making. In line with observations that mortality in ARDS is generally due to multiple-organ system failure, the best-performing determinants of prognosis in ARDS are age, the severity of disease indices (eg, APACHE scores),[17, 18] and predisposing conditions for ARDS. For example, trauma-induced ARDS has a much more favourable prognosis (approximately 10% mortality) than other conditions.[14, 19] Clinical risk factors for ARDS mortality include poor oxygenation[3, 18] and poor lung compliance,[15] although

the Berlin ARDS Definition Task Force did not find that lung compliance added significant predictive value over oxygenation alone.[3] Other predictors of ARDS mortality include pulmonary vascular dysfunction,[20] lack of temporal improvement in dead-space fraction,[21] lung compliance,[22] oxygenations, or shock.[23]

The diagnosis of ARDS is often clinically challenging because of nonspecific features of this condition. Highlighting the difficulty of ARDS diagnosis, Ferguson et al[24] identified that only 48% of patients with autopsy-proven ARDS had a diagnosis of ARDS noted in their charts. ARDS mimics include cardiogenic pulmonary oedema, acute eosinophilic pneumonia, acute interstitial pneumonitis, cryptogenic organizing pneumonia, and diffuse alveolar haemorrhage. To differentiate these conditions from ARDS, various diagnostic modalities are utilized, such as sophisticated chest-imaging studies, echocardiography, right-heart catheterization, and bronchoscopy. Lung biopsy has been reported to change management in 60%–80% of select cases in which the diagnosis of ARDS remains uncertain,[25-27] even though it is unclear whether outcomes are improved through biopsy triggered management change. Importantly, lung biopsy is reserved for a minority of patients in experienced centres because of its high rate of severe complications (10%) in critically ill patients. Therapeutic strategies for ARDS focus upon treating the underlying aetiology and providing supportive care that reduces the progression of lung injury. This algorithm for an evidence-based approach to ARDS is shown in Figure 1

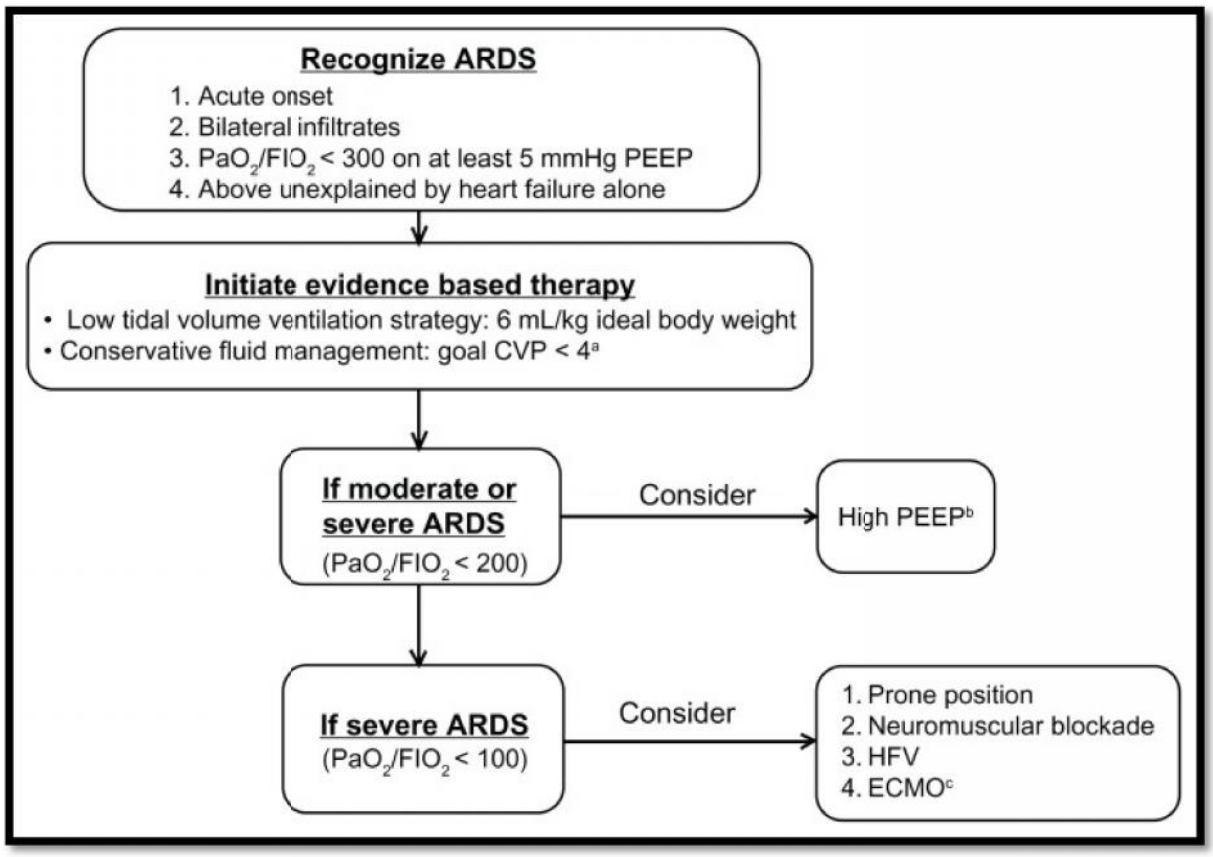



***Figure 1:*** **An evidence-based approach to the management of acute lung injury and acute respiratory distress syndrome.**

If the urine output is >0.5ml/kg/hr and the mean arterial pressure is >60 mmHg with no vasopressor support, consider the use of positive end-expiratory pressure (PEEP) until plateau pressure reaches 30 mmHg, or use stress index to titrate PEEP.

**NEED FOR THE STUDY:**

Although ARDS represents a complex syndrome with considerable morbidity and mortality, recent advances in clinical care have improved outcomes. Support of ARDS patients with low tidal volume ventilation has become the standard of care, and this approach has revealed important underlying mechanisms that have led to new areas of investigation in lung injury. Use of the Berlin Criteria has aided in the identification of the most afflicted ARDS patients who might benefit from rescue therapies, and targeting of neuromuscular blockade and prone positioning in severe ARDS has recently proven beneficial regarding improved ARDS mortality. Ongoing studies will be important for providing additional information for helping target these modalities to the patients most likely to benefit from them as well as to gain further understanding of the mechanisms underlying benefit of these modalities. Majority of data available on the clinical profile of patients with ARDS is from western literature. There are retrospective studies on clinical course and outcome and only a few prospective studies in Indian literature. This study was a cross sectional prospective study where an attempt was made to study the clinical profile, and outcome of patients with ARDS admitted in ICU at DrPrabhakar Kore Hospital and MRC, Belagavi.

# AIMS AND OBJECTIVES

- To study the etiology, risk factors and clinical features of ARDS.
- To study the outcome of the patients of ARDS.

# REVIEW OF LITERATURE

In 1821 the first known literature, in which Laennec described the gross pathology of the heart and lungs and described idiopathic anasarca of the lungs; pulmonary oedema without heart failure in "A Treatise on Diseases of the chest" [28] fatal form of "double pneumonia" was the development of methods of establishing secure airway access using tubes that could be attached to mechanical ventilators to deliver adequate pulmonary distending pressures. Since acute, diffuse, and dense bilateral infiltrates were almost never observed except in patients requiring prolonged mechanical ventilation, many surmised the cause of such infiltrates the ventilator, hence the term "respirator lung".[29]For a period ARDS went by the name of inciting injuries (e.g. shock lung, post-traumatic lung, etc.). It wasn't until 1967, in a landmark article published in Lancet which described the clinical entity that they called" acute respiratory distress in adults" [30] This article recognized for the first time that ARDS was a constellation of pathophysiological abnormalities common to a relatively large number of patients but that was initiated by a wide variety of unrelated insults-for example, gastric aspiration, sepsis, blunt trauma, near-drowning, etc. Also, notable in this 1967 report, ARDS was "acute" respiratory distress syndrome.

## ARDS - DEFINITION AND HISTORY

ARDS is a syndrome with multiple risk factors that trigger the acute onset of respiratory insufficiency. The pathogenic mechanisms vary depending on the inciting insult, but as demonstrated on autopsy findings, there are some common pathological pulmonary features [31], such as increased permeability as reflected by alveolar oedema due to epithelial and endothelial cell damage, and neutrophil infiltration in the early phase of ARDS. Until recently, the most accepted definition of ARDS for use at the

bedside or to conduct clinical trials [32] was the American-European Consensus Conference (AECC) definition, published in 1994 [30]. ARDS was defined as: the acute onset of respiratory failure, bilateral infiltrates on chest radiograph, hypoxemia as defined by a PaO2/FiO2 ratio ≤200 mmHg, and no evidence of left atrial hypertension or a pulmonary capillary pressure <18 mmHg (if measured) to rule out cardiogenic oedema. Also, Acute Lung Injury (ALI), the less severe form of acute respiratory failure, was different from ARDS only for the degree of hypoxemia, in fact, it was defined by a 200 < PaO2/FiO2 ≤300 mmHg.

Over the past 18 years of practice, the diagnostic accuracy of the ARDS definition by AECC has been questioned. In a series of 138 ARDS patients, the definition had relatively low specificity (51%) when compared with autopsy findings demonstrating diffuse alveolar damage as assessed by two independent pathologists [24, 33]. The reliability of the chest radiographic criteria of ARDS has been demonstrated to be moderate, with substantial interobserver variability.[34] In addition, the hypoxemia criterion (i.e. PaO2/FiO2 <200 mmHg) can be markedly affected by the patient's ventilator settings; especially the PEEP level used.[35]

Finally, the wedge pressure can be difficult to interpret and if a patient with ARDS develops a high wedge pressure that should not preclude diagnosing that patient as having ARDS. Based on these concerns, the European Society of Intensive Care Medicine with an endorsement from the American Thoracic Society and the Society of Critical Care Medicine convened an international expert panel to revise the ARDS definition; the panel met in 2011 in Berlin, and hence the new definition was coined the Berlin definition. The goal of developing the Berlin definition was to try and improve feasibility, reliability, face and predictive validity. Of interest, this definition was empirically evaluated for predictive validity for mortality compared

with the AECC definition, using data derived from multi and single centre clinical trials. [3]

There are a few key modifications (oxygenation, the timing of acute onset, Chest X-ray, and wedge pressure criterion) in the Berlin definition as compared with the AECC definition.

***Oxygenation***

In the Berlin definition, there is no use of the term Acute Lung Injury (ALI). The committee felt that this term was used inappropriately in many contexts and hence was not helpful. In the Berlin definition, ARDS was classified as mild, moderate and severe according to the value of $PaO_2/FiO_2$ ratio. Importantly, the $PaO_2/FiO_2$ ratio value is considered only with a CPAP or PEEP value of at least 5 $cmH_2O$.

| | |
|---|---|
| Timing | Within 1 week of a known clinical insult or new or worsening respiratory symptoms |
| Chest imaging | Bilateral opacities — not fully explained by effusions, lobar/lung collapse, or nodules |
| Origin of edema | Respiratory failure not fully explained by cardiac failure or fluid overload.Need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present |
| **CLASSIFICATION OF OXYGENATION** [b] | |
| **Mild** | 200 mmHg < $PaO_2/FIO_2$ ≤300 mmHg with PEEP or CPAP ≥5 $cmH_2O$[c] |
| **Moderate** | 100 mmHg < $PaO_2/FIO_2$ ≤200 mmHg with PEEP ≥5 $cmH_2O$ |
| **Severe** | $PaO_2/FIO_2$ ≤100 mmHg with PEEP ≥5 $cmH_2O$ |

*Abbreviations: CPAP, continuous positive airway pressure; $F_IO_2$, fraction of inspired oxygen; $PaO_2$, partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure; [a]Chest radiograph or computed tomography scan; [b]If altitude is higher than 1,000 m, the correction factor should be calculated as follows: [$PaO_2/FIO_2$_(barometric pressure/760)]; [c]This may be delivered noninvasively in the mild acute respiratory distress syndrome group.*

***The timing of acute onset***

The timing of acute onset of respiratory failure to make a diagnosis of ARDS is clearly defined in Berlin definition. It defines the exposure to a known risk factor or worsening of the respiratory symptoms within one week. It is important to identify risk factors that explain the context of acute respiratory failure (Table 1).

**Table 1: Risk factors for ARDS**

| **Direct** | **Indirect** |
|---|---|
| Pneumonia | Non-pulmonary sepsis |
| Aspiration of gastric contents | Major trauma |
| Inhalational injury | Pancreatitis |
| Pulmonary contusion | Severe burns |
| Pulmonary vasculitis | Non-cardiogenic shock |
| Drowning | Drug overdose |
| | Multiple transfusions or transfusion associated acute lung injury (TRALI) |

***Chest X-ray***

The chest radiograph is characterized by bilateral opacities involving at least 3 quadrants that are not fully explained by pleural effusions, atelectasis and nodules. In the absence of known risk factors, a cardiogenic origin of oedema is to be excluded by objective evaluation of cardiac function with echocardiography. Consequently, the wedge pressure measurement was abandoned because ARDS may coexist with hydrostatic oedema caused by fluid overload or cardiac failure [32]. The ARDS Berlin definition was empirically evaluated to test predictive validity for mortality [3] by using a large clinical database from multicentre and single centre clinical trials that included 3,670 patients. The mortality rate was 27% for mild, 32% for moderate and 45% for severe ARDS. Moreover, the number of ventilator-free days declined from mild to severe ARDS, and the more severe stages of ARDS were associated with a progressive increase in lung weight as evaluated by CT scan and shunt fraction.

Acute respiratory distress syndrome (ARDS) is defined as distress occurring within 1 week of a known clinical insult or new or worsening respiratory symptoms with chest imaging showing bilateral opacities – not fully explained by effusions, lobar/lung collage, or nodules and the origin of oedema leading to the respiratory failure not fully explained by cardiac failure of fluid overload. There is a need for objective assessment (eg., echocardiography) to exclude hydrostatic oedema if no risk factor present. The definition categorises ARDS based on degree of hypoxemia as mild (200 mm Hg < $PaO_2/FIO_2$ ≤ 300 mm Hg or CPAP >5cm$H_2O$), moderate (100 mm Hg < $PaO_2/FIO_2$ ≤ 200 mm Hg or CPAP >5cm$H_2O$), and severe ($PaO_2/FIO_2$ ≤ 100 mm Hg or CPAP >5cm$H_2O$).**[1]**

## DIAGNOSTIC CRITERIA FOR ARDS[1]

Acute respiratory distress syndrome (ARDS) is a non-cardiogenic pulmonary oedema and diffuse lung inflammation syndrome that often complicates critical illness. The diagnosis of ARDS is based on fulfilling 3 criteria:

• Acute onset (within 1 week)

• Bilateral opacities on chest x-ray

• $PaO_2/FiO_2$ (arterial to inspired oxygen) ratio of ≤300 on positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) ≥5 cm $H_2O$.

If no risk factors for ARDS are present, then acute pulmonary oedema as a result of heart failure should be ruled out.

## COMMON ETIOLOGIES OF ADULT ARDS

Multiple risk factors exist for ARDS. Approximately 20% of patients with ARDS have no identified risk factor. ARDS risk factors include direct lung injury (most commonly, aspiration of gastric contents), systemic illnesses, and injuries. The most common risk factor for ARDS is sepsis.

Given the number of adult studies, major risk factors associated with the development of ARDS include the following:

- Bacteraemia
- Sepsis – The most common cause of ARDS is sepsis, a serious and widespread infection of the bloodstream.
- Trauma, with or without pulmonary contusion - Accidents, such as falls or car crashes, can directly damage the lungs or the portion of the brain that controls breathing.
- Fractures, particularly multiple fractures and long bone fractures

- Burns
- Massive transfusion
- Pneumonia - Severe cases of pneumonia usually affect all five lobes of the lungs.
- Inhalation/ Aspiration - Breathing high concentrations of smoke or chemical fumes can result in ARDS, as can inhaling (aspirating) vomit or near-drowning episodes.
- Drug overdose
- Post perfusion injury after cardiopulmonary bypass
- Pancreatitis
- Fat embolism

General risk factors for ARDS have not been prospectively studied using the 1994 EACC criteria. However, several factors appear to increase the risk of ARDS after an inciting event, including advanced age, female sex (noted only in trauma cases), cigarette smoking, [36] and alcohol use. For any underlying cause, increasingly severe illness as predicted by a severity scoring system such as the Acute Physiology and Chronic Health Evaluation (APACHE) increases the risk of development of ARDS.

- **Genetic factors**

A study by Glavanet al. examined the association between genetic variations in the *FAS* gene and ALI susceptibility. The study identified associations between four single nucleotide polymorphisms and increased ALI susceptibility. [37] Further studies are needed to examine the role of *FAS* in ALI.

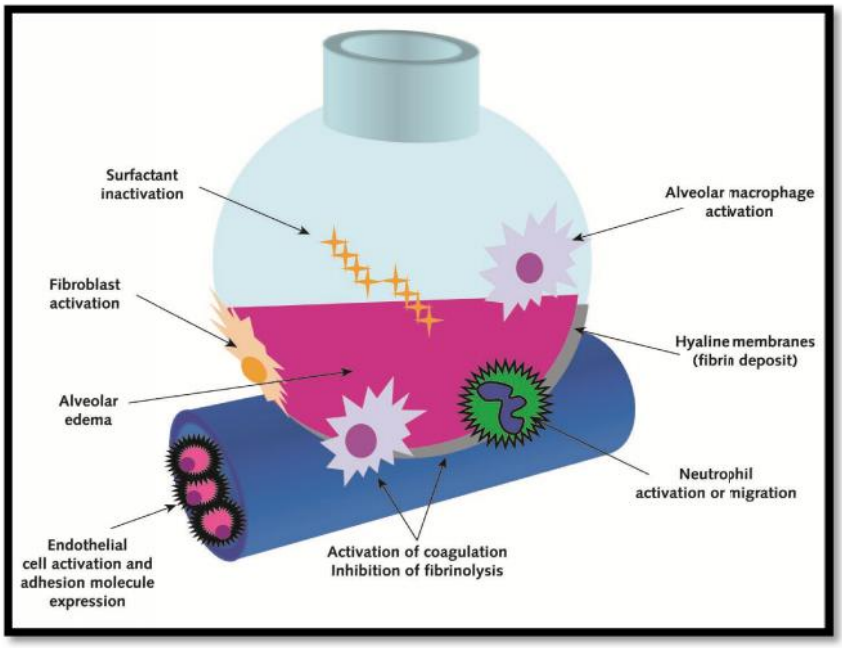
**PATHOPHYSIOLOGICAL MECHANISM OF DEVELOPMENT OF ARDS**

Increased capillary permeability is the hallmark of ARDS. Damage of the capillary endothelium and alveolar epithelium in correlation to impaired fluid remove from the alveolar space result in accumulation of protein-rich fluid inside the alveoli,

thereby producing diffuse alveolar damage, with release of pro-inflammatory cytokines, such as Tumour Necrosis Factor (TNF), IL-1 and IL-6.[38] Neutrophils are recruited to the lungs by cytokines, become activated and release toxic mediators, such as reactive oxygen species and proteases.[39] Extensive free radical production overwhelms endogenous anti-oxidants and causes oxidative cell damage.[40]

Inflammation due to neutrophil activation is key in the pathogenesis of ARDS. Fundamental transcription abnormalities, involving NF-kappa B that is required for transcription of genes for many pro-inflammatory mediators, are present in the lungs of ARDS patients.[41] In addition, other factors such as endothelin-1, angiotensin-2 and phospholipase A-2 increase vascular permeability and destroy micro-vascular architecture, enhancing inflammation and lung damage. In conclusion, as several different pathways are involved in ARDS development, no single biomarker can predict outcome in ARDS patients. [42]

**Figure 2: Cellular and molecular events that interfere with gas exchange in the acute respiratory distress syndrome.**



*These events include endothelial activation, recruitment of inflammatory cells, activation of coagulation, and inhibition of fibrinolysis.*

Computed Tomography studies in the 1980s helped us understand the pathophysiologic alterations in the lungs of ARDS patients.[43] In addition, as lung compliance correlates with the degree of the normally ventilated tissue, lung compliance decreases in ARDS because of decreased lung size, rather than because of lung stiffness, and this hypothesis introduced the concept of "baby lung" in ARDS.[44] Pulmonary hypertension (PH) is widely recognized as a characteristic feature of ARDS.[45] PH aetiology includes parenchymal destruction and airway collapse, hypoxic pulmonary vasoconstriction, presence of other pulmonary vasoconstrictors and vascular compression.[46]

The initial phase of fluid accumulation is followed by a proliferation phase characterized by resolution of pulmonary edema, proliferation of type II alveolar cells, fibroblasts and myofibroblasts, and new matrix deposition. This phase starts early (within 72 h) in ARDS, and lasts for more than 7 days. Factors influencing the progression to fibro-proliferation vs. resolution and reconstitution of normal pulmonary parenchymal architecture are poorly understood,[47] but patients who develop pulmonary fibrosis exhibit deterioration of pulmonary compliance, progressive hypoxia and ventilator dependence, and increased mortality (> 57%).[48]

Multiple Organ Failure (MOF) is the leading cause of death in ARDS, but the pathophysiologic link between ARDS and MOF is not well defined.[49] However, based on existing data it is not clear whether ARDS is the manifestation of a disease, or it is a disease that causes the MOF syndrome.

**STAGES**

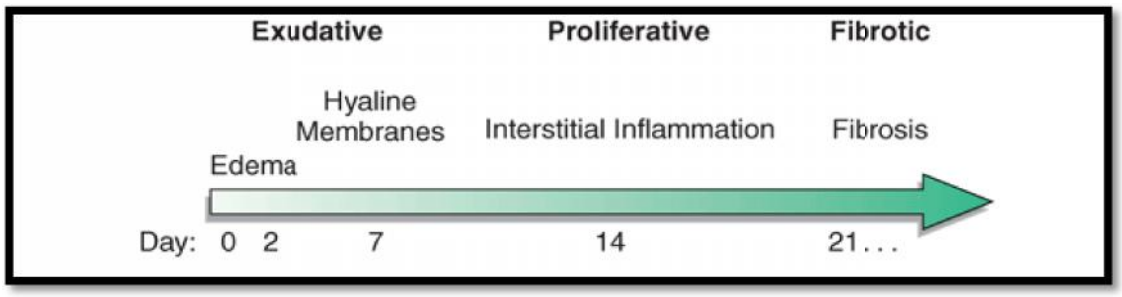



**Figure 3: stages of ARDS**

1. EXUDATIVE STAGE Alveolar capillary endothelial cells and type I pneumocytes is injured, leading to the loss of the normally tight alveolar barrier to fluid and macromolecules. oedema fluid that is rich in protein accumulates in the interstitial and alveolar spaces. Significant concentrations of cytokines, Lipid mediators (e.g. leukotriene B4) are present in the lung in this acute phase. In response to proinflammatory mediators, leukocytes (especially neutrophils) traffic into the pulmonary interstitium and alveoli. Pulmonary vascular injury also occurs early in ARDS, with alveolar oedema predominantly involving the dependent portions of the lung, leading to the diminished aeration and atelectasis.

Collapse of large sections of dependent lung markedly decreases lung compliance. Consequently, intrapulmonary shunting and hypoxemia develop and the work of breathing rises, leading to dyspnoea. Thus, in addition to severe hypoxemia, hypercapnia secondary to an increase in pulmonary dead space is also prominent in early ARDS.

2. PROLIFERATIVE STAGE This phase of ARDS usually lasts from day 7 to day 21. Most patients recover rapidly and are liberated from mechanical ventilation during this phase. Despite this improvement, many still experience dyspnoea, tachypnea, and hypoxemia. Histologically, the first signs of resolution are often evident in this phase

with the initiation of lung repair, organization of alveolar exudates, and a shift from a neutrophil to a lymphocyte-predominant pulmonary infiltrate. As part of the reparative process, there is a proliferation of type II pneumocytes along alveolar basement membranes. The presence of alveolar type III procollagen peptide, a marker of pulmonary fibrosis, is associated with a protracted clinical course and increased mortality from ARDS.

3. FIBROTIC PHASE While many patients with ARDS recover lung function 3-4 weeks after the initial pulmonary injury, some will enter a fibrotic phase that may require long term support on mechanical ventilators and/or supplemental oxygen. There is extensive alveolar and interstitial fibrosis. Acinar architecture is markedly disrupted, leading to emphysema-like changes with large bullae.

**CLINICAL FEATURES /CLINICAL COURSE**

Physical findings often are nonspecific and include tachypnea, tachycardia, and the need for a high fraction of inspired oxygen ($FiO_2$) to maintain oxygen saturation. The patient may be febrile or hypothermic. Because ARDS often occurs in the context of sepsis, associated hypotension and peripheral vasoconstriction with cold extremities may be present. Cyanosis of the lips and nail beds may occur. Examination of the lungs may reveal bilateral rales. Rales may not be present despite widespread involvement. Because the patient is often intubated and mechanically ventilated, decreased breath sounds over 1 lung may indicate a pneumothorax or endotracheal tube down the right main bronchus. Manifestations of the underlying cause (eg, acute abdominal findings in the case of ARDS caused by pancreatitis) are present. Because cardiogenic pulmonary oedema must be distinguished from ARDS signs of congestive heart failure or intravascular volume overload, including jugular

venous distention, cardiac murmurs and gallops, hepatomegaly, and oedema must be assessed.

**MANAGEMNT OF ADULT ARDS, ROLE OF DIFFERENT INTERVENTIONS**

Improved understanding of ARDS pathophysiology and advances in technology have introduced new treatments and improved therapeutic strategies. The following paragraphs discuss recent developments in the therapeutic approach to ARDS.

Low tidal volume ventilation

The concept of "baby lung" was introduced in 1980s by Gattinoniet al and generated interest in the use of low tidal volume ventilation as therapeutic strategy in ARDS. Several animal studies showed that ventilation with large tidal volumes and high inspiratory pressures resulted in development of hyaline membranes and inflammatory infiltrates in the lungs, and development of respiratory failure.[50]

In the late 1990s four randomized controlled trials (RCTs) evaluated the potential benefit of low tidal volume ventilation in ARDS.[51-53] Although all four studies had limited power, one study by Amato et al [53] demonstrated that the low tidal volume group had higher survival, higher rate of weaning from mechanical ventilation and reduced rate of barotrauma.

Because of conflicting results from these studies, the National Heart Lung and Blood Institute ARDS Network conducted a multicentre RCT on 861 ARDS patients [54], comparing two group of patients ventilated with low vs. high tidal volumes. In-hospital mortality was significantly lower and the number of days without mechanical ventilation was significantly higher in the low tidal volume group. Although this

study has been criticized for the high difference of tidal volume between groups, it demonstrated that high tidal volumes should be avoided, and underlined the importance of maintaining low plateau pressures, with 30 cm $H_2O$ as an acceptable cut-off.

Low tidal volume ventilation is generally well tolerated and it has not been associated with clinically important adverse outcomes, except for hypercapnia respiratory acidosis in some patients. In conclusion, hypercapnia and respiratory acidosis are expected consequences of low tidal volume ventilation. However, there is no evidence that hypercapnia is harmful in ARDS patients, and it may in fact confer some protection against ventilator-associated lung injury.

PEEP

PEEP is an essential component of mechanical ventilation for patients with ARDS, as it was early observed that PEEP greatly improves oxygenation in ARDS patients. High PEEP levels may open collapsed alveoli and decrease intrapulmonary shunt. Additionally, ventilation-induced alveolar injury is reduced by decreasing alveolar over-distention, because the volume of each subsequent tidal breath is shared by more open alveoli.[55] On the other hand, high PEEP levels may decrease repetitive alveolar opening and closing during the respiratory cycle, thereby promoting lung injury[56].

Three RCTs have evaluated modest vs. high levels of PEEP in patients with ARDS. The NHLB ARDS Network conducted the ALVEOLI trial (Assessment of Low tidal Volume and Elevated end expiratory pressure to Obviate Lung Injury).[57] This study showed improved PaO2/FiO2 ratio but no benefits with regards to survival or duration of mechanical ventilation in the high PEEP group. Several years later, the

Canadian Critical Care Trials Group performed a similar study to determine whether the combination of low tidal volume ventilation with high PEEP could improve mortality to a greater extent compared to low tidal ventilation alone.[34] Results of this study showed reduced need for other rescue therapies such as prone position or NO, but did not show any benefit in survival.

In conclusion, based on published data, high levels of PEEP do not seem to confer any benefit with regards to mortality in ARDS. Because ARDS patients are a heterogeneous population, the apparent absence of benefit from high levels of PEEP could be due to the beneficial effects of high PEEP in some ARDS patients being offset by detrimental effects in other patients.[58] However, data from the RCTs mentioned above suggest that high PEEP levels improve lungs function without any adverse effect on mortality.[59]

Recruitment manoeuvres

A recruitment manoeuvre is a transient increase of trans-pulmonary pressure intended to promote reopening of collapsed alveoli.[60] Techniques described for recruitment manoeuvres include sustained high-pressure inflation and increased PEEP, with concurrent reduction of tidal volume,[61] but it is not clear if any manoeuvre is superior to others. Several studies have shown improved gas exchange with recruitment manoeuvres, but no RCT has shown benefit on ARDS mortality [62] and a recent systematic review by Fan et al[63] showed that hypotension and decreased saturation occur in 12% and 8% of patients respectively during or after such manoeuvres. Based on currently available data, although routine recruitment manoeuvres are not recommended in ARDS, such manoeuvres can dramatically

improve oxygenation in certain patients, and should be considered as rescue therapy in patients with life-threatening refractory hypoxia.[64]

Prone position

Prone positioning has been used in ARDS for over 30 years. In 1976 Piehl et al.[65] reported improved oxygenation in ARDS patients when they were turned to the prone position. Since then, several observational studies on ARDS have found similar results, and improvement in oxygenation can sometimes be dramatic.[66] Mechanisms proposed to explain the observed beneficial effects of prone positioning include increased chest wall elastance decreased compression of lung tissue in the dependent regions and recruitment of alveoli, more homogeneous ventilation due to decreased ventilation-perfusion inequalities and reduced ventilator-induced lung injury.[67]

Four RCTs have investigated the effect of prone positioning on outcome. The first trial by the Prone-Supine Study group randomized 304 patients with a wide range of severity of acute lung injury. [68] Patients remained prone for 7 h/day on average, for up to 10 days, but there was no effect on survival. Three years later, Guerin C et al[69] conducted a similar multicentre study: patients remained prone for about 8 h/day, and prone positioning continued until clinical criteria for improvement were met, but this study also did not show a reduction in mortality. Two subsequent RCTs attempted to correct some shortcomings of the earlier study: they only included patients with ARDS, and patients remained prone for most of the day (about 20 h). The first RCT by Manceboet al[70] was terminated prematurely, after only including 142 patients, because of problems with patient recruitment. A more recent multicentre RCT by Tacconeet al[71], included 344 patients, and showed significantly increased frequency

of adverse events (airway obstruction, hypotension, vomiting, accidental extubation) in patients treated with prone position. Neither of the last two studies showed any survival benefit using the prone position in patients with severe ARDS.

In conclusion, existing data do not support routine use of the prone position in ARDS. However, because all published studies have shown improved oxygenation, prone positioning is an attractive rescue treatment for ARDS patients with severe hypoxemia, even though a survival benefit has never been demonstrated.

High-frequency ventilation

The idea of high frequency ventilation (HFV) is to provide tidal volumes below that of anatomic dead space at high frequency (> 60 breaths per minute). Compared to conventional mechanical ventilation, mean airway pressure is higher. Two studies, by Hamilton [72] and Chan [73], showed reduced risk for barotrauma and lung over-distention, after performing high frequency ventilation. High frequency ventilation can be applied by different modes, such as high-frequency percussive ventilation, high-frequency jet ventilation and high-frequency oscillatory ventilation (HFOV). In the absence of studies showing superiority of one method over another, HFOV is the HFV method used more often in adult critical care [73].

In HFOV very small tidal volumes (1 - 4 ml/kg) are delivered at high frequency (3 - 15 Hz) by an oscillatory pump. However, the use of HFOV as rescue therapy in patients with refractory hypoxia remains controversial. There are two RCTs comparing HFOV with conventional mechanical ventilation. The first RCT by Derdaket al[74] found a trend for decreasing 30-day mortality even though relatively high tidal volume was used in the control group. The second RCT by Bollenet al[75] was terminated prematurely because of slow enrolment, but found an opposite trend

in mortality. A more recent study by Sudet al included 8 RCTs and found reduced 30-day mortality with HFOV compared to conventional ventilation [76]. In conclusion, the role of HFOV in ARDS is not well defined, and deserves further study from well-designed RCTs.

Supportive treatment of ARDS

***Fluid management***

Early data indicate that increased fluid administration is correlated with worse outcome in ARDS, whereas negative fluid balance was associated with better outcome. The ARDS network conducted a RCT with 1000 patients randomized to receive conservative or liberal fluid administration. The conservative strategy group showed improved lung function and shortened duration of mechanical ventilation, but there was no difference in non-pulmonary organ failures and 60-day mortality.

***Transfusions***

Allogenic blood transfusion is associated with detrimental immuno-modulatory effects that may result in ARDS. Consequently, conservative transfusion strategies may decrease the incidence of ARDS.

**Sedation**

Several studies have shown that newer ventilation strategies using low tidal volume and high levels of PEEP do not require high doses of sedation [77]. Furthermore, evidence suggests that use of sedatives may increase duration of mechanical ventilation and ICU length of stay and may even be associated with higher mortality. In addition, there is evidence that spontaneously breathing ARDS patients have improved cardiopulmonary function, presumably by recruiting non

ventilated lung units [78]. Therefore, based on current evidence, avoidance or minimization of sedation and paralysis is preferred in ARDS.

***Neuromuscular blocking agents***

Administration of neuromuscular blocking agents (NMBA) in addition to sedation can result in improvement in severe hypoxemia, because paralysis improves patient-ventilator synchronism and reduces oxygen consumption. Muscle relaxation may also improve chest wall compliance. NMBAs may also have anti-inflammatory effects that could decrease the inflammation associated with ARDS. However, because there is evidence that NMBAs increase the risk of acquired neuromuscular weakness, thereby making weaning from mechanical ventilation more difficult, and may even increase mortality [79].

***Nutrition***

Two RCTs [80, 81] and a meta-analysis by Puntes-Arrudaet al[82] showed that administration of enteral nutrition containing high concentrations of eicosapentanoic acid and γ-linoleic acid and ω-3 fatty acids increased oxygenation and decreased ICU stay and 28-day mortality in ARDS.

**Pharmacologic agents**

***Vasodilators***

Because diffuse pulmonary vasoconstriction is part of ARDS pathophysiology, selective vasodilatation of well-ventilated areas seems an attractive method to improve gas exchange in ARDS patients.

Inhaled nitric oxide (iNO) causes vasodilation of ventilated lung units and redistribution of pulmonary blood flow away from non-ventilated lung areas, without adverse systemic hemodynamic effects. Four RCTs evaluated the effects of iNO and showed transient improvement in oxygenation, but no improvement in mortality. Similarly, one meta-analysis found transient oxygenation improvement but no survival benefit with iNO[83]. Consequently, iNO may be useful as short-term rescue therapy in patients with severe hypoxemic respiratory failure.

Inhaled prostacycline is another selective pulmonary vasodilator. Importantly, liposomal PGE1 influences neutrophil function and decreases neutrophil accumulation and lung leak. Although inhaled prostacycline improves oxygenation, it has not been shown to reduce duration of mechanical ventilation or mortality in ARDS patients. Despite the lack of sufficient data supporting the use of prostacycline as alternative to iNO, prostacyclineis increasingly used as pulmonary vasodilator, because of the high cost of iNO[84].

***Vasoconstrictors***

Vasoconstrictors can improve oxygenation in ARDS patients by decreasing intrapulmonary shunt. Phenylephrine and almitrine[85] have been used in small studies, mainly as adjuncts during administration of NO. B-blockers have also been shown to increase arterial oxygenation in patients with ARDS. However, the role of these agents in ARDS has not been adequately evaluated, and deserves further study.

***Anti inflammatory agents***

The interaction between nuclear factor-kappa B (NF-kB) and glucocorticoid receptor alpha (GRa) is a key mechanism regulating the progression of systemic and

pulmonary inflammation in ARDS. The ability of GC-GRa to down-regulate NF-kB activation is critical for the resolution of systemic and pulmonary inflammation in ARDS [86]. Although several studies showed that corticosteroids confer no benefit and may even cause harm, corticosteroids are still used in clinical practice.

Timing of corticosteroid administration and duration of therapy may be important, and should be taken into consideration. A RCT conducted by the ARDS Network, randomized 180 patients with persistent (> 7 days) ARDS, to receive methylprednisolone (2 mg/kg/d) or placebo for 21 days, and showed improved oxygenation and more ventilator-free days in the methylprednisolone group, but no significant improvement in mortality[87]. Another RCT [88] evaluated early corticosteroid administration, and showed that methylprednisolone administration (1mg/kg/d) less than 72 after the onset of ARDS reduced mortality. However, these results should be interpreted with caution, because this study included a large number of patients with septic shock.

Conflicting data exist concerning the correlation between corticosteroids and ICU neuromyopathy. A sub-analysis of study survivors did not show any association between randomization to corticosteroids and increased risk of neuromyopathy. In conclusion, the relationship between corticosteroids and ICU neuromyopathy is an important issue that deserves further study.

Several other anti-inflammatory factors like Ibuprofen, ketoconazole, neutrophil elastase inhibitors (ONO 5046), NF-KB inhibitors, recombinant soluble complement receptor-1, and liposomal prostaglandin E1 have been evaluated in ARDS patients without success. [89]

**$_2$ AGONISTS**:

There are substantial evidence that $\beta_2$ agonistsmay play a potential role in the treatment of patients with ARDS. $\beta_2$ agonists have been found to have anti-inflammatory effects by direct influence on neutrophil function and by reducing the secretion of several pro-inflammatory cytokines. Additionally, $\beta_2$ agonistscan reduce the endothelial permeability and stimulate the fluid clearance from the lungs [90]. In a small RCT [91] using the thermodilution method (PiCCO), intravenous salbutamol (15μg/kg/h) use for seven days reduced extravascular lung water compared to placebo. The effects of inhaled $\beta_2$ agonists have not, to this date, been adequately evaluated, but will be investigated in an ongoing study conducted by ARDS network. Several other pharmacological agents, including glutathione lisofylline, N-Acetylcysteine, and surfactant have been evaluated, but none of them has been shown to be effective for treatment of ARDS.

**Extracorporeal techniques**

Extracorporeal membrane oxygenation (ECMO) has been studied since 1970s as a method for supporting gas exchange in patients failing conventional ventilation. An RCT[92] conducted in 1979 showed that ECMO use did not affect long-term survival of ARDS patients. Nowadays, ECMO is used to support oxygenation of patients with severe ARDS, thereby allowing the use of decreased ventilator settings (tidal volume, respiratory rate, FiO2), in an attempt to minimiseventilator-induced lung injury.

In a more recent study 180 patients with severe ARDS were randomized to support by ECMO vs conventional treatments. This study showed significantly

improved survival (63% vs 47%, P = 0.03) at 6 months in the ECMO group [93]. Although no definite conclusions can be drawn from this study [94], the results of this study suggest that ECMO can be used as a rescue therapy in cases of very severe ARDS.

Extracorporeal CO2 removal (ECCO2R) is an alternative device that uses veno-venous circuit for removal of CO2 at much lower extracorporeal flow rates compared to ECMO. An RCT conducted before the year 2000 used ECCO2R and showed no effect on mortality [95]. In another study ECCO2R was combined with low frequency positive pressure ventilation (2 - 3 b/min), and showed improvement in lung mechanics [96]. Overall, extracorporeal support technologies produce significant temporary improvement in ARDS patients with severe respiratory dysfunction, but this improvement does not seem to affect the outcome. New, well conducted clinical studies are needed to better evaluate the role of ECMO and ECCO2R on survival in ARDS.

**TREATMENT OUTCOMES FOLLOWING ARDS**

Ingle VV et al[97] studied subjects and reported more males than females. Common etiological causes of ARDS were pneumonia, tropical infections including malaria and sepsis. Mortality was observed in 60% cases. ARDS was one of the important causes of mortality in ICU.

Agarwal R et al[98] reported that the most common cause of ARDS was infective pneumonia and sepsis. The median length of ICU stay was 5 days. The hospital mortality rate was 47.8%. Multivariate analysis showed SOFA scores as a risk factor for death in the ICU. There was no significant effect of the category of ARDS on the outcome (OR, 1.6; 95% CI, 0.8 to 3.2).

Conflicting data exist about the evolution of ARDS mortality over time. A meta-analysis by Phuaet al[99] did not find any mortality reduction in recent years, whereas another meta-analysis by Zambonet al[100] showed reduced mortality in recent years. In the past, several studies evaluated patterns of ARDS mortality over time within the same institution and all studies, except for two found decreasing mortality in ARDS. The observed discrepancy between different studies may be due to different investigational methods, but we can conclude that ARDS mortality remains high (41 - 46%). Regardless of improvements in recent years, ARDS mortality is higher in older patients and medical patients[101]. However, the impact, if any, of newer treatment strategies on ARDS mortality, has not been evaluated, because most studies are referred to the period before the year 2000.

Lu Y et al[102] reported the most common predisposing factors for ARDS were pneumonia (34.3%) and nonpulmonary sepsis (30.6%). The overall ICU mortality was 10.3%. In-hospital and 90-day mortalities of ARDS patients were 68.5 and 70.4%, respectively, and accounted for 13.5% of the overall ICU mortality. For ARDS patients, multiple organ dysfunction syndrome was a major risk factor associated with death (59.5%).

## FACTORS ASSOCIATED WITH ADVERSE OUTCOME AMONG ARDS PATIENTS

Meduri et al[49] reported that experimental and clinical evidence demonstrated a strong cause and effect relationship between persistence vs reduction in systemic inflammation and progression (unresolving) vs resolution (resolving) of ARDS. In their review, the cellular mechanisms involved in activating and regulating inflammation are contrasted between patients with resolving and unresolving ARDS. At the cellular level, patients with unresolving ARDS have deficient glucocorticoid

(GC) - mediated down-regulation of inflammatory cytokine and chemokine transcription despite elevated levels of circulating cortisol, a condition defined as systemic inflammation-associated acquired GC resistance. These patients, contrary to those with resolving ARDS, have persistent elevation in levels of both systemic and BAL fluid inflammatory cytokines and chemokines, markers of alveolar-capillary membrane permeability and fibrogenesis. At the tissue level, the continued production of inflammatory mediators leads to tissue injury, intravascular and extravascular coagulation, and the proliferation of mesenchymal cells, all resulting in maladaptive lung repair and progression of extrapulmonary organ dysfunction. In ARDS, down-regulation of systemic inflammation is essential to restoring homeostasis, decreasing morbidity, and improving survival. Prolonged low-to-moderate dose GC therapy promotes the down-regulation of inflammatory cytokine transcription at the cellular level. Eight controlled studies have consistently reported a significant reduction in markers of systemic inflammation, pulmonary and extrapulmonary organ dysfunction scores, duration of mechanical ventilation, and ICU length of stay. In the aggregate (n = 628), reduction in mortality was substantial for all patients (relative risk [RR], 0.75; 95% CI, 0.63 to 0.89; $p < 0.001$; I(2), 43%) and for those treated before day 14 (RR, 0.71; 95% CI, 0.59 to 0.85; $p < 0.001$; I(2), 40%).

Meade Mo et al[34] applied control strategy that included target tidal volumes of 6 mL/kg of predicted body weight, plateau airway pressures not exceeding 30 cm H2O, and conventional levels of positive end-expiratory pressure (n = 508). The experimental strategy included target tidal volumes of 6 mL/kg of predicted body weight, plateau pressures not exceeding 40 cm H2O, recruitment manoeuvres, and higher positive end-expiratory pressures (n = 475). The main outcome measure studied in this study was all-cause hospital mortality. Eighty-five per cent of the 983

study patients met criteria for acute respiratory distress syndrome at enrollment. Tidal volumes remained similar in the 2 groups, and mean positive end-expiratory pressures were 14.6 (SD, 3.4) cm H2O in the experimental group vs 9.8 (SD, 2.7) cm H2O among controls during the first 72 hours (P < .001). All-cause hospital mortality rates were 36.4% and 40.4%, respectively (relative risk [RR], 0.90; 95% confidence interval [CI], 0.77-1.05; P = .19). Barotrauma rates were 11.2% and 9.1% (RR, 1.21; 95% CI, 0.83-1.75; P = .33). The experimental group had lower rates of refractory hypoxemia (4.6% vs 10.2%; RR, 0.54; 95% CI, 0.34-0.86; P = .01), death with refractory hypoxemia (4.2% vs 8.9%; RR, 0.56; 95% CI, 0.34-0.93; P = .03), and previously defined eligible use of rescue therapies (5.1% vs 9.3%; RR, 0.61; 95% CI, 0.38-0.99; P = .045). For patients with acute lung injury and acute respiratory distress syndrome, a multifaceted protocolized ventilation strategy designed to recruit and open the lung resulted in no significant difference in all-cause hospital mortality or barotrauma compared with an established low-tidal-volume protocolized ventilation strategy. This "open-lung" strategy did appear to improve secondary end points related to hypoxemia and use of rescue therapies.

Singh G et al[103] reported the incidence of ARDS among those who were mechanically ventilated was 11.4%. Sepsis was the most common (34.6%) etiology. Among those with risk factors, the incidence of ARDS was 30% and that of ALI was 32.7%. The mortality in those with ARDS was 41.8%. Those who develop ARDS had higher APACHE II scores, lower pH and higher $PaCO_2$ at admission compared with those who developed ALI or no lung injury.

Gupta D et al[104] reported that sepsis (28.6%), followed by malaria (21.4%), were the commonest risk factors for ARDS. Seven out of eight patients (87.5%) with

sepsis died. The presence of sepsis, more than three organ failure prior to admission, APACHE III score > 57 and SAPS II score > 39 were significantly associated with mortality. Only APACHE III score > 57 or SAPS II score > 39 were, however, independently predictive of a poor outcome following multivariate analysis. They concluded with sepsis, associated with a very poor outcome, and malaria were important risk factors for the development of ARDS. APACHE III score > 57 or SAPS II score > 39 were associated with increased risk of mortality.

Grasso et al[58] observed a recent study by the Acute Respiratory Distress Syndrome Network comparing the traditional lower end-expiratory pressure strategy with a higher end-expiratory pressure strategy in patients with the acute respiratory distress syndrome ventilated with low tidal volumes. Clinical outcomes were similar whether lower or higher positive end-expiratory pressure (PEEP) levels were used. They applied both the lower (9 +/- 2 cm $H_2O$) and higher (16 +/- 1 cm $H_2O$) PEEP strategy in 19 patients. In nine recruiters, the higher end-expiratory pressure strategy resulted in significant alveolar recruitment (587 +/- 158 ml), improvement in arterial oxygen partial pressure/inspired oxygen fraction ratio (from 150 +/- 36 to 396 +/- 138), and reduction in static lung elastance (from 23 +/- 3 to 20 +/- 2 cm $H_2O$/L). In 10 nonrecruiters, alveolar recruitment was minimal, oxygenation did not improve, and static lung elastance significantly increased (from 26 +/- 5 to 28 +/- 6 cm $H_2O$/L). The increase in oxygenation, the reduction in static lung elastance, and the shape of the volume-pressure curve during the lower PEEP strategy were independently associated with alveolar recruitment. In conclusion, the protocol proposed by the Acute Respiratory Distress Syndrome Network, lacking solid physiologic basis, frequently fails to induce alveolar recruitment and may increase the risk of alveolar overinflation.

Borges JB et al[61] studied twenty-six patients received sequential increments in inspiratory airway pressures, in 5 cm H(2)O steps, until the detection of $PaO_2$ + $PaCO_2$>or= 400 mm Hg. Whenever this primary target was not met, despite inspiratory pressures reaching 60 cm $H_2O$, the maneuver was considered incomplete. If there was hemodynamic deterioration or barotrauma, the maneuver was to be interrupted. Late assessment of recruitment efficacy was performed by computed tomography (9 patients) or by online continuous monitoring in the intensive care unit (15 patients) up to 6 h. It was possible to open the lung and to keep the lung open in the majority (24/26) of patients, at the expense of transient hemodynamic effects and hypercapnia but without major clinical consequences. No barotrauma directly associated with the maneuver was detected. There was a strong and inverse relationship between arterial oxygenation and percentage of collapsed lung mass ($R = - 0.91$; $p < 0.0001$). It is often possible to reverse hypoxemia and fully recruit the lung in early acute respiratory distress syndrome. Due to transient side effects, the required maneuver still awaits further evaluation before routine clinical application.

Martin et al[48]studied twenty-two lung specimens were obtained from 25 consecutive patients with ARDS of various origin (postsurgical complications, 7 patients; multiple trauma, 8 patients; medical problems, 7 patients). Transbronchial lung biopsy was complicated by small or moderate hemorrhage in three patients. No case of pneumothorax was identified. Pathologic findings showed that 14 patients (64%) had pulmonary fibrosis, either mild (9 patients) or moderate to severe fibrosis (5 patients). In the patients with pulmonary fibrosis, mortality rate was 57% (8 out of 14 patients), which was significantly different ($p < 0.02$) from the 0% mortality rate observed in patients without pulmonary fibrosis. Severity of pulmonary fibrosis (mild vs moderate and severe) did not influence outcome. With the exception of pathologic

findings, characteristics of patients with and without pulmonary fibrosis ($PaO_2$, $PaCO_2$, the ratio of $PaO_2$ to fraction of inspired oxygen, and positive end-expiratory pressure) were not different. In the study patients, pulmonary fibrosis diagnosed on the basis of TBLB was closely related to fatality in established ARDS.

Brower RG et al[51] observed that mean tidal volumes during the first 5 days in traditional and small tidal volume patients were 10.2 and 7.3 mL/kg, respectively ($p < .001$), with mean plateau pressure = 30.6 and 24.9 cm $H_2O$ (3.3 kPa), respectively ($p < .001$). There were no significant differences in requirements for positive end-expiratory pressure or $FiO_2$, fluid intakes/outputs, requirements for vasopressors, sedatives, or neuromuscular blocking agents, percentage of patients that achieved unassisted breathing, ventilator days, or mortality.

Gattinoni L et al[62] Sixty-eight patients with acute lung injury or ARDS underwent whole-lung CT during breath-holding sessions at airway pressures of 5, 15, and 45 cm of water. The percentage of potentiallyrecruitable lung was defined as the proportion of lung tissue in which aeration was restored at airway pressures between 5 and 45 cm of water. The percentage of potentially recruitable lung varied widely in the population, accounting for a mean (+/-SD) of 13+/-11 percent of the lung weight, and was highly correlated with the percentage of lung tissue in which aeration was maintained after the application of PEEP ($r2=0.72$, $P<0.001$). On average, 24 percent of the lung could not be recruited. Patients with a higher percentage of potentially recruitable lung (greater than the median value of 9 percent) had greater total lung weights ($P<0.001$), poorer oxygenation (defined as a ratio of partial pressure of arterial oxygen to fraction of inspired oxygen) ($P<0.001$) and respiratory-system compliance ($P=0.002$), higher levels of dead space ($P=0.002$), and higher rates of death ($P=0.02$) than patients with a lower percentage of potentially recruitable lung.

The combined physiological variables predicted, with a sensitivity of 71 percent and a specificity of 59 percent, whether a patient's proportion of potentially recruitable lung was higher or lower than the median. In ARDS, the percentage of potentiallyrecruitable lung is extremely variable and is strongly associated with the response to PEEP.

Fan E et al[63] conducted a systemic review of case series, observational studies, and randomized clinical trials with pooling of study-level data. Forty studies (1,185 patients) met inclusion criteria. Oxygenation (31 studies; 636 patients) was significantly increased after an RM (PaO2): 106 versus 193 mm Hg, P = 0.001; and PaO2/FiO2 ratio: 139 versus 251 mm Hg, P < 0.001). There were no persistent, clinically significant changes in hemodynamic parameters after an RM. Ventilatory parameters (32 studies; 548 patients) were not significantly altered by an RM, except for higher PEEP post-RM (11 versus 16 cm H2O; P = 0.02). Hypotension (12%) and desaturation (9%) were the most common adverse events (31 studies; 985 patients). Serious adverse events (e.g., barotrauma [1%] and arrhythmias [1%]) were infrequent. Only 10 (1%) patients had their RMs terminated prematurely due to adverse events. Adult patients with ALI receiving RMs experienced a significant increase in oxygenation, with few serious adverse events. Transient hypotension and desaturation during RMs is common but is self-limited without serious short-term sequelae. Given the uncertain benefit of transient oxygenation improvements in patients with ALI and the lack of information on their influence on clinical outcomes, the routine use of RMs cannot be recommended or discouraged at this time. RMs should be considered for use on an individualized basis in patients with ALI who have life-threatening hypoxemia.

Hodgson C et al[64] included randomized controlled trials of adults who were mechanically ventilated comparing recruitment manoeuvres to standard care for those patients diagnosed with ALI or ARDS. Two authors independently assessed trial quality and extracted data. We contacted study authors for additional information. Seven trials met the inclusion criteria for this review (the total number of included participants was 1170). All trials included a recruitment manoeuvre as part of the treatment strategy for patients on mechanical ventilation for ARDS or ALI. However, two of the trials included a package of ventilation that was different from the control ventilation in aspects other than the recruitment manoeuvre. The intervention group showed no significant difference on 28-day mortality (RR 0.73, 95% CI 0.46 to 1.17, P = 0.2). Similarly there was no statistical difference for risk of barotrauma (RR 0.50, 95% CI 0.07 to 3.52, P = 0.5) or blood pressure (MD 0.9 mm Hg, 95% CI -4.28 to 6.08, P = 0.73). Recruitment manoeuvres significantly increased oxygenation above baseline levels for a short period of time in four of the five studies that measured oxygenation. There were insufficient data on length of ventilation or hospital stay to pool results. The authors concluded that there is not enough evidence to make conclusions on whether recruitment manoeuvres reduce mortality or length of ventilation in patients with ALI or ARDS.

Blanch L et al[66] measured gas exchange and hemodynamic variables in all patients and in 16 patients calculated respiratory system compliance when they were supine and 60 to 90 min after turning them to a prone position. This latter position was remarkably well toleratedand no clinically relevant complications or events were detected either during turning or while prone. The partial pressure of oxygen in arterial blood (PaO2)/FIO2 ratio improved from 78 +/- 37 mm Hg supine to 115 +/- 31 mm Hg prone ($p < 0.001$), and intrapulmonary shunt decreased from 43 +/- 11 to

34 +/- 8% ($p < 0.001$). Cardiac output and other hemodynamic parameters were not affected. Respiratory system compliance slightly improved from 24.7 +/- 10.2 ml/cmH20 supine to 27.8 +/- 13.2 ml/cmH20 prone ($p < 0.05$). An improvement in PaO2/FIO2 of more than 15% from changing from supine to prone was found in 16 patients (responders). Responders had more hypoxemia (PaO2/FIO2 70 +/- 23 vs 99 +/- 53 mm Hg in non-responders, $p < 0.01$), more hypercapnia (partial pressure of carbon dioxide in arterial blood (70 +/- 27 vs 64 +/- 9 mm Hg, $p < 0.01$) and a shorter elapsed time to the onset of ARDS and turning to the prone position (11.8 +/- 16 vs 32.8 +/- 42 days, $p < 0.01$). Turning critically ill, severely hypoxemic patients from the supine to the prone position is a safe and useful therapeutic intervention. Their data suggest that prone positioning should be carried out early in the course of ARDS.

Gattinoni L et al[68], in a multicenter, randomized trial, compared conventional treatment (in the supine position) of patients with acute lung injury or the acute respiratory distress syndrome with a predefined strategy of placing patients in a prone position for six or more hours daily for 10 days. They enrolled 304 patients, 152 in each group. The mortality rate was 23.0 percent during the 10-day study period, 49.3 percent at the time of discharge from the intensive care unit, and 60.5 percent at 6 months. The relative risk of death in the prone group as compared with the supine group was 0.84 at the end of the study period (95 percent confidence interval, 0.56 to 1.27), 1.05 at the time of discharge from the intensive care unit (95 percent confidence interval, 0.84 to 1.32), and 1.06 at six months (95 percent confidence interval, 0.88 to 1.28). During the study period the mean (+/-SD) increase in the ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen, measured each morning while patients were supine, was greater in the prone than the supine group (63.0+/-66.8 vs. 44.6+/-68.2, P=0.02). The incidence of complications related

to positioning (such as pressure sores and accidental extubation) was similar in the two groups. Although placing patients with acute respiratory failure in a prone position improves their oxygenation, it does not improve survival.

Guerin C et al[69] studied patients above 18 years, hemodynamically stable, receiving mechanical ventilation, and intubated and had to have a partial pressure of arterial oxygen (PaO2) to fraction of inspired oxygen (FIO2) ratio of 300 or less and no contraindications to lying prone. The 28-day mortality rate was 32.4% for the prone group and 31.5% for the supine group (relative risk [RR], 0.97; 95% confidence interval [CI], 0.79-1.19; P = .77). Ninety-day mortality for the prone group was 43.3% vs 42.2% for the supine group (RR, 0.98; 95% CI, 0.84-1.13; P = .74). The mean (SD) duration of mechanical ventilation was 13.7 (7.8) days for the prone group vs 14.1 (8.6) days for the supine group (P = .93) and the VAP incidence was 1.66 vs 2.14 episodes per 100-patient's days of intubation, respectively (P = .045). The PaO2/FIO2 ratio was significantly higher in the prone group during the 28-day follow-up. However, pressure sores, selective intubation, and endotracheal tube obstruction incidences were higher in the prone group. This trial demonstrated no beneficial outcomes and some safety concerns associated with prone positioning. For patients with hypoxemic Acute Respiratory failure (ARF), prone position placement may lower the incidence of VAP.

Derdaks et al[74] designed a multicenter, randomized, controlled trial comparing the safety and effectiveness of high-frequency oscillatory ventilation with conventional ventilation in adults with acute respiratory distress syndrome; 148 adults with acute respiratory distress syndrome (Pa(O2)/fraction of inspired oxygen <or= 200 mm Hg on 10 or more cm H2O positive end-expiratory pressure) were randomized to high-frequency oscillatory ventilation (n = 75) or conventional

ventilation (n = 73). Applied mean airway pressure was significantly higher in the high-frequency oscillation group compared with the conventional ventilation group throughout the first 72 hours (p = 0.0001). The high-frequency oscillation group showed early (less than 16 hours) improvement in Pa(O2)/fraction of inspired oxygen compared with the conventional ventilation group (p = 0.008); however, this difference did not persist beyond 24 hours. Oxygenation index decreased similarly over the first 72 hours in both groups. Thirty-day mortality was 37% in the high-frequency oscillation group and was 52% in the conventional ventilation group (p = 0.102). The percentage of patients alive without mechanical ventilation at Day 30 was 36% and 31% in the high-frequency oscillation and conventional ventilation groups, respectively (p = 0.686). There were no significant differences in hemodynamic variables, oxygenation failure, ventilation failure, barotraumas, or mucus plugging between treatment groups. We conclude that high-frequency oscillation is a safe and effective mode of ventilation for the treatment of acute respiratory distress syndrome in adults.

Bollen CW et al[75]prematurely stopped the study. Thirty-seven patients received HFOV and 24 patient's CV (average APACHE II score 21 and 20, oxygenation index 25 and 18 and duration of mechanical ventilation prior torandomization 2.1 and 1.5 days, respectively). There were no statistically significant differences in survival without supplemental oxygen or on ventilator, mortality, therapy failure, or crossover. Adjustment by a priorly defined baseline characteristics showed an odds ratio of 0.80 (95% CI 0.22-2.97) for survival without oxygen or on ventilator, and an odds ratio for mortality of 1.15 (95% CI 0.43-3.10) for HFOV compared with CV. The response of the oxygenation index (OI) to treatment did not differentiate between survival and death. In the HFOV group the OI response was

significantly higher than in the CV group between the first and the second day. A post hoc analysis suggested that there was a relatively better treatment effect of HFOV compared with CV in patients with a higher baseline OI. No significant differences were observed, but this trial only had power to detect major differences in survival without oxygen or on ventilator. In patients with ARDS and higher baseline OI, however, there might be a treatment benefit of HFOV over CV. More research is needed to establish the efficacy of HFOV in the treatment of ARDS. We suggest that future studies are designed to allow for informative analysis in patients with higher OI.

Sud S et al[76] included eight randomised controlled trials (n=419 patients); almost all patients had ARDS. Methodological quality was good. The ratio of partial pressure of oxygen to inspired fraction of oxygen at 24, 48, and 72 hours was 16-24% higher in patients receiving high frequency oscillation. There were no significant differences in oxygenation index because mean airway pressure rose by 22-33% in patients receiving high frequency oscillation (P</=0.01). In patients randomised to high frequency oscillation, mortality was significantly reduced (risk ratio 0.77, 95% confidence interval 0.61 to 0.98, P=0.03; six trials, 365 patients, 160 deaths), and treatment failure (refractory hypoxaemia, hypercapnoea, hypotension, or barotrauma) resulting in discontinuation of assigned therapy was less likely (0.67, 0.46 to 0.99, P=0.04; five trials, 337 patients, 73 events). Other risks were similar. There was substantial heterogeneity between trials for physiological (I(2)=21-95%) but not clinical (I(2)=0%) outcomes. Pooled results were based on few events for most clinical outcomes.High frequency oscillation might improve survival and is unlikely to cause harm. As ongoing large multicentre trials will not be completed for several

years, these data help clinicians who currently use or are considering this technique for patients with ARDS.

Pontes-Arruda, A et al[81] conducted a prospective, double-blind, placebo-controlled, randomized trial in three different intensive care units of a tertiary hospital in Brazil. The study enrolled 165 patients. Patients were randomized to be continuously tube-fed with either a diet enriched with EPA, GLA, and elevated antioxidants or an isonitrogenous and isocaloric control diet, delivered at a constant rate to achieve a minimum of 75% of basal energy expenditure x 1.3 during a minimum of 4 days. Patients were monitored for 28 days. Patients who were fed with the study diet experienced a significant reduction in mortality rate compared with patients fed with the control diet, the absolute mortality reduction amounting to 19.4% ($p = .037$). The group who received the study diet also experienced significant improvements in oxygenation status, more ventilator-free days (13.4 +/- 1.2 vs. 5.8 +/- 1.0, $p < .001$), more intensive care unit (ICU)-free days (10.8 +/- 1.1 vs. 4.6 +/- 0.9, $p < .001$), and a lesser development of new organ dysfunctions ($p < .001$). In patients with severe sepsis or septic shock and requiring mechanical ventilation and tolerating enteral nutrition, a diet enriched with EPA, GLA, and elevated antioxidants contributed to better ICU and hospital outcomes and was associated with lower mortality rates.

Pontes Arruda A et al [82] conducted a meta-analysis including three randomized controlled studies (n = 411 patients). Among the most important findings of this evaluation is a significant reduction in the risk of mortality (odds ratio [OR] = 0.40; 95% confidence interval [CI] = 0.24-0.68; P = .001), with significant reductions in the risk of developing new organ failures (OR = 0.17; 95% CI = 0.08-0.34; P < .0001), time on mechanical ventilation (standardized mean difference [SMD] = 0.56;

95% CI = 0.32-0.79; P < .0001), and ICU stay (SMD = 0.51; 95% CI = 0.27-0.74; P < .0001) in patients who received EPA + GLA. The meta-analysis showed a significant reduction in the risk of mortality as well as relevant improvements in oxygenation and clinical outcomes of ventilated patients with ALI/ARDS given EPA + GLA.

Steinberg KP et al [87] reported that at 60 days, the hospital mortality rate was 28.6 percent in the placebo group (95 percent confidence interval, 20.3 to 38.6 percent) and 29.2 percent in the methylprednisolone group (95 percent confidence interval, 20.8 to 39.4 percent; P=1.0); at 180 days, the rates were 31.9 percent (95 percent confidence interval, 23.2 to 42.0 percent) and 31.5 percent (95 percent confidence interval, 22.8 to 41.7 percent; P=1.0), respectively. Methylprednisolone was associated with significantly increased 60- and 180-day mortality rates among patients enrolled at least 14 days after the onset of ARDS. Methylprednisolone increased the number of ventilator-free and shock-free days during the first 28 days in association with an improvement in oxygenation, respiratory-system compliance, and blood pressure with fewer days of vasopressor therapy. As compared with placebo, methylprednisolone did not increase the rate of infectious complications but was associated with a higher rate of neuromuscular weakness. These results do not support the routine use of methylprednisolone for persistent ARDS despite the improvement in cardiopulmonary physiology. In addition, starting methylprednisolone therapy more than two weeks after the onset of ARDS may increase the risk of death.

Meduri GU et al [88] measured the predefined primary end point as a 1-point reduction in lung injury score (LIS) or successful extubation by day 7. In intention-to-treat analysis, the response of the two groups (63 treated and 28 control) clearly diverged by day 7, with twice the proportion of treated patients achieving a 1-point reduction in LIS (69.8% vs 35.7%; p = 0.002) and breathing without assistance

(53.9% vs 25.0%; p = 0.01). Treated patients had significant reduction in C-reactive protein levels, and by day 7 had lower LIS and multiple organ dysfunction syndrome scores. Treatment was associated with a reduction in the duration of mechanical ventilation (p = 0.002), ICU stay (p = 0.007), and ICU mortality (20.6% vs 42.9%; p = 0.03). Treated patients had a lower rate of infections (p = 0.0002), and infection surveillance identified 56% of nosocomial infections in patients without fever. Methylprednisolone-induced down-regulation of systemic inflammation was associated with significant improvement in pulmonary and extrapulmonary organ dysfunction and reduction in duration of mechanical ventilation and ICU length of stay.

Perkins GD et al [90] reported that intravenous salbutamol reduced measures of alveolar-capillary permeability in patients with acute respiratory distress syndrome (ARDS). In vitro, salbutamol stimulated both wound repair, and spreading and proliferation of A549 cells and distal lung epithelial cells. Lung lavage fluid from patients treated with salbutamol enhanced wound repair responses compared with placebo treated patients in vitro by an interleukin 1beta dependent mechanism.Their in vivo and in vitro work suggests that salbutamol may stimulate epithelial repair--potentially a pharmacological first in ARDS. Clearly establishing the mechanisms and pathways responsible for this is important for the future, and may allow identification of novel therapeutic targets to promote alveolar epithelial repair in humans with ARDS.

Perkins GD et al [91] conducted a single-center, double-blind, randomized controlled trial. Patients with ALI/ARDS were randomized to treatment with intravenous salbutamol (15 microg kg(-1) h(-1)) or placebo for 7 d. The primary endpoint was extravascular lung water measured by thermodilution (PiCCO) at Day 7.

Sixty-six patients were screened; of these, 40 met the inclusion criteria and were enrolled during 2001-2003. Patients in the salbutamol group had significantly lower lung water at Day 7 than the placebo group (9.2 +/- 6 vs. 13.2 +/- 3 ml kg(-1); 95% confidence interval difference, 0.2-8.3 ml kg(-1); p = 0.038). Plateau airway pressure was lower at Day 7 in the salbutamol group (23.9 +/- 3.8 cm H2O) versus placebo (29.5 +/- 7.2 cm H2O; p = 0.049). There was a trend toward lower Murray lung injury score at Day 7 in the salbutamol group (1.7 +/- 0.9) versus placebo (2.0 +/- 0.6; p = 0.2). Patients in the salbutamol group had a higher incidence of supraventricular arrhythmias (26 vs. 10%; p = 0.2). Although further research is required to confirm the efficacy and safety of intravenous salbutamol in ALI/ARDS, this trial provides the first proof of principle that, in humans with ALI/ARDS, sustained treatment with intravenous beta-agonists reduces extravascular lung water.

Phua J et al [99]searched multiple databases (MEDLINE, EMBASE, CINAHL, Cochrane CENTRAL) for prospective observational studies or randomized controlled trials (RCTs) published during the period 1984 to 2006 that enrolled 50 or more patients with ALI/ARDS and reported mortality. They pooled mortality estimates using random-effects meta-analysis and examined mortality trends before and after 1994 (when a consensus definition of ALI/ARDS was published) and factors associated with mortality using meta-regression models. Of 4,966 studies, 89 met inclusion criteria (53 observational, 36 RCTs). There was a total of 18,900 patients (mean age 51.6 years; 39% female). Overall pooled weighted mortality was 44.3% (95% confidence interval [CI], 41.8-46.9). Mortality decreased with time in observational studies conducted before 1994; no temporal associations with mortality were demonstrated in RCTs (any time) or observational studies (after 1994). Pooled mortality from 1994 to 2006 was 44.0% (95% CI, 40.1-47.5) for observational

studies, and 36.2% (95% CI, 32.1-40.5) for RCTs. Meta-regression identified study type (observational versus RCT, odds ratio, 1.36; 95% CI, 1.08-1.73) and patient age (odds ratio per additional 10 yr, 1.27; 95% CI, 1.07-1.50) as the only factors associated with mortality. A decrease in ARDS mortality was only seen in observational studies from 1984 to 1993. Mortality did not decrease between 1994 (when a consensus definition was published) and 2006, and is lower in RCTs than observational studies.

Zambon M et al [100] used the Medline database to select studies with the key words "acute lung injury," "ARDS," "acute respiratory failure," and "mechanical ventilation." All studies that reported mortality rates for patients with ALI/ARDS defined according to the criteria of the American European Consensus Conference were selected. They excluded studies with < 30 patients and studies limited to specific subgroups of ARDS patients such as sepsis, trauma, burns, or transfusion-related ARDS. Seventy-two studies were included in the analysis. There was a wide variation in mortality rates among the studies (15 to 72%). The overall pooled mortality rate for all studies was 43% (95% confidence interval, 40 to 46%). Metaregression analysis suggested a significant decrease in overall mortality rates of approximately 1.1%/yr over the period analyzed (1994 to 2006). The mortality reduction was also observed for hospital but not for ICU or 28-day mortality rates. In this literature review, the data are consistent with a reduction in mortality rates in general populations of patients with ALI/ARDS over the last 10 years.

Eachampati et al [105]included 343 patients with ARDS, 210 of whom were >65 years old. Overall, age was 65.2 +/- 0.2 years, with a mean APACHE III score of 83.4 +/- 2.0 points. Sixty-six percent were men. The initial Pao2:FIO2 for the entire group was 104.3 +/- 4.1, and was less in younger patients. Maximum positive end-

expiratory pressure was 15.6 +/- 0.5 cm H2O, and mean LIS was 3.3 +/- 0.6 points; these values did not differ between cohorts. Elderly patients had a mortality of 51.9% when compared with 41.7% for younger patients (p = not significant). By logistic regression analysis, factors predicting mortality included APACHE III score (each point, odds ratio [OR], 1.022; 95% confidence interval [CI], 1.008-1.035; $p < 0.01$) and nonpulmonary multiple organ dysfunction score (each point, OR, 1.366; 95% CI, 1.223-1.526; $p < 0.0001$), but neither age ($p = 0.37$), LIS ($p = 0.49$), multiple organ dysfunction pulmonary ($p = 0.90$), nor year of treatment ($p = 0.74$) had any effect on mortality. The mortality rate for elderly patients with ARDS is lower in our experience when compared with historical series, even though illness severity may be higher, and comparable to that of other patients. Careful hemodynamic monitoring and resuscitation combined with other strategies to ameliorate nonpulmonary organ dysfunction achieved good outcomes in high-risk patients and could contribute in the future to further improved outcomes of elderly patients with ARDS.

Suchyta MR et al [101] reported that 72 of 112 patients older than 55 years (64%) died vs 65 of 144 patients 55 years and younger (45%) ($p = 0.002$). Examination of patient groups using age identified older than 55 years as a "cutpoint" above which mortality was greater ($p = 0.002$). Older nonsurvivors did not differ from nonsurvivors 55 years or younger with respect to gender, smoking history, ARDS risk factors, ARDS identifying characteristics, APACHE II (acute physiology and chronic health evaluation), number of organ failures, or the incidence of sepsis. In the 48 h prior to death, nonsurvivors 55 years and younger had more organ failure (3.4 +/- 0.2 vs 2.8 +/- 0.2; $p = 0.03$), higher fraction of inspired oxygen (0.82 +/- 0.03 vs 0.68 +/- 0.03; $p = 0.008$), and higher positive end-expiratory pressure levels (13 +/- 1 vs 8 +/- 1; $p = 0.001$) than older nonsurvivors. Despite more severe expression of disease,

only 32 (50%) nonsurvivors 55 years and younger had support withdrawn. Significantly more nonsurvivors older than 55 years (73%) had support withdrawn ($p = 0.009$). Even in the absence of chronic disease states, withdrawal was more likely for patients older than 55 years (21/51) than in those 55 years and younger (3/32; $p < 0.001$). Mortality is significantly higher for patients with ARDS older than 55 years. Decisions to withdraw support are made more often in ARDS patients older than 55 years. These data suggest that age bias may influence decisions to withdraw support.

Magazine R et al [11] reported that the mean age of their study population was 42.92 ± 13.91 years. The causes of ARDS included pneumonia (*n* = 35, 23.3%), scrub typhus (*n* = 33, 22%), leptospirosis (*n* = 11, 7.3%), malaria (*n* = 6, 4%), influenza (H1N1) (*n* = 10, 6.7%), pulmonary tuberculosis (*n* = 2, 1.3%), dengue (*n* = 1, 0.7%), abdominal sepsis (*n* = 16, 10.7%), skin infection (*n* = 3, 2%), unknown cause of sepsis (*n* = 18, 12%), and nonseptic causes (*n* = 15, 10%). A total of 77 (51.3%) patients survived, 66 (44%) expired, and 7 (4.7%) were discharged against medical advice (AMA). Pre-existing comorbidities (46) were present in 13 survivors, 19 nonsurvivors, and four discharged AMA. History of surgery prior to the onset of ARDS was present in one survivor, 13 nonsurvivors, and one discharge AMA. Mean Acute Physiology and Chronic Health Evaluation (APACHE) II, APACHE III, and Sequential Organ Failure Assessment scores in survivors were 9.06 ± 4.3, 49.22 ± 14, and 6.43 ± 2.5 and in nonsurvivors 21.11 ± 7, 86.45 ± 23.5, and 10.6 ± 10, respectively. The most common cause of ARDS in our study was pneumonia, but a large percentage of cases were due to the tropical infections. Pre-existing comorbidity, higher severity scores, and organ failure scores were more frequently observed among nonsurvivors than survivors.

# MATERIALS & METHODS

**Study site:** This study was conducted in the Intensive Care Unit (ICU), at KLES Dr. Prabhakar Kore Hospital and MRC Belagavi

**Study population:** All the eligible patients above 18 years admitted to the Intensive care unit and confirmed cases of ARDS based on the Berlin definition of ARDS were considered as study population.

**Study design:** cross sectional prospective study

**Sample size:** The sample size was calculated assuming the expected mortality among the ARDS patients as 47.8% as per the study by Agarwal, R., et al.[12] hence the expected proportion of subjects with and without mortality was considered as 1:1. By considering the mean APACHE II score among survivors as 15.9 (SD= 7.1) and among non survivors as 20 (SD=8.2). To be able to detect the differences in the above mentioned mean values between the two groups, with 80% power and 5% alpha error, the required sample size was calculated as 55 subjects. To account for non-participation or loss to follow up of about 5%, another 2 subjects were added to sample size. Hence the required sample size was 57. The study had included 60 subjects in the final analysis.

**Sampling method:** All the eligible subjects were recruited into the study consecutively by convenient sampling till the sample size is reached.

**Study duration:** The data collection for the study was done between January 2017 to December 2017 for a period of 1 year.

**Inclusion Criteria:**

Patients above age of 18 years admitted in intensive care unit and confirmed cases of ARDS based on The Berlin Definition of ARDS as follows.[3]

| | |
|---|---|
| Timing | Within 1 week of a known clinical insult or new or worsening respiratory symptoms |
| Chest imaging[a] | Bilateral opacities — not fully explained by effusions, lobar/lung collapse, or nodules |
| Origin of edema | Respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present |
| **CLASSIFICIATION OF OXYGENATION**[b] | |
| **Mild** | 200 mmHg < $PaO_2/FIO_2$ ≤300 mmHg with PEEP or CPAP ≥5 $cmH_2O$[c] |
| **Moderate** | 100 mmHg < $PaO_2/FIO_2$ ≤200 mmHg with PEEP ≥5 $cmH_2O$ |
| **Severe** | $PaO_2/FIO_2$ ≤100 mmHg with PEEP ≥5 $cmH_2O$ |

**Exclusion criteria:**

1. Clinical or investigative procedures suggestive or left sided cardiac dysfunction.
2. Significant underlying lung disease.

**Ethical considerations:** Study was approved by institutional human ethics committee. Informed written consent was obtained from all the study participants and only those participants willing to sign the informed consent were included in the study. The risks and benefits involved in the study and voluntary nature of participation were explained to the participants before obtaining consent. Confidentiality of the study participants was maintained.

**Data collection tools:** All the relevant parameters were documented in a structured study proforma.

**Methodology:**

All patients fulfilling the inclusion criteria that was confirmed cases of ARDS according to Berlin criteria were taken. Informed consent was obtained. The enrolled patient's demographic data including age, sex, address, were noted. Patient's premorbid illness was noted including history of alcohol abuse and smoking. Patient's detailed history was taken. Presenting chief complaints were recorded in the pre-designed proforma and detailed examination was done.

Investigations needed for diagnosis, assess severity and to identify risk factors were done according to clinical picture. The etiology of ARDS was ascertained on the basis of medical history and physical examination, radiology and biochemical and microbiological investigations. Routine investigations namely complete blood count, liver function test, renal function test, arterial blood gas analyses and chest X-ray was done for all patients. Blood culture were sent for all patients and other site cultures were sent based of clinical picture.

Dengue infection was identified by NS1 antigen, IgM antibody. Malarial parasite was identified by peripheral smear and malaria card test. Other sepsis work up HIV, HbSAg, Brucella, Leptospira antibody, Widal and Weil Felix test, H1N1 was sent. 2D echo was done whenever necessary. Duration of hospital stay, duration of mechanical ventilation and the ultimate hospital outcome were documented at the time of discharge or death.

**SEVERITY OF ILLNESS**

The severity scores used in our study were as follows:

1) APACHE II (Acute Physiology and Chronic Health Evaluation II)
2) APACHE III (Acute Physiology and Chronic Health Evaluation III)
3) The Sequential Organ Failure Assessment (SOFA) score
4) q SOFA (quick SOFA)

Acute Physiology and Chronic Health Evaluation (APACHE) Score was developed first in 1981 by Knaus et al. The APACHE score has become the most commonly used survival prediction model in ICUs worldwide. [106]

The APACHE II score is a revised and simplified version of the original prototype, uses a point score based on initial values of 12 routine physiologic measures, age and previous health status to provide a general measure of severity of disease. The maximum possible APACHE II score is 71 and high scores have been well correlated with mortality. The APACHE II severity-of disease classification was devised to stratify prognosis in groups of critically ill patients and to determine the success of treatment. [107]

APACHE III scoring system uses 17 physiological and biochemical parameters along with age and co morbities to assess the severity of the disease.The score can be used for predicting the risk of hospital mortality in critically ill patients .[108]

The Sequential Organ Failure Assessment (SOFA) score is a simple and objective score that allows for calculation of both the number and the severity of organ dysfunction in six organ systems (respiratory, coagulatory, liver, cardiovascular, renal, and neurologic) and the score can measure individual or aggregate organ dysfunction.[109]

Quick SOFA (qSOFA) score: This score is a modified version of the Sequential (Sepsis-related) Organ Failure Assessment score (SOFA). qSOFA consists of only three components that are each allocated one point. These components include respiratory rate of 22/min or greater, altered mentation, or systolic blood pressure of 100 mm Hg or less.[110]

Sepsis was defined as per, the third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) by ESICM-SCCM sepsis redefinition task force. As per this definition, sepsis was definedas life-threatening organ dysfunction caused by a dysregulated host response to infection. For clinical operationalization, organ dysfunction can be represented by an increase in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more. [110]

**Statistical methods:**

APACHE II, APACHE III and SOFA qSOFA score were considered as primary outcome variables. Study group (improved Vs expired) was considered as Primary explanatory variable.

All the quantitative variables like Hb%, total WBC count, platelets, bilirubin, creatinine, pao2/fio2, APACHE II and III score, SOFA score, duration of mechanical ventilation days, duration of stay in hospital days and ICU stay were checked for normal distribution within each category of outcome (improved expired) by using visual inspection of histograms and normality Q-Q plots. Shapiro- wilk test was also conducted to assess normal distribution. Shapiro wilk test p value of >0.05 was considered as normal distribution.ddr

For normally distributed APACHE II & III score the mean values were compared between study groups (improved Vs expired) using Independent sample t-test.

For non-normally distributed SOFA score, Medians and Interquartile range (IQR) were compared between study groups (improved Vs expired) using Mann Whitney u test.

Categorical qSOFA was compared between study groups outcome (improved vs expired) using Chi square test. Association between APACHE II, APACHE III and

SOFA score and duration of mechanical ventilation days, duration of stay in hospital days and ICU stay variables was assessed by calculating spearman rank correlation coefficient and the data was represented in a scatter diagram

The utility of APACHE II& III in predicting outcome (improved Vs expired) was assessed by Receiver Operative curve (ROC) analysis. Area under the ROC curve along with it's 95% CI and p value are presented.

P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.[111]

# RESULTS

A total of 60 subjects were included in the final analysis

**Table 2: Descriptive analysis of age in study population (N=60)**

| Parameter | Mean ± SD | Median | Min | Max | 95% C.I | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| **Age** | 41.4 ± 14.51 | 40.00 | 18.00 | 77.00 | 37.65 | 45.15 |

The mean age of study population was 41.4 ± 14.51 with the ranged between 18 to 77 years. (Table 2)

**Table 3: Descriptive analysis of age group in the study population (N=60)**

| Age group | Frequency | Percentage |
|---|---|---|
| Upto 30 | 15 | 25% |
| 30 to 39 | 12 | 20% |
| 40 to 49 | 18 | 30% |
| 50 to 59 | 7 | 11.7% |
| 60 and above | 8 | 13.3% |

Among the study population, 15(25%) participants were aged upto 30 years,12(20%) were aged 30 to 39 years,18(30%) were aged 40 to 49 years, 7(11.7%) were aged 50 to 59 years and 8(13.3%) were aged 60 years and above. (Table 3& figure 4)

**Figure 4: Bar chart of age group distribution in the study population (N=60)**

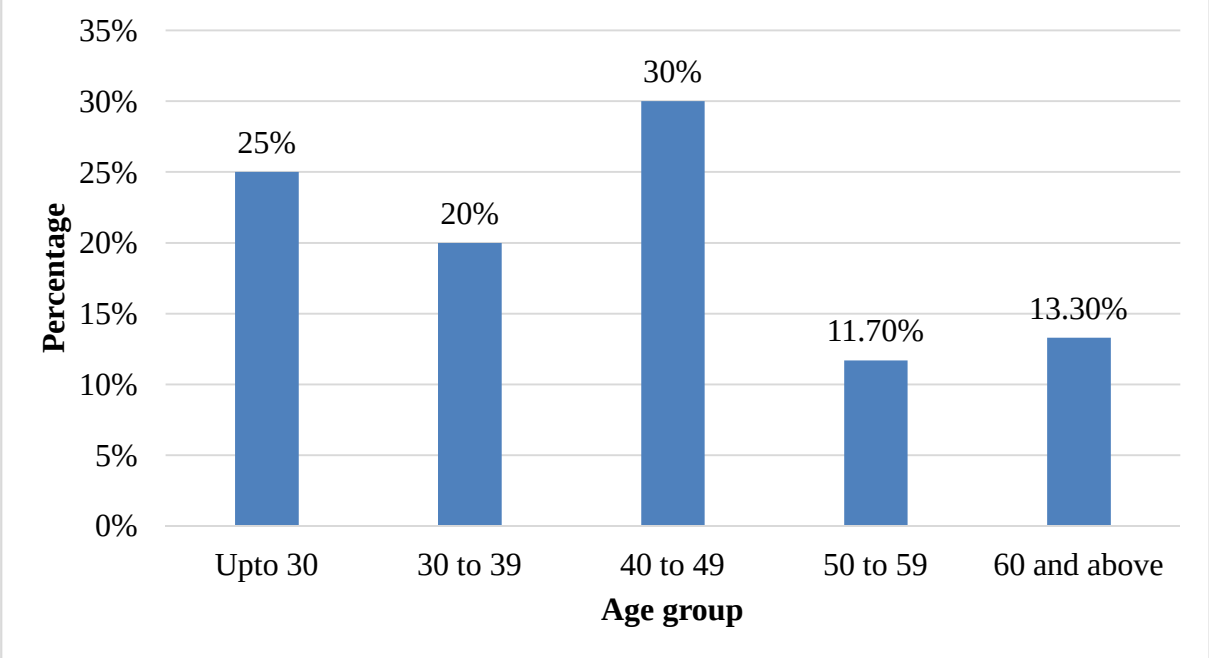



**Table 4: Descriptive analysis of gender in the study population (N=60)**

| Gender | Frequency | Percentage |
|---|---|---|
| Male | 34 | 56.7% |
| Female | 26 | 43.3% |

Among the study participants, 34(56.7%) participants were males and remaining 26(43.3%) were females. (Table 4 &figure 5)

**Figure 5: Bar chart of gender distribution in the study population (N=60)**

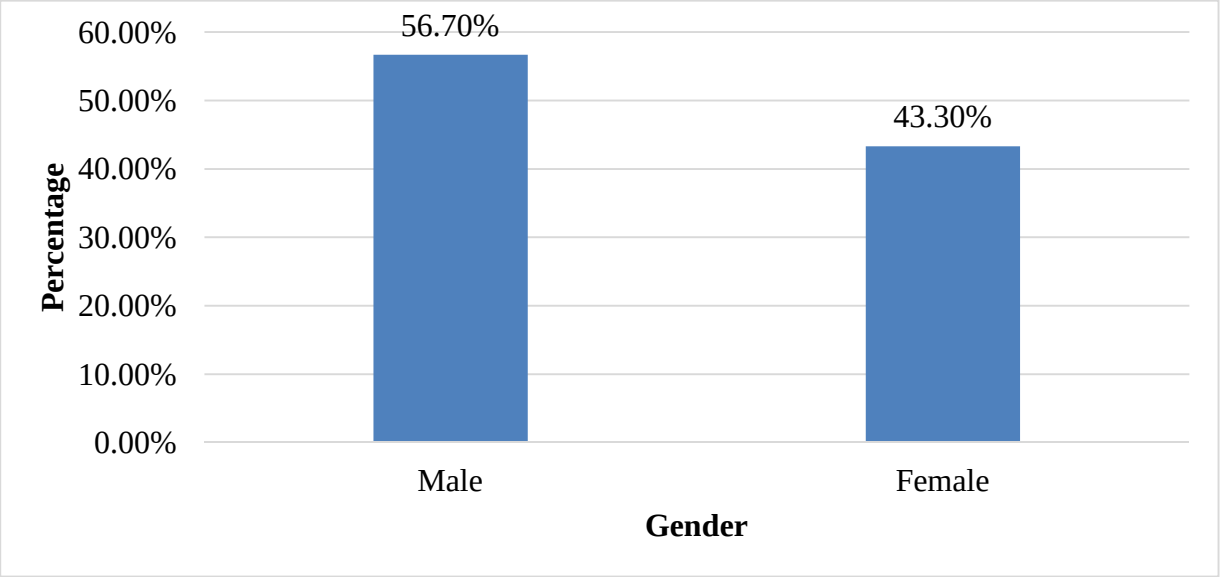



**Table 5: Descriptive analysis of locality in the study population (N=60)**

| Rural/urban | Frequency | Percentage |
|---|---|---|
| Rural | 33 | 55% |
| urban | 27 | 45% |

Among the study population,33(55%) participant were from the rural area and 27(45%) were urban locality. (table 5 &figure 6)

**Figure 6: Pie chart of rural /urban in the study population(N=60)**

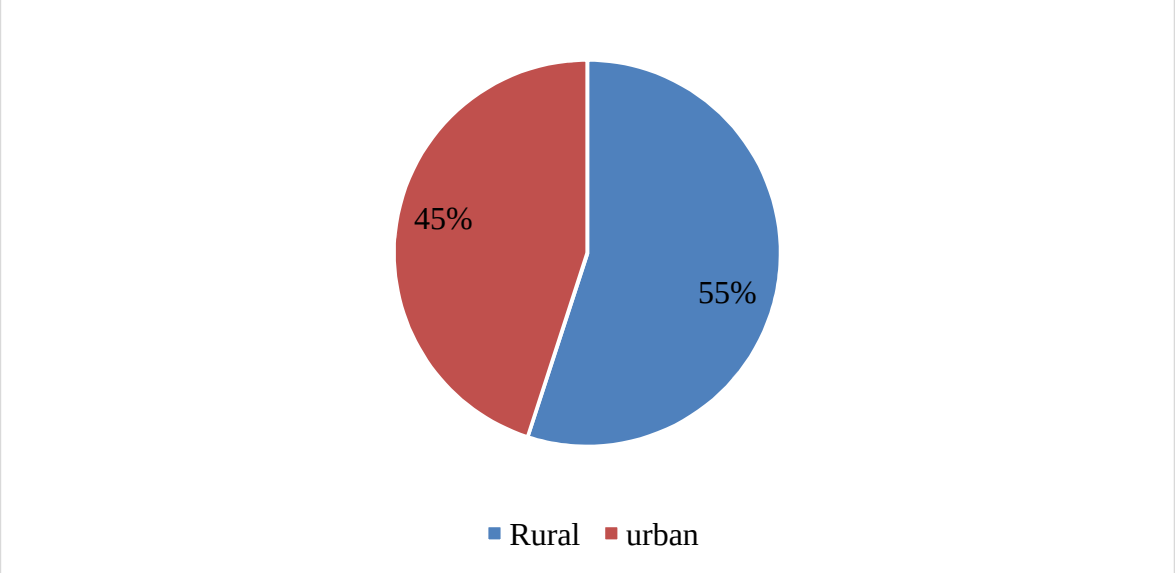



**Table 6: Descriptive analysis of aetiology in the study population (N=60)**

| **Aetiology** | **Frequency** | **Percentage** |
|---|---|---|
| Pneumonia | 17 | 28.3% |
| Organophosphorus poisoning | 6 | 10% |
| Abdominal sepsis | 3 | 5.0% |
| Dengue | 5 | 8.3% |
| H1N1 | 5 | 8.3% |
| Undiagnosed fever | 4 | 6.7% |
| Pancreatitis | 3 | 5.0% |
| Sepsis-chronic liver disease | 4 | 6.7% |
| Sepsis-intra uterine death | 2 | 3.3% |
| Snake bite | 2 | 3.3% |
| Urinary Tract Infection (UTI) | 2 | 3.3% |
| Leptospirosis | 2 | 3.3% |

| | | |
|---|---|---|
| Paraquat poisoning | 2 | 3.3% |
| Acute fulminant viral hepatitis | 1 | 1.7% |
| Malaria | 1 | 1.7% |
| Scrub typhus | 1 | 1.7% |

Among the study population, 17(28.3%) participants had pneumonia. The number of OP poisoning, abdominal sepsis, dengue, H1N1, undiagnosed fever, pancreatitis, sepsis-chronic liver diseases, sepsis-intra uterine death, snake bite, UTI, leptospirosis, paraquat poisoning, acute fulminant viral hepatitis, malaria and scrub typhus was 6(10%), 3(5%), 5(8.3%), 5(8.3%), 4(6.7%), 3(5%), 4(6.7%), 2(3.3%), 2(3.3%), 2(3.3%), 1(1.7%), 1(1.7%) and 1(1.7%) respectively. (Table 6)

**Table 7: Descriptive analysis of symptoms in the study population (N=60)**

| Symptoms | Frequency | Percentage |
|---|---|---|
| Fever | 31 | 51.7% |
| Sore throat | 27 | 45% |
| Cough | 22 | 36.7% |
| Pain abdomen | 14 | 23.3% |
| Vomiting | 12 | 20% |
| Body ache | 9 | 15% |
| Loose motions | 5 | 8.3% |
| Altered mentation | 6 | 10% |
| Head ache | 4 | 6.7% |

Among the study population, 31(51.7%) participants had fever. The number participants with sore throat, cough, pain abdomen, vomiting, body ache, loose motions, altered mentation and head ache were 27(45%), 22(36.7%), 14(23.3%), 12(20%), 9(15%), 5(8.3%), 6(10%) and 4(6.7%) respectively. (Table 7)

**Table 8: Descriptive analysis of comorbidities in the study population (N=60)**

| Comorbidities | Frequency | Percentage |
|---|---|---|
| Hypertension | 12 | 45% |
| DM type 2 | 11 | 18.3% |
| Liver disease | 5 | 8.3% |
| Coronary artery disease (CAD) | 1 | 1.7% |
| Cerebrovascular Accident (CVA) | 1 | 1.7% |
| COPD | 1 | 1.7% |
| Asthma | 1 | 1.7% |
| HIV | 1 | 1.7% |

Among the study population, 12(45%) participants had hyper tension. The number of DM type 2, liver disease, CAD, CVA, COD, Asthma and HIV was 11(18.3%), 5(8.3%) and 1(1.7%) each respectively. (Table 8)

**Table 9: Descriptive analysis of substance use in the study population (N=60)**

| Substance use | Frequency | Percentage |
|---|---|---|
| Smoking | 13 | 21.7% |
| Alcohol | 12 | 20% |
| Tobacco chewing | 11 | 18.3% |

Among the study population, 13(21.7%) participants were smokers. The number of subjects using alcohol were 12(20%) and 11(18.3%) chewed tobacco. (Table 9)

**Table 10: Descriptive analysis of vital signs in the study population (N=60)**

| Vital signs | Frequency | Percentage |
|---|---|---|
| **Pulse rate** | | |
| <90 | 5 | 8.3% |
| >90 | 55 | 91.7% |
| **Respiratory rate** | | |
| <20 | 0 | 0% |
| >20 | 60 | 100% |
| **Systolic BP** | | |
| <90 | 25 | 41.7% |
| >90 | 35 | 58.3% |

Among the study population, 5(8.3%) participant had <90 beats per minute pulse rate and remaining 55(91.7%) had >90 beats per minute pulse rate. 60(100%) participants had >20 respiratory rate. Among the study population, 25(41.7%) participants had systolic BP <90 and remaining 35(58.3%) participants had systolic BP >90.

**Table 11: Descriptive analysis of clinical signs in the study population (N=60)**

| Clinical signs | Frequency | Percentage |
|---|---|---|
| Pallor | 18 | 30.00% |
| pedal oedema | 8 | 13.3% |
| Icterus | 5 | 8.30% |
| Petechiae | 3 | 5% |
| cyanosis | 1 | 1.7% |

Among the study population, 18(30%) participants had pallor. The number of pedal edema, icterus, petchiae and cyanosis was 8(13.3%),5(8.30%),3(5%) and 1(1.7%) respectively. (Table 11)

**Figure 7: Bar chart of clinical signs in the study population(N=60)**

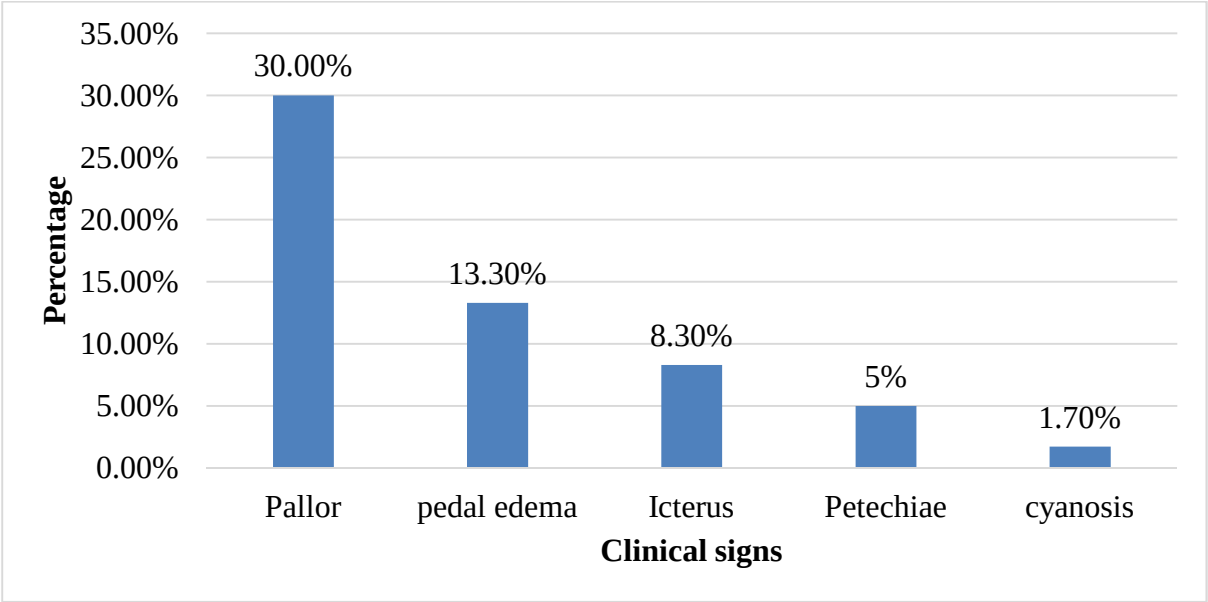


**Table 12: Descriptive analysis of laboratory parameters in study population (N=60)**

| Lap parameter | Mean ± SD | Minimum | Maximum |
|---|---|---|---|
| Haemoglobin g/dl | 11.66 ± 1.82 | 7.60 | 15.00 |
| Total count mm | 13926.67 ± 7344.78 | 2300.00 | 32000.00 |
| Platelets | 130250 ± 60549.64 | 12000.00 | 280000.00 |
| Bilirubin mg/dl | 1.65 ± 1.32 | 0.30 | 6.80 |
| Creatinine mg/dl | 1.41 ± 0.6 | 0.60 | 3.00 |

The mean haemoglobin of study population was 11.66 ± 1.82 with the ranged between 7.60 to 15 g/dl. The mean total count of study population was 13926.67 ± 7344.78with the ranged between 2300 to 32000.The mean platelets of study population was 130250 ± 60549.64with the ranged between 12000 to 280000.The mean bilirubin of study population was 1.65 ± 1.32 with the ranged between 0.30 to 6.80 mg/dl. The mean creatinine of study population was 1.41 ± 0.6 with the ranged between 0.60 to 3 mg/dl.

**Table 13: Descriptive analysis of sputum Culture in the study population (N=3)**

| Sputum | Frequency | Percentages |
|---|---|---|
| Klebsiella | 2 | 66.67% |
| Pseudomonas | 1 | 33.33% |

Among the study population,2(66.67%) participants had Klebsiella and remaining 1(33.33%) had Pseudomonas isolated in sputum. (Table 13)

**Table 14: Descriptive analysis of urine Culture in the study population (N=4)**

| Urine | Frequency | Percentages |
|---|---|---|
| E. coli | 2 | 50% |
| Enterobacter | 1 | 25% |
| Pseudomonas | 1 | 25% |

Among the study population, 2(50%) participants had E. coli. 1(25%) person each had Enterobacter and Pseudomonas isolated from urine sample. (Table 14)

**Table 15: Descriptive analysis of blood culture sensitivity in the study population (N=14)**

| Blood culture sensitivity | Frequency | Percentages |
|---|---|---|
| Staphylococcus | 6 | 42.85% |
| klebsiella | 2 | 14.30% |
| MRSA | 2 | 14.30% |
| E coli | 2 | 14.30% |
| Enterococus | 1 | 7.10% |
| Pseudomonas | 1 | 7.10% |

Among the study population, 6(42.85%) participants had staphylococcus. The number of participants with Klebsiella, MRSA, E.coli, enterococcus and pseudomonas was 2(14.30%),2(14.30%),2(14.30%),1(7.10%) and 1(7.10%) respectively. (Table 15)

**Table 16: Descriptive analysis of pH in the study population (N=60)**

| PH | Frequency | Percentages |
|---|---|---|
| <7.35 | 37 | 61.7% |
| >7.35 | 23 | 38.3% |

Among the study population,37(61.7%) participants had and <7.35 pH and 23(38.3%) had >7.35 pH.(table 16)

**Table 17: Descriptive analysis of PAO2/ FIO2in study population (N=60)**

| Parameter | Mean ± SD | Median | Min | Max | 95% C.I | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| **PO2/FIO 2** | 98.92 ± 41.1 | 95.10 | 10.20 | 190.00 | 88.30 | 109.54 |

The mean po2/Fio2 of study population was 98.92 ± 41.1 with the ranged between 10.20 to 190. (Table 17)

**Table 18: Descriptive analysis of endotracheal tube culture in the study population (N=4)**

| Endotracheal tube culture | Frequency | Percentages |
|---|---|---|
| Acinetobacter | 2 | 50% |
| Klebsiella | 1 | 25% |
| Pseudomonas | 1 | 25% |

Among the study population, 2(50%) participants had acinetobacter,1(25%) participants had Klebsiella and 1(25%) had Pseudomonas. (Table 18)

**Table 19: Descriptive analysis of dengue serology in the study population (N=60)**

| Dengue serology | Frequency | Percentages |
|---|---|---|
| Positive | 5 | 8.4% |
| Negative | 23 | 38.3% |
| Not done | 32 | 53.3% |

Out of the study 5(8.3%) participants had dengue serology positive, another 23 (38.3% were tested for dengue and were found negative. (Table 19)

**Table 20: Descriptive analysis of HbsAg in the study population (N=60)**

| HbsAg | Frequency | Percentages |
|---|---|---|
| Yes | 1 | 1.7% |
| No | 59 | 98.3% |

Out of 1(1.7%) participants had HbSAg positive. (Table 20)

**Table 21: Descriptive analysis of APACHE II and APACHE III in the study population (N=60)**

| APACHE Scores | Mean ± SD | Median | Mini | Maxi | 95% C.I | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| APACHE II score | 16.9 ± 7.09 | 15.50 | 2.00 | 35.00 | 15.07 | 18.73 |
| APACHE III score | 71.58 ± 28.63 | 69.50 | 10.00 | 139.00 | 64.19 | 78.98 |

The mean APACHE II score of study population was 16.9 ± 7.09 with the ranged between 2 to 35. The mean APACHE III score of study population was 71.58 ± 28.63 with the ranged between 10 to 139.

**Table 22: Descriptive analysis of SOFA score in study population (N=60)**

| parameter | Median | Inter quartile range (IQR) |
|---|---|---|
| SOFA score | 7.50 | (5, 9) |

The median SOFA score in the study population was 7.5(IQR:5,9)

**Table 23: Descriptive analysis of intubation in the study population (N=60)**

| Intubation | Frequency | Percentages |
|---|---|---|
| Yes | 18 | 30% |
| No | 42 | 70% |

Out of 60 people, 18(30%) participants were intubated. (table23)

**Figure 8: Pie chart of intubation in the study population(N=60)**

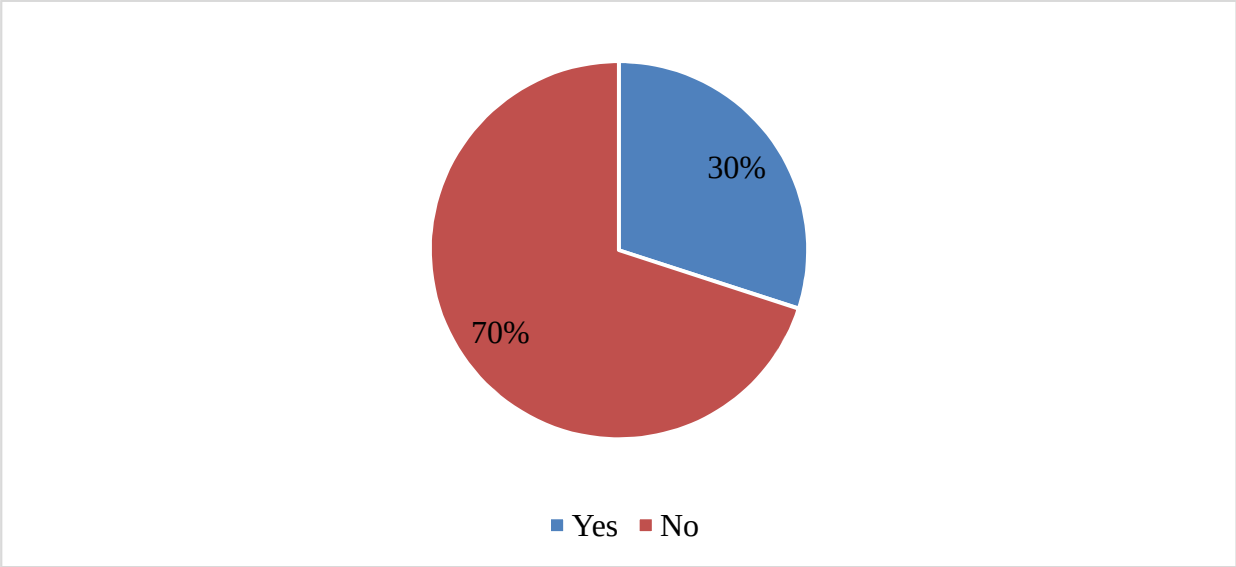



**Table 24: Descriptive analysis of sepsis in the study population (N=60)**

| Sepsis | Frequency | Percentages |
|---|---|---|
| Yes | 45 | 75% |
| No | 15 | 25% |

Out of 60 people,45(75%)participants had sepsis. (Table 24)

**Table 25: Descriptive analysis of qSOFA in the study population (N=60)**

| qSOFA | Frequency | Percentages |
|---|---|---|
| 1 | 29 | 48.33% |
| 2 | 27 | 45% |
| 3 | 4 | 6.67% |

Among the study population, 29(48.33%) participants had qSOFA score of 1, 27(45%) had q SOFAof 2 and 4 (6.67%) had qSOFA score of 3. (Table 25)

**Table 26: Descriptive analysis of duration days in study population (N=60)**

| Durations of days | Mean ± SD | Median | Min | Max | 95% C.I | |
|---|---|---|---|---|---|---|
| | | | | | Lower | Upper |
| Mechanical ventilation Days | 5.08 ± 2.76 | 4.00 | 2.00 | 14.00 | 4.37 | 5.80 |
| Stay in hospital Days | 8.43 ± 4.06 | 7.50 | 3.00 | 18.00 | 7.39 | 9.48 |
| ICU stay Days | 6.48 ± 3.04 | 6.00 | 2.00 | 17.00 | 5.70 | 7.27 |

The mean mechanical ventilation days of study population was 5.08 ± 2.76 with the ranged between 2 to 14 days. The mean stay in hospital days of study population was 8.43 ± 4.06 with the range between 3 to 18. Days. The mean ICU stay of study population was 6.48 ± 3.04 with the ranged between 2 to 17 days.

**Table 27: Descriptive analysis of outcome in the study population (N=60)**

| Outcome | Frequency | Percentages |
|---|---|---|
| Improved | 31 | 51.7%% |
| Expired | 29 | 48.3% |

Among the study population 31(51.7%) participants had 29(48.3%) participants had expired. (Table 27&figure 9)

**Figure 9: Pie chart of outcome in the study population(N=60)**

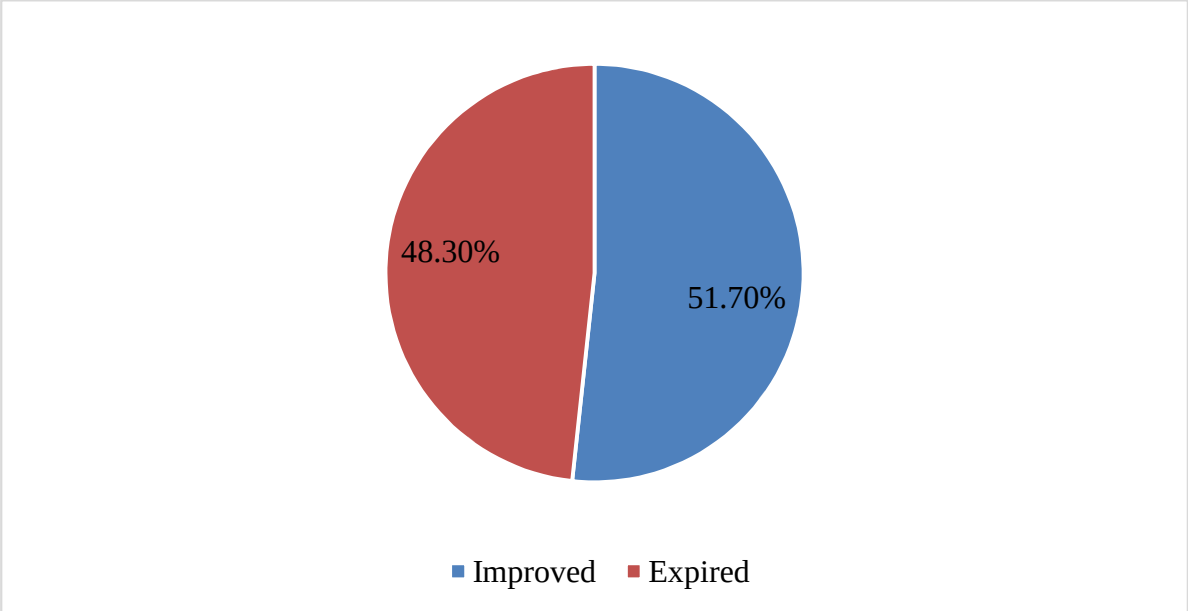


**Table 28: Comparison of q SOFA with outcome (N=60)**

| q SOFA | outcome | | Chi square | P-value |
|---|---|---|---|---|
| | Improved | Expired | | |
| 1(N=29) | 19 (61.3%) | 10 (34.5%) | 4.658 | 0.097 |
| 2(N=27) | 11 (35.5%) | 16 (55.2%) | | |
| 3(N=4) | 1(3.2%) | 3(10.3%) | | |

Out of 29 people with q SOFA score of 1, 19 (61.3%) people had improved and 10 (34.5%) had expired. Out of 27 people q SOFA score of 2, 11 (35.5%) people had improved and 16 (55.2%) had expired. Out of 3 people q SOFA score of 3, 1 (3.2%) people had improved and 3 (10.3%) had expired. The difference in the proportion of outcome between q sofa was statistically not significant (p value 0.097)

**Figure 10: Comparative bar chart of q SOFA with outcome (N=60)**

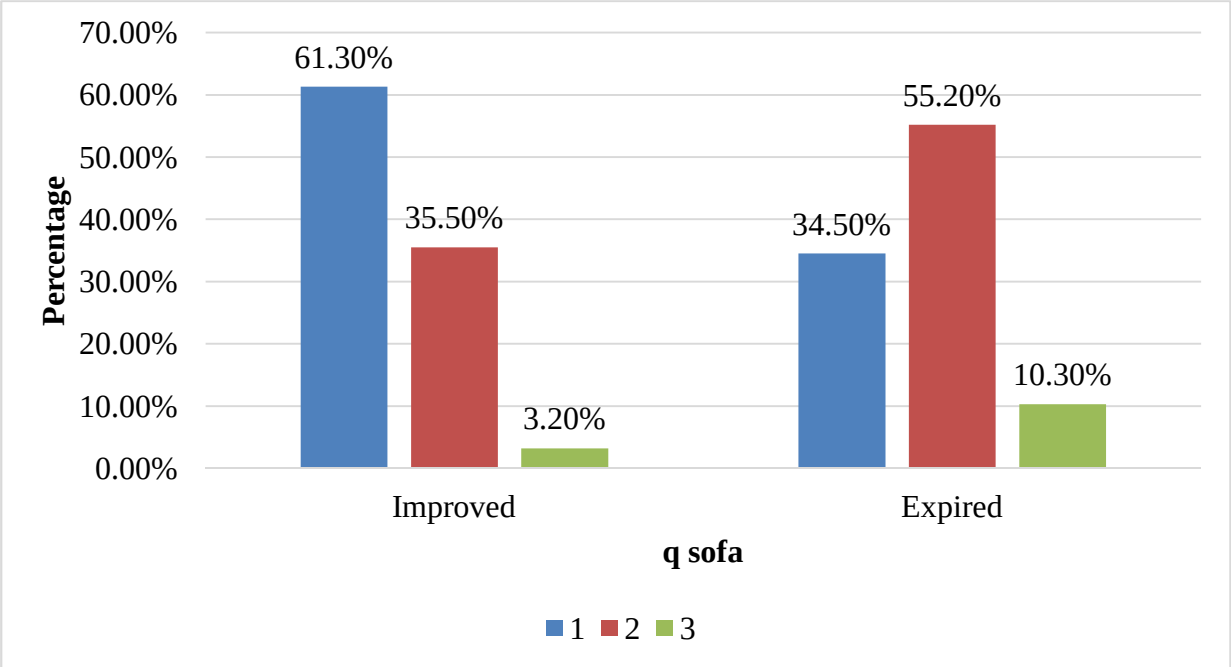


**Table 29: Comparison of mean APACHE II & III score between study group (N=60)**

| Parameter | Outcome (Mean ± SD) | | P value |
|---|---|---|---|
| | Improved (N=31) | Expired (N=29) | |
| APACHE II score | 14.39 ± 6.27 | 19.59 ± 7.01 | 0.004 |
| APACHE III score | 51.65 ± 16.09 | 92.90 ± 23.27 | <0.001 |

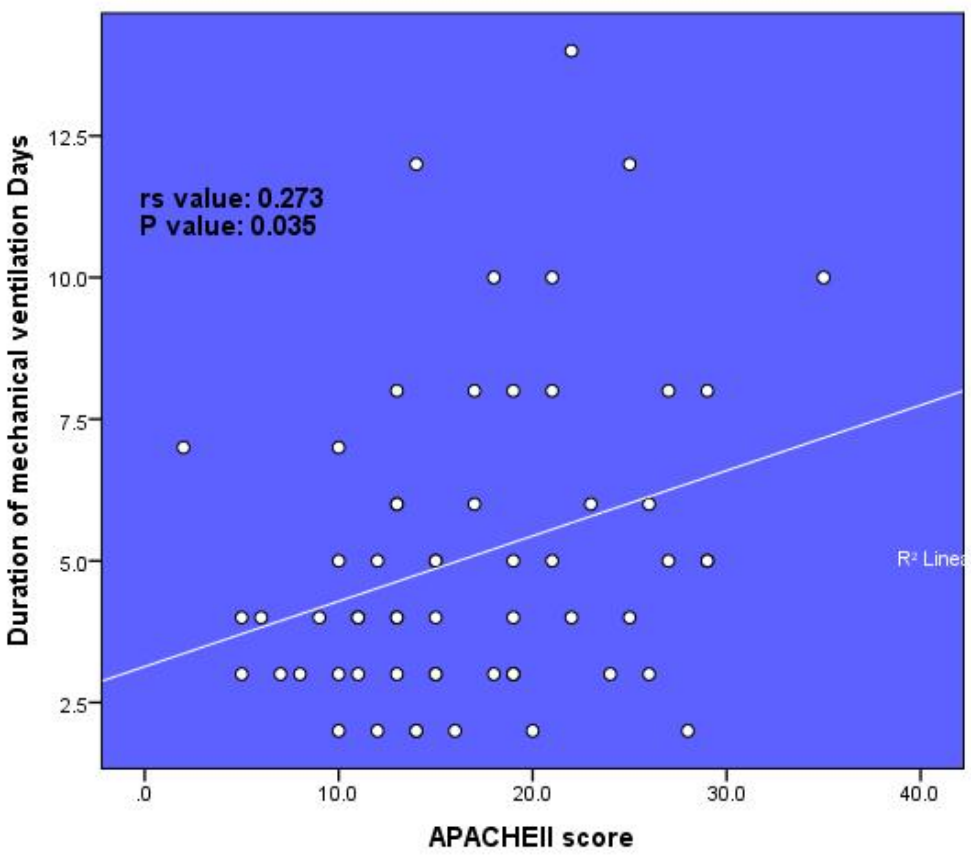
The mean APACHE II score of people with improved was 14.39 ± 6.27 and it was 19.59 ± 7.01in people with expired group, the difference in the mean APACHE II score between study group was statistically significant. (P value 0.004). The mean APACHE III score of people with improved was 51.65 ± 16.09 and it was 92.90 ± 23.27 in people with expired group, the difference in the mean APACHE III score between study group was statistically significant. (P value <0.001).

**Table 30: Comparison of mean SOFA score between study group (N=60)**

| Parameter | Outcome(Median IQR) | | Mann Whitney U test (P value) |
|---|---|---|---|
| | Improved (N=31) | Expired (N=29) | |
| SOFA score | 5 (IQR 4 to 7) | 9 (IQR 8 to 11) | *<0.001* |

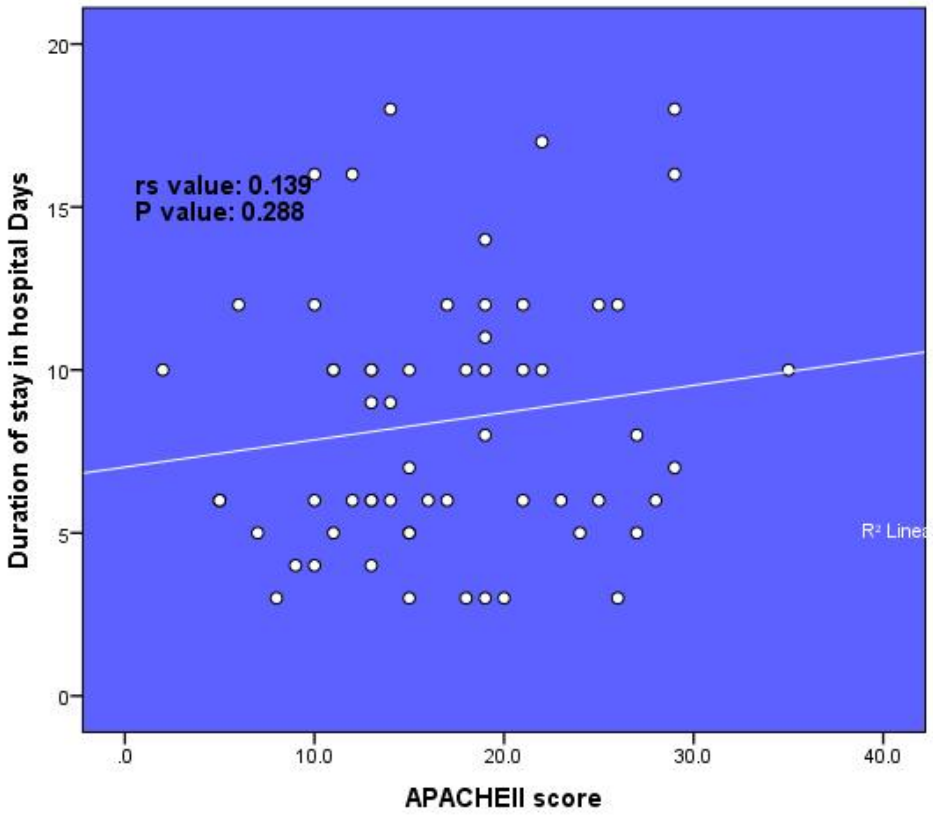
Among the people with, improved median SOFA score was 5 (IQR 4 to7) and in people with expired it was 9 (IQR 8 to 11), the difference in the SOFA score between outcome was statistically significant (P Value <0.001). (Table 30)

**Figure 11: Correlation between duration of mechanical ventilation days and APACHE II score in the study population (N= 60)**



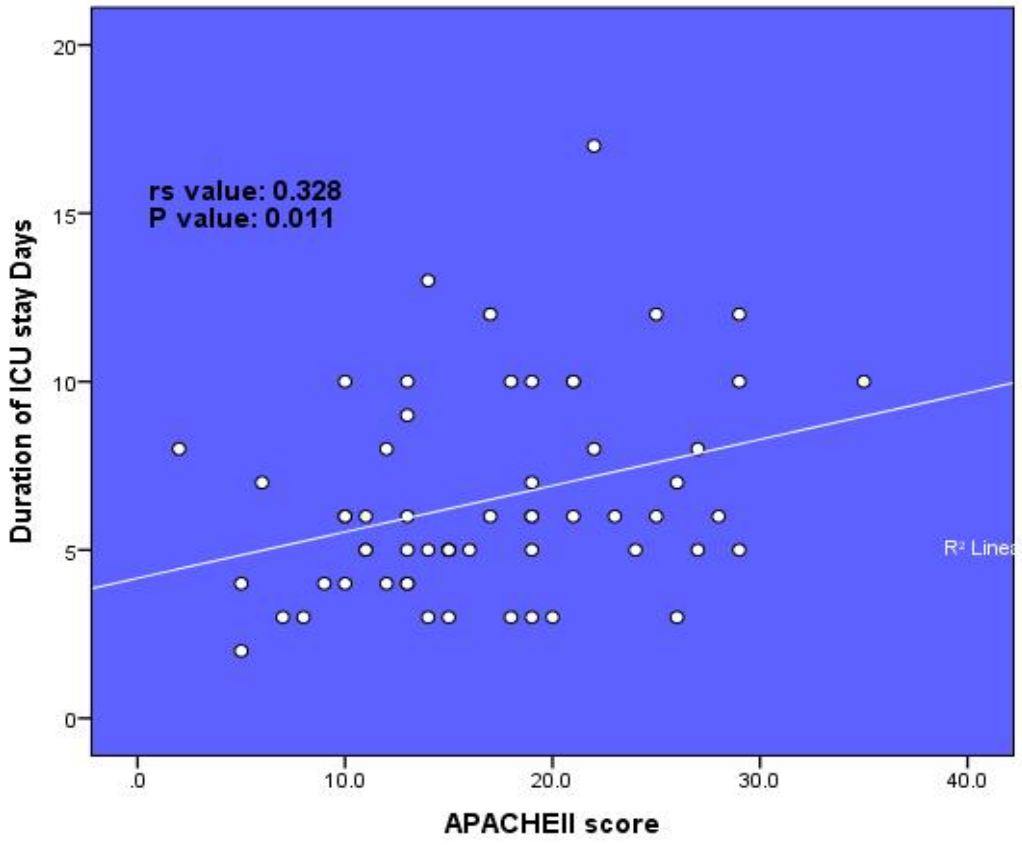

There was a weak positive correlation between APACHE II score and duration of mechanical ventilation days ($r_s$value 0.273, p value 0.035)

**Figure 12: Correlation between duration of stay in hospital days and APACHE II score in the study population (N= 60)**



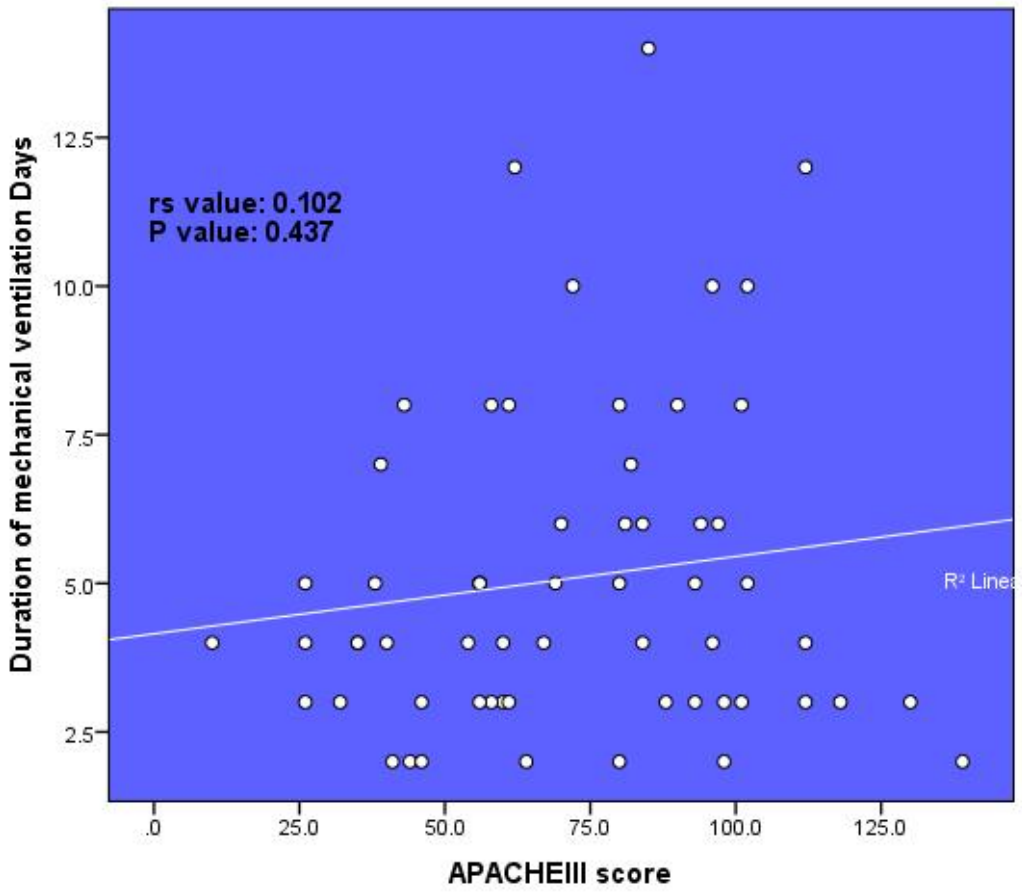

There was a weak positive correlation between APACHE II score and duration of stay in hospital days ($r_s$value 0.139, p value 0.288)

**Figure 13: Correlation between duration of ICU stay days and APACHE II score in the study population (N= 60)**



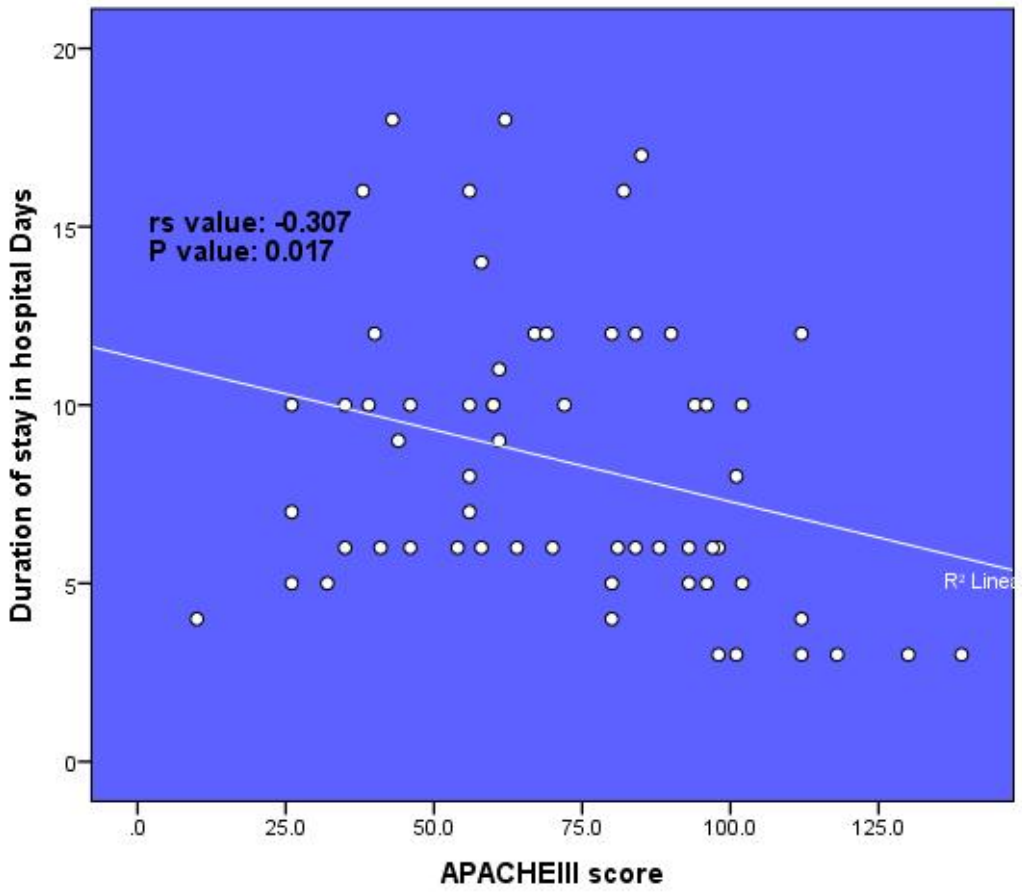

There was a weak positive correlation between APACHE II score and duration of ICU stays ($r_s$value 0.328, p value 0.011)

**Figure 14: Correlation between duration of mechanical ventilation days and APACHE III score in the study population (N= 60)**



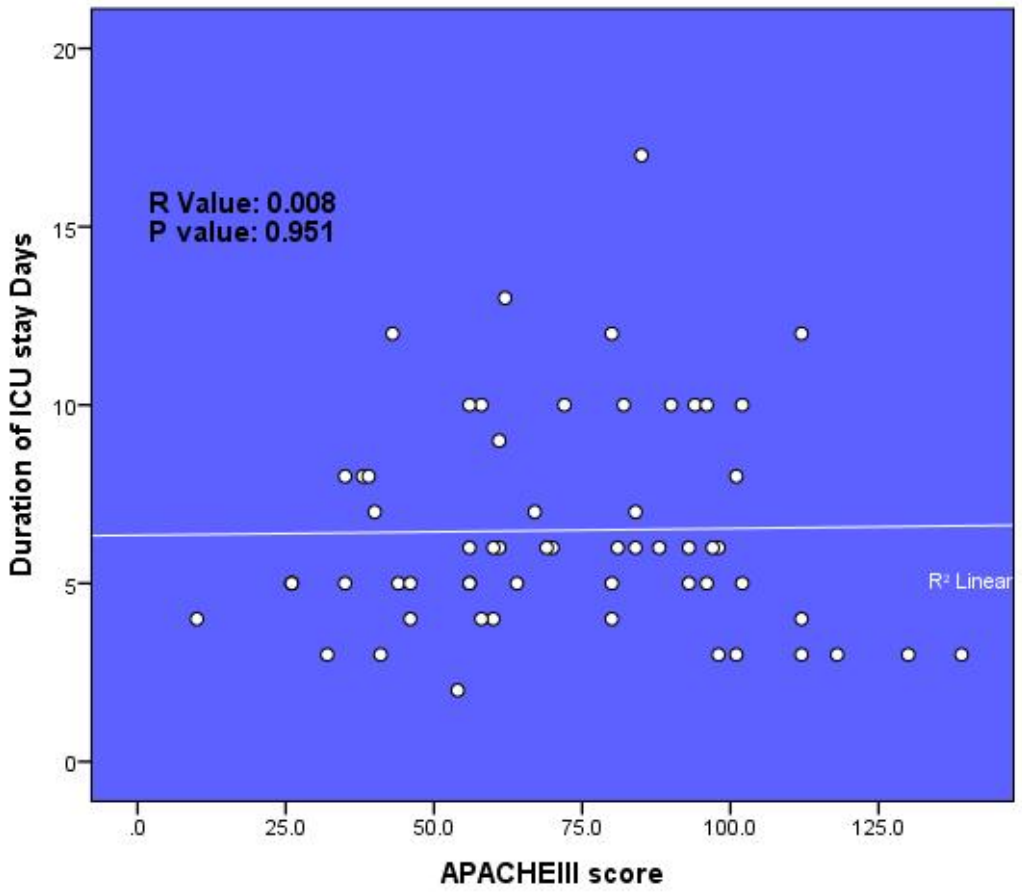

There was a weak positive correlation between APACHE III score and duration of mechanical ventilation days ($r_s$value 0.102, p value 0.437)

**Figure 15: Correlation between duration of stay in hospital days and APACHE III score in the study population (N= 60)**



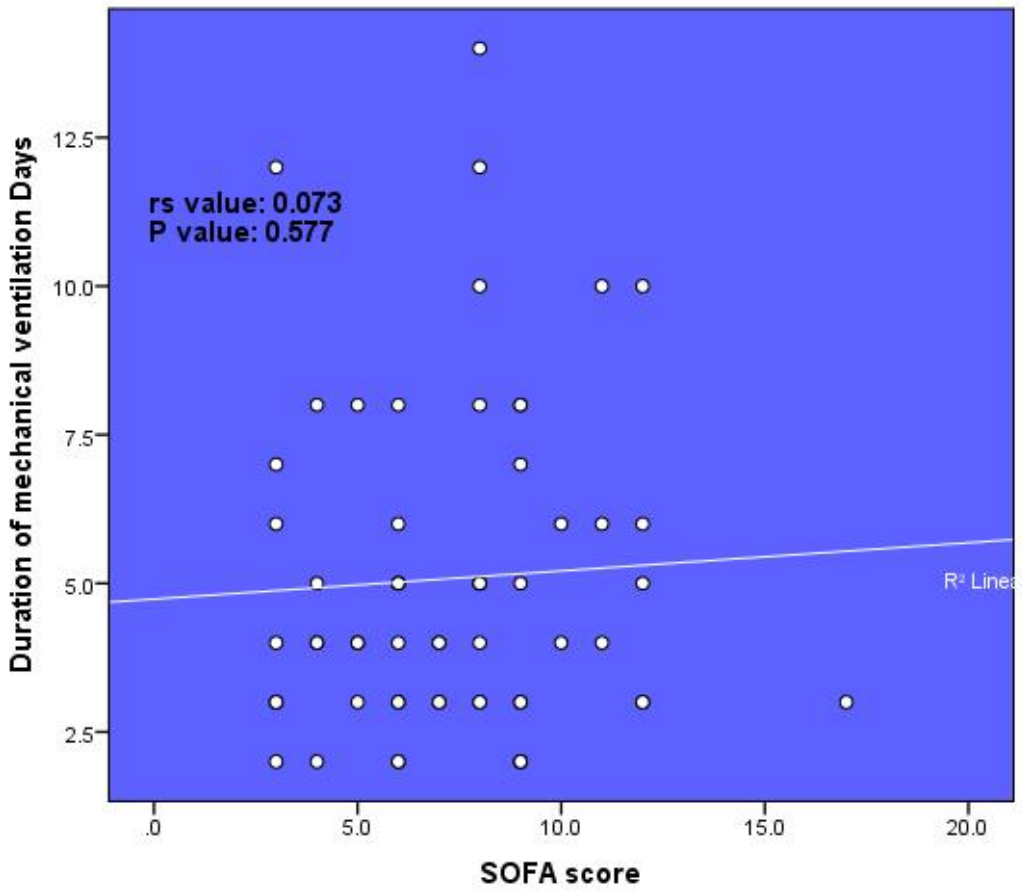

There was a negative correlation between APACHE III score and duration of stay in hospital days ($r_s$value -0.307, p value 0.017)

**Figure 16: Correlation between duration of ICU stay in days and APACHE III score in the study population (N= 60)**



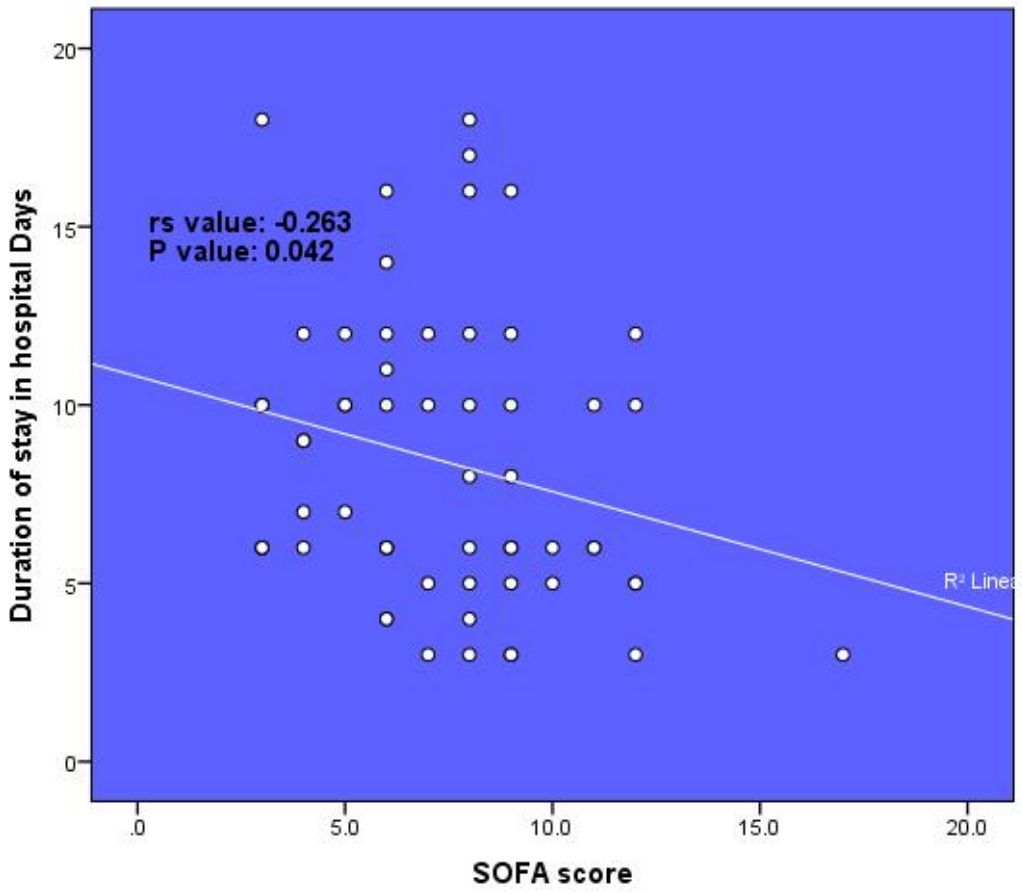

There was a weak positive correlation between APACHE III score and duration of ICU stays ($r_s$value 0.008, p value 0.951)

**Figure 17: Correlation between duration of mechanical ventilation days and SOFA score in the study population (N= 60)**



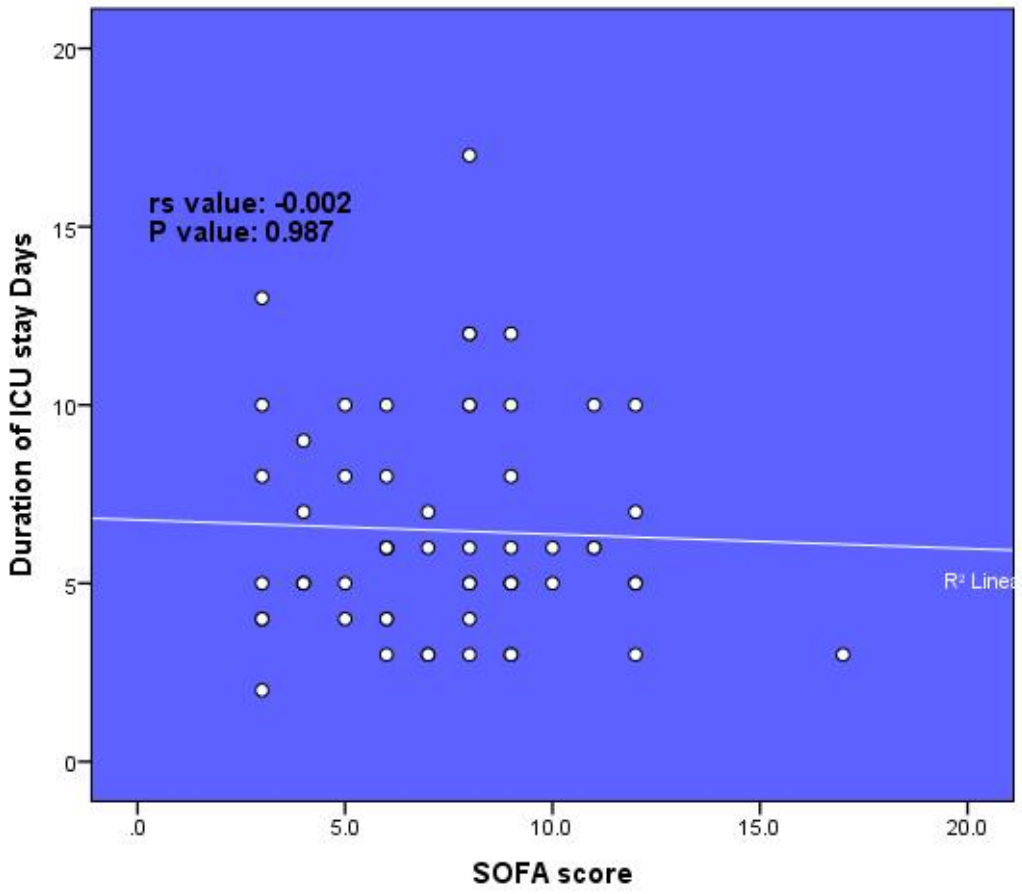

There was a weak positive correlation between SOFA score and duration of mechanical ventilation days ($r_s$value 0.073, p value 0.577)

**Figure 18: Correlation between duration of stay in hospital days and SOFA score in the study population (N= 60)**



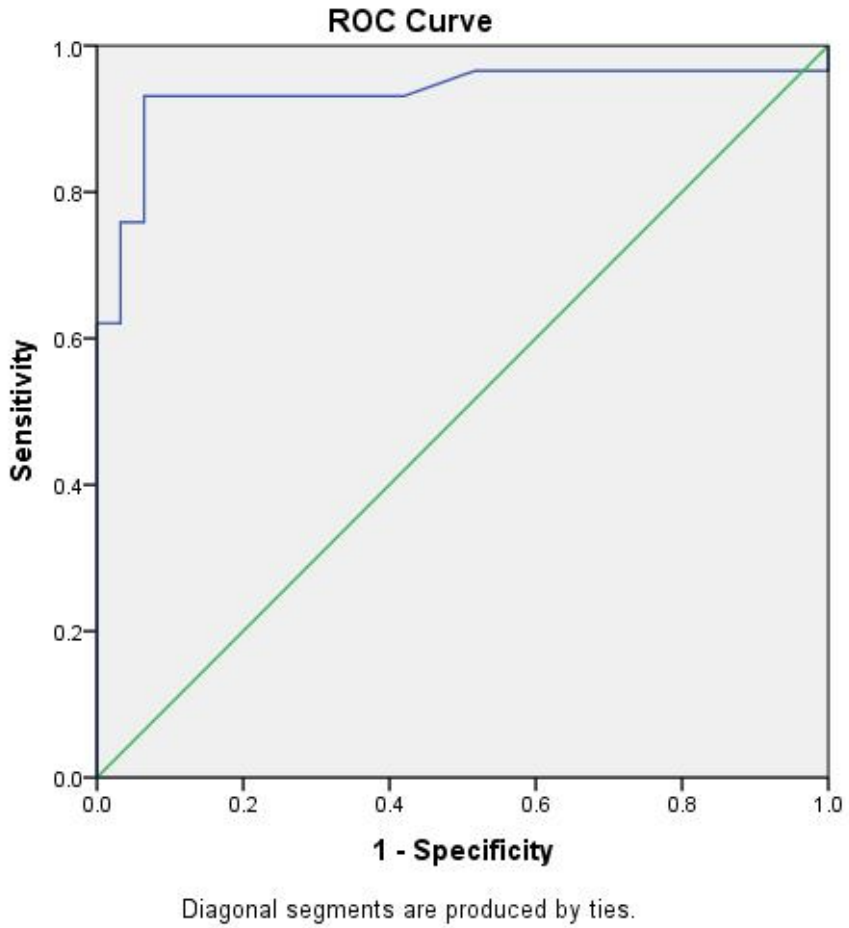

There was a weak negative correlation between SOFA score and duration of stay in hospital days ($r_s$value -0.263, p value 0.042)

**Figure 19: Correlation between duration of ICU stay days and SOFA score in the study population (N= 60)**




There was a weak negative correlation between SOFA score and duration of ICU stays ($r_s$value -0.002, p value 0.987)

**Figure 20: Predictive validity of APACHE II in predicting outcome(Expired) N=60)**

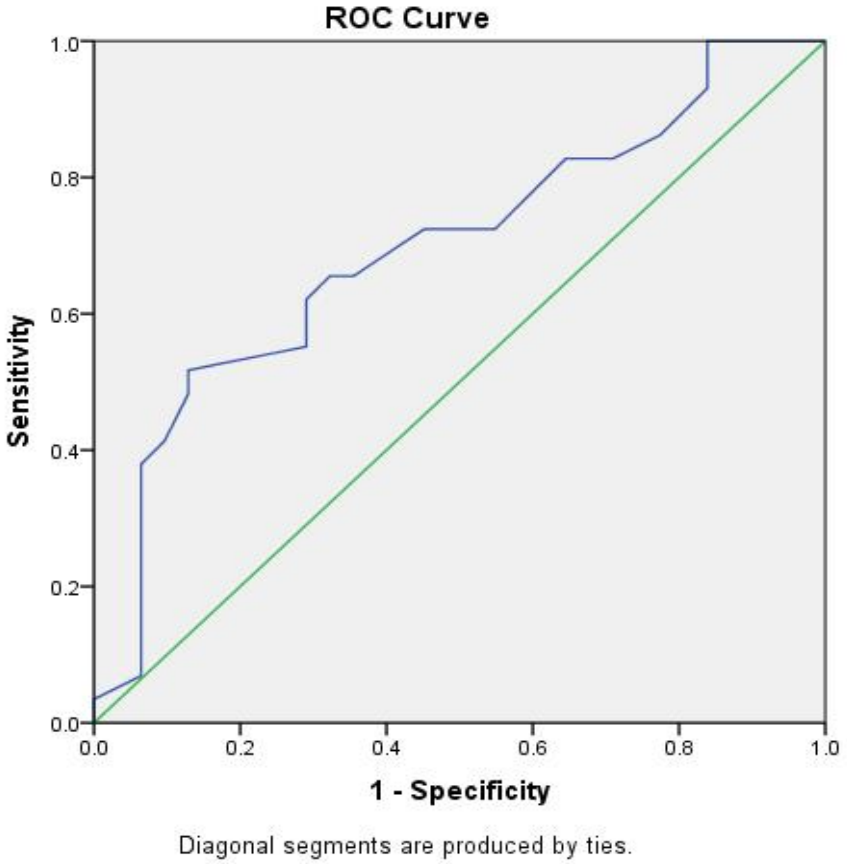



| Test Result Variable(s): APACHE II | | | | |
|---|---|---|---|---|
| **Area Under the Curve** | Std. Error | 95% Confidence Interval of AUC | | P value |
| | | Lower Bound | Upper Bound | <0.001 |
| 0.934 | 0.039 | 0.000 | 1.000 | |

The apache II had excellent predictive validity in predicting expired, as indicated by area under the curve of 0.934 (95% CI 0.000 to 1, P value <0.001) (Figure 20)

**Figure 21: Predictive validity of APACHE III in predicting outcome(Expired)**

**N=(60)**




| Test Result Variable(s): APACHE III | | | | |
|---|---|---|---|---|
| **Area Under the Curve** | Std. Error | 95% Confidence Interval of AUC | | P value |
| | | Lower Bound | Upper Bound | 0.009 |
| 0.697 | 0.069 | 0.562 | 0.833 | |

The apache III had poor predictive validity in predicting expired, as indicated by area under the curve of 0.697 (95% CI 0.562 to 0.833, P value 0.009) (Figure 21)

**Figure 22: Predictive validity of APACHE II & III and SOFA scores in predicting outcome(Expired) N= (60)**

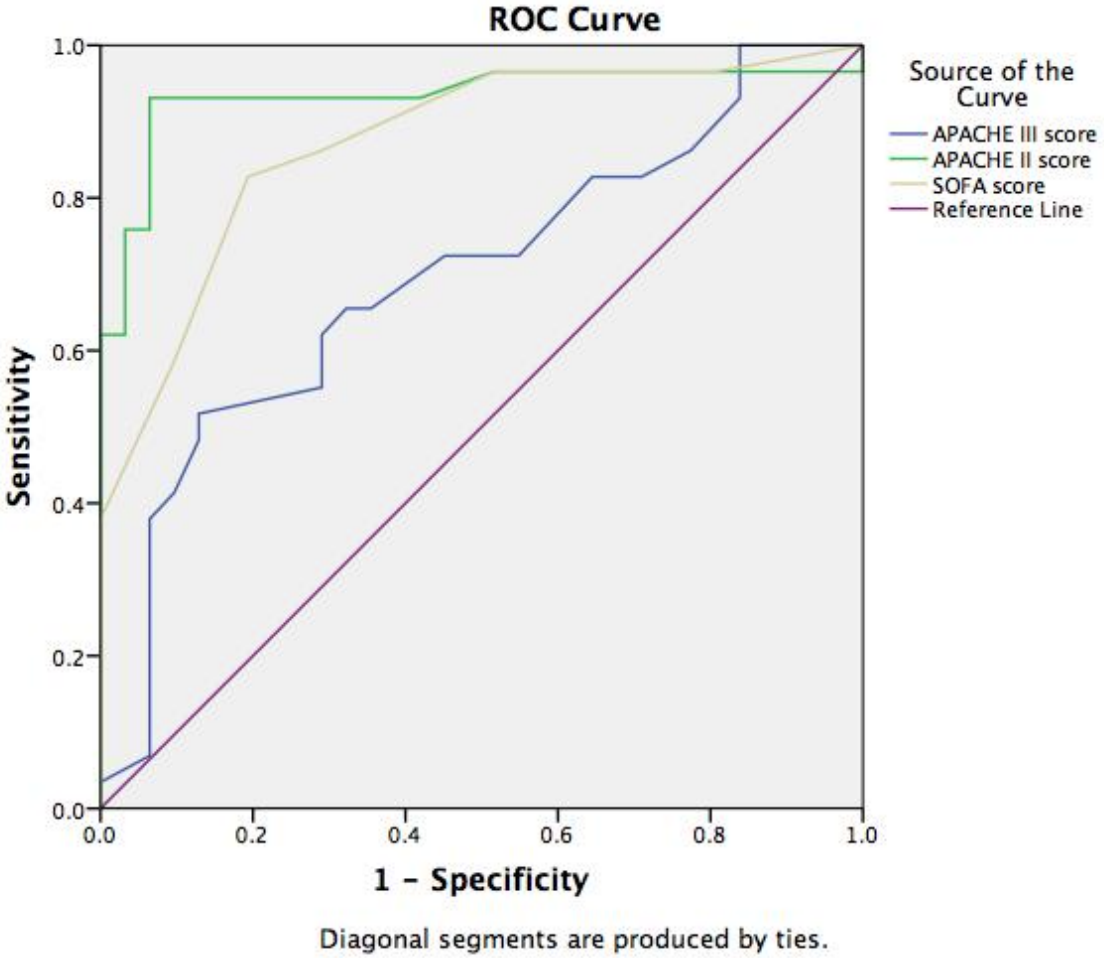


**Table 31: Comparison of predictive validity of different scoring systems.**

| Parameter | Area Under the Curve | Std. Error | 95% Confidence Interval of AUC | | P value |
|---|---|---|---|---|---|
| | | | Lower Bound | Upper Bound | |
| APACHE II score | 0.933 | 0.039 | 0.857 | 1.000 | <0.001 |
| APACHE III score | 0.696 | 0.070 | 0.559 | 0.834 | 0.010 |
| SOFA score | 0.871 | 0.047 | 0.779 | 0.963 | <0.001 |

The APACHE II score had excellent predictive validity in predicting mortality, as indicated by area under the curve of 0.933 (95% CI 0.857 to 1, P value <0.001). The APACHE III score had poor predictive validity in predicting expired, as indicated by area under the curve of 0.696 (95% CI 0.559 to 834, P value 0.010).The SOFA score had good predictive validity in predicting expired, as indicated by area under the curve of 0.871 (95% CI 0.779 to 963, P value <0.001) (Figure 21)

# DISCUSSION

Acute respiratory distress syndrome (ARDS) occur in response to a variety of insults and are characterized by the development of non-cardiogenic pulmonary oedema, impaired gas exchange and need for mechanical ventilation. ARDS is a major cause of acute respiratory failure associated with significant morbidity and mortality.[112] Patients are usually treated with supportive ventilation.[113] ARDS still remains a syndrome with an elevated overall incidence, and with mortality ranging from 40% to 60%.[114]Nowadays, approximately 5% of hospitalized, mechanically ventilated patients meet the diagnostic criteria for ARDS. As for the severity of the clinical presentation, it has been shown how only 25% of patients have a mild form of ARDS, while the remaining 75% display a moderate or severe form.[114] The primary targets for ARDS treatment are to ensure adequate gas exchange while minimizing the risk of VILI. To date, the leading cause of death among patients with ARDS is multiple organ failure (MOF).[115]

There is a paucity of literature on this condition from developing countries especially in India. Hence this study was done to analyse the clinical characteristics of ARDS patients. In the present study a total of 60 subjects were included in the final analysis.

**AGE AND GENDER**

**Table 32: Comparison of average age and gender of the current study population with published literature.**

| STUDIES | AGE | GENDER |
|---|---|---|
| Present study | 41.4 | Males: 56.7% |
| Magazine R et al [11] | 42.92 | Males: 90 (60%)<br>Females: 60 (40%) |
| Suchyta et al.[101] | Older than 55 years | 135(52%) were females |
| Eachampati et al[105] | 65.2 | 66% were men |
| Phua J et al[99] | 51.6 | Males:61%<br>Females: 39% |
| Ingle VV et al[97] | 48 | 42(70%) |

The mean age of the present study population was 41.4 years with 56.7% participants being males. This finding was similar to the study conducted by Ingle VV et al[97] in which 70% of ARDS patients were males.The Bhadade RR et al.[10] study comprised of 74% males and 26% females. The mean age of the patients in the study was 37.9 years. The ARDS was mostly found in older age groups. The males were predominantly involved. The reason behind predominant involvement of males in this study is the higher environmental exposure in working males, causing more vector borne tropical infections such as dengue, malaria, scrub typhus and undiagnosed febrile illnesses-in them with ALI/ARDS as a complication.

**ETIOLOGICAL FACTORS OF ARDS**

**Table 33 : Comparison of Various etiological factors of ARDS of current study with other studies**

| STUDIES | Pneumonia | Scrub typhus | Pulmonary TB | Leptospirosis | Influenza | Malaria | Abdominal sepsis | Non infectious |
|---|---|---|---|---|---|---|---|---|
| Present study | 28.3% | 1.7% | - | 3.3% | 8.3% | 1.7% | 5% | - |
| Magazine R et al [11] | 23.3% | 22% | 1.3% | 7.3% | 6.7% | 6.4% | 10.7% | 10% |
| Ingle VV et al[97] | 28.3% | - | - | - | - | - | - | - |

Apart from the above mentioned causes the other observed causes for ARDS in the present study were OP poisoning 10%, dengue 8.3%, undiagnosed fever 6.7%, pancreatitis 5%, sepsis-chronic liver diseases 6.7%, sepsis-intra uterine death 3.3%, snake bite3.3%, UTI 3.3%, paraquat poisoning 1.7%, acute fulminant viral hepatitis 1.7% which were seen in 6(10%), 5(8.3%), 5(8.3%), 4(6.7%), 3(5%), 4(6.7%), 2(3.3%), 2(3.3%), 1(1.7%) respectively. Ingle VV et al[97] reported that 28.3% participants had pneumonia. Out of 60 people, 75% participants had sepsis. Lu Y et al [102] reported the most common predisposing factors for ARDS were pneumonia (34.3%) and nonpulmonary sepsis (30.6%) and this was true for the study by Ingle VV et al. [97] Magazine R et al [11] reported that the most common cause of ARDS in their study was pneumonia, but a large percentage of cases were due to the tropical infections. Agarwal R et al [98] reported that the most common cause of ARDS was infective pneumonia and sepsis.

**OUTCOMES**

**Table 34: Comparison of adverse outcome (Mortality) with published literature**

| STUDIES | MORTALITY |
|---|---|
| Lu Y et al[102] | 70.4% |
| Ingle VV et al[97] | 60% |
| Suchyta et al[101] | 64% |
| Eachampati et al[105] | 51.9% for elderly and 41.9% for younger |
| Zambon M et al[100] (pooled mortality) | 43% |
| Phua J et al[99] (pooled mortality) | 44.3% |
| Derdaks et al[74] | 52% |
| Guerin C et al[69] | 42.7% |
| Singh G et al[103] | 41.8% |
| Gupta et al[104] | 42.9% |
| Present study | 48.3% |

Agarwal R et al[12] reported that the hospital mortality rate was 47.8%. Multivariate analysis showed SOFA scores as risk factors for death in the ICU. There was no significant effect of the category of ARDS on outcome (OR, 1.6; 95% CI, 0.8 to 3.2). Conflicting data exist about the evolution ARDS mortality over time. A meta-analysis by Phua J et al[99] did not find any mortality reduction in recent years, whereas another meta-analysis by Zambonet al[100] showed reduced mortality in recent years. In the past, several studies evaluated patterns of ARDS mortality over time within the same institution and all studies, except for two, found decreasing mortality in ARDS. The observed discrepancy between different studies may be due to different investigational methods, but we can conclude that ARDS mortality remains high (41 -

46%). Regardless of improvements in recent years, ARDS mortality is higher in older patients and in medical patients[101]. However, the impact, if any, of newer treatment strategies on ARDS mortality has not been evaluated, because most studies are referred to the period before the year 2000. Phua J et al[99]Overall pooled weighted mortality was 44.3% (95% confidence interval [CI], 41.8-46.9). Mortality decreased with time in observational studies conducted before 1994; no temporal associations with mortality were demonstrated in RCTs (any time) or observational studies (after 1994). Pooled mortality from 1994 to 2006 was 44.0% (95% CI, 40.1-47.5) for observational studies, and 36.2% (95% CI, 32.1-40.5) for RCTs.

**Table 35: Comparison Severity scores between survivors and nonsurvivors among survivors of current study with literature**

| | | APACHE II | APACHE III | SOFA |
|---|---|---|---|---|
| Present study | Survivors | 14.39 ± 6.27 | 51.65 ± 16.09 | 5 (IQR 4 to 7) |
| | Non survivors | 19.59 ± 7.01 | 92.90 ± 23.27 | 9 (IQR 8 to 11) |
| Magazine R et al [11] | Survivors | 9.06 ± 4.3 | 49.22 ± 14 | 6.43 ± 2.5 |
| | Non survivors | 21.11 ± 7 | 86.45 ± 23.5 | 10.6 ± 10 |
| Eachampati et al[105] | Survivors | - | 83.4 +/- 2.0 | - |
| | Non-survivors | - | - | - |
| Agarwal, R., et al.[12] | Survivors | 15.9 (8.1) | - | 6.5 (3.3) |
| | Non survivors | 20 (9.2) | - | 7.9 (3.9) |
| Balzer, F., et al.[116] | Survivors | 25.0 (18.0;35.2) | - | 11.0 (9.0;14.0)* |
| | Non survivors | 29.0 (24.0;37.0) | - | 13.0 (9.0;16.0)* |

In the current study, The mean APACHE II score of the study population was 16.9. The mean APACHE III score of the study population was 71.58. qSOFA score of 1 was seen in 48.33% participants, 45% had qSOFA score of 2, and 6.67% had qSOFA score of 3. Magazine R et al.[11] reported mean Acute Physiology and Chronic Health Evaluation (APACHE) II was 21.11, APACHE III was 86.45, and Sequential Organ Failure Assessment score was 10.6.

**Table 36: Duration of hospital stay and Mechanical ventilation of current study with published literature**

| **Study** | Duration of hospital stay | Duration of mechanical ventilation |
|---|---|---|
| Magazine R et al.[11] | 61.33%, (*n* = 92) was more than 7 days. | - |
| Agarwal, R., et al.[98] | Survivors: 8.4 (4.6)<br>Non survivors: 9.8 (4.3) | Survivors: 8.2 (5)<br>Non survivors: 9.4 (11.8) |
| Suchyta, M. R.,[101] | - | 14 +/-2 days |
| The Irish Critical Care Trials Group | 10.0 (5.0 to 18.5) | 6.0 (2.0 to 12.8) |
| Balzer, F., et al.[116] | Survivors: 6.0 (3.0;10.2)<br>Non survivors: 11.0 (4.0;23.0) | Survivors: 3.0 (2.0;6.0)<br>Non survivors4.0 (2.0;11.0) |
| Current study | 8.43±4.06 days | 5.08±2.76 days |

Among the study population, 48.3% participants expired. Lu Y et al.[102] reported overall ICU mortality of 10.3% and In-hospital and 90-day mortalities of ARDS patients were 68.5 and 70.4%, respectively, and accounted for 13.5% of the overall ICU mortality. Multiple organ dysfunction syndromes was a major risk factor associated with death [102].In the past two decades, there are studies reporting mortality decreased to up to 30%. The study done by Widdermannet al.[32] had observed mortality of 30%, which may have been as a result of improvement in the specific management of patients of ARDS such lung protective ventilation as well as in the general management of ICU patients. However, in another study in India by Agrawal R et al.[98], the mortality rates were again higher but similar to our study. The mean duration of mechanical ventilation was 5.08 ± 2.76 days. The mean stay in hospital was 8.43 days, and the mean ICU stay was 6.48 days.Ingle VV et al.[97] reported higher mean stay in MICU of 10.4 days and average in-hospital mortality in our study was observed in 60% which was more than that observed during recent studies.

The mean PaO2 /FiO2 of the study population was 98.92 with the ranged between 10.20 to 190. Mean PaO2 /FiO2 ratio on admission in our patients was 92 and Ziberberg, and Epstein found mortality rate in patients with PaO2 /FiO2 less than 200. [117]

In the current study, we found statistical significance between both scoring scales to the duration of hospitalization. Individuals with high APACHE II scoring had a significant duration of ICU stay and duration of ventilation. There was a weak negative correlation between qSOFA score and duration of ICU stays and duration of stay in hospital days. There was a weak positive correlation between qSOFA score and duration of mechanical ventilation days. There was a weak positive correlation between the APACHE III score and duration of ICU stays. There was a negative

correlation between the APACHE III score and duration of stay in hospital days. There was a weak positive correlation between the APACHE III score and duration of mechanical ventilation days. There was a weak positive correlation between APACHE II score and duration of stay in hospital days, duration of ICU and duration of mechanical ventilation days stayand this was statistically significant.

The APACHE II had excellent predictive validity in predicting expired, APACHE III had poor predictive validity in predicting expired and SOFA score had good predictive validity in predicting expired.

Naqvi, I. H., et[118] al in their study concluded that each model in their study showed good discriminative power as assessed by area under the ROC (Receiver operator curve) while APACHE II showed better discriminative power than SAP II and SOFA due to its greater value(.83) of area under ROC (Receiver operator curve) as compared to .75 for both SAPS II and SOFA. The discrimination power was weak for SOFA, but it was acceptable for APACHE II (AUC = 0.634 vs AUC = 0.737, respectively) in the study by Hosseini, M. and J. Ramazani.[119] The ROC analysis done by Sharma, S., et al[120] shows that the best discrimination was provided by APACHE II (AUROC=0.978) followed by SOFA (AUROC=0.911).

Sadaka, F., et al.[121] in their study had APACHE III score as 68 ± 28. ICU mortality was 11.8% and hospital mortality was 18.3%. Both APACHE II (r = 0.41) and APACHE III scores (r = 0.44) had good correlations with hospital mortality. There was no statistically significant difference between the two correlations (P = 0.1). ROC area under the curve (AUC) was 0.80 (95% confidence interval (CI): 0.78 - 0.82) for APACHE II, and 0.83 (95% CI: 0.81 - 0.85) for APACHE III, suggesting that both scores have very good discriminative powers for predicting hospital mortality. Cho, D. Y., et al.[122] found the correct prediction of outcome was 85.5% in

APACHE III, 77.5% in APACHE II and 75.0% in GCS. The area under the Receiver Operating Characteristic (ROC) curve was 0.892 in APACHE III, and 0.826 in APACHE II. Gilani, M. T., et al.[123] found discrimination was excellent for APACHE II (AUC: 0.828) score and acceptable for APACHE III (AUC: 0.782) scores. APACHE II provided better discrimination than APACHE III.

The qSOFA in itself had no statistically significant association with mortality in our study. Hence overall it can be summarised that, among all the scoring systems, APACHE-II had the highest predictive validity, followed by SOFA score and APACHE-III. The utility of qSOFA in risk stratification appears to be limited.

# LIMITATIONS

1. Limited sample size did not allow us to conduct inferential statistical analysis to assess factors associated with adverse outcomes.
2. The findings of the study should be generalised with caution, as the study was limited to a single centre, with limited sample size.

# RECOMMENDATIONS

1. There is a need to conduct large-scale prospective studies to document various factors associated with adverse outcomes like duration of mechanical ventilation, mortality etc. This may aid in effective risk stratification and risk communication at the time of admission.
2. Thereis also a need to test the utility of various structured clinical scoring systems in their predictive validity to identify the score with best predictive validity among Indian population. This may again help in effective risk stratification and efficient utilisation of limited resources in the management of ARDS patients.

# CONCLUSIONS

- The current study has assessed the clinical profile and outcome of patients with ARDS in a tertiary care teaching hospital. Also, it has assessed the predictive validity of various commonly used disease severity assessment scores.
- The mean age of the study population was 41.4 ± 14.51 years with the ranged between 18 to 77 years and males slightly outnumbered female population.
- The most common underlying disease was Pneumonia, followed by OP poisoning, H1N1 and Dengue. Undiagnosed fever and Sepsis due to chronic liver disease were the other common conditions.
- The most common comorbidity was hypertension, followed by diabetes mellitus. CAD, CVA, COPD, Asthma and HIV were the other common co-morbidities.
- The most common presenting symptom was fever in more than 50% of the population. The other common presenting features were sore throat, cough, pain abdomen, vomiting etc. Altered sensorium and headache were present in the minor portion of subjects. Pallor was the most common clinical sign Among the study population. Pedal edema, icterus, Petechiae and cyanosis were the other clinical signs
- Staphylococcus was the most common organism isolated from blood culture. The other organisms isolated were Klebsiella, MRSA, E.coli, enterococcus and pseudomonas in blood.
- Among sputum specimens, Klebsiella and pseudomonas were isolated.
- In urine specimens, E.coli was the most common organism, followed by Enterobacter and Pseudomonas.
- Acinetobacter, Klebsiella and Pseudomonas were isolated from fluid collected from ET.

- Dengue and HBsAg positivity was seen in the minor proportion of subjects.
- In the study population, 75% of the patients were in sepsis.
- The mean po2/Fio2 of the study population was 98.92 ± 41.1.
- In the study, Out of 60 people, 18(30%) participants were intubated.
- The mean duration of mechanical ventilation was 5.08 ± 2.76 days, ranged between 2 to 14 days. The mean stay in hospital was 8.43 ± 4.06 days, ranged between 3 to 18 days. The mean ICU stay was 6.48 ± 3.04 days, ranged between 2 to 17 days.
- Among the study population, 31(51.7%) participants had improved, and 29(48.3%) participants met with mortality.
- The APACHE II had excellent predictive validity in predicting mortality, as indicated by the area under the curve of 0.934 (95% CI 0.000 to 1, P value <0.001). The APACHE III had poor predictive validity in predicting mortality, as indicated by the area under the curve of 0.697 (95% CI 0.562 to 0.833, P value 0.009). The SOFA score had good predictive validity in predicting mortality as indicated by the area under the curve of 0.871 (95% CI 0.779 to 963, P value <0.001)
- The qSOFA score had no statistically significant association with mortality. Hence it's usefulness in identifying subjects with a high risk of mortality may be very limited.

# SUMMARY

The current study has assessed the clinical profile and outcome of patients with ARDS in a tertiary care teaching hospital. Also, it has assessed the predictive validity of various commonly used disease severity assessment scores. The mean age of study population was 41.4 ± 14.51 years. With the ranged between 18 to 77 years and males slightly outnumbered female population. The most common underlying disease was Pneumonia, followed by OP poisoning, H1N1 and Dengue. Undiagnosed fever and Sepsis due to chronic liver disease were the other common conditions.The most common co-morbidity was hypertension, followed by diabetes mellitus. CAD, CVA, COPD, Asthma and HIV were the other common co-morbidities. The most common presenting symptom was fever in more than 50% of the population. The other common presenting features were sore throat, cough, pain abdomen, vomiting etc. Altered sensorium and headache were present in minor portion of subjects. Pallor was the most common clinical sign Among the study population. Pedal edema, icterus, Petechiae and cyanosis were the other clinical signs. Staphylococcus was the most common organism isolated from blood culture. The other organisms isolated were Klebsiella, MRSA, E.coli, enterococcus and pseudomonas in blood. Among sputum specimens Klebsiella and pseudomonas were isolated. In urine specimens, E.coli was the most common organism, followed by Enterobacter and Pseudomonas. Acinetobacter, Klebsiella and Pseudomonas were isolated from fluid collected from ET. Dengue and HbSAg positivity was seen in minor proportion of subjects. The mean duration of mechanical ventilation was 5.08 ± 2.76 days, ranged between 2 to 14 days. The mean stay in hospital was 8.43 ± 4.06 days, ranged between 3 to 18 days. The mean ICU stay was 6.48 ± 3.04 days, ranged between 2 to 17 days. Among the study population 31(51.7%) participants had improved and 29(48.3%) participants

met with mortality. The APACHE II had excellent predictive validity in predicting mortality, as indicated by area under the curve of 0.934 (95% CI 0.000 to 1, P value <0.001). The APACHE III had poor predictive validity in predicting mortality, as indicated by area under the curve of 0.697 (95% CI 0.562 to 0.833, P value 0.009). The SOFA score had good predictive validity in predicting mortality as indicated by area under the curve of 0.871 (95% CI 0.779 to 963, P value <0.001). The qSOFA score did not show any statistically significant association with mortality, hence it's utility in risk stratification of the subjects is questionable.

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# ANNEXURE:I – CONSENT FORM

**INFORMED CONSENT FORM**

**TITLE :CLINICAL PROFILE AND OUTCOME OF PATIENT WITH ACUTE RESPIRATORY DISTR**
**SYNDROME IN INTENSIVE CARE UNIT - ONE YEAR HOSPITAL BASED CROSS SECTIONAL STU**

PRINCIPAL INVESTIGATOR :

DEPARTMENT OF GENERAL MEDICINE
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELGAUM 590010
KARNATAKA

**Objective and purpose of the study:**

. This research is intended to assess **CLINICAL PROFILE AND OUTCOME OF PATIENT WITH ACUTE RESPIRATORY DISTRESS SYNDROME IN INTENSIVE CARE UNIT .**The principal investigator of the study is under the guidance of

Acute respiratory distress syndrome (ARDS) is a clinical syndrome of severe dyspnoea of rapid onset, hypoxemia and diffuse pulmonary infiltrates leading to respiratory failure.

Acute respiratory distress syndrome is a devastating clinical disorder that is seen in critically ill patients withvariable clinical manifestations. There are very few studies on the pattern of ARDS seen in our country. Much of the available data on clinical course of patients with ARDS is from western literature.

Mortality rates in the North Indian and Western Indian population were 47.8% and 57%, respectively. This is a prospective study where an attempt is made to evaluate the etiology,clinical features,prognostic factors and outcome of ARDS of patients admitted in ICU .

**Procedure:**
If you agree to be part of the research study you will be asked the relevant history and will be subjected to relevant clinical examination and investigations.

**Risk and Benefits:** The only risk and possible discomfort you might get is while taking blood from my arm for the investigations. It may cause swelling, pain, redness, bruising or infection (rarely happens) at the site from where the blood is drawn

**Alternatives**

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

**Privacy and Confidentiality:**

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

**Institution / Sponsor's policy:**

Does not apply to this research

**VOLUNTARY PARTICIPATION/ WITHDRAWAL:**

Your participation in this study is entirely voluntary and you may withdraw from the study at any time.

**.Financial incentives for participation**

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

**Authorization to publish the result**

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

If you have any questions about your rights as a participant you may call :

# संशोधन अभ्यास सहभाग संमती

संशोधन अध्ययन: **"क्लिनिकल प्रोपैल ऍन्ड अवटकं ऑफ पेसेन्ट विथ अक्यूट रिसपीरेट्री डिस्ट्रिसिंड्रोम इन इंट्नसहिव केयर युनिट–वन इयर बेसड क्रॉस सेक्शनल स्टडि" एक अध्ययन,** अट **के.एल.ई. के डॉ. प्रभाकर कोरे हॉस्पिटल आणि एम.आर.सी. बेलगावी ,** पी.जी. विद्यार्थि, जे.एन. मेडीकल कॉलेज बेळगावी, द्वारा आयोजित प्रिन्सिपाल ऍन्ड प्रोफेसर, मेडिसिन विभाग, जे.एन. मेडीकल कॉलेज बेळगावी यांच्या मार्गदर्शनाखाली करत आहेत.

प्रक्रिया सहभाग:

तुम्ही माझ्या अभ्यासात स्वत: नावनोंदणी करणेस सहमत असल्यास, नंतर वैद्यकीय तपासणी केली जाईल, आणि त्यानुसार, तुमच्या सध्याच्या मगील आणि कुटुंबाचा इतिहास या संबंधित मुलाखत घेतली जाईल.

धोके आणि फ़ायदे

या अभ्यासातील धोके आणि फ़ायदे मला समजावून सांगितळे आहेत.

प्रलियेतीळ सहभाग

सहभाग ऐच्छिक आहे. आपण स्वत: ला या अभ्यासात सहभागीकरू शकता. किंवा नाकरू शकता.नाकारत्यास रूग्णोलयोशी असलेल्या सबंधात काही फरक पडणार नाही. तुम्ही या अभ्यासातून कधीही माघार घेऊ शकता

पर्याय : आपण अभ्यास सहभाग सोडला तरी आपत्याला रूग्णालयातीळ उपचार नियमा प्रमाणे मिळेतील.

गोपनीयता : तुम्ही. दिलेली संशोधना दरम्यानची माहिती ही फक्त संशोधन संघातील लोकांनाच माहित असेल. व संशोधनासाहीच वापरली जाहील तुमच्या लेखी परवानगीशिवाय कोणतीच माहिती उघड केली जाणार नाही.

परिणाम छापण्याबाबत : संशोधनच्या परिणामांबाबत चर्चा करताना, तुमची ओळख पटेल अशी माहिती उघड केली जाणार नाही.

नुकसानभरपाई : काहीही आरोग्यिक नुकसान झाल्यास रूग्णालय कोणतीहीं आर्थिक नुकसानभरपाई देण्यास बंधील नाही.

संशोधनाबाबत काहीही प्रश्न वा शंका असल्यास संपर्क साधावा :

**३. डॉ. गंगा. एस. पिळहे: चेअरमन, इन्स्टिटूशनल एथिक्स कमिटी, प्रोफेसर, पॅथॉलाजि विभाग, जे.एन. मेडीकल कॉलेज, बेळगावी । मो–९४८०२७५६०१**

## सम्मती पत्र

मी खाली सही करणार स्वत:हून अभ्यासामध्ये भाग घेण्यासाठी हे मान्य करत आहे. मी माझे नांव यातून कोणत्याही क्षणी काढून घेवू शकतो/शकते हा नमूना फार्म सही केल्यामुळे मी माझे कोणतेही नैतिक अधिकार सोडून देत नाही आहे. हे वाचून पाहिल्यानंतर किंवा ते वाचून दाखविल्या नंतर मी माझी सही या सम्मती पत्रावर करत आहे. व अशा प्रकारे मी सर्व प्रश्नाची उत्तरे देत आहे.

भाग घेणायाचे नांव :

सही अथवा डाव्या हाताचा अंगठा :

साक्षीदाराचे नांव :

साक्षीदाराची सही :

तपासणान्याचे नांव :

तपासणान्याचे सही :

तारीख: ठिकाण :

## संशोधन में भाग लेने केलिए सम्मती पत्र.

आपको इस संशोधन **"क्लिनिकल प्रोपैल ऍन्ड अवटकं ऑफ पेसेन्ट विथ अक्यूट रिसपीरेट्री डिस्ट्रिसिंड्रोम इन इंट्नसहिव केयर युनिट–वन इयर बेसड क्रॉस सेक्शनल स्टडि", के बारे में एक अध्ययन"** अट **के.एल.ई. के डॉ. प्रभाकर कोरे हॉस्पिटल और एम.आर.सी. बेलगावी** में भाग लेने के लिये निमंत्रित करता हु । ये संशोधन पी.जी. विद्यार्थि, जे.एन. मेडीकल कॉलेज बेळगावी. और मार्गदर्शक : व्हायिस प्रिन्सिपॉल ऍन्ड प्रोफेसर, मेडिसिन विभाग, जे.एन. मेडीकल कॉलेज बेळगावी. द्वारा किया जा रहा है ।

मुझे इस संशोधन के बारे में और इसके फायदे और इसके रिस्क के बारेमे पुरे तरिके से बतादिये गये है ।

मै अपनी मर्जी से संशोधन में भाग लेना चाहता हुं और इसके लिये मेरी सहमती है । मैं अपनी मर्जी से कभी भी संशोधन में भाग लेने के लिये मना कर सकता हुँ । मेरे पास संशोधन के बारे मे प्रश्न पुछने के लिये पूरा समय है और इसके लिय मैं कभी भी प्रश्न पुछ सकता हुँ ।

मेरा स्वाक्षरी / अगूंठा साक्षी है कि मै सहमती पत्र के लिय तैयार हूँ ।

इस विषय पर और अधिक जानकरी केलिये या संपर्क किजिए

**डॉ. गंगा. एस. पिळहे चेअरमन, इन्स्टिट्यूशनल एथिक्स कमिटी, प्रोफेसर, पॅथॉलाजि विभाग, जे.एन. मेडीकल कॉलेज, बेळगावी । मो–९४८०२७५६०१**

# सम्मती पत्र

मै नीचे सही करनेवाला स्वेइच्छेसे इस अभ्यासमें भाग लेने के लिए मान्यता देता हूँ । मै अपना नाम किसी भी वक्त इसमेसे वापस ले सकता हूँ और इस सम्मती के कारण मै मेरे कोई भी कानूनी हक नहीं छोड रहा हूँ। यह सब उपर के विषय के बारे में स्वयं पढकर या पढने के, सुनने के बाद मैं इस सम्मती पत्र पर अपने हस्ताक्षर कर के सभी प्रश्नों का उत्तर हे रहा हूँ।

सहभागी का नाम :

हस्ताक्षर :

साक्षीदार का नाम :

हस्ताक्षर :

संशोधक का नाम :

हस्ताक्षर :

दिनांक :

स्थळ :

# ಸಂಶೋಧನಾ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವಿಕೆಗಾಗಿನ ಸಮ್ಮತಿ ಪತ್ರ

ನಾವು ನಿಮ್ಮನ್ನು ಸಂಶೋಧನೆಯಲ್ಲಿ ತೊಡಗಿಸಿಕೊಳ್ಳಲು ವಿನಂತಿಸುತ್ತಿದ್ದೇವೆ **"ಕ್ಲಿನಿಕಲ್ ಪ್ರೋಫೈಲ್ ಆಂಡ್ ಅವಟಕಂ ಆಫ್ ಪೇಸೆಂಟ್ ವಿಥ್ ಅಕ್ಯೂಟ್ ರಿಸಪೀರೆಟ್ರೀ ಡಿಸ್ಟ್ರಿಸಿಂಡ್ರೋಮ್ ಇನ್ ಇಂಟನಸ್ಹೀವ್ ಕೇಯರ್ ಯುನಿಟ್--ಒನ್ ಇಯರ್ ಹಾಸ್ಪಿಟಲ್ ಬೇಸಡ್ ಕ್ರಾಸ್ ಸೆಕ್ಷನಲ್ ಸ್ಟಡಿ". ಆಟ್ ಕೆ.ಎಲ್.ಇ.ಎಸ್. ಡಾ॥ ಪ್ರಭಾಕರ ಕೋರೆ ಹಾಸ್ಪೀಟಲ್ ಮತ್ತು ಎಮ್.ಆರ್.ಸಿ. ಬೆಳಗಾವಿಯಲ್ಲಿ ಮಾಡುವ ಒಂದು ಅಧ್ಯಯನ"**

**ಸ್ನಾತಕೋತ್ತರ ವಿದ್ಯಾರ್ಥಿ ಜೆ.ಎನ್.ಮೆಡಿಕಲ್ ಕಾಲೇಜ, ಬೆಳಗಾವಿ ಇವರು**

**ವ್ಹಾಯಿಸ್ ಪ್ರಿನ್ಸಿಪಾಲ್ & ಪ್ರೊಫೇಸರ, ಮೇಡಿಸಿನ ವಿಭಾಗ, ಜೆ.ಎನ್.ಮೇಡಿಕಲ್ ಕಾಲೇಜ, ಬೆಳಗಾವಿ,** ಇವರ ಮಾರ್ಗದರ್ಶದಲ್ಲಿ ನಡೆಸುತ್ತಿದ್ದೇವೆ.

ಗೌರವಾನ್ವಿತರೇ ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ಅರ್ಹರಿದ್ದಿರಿ.

ಸಂಶೋಧನೆಯಲ್ಲಿ ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆ ವೈಯಕ್ತಿಕವಾಗಿದ್ದು, ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವುದು ನಿಮ್ಮ ನಿರ್ಧಾರವಾಗಿರುತ್ತದೆ. ಇದರಿಂದ ಜೆ.ಎನ್ ಮೇಡಿಕಲ್ ಕಾಲೇಜಿಗೆ ನಿಮಗಿರುವ ಸಂಬಂಧಕ್ಕೆ ಪರಿಣಾಮ ಬೀರುವುದಿಲ್ಲ. ನೀವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ಹಿಂದೆ ಸರಿಯಬಹುದು.

ನೀವು ನನ್ನ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮನ್ನು ತೊಡಗಿಸಿಕೊಳ್ಳಲು ಒಪ್ಪಿದ ನಂತರ ಪ್ರಾಯೋಗಿಕವಾಗಿ ವಿಚಾರಣೆ ಹಾಗೂ ಅದಕ್ಕೆ ತಕ್ಕಂತೆ ತನಿಖೆ ನಡೆಸಲಾಗುವುದು. ನಿಮ್ಮ ಹಾಗೂ ಕುಟುಂಬದ ಇತಿಹಾಸದ ಬಗ್ಗೆ ಸಂಧರ್ಶನ ನಡೆಯಿಸಲಾಗುವುದು.

ತಾವುಗಳು ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವಾಗ ಮುನ್ನೆಚ್ಚರಿಕೆ ಕ್ರಮಗಳನ್ನು ಅನುಸರಿಸಲಾಗುವುದು. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವುದರಿಂದ ಖಾಯಿಲೆಯ ಸಂಪೂರ್ಣ ಮಾಹಿತಿ ಪಡೆಯಬಹುದು. ಇದರಿಂದ ಇದೇ ಖಾಯಿಲೆಯಿಂದ ಬಳಲುತ್ತಿರುವ ಇತರರಿಗೆ ತುಂಬಾ ಸಹಾಯವಾಗುವುದು.

ಈ ಪರೀಕ್ಷೆಯ ವೆಚ್ಚವನ್ನು ಆಸ್ಪತ್ರೆಯ ನಿಯಮದಂತೆ ತಾವೇ ಭರಿಸಬೇಕು. ಆದರೆ ಇದರಲ್ಲಿ ಯಾವುದೇ ಇತರ ವೆಚ್ಚುಗಳು ಇರುವುದಿಲ್ಲ.

ತಾವು ಈ ಪರೀಕ್ಷೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವುದನ್ನು ಸಂಪೂರ್ಣವಾಗಿ ಗೌಪ್ಯವಾಗಿ ಇಡಲಾಗುವುದು.

ತಮ್ಮ ಖಾಯಿಲೆ ಹಾಗೂ ಸಂಶೋಧನೆಯ ವಿವರಗಳನ್ನು ಎಲ್ಲಿಯೂ ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ಸಂಶೋಧನೆಯ ವಿವರಗಳನ್ನು ಪ್ರಕಟಿಸಲಿಕ್ಕೆ ಉಪಯೋಗ ಮಾಡಬಹುದು. ಆದರೆ ಇಲ್ಲಿ ನಿಮ್ಮ ಗೌಪ್ಯತೆಯನ್ನು ಕಾಪಾಡಲಾಗುವುದು. ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ಆಗುವ ಯಾವುದೇ ವ್ಯತಿರಿಕ್ತ ಪರಿಣಾಗಳಿಗೆ ಕೆ.ಎಲ್.ಇ.ಆಸ್ಪತ್ರೆಯ ಮೂಲಕ ಚಿಕಿತ್ಸೆ ನೀಡಲಾಗುವುದು.

## संशोधन में भाग लेने केलिए सम्मती पत्र.

आपको इस संशोधन **"क्लिनिकल प्रोपैल ऍन्ड अवटकं ऑफ पेसेन्ट विथ अक्यूट रिसपीरेट्री डिस्ट्रिसिंड्रोम इन इंट्नसहिव केयर युनिट–वन इयर बेसड क्रॉस सेक्शनल स्टडि", के बारे में एक अध्ययन"** अट **के.एल.ई. के डॉ. प्रभाकर कोरे हॉस्पिटल और एम.आर.सी. बेलगावी** में भाग लेने के लिये निमंत्रित करता हु । ये संशोधन, पी.जी. विद्यार्थि, जे.एन. मेडीकल कॉलेज बेळगावी. और मार्गदर्शक : व्हायिस प्रिन्सिपॉल ऍन्ड प्रोफेसर, मेडिसिन विभाग, जे.एन. मेडीकल कॉलेज बेळगावी. द्वारा किया जा रहा है ।

मुझे इस संशोधन के बारे में और इसके फायदे और इसके रिस्क के बारेमे पुरे तरिके से बतादिये गये है ।

मै अपनी मर्जी से संशोधन में भाग लेना चाहता हुं और इसके लिये मेरी सहमती है । मैं अपनी मर्जी से कभी भी संशोधन में भाग लेने के लिये मना कर सकता हुँ । मेरे पास संशोधन के बारे मे प्रश्न पुछने के लिये पूरा समय है और इसके लिय मैं कभी भी प्रश्न पुछ सकता हुँ ।

मेरा स्वाक्षरी / अगूंठा साक्षी है कि मै सहमती पत्र के लिय तैयार हूँ ।

इस विषय पर और अधिक जानकरी केलिये या संपर्क किजिए

**डॉ. गंगा. एस. पिळहे चेअरमन, इन्स्टिटूशनल एथिक्स कमिटी, प्रोफेसर, पॅथॉलाजि विभाग, जे.एन. मेडीकल कॉलेज, बेळगावी । मो–९४८०२७५६०१**

# सम्मती पत्र

मै नीचे सही करनेवाला स्वेइच्छेसे इस अभ्यासमें भाग लेने के लिए मान्यता देता हूँ । मै अपना नाम किसी भी वक्त इसमेसे वापस ले सकता हूँ और इस सम्मती के कारण मै मेरे कोई भी कानूनी हक नहीं छोड रहा हूँ। यह सब उपर के विषय के बारे में स्वयं पढकर या पढने के, सुनने के बाद मैं इस सम्मती पत्र पर अपने हस्ताक्षर कर के सभी प्रश्नों का उत्तर हे रहा हूँ।

सहभागी का नाम :

हस्ताक्षर :

साक्षीदार का नाम :

हस्ताक्षर :

संशोधक का नाम :

हस्ताक्षर :

दिनांक :

स्थळ :

# ಸಂಶೋಧನಾ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವಿಕೆಗಾಗಿನ ಸಮ್ಮತಿ ಪತ್ರ

ನಾವು ನಿಮ್ಮನ್ನು ಸಂಶೋಧನೆಯಲ್ಲಿ ತೊಡಗಿಸಿಕೊಳ್ಳಲು ವಿನಂತಿಸುತ್ತಿದ್ದೇವೆ **"ಕ್ಲಿನಿಕಲ್ ಪ್ರೋಫೈಲ್ ಆಂಡ್ ಅವಟಕಂ ಆಫ್ ಪೇಸೆಂಟ್ ವಿಥ್ ಅಕ್ಯೂಟ್ ರಿಸಪೀರೆಟ್ರೀ ಡಿಸ್ಟ್ರಿಸಿಂಡ್ರೋಮ್ ಇನ್ ಇಂಟನಸ್ಹೀವ್ ಕೇಯರ್ ಯುನಿಟ್–ಒನ್ ಇಯರ್ ಹಾಸ್ಪಿಟಲ್ ಬೇಸಡ್ ಕ್ರಾಸ್ ಸೆಕ್ಷನಲ್ ಸ್ಟಡಿ". ಆಟ್ ಕೆ.ಎಲ್.ಇ.ಎಸ್. ಡಾ॥ ಪ್ರಭಾಕರ ಕೋರೆ ಹಾಸ್ಪೀಟಲ್ ಮತ್ತು ಎಮ್.ಆರ್.ಸಿ. ಬೆಳಗಾವಿಯಲ್ಲಿ ಮಾಡುವ ಒಂದು ಅಧ್ಯಯನ"**
**ಅನೇಜಾ ಸ್ನಾತಕೋತ್ತರ ವಿದ್ಯಾರ್ಥಿ ಜೆ.ಎನ್.ಮೆಡಿಕಲ್ ಕಾಲೇಜ, ಬೆಳಗಾವಿ ಇವರು ಡಾ॥ ವಿ.ಎ.ಕೊಟಿವಾಲೆ, ಪ್ರಿನ್ಸಿಪಾಲ್ & ಪ್ರೊಫೇಸರ, ಮೇಡಿಸಿನ ವಿಭಾಗ, ಜೆ.ಎನ್.ಮೇಡಿಕಲ್ ಕಾಲೇಜ, ಬೆಳಗಾವಿ,** ಇವರ ಮಾರ್ಗದರ್ಶದಲ್ಲಿ ನಡೆಸುತ್ತಿದ್ದೇವೆ.

ಗೌರವಾನ್ವಿತರೇ ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ಅರ್ಹರಿದ್ದಿರಿ.

ಸಂಶೋಧನೆಯಲ್ಲಿ ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆ ವೈಯಕ್ತಿಕವಾಗಿದ್ದು, ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವುದು ನಿಮ್ಮ ನಿರ್ಧಾರವಾಗಿರುತ್ತದೆ. ಇದರಿಂದ ಜೆ.ಎನ್ ಮೇಡಿಕಲ್ ಕಾಲೇಜಿಗೆ ನಿಮಗಿರುವ ಸಂಬಂಧಕ್ಕೆ ಪರಿಣಾಮ ಬೀರುವುದಿಲ್ಲ. ನೀವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ಹಿಂದೆ ಸರಿಯಬಹುದು.

ನೀವು ನನ್ನ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮನ್ನು ತೊಡಗಿಸಿಕೊಳ್ಳಲು ಒಪ್ಪಿದ ನಂತರ ಪ್ರಾಯೋಗಿಕವಾಗಿ ವಿಚಾರಣೆ ಹಾಗೂ ಅದಕ್ಕೆ ತಕ್ಕಂತೆ ತನಿಖೆ ನಡೆಸಲಾಗುವುದು. ನಿಮ್ಮ ಹಾಗೂ ಕುಟುಂಬದ ಇತಿಹಾಸದ ಬಗ್ಗೆ ಸಂಧರ್ಶನ ನಡೆಯಿಸಲಾಗುವುದು.

ತಾವುಗಳು ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವಾಗ ಮುನ್ನೆಚ್ಚರಿಕೆ ಕ್ರಮಗಳನ್ನು ಅನುಸರಿಸಲಾಗುವುದು. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವುದರಿಂದ ಖಾಯಿಲೆಯ ಸಂಪೂರ್ಣ ಮಾಹಿತಿ ಪಡೆಯಬಹುದು. ಇದರಿಂದ ಇದೇ ಖಾಯಿಲೆಯಿಂದ ಬಳಲುತ್ತಿರುವ ಇತರರಿಗೆ ತುಂಬಾ ಸಹಾಯವಾಗುವುದು.

ಈ ಪರೀಕ್ಷೆಯ ವೆಚ್ಚವನ್ನು ಆಸ್ಪತ್ರೆಯ ನಿಯಮದಂತೆ ತಾವೇ ಭರಿಸಬೇಕು. ಆದರೆ ಇದರಲ್ಲಿ ಯಾವುದೇ ಇತರ ವೆಚ್ಚುಗಳು ಇರುವುದಿಲ್ಲ.

ತಾವು ಈ ಪರೀಕ್ಷೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವುದನ್ನು ಸಂಪೂರ್ಣವಾಗಿ ಗೌಪ್ಯವಾಗಿ ಇಡಲಾಗುವುದು.

ತಮ್ಮ ಖಾಯಿಲೆ ಹಾಗೂ ಸಂಶೋಧನೆಯ ವಿವರಗಳನ್ನು ಎಲ್ಲಿಯೂ ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ಸಂಶೋಧನೆಯ ವಿವರಗಳನ್ನು ಪ್ರಕಟಿಸಲಿಕ್ಕೆ ಉಪಯೋಗ ಮಾಡಬಹುದು. ಆದರೆ ಇಲ್ಲಿ ನಿಮ್ಮ ಗೌಪ್ಯತೆಯನ್ನು ಕಾಪಾಡಲಾಗುವುದು. ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ಆಗುವ ಯಾವುದೇ ವ್ಯತಿರಿಕ್ತ ಪರಿಣಾಗಳಿಗೆ ಕೆ.ಎಲ್.ಇ.ಆಸ್ಪತ್ರೆಯ ಮೂಲಕ ಚಿಕಿತ್ಸೆ ನೀಡಲಾಗುವುದು.

ತಮಗೆ ಯಾವುದಾದರೂ ಸಂಶಯಗಳಿದ್ದಲ್ಲಿ ಅಥವಾ ಹೆಚ್ಚಿನ ಮಾಹಿತಿ ಬೇಕಾಗಿದ್ದಲ್ಲಿ ಈ ಕೆಳಗಿನ ವೈದ್ಯರನ್ನು ಸಂಪರ್ಕಿಸಬಹುದು.

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವವರ ಹಕ್ಕುಗಳ ವಿವರಗಳಿಗಾಗಿ ಈ ಕೆಳಗಿನ ವೈದ್ಯರನ್ನು ಸಂಪರ್ಕಿಸಬಹುದು.
**ಡಾ॥ ಗಂಗಾ ಎಸ್. ಪಿಳ್ಳಿ,** ಚೇರಮನ್, ಇನಸ್ಟಿಟ್ಯೂಶನಲ್ ಎಥಿಕ್ಸ್ ಕಮಿಟಿ, ಪ್ರೊಫೇಸರ, ಪೆಥಾಲಾಜಿ ವಿಭಾಗ, ಜೆ.ಎನ್.ಮೇಡಿಕಲ್ ಕಾಲೇಜ, ಬೆಳಗಾವಿ. (ಮೋ) 9480275601.

**ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ಸ್ವ–ಒಪ್ಪಿಗೆ ಪ್ರಮಾಣ ಪತ್ರ :**

ಈ ಸಂಶೋಧನೆಯ ಬಗ್ಗೆ ನನ್ನ ಸ್ವಂತ ಭಾಷೆಯಲ್ಲಿ ಸಂಪೂರ್ಣ ವಿವರವಾಗಿ ನನಗೆ ಅರ್ಥವಾಗಿರುತ್ತದೆ. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ನನಗೆ ಸಂಪೂರ್ಣವಾದ ಒಪ್ಪಿಗೆ ಇರುತ್ತದೆ. ಈ ಸಂಶೋಧನೆಯ ವಿವರಗಳು ಹಾಗೂ ಪರಿಣಾಮಗಳ ಬಗ್ಗೆ ನನಗೆ ಸಂಪೂರ್ಣವಾದ ಮಾಹಿತಿ ಇರುತ್ತದೆ. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಸ್ವ ಇಚ್ಛೆಯಿಂದ ಪಾಲ್ಗೊಳ್ಳಲು ಬಯಸುತ್ತೇನೆಂದು ಈ ಮೂಲಕ ದೃಢೀಕರಿಸುತ್ತೇನೆ. ನಾನು ಈ ಸಮ್ಮತಿ ಪತ್ರಕ್ಕೆ ಸಹಿ ಮಾಡುವುದರಿಂದ ನನಗೆ ಲಭ್ಯವಿರುವ ಕಾನೂನಿನ ಯಾವುದೇ ಹಕ್ಕುಗಳನ್ನು ಬಿಟ್ಟುಕೊಟ್ಟಿರುವುದಿಲ್ಲ. ನಾನು ಮೇಲಿನ ವಿಷಯ ಓದಿ ಅಥವಾ ಓದಿಸಿ ಕೇಳಿ ಸಮ್ಮತಿ ಪತ್ರದಲ್ಲಿರುವ ಎಲ್ಲ ಪ್ರಶ್ನೆಗಳಿಗೆ ಉತ್ತರಿಸಿರುತ್ತೇನೆ.

ಭಾಗವಹಿಸುವವರ ಹೆಸರು : _____

ಭಾಗವಹಿಸುವವರ ಸಹಿ : _____

ಭಾಗವಹಿಸುವವರ ಹೆಬ್ಬಟ್ಟಿನ ಗುರುತು : _____

ಸಾಕ್ಷಿದಾರರ ಹೆಸರು : _____

ಸಾಕ್ಷಿದಾರರ ಸಹಿ : _____

ಸಂಶೋಧಕರ ಹೆಸರು : _____

ಸಂಶೋಧಕರ ಸಹಿ : _____

ಸ್ಥಳ : _____

ದಿನಾಂಕ : _____

**CONSENT STATEMENT**

I voluntarily agree to take part in this study by signing on the line below. I may withdraw at any time. I am not giving up any of my legal rights by signing this form. My signature below indicated that I have read this entire consent form or it has been read to me, and has been explained to me in my vernacular language and had all my questions answered. I will be given a copy of this consent form.

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

Participant's Name/ : .....

Signature/ Left Thumb
Impression of the participant's : .....

Name of the legally
authorized representative/ Guardian : .....

Signature/ Left Thumb
Impression. : .....

Witness's Name : .....

Signature/ Left Thumb
Impression. :.....

Investigators name and Signature : .....

Date and Place : .....

Date: Place :

## सम्मती पत्र

मी खाली सही करणारा स्वत:हून अभ्यासामध्ये भाग घेण्यासाठी हे मान्य करत आहे. मी माझे नांव यातून कोणत्याही क्षणी काढून घेवू शकतो. हा नमूना फार्म सही केल्यामुळे मी माझे कोणतेही नैतिक अधिकार सोडून देत नाही आहे. हे वाचून पाहिल्यानंतर किंवा ते वाचून दाखविल्या नंतर मी माझी सही या सम्मती पत्रावर करत आहे. व अशा प्रकारे मी सर्व प्रश्नाची उत्तरे देत आहे.

भाग घेणाऱ्याचे नांव : .....सही/अंगठा

साक्षीदाराचे नांव: .....सही/अंगठा

तपासणाऱ्याचे नांव:.....सही

तारीख: ठिकाण:

## सम्मती पत्र

मै निचे सही करनेवाला स्वइच्छेसे इस अभ्यासमें भाग लेने के लिए मान्यता देता हू । मै अपना नाम किसी भी वक्त इसमेसे वापस ले सकता हू और इस सम्मती के कारण मै मेरे कोई भी कानुनी हक्क नही छोड़ रहा हू । यह सब उपर के विषय के बारे में स्वयं पढकर या पढने के सूनने के बाद मैं इस सम्मती पत्र पर अपने हस्ताक्षर कर के सभी प्रश्नो का उत्तर दिया हू ।

हिस्सा लेने वाले का नाम : .....सही/अंगठा

साक्षीदार का नाम: .....सही/अंगठा

परीक्षण करने वाले का नाम:..... .....सही

तारीख: स्थळ:

## ಸಮ್ಮತಿ ಪತ್ರ

ನಾನು ಈ ಕೆಳಗೆ ಸಹಿ ಮಾಡಿ ಸ್ವಚ್ಛೆಯಿಂದ ಅಭ್ಯಾಸದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪಿಕೊಂಡಿರುತ್ತೇನೆ. ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನನ್ನ ಒಪ್ಪಿಗೆಯನ್ನು ಹಿಂದೆ ಪಡೆಯಬಹುದು. ನಾನು ಈ ಸಮ್ಮತಿ ಪತ್ರಕ್ಕೆ ಸಹಿ ಮಾಡುವುದರಿಂದ ನನಗೆ ಲಭ್ಯವಿರುವ ಕಾನೂನಿನ ಯಾವುದೇ ಹಕ್ಕುಗಳನ್ನು ಬಿಟ್ಟುಕೊಟ್ಟಿರುವುದಿಲ್ಲ. ಕೆಳಗೆ ನಾನು ಸಹಿ ಮಾಡಿರುವುದರ ಅರ್ಥ ಏನೆಂದರೆ ಮೇಲಿನ ವಿಷಯ ಓದಿ ಅಥವಾ ಓದಿಸಿ ಕೇಳಿ ಪೂರ್ಣ ಸಮ್ಮತಿ ಪತ್ರದಲ್ಲಿರುವ ಎಲ್ಲ ಪ್ರಶ್ನೆಗಳಿಗೆ ಉತ್ತರಿಸಿರುತ್ತೇನೆ.

ಭಾಗವಹಿಸುವವರ ಹೆಸರು — ಸಹಿ/ಹೆಬ್ಬರಳಿನ ಗುರುತು

ಸಾಕ್ಷಿಯ ಹೆಸರು — ಸಹಿ/ಹೆಬ್ಬರಳಿನ ಗುರುತು

ಸಂಶೋಧಕರ ಹೆಸರು — ಸಹಿ

ದಿನಾಂಕ: — ಸ್ಥಳ:

# ANNEXURE : II – PROFORMA

## CLINICAL PROFILE AND OUTCOME OF PATIENT WITH ACUTE RESPIRATORY DISTRESS SYNDROME IN INTENSIVE CARE UNIT

**PROFORMA** **CASE NO**:

Name: Age: yrs Sex: M / F Education: OP / IP

Address: Occupation: Rural/Urban: No:

Interval between symptoms onset and admission: days

Etiology of ARDS

**HISTORY OF PRESENTING ILLNESS**

Fever: Y / N Duration: days Sore throat: Y / N Duration: days

Body ache: Y / N Duration: days Headache: Y / N Duration: days

Cough: Y / N Duration: days Breathlessness: Y / N Duration: days

Vomiting: Y / N Duration: days Loose motions: Y / N Duration: days

Altered mentation: Y / N Duration: days Pain abdomen: Y / N Duration: days

**CO-MORBID ILLNESS**

DM-Type 1 / 2./ HTN/ CAD/ RHD/ CVA/ COPD/ Asthma/ HIV/ CRF/PREVIOUS PNEUMONIA/TUBERCULOSIS/LIVER DISEASE

Others (if any)

**PERSONAL HISTORY-**smoking/alcohol /tobacco chewing/drug abuse/others

**GENERAL PHYSICAL EXAMINATION**

PR: bpm BP: mm/Hg RR: cpmSpO2:

Pallor/ icterus/ cyanosis/ clubbing/lymphadenopathy/pedal edema/congested throat/petechiae/ecchymosis/rashes/others

**SYSTEMIC EXAMINATION**

**Respiratory system:**

**Cardiovascular system:**

**Abdomen:** hepatomegaly/ splenomegaly/ free fluid

**Abdomen:** hepatomegaly/ splenomegaly/ free fluid

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Central nervous system:** | | | | | | | | |
| Glasgow coma scale: | | E- | | | V- | | M- | Total- /15 |
| Signs of meningeal irritation | | | | | | | | |
| | | | **INVESTIGATIONS** | | | | | |
| Hb: g/dl | TC: | c/mm | | N: | L: | E: | M: B: | Platelets: |
| lakhs/L | | | | | | | | |
| RBS: mg/dl | PCV: | % | | | | | | |
| BU: Bilirubin: | | mg/ dl | | SGOT: | SGPT: | | ALP:CPK: | |
| Electrolytes: | sodium- | meq/L | | potassium: | | | meq/L | chloride: meq/L |
| Albumin: | Creat | mg/dl | | | | | | |
| PT: | APTT: | | | INR: | | | | |
| USG: | | | | | | | | |
| CXR: | | | | | | | | |
| Blood C/S: | | | | | | | | |
| ABG: pH: | pO2: | | | pO2:FiO2: | | | | |
| Wound culture(if relevant) | | | | | | | | |
| Urine culture(if relevant) | | | | | | | | |
| Endotracheal tube C/S : | | | | | | | | |
| Any other culture sensitivity which is available | | | | | | | | |
| Weil felix test: | Ox 19 Ox 2: | | | | | Ox K: | | |
| Widal Test: | | S.Typhi O: | | | | H: | | |
| Dengue serology: NS1 antigen | | IgG : | | | | IgM: | | |
| Brucella/ HIV/ HBsAg/ HCV | | | | | | | | |

Other relevant investigations

**SEPSIS:**YES /NO

# APACHE II SCORE

1. Age points-

| Age, Years | Score |
|---|---|
| <45 | 0 |
| 45–54 | 2 |
| 55–64 | 3 |
| 65–74 | 5 |
| 75 | 6 |
| | |

2.Chronic health points-

None 0

If patient is admitted after elective surgery 2

If patient is admitted after emergency surgery or for reason other than after elective surgery 5

3. Glasgow coma score-

**ACUTE PHYSIOLOGY SCORE**

| **Score** | **4** | **3** | **2** | **1** | **0** | **1** | **2** | **3** | **4** |
|---|---|---|---|---|---|---|---|---|---|
| 1)Rectal temperature, °C | 41 | 39.0–40.9 | | 38.5–38.9 | 36.0–38.4 | 34.0–35.9 | 32.0–33.9 | 30.0–31.9 | 29.9 |
| 2)Mean blood pressure, mmHg | 160 | 130–159 | 110–129 | | 70–109 | | 50–69 | | 49 |
| 3)Heart rate | 180 | 140–179 | 110–139 | | 70–109 | | 55–69 | 40–54 | 39 |
| 4)Respiratory rate | 50 | 35–49 | | 25–34 | 12–24 | 10–11 | 6–9 | | 5 |
| 5Arterial pH | 7.70 | 7.60–7.69 | | 7.50–7.59 | 7.33–7.49 | | 7.25–7.32 | 7.15–7.24 | <7.15 |
| Oxygenation | | | | | | | | | |
| If $FI_{O2}$> 0.5, use (A – a) $D_{O2}$ | 500 | 350–499 | 200–349 | | <200 | | | | |
| If $FI_{O2}$<0.5, use $Pa_{O2}$ | | | | | >70 | 61–70 | | 55–60 | <55 |
| Serum sodium, meq/L | 180 | 160–179 | 155–159 | 150–154 | 130–149 | | 120–129 | 111–119 | 110 |
| Serum potassium, meq/L | 7.0 | 6.0–6.9 | | 5.5–5.9 | 3.5–5.4 | 3.0–3.4 | 2.5–2.9 | | <2.5 |
| Serum creatinine, mg/dL | 3.5 | 2.0–3.4 | 1.5–1.9 | | 0.6–1.4 | | <0.6 | | |
| Hematocrit | 60 | | 50–59.9 | 46–49.9 | 30–45.9 | | 20–29.9 | | <20 |
| WBC count, $10^3$/mL | 40 | | 20–39.9 | 15–19.9 | 3–14.9 | | 1–2.9 | | <1 |

SCORE=

APACHE II SCORE=acute physiology score + age points+ chronic health points + Glasgow coma scale

TOTAL SCORE=

APACHE III SCORE=

SOFA SCORE

| | 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| Respiratory Pao2:fio2 ratio (mm hg) | >400 | <400 | <300 | <200 | <100 |
| Renal Creatinine (mg/dl)or urine output (Ml/d) | <1.2 | 1.2-1.9 | 2.0-3.4 | 3.5-4.9 urine output <500ml/day | >5 urine output <20ml/day |
| Hepatic bilirubin (mg/dl) | <1.2 | 1.2-1.9 | 2.0-59 | 6.0-11.9 | >12 |
| Cardiovascular mean arterial pressure (mmhg) | MAP>70mm hg | MAP<70mmhg | *Dopamine <5 or dobutamine any dose | *Dopamine <5 or epinephrine <0.1 or nor epinephrine <0.1 | *Dopamine <5 epinephrine >0.1 or norepinephrine >0.1 |
| Haematological platelet count ($x10^3/mm^3$) | >150 | <150 | <100 | <50 | <20 |
| Neurological Glasgow coma score | 15 | 13-14 | 10-12 | 6-9 | <6 |

*adrenergic agents administered for atleast 1 hr

TOTAL SCORE =

qSOFA score

| | NO | YES |
|---|---|---|
| Altered mental status GCS <15 | | |
| Respiratory rate >22 | | |
| Systolic bp<100 | | |

TOTAL SCORE =

## COURSE IN HOSPITAL

| | | | | |
|---|---|---|---|---|
| Intubation: Y/N | | | | |
| Mechanical ventilation: Y/ N | | duration: | Days | |
| | | | | |
| Duration of stay in hospital: | days | Duration of ICU stay: | | days |
| ICU free days: | | | | |

**OUTCOME:** Improved /Expired

# ANNEXURE:III – SCORING SYSTEM

Table 1 The Sequential Organ Failure Assessment (SOFA) score[a]

| Organ system | SOFA score | | | | |
|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 |
| Respiratory, $PO_2/FiO_2$, mmHg (kPa) | ≥400 (53.3) | <400 (53.3) | <300 (40) | <200 (26.7) with respiratory support | <100 (13.3) with respiratory |
| Coagulation, Platelets, $\times 10^3/mm^3$ | ≥150 | <150 | <100 | <50 | <20 |
| Liver, Bilirubin, mg/dL | <1.2 | 1.2–1.9 | 2.0–5.9 | 6.0–11.9 | >12.0 |
| Cardiovascular | MAP ≥70 mmHg | MAP <70 mmHg | Dopamine <5 or dobutamine (any dose)[b] | Dopamine 5.1–15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b] | Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b] |
| Central nervous system, Glasgow Coma Scale | 15 | 13–14 | 10–12 | 6–9 | <6 |
| Renal, Creatinine, mg/dL. Urine output, mL/d | <1.2 | 1.2–1.9 | 2.0–3.4 | 3.5–4.9<br><500 | >5.0<br><200 |

[a], adapted from Vincent *et al*. (7); [b], Catecholamine doses are given as μg/kg/min for at least 1 hour. $FiO_2$, fraction of inspired oxygen; MAP, mean arterial pressure; $PO_2$, partial pressure of oxygen.

| APACHE II score | N | Alive | Dead | Mortality rate |
|---|---|---|---|---|
| 0–5 | 204 | 198 | 6 | 2·94% |
| 6–10 | 117 | 89 | 28 | 23·93% |
| 11–15 | 125 | 79 | 46 | 36·8% |
| 16–20 | 119 | 61 | 58 | 48·74% |
| 21–25 | 91 | 22 | 69 | 75·82% |
| 26–30 | 47 | 9 | 38 | 80·85% |
| 31–35 | 34 | 4 | 30 | 88·24% |
| 36–40 | 10 | 5 | 5 | 50% |
| 41–45 | 7 | 0 | 7 | 100% |
| >46 | 2 | 0 | 2 | 100% |

| Variables | Scores | Variables | Scores |
|---|---|---|---|
| Heart Rate | | Ht (%) | |
| ≤ 54 | 5 | < 0 | 9 |
| 55-69 | 1 | 20-29.9 | 2 |
| 70-109 | 0 | 30-45.9 | 0 |
| 110-139 | 1 | 46-59.9 | 2 |
| ≥ 140 | 5 | > 60 | 9 |
| Respiratory Rate | | WBC( × $10^3/mm^3$) | |
| ≤ 5 | 10 | < 2.9 | 3 |
| 11-Jun | 2 | 3-19.9 | 0 |
| 24-Dec | 0 | ≥ 20 | 3 |
| 25-34 | 2 | GCS | |
| 35-49 | 6 | 3 | 12 |
| ≥ 50 | 10 | 4 | 11 |
| If $FIO_2 \geq 0.5$:(A-a)$O_2$ (mmHg) | | 5 | 10 |
| < 00 | 0 | 6 | 9 |
| 200-349 | 2 | 7 | 8 |
| ≥ 350 | 3 | 8 | 7 |
| If $FIO_2 < 0.5$:(A-a)$O_2$ (mmHg) | | 9 | 6 |
| <60 | 7 | 10 | 5 |
| ≥ 61 | 0 | 11 | 4 |
| PH | | 12 | 3 |
| < 7.24 | 4 | 13 | 2 |
| 7.25-7.32 | 0 | 14 | 1 |
| 7.33-7.59 | 2 | 15 | 0 |
| ≥ 7.6 | 4 | Chronic Organ Insufficiency immune-compromised and: | |
| Age | | | |
| ≤ 44 | 0 | Non-Operative | 3 |
| 45-74 | 2 | Emergency-postoperative | 3 |
| ≥ 75 | 6 | Elective-Postoperative | 2 |
| Total Score Sum of scores | | | |

*Ht: Hematocrit, WBC: White blood cells count, GCS: Glasgow coma score

**Table 2** Quick Sequential Organ Failure Assessment (SOFA) score

| qSOFA (Quick SOFA) Criteria | Points |
|---|---|
| Respiratory rate ≥22/min | 1 |
| Change in mental status | 1 |
| Systolic blood pressure ≤100 mmHg | 1 |

# ANNEXURE:IV – MASTERSHEET

| S.no | IpNo | Age | Gender | Rural urban | Etiology | Fever | Sore throat | Body ache | Head ache | Cough | Vomiting | Loose motions | Alteredmentation | Pain abdomen | DM Type 2 | Hyper tension | CAD | CVA | COPD | Asthma | HIV | Liver disease | Smoking | Alcohol | Tobacco chewing | Pulse rate bpm | Systolic blood pressure mmHg | Respiratory rate cpm | Pallor | Icterus | Cyanosis | Pedal edema |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 838575 | 47 | Male | Rural | dengue | Yes | No | Yes | Yes | No | No | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | <90 | <90 | >20 | No | No | No | No |
| 2 | 802988 | 57 | Male | Urban | dengue | Yes | No | Yes | Yes | No | Yes | No | No | No | No | Yes | No | No | No | No | No | No | No | No | Yes | >90 | <90 | >20 | No | No | No | No |
| 3 | 819907 3 | 55 | Male | Urban | dengue | Yes | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | Yes | Yes | Yes | >90 | <90 | >20 | No | No | No | No |
| 4 | 814803 | 73 | Male | Rural | dengue | Yes | No | No | No | No | No | No | No | Yes | Yes | Yes | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | No | No | No | No |
| 5 | 793162 | 53 | Male | Urban | dengue | Yes | No | Yes | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | Yes | No | Yes | >90 | >90 | >20 | No | No | No | No |
| 6 | 788824 | 46 | Female | Rural | leptospirosis | Yes | No | Yes | No | No | Yes | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | Yes | Yes | No | No |
| 7 | 797283 | 36 | Male | Urban | Chronic liver disease sepsis | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | Yes | No | Yes | Yes | >90 | <90 | >20 | No | No | No | Yes |
| 8 | 823274 | 32 | Male | Rural | snake bite | Yes | Yes | No | No | No | No | No | No | Yes | No | No | No | No | No | No | No | No | Yes | No | No | >90 | <90 | >20 | No | No | No | No |
| 9 | 804762 | 49 | Female | Urban | leptospirosis | Yes | No | Yes | No | Yes | No | Yes | No | No | No | Yes | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | Yes | Yes | No | No |
| 10 | 825166 | 28 | Male | Rural | acute fulminant viral hepatitis | No | No | No | No | No | Yes | No | Yes | Yes | No | No | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | No | Yes | No | No |
| 11 | 824408 | 25 | Female | Urban | sepsis-intrauterine death | No | No | No | No | No | Yes | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | >90 | <90 | >20 | No | No | No | Yes |
| 12 | 825166 | 48 | Male | Urban | Chronic liver disease sepsis | No | No | No | No | No | No | No | Yes | No | No | No | No | No | No | No | No | Yes | No | No | No | >90 | >90 | >20 | No | Yes | No | Yes |
| 13 | 817794 5 | 48 | Male | Urban | Chronic liver disease sepsis | No | No | No | No | Yes | No | No | No | Yes | No | No | No | No | No | No | No | Yes | No | Yes | No | >90 | >90 | >20 | Yes | No | No | Yes |
| 14 | 801773 | 38 | Male | Rural | abdominal sepsis | No | Yes | No | No | No | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | Yes | >90 | <90 | >20 | No | No | No | No |
| 15 | 812291 | 50 | Female | Rural | abdominal sepsis | No | Yes | No | No | No | Yes | Yes | No | Yes | Yes | No | No | No | No | No | No | No | No | No | No | >90 | <90 | >20 | Yes | No | No | No |
| 16 | 796576 | 40 | Male | Rural | Chronic liver disease sepsis | No | No | No | No | No | No | No | Yes | Yes | No | No | No | No | No | No | No | Yes | No | Yes | Yes | >90 | >90 | >20 | Yes | Yes | No | Yes |
| 17 | 797417 | 42 | Male | Urban | pneumonia | No | Yes | No | No | Yes | No | No | No | No | No | No | No | No | No | No | Yes | No | No | No | No | >90 | <90 | >20 | No | No | No | No |
| 1 | 81774 | 3 | Male | Rur | scrub typhus | Y | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | Y | N | >9 | >9 | >2 | N | N | N | N |

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| 8 | 7 | 2 | | al | | es | o | o | o | o | o | o | o | o | o | o | o | o | o | o | o | o | o | es | o | 0 | 0 | 0 | o | o | o | o |
| 19 | 803384 | 18 | Female | Rural | pneumonia | Yes | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | >90 | <90 | >20 | Yes | No | No | No |
| 20 | 827019 | 40 | Female | Rural | snake bite | No | No | No | No | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | >90 | <90 | >20 | No | No | No | No |
| 21 | 830587 | 24 | Female | Rural | sepsis-intrauterine death | No | No | No | No | No | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | >90 | <90 | >20 | Yes | No | No | Yes |
| 22 | 819535 | 40 | Male | Rural | pancreatitis | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | Yes | Yes | No | >90 | <90 | >20 | Yes | No | No | No |
| 23 | 848260 | 59 | Male | Rural | Urinary tract infection | Yes | No | No | No | No | No | No | No | Yes | Yes | Yes | No | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | No | No | No | Yes |
| 24 | 801630 | 45 | Female | Rural | pneumonia | Yes | No | No | No | Yes | No | No | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | >90 | <90 | >20 | Yes | No | No | No |
| 25 | 809044 | 40 | Male | Rural | abdominal sepsis | Yes | No | No | No | No | No | Yes | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | >90 | <90 | >20 | No | No | No | No |
| 26 | 802445 | 64 | Male | Rural | undiagnosed fever | Yes | No | No | No | No | No | No | No | No | Yes | Yes | No | No | No | No | No | No | Yes | Yes | No | No | >90 | <90 | >20 | No | No | No | No |
| 27 | 832168 | 40 | Male | Rural | h1n1 | Yes | Yes | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | Yes | No | Yes | No | >90 | >90 | >20 | No | No | No | No |
| 28 | 794497 | 22 | Female | Rural | pneumonia | Yes | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | No | No | No | No |
| 29 | 831721 | 31 | Male | Rural | pneumonia | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | Yes | No | No | No | No | >90 | >90 | >20 | No | No | No | No |
| 30 | 790525 | 60 | Male | Rural | Urinary tract infection | Yes | No | No | No | No | No | No | No | Yes | No | Yes | No | No | No | No | No | No | No | Yes | Yes | Yes | <90 | <90 | >20 | No | No | No | No |
| 31 | 785495 | 33 | Female | Urban | h1n1 | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | >90 | <90 | >20 | No | No | No | No |
| 32 | 816336 | 40 | Male | Rural | h1n1 | Yes | No | No | No | Yes | No | Yes | No | No | No | No | No | No | No | No | No | No | No | Yes | No | Yes | >90 | >90 | >20 | No | No | No | No |
| 33 | 824648 | 77 | Male | Urban | pneumonia | Yes | No | No | No | Yes | No | No | No | No | Yes | Yes | No | Yes | No | No | No | No | No | No | No | No | >90 | >90 | >20 | Yes | No | No | No |
| 34 | 788826 | 55 | Female | Urban | pneumonia | Yes | No | No | No | Yes | No | No | No | No | Yes | Yes | No | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | No | No | No | No |
| 35 | 811603 | 34 | Male | Rural | pneumonia | Yes | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | <90 | >90 | >20 | No | No | No | No |
| 36 | 829696 | 58 | Male | Urban | pneumonia | Yes | No | No | No | No | No | No | No | Yes | No | No | Yes | No | No | No | No | No | No | No | Yes | No | >90 | >90 | >20 | Yes | No | No | No |
| 37 | 793721 | 48 | Male | Urban | pneumonia | Yes | No | Yes | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | Yes | Yes | No | >90 | >90 | >20 | No | No | No | Yes |
| 38 | 790606 | 61 | Male | Urban | malaria | Yes | Yes | No | No | No | No | No | Yes | No | No | Yes | No | No | Yes | No | No | No | No | Yes | No | No | >90 | >90 | >20 | No | No | No | No |
| 39 | 846190 | 25 | Male | Rural | Organophosphorus poisoning | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | >90 | <90 | >20 | No | No | No | No |
| 40 | 828927 | 45 | Female | Rural | paraquat poisoning | No | No | No | No | No | No | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | >90 | <90 | >20 | No | No | No | No |

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 41 | 829374 | 32 | Female | Rural | pneumonia | Yes | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | <90 | >90 | >20 | No | No | No | No |
| 42 | 814840 | 21 | Male | Urban | h1n1 | No | No | Yes | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | <90 | >90 | >20 | No | No | No | No |
| 43 | 821148 | 23 | Male | Urban | pancreatitis | No | No | No | No | No | Yes | No | No | Yes | No | No | No | No | No | No | No | No | No | Yes | No | No | >90 | <90 | >20 | No | No | No | No |
| 44 | 785337 | 35 | Female | Urban | pneumonia | Yes | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | >90 | <90 | >20 | No | No | No | No |
| 45 | 818613 | 23 | Female | Urban | paraquat poisoning | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | Yes | No | No | No |
| 46 | 794563 | 30 | Female | Urban | Organophosphorus poisoning | No | No | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | No | No | No | No |
| 47 | 832310 | 40 | Female | Urban | pancreatitis | No | No | No | No | No | Yes | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | >90 | <90 | >20 | Yes | No | No | Yes |
| 48 | 806749 | 70 | Female | Urban | Organophosphorus poisoning | No | No | No | No | No | No | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | >90 | <90 | >20 | No | No | No | No |
| 49 | 807394 | 34 | Male | Rural | h1n1 | Yes | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | Yes | Yes | Yes | >90 | >90 | >20 | Yes | No | No | No |
| 50 | 807023 | 32 | Female | Urban | Organophosphorus poisoning | No | No | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | Yes | No | No | No | >90 | >90 | >20 | No | No | No | No |
| 51 | 841174 | 18 | Female | Rural | undiagnosed fever | Yes | No | No | No | Yes | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | Yes | No | No | No |
| 52 | 797200 | 30 | Male | Rural | pneumonia | No | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | Yes | >90 | <90 | >20 | No | No | No | No |
| 53 | 801630 | 64 | Female | Urban | pneumonia | No | No | No | No | Yes | No | No | No | No | Yes | Yes | No | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | No | No | No | No |
| 54 | 794497 | 30 | Female | Urban | undiagnosed fever | Yes | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | No | No | No | No |
| 55 | 802713 | 35 | Female | Rural | Organophosphorus poisoning | No | No | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | No | No | No | No |
| 56 | 795927 | 30 | Male | Rural | pneumonia | Yes | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | Yes | No | >90 | >90 | >20 | No | No | No | No |
| 57 | 821121 | 48 | Female | Rural | pneumonia | No | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | Yes | No | No | No |
| 58 | 805492 | 43 | Female | Urban | undiagnosed fever | No | Yes | No | No | No | Yes | No | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | No | No | No | No |
| 59 | 806791 | 66 | Female | Rural | Organophosphorus poisoning | No | No | No | No | No | No | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | >90 | >90 | >20 | Yes | No | No | No |
| 60 | 788591 | 22 | Male | Urban | pneumonia | Yes | No | No | No | Yes | No | No | No | No | No | No | No | No | No | No | No | No | No | Yes | No | No | >90 | >90 | >20 | Yes | No | No | No |

| Petechiae | Hbgdl | TCcmm | Platelets | Bilirubin mgdl | Albumin mgdl | Creatinine mgdl | sputum c/s | Urine c/s | Blood c/s | Ph | pao 2/fio 2 | Urine culture | Endotracheal tubec/s | Dengue serology | Dengue serology (NS1 antigen | HBsAg | APACHEII score | APACHEIII score | SOFA score | Intubation | sepsis | q SOFA | Duration of mechanical ventilation Days | Duration of stay in hospital Days | Duration of ICU stay Days | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No | 11.0 | 4,200.00 | 12,000.00 | 0.54 | 2 | 2.00 | | | | 1 | 75.0 | No | | Positive | Positive | 2 | 18 | 130 | 12 | No | Yes | 3 | 3 | 3 | 3 | Expired |
| Yes | 15.0 | 6,000.00 | 13,000.00 | 2.10 | | 2.00 | | | | 1 | 86.0 | No | | | Positive | 2 | 26 | 118 | 17 | No | Yes | 2 | 3 | 3 | 3 | Expired |
| No | 15.0 | 10,400.00 | 30,000.00 | 0.80 | | 1.60 | | | | 2 | 108.0 | No | | Positive | Positive | 2 | 15 | 26 | 9 | No | Yes | 2 | 3 | 10 | 5 | Improved |
| Yes | 12.0 | 3,000.00 | 40,000.00 | 1.00 | | 1.00 | | | | 1 | 118.0 | No | | Positive | | 2 | 19 | 58 | 6 | No | Yes | 1 | 8 | 14 | 10 | Improved |
| No | 14.0 | 15,000.00 | 50,000.00 | 0.70 | 2 | 0.80 | | | | 1 | 120.0 | No | | Positive | Positive | 2 | 13 | 60 | 5 | No | No | 1 | 3 | 10 | 4 | Improved |
| Yes | 11.0 | 18,000.00 | 50,000.00 | 5.20 | | 2.40 | | | | 1 | 57.0 | No | | | | 2 | 21 | 102 | 12 | No | Yes | 1 | 10 | 10 | 10 | Expired |
| No | 14.0 | 2,800.00 | 60,000.00 | 4.20 | | 2.00 | | | staphylococcus | 1 | 77.1 | No | | | | 2 | 26 | 84 | 12 | No | Yes | 2 | 6 | 12 | 7 | Expired |
| No | 12.0 | 3,300.00 | 60,000.00 | 0.80 | 2 | 1.70 | | | | 2 | 118.0 | No | | | | 2 | 19 | 56 | 8 | No | No | 2 | 3 | 8 | 5 | Improved |
| No | 11.0 | 4,000.00 | 60,000.00 | 2.20 | | 0.90 | | | | 2 | 180.0 | No | | | | 2 | 7 | 32 | 7 | No | Yes | 1 | 3 | 5 | 3 | Improved |
| No | 10.0 | 16,000.00 | 60,000.00 | 6.80 | | 1.60 | | | | 1 | 60.0 | No | | | | 2 | 18 | 72 | 11 | No | Yes | 2 | 10 | 10 | 10 | Expired |
| No | 10.0 | 16,000.00 | 60,000.00 | 1.80 | | 2.20 | | pseudomonas | MRSA | 1 | 53.8 | Yes | | | | 2 | 24 | 93 | 12 | Yes | Yes | 2 | 3 | 5 | 5 | Expired |
| No | 14.0 | 17,000.00 | 60,000.00 | 1.20 | | 0.80 | | | enterococcus | 1 | 77.8 | No | | | | 2 | 11 | 60 | 7 | Yes | Yes | 3 | 4 | 10 | 6 | Improved |
| No | 7.6 | 32,000.00 | 60,000.00 | 4.20 | | 0.87 | | | pseudomonas | 1 | 102.2 | No | | | | 2 | 17 | 80 | 9 | No | Yes | 2 | 8 | 12 | 12 | Expired |
| No | 11.0 | 32,000.00 | 80,000.00 | 2.20 | | 1.00 | | | e coli | 1 | 49.8 | No | | | | 2 | 27 | 102 | 12 | Yes | Yes | 2 | 5 | 5 | 5 | Expired |
| No | 11.0 | 2,300.00 | 90,000.00 | 0.80 | | 1.20 | | | staphylococcus | 1 | 60.0 | No | | | | 2 | 23 | 81 | 11 | Yes | Yes | 2 | 6 | 6 | 6 | Expired |
| No | 9.0 | 10,500.00 | 90,000.00 | 3.20 | | 1.70 | | | | 1 | 116.0 | No | | | | 2 | 19 | 56 | 6 | No | Yes | 2 | 5 | 10 | 6 | Improved |
| No | 13.1 | 5,600.00 | 1,00,000.00 | 0.69 | | 1.03 | | | klebsiella | 1 | 109.0 | No | klebsiella | | | 2 | 22 | 85 | 8 | Yes | Yes | 2 | 14 | 17 | 17 | Expired |
| No | 11.0 | 8,600.00 | 1,00,000.00 | 2.80 | | 2.00 | | | | 2 | 77.6 | No | | | | 2 | 10 | 82 | 9 | No | Yes | 1 | 7 | 16 | 10 | Improved |
| No | 9.8 | 13,300.00 | 1,00,000.00 | 1.60 | | 1.00 | | | | 2 | 158.0 | No | | | | 2 | 15 | 26 | 5 | No | Yes | 2 | 4 | 7 | 5 | Improved |
| No | 11.0 | 15,000.00 | 1,00,000.00 | 2.60 | 2 | 1.00 | | | | 2 | 180.0 | No | | | | 2 | 16 | 64 | 9 | No | No | 2 | 2 | 6 | 5 | Improved |
| No | 9.0 | 21,000.00 | 1,00,000.00 | 2.60 | | 2.00 | | e coli | e coli | 1 | 112.5 | Yes | | | | 2 | 29 | 56 | 8 | No | Yes | 2 | 5 | 16 | 10 | Expired |
| No | 8.0 | 26,000.00 | 1,00,000.00 | 4.20 | 2 | 1.00 | | | | 2 | 65.3 | No | | | | 2 | 27 | 101 | 9 | No | Yes | 3 | 8 | 8 | 8 | Expired |
| No | 11.0 | 17,000.00 | 1,10,000.00 | 0.30 | | 1.20 | | e coli | | 1 | 70.0 | Yes | | | | 2 | 22 | 35 | 5 | No | Yes | 1 | 4 | 10 | 8 | Improved |
| No | 11.0 | 13,000.00 | 1,20,000.00 | 2.40 | | 1.00 | | | klebsiella | 1 | 47.9 | No | | | | 2 | 11 | 96 | 10 | Yes | Yes | 1 | 4 | 5 | 5 | Expired |
| No | 11.0 | 21,000.00 | 1,20,000.00 | 1.00 | 2 | 1.00 | | | staphylococcus | 2 | 140.0 | No | | | | 2 | 6 | 40 | 7 | No | Yes | 2 | 4 | 12 | 7 | Improved |
| No | 11.0 | 29,000.00 | 1,20,000.00 | 1.00 | | 1.30 | | | staphylococcus | 1 | 59.2 | No | | | | 2 | 35 | 96 | 8 | Yes | Yes | 2 | 10 | 10 | 10 | Expired |
| No | 14.0 | 3,500.00 | 1,30,000.00 | 2.00 | | 1.20 | | | | 1 | 58.5 | No | | | | 2 | 15 | 98 | 8 | No | Yes | 1 | 3 | 3 | 3 | Expired |
| No | 12.0 | 14,000.00 | 1,30,000.00 | 1.40 | | 0.80 | | | | 2 | 92.0 | No | | | | 2 | 12 | 38 | 6 | No | Yes | 1 | 5 | 16 | 8 | Improved |
| No | 12.8 | 18,000.00 | 1,30,000.00 | 2.20 | | 0.90 | | | | 2 | 60.0 | No | | | | 2 | 13 | 112 | 8 | No | Yes | 1 | 4 | 4 | 4 | Expired |
| No | 13.0 | 19,000.00 | 1,30,000.00 | 2.30 | | 1.30 | | | | 2 | 60.0 | No | | | | 2 | 25 | 84 | 11 | No | Yes | 2 | 4 | 6 | 6 | Expired |

| | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No | 11.0 | 10,800.00 | 1,40,000.00 | 1.00 | 2 | 1.80 | | | | 2 | 64.6 | No | | | | 2 | 15 | 80 | 9 | Yes | Yes | 2 | 5 | 5 | 5 | Expired |
| No | 11.0 | 20,000.00 | 1,40,000.00 | 1.40 | | 2.30 | | | | 2 | 74.0 | No | | | | 2 | 28 | 98 | 9 | Yes | Yes | 1 | 2 | 6 | 6 | Expired |
| No | 10.0 | 9,000.00 | 1,40,000.00 | 0.40 | | 2.00 | klebsiella | | MRSA | 1 | 98.2 | No | | | | 2 | 25 | 112 | 8 | Yes | Yes | 1 | 12 | 12 | 12 | Expired |
| No | 11.0 | 9,800.00 | 1,50,000.00 | 1.00 | | 1.70 | | | | 1 | 74.0 | No | | | | 2 | 8 | 101 | 7 | No | Yes | 1 | 3 | 3 | 3 | Expired |
| No | 14.0 | 11,000.00 | 1,50,000.00 | 0.40 | 2 | 1.00 | | | | 2 | 110.0 | No | | | | 1 | 12 | 46 | 3 | No | No | 1 | 2 | 6 | 4 | Improved |
| No | 7.8 | 12,000.00 | 1,50,000.00 | 0.90 | 2 | 0.70 | | | staphylococcus | 1 | 68.7 | No | acinetobacter | | | 2 | 19 | 67 | 4 | Yes | No | 1 | 4 | 12 | 7 | Improved |
| No | 14.0 | 14,000.00 | 1,50,000.00 | 1.60 | | 2.00 | | | | 1 | 10.2 | No | | | | 2 | 21 | 93 | 8 | No | Yes | 1 | 5 | 6 | 6 | Expired |
| No | 15.0 | 14,500.00 | 1,50,000.00 | 2.60 | | 2.00 | | | | 1 | 108.0 | No | | | | 2 | 15 | 26 | 8 | No | Yes | 2 | 5 | 5 | 5 | Improved |
| No | 11.0 | 17,000.00 | 1,50,000.00 | 0.40 | 2 | 0.60 | | | | 2 | 162.0 | No | | | | 2 | 10 | 80 | 6 | No | No | 2 | 2 | 4 | 4 | Expired |
| No | 12.0 | 11,000.00 | 1,60,000.00 | 1.20 | 2 | 3.00 | | | | 1 | 47.9 | No | | | | 2 | 20 | 139 | 9 | No | Yes | 2 | 2 | 3 | 3 | Expired |
| No | 12.0 | 11,800.00 | 1,60,000.00 | 0.50 | | 0.80 | | | | 2 | 112.0 | No | pseudomonas | | | 2 | 11 | 46 | 3 | No | No | 1 | 3 | 10 | 5 | Improved |
| No | 13.0 | 12,000.00 | 1,60,000.00 | 0.60 | | 0.70 | | | | 2 | 149.0 | No | | | | 2 | 2 | 39 | 3 | No | Yes | 1 | 7 | 10 | 8 | Improved |
| No | 14.0 | 21,000.00 | 1,60,000.00 | 3.40 | | 1.90 | | | | 1 | 72.0 | No | | | | 2 | 29 | 43 | 8 | Yes | Yes | 2 | 8 | 18 | 12 | Improved |
| No | 12.4 | 24,000.00 | 1,60,000.00 | 0.50 | | 0.80 | | | | 2 | 164.0 | No | | | | 2 | 10 | 69 | 6 | No | Yes | 2 | 5 | 12 | 6 | Improved |
| No | 10.8 | 5,000.00 | 1,70,000.00 | 0.70 | 2 | 2.60 | | | | 2 | 54.3 | No | | | | 2 | 10 | 88 | 6 | No | No | 1 | 3 | 6 | 6 | Expired |
| No | 12.0 | 12,400.00 | 1,70,000.00 | 0.60 | 2 | 0.70 | | | | 2 | 190.0 | No | | | | 2 | 13 | 94 | 3 | No | No | 2 | 6 | 10 | 10 | Expired |
| No | 11.0 | 16,400.00 | 1,70,000.00 | 2.20 | | 1.00 | | | | 1 | 120.0 | No | | | | 2 | 19 | 61 | 6 | No | No | 2 | 3 | 11 | 6 | Improved |
| No | 10.0 | 27,000.00 | 1,70,000.00 | 2.20 | 2 | 2.60 | | | | 2 | 158.0 | No | | | | 2 | 13 | 97 | 10 | No | Yes | 2 | 6 | 6 | 6 | Expired |
| No | 8.0 | 3,000.00 | 1,80,000.00 | 2.40 | | 1.60 | | | | 1 | 77.4 | No | | | | 2 | 19 | 112 | 9 | No | Yes | 1 | 3 | 3 | 3 | Expired |
| No | 12.0 | 17,000.00 | 1,80,000.00 | 1.00 | 2 | 1.00 | | | | 1 | 156.2 | No | | | | 2 | 14 | 62 | 3 | Yes | No | 1 | 12 | 18 | 13 | Improved |
| No | 11.0 | 18,000.00 | 1,80,000.00 | 1.20 | | 0.80 | | | staphylococcus | 1 | 157.0 | No | | | | 2 | 14 | 44 | 4 | No | Yes | 1 | 2 | 9 | 5 | Improved |
| No | 14.0 | 9,800.00 | 2,00,000.00 | 1.80 | | 1.80 | | | | 1 | 140.0 | No | acinetobacter | | | 2 | 14 | 41 | 6 | No | Yes | 2 | 2 | 6 | 3 | Improved |
| No | 12.0 | 9,800.00 | 2,00,000.00 | 0.60 | | 0.90 | pseudomonas | enterobacter | | 1 | 47.5 | No | | | | 2 | 9 | 10 | 6 | Yes | Yes | 3 | 4 | 4 | 4 | Expired |
| No | 13.0 | 10,900.00 | 2,00,000.00 | 0.70 | 2 | 0.90 | | | | 1 | 68.8 | No | | | | 2 | 13 | 35 | 4 | Yes | No | 1 | 4 | 6 | 5 | Improved |
| No | 12.0 | 4,400.00 | 2,20,000.00 | 0.50 | 2 | 1.80 | | | | 1 | 130.0 | No | | | | 2 | 29 | 56 | 4 | Yes | No | 1 | 5 | 7 | 5 | Improved |
| No | 11.0 | 16,500.00 | 2,20,000.00 | 0.70 | 2 | 1.70 | | | | 1 | 100.6 | No | | | | 2 | 13 | 61 | 4 | No | No | 1 | 8 | 9 | 9 | Improved |
| No | 10.4 | 9,000.00 | 2,30,000.00 | 0.45 | | 0.60 | | | | 1 | 136.0 | No | | | | 2 | 5 | 54 | 3 | No | Yes | 1 | 4 | 6 | 2 | Improved |
| No | 13.0 | 19,000.00 | 2,30,000.00 | 0.90 | | 2.00 | | | | 2 | 140.0 | No | | | | 2 | 21 | 90 | 5 | Yes | Yes | 1 | 8 | 12 | 10 | Improved |
| No | 11.0 | 21,000.00 | 2,70,000.00 | 1.70 | 2 | 1.80 | | | | 1 | 75.0 | No | | | | 2 | 17 | 70 | 6 | Yes | No | 1 | 6 | 6 | 6 | Improved |
| No | 14.0 | 22,000.00 | 2,80,000.00 | 0.30 | | 0.60 | klebsiella | | | 2 | 121.0 | No | | | | 2 | 5 | 58 | 3 | No | Yes | 1 | 3 | 6 | 4 | Improved |