# "A CROSS SECTIONAL STUDY TO ESTIMATE THE PREVALENCE OF ACUTE KIDNEY INJURY AND IT'S CORRELATION WITH SEVERITY OF ILLNESS AMONG CRITICALLY ILL COVID 19 PATIENTS"

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**CHENNAI, TAMIL NADU**

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**GOVERNMENT STANLEY MEDICAL COLLEGE AND HOSPITAL**

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**MAY 2021**

# CERTIFICATE

This is to certify that this dissertation entitled **"A CROSS SECTIONAL STUDY TO ESTIMATE THE PREVALENCE OF ACUTE KIDNEY INJURY AND IT'S CORRELATION WITH SEVERITY OF ILLNESS AMONG CRITICALLY ILL COVID 19 PATIENTS"** presented here is the original work done by **Dr. KIRUTHIKA SUBRAMANIYAN** in the Department of General Medicine, Government Stanley Hospital,Stanley Medical College, Chennai-600001 in partial fulfillment of the University rules and regulations for the award of M.D DEGREE BRANCH-I (GENERAL MEDICINE) - under my direct supervision and guidance during the academic period from 2020-2021

**GUIDE**

**Prof. Dr. I.ROHINI MD**

Chief, Medical Unit-3,

Department of Medicine,

Stanley Medical College and Hospital,

Chennai – 1

**HOD**

**Prof. Dr. S.CHANDRASEKAR M.D.**,

Head of the Department,

Department of Medicine,

Stanley Medical College and Hospital,

Chennai- 1.

**PROF. DR. P. BALAJI MS, FRCS, PhD, FCLS**

DEAN

Government Stanley Medical College and Hospital

Chennai-600001

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I owe my thanks to almighty for successful completion of this study.

Signature of the candidate

Dr. KIRUTHIKA SUBRAMANIYAN

# DECLARATION

I, Dr. KIRUTHIKA SURAMANIYAN, solemnly declare that the dissertation titled **"A CROSS SECTIONAL STUDY TO ESTIMATE THE PREVALENCE OF ACUTE KIDNEY INJURY AND IT'S CORRELATION WITH SEVERITY OF ILLNESS AMONG CRITICALLY ILL COVID 19 PATIENTS"** is a bonafide work done by me at Government Stanley Hospital, Chennai during May 2020 to October 2020under the guidance and supervision of Prof.Dr.I.ROHINI, Professor of Medicine, Government Stanley Hospital, Chennai. I also declare that this bonafide work or a part of this work was not submitted by me or any other forward degree or diploma to any other university, board either in India or abroad. This dissertation is submitted to the Tamilnadu Dr. M.G.R Medical University, towards the partial fulfillment of requirement for the award of M.D. Degree (Branch – I) in General Medicine.

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**Date:**

**(Dr. KIRUTHIKA SUBRAMANIYAN)**

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# ABBREVIATION

| | |
|---|---|
| SARS CoV-2 | Severe Acute Respiratory Syndrome CoronaVirus -2 |
| WHO | World health organisation |
| SHT | Systemic hypertension |
| DM | Diabetes mellitus |
| CAD | Coronary artery disease |
| CKD | Chronic kidney disease |
| CVA | Cerebrovacular accident |
| AKI | acute kidney injury |
| CKD | chronic kidney disease |
| RRT | renal replacement therapy |
| COVID 19 | Coronavirus disease 2019 |
| ARDS | Acute respiratory distress syndrome |
| MERSCoV | Middle East respiratory syndrome- related coronavirus |
| ICU | Intensive care unit |
| NRM | Non-Rebreathing Mask |
| HFNO | High Flow Nasal Oxygen |
| NIV | Non-Invasive Ventilation |
| MV | Mechanical ventilation |
| CPAP | Continuous positive airway pressure |
| ACC | Acetyl coenzyme A carboxylase α |
| AMPKα | Adenosine monophosphate kinase α |

| | |
|---|---|
| HIF-1α | Hypoxia-inducible factor-1α |
| LDH | Lactic acid dehydrogenase |
| ER | endoplasmic reticulum |
| NGAL | neutrophil gelatinase-associated lipocalin |
| KIM-1 | kidney injury molecule-1 |
| TIMP-2 | tissue inhibitor of metalloproteinase-2 |
| TNF | tumor necrosis factor |
| IGFBP7 | insulin-like growth factor binding protein 7 |
| mTORC1 | mammalian target of rapamycin complex 1 |
| PDH | , pyruvate dehydrogenase |
| PGC-1α | peroxisome proliferator-activated receptor gamma coactivator-1α |
| PKM2 | pyruvate kinase isozyme M2 |
| Ang-1 | angiopoietin-1 |
| AUC | area under the receiver operating characteristic curve |
| CI | confidence interval |
| IGFBP7 | insulin-like growth factor-binding protein 7 |
| L-FABP | liver-type fatty acid binding protein; |
| OR | odds ratio |
| sTREM-1 | soluble triggering receptor expressed on myeloid cells 1 |
| TIMP-2 | tissue inhibitor of metalloproteinases-2 |
| VE | vascular endothelial. |

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# INTRODUCTION

The worldwide rapidly spreading coronavirus, Severe Acute Respiratory Syndrome CoronaVirus -2 (SARS CoV-2), originated in Wuhan, China in December 2019, has been declared pandemic by WHO on 11 March 2020(1).Though the new coronavirus has high infectivity and low fatality rate than SARS, patients with underlying disease such as diabetes mellitus, hypertension,coronary artery disease and chronic kidney disease are more likely to progress to severe disease(2). Relationship between Acute Kidney Injury and coronavirus had been identified previously in SARCoV and MERS CoV as 6.3% and 43% respectively(3).

Since the outbreak several studies established pulmonary complications like ARDS as the leading cause of ICU admission and associated with high mortality. Lately several studies focused SARS CoV-2 invasion of kidneys through various mechanisms.

In order to fully understand the impact of renal involvement, a retrospective study was undertaken, not only to evaluate the prevalence of AKI but also to access the severity in critically ill COVID 19 positive patients.

## AIM

To determine the prevalence and correlation of severity of illness of AKI in COVID positive patients admitted in the ICU.

## PRIMARY OBJECTIVE

To observe the prevalence of AKI in critically ill COVID positive patients.

## SECONDARY OBJECTIVE

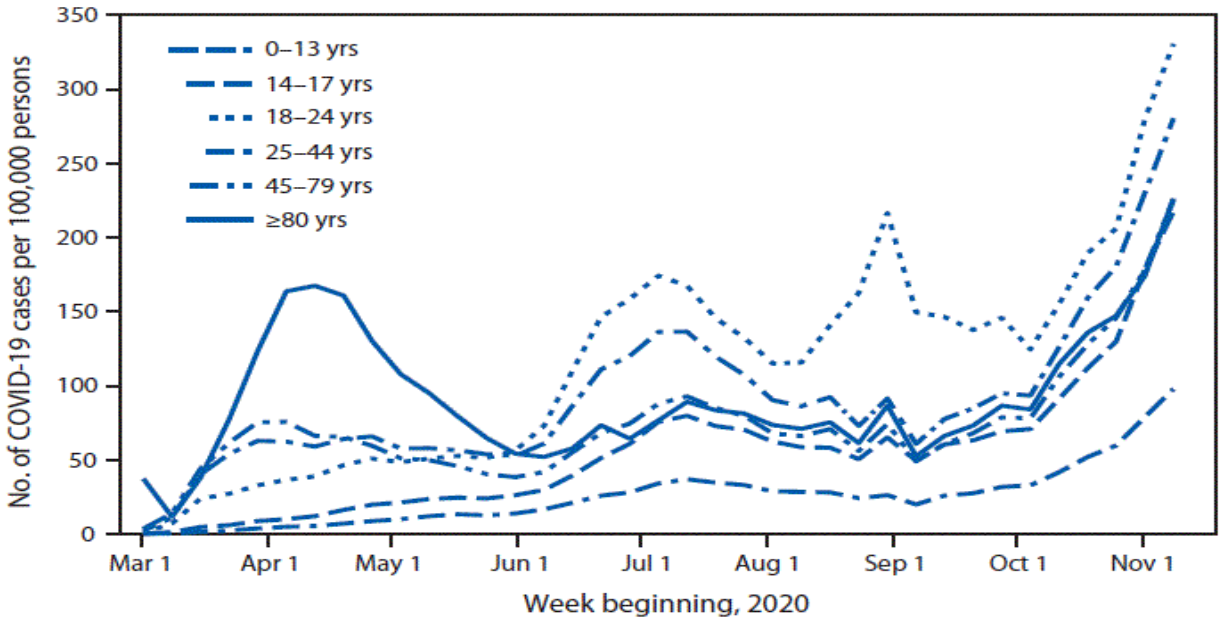
To determine the proportion of patients with AKI requiring nasal oxygen, Non Re-breathing Mask, High Flow Nasal Oxygen, Non-Invasive Ventilation and Invasive ventilation.

# REVIEW OF LITERATURE

## COVID-19 INFECTION:

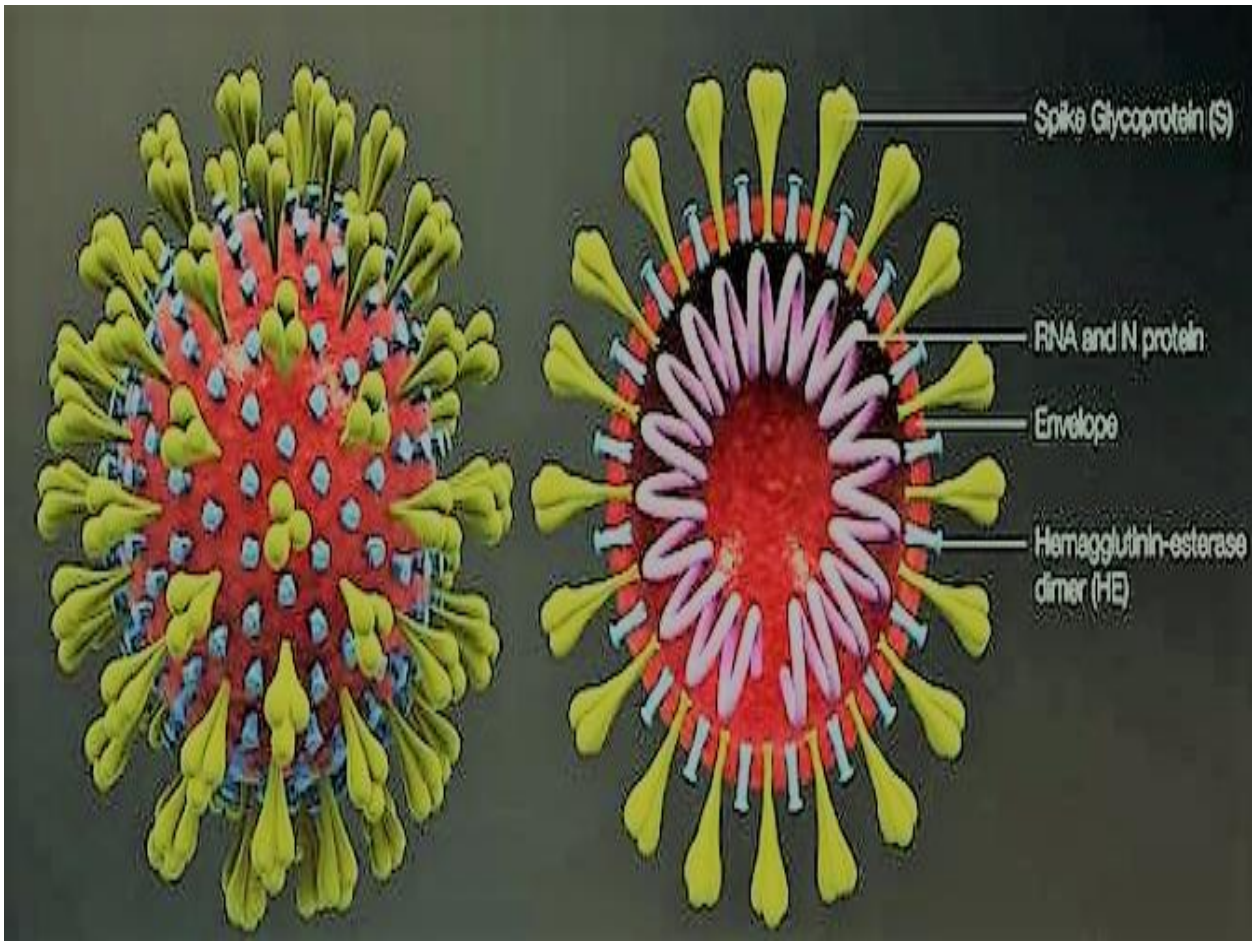
COVID-19 is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Virus is transmitted by human-to-human contact by droplet or aerosol. Coronaviruses constitute the subfamily Orthocoronavirinae(4), in the family Coronaviridae.They are enveloped viruses with a positive sense single stranded RNA genome, one of the largest among RNA viruses(5). They have club-shaped spikes that project from their surface,that create an image similar to solar corona, hence the etymology(6,7).

The first cases of COVID-19 in India were reported on 30 January 2020 in Kerala.Cases peaked during mid-September with over 90,000 cases reported per-day and eventually dropping to below 15,000 in January 2021(8).

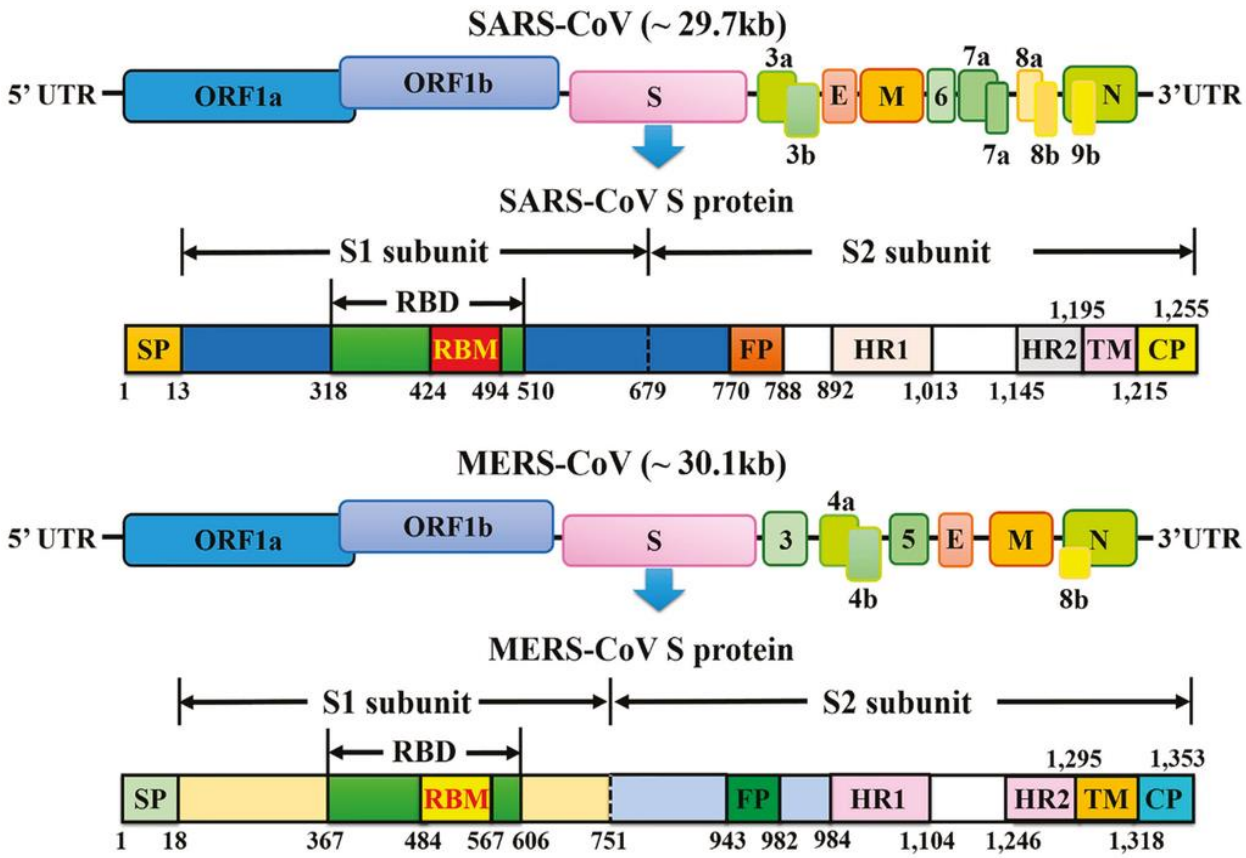



## COVID VIRUS:

Their envelope is made up of a lipid bilayer in which the membrane(M), envelope (E) and spike (S) proteins are anchored(9). These are the structural proteins. The E and M proteins are structural proteins that combined with the lipid bi-layer maintain the shape of the virus. In the human coronavirus NL63, M protein binds with the host cell and not the S protein(10).




## GENOME OF THE VIRUS:



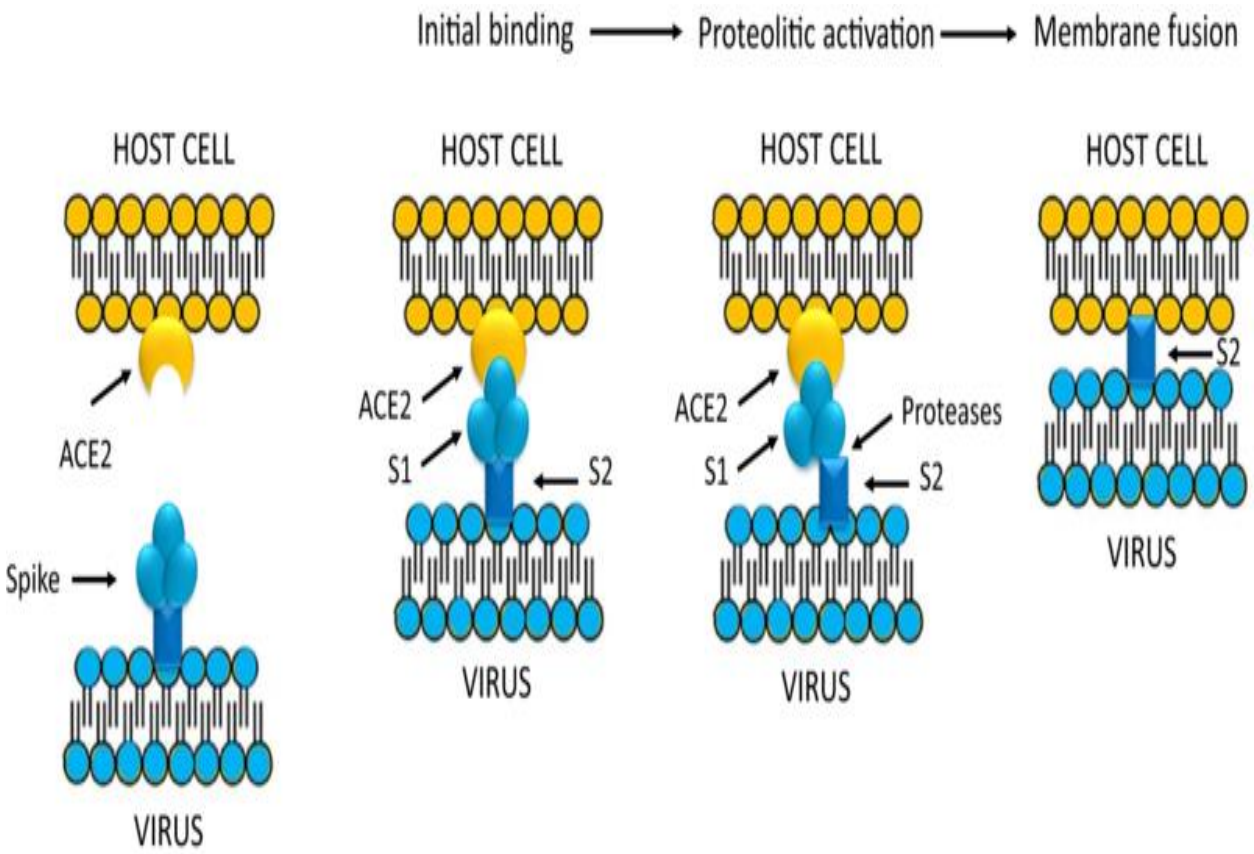

The genomic size for coronaviruses ranges from 26.4 to 31.7 kilobases(11). It is one of the largest among RNA viruses. It has a 5′ methylated cap and a 3′ poly-adenylated tail(12).The genome organization is 5′-leader-UTR-replicase (ORF1ab)-spike (S)-envelope (E)-membrane (M)-nucleocapsid (N)-3′UTR-poly (A) tail.

The open reading frames 1a and 1b, occupying the first two-thirds of the genome, encodes the replicase polyprotein (pp1ab)(13). The four major structural proteins: spike, envelope, membrane, and nucleocapsid are encoded by the later reading frames(14).

The reading frames for the accessory proteins are interspersed between these reading frames. Depending on the specific coronavirus. The number of accessory proteins and their function is unique(13).

## **REPLICATION CYCLE OF THE VIRUS**;

When the viral spike protein attaches to its complementary host cell receptor, infection begins and protease of the host, cleaves and activates the receptor-attached spike protein. Thus the virus enters the host cell by endocytosis  or direct fusion of the viral envelope(15).



1.With their S- protein, corona viruses bind on the surface molecules such as the metalloprotease-amino-peptidase N-alpha.

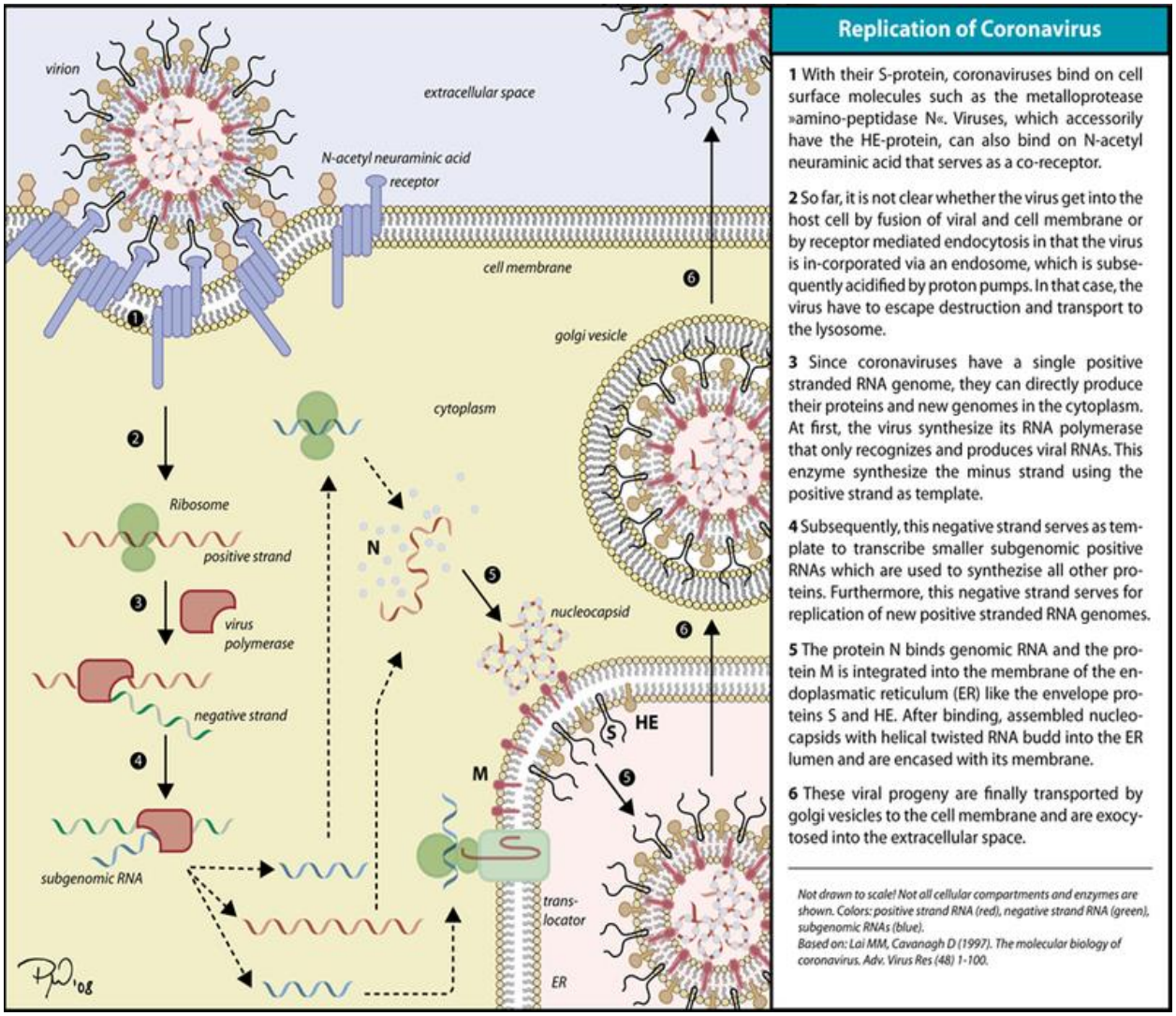
2.So far, it is not clear whether the virus get into the host cell by fusion of viral and cell membrane or by receptor mediated endocytosis in that the virus gets in corporate via a endosome, which is subsequently acidified by proton pumps. In that case, the virus has to escape destruction and transport to the lysosome.

3.At first, the virus synthesizes its RNA polymerase that only recognizes and produces viral RNAs. This enzyme synthesizes the minus strand using the positive strand as template.

4.Subsequently, this negative strand serves as template to transcribe smaller subgenomic positive RNAs which are used to synthesize all other proteins. This negative strand serves for replication of new positive stranded RNA genomes.

5.The protein N binds genomic RNA and the protein M is integrated into the membrane of the ER like the envelope protein S and HE. After binding, assembled nucleocapsids with helicaltwisted RNA budd into the ER lumen and are encased with its membrane.

6.These viral progeny are finally transported by golgi vesicles to the cell membrane and are exocytosies into the extracellular space.




## TRANSMISSION:

Infected carriers don't shed the virus. They are transmitted by either an aerosol, fomite or feco-oral route(16).They infects the human epithelial cells of the lungs via aerosol route by binding to the epithelial cells of the lungs(17).

They can produce a mild flu like illness to fatal pneumonia. MERS CoV has a fatality rate of upto 30%(13,18).

1.Virus enters oral and repiratorycells by ACE2 and TMPRSS2 interaction.

2. It enters the epithelium.

3. Virus fuses with vesicles and its RNA is released.

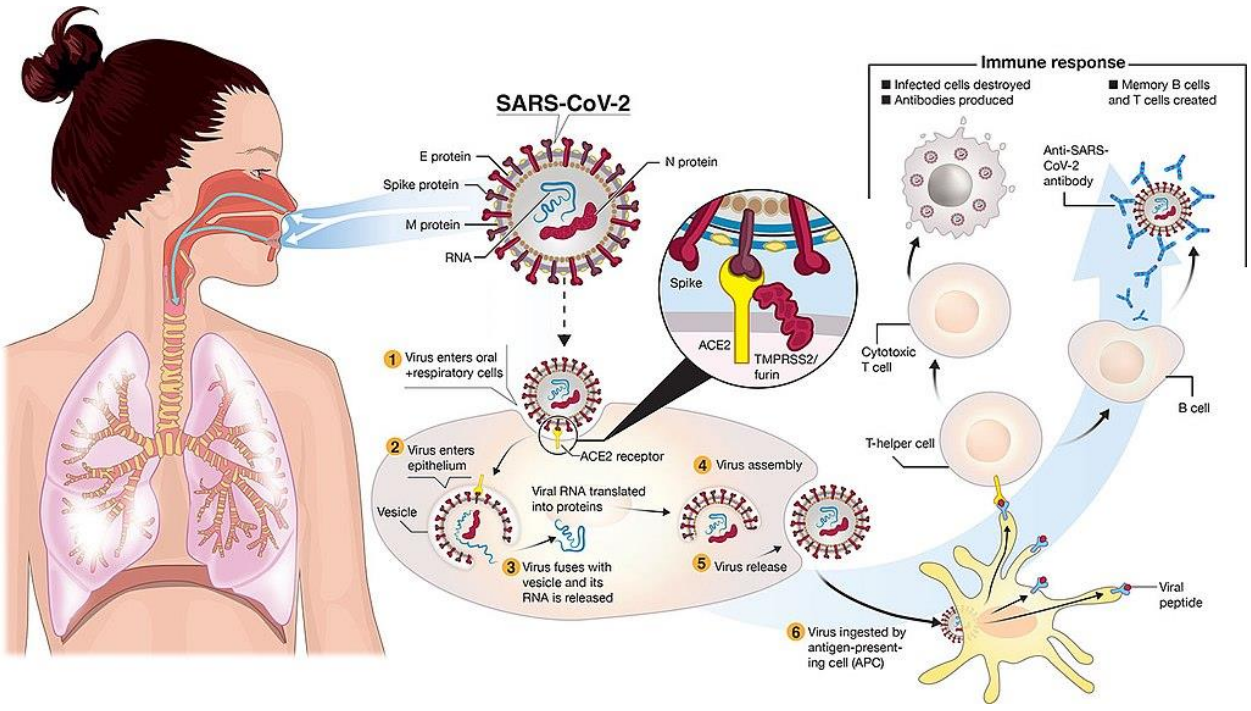
4. Virus is assembled.

5. Virus is released.

6. Virus ingested by antigen-presenting cells (APC) and viral peptide is separated.

7. It is presented to the T-helper cells , B cells and cytotoxic T cell.

8. Immune response: infected cells are destroyed, antibodies produced, memory B cells and T cells created.



## PATHOGENESIS AND COMPLICATIONS:

The most common reasons for ICU admission in COVID-19 are either hypoxemic respiratory failure leading to mechanical ventilation or hypotension requiring vasopressor support. AKI also can be a severe complication(19).

Prominent acute proximal tubular injury, peritubular erythrocyte aggregation and glomerular fibrin thrombi with ischemic collapse along with endothelial damage, hemosiderin deposition, pigment casts related to rhabdomyolysis, and inflammation are common pathogenetic processes in the kidneys.

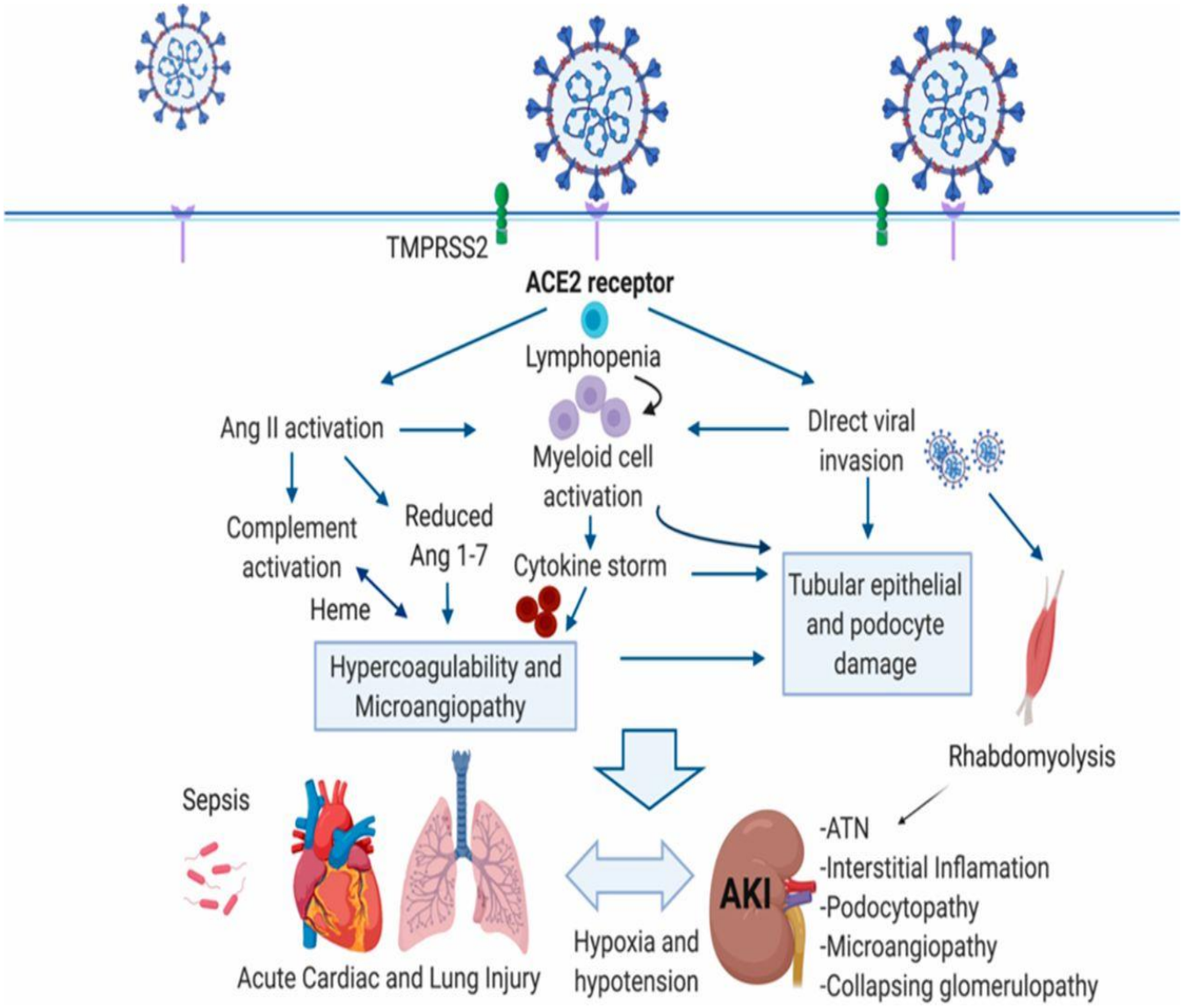
Increased clotting time and disseminated intravascular coagulation with small vessel thrombosis and pulmonary infarction are major contributors.Elevated d-dimer and low platelet levels carry prognostic values. There are also cases reported with evidence of microangiopathy in other organ systems, such as myocarditis, microangiopathy, splenic infarction, renal infarction or ATN.

Macrophage activation, increased ferritin levels, cytokine storm, and release of pathogen-associated molecular patterns and damage-associated molecular proteins can result in release of tissue factor and activation of coagulation factors that create a predisposition to hypercoagulability. It targets lymphocytes as they express angiotensin-converting enzyme 2 (ACE2), leading to lymphocyte activation and activation-induced cell death than can result in lymphopenia of both $CD4^+$ and $CD8^+$ T cells(20). Organ crosstalk between the injured lung, the heart, and the kidney can worsen pathology(21).

SARS-CoV-2 could directly infect human kidney tubules and induce cytoplasmic renal tubular inclusions, ACE2 protein, which is expressed on the brush border of the proximal tubule and

podocytes of the kidney much more than the lungs, the virus enters and gains easy access to the tubular fluid present at lower levels in podocytes.

In the kidney, Transmembrane protease, serine 2 (TMPRSS2) required for viral priming, is expressed in the distal nephron rather than the proximal tubule(22–24).



## ACUTE KIDNEY INJURY:

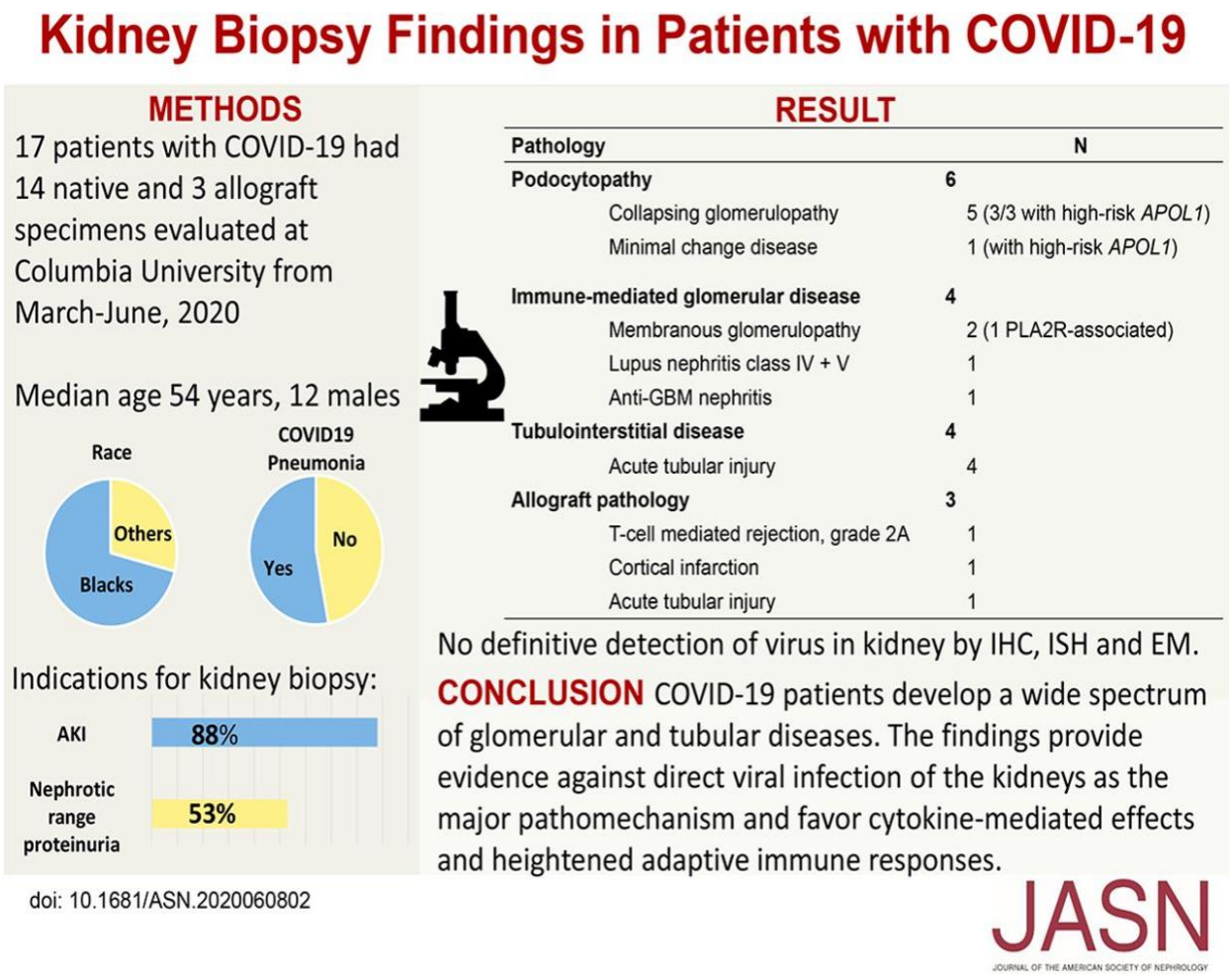
Acute kidney injury is characterized by sudden deterioration in kidney function, characterized by an increase in serum creatinine level with or without reduced urine output. The spectrum of injury ranges from mild to advanced and may also require renal replacement therapy.

AKI is defined as any of the following (Not Graded): K Increase in S.Cr by X0.3 mg/dl (X26.5 lmol/l) within 48 hours; or K Increase in S.Cr to X1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or K Urine volume of 0.5 ml/kg/h for 6 hours.

## STAGING OF SEVERITY OF AKI:

| Stage | Serum Creatinine | Urine output |
|---|---|---|
| 1 | 1.5–1.9 times baseline<br>or<br>≥ 0.3 mg $dl^{-1}$ (≥26.5 µmol $litre^{-1}$)<br>increase within 48 h | ≤0.5 ml $kg^{-1}$ $h^{-1}$ for 6–12 h |
| 2 | 2.0–2.9 times baseline | ≤0.5 ml $kg^{-1}$ $h^{-1}$ for 12 h |
| 3 | 3.0 times baseline<br>or<br>Increase in serum creatinine to ≥4.0 mg $dl^{-1}$ (≥353.6 µmol $litre^{-1}$)<br>or<br>Initiation of renal replacement therapy<br>or<br>In patients <18 yr, decrease in eGFR to <35 ml $min^{-1}$ per 1.73 $m^2$ | ≤0.3 ml $kg^{-1}$ $h^{-1}$ for 24 h<br>or<br>Anuria for × 12 h |

A recently published study in China that utilized autopsy specimen from 14 patients (25), that died of COVID 19, demonstrated that there is evidence of invasion of SARS CoV-2 into the kidney tissues along with significant acute tubular injury, endothelial damage as well as glomerular and vascular injury. AKI is an independent risk factor for severity in COVID 19 patients. High Angiotensin Converting Enzyme-2 receptor expression (26), imbalance of Renin Angiotensin Aldosterone system,immune mediated injury and micro-thrombus play important role in pathogenesis. Synergistic effect of virus induced direct cytotoxic effect and cytokines induced systemic inflammatory response contributed to development of AKI in these patients.



AKI is strongly associated with poor clinical outcomes. Among critically ill patients with AKI. AKI was associated with higher risk of in-hospital death and a longer hospital stay compared with AKI from any other causes. In-hospital RRT requirement was strongly associated with hospital mortality.Those who have renal recovery after S-AKI have dramatically improved survival. Patients who had reversal of S-AKI within 24 hours of shock have reduced mortality. Relapse of AKI is also common after initial recovery.

Recurrence of AKI is also common in upto 32% of the patients. The long-term outcomes of patients recovered from AKI is determined by of AKI and recovery status at hospital discharge. Those with even partial recovery have similar prognosis to those without AKI. AKI in patients with severe pneumonia leads upto 44% mortality.

After recovery from AKI, patients still carry the risk of developing chronic kidney disease (CKD), end-stage renal disease, and death. The severity of AKI, RRT requirement, and recovery status during hospitalization determines the risk of progression to CKD.In over 1 year, CKD developed in 21% patients with reversal of renal parameters , 30% of patients with recovery from AKI, and 79% of patients with non recovery from AKI, according to a recent study data.

**PATHOPHYSIOLOGY OF AKI:**

SARS-CoV-2–infected patients developed diverse glomerular and tubular diseases. The most common glomerular disorder was podocytopathy, out of which five patients had collapsing glomerulopathy and one developed minimal change disease. All occurred in black patients (including four with documented APOL1 high-risk genotype) and presented with nephrotic

syndrome or nephrotic-range proteinuria and AKI with associated ATI. These findings enlarge the literature on collapsing glomerulopathy (27)

The association between IFN therapy with both collapsing glomerulopathy and minimal change disease(28,29), as well as the presence of TRI (so-called IFN footprints), the findings indicate a role for cytokine-mediated podocyte injury in genetically susceptible individuals with SARS-CoV-2 infection(30). The lack of demonstrable viral particles in the podocytes disproved direct glomerular viral infection.

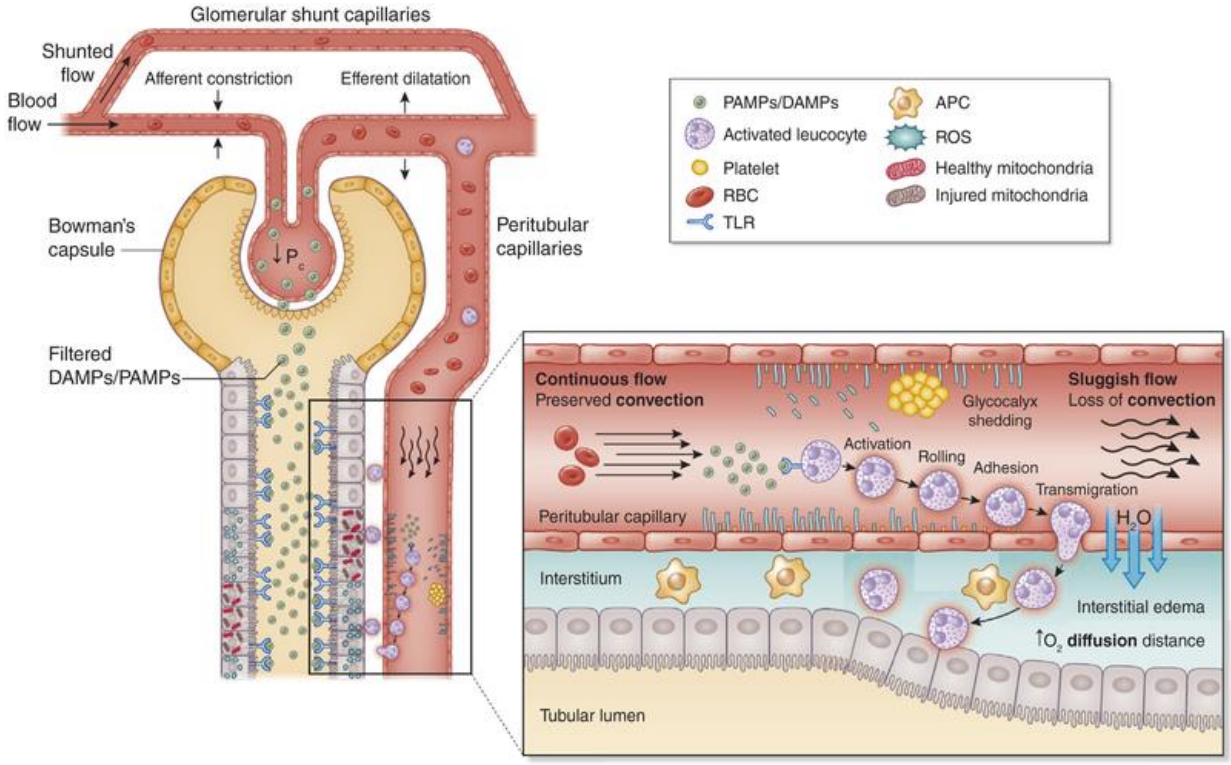
The inflammatory milieu surrounding COVID-19 also may trigger or exacerbate immune-(31)longstanding preexisting class 2 lupus nephritis and development of acute T cell–mediated rejection in a patient with preformed donor-specific antibodies. IFN and granulocyte colony–stimulating factor play an important role in triggering acute rejection23 or exacerbating immune complex–mediated GN,24 and both cytokines are known to be elevated in patients with COVID-19. Other glomerular diseases included new onset of anti-GBM nephritis and membranous glomerulopathy.

Pulmonary injury from influenza or other insults has been postulated to precede onset of anti-GBM nephritis by exposing the cryptic target Goodpasture antigen, consisting of distinct epitopes in COL4A3 and COL4A5, in damaged alveolar capillary basement membranes.(32) COVID-19 pneumonia could play a similar priming role. The major target antigen in membranous glomerulopathy, PLA2R, is also expressed in the respiratory tract,(33) suggesting a potential source for antigen presentation to incite or potentiate anti-PLA2R autoimmune responses. Coincidental associations with COVID-19 cannot be excluded.

ATI has also been identified as the predominant finding in autopsy series. Etiology is likely to be multifactorial with complex interplay of sepsis, hypoxia, hemodynamic instability, nephrotoxin exposure, and multiorgan complications, such as rhabdomyolysis.

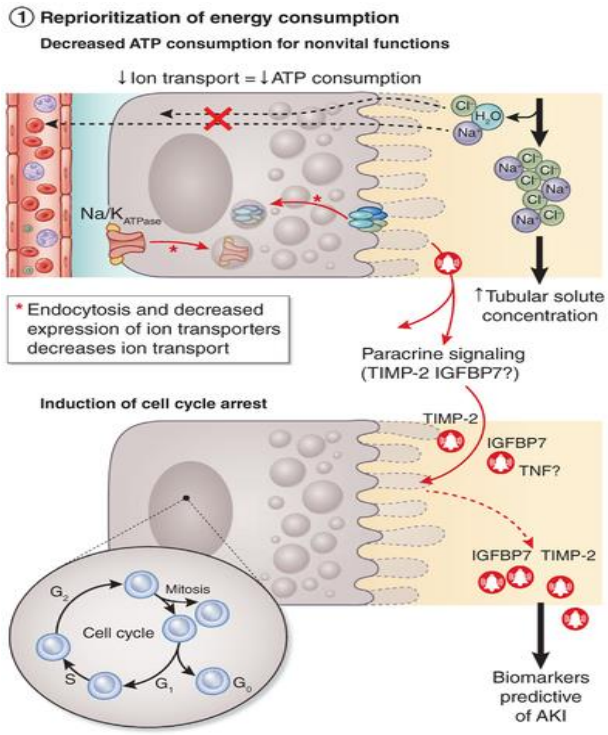
In an attempt to detect virus in kidney cells, five distinct methodologies, namely immunostains for viral spike and nucleocapsid proteins, ISH for viral RNA (by automated platform and manual RNAScope), and ultrastructural examination, all of which failed to reveal definitive viral particles (34,35) .The possibility that these techniques lack sufficient sensitivity for definitive viral detection cannot be ruled out.Such rare and low abundance of virus is sufficient to account for the pathologic changes and favor predominant roles for cytokine-mediated and other systemic effects.(36).

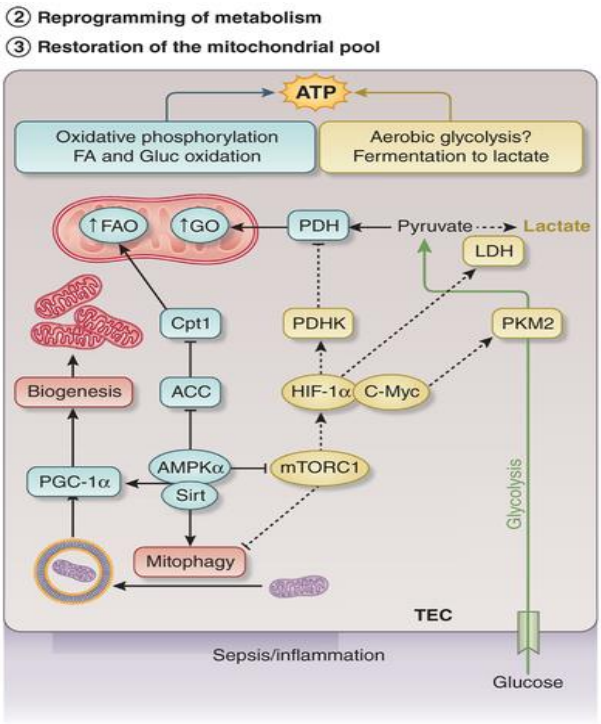
The biopsy series reveals diverse kidney pathology in SARS-CoV-2–infected patients. The findings highlight the potential for viral infection to influence innate or adaptive immune responses that in turn trigger new glomerular diseases (such as podocytopathies and anti-GBM nephritis) or exacerbate preexisting autoimmune or alloimmune conditions (such as lupus nephritis, membranous glomerulopathy, and allograft rejection). ATI is common and likely multifactorial. The lack of definitive virus in kidney cells argues against direct viral infection as the major pathomechanism.




## METABOLIC REPROGRAMMING:

During acute kidney injury (AKI), a reprioritization of energy occurs at the expense of cell function. Multiple highly consuming adenosine triphosphate (ATP) functions are down-regulated to save energy, including protein synthesis and ion transportation, especially in the proximal tubular epithelial cells (TECs).TECs reprograms their metabolism switching to aerobic glycolysis and oxidative phosphorylation to fulfill energy requirements. Preservation of functional mitochondrial poll is necessary to carry out all the metabolic changes. Mitochondria enter a series of quality control processes such as mitophagy and biogenesis to preserve the mitochondrial pool to confer protection and fulfill the necessary energetic requirements.




## ROLE OF BIOMARKERS IN AKI:

| | | | |
|---|---|---|---|
| NGAL | Urine, plasma | chelates labile Fe released from damaged tubules and prevents formation of hydroxy radicals; upregulatesheme-oxygenase-1 | Higher plasma and urine NGAL levels in patients with S-AKI compared with AKI due to other causes. Plasma NGAL appeared to be useful for predicting renal recovery |
| KIM-1 | URINE | promotes apoptotic and necrotic cell clearance and remodeling of injured epithelia | Urinary KIM-1 at 24 h predicted S-AKI with an AUC of 0.91 |

| | | | |
|---|---|---|---|
| L-FABP | URINE | protects against damage caused by reactive oxygen species; upregulated during ischemia-reperfusion injury | Urinary L-FABP levels at admission were significantly higher in nonsurvivors than in survivors with S-AKI |
| Angiopoietins | PLASMA | Ang-1 has been found to be protective by stabilizing endothelium, while Ang-2 promotes vascular leak, which can worsen sepsis | Higher levels of Ang-1 were associated with lower risk of AKI and higher levels of Ang-2 were associated with higher risk of AKI and are an independent predictor of 28-day mortality in ICU patients with AKI requiring RRT |
| [TIMP-2] [IGFBP7] | URINE | block cyclin-dependent protein kinase complexes on cell cycle promotion | Levels did not increase in nonrenal, organ failures in sepsis |
| Interleukin-6 | PLASMA | helps control the induction of the acute-phase response; a mediator for immunoglobulin class switching | Baseline interleukin-6 at admission predicted AKI in patients with severe sepsis. |
| sTREM-1 | URINE PLASMA | associated with the inflammatory response triggered by bacterial infection | In patients with sepsis, urine sTREM-1 at ICU admission predicted AKI at 48 h with AUC of 0.922 |

## EVALUATION AND GENERAL MANAGEMENT OF PATIENTS WITH AND AT RISK FOR AKI:

- Evaluate patients with AKI promptly to determine the cause, with special attention to reversible causes.
- Monitor patients with AKI with measurements of SCr and urine output to stage the severity.
- Manage patients with AKI according to the stage and cause.
- Evaluate patients 3 months after AKI for resolution, new onset, or worsening of pre-existing CKD. If patients have CKD, manage these patient accordingly.If patients do not have CKD, consider them to be at increased risk for CKD at later life.

## PATTERNS AND ASSOCIATED MECHANISMS OF ACUTE KIDNEY INJURY IN PATIENTS WITH COVID-19

| | |
|---|---|
| Viral cytopathic effect | Proteins critical for mediating cellular SARS-CoV-2 infection– ACE2, TMPRSS2, and CTSL–are highly expressed in kidney. Expression is mainly localized to the apical brush border of proximal tubular cells and podocytes. Viral protein and RNA have been demonstrated at the cellular level in kidney tissue, supporting a potential role for direct viral infection |

| | |
|---|---|
| | in the pathogenesis of AKI. Studies have demonstrated presence of mRNA in post mortem kidney tissues and its presence may correlate with clinical outcomes. However, the specificity of these reports have been questioned, and the actual presence of replicating virus in renal epithelium remains controversial, as nucleic acid tests and immunohistochemistry failed to detect the virus in kidney tissues. |
| Hemodynamic compromise | AKI is more common in patients requiring mechanical ventilation and vasopressor support. Inadequate volume resuscitation and tissue hypoperfusion may lead to AKI. Hemodynamic compromise from pulmonary embolism, right ventricular dysfunction, and myocardial injury may contribute. |
| The ARDS-AKI axis | AKI is the most common extra-pulmonary organ injury in ARDS via mechanisms including hypoxemia, reduced cardiac output, and systemic inflammation. Moreover, AKI-induced lung injury may further propagate severity of disease. |
| Glomerular injury | Possible direct viral effect and/or cytokine induced podocyte injury, along with a genetic predisposition, may result in collapsing glomerulopathy |
| Rhabdomyolysis | Rhabdomyolysis with histologic evidence of pigment deposition in renal tubules |

## AKI PROGRESSION TO CKD:

Acute kidney injury (AKI) and chronic kidney disease (CKD) are closely linked and likely promote one another.

Underlying CKD is a clear risk factor for AKI, as both decreased glomerular filtration rate (GFR) and increased proteinuria are strongly associated with AKI. Evidences prove that AKI accelerates the progression of CKD. Individuals who suffered dialysis-requiring AKI are particularly more susceptible to worse long-term renal outcomes, including end-stage renal disease (ESRD). The association between AKI and subsequent renal function decline is amplified by pre-existing severity of CKD, higher stage AKI, and cumulative number of AKI episodes. As the number of AKI survivors increases, there is a need to identify those at highest risk for the most adverse sequelae, and develop strategies to optimize their care.

The stages of CKD are (37):

Stage 1: Kidney damage with normal or increased GFR (>90 mL/min/1.73 m 2)

Stage 2: Mild reduction in GFR (60-89 mL/min/1.73 m 2)

Stage 3a: Moderate reduction in GFR (45-59 mL/min/1.73 m 2)

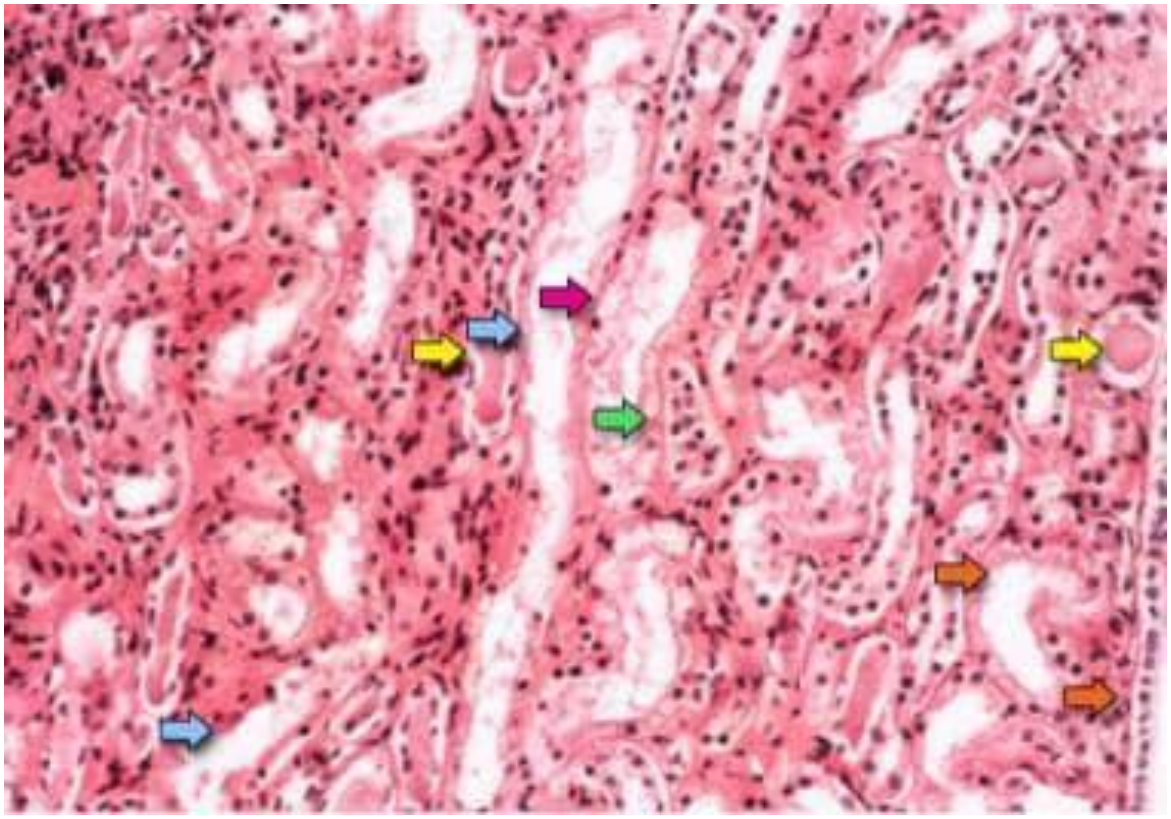
Stage 3b: Moderate reduction in GFR (30-44 mL/min/1.73 m 2)

Stage 4: Severe reduction in GFR (15-29 mL/min/1.73 m 2)

Stage 5: Kidney failure (GFR < 15 mL/min/1.73 m 2 or dialysis or ESRD)

Measurement of GFR may not be sufficient  for identifying stage 1 and stage 2 CKD, because in those patients the GFR may in fact be normal or borderline normal. In such cases, the presence of one or more of the following markers of kidney damage can establish the diagnosis :(38)

a. Albuminuria (albumin excretion > 30 mg/24 hr or albumin:creatinine ratio > 30 mg/g
b. Urine sediment abnormalities
c. Electrolyte and other abnormalities due to tubular disorders
d. Histologic abnormalities
e. Structural abnormalities detected by imaging
f. History of kidney transplantation in such cases



**Renal biopsy specimen shows renal medulla, which is composed mainly of renal tubules.**

**Features suggesting:**

**BLUE ARROW**- acute tubular necrosis are the patchy or diffuse denudation of the renal tubular cells with loss of brush border;

**ORANGE ARROW**-flattening of the renal tubular cells due to tubular dilation

**YELLOW ARROW:** intratubular cast formation

**RED ARROW:** sloughing of cells, which is responsible for the formation of granular casts

**GREEN ARROW:** Intratubular obstruction due to the denuded epithelium and cellular debris is evident. The denuded tubular epithelial cells clump together because of rearrangement of intercellular adhesion molecules.

## DIAGNOSIS:

The following tests can aid in the diagnosis and assessment of AKI:

Kidney function studies: 1. Increased levels of blood urea nitrogen (BUN) and creatinine are the hallmarks of renal failure;

2. The ratio of BUN to creatinine can exceed 20:1 in conditions that favor the enhanced reabsorption of urea, such as volume contraction (this suggests prerenal AKI)

3. urine analysis with microscopy

4. urine electrolytes

5. Fractional excretion of sodium

-

- Complete blood count (can indicate infection; acute blood loss or chronic anemia; thrombotic microangiopathy)
- Peripheral smear (eg, schistocytes such as hemolytic-uremic syndrome and thrombotic thrombocytopenic purpura)
- Serologic tests: For conditions associated with AKI, such as in lupus nephritis, ANCA vasculitis or anti-GBM disease or syndrome
- Complement testing: Pattern may indicate AKI related to endocarditis or various glomerulonephritidites
- Bladder pressure: Patients with a bladder pressure above 25 mm Hg should be suspected of having AKI caused by abdominal compartment syndrome
- Ultrasonography: Renal ultrasonography is useful for evaluating existing renal disease and obstruction of the urinary collecting system. The American College of Radiology recommends ultrasonography, preferably with Doppler methods, as the most appropriate imaging method in AKI.
- Aortorenal angiography : Can be helpful in establishing the diagnosis of renal vascular diseases, such as renal artery stenosis, renal atheroembolic disease, atherosclerosis with aortorenal occlusion, and certain cases of necrotizing vasculitis (eg, polyarteritis nodosa)
- Renal biopsy: Can be useful in identifying intrarenal causes of AKI and directing targeted therapy

## MANAGEMENT:

Measures to correct underlying causes of acute kidney injury (AKI) should begin at the earliest indication of renal dysfunction. Serum creatinine does not rise to abnormal levels until a large proportion of the renal mass is damaged, because the relationship between the glomerular filtration rate (GFR) and the serum creatinine level is not linear, especially early in disease. The rise of serum creatinine may not be evident before 50% of the GFR is lost.

It cannot be overstated that the current treatment for AKI is mainly supportive in nature; no therapeutic modalities to date have shown efficacy in treating the condition. Therapeutic agents (eg, dopamine, nesiritide, fenoldopam, mannitol) are not indicated in the management of AKI and may be harmful for the patient.

Maintenance of volume homeostasis and correction of biochemical abnormalities remain the primary goals of treatment and may include the following measures:

Correction of fluid overload with furosemide

Correction of severe acidosis with bicarbonate administration, which can be important as a bridge to dialysis

Correction of hyperkalemia

Correction of hematologic abnormalities (eg, anemia, uremic platelet dysfunction) with measures such as transfusions and administration of desmopressin or estrogens

# MATERIAL AND METHODOLOGY

1. **Study center:** COVID ICU, Government Stanley Medical Hospital, Chennai

2. **Study population:** COVID- 19 RT-PCR positive patients with severe disease admitted in the COVID ICU in a tertiary care centre in Chennai.

3. **Sampling:** convenient sampling

4. **Sample size:** All critically ill COVID positive patients admitted during the study period.

5. **Study design:** record based cross sectional study

6. **Data collection**: Manual medical health records of the patients.(case sheets)

7. **Period of study:** May 2020 to October 2020

## INCLUSION CRITERIA:

1. Patients with fever/myalgia and/or shortness of breath onset within 10 days with RT PCR COVID 19 positive.

2. Age more than 18yrs of age

3. AKI as per KDIGO guidelines, S. Creatinine increase > 0.3 from baseline or more than 1.5 fold the upper limit of normal

## EXCLUSION CRITERIA :

1. Age less than 18 yrs
2. End stage renal disease
3. Renal transplant
4. Symptomatic patients with RTPCR negative
5. Mild cases with spo2 >95%
6. Pregnant women.

## LABORATORY PROCEDURES:

1. Laboratory confirmation of COVID infection will be done by RT-PCR of nasopharyngeal swab in patients with history of contact with COVID positive patients, fever >38 deg C, cough, breathlessness onset within 7 days.

2. Blood examination include complete blood count, renal and liver function tests, inflammatory markers (interleukin- 6, ferritin, Lactate dehydrogenase), d-dimer.

3. Urine examination include monitoring urine output, urine analysis.

4. Laboratory parameters will be measured at the time of admission, 48 hours after admission, one week after clinical onset, and at discharge or before death.

5. Clinical improvement , stability or worsening will be based on need for non-invasive/invasive ventilation;worsening of renal function tests and need for renal replacement therapy(peritoneal or hemodialysis).

6. Unfavorable evolution was defined as increase in serum creatinine by more than or equal to 0.3 mg/dL within 48 hours or increase in serum creatinine to more than or equal to 1.5 times from baseline which is known and/or need for RRT.

## INDICATION FOR DIALYSIS:

1. KDIGO stage 3 AKI: Serum Creatinine more than or equal to 4 mg/dL; S. Creatinine increase to more than or equal to 3 times from baseline.

2. Urine output < 0.3ml/kg/hour for more than 24 hours or anuria for more than 12 hours.

3. Patient with AKI due to presumed acute tubular necrosis due to ischemia or direct virus mediated injury who are either on Mechanical Ventilation or vasopressors.

## STATISTICAL ANALYSIS:

**Data entry:** Microsoft Excel.

**Data analysis:** SPSS software.

**Result analysis:** Based on the reference study done by Yichung Cheng et al, Wuhan

## Formula: n= Z2pq / d2

Where Z= 1.96 (statistical significant constant for 95% CI)

p= 17.8 % (Prevalence of AKI among critically ill COVID 19 patients from previous study)

q = 82.2%(100-p)

d= 5% absolute precision

On substituting, in the formula

n= 3.84 x 17.8x 82.2 /25

n= 224

Adding 10% non response rate (ie 10% of 224 = 22)

n=246(minimum sample size)

**Therefore Sample size n= 250 (1 group)**

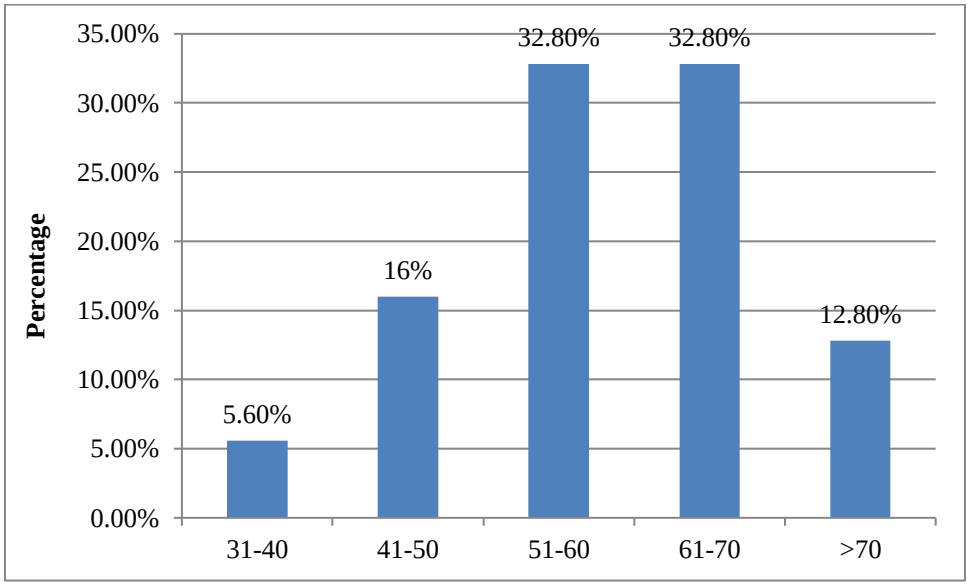
# STATISTICAL ANALYSIS

A total 250 people were included in the final analysis.

Table 1: Descriptive analysis of age group in study population (N=250)

| Age group | Frequency (N) | Percentage (%) |
|---|---|---|
| 31-40 | 14 | 5.6% |
| 41-50 | 40 | 16% |
| 51-60 | 82 | 32.8% |
| 61-70 | 82 | 32.8% |
| >70 | 32 | 12.8% |
| Total | 250 | 100% |

Figure 1: Age group distribution

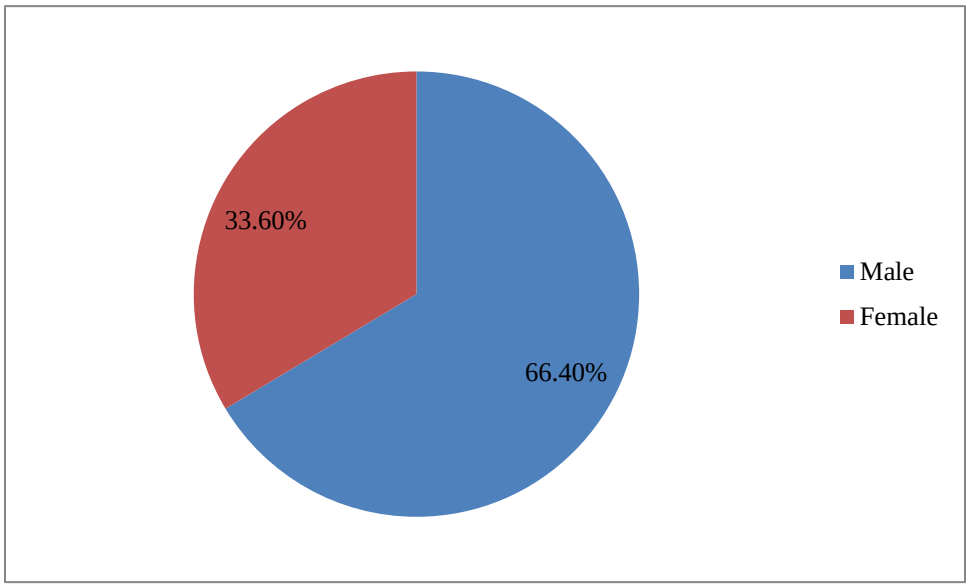



The above chart depicts the age distribution in this study which shows a maximum distribution between 51-70 at 65.60%. The next highest percentage holds between 41-50 years 16% followed by more than 70 years at 12.80%.

Table 2: Descriptive analysis of gender in study population (N=250)

| Gender | Frequency (N) | Percentage (%) |
|---|---|---|
| Male | 166 | 66.4% |
| Female | 84 | 33.6% |
| Total | 250 | 100% |

Figure 2: Gender distribution

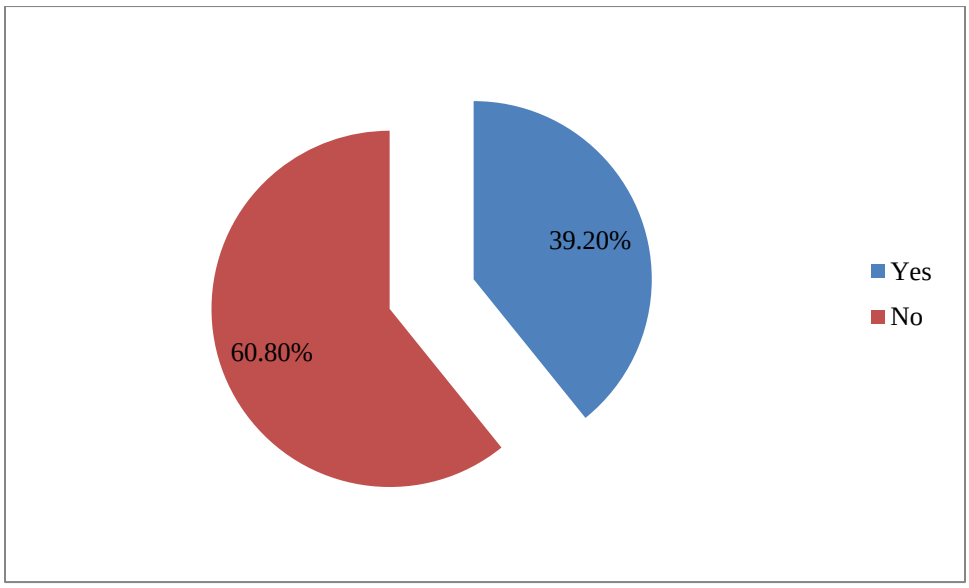



The above chart depicts the gender distribution in this study which shows male preponderance at 66.40% and female at 33.60%.

Table 3: Descriptive analysis of travel history in study population (N=250)

| Travel history | Frequency (N) | Percentage (%) |
|---|---|---|
| Yes | 98 | 39.2% |
| No | 152 | 60.8% |
| Total | 250 | 100% |

Figure 3: Travel historydistribution

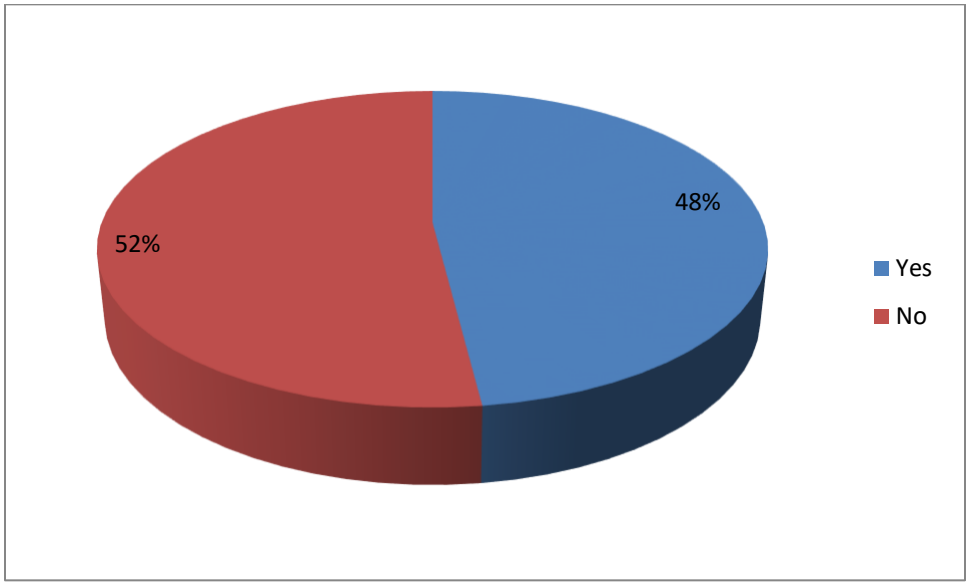



The above chart depicts the travel history distribution in this study which shows that about 60.80% had no positive travel history. As the population contained tertiary cases, travel history did not play a major role in patients becoming positive for COVID disease. This chart signifies that more than half of the study population were tertiary cases.

Table 4: Descriptive analysis of Contact with COVID 19 patients in study population (N=250)

| Contact with COVID 19 patients | Frequency (N) | Percentage (%) |
|---|---|---|
| Yes | 120 | 48% |
| No | 130 | 52% |
| Total | 250 | 100% |

Figure 4: Contact with COVID 19 patients distribution

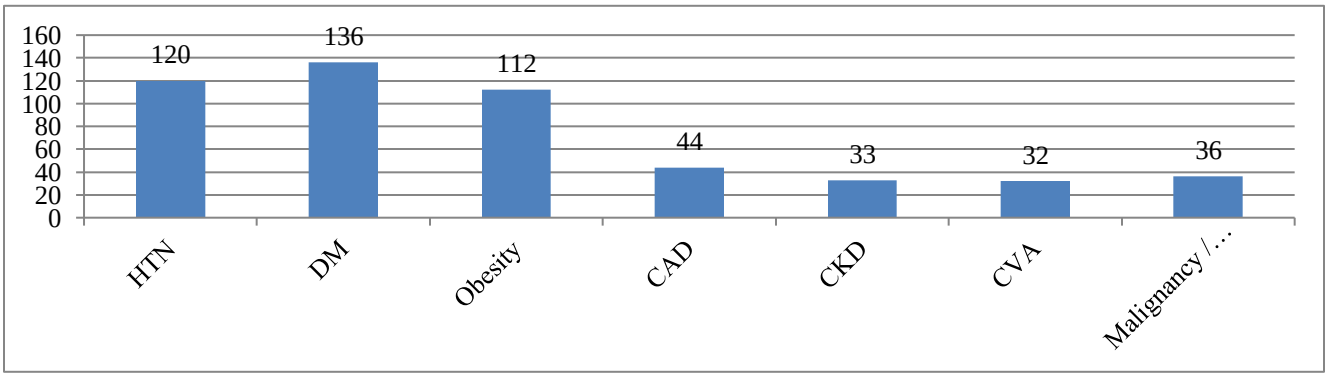



The above chart depicts the contact with COVID patients distribution in this study which shows that almost half of the study population (48%) had a history of contact with positive patients.

Table 5: Descriptive analysis of comorbidities in study population (N=250)

| Comorbidities | Frequency (N) | Percentage (%) |
|---|---|---|
| HTN | 120 | 48% |
| DM | 136 | 54.4% |
| Obesity | 112 | 44.8% |
| CAD | 44 | 17.6% |
| CKD | 33 | 13.2% |
| CVA | 32 | 12.8% |
| Malignancy / immunosuppression | 36 | 14.4% |

Figure 5: Comorbidities distribution

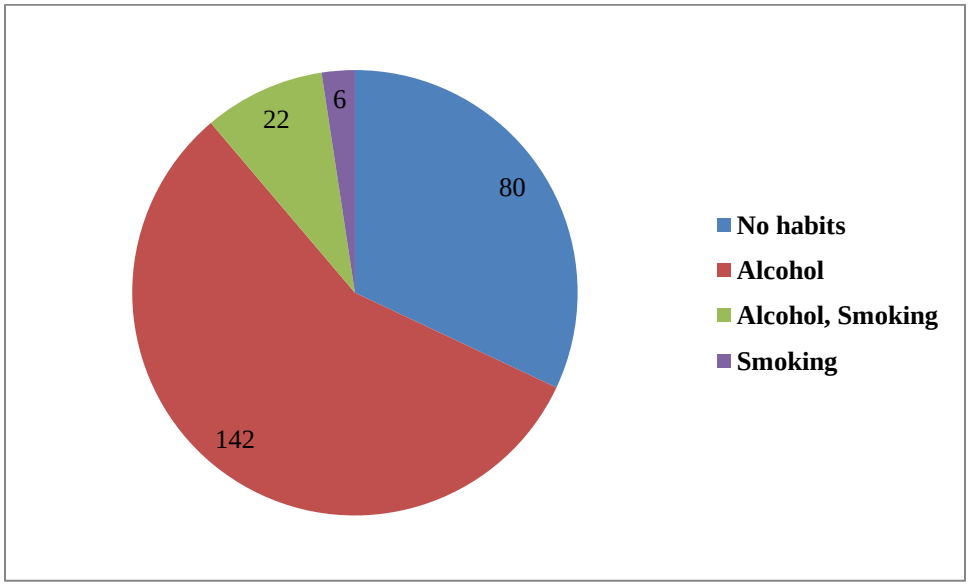



The above chart depicts the co-morbidities distribution in this study which shows that 54% were diabetics and 48% were hypertensive with almost half of the population (44.8%) being obese.

Table 6: Descriptive analysis of habits in study population (N=250)

| Habits | Frequency (N) | Percentage (%) |
|---|---|---|
| No habits | 80 | 32% |
| Alcohol | 142 | 56.8% |
| Alcohol, Smoking | 22 | 8.8% |
| Smoking | 6 | 2.4% |
| Total | 250 | 100% |

Figure 6: Habits distribution

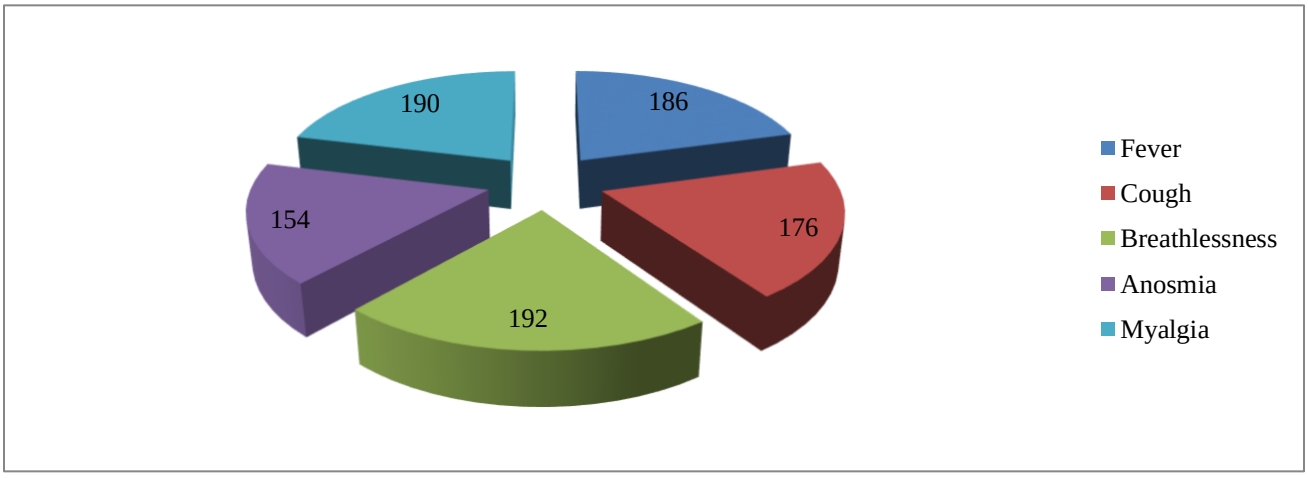



The above chart depicts the habits distribution in this study which shows that 56.8% were alcoholics and 32% had no habits. Only smokers were only 2.4%.

Table 7: Descriptive analysis of symptoms in study population (N=250)

| Symptoms | Frequency (N) | Percentage (%) |
|---|---|---|
| Fever | 186 | 74.4% |
| Cough | 176 | 70.4% |
| Breathlessness | 192 | 76.8% |
| Anosmia | 154 | 61.6% |
| Myalgia | 190 | 76% |

Figure 7: Symptoms distribution

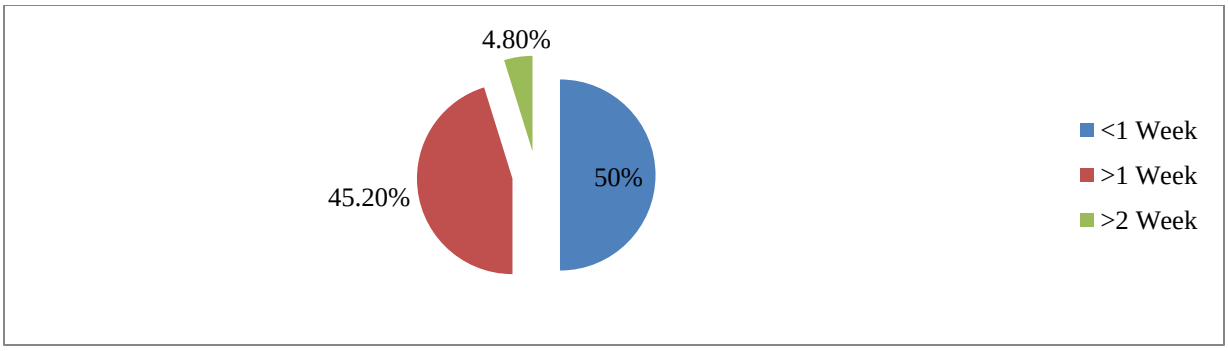



The above chart depicts the symptoms distribution in this study which shows that breathlessness(76.8%), myalgia(76%), fever(74.4%) and cough(70.4%) were the most common.

Table 8: Descriptive analysis of time from onset of illness to hospital in study population (N=250)

| Time from onset of illness to hospital | Frequency (N) | Percentage (%) |
|---|---|---|
| <1 Week | 125 | 50% |
| >1 Week | 113 | 45.2% |
| >2 Week | 12 | 4.8% |
| Total | 250 | 100% |

Figure 8: Time from onset of illness to hospital distribution

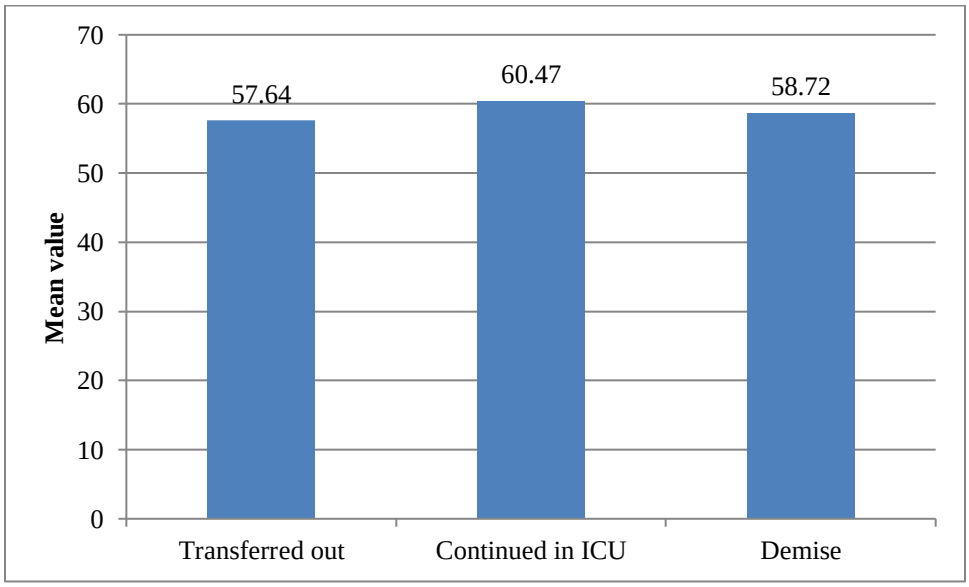



The above chart depicts the onest of symptom distribution in this study which shows that half of them were admitted during the 1st week 50% and 45.2 % within the 2nd week. Only 4.8% were admitted beyond the 2nd week.

Table 9: Comparison of mean age with outcome (N=250)

| Parameter | Outcome | | | Unpaired t test P Value |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Age | 57.64 ± 11.28 | 60.47 ± 10.77 | 58.72 ± 11.12 | 0.630 |

Figure 9: Bar chart of mean age among outcome (N=250)

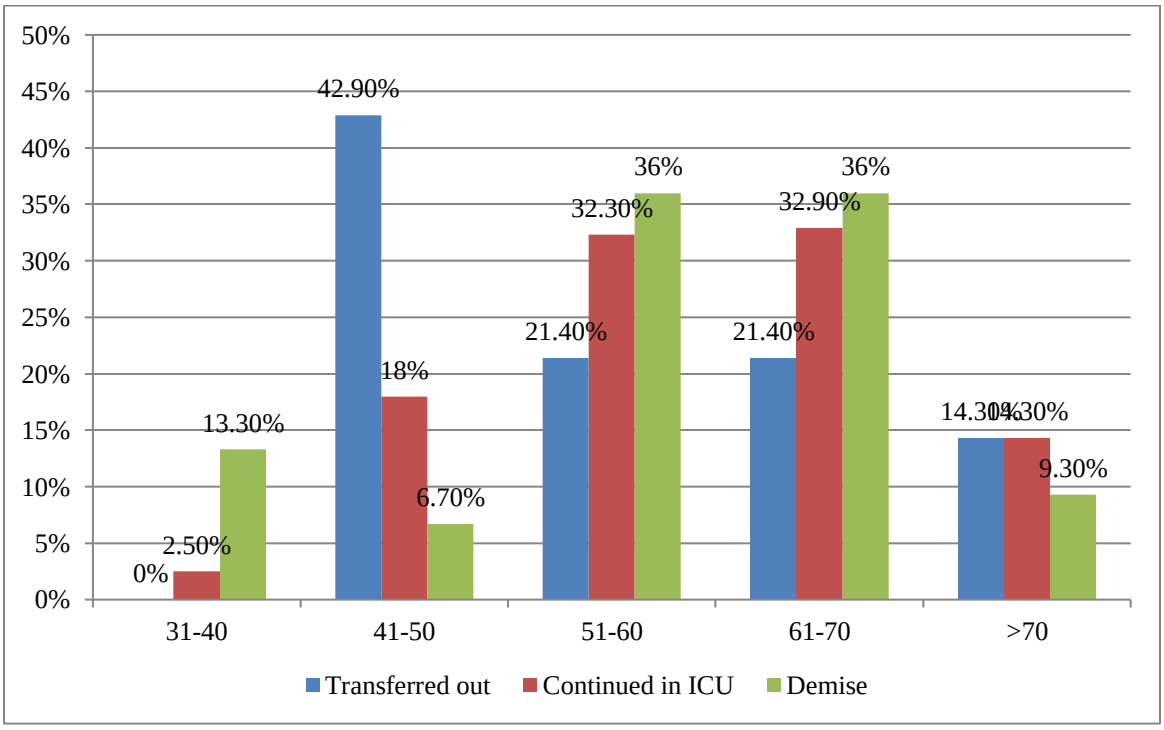



The above chart depicts the comparison of mean age among outcome in this study which shows that patients with a mean age of 57.64 were transferred out of the ICU, 60.47 continued in the ICU and those who died were of a mean age of 58.72 with a p value of 0.630 by unpaired t test.

Table 10: Comparison of age group among outcome (N=250)

| Age group | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| 31-40 | 0 (0%) | 4 (2.5%) | 10 (13.3%) | 14 (5.6%) |
| 41-50 | 6 (42.9%) | 29 (18%) | 5 (6.7%) | 40 (16%) |
| 51-60 | 3 (21.4%) | 52 (32.3%) | 27 (36%) | 82 (32.8%) |
| 61-70 | 3 (21.4%) | 53 (32.9%) | 27 (36%) | 82 (32.8%) |
| >70 | 2 (14.3%) | 23 (14.3%) | 7 (9.3%) | 32 (12.8%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 24.82 | | | | |
| P value – 0.002 (Significant) | | | | |

Figure 10: Age group among outcome (N=250)

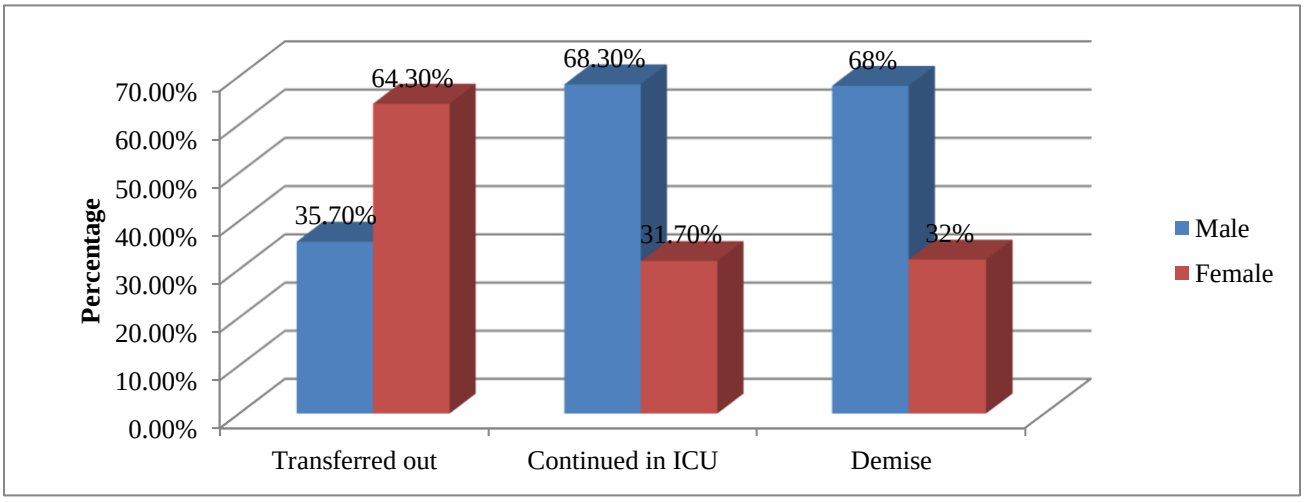



This chart depicts the Comparison of age group among outcome which shows that about 72% of the population who died were between 51-70 years of age. About 32% each among 51-60 years and 61-70 years continued within the ICU in critical situation. This chart was prepared by Chi square test with = 24.82 (p value of 0.002), hence the finding are statistically significant.

Table 11: Comparison of gender among outcome (N=250)

| Gender | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Male | 5 (35.7%) | 110 (68.3%) | 51 (68%) | 166 (66.4%) |
| Female | 9 (64.3%) | 51 (31.7%) | 24 (32%) | 84 (33.6%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 6.26 | | | | |
| P value – 0.044 (Significant) | | | | |

Figure 11: Gender among outcome (N=250)

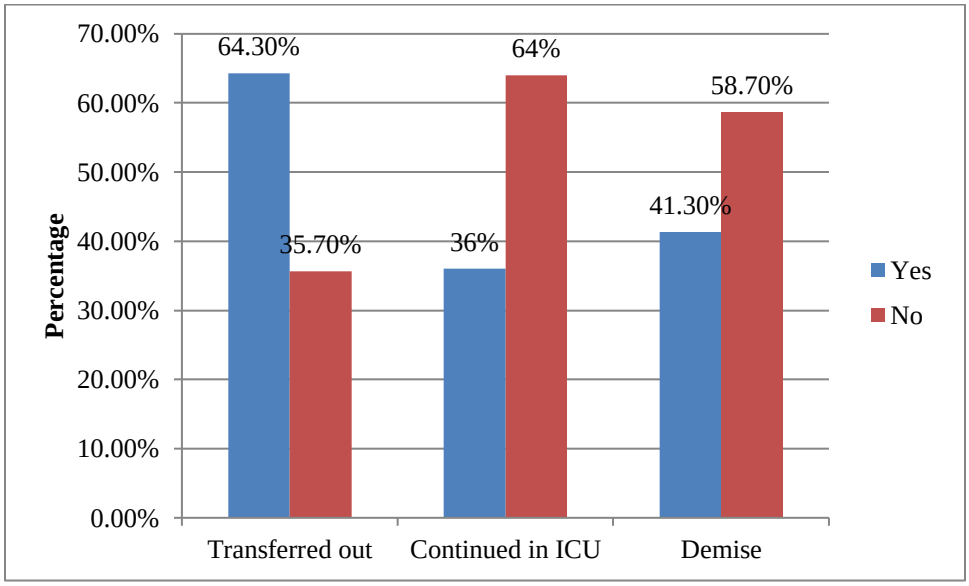


This chart depicts the Comparison of gender among outcome which shows that out of the patients transferred out 64.30%, out of the patients who remained critical in ICU 35.70% and out of the patients who succumbed to the illness 68% were male. Chi square test was 6.26 with a p value of 0.044 which is statistically significant. Hence, there is a male preponderance in poor outcome.

Table 12: Comparison of Travel history among outcome (N=250)

| Travel history | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Yes | 9 (64.3%) | 58 (36%) | 31 (41.3%) | 98 (39.2%) |
| No | 5 (35.7%) | 103 (64%) | 44 (58.7%) | 152 (60.8%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 4.52 | | | | |
| P value – 0.104 (Insignificant) | | | | |

Figure 12: Travel history among outcome (N=250)



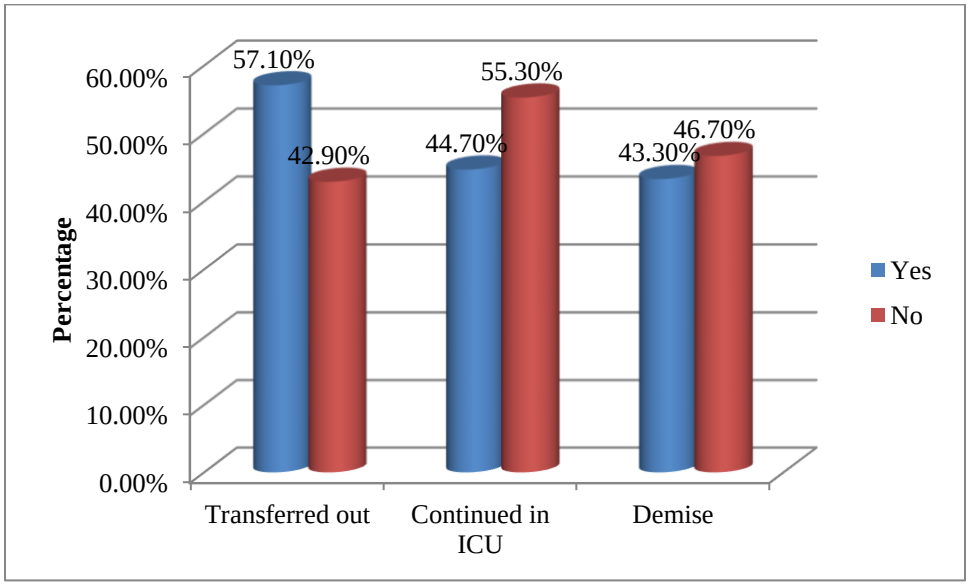

The above chart depicts comparison of Travel history among outcome with Chi square test of 4.52 and a p value of 0.104 which is statistically insignificant. Hence, there is no correlation between travel history and outcome.

Table 13: Comparison of Contact with COVID 19 patients among outcome (N=250)

| Contact with COVID 19 patients | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Yes | 8 (57.1%) | 72 (44.7%) | 40 (43.3%) | 120 (48%) |

| | | | | |
|---|---|---|---|---|
| No | 6 (42.9%) | 89 (55.3%) | 35 (46.7%) | 130 (52%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 2.02 | | | | |
| P value – 0.365 (Insignificant) | | | | |

Figure 13: Contact with COVID 19 patients among outcome (N=250)

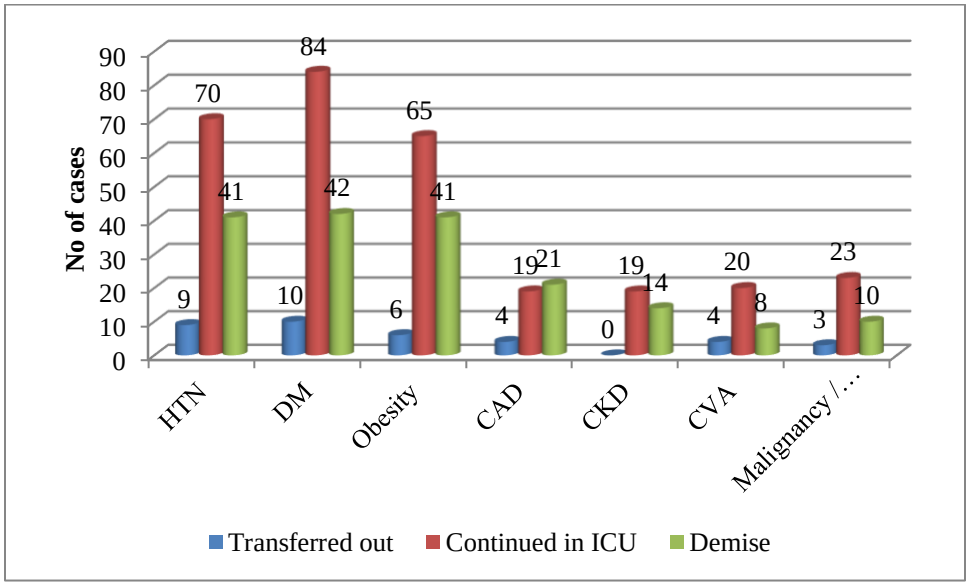



The above chart depicts comparison of contact history among outcome with Chi square test of 2.02 and a p value of 0.365 which is statistically insignificant. Hence, there is no correlation between contact history and outcome.

Table 14: Comparison of comorbidities among outcome (N=250)

| Comorbidities | Outcome | | | Total | P value |
|---|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | | |
| HTN | 9 (64.3%) | 70 (43.5%) | 41 (54.7%) | 120 (48%) | 0.126 |
| DM | 10 (71.4%) | 84 (52.2%) | 42 (56%) | 136 (54.4%) | 0.361 |
| Obesity | 6 (42.9%) | 65 (40.4%) | 41 (54.7%) | 112 (44.8%) | 0.119 |
| CAD | 4 (28.6%) | 19 (11.8%) | 21 (28%) | 44 (17.6%) | 0.005 |
| CKD | 0 (0%) | 19 (11.8%) | 14 (18.7%) | 33 (13.2%) | 0.113 |
| CVA | 4 (28.6%) | 20 (12.4%) | 8 (10.7%) | 32 (12.8%) | 0.179 |
| Malignancy / immunosuppression | 3 (21.4%) | 23 (14.3%) | 10 (13.3%) | 36 (14.4%) | 0.729 |

Figure 14: Co-morbidities among outcome (N=250)



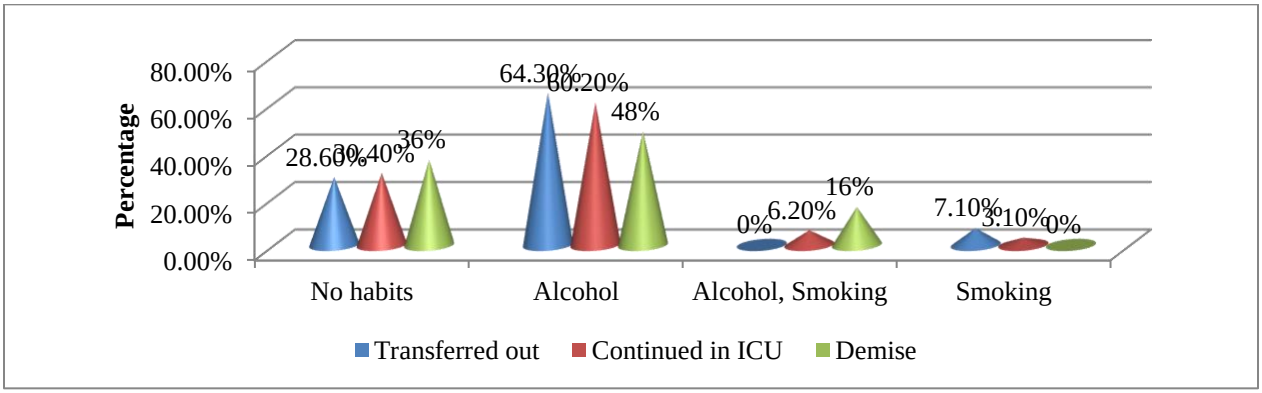

The above chart depicts comparison of co-morbidities among outcome that showed 56% of diabetics, 54.7% each of hypertensive and obese patients died at outcome. 52.2% of diabetics, 43.5% of hypertensive and 40.4% of obese patients continued in the ICU.

Table 15: Comparison of habits among outcome (N=250)

| Habits | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| No habits | 4 (28.6%) | 49 (30.4%) | 27 (36%) | 80 (32%) |

| | | | | |
|---|---|---|---|---|
| Alcohol | 9 (64.3%) | 97 (60.2%) | 36 (48%) | 142 (56.8%) |
| Alcohol, Smoking | 0 (0%) | 10 (6.2%) | 12 (16%) | 22 (8.8%) |
| Smoking | 1 (7.1%) | 5 (3.1%) | 0 (0%) | 6 (2.4%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 12.370 | | | | |
| P value – 0.054 (Insignificant) | | | | |

Figure 15: Habits among outcome (N=250)

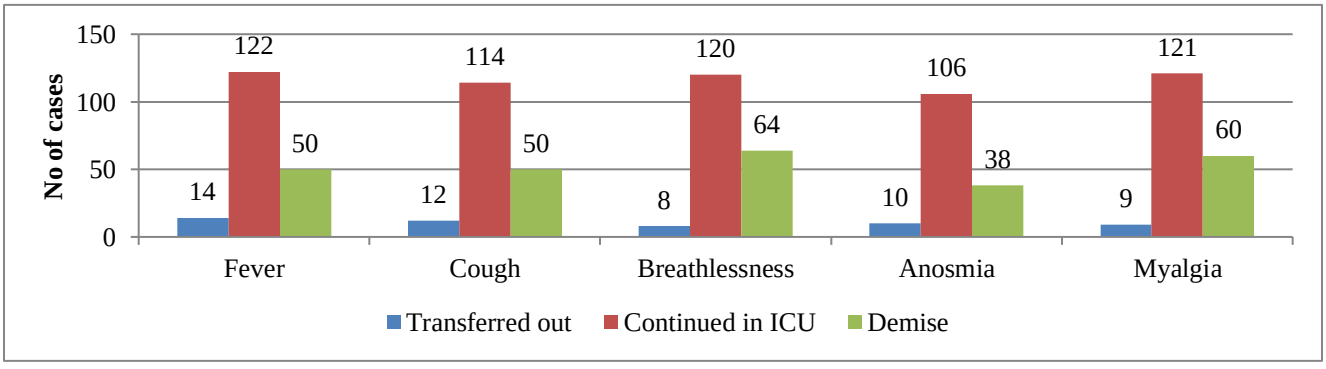



The above chart depicts comparison of habits among outcome with a Chi square test of 12.370 and a p value of 0.054 which is statistically insignificant. Hence, there is no correlation of habits on outcome.

Table 16: Comparison of symptoms among outcome (N=250)

| Symptoms | Outcome | | | Total | P value |
|---|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | | |
| Fever | 14 (100%) | 122 (75.8%) | 50 (66.7%) | 186 (74.4%) | 0.026 |
| Cough | 12 (85.7%) | 114 (70.8%) | 50 (66.7%) | 176 (70.4%) | 0.352 |
| Breathlessness | 8 (57.1%) | 120 (74.5%) | 64 (85.3%) | 192 (76.8%) | 0.036 |
| Anosmia | 10 (71.4%) | 106 (65.8%) | 38 (50.7%) | 154 (61.6%) | 0.061 |
| Myalgia | 9 (64.3%) | 121 (75.2%) | 60 (80%) | 190 (76%) | 0.412 |

Figure 16: Symptoms among outcome (N=250)

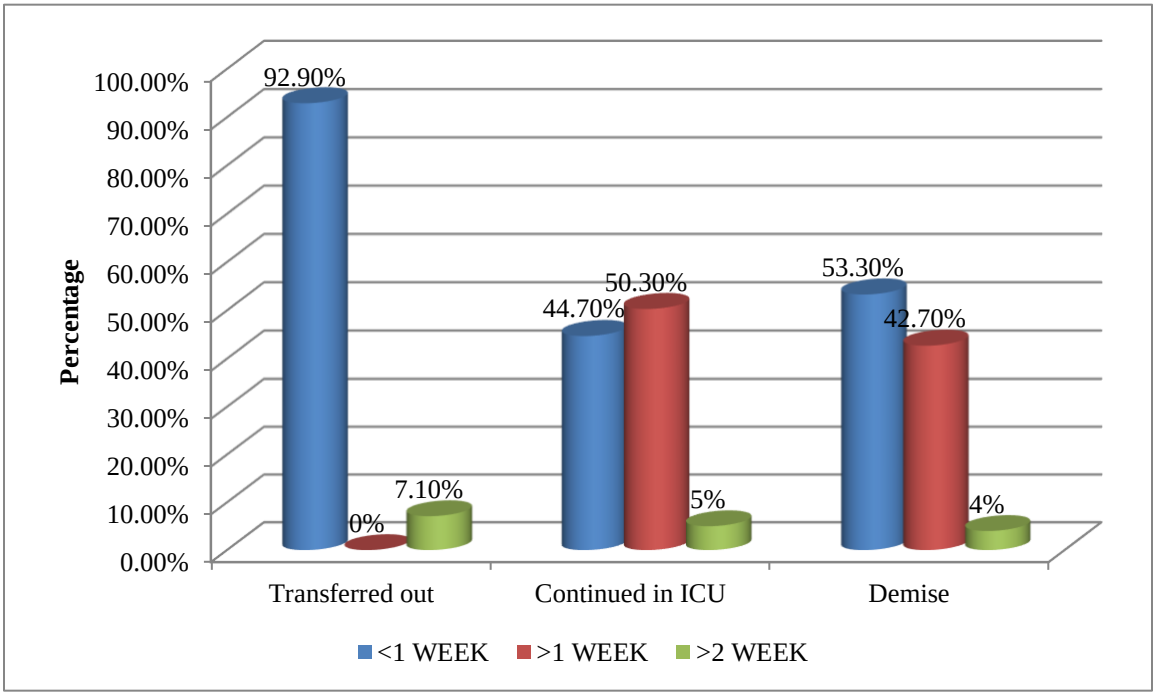



The chart depicts comparison of symptoms among outcome and shows that 85.3% of patients with breathlessness, 80% with myalgia, 66.7% of patients with fever and cough and 50.7% with anosmia underwent demise at the end of the study.

Table 17: Comparison of time from onset of illness to hospital among outcome (N=250)

| Time from onset of illness to hospital | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| <1 WEEK | 13 (92.9%) | 72 (44.7%) | 40 (53.3%) | 125 (50%) |
| >1 WEEK | 0 (0%) | 81 (50.3%) | 32 (42.7%) | 113 (45.2%) |
| >2 WEEK | 1 (7.1%) | 8 (5%) | 3 (4%) | 12 (4.8%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 13.84 | | | | |
| P value – 0.008 (Significant) | | | | |

Figure 17: Time from onset of illness to hospital among outcome (N=250)



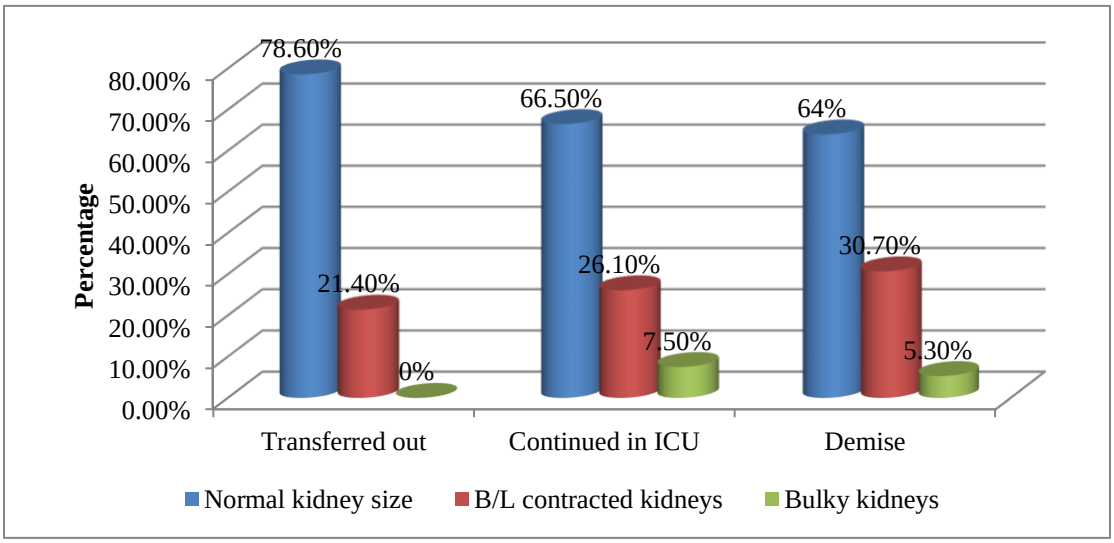

The chart depicts comparison of time from onset of illness to hospital among outcome with a Chi square test of 13.84 and a p value of 0.008 which holds statistical significance. Hence, out of the patients that met with demie at the end of the study 53.3% were in the 1st week if illness, 42.7% in their 2nd week and 4% were admitted beyond 2 weeks of illness.

Table 18: Comparison of USG ABD/PELVIS among outcome (N=250)

| USG ABD/PELVIS | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |

| | | | | |
|---|---|---|---|---|
| Normal kidney size | 11 (78.6%) | 107 (66.5%) | 48 (64%) | 166 (66.4%) |
| B/L contracted kidneys | 3 (21.4%) | 42 (26.1%) | 23 (30.7%) | 68 (27.2%) |
| Bulky kidneys | 0 (0%) | 12 (7.5%) | 4 (5.3%) | 16 (6.4%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 2.26 | | | | |
| P value – 0.688 (Insignificant) | | | | |

Figure 18: USG ABD/PELVIS among outcome (N=250)

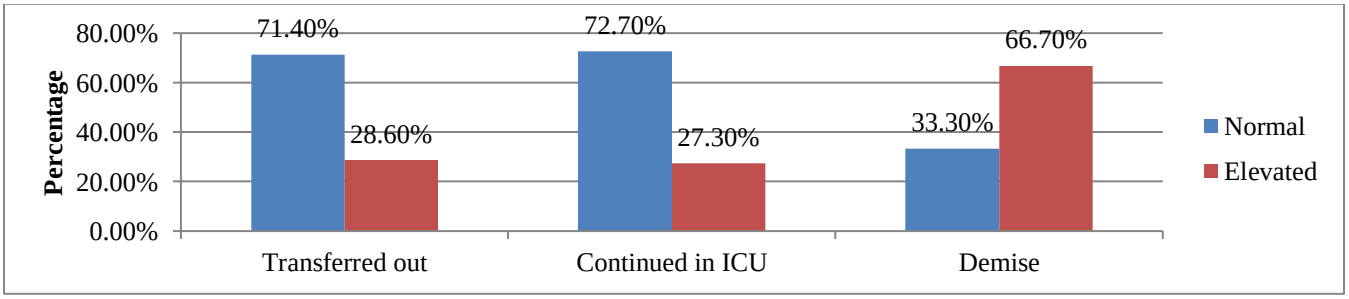



The chart depicts comparison of USG ABD/PELVIS among outcome that shows Chi square test of 2.26 and a p value of 0.688 which is statistically insignificant. Hence, there is no correlation between USG ABD/PELVIS findings and outcome.

Table 19: Comparison of lymphocyte count (*109 ) among outcome (N=250)

| lymphocyte count (*109 ) | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Normal | 10 (71.4%) | 117 (72.7%) | 25 (33.3%) | 152 (60.8%) |
| Elevated | 4 (28.6%) | 44 (27.3%) | 50 (66.7%) | 98 (39.2%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 33.92 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 19: lymphocyte count (*109 ) among outcome (N=250)

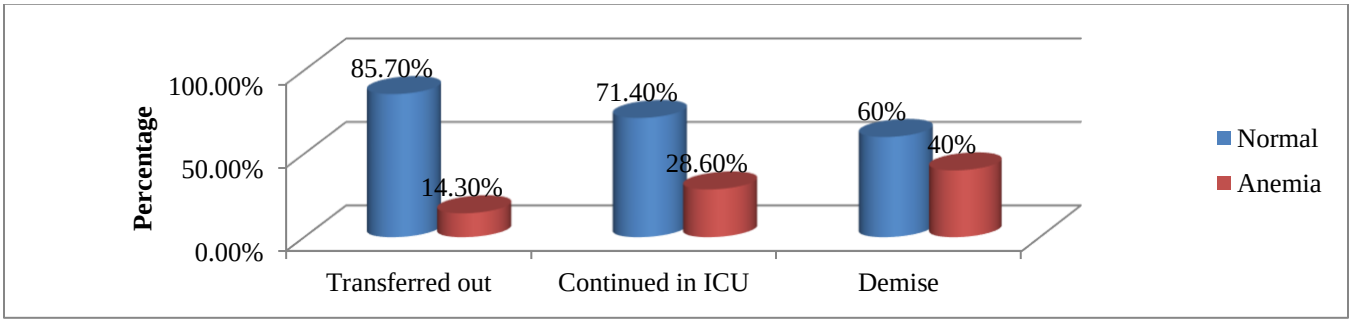



The chart depicts lymphocyte count (*109 ) among outcome that shows Chi square test of 33.92 and a p value of <0.001 which is statistically significant. Hence, there is correlation between lymphocyte count (*109 ) and outcome in that out of the people who died at the end of the study 66.7% had elevated lymphocyte count.

Table 20: Comparison of Hemoglobin (g/dl) among outcome (N=250)

| Hemoglobin (g/dl) | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Normal | 12 (85.7%) | 115 (71.4%) | 45 (60%) | 172 (68.8%) |
| Anemia | 2 (14.3%) | 46 (28.6%) | 30 (40%) | 78 (31.2%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 5.090 | | | | |
| P value – 0.078 (Significant) | | | | |

Figure 20: Hemoglobin (g/dl) among outcome (N=250)



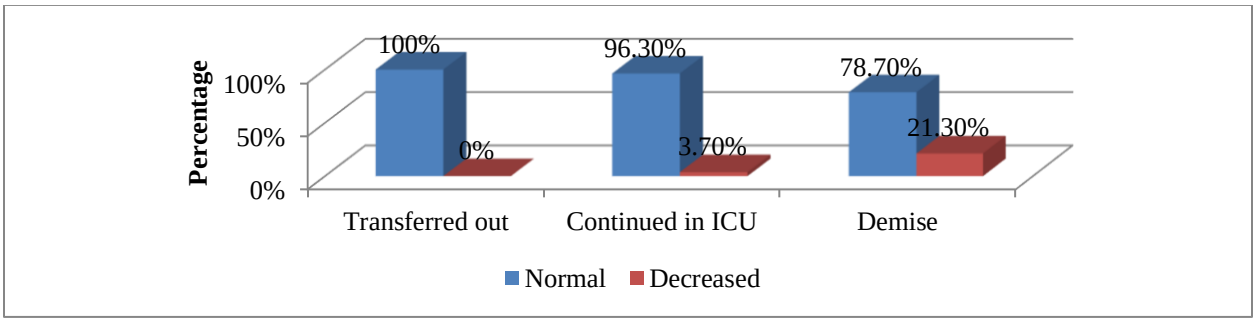

The chart depicts comparison of Hemoglobin (g/dl) among outcome that shows even though 60% of those who died had normal Hemoglobin, 40 % had anemia with Chi square test of 5.090

and a p value of <0.078 which is statistically significant. Hence, the anemia could be attributed to the anemia of chronic disease among patients admitted with preexisting CKD.

Table 21: Comparison of Platelet count (x109) among outcome (N=250)

| Platelet count (x109) | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Normal | 14 (100%) | 115 (96.3%) | 59 (78.7%) | 228 (91.2%) |
| Decreased | 0 (0%) | 6 (3.7%) | 16 (21.3%) | 22 (8.8%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 21.19 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 21: Platelet count (x109)among outcome (N=250)



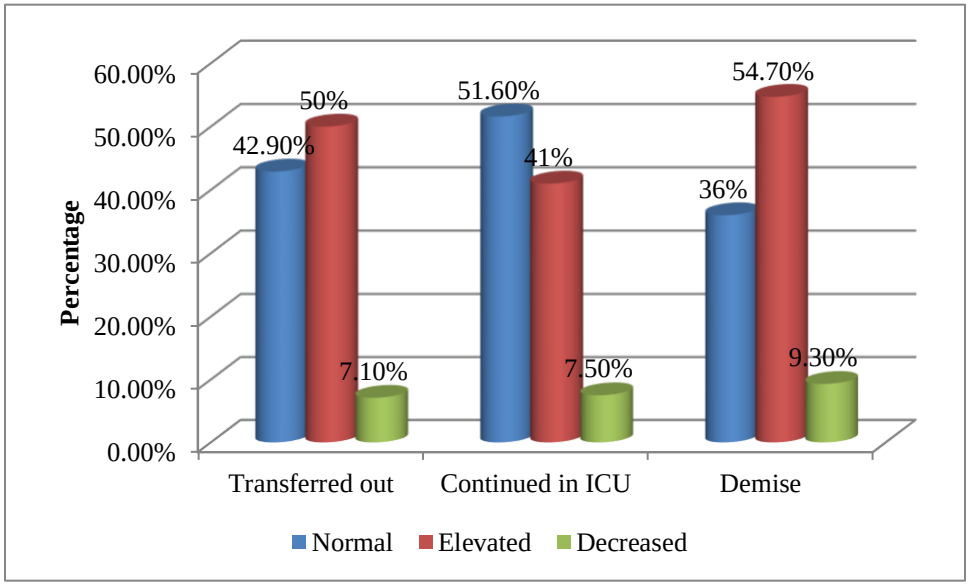

The chart depicts comparison of Platelet count (x109) among outcome that shows even though

78.7 of those who died had normal platelet count, 21.3% had reduced platelet count with Chi square test of 21.19 and a p value of <0.001 which is statistically significant. Hence, thrombhocytopenia is associated with poor outcome.

Table 22: Comparison of Random blood glucose (mg/dL) among outcome (N=250)

| Random blood glucose (mg/dL) | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Normal | 6 (42.9%) | 83 (51.6%) | 27 (36%) | 116 (46.4%) |
| Elevated | 7 (50%) | 66 (41%) | 41 (54.7%) | 114 (45.6%) |
| Decreased | 1 (7.1%) | 12 (7.5%) | 7 (9.3%) | 20 (8%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 5.11 | | | | |
| P value – 0.276 (Insignificant) | | | | |

Figure 22: Random blood glucose (mg/dL) among outcome (N=250)



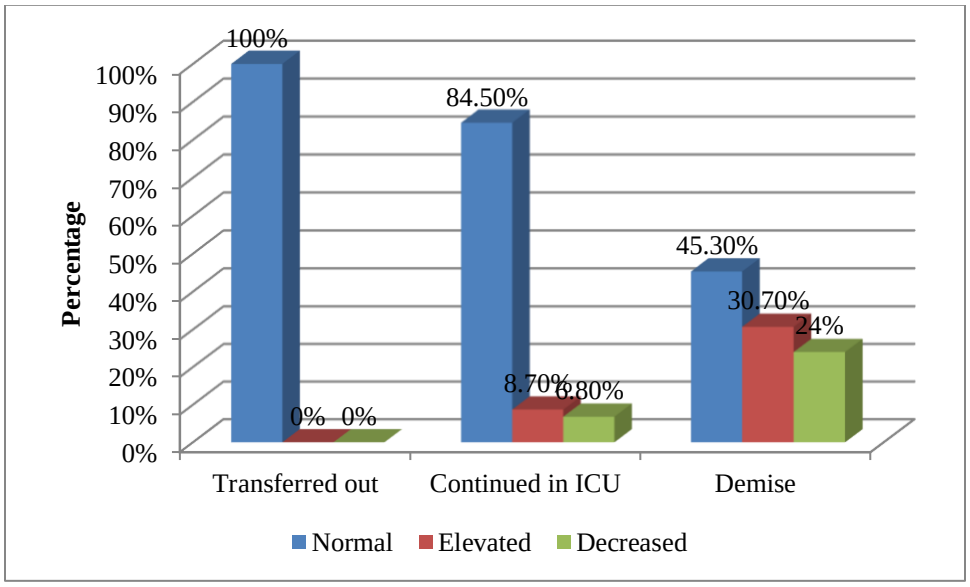

The chart depicts blood glucose (mg/dL)among outcome which shows Chi square test of 5.11 with a p value of <0.276 which is statistically insignificant. Hence, there is no correlation between RBS levels and outcome. Out of the paients who continued to be critically ill in the ICU and those who died 41%,54.7% had elevated RBS and 7.5%, 9.3% had RBS levels.

Table 23: Comparison of Sodium(in mEq/dL) among outcome (N=250)

| Sodium(in mEq/dL) | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Normal | 14 (100%) | 136 (84.5%) | 34 (45.3%) | 184 (73.6%) |
| Elevated | 0 (0%) | 14 (8.7%) | 23 (30.7%) | 37 (14.8%) |

| | | | | |
|---|---|---|---|---|
| Decreased | 0 (0%) | 11 (6.8%) | 18 (24%) | 29 (11.6%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 45.65 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 23: Sodium(in mEq/dL) among outcome (N=250)

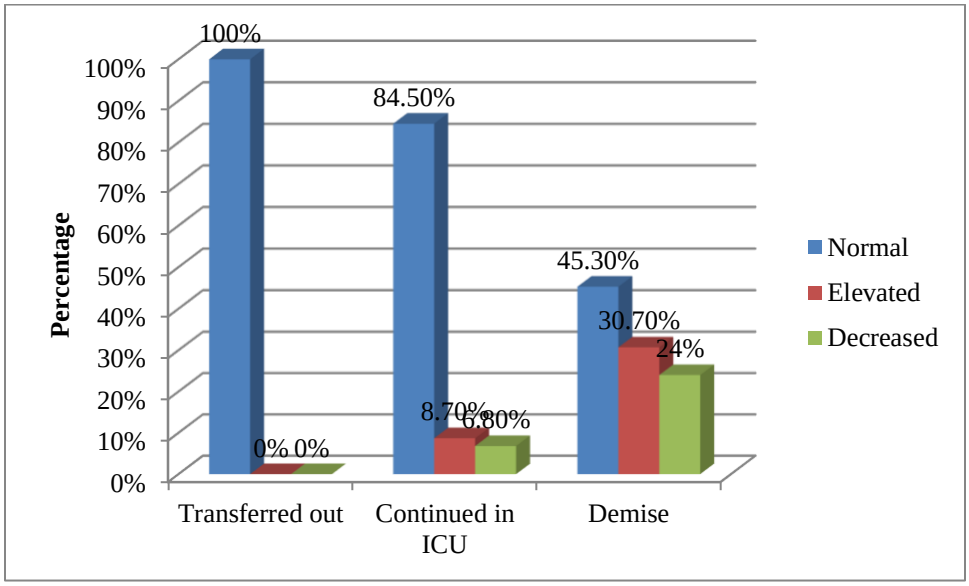



The chart depicts Sodium(in mEq/dL) among outcome which shows Chi square test of 45.65 with a p value of <0.001 which is statistically significant. Hence, there is correlation between sodium levels and outcome. Out of the paients who continued to be critically ill in the ICU and those who died 39.4% had elevated sodium and 30.8% had low sodium levels.

Table 24: Comparison of Potassium(in mEq/dL) among outcome (N=250)

| Potassium(in mEq/dL) | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Normal | 14 (100%) | 148 (91.9%) | 46 (61.3%) | 208 (83.2%) |
| Elevated | 0 (0%) | 6 (3.7%) | 10 (13.3%) | 16 (6.4%) |
| Decreased | 0 (0%) | 7 (4.3%) | 19 (25.3%) | 26 (10.4%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 37.79 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 24: Potassium(in mEq/dL) among outcome (N=250)



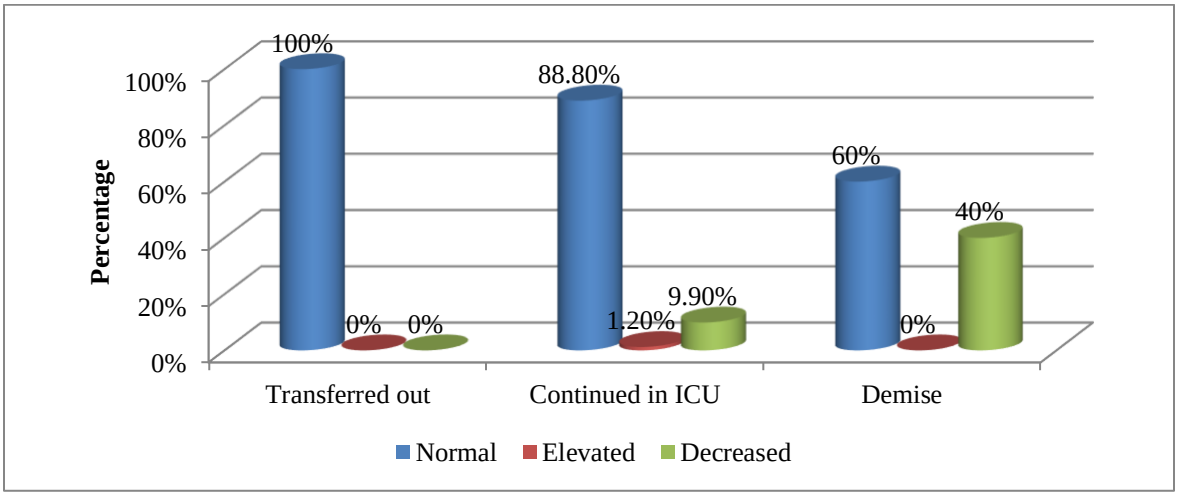

The chart depicts Potassium (in mEq/dL) among outcome which shows Chi square test of 37.79 with a p value of <0.001 which is statistically significant. Hence, there is correlation between potassium levels and outcome. Out of the paients who continued to be critically ill in the ICU and those who died 17% had elevated potassium and 29.6% had low potassium levels.

Table 25: Comparison of Bicarbonate(in mEq/dL) among outcome (N=250)

| Bicarbonate(in mEq/dL) | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Normal | 14 (100%) | 143 (88.8%) | 45 (60%) | 202 (80.8%) |
| Elevated | 0 (0%) | 2 (1.2%) | 0 (0%) | 2 (0.8%) |

| | | | | |
|---|---|---|---|---|
| Decreased | 0 (0%) | 16 (9.9%) | 30 (40%) | 46 (18.4%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| | | | | |
| Chi square test – 37.79 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 25: Bicarbonate(in mEq/dL) among outcome (N=250)

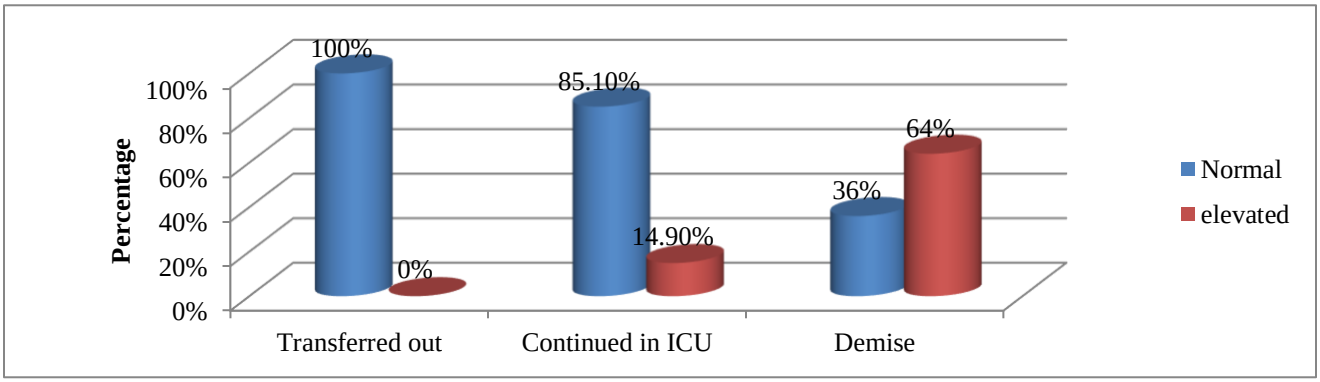



The chart depicts Bicarbonate (in mEq/dL) among outcome which shows Chi square test of 37.79 with a p value of <0.001 which is statistically significant. Hence, there is correlation between bicarbonate levels and outcome. Out of the paients who continued to be critically ill in the ICU and those who died 1.2% had elevated bicarbonate and 49.9% had low bicarbonate levels.

Table 26: Comparison of Serum AST/ALT (U/L) among outcome (N=250)

| Serum AST/ALT (U/L) | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Normal | 14 (100%) | 137 (85.1%) | 27 (36%) | 178 (71.2%) |
| elevated | 0 (0%) | 24 (14.9%) | 48 (64%) | 72 (28.8%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 66.136 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 26: Serum AST/ALT (U/L) among outcome (N=250)

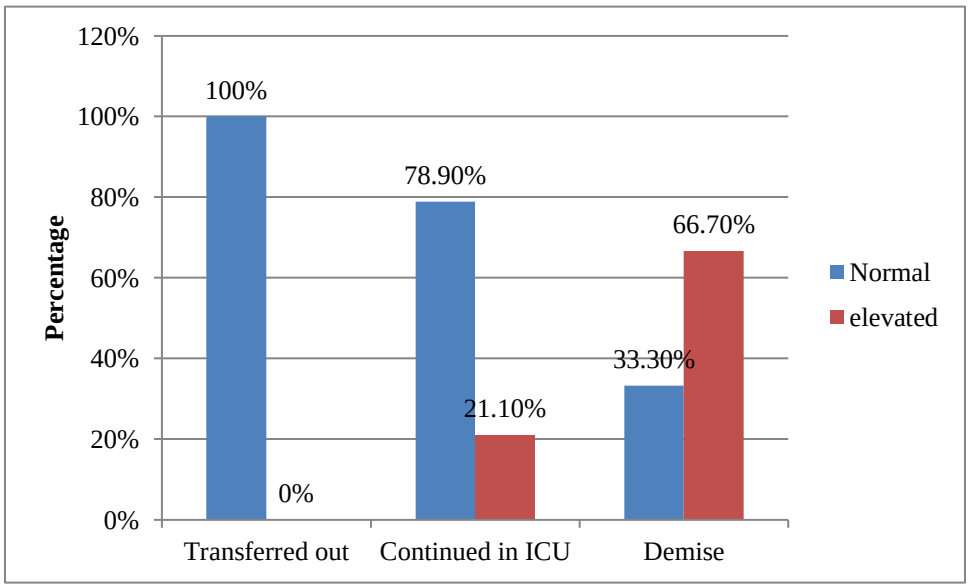



The chart depicts serum AST/ALT (U/L) among outcome which shows Chi square test of 66.136 with a p value of <0.001 which is statistically significant. Hence, there is correlation between elevatedAST/ALT levels and outcome. Out of the paients who continued to be critically ill in the ICU and those who died 78.9% had elevated AST/ALT.

Table 27: Comparison of Serum Alkaline phosphatase (U/L) among outcome (N=250)

| Serum Alkaline phosphatase (U/L) | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Normal | 14 (100%) | 127 (78.9%) | 25 (33.3%) | 166 (66.4%) |
| elevated | 0 (0%) | 34 (21.1%) | 50 (66.7%) | 84 (33.6%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 55.084 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 27: Serum Alkaline phosphatase (U/L) among outcome (N=250)



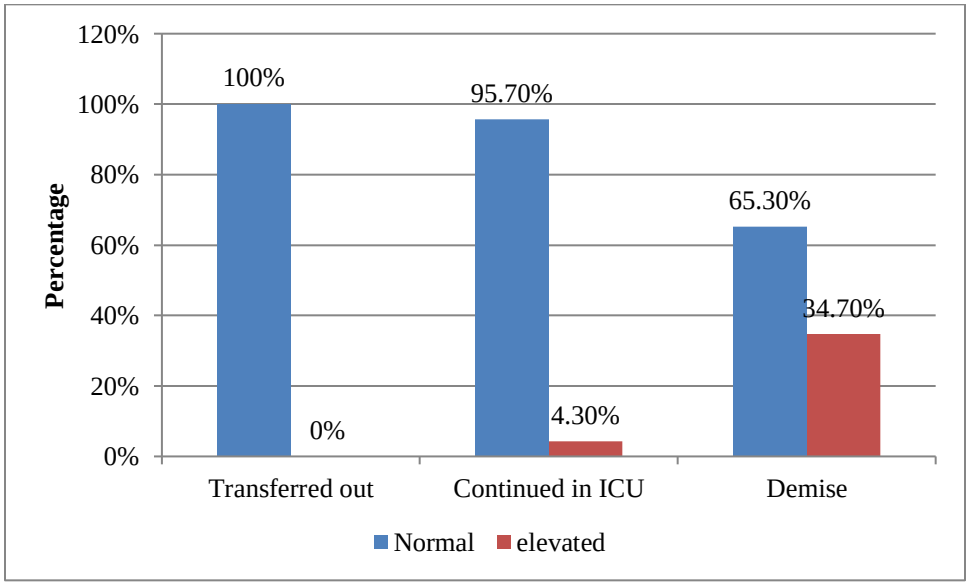

The chart depicts serum Alkaline phosphatase (U/L) among outcome which shows Chi square test of 55.084 with a p value of <0.001 which is statistically significant. Hence, there is correlation between elevated Alkaline phosphatase levels and outcome. Out of the paients who continued to be critically ill in the ICU and those who died 87.8% had elevated Alkaline phosphatase.

Table 28: Comparison of Serum total bilirubin (mg/dL) among outcome (N=250)

| Serum total bilirubin (mg/dL) | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Normal | 14 (100%) | 154 (95.7%) | 49 (65.3%) | 217 (86.8%) |

| | | | | |
|---|---|---|---|---|
| elevated | 0 (0%) | 7 (4.3%) | 26 (34.7%) | 33 (13.2%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 43.30 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 28: Serum total bilirubin (mg/dL) among outcome (N=250)

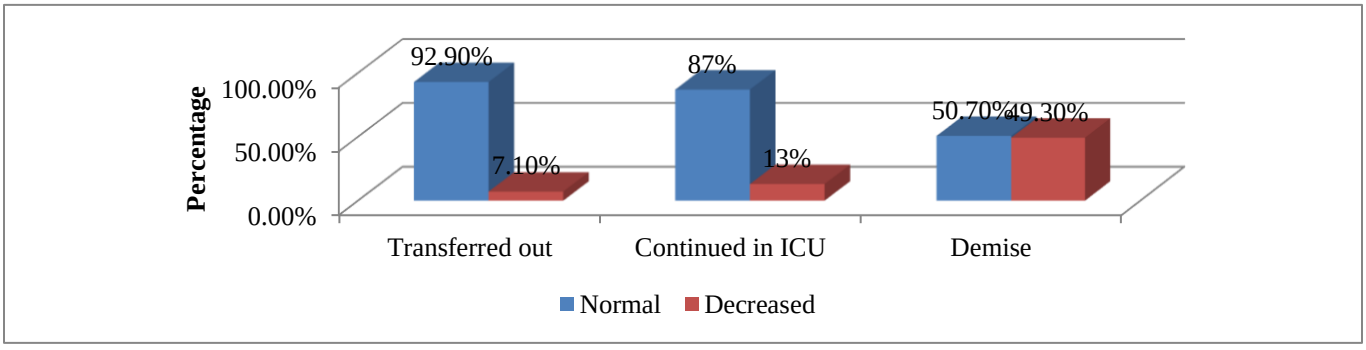



The chart depicts serum total bilirubin (mg/dL) among outcome which shows Chi square test of 43.30 with a p value of <0.001 which is statistically significant. Hence, there is correlation between elevated total bilirubin levels and outcome. Out of the paients who continued to be critically ill in the ICU and those who died 38% had elevated total bilirubin.

Table 29: Comparison of Serum albumin (mg/dL) among outcome (N=250)

| Serum albumin (mg/dL) | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Normal | 13 (92.9%) | 140 (87%) | 38 (50.7%) | 191 (76.4%) |
| Decreased | 1 (7.1%) | 21 (13%) | 37 (49.3%) | 59 (23.6%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 39.60 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 29: Serum albumin (mg/dL) among outcome (N=250)



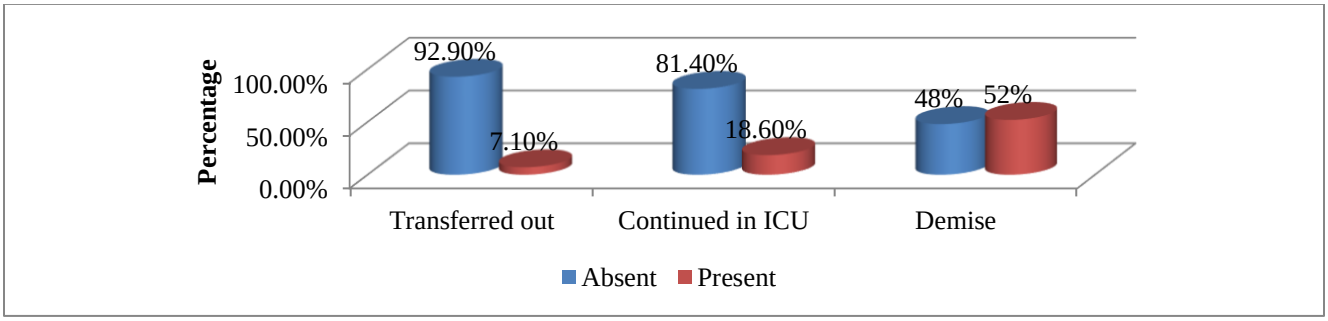

The chart depicts serum total albumin (mg/dL) among outcome which shows Chi square test of 39.60 with a p value of <0.001 which is statistically significant. Hence, there is correlation

between low albumin levels and outcome. Out of the paients who continued to be critically ill in the ICU and those who died 62.3% had low albumin levels.

Table 30: Comparison of Urine sugar among outcome (N=250)

| Urine sugar | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Absent | 13 (92.9%) | 131 (81.4%) | 36 (48%) | 180 (72%) |
| Present | 1 (7.1%) | 30 (18.6%) | 39 (52%) | 70 (28%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 31.46 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 30: Urine sugar among outcome (N=250)



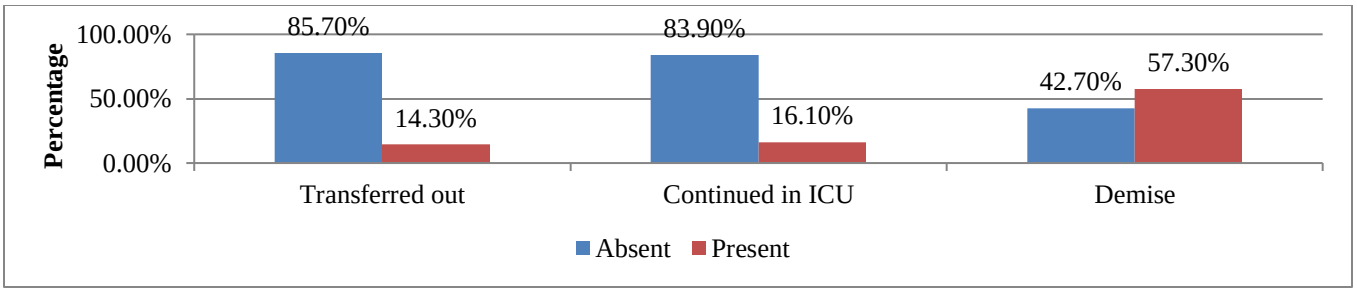

The chart depicts urine sugar among outcome which shows Chi square test of 31.96 with a p

value of <0.001 which is statistically significant. Hence, there is correlation between presence of urine sugar and outcome. Out of the paients who continued to be critically ill in the ICU and those who died 70.6% had sugar in urine.

Table 31: Comparison of Urine Pus cells among outcome (N=250)

| Urine Pus cells | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Absent | 12 (85.7%) | 135 (83.9%) | 32 (42.7%) | 179 (71.9%) |
| Present | 2 (14.3%) | 26 (16.1%) | 43 (57.3%) | 71 (28.4%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 44.131 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 31: Urine Pus cells among outcome (N=250)



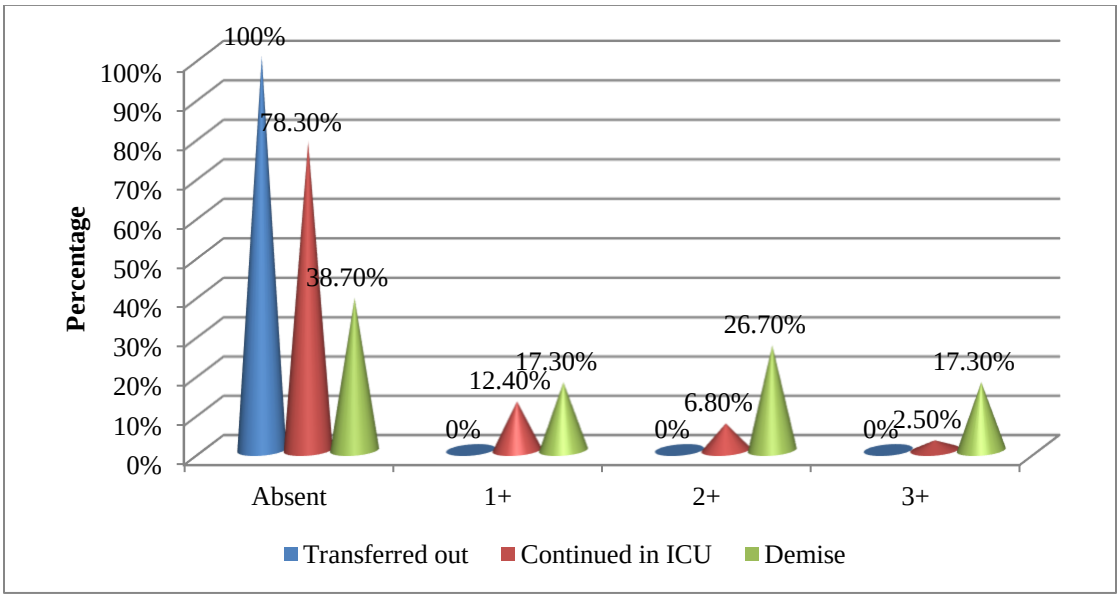

The chart depicts urine pus cells among outcome which shows Chi square test of 44.131 with a p value of <0.001 which is statistically significant. Hence, there is correlation between presence of pus in urine and outcome. Out of the patients who continued to be critically ill in the ICU and those who died 73.4% had pus in urine indicating it as a source of sepsis.

Table 32: Comparison of Urine protein/albumin among outcome (N=250)

| Urine protein/albumin | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Absent | 14 (100%) | 126 (78.3%) | 29 (38.7%) | 169 (67.6%) |
| 1+ | 0 (0%) | 20 (12.4%) | 13 (17.3%) | 33 (13.2%) |
| 2+ | 0 (0%) | 11 (6.8%) | 20 (26.7%) | 31 (12.4%) |
| 3+ | 0 (0%) | 4 (2.5%) | 13 (17.3%) | 17 (6.8%) |

| | | | | |
|---|---|---|---|---|
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 52.73 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 32: Urine protein/albumin among outcome (N=250)



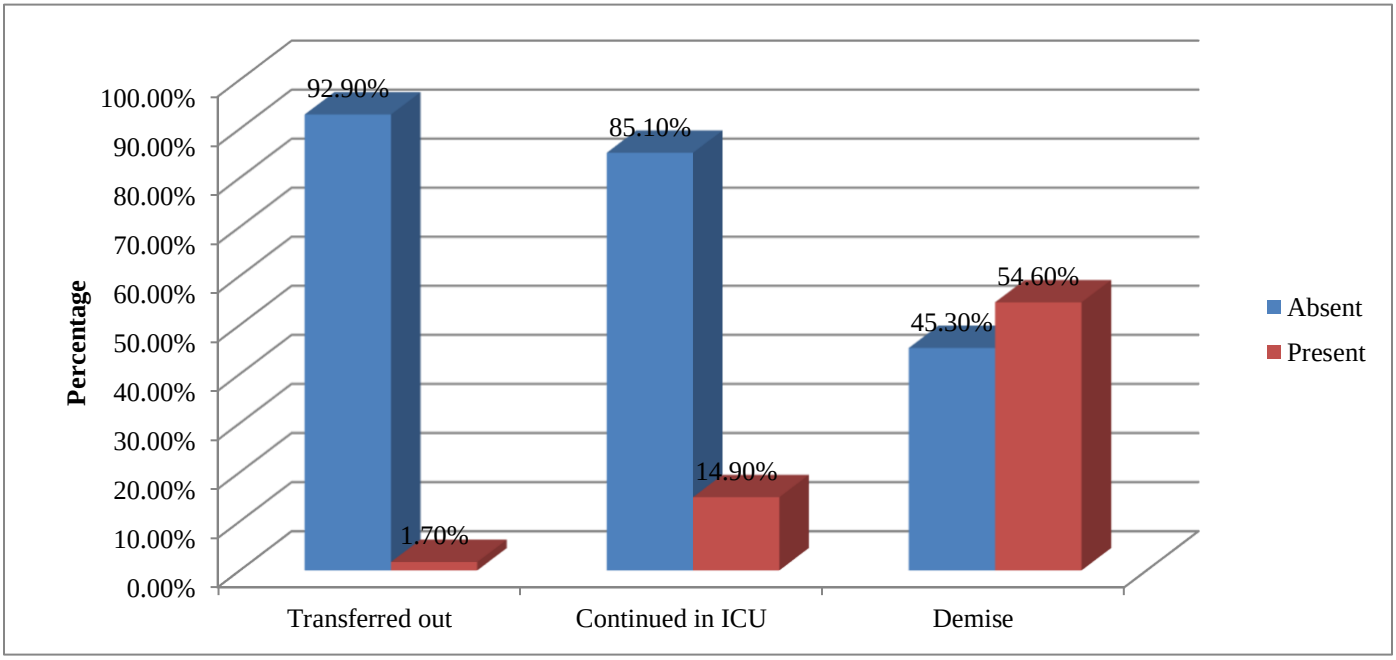

The chart depicts urine protein/albumin among outcome which shows Chi square test of 52.73 with a p value of <0.001 which is statistically significant. Hence, there is correlation between urine protein/albumin and outcome. Out of the patients who continued to be critically ill in the

ICU and those who died 29.7% had 1+, 33.5% had 2+ and 19.8%had 3+ protein/albumin in urine.

Table 33: Comparison of Blood in urine among outcome (N=250)

| Blood in urine | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Absent | 13 (92.9%) | 137 (85.1%) | 34 (45.3%) | 185 (73.6%) |
| Present | 1 (1.7%) | 24 (14.9%) | 41 (54.6%) | 66 (26.4%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 45.16 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 33: Blood in urine among outcome (N=250)



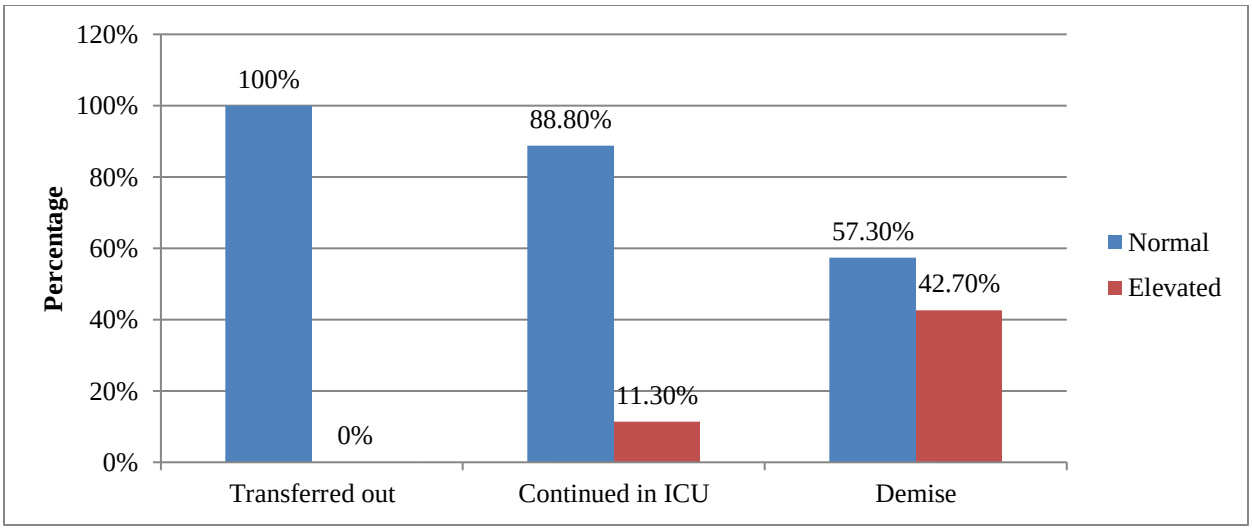

The chart depicts blood in urine among outcome which shows Chi square test of 45.16 with a p value of <0.001 which is statistically significant. Hence, there is correlation between presence of blood in urine and outcome. Out of the patients who continued to be critically ill in the ICU and those who died 69.5% had blood in urine.

Table 34: Comparison of Serum Urea (mg/dL) among outcome (N=249)

| | Outcome | Total |
|---|---|---|

| Serum Urea (mg/dL) | Transferred out | Continued in ICU | Demise | |
|---|---|---|---|---|
| Normal | 14 (100%) | 142 (88.8%) | 43 (57.3%) | 199 (79.9%) |
| Elevated | 0 (0%) | 18 (11.3%) | 32 (42.7%) | 50 (20.1%) |
| Total | 14 (100%) | 160 (100%) | 75 (100%) | 249(100%) |
| Chi square test – 35.13 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 34: Serum Urea (mg/dL) among outcome (N=249)



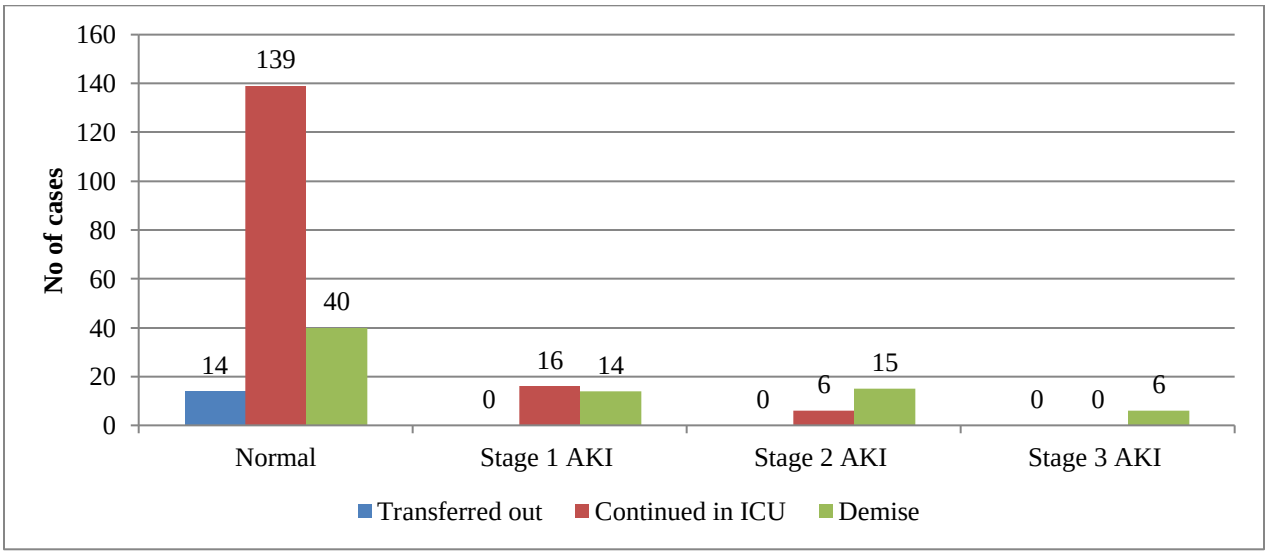

The chart depicts serum urea (mg/dL) among outcome which shows Chi square test of 35.13 with a p value of <0.001 which is statistically significant. Hence, there is correlation between elevated serum urea and outcome. Out of the patients who continued to be critically ill in the ICU and those who died 54% had elevated serum urea.

Table 35: Comparison of Serum Creatinine (mg/dL) on admission among outcome (N=250)

| Serum Creatinine (mg/dL) on admission | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Normal | 14 (100%) | 139 (86.3%) | 40 (53.3%) | 193 (77.2%) |
| Stage 1 AKI | 0 (0%) | 16 (9.9%) | 14 (18.7%) | 30 (12%) |
| Stage 2 AKI | 0 (0%) | 6 (3.7%) | 15 (20%) | 21 (8.4%) |

| | | | | |
|---|---|---|---|---|
| Stage 3 AKI | 0 (0%) | 0 (0%) | 6 (8%) | 6 (2.4%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 44.62 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 35: Serum Creatinine (mg/dL) on admission among outcome (N=250)

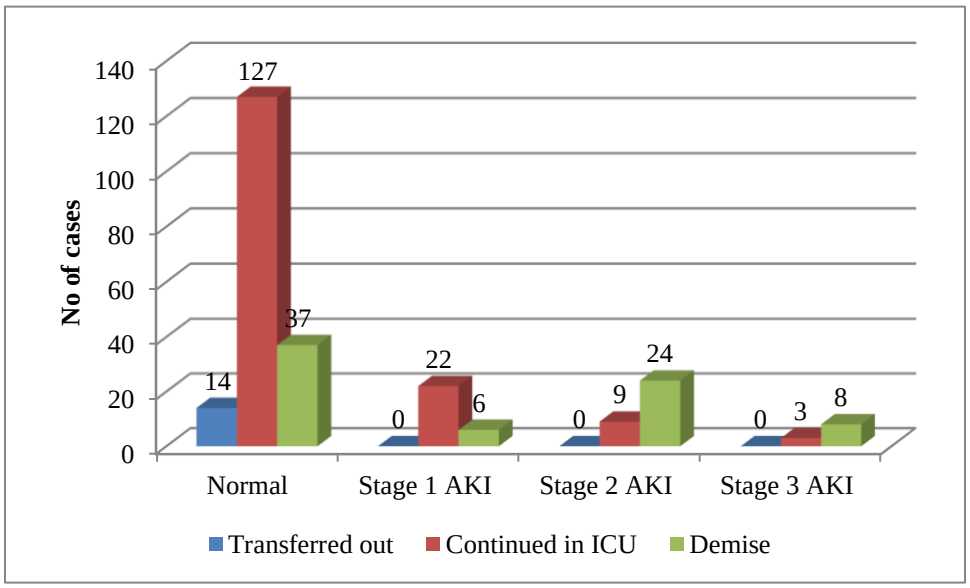



The chart depicts serum creatinine (mg/dL) on admission among outcome which shows Chi square test of 44.62 with a p value of <0.001 which is statistically significant. Hence, there is correlation between elevated serum creatinine on admission and outcome. Out of the patients who continued to be critically ill in the ICU and those who died 28.6% had stage 1, 23.7% had stage 2 and 8% had stage 3 AKI based on serum creatinine on admission.

Table 36: Comparison of Serum Creatinine (mg/dL) after 48 hrs among outcome (N=250)

| Serum Creatinine (mg/dL) after 48 hrs | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Normal | 14 (100%) | 127 (78.9%) | 37 (49.3%) | 178 (71.2%) |
| Stage 1 AKI | 0 (0%) | 22 (13.7%) | 6 (8%) | 28 (11.2%) |
| Stage 2 AKI | 0 (0%) | 9 (5.6%) | 24 (32%) | 33 (13.2%) |
| Stage 3 AKI | 0 (0%) | 3 (1.9%) | 8 (10.7%) | 11 (4.4%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 49.79 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 36: Serum Creatinine (mg/dL) after 48 hrs among outcome (N=250)



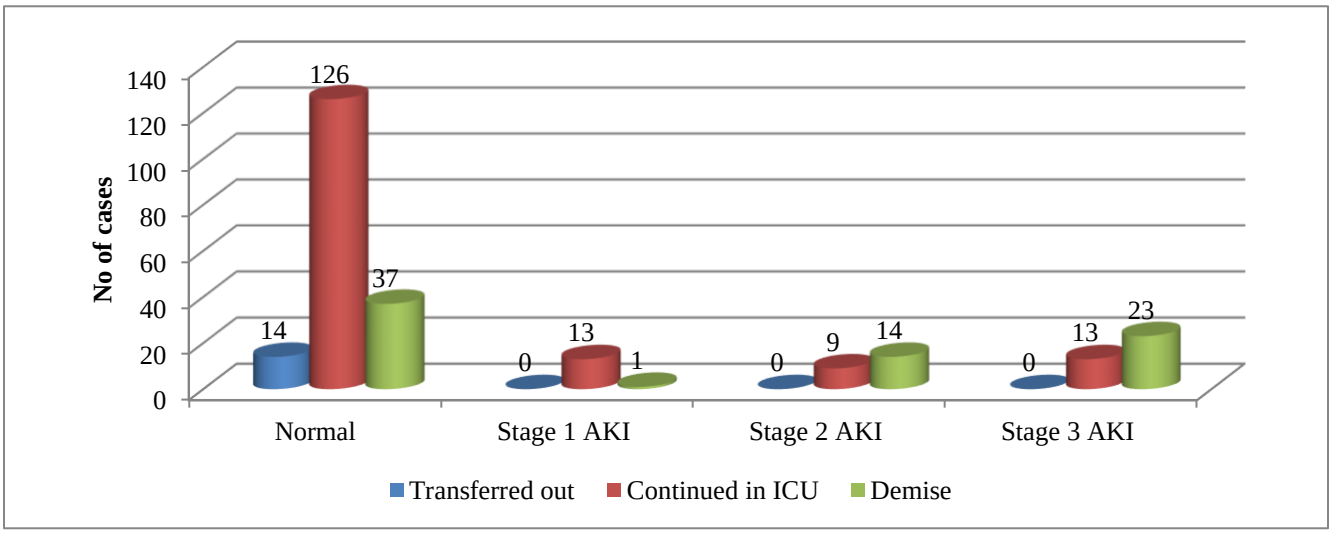

The chart depicts serum creatinine (mg/dL) at 48 hours among outcome which shows Chi square test of 49.79 with a p value of <0.001 which is statistically significant. Hence, there is correlation between elevated serum creatinine at 48 hours and outcome. Out of the patients who continued to be critically ill in the ICU and those who died 21.7% had stage 1, 37.6% had stage 2 and 12.6% had stage 3 AKI based on serum creatinine at 48 hours.

Table 37: Comparison of Serum Creatinine (mg/dL) at outcome among outcome (N=250)

| Serum Creatinine (mg/dL) at outcome | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Normal | 14 (100%) | 126 (78.3%) | 37 (49.3%) | 177 (70.8%) |

| | | | | |
|---|---|---|---|---|
| Stage 1 AKI | 0 (0%) | 13 (8.1%) | 1 (1.3%) | 14 (5.6%) |
| Stage 2 AKI | 0 (0%) | 9 (5.6%) | 14 (18.7%) | 23 (9.2%) |
| Stage 3 AKI | 0 (0%) | 13 (8.1%) | 23 (30.7%) | 36 (14.4%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 43.96 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 37: Serum Creatinine (mg/dL) at outcome among outcome (N=250)

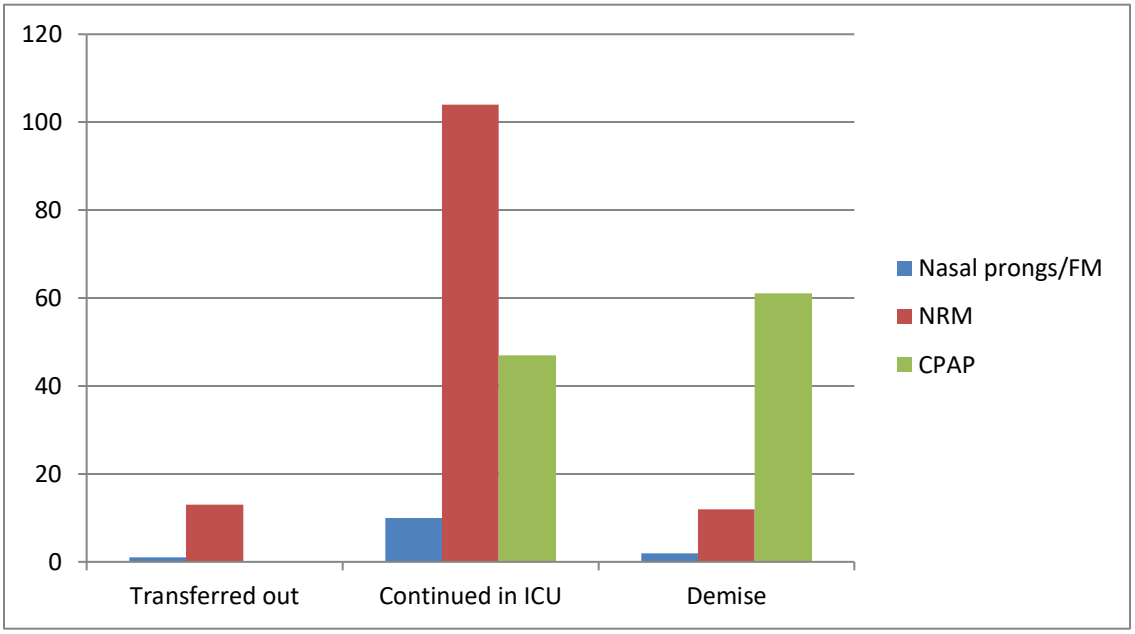



The chart depicts serum creatinine (mg/dL) at outcome among outcome which shows Chi square test of 43.96 with a p value of <0.001 which is statistically significant. Hence, there is correlation between elevated serum creatinine at outcome and outcome. Out of the patients who continued to be critically ill in the ICU and those who died 9.4% had stage 1, 24.3% had stage 2 and 38.8% had stage 3 AKI based on serum creatinine at outcome.

Table 38: Comparison of Oxygen Requirement (on admission) among outcome (N=250)

| Oxygen Requirement (on admission) | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Nasal prongs/FM | 1 (7.1%) | 10 (6.2%) | 2 (2.7%) | 13 (5.2%) |
| NRM | 13 (92.9%) | 104 (64.6%) | 12 (16%) | 129 (51.6%) |
| CPAP | 0 (0%) | 47 (29.2%) | 61 (81.3%) | 108 (43.2%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 68.26 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 38: Oxygen Requirement (on admission) among outcome (N=250)



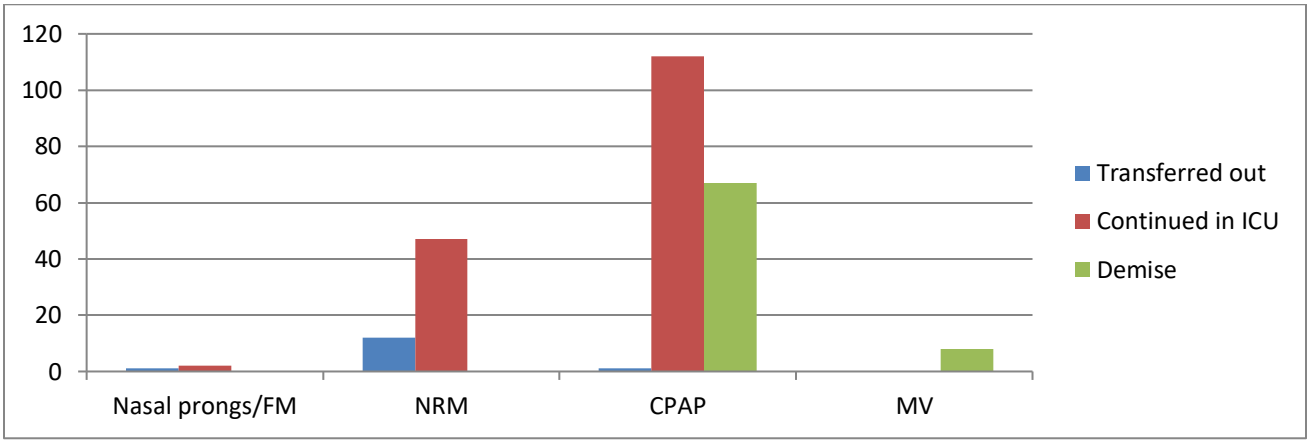

The chart depicts oxygen requirement (on admission) among outcome which shows Chi square test of 68.26 with a p value of <0.001 which is statistically significant. Hence, there is correlation between oxygen requirement (on admission) among outcome. Out of the patients who continued to be critically ill in the ICU and those who died 5.2% were on nasal prongs/face mask, 51.6% were on NRM, 43.2% on CPAP on admission.

Table 39: Comparison of Oxygen Requirement (after 48 hrs) among outcome (N=250)

| Oxygen Requirement (after 48 hrs) | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |

| | | | | |
|---|---|---|---|---|
| Nasal prongs/FM | 1 (7.1%) | 2 (1.2%) | 0 (0%) | 3 (1.2%) |
| NRM | 12 (85.7%) | 47 (29.2%) | 0 (0%) | 59 (23.6%) |
| CPAP | 1 (7.1%) | 112 (69.6%) | 67 (89.3%) | 180 (72%) |
| MV | 0 (0%) | 0 (0%) | 8 (10.7%) | 8 (3.2%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 77.85 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 39: Oxygen Requirement (after 48 hrs) among outcome (N=250)



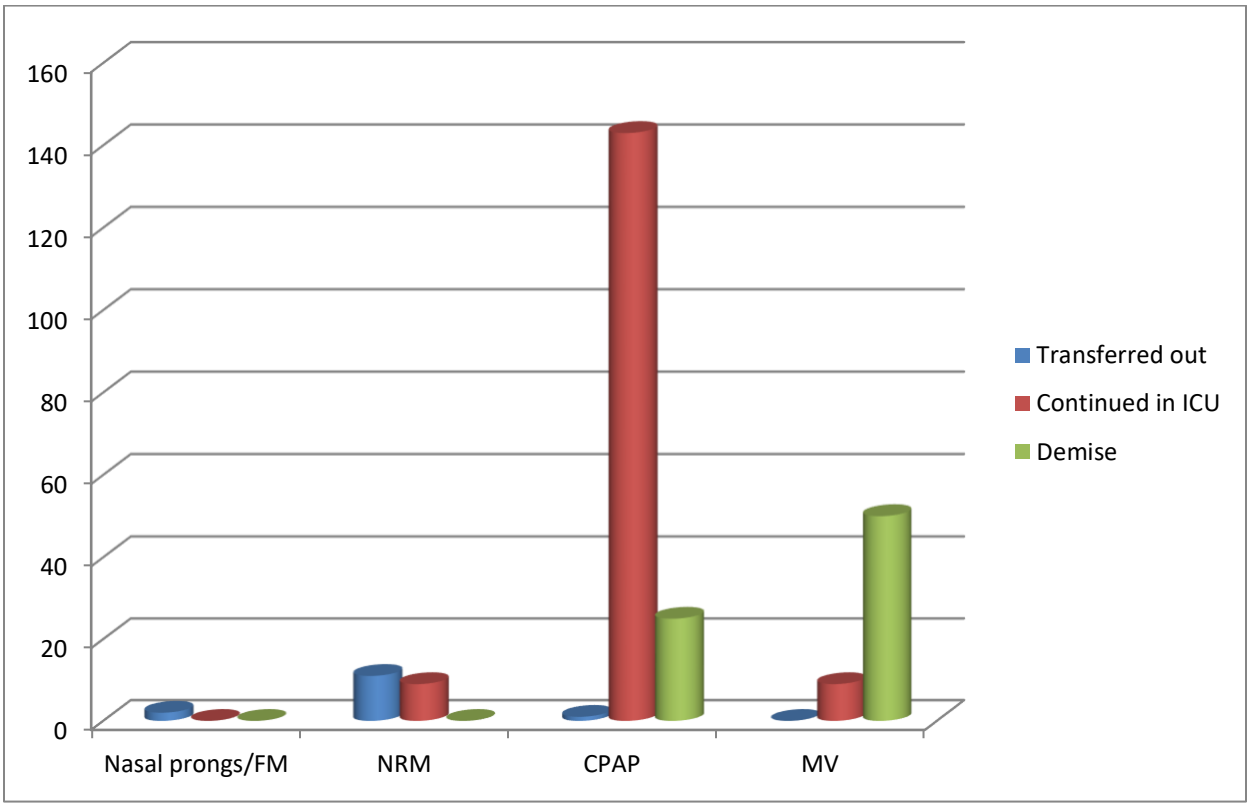

The chart depicts oxygen requirement (after 48 hours) among outcome which shows Chi square test of 77.85 with a p value of <0.001 which is statistically significant. Hence, there is correlation between oxygen requirement (after 48hrs of admission) among outcome. Out of the patients who

continued to be critically ill in the ICU and those who died 1.2% were on nasal prongs/face mask, 23.6% were on NRM, 72% on CPAP and 3.2% on MV after 48 hours.

Table 40: Comparison of OXYGEN REQIUREMENT (at end of study) among outcome (N=250)

| OXYGEN REQIUREMENT (at end of study) | Outcome | | | Total |
|---|---|---|---|---|
| | Transferred out | Continued in ICU | Demise | |
| Nasal prongs/FM | 2 (14.3%) | 0 (0%) | 0 (0%) | 2 (0.8%) |
| NRM | 11 (78.6%) | 9 (5.6%) | 0 (0%) | 20 (8%) |
| CPAP | 1 (7.1%) | 143 (88.8%) | 25 (33.3%) | 169 (67.9%) |
| MV | 0 (0%) | 9 (5.6%) | 50 (66.7%) | 59 (23.6%) |
| Total | 14 (100%) | 161 (100%) | 75 (100%) | 250 (100%) |
| Chi square test – 243.73 | | | | |
| P value – <0.001 (Significant) | | | | |

Figure 40: OXYGEN REQIUREMENT (at end of study) among outcome (N=250)




The chart depicts oxygen requirement (at end of study) among outcome which shows Chi square test of 243.73 with a p value of <0.001 which is statistically significant. Hence, there is correlation between oxygen requirement (at end of study) among outcome. Out of the patients who continued to be critically ill in the ICU and those who died 0.8% were on nasal prongs/face mask, 8% were on NRM, 67.9% on CPAP and 23.6% on MV at end of study.

Table 41: Consolidated comparison of Serum Urea and Creatinine (mg/dL) among Oxygen Requirement (on admission) (N=250)

| | Oxygen Requirement (on admission) | | | Total | P value |
|---|---|---|---|---|---|
| | Nasal prongs/FM | NRM | CPAP | | |
| Serum Urea (mg/dL) | | | | | |
| Normal | 12 (92.3%) | 117 (90.7%) | 70 (65.4%) | 199 (79.9%) | <0.001 |
| Elevated | 1 (7.7%) | 12 (9.3%) | 27 (36%) | 50 (20.1%) | |
| Serum Creatinine (mg/dL) on admission | | | | | |
| Normal | 12 (92.3%) | 115 (89.1%) | 66 (61.1%) | 193 (77.2%) | |

| | | | | | |
|---|---|---|---|---|---|
| Stage 1 AKI | 1 (7.7%) | 9 (7%) | 20 (18.5%) | 30 (12%) | <0.001 |
| Stage2 AKI | 0 (0%) | 4 (3.1%) | 17 (15.7%) | 21 (8.4%) | |
| Stage 3 AKI | 0 (0%) | 1 (0.8%) | 5 (4.6%) | 6 (2.4%) | |
| Serum Creatinine (mg/dL) after 48 hrs | | | | | |
| Normal | 12 (92.3%) | 104 (80.6%) | 62 (57.4%) | 178 (71.2%) | 0.001 |
| Stage 1 AKI | 1 (7.7%) | 13 (10.1%) | 14 (13%) | 28 (11.2%) | |
| Stage2 AKI | 0 (0%) | 9 (7%) | 24 (22.2%) | 33 (13.2%) | |
| Stage 3 AKI | 0 (0%) | 3 (2.3%) | 8 (7.4%) | 11 (4.4%) | |
| Serum Creatinine (mg/dL) at outcome | | | | | |
| Normal | 12 (92.3%) | 103 (79.8%) | 62 (57.4%) | 177 (70.8%) | <0.001 |
| Stage 1 AKI | 0 (0%) | 10 (7.8%) | 4 (3.7%) | 14 (5.6%) | |
| Stage2 AKI | 1 (7.7%) | 8 (6.2%) | 14 (13%) | 23 (9.2%) | |

| | | | | | |
|---|---|---|---|---|---|
| Stage 3 AKI | 0 (0%) | 8 (6.2%) | 28 (25.9%) | 36 (14.4%) | |

Table 42: Consolidated comparison of Serum Urea and Creatinine (mg/dL) among Oxygen Requirement (after 48 hrs) (N=250)

| | Oxygen Requirement (after 48 hrs) | | | | Total | P value |
|---|---|---|---|---|---|---|
| | Nasal prongs/FM | NRM | CPAP | MV | | |
| Serum Urea (mg/dL) | | | | | | |
| Normal | 3 (100%) | 56 (94.9%) | 136 (76%) | 4 (50%) | 199 (79.9%) | 0.002 |
| Elevated | 0 (0%) | 3 (5.1%) | 43 (24%) | 4 (50%) | 50 (20.1%) | |
| Serum Creatinine (mg/dL) on admission | | | | | | |
| Normal | 3 (100%) | 56 (94.9%) | 130 (72.2%) | 4 (50%) | 193 (77.2%) | 0.021 |
| Stage 1 AKI | 0 (0%) | 2 (3.4%) | 26 (14.4%) | 2 (25%) | 30 (12%) | |
| Stage2 AKI | 0 (0%) | 1 (1.7%) | 19 (10.6%) | 1 (12.5%) | 21 (8.4%) | |
| Stage 3 AKI | 0 (0%) | 0 (0%) | 5 (2.8%) | 1 (12.5%) | 6 (2.4%) | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Serum Creatinine (mg/dL) after 48 hrs | | | | | | |
| Normal | 3 (100%) | 50 (84.7%) | 121 (67.2%) | 4 (50%) | 178 (71.2%) | 0.112 |
| Stage 1 AKI | 0 (0%) | 7 (11.9%) | 20 (11.1%) | 1 (12.5%) | 28 (11.2%) | |
| Stage2 AKI | 0 (0%) | 2 (3.4%) | 29 (16.1%) | 2 (25%) | 33 (13.2%) | |
| Stage 3 AKI | 0 (0%) | 0 (0%) | 10 (5.6%) | 1 (12.5%) | 11 (4.4%) | |
| Serum Creatinine (mg/dL) at outcome | | | | | | |
| Normal | 3 (100%) | 50 (84.7%) | 120 (66.7%) | 4 (50%) | 177 (70.8%) | 0.016 |
| Stage 1 AKI | 0 (0%) | 6 (10.2%) | 8 (4.4%) | 0 (0%) | 14 (5.6%) | |
| Stage2 AKI | 0 (0%) | 1 (1.7%) | 20 (11.1%) | 2 (25%) | 23 (9.2%) | |
| Stage 3 AKI | 0 (0%) | 2 (3.4%) | 32 (17.8%) | 2 (25%) | 36 (14.4%) | |

Table 43: Consolidated comparison of Serum Urea and Creatinine (mg/dL) among OXYGEN REQIUREMENT (at end of study) (N=250)

| | OXYGEN REQIUREMENT (at end of study) | | | | Total | P value |
|---|---|---|---|---|---|---|
| | Nasal prongs/FM | NRM | CPAP | MV | | |
| Serum Urea (mg/dL) | | | | | | |
| Normal | 2 (100%) | 2 (100%) | 145 (86.3%) | 32 (54.2%) | 199 (79.9%) | <0.001 |
| Elevated | 0 (0%) | 0 (0%) | 23 (13.7%) | 27 (45.8%) | 50 (20.1%) | |
| Serum Creatinine (mg/dL) on admission | | | | | | |
| Normal | 2 (100%) | 20 (100%) | 141 (83.4%) | 30 (50.8%) | 193 (77.2%) | <0.001 |
| Stage 1 AKI | 0 (0%) | 0 (0%) | 18 (10.7%) | 12 (20.3%) | 30 (12%) | |
| Stage2 AKI | 0 (0%) | 0 (0%) | 9 (5.3%) | 12 (20.3%) | 21 (8.4%) | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Stage 3 AKI | 0 (0%) | 0 (0%) | 1 (0.6%) | 5 (8.5%) | 6 (2.4%) | |
| Serum Creatinine (mg/dL) after 48 hrs | | | | | | |
| Normal | 2 (100%) | 18 (90%) | 130 (76.9%) | 28 (47.8%) | 178 (71.2%) | <0.001 |
| Stage 1 AKI | 0 (0%) | 2 (10%) | 22 (13%) | 4 (6.8%) | 28 (11.2%) | |
| Stage2 AKI | 0 (0%) | 0 (0%) | 13 (7.7%) | 20 (33.9%) | 33 (13.2%) | |
| Stage 3 AKI | 0 (0%) | 0 (0%) | 4 (2.4%) | 7 (11.9%) | 11 (4.4%) | |
| Serum Creatinine (mg/dL) at outcome | | | | | | |
| Normal | 2 (100%) | 18 (90%) | 129 (76.3%) | 28 (47.5%) | 177 (70.8%) | <0.001 |
| Stage 1 AKI | 0 (0%) | 2 (10%) | 12 (7.1%) | 0 (0%) | 14 (5.6%) | |
| Stage2 AKI | 0 (0%) | 0 (0%) | 11 (6.5%) | 12 (20.3%) | 23 (9.2%) | |
| Stage 3 AKI | 0 (0%) | 0 (0%) | 17 (10.1%) | 19 (32.2%) | 36 (14.4%) | |

# RESULTS

1. The age distribution was 51-70 -65.60%, 41-50 years-16% and more than 70 years- 12.80%.

2. The gender distribution was male at 66.40% and female at 33.60%.

3. The travel history distribution was 60.8% with no travel history and 39.20% with positive travel history.

4. The contact with COVID 19 patients distribution was 52% with no history of contact and 48% with a history of contact with positive patients.

5. The comorbidities distribution was SHT-48%,DM-54.4%,Obesity – 44.8%,CAD-17.6%,CKD-13.2%,CVA- 12.58% and malignancy/immunosuppression – 14.4%

6. The habits distribution was no habits- 32%, alcohol – 56.8%, alocohol and smoking- 8.8%, smoking- 2.4%.

7. The symptoms distribution was fever-74.4%, cough- 70.4%, breathlessness-76.8%, anosmia – 61.6%, myalgia – 76%.

8. The time from onset of illness to hospital distribution was <1 week- 50%, >1 week – 45.2% and > 2 weeks 4.8%.

9. Comparison of mean age with outcome shows statistical significant correlation with p value of 0.630 by unpaired t test.

10. Comparison of age group with outcome shows statistical significant correlation with p value of 0.002.

11. Comparison of gender with outcome shows statistical significant correlation with p value of 0.044.

12. Comparison of travel history with outcome shows no statistical significant correlation with p value of 0.104.

13. Comparison of contact history with COVID 19 with outcome shows no statistical significant correlation with p value of 0.365.

14. Comparison of co-morbidities with outcome shows statistical significant correlation with p value of 0.126 for SHT, 0.361 for DM, 0.119 for obesity, 0.005 for CAD, 0.113 for CKD, 0.179 for CVA, 0.729 for malignancy/immunosuppression.

15. Comparison of habits with outcome shows no statistical significant correlation with p value of 0.054.

16. Comparison of symptoms with outcome shows statistical significant correlation with p value of 0.026 for fever, 0.352 for cough, 0.036 for breathlessness, 0.061 for anosmia and 0.412 for myalgia.

17. Comparison of time from onset of illness to hospital with outcome shows statistical significant correlation with p value of 0.008.

18. Comparison of USG ABD/PELVIS with outcome shows no statistical significant correlation with p value of 0.688.

19. Comparison of lymphocyte count (*109 ) with outcome shows highly statistical significant correlation with p value of 0.001.

20. Comparison of Hemoglobin (g/dl) with outcome shows highly statistical significant correlation with p value of 0.078.

21. Comparison of Platelet count (x109) with outcome shows highly statistical significant correlation with p value of 0.001.

22. Comparison of Random blood glucose (mg/dL) with outcome shows no statistical significant correlation with p value of 0.276.

23. Comparison of Sodium(in mEq/dL) with outcome shows statistical significant correlation with p value of <0.001.

24. Comparison of Potassium(in mEq/dL) with outcome shows statistical significant correlation with p value of <0.001.

25. Comparison of Bicarbonate (in mEq/dL) with outcome shows statistical significant correlation with p value of <0.001.

26. Comparison of AST/ALT (U/L) with outcome shows statistical significant correlation with p value of <0.001.

27. Comparison of Alkaline phosphatase (U/L) with outcome shows statistical significant correlation with p value of <0.001.

28. Comparison of total bilirubin (mg/dL) with outcome shows statistical significant correlation with p value of <0.001.

29. Comparison of albumin (mg/dL) with outcome shows statistical significant correlation with p value of <0.001.

30. Comparison of Urine sugar with outcome shows statistical significant correlation with p value of <0.001.

31. Comparison of Urine Pus cells with outcome shows statistical significant correlation with p value of <0.001.

32. Comparison of Urine protein/albumin with outcome shows statistical significant correlation with p value of <0.001.

33. Comparison of Blood in urine with outcome shows statistical significant correlation with p value of <0.001.

34. Comparison of Serum Urea (mg/dL) with outcome shows statistical significant correlation with p value of <0.001.

35. Comparison of Serum Creatinine (mg/dL) on admission with outcome shows statistical significant correlation with p value of <0.001.

36. Comparison of Serum Creatinine (mg/dL) after 48hours with outcome shows statistical significant correlation with p value of <0.001.

37. Comparison of Serum Creatinine (mg/dL) at outcome with outcome shows statistical significant correlation with p value of <0.001.

38. Comparison of Oxygen Requirement (on admission) with outcome shows statistical significant correlation with p value of <0.001.

39. Comparison of Oxygen Requirement (after 48hours) with outcome shows statistical significant correlation with p value of <0.001.

40. Comparison of Oxygen Requirement (at end of study) with outcome shows statistical significant correlation with p value of <0.001.

# DISCUSSION

1. Yichung Cheng et al, determined 7% prevalence of AKI in hospitalized COVID patients, 40% of which occurred within 1 week of admission. The study showed that the in-hospital mortality in patients with AKI stage 1, stage 2, and stage 3 was 62%, 77%, and 80%, respectively. AKI was associated with in-hospital mortality even after adjustment for confounders.

2. Claudio Ranco,Thiago Reid, Faeq Husain-Syed reviewed management of AKI in patients with COVID and reported symptoms ranging from mild proteinuria to progressive AKI requiring RRT.

3. Sreedhar Adapa et al, did a Cohort study and analyzed the impact of COVID 19 on patients with CKD and on RRT leading to acute kidney injury. The study l analyzed 101 patients who died from COVID-19 infection showed that 23% had AKI and 11% of patient had underlying CKD. BUN and myoglogin levels were higher in patients who died within 3 days and median time from hospitalization to death is 4 days. The analysis showed that elevated baseline serum creatinine, elevated BUN, peak serum creatinine > 1.5, proteinuria, hematuria, AKI stages 2 and 3 are all associated with mortality after adjusting for confounding factors.

4. Paul Gabarre et al, did a case series report on AKI in critically ill COVID 19 patients and reported the various mechanisms leading to kidney injury.

5. Xianghong Yang et al, did a systematic review and meta analysis on the prevalence and impact of AKI on COVID 19. It was concluded that the incidence of abnormal urine analysis and kidney dysfunction in COVID 19 was high and AKI was closely associated with severity and prognosis of COVID 19 patients.

6. Jamie S.Hirsch et al, studied AKI in patients hospitalized with COVID 19 andconcluded a strong link to respiratory failure.

7. Lili Chan et al, did a observational study on the incidence and outcomes of AKI in COVID 19 patients and reported worse association with poor recovery of kidney function.

8.Michael G Argenziano et al, characterized the clinical course of COVID 19 patients in the emergency department and concluded significant morbidity and mortality with high rates of AKI, dialysis and a bimodal distribution in time to intubation from symptom onset.

9.Jonge-Hoon Lim et al, studied the outcomes of COVID 19 in patients with AKI and reported low mortality rate among mild to moderate AKI.Patients those with ARDS and low albumin on admission developed severe AKI.

10. Joseph A Lewnard et al, made a study regarding the all-cause mortality during the COVID-19 pandemic in Chennai and observed that mortality in Chennai increased substantially but heterogeneously during the COVID-19 pandemic, with the greatest burden concentrated in disadvantaged communities. The reported COVID-19 deaths were greatly underestimated pandemic-associated mortality(39).

# CONCLUSION

COVID-19 infection is spreading rapidly and causing mortality daily worldwide. Unfortunately, knowledge about the novel virus is limited, and it causes a significant clinical threat to the general population and healthcare worker.

We conclude that:

a. The prevalence of AKI in our study was 29.2% which is high.
b. The prevalence of total AKI in our study was 29.2%
c. The prevalence of AKI among CKD patients in our study was 12.8%
d. The prevalence of AKI in patients with normal renal function in our study was 16.4%.
e. The mortality in our study was 30%.
f. The mortality rate among patients with AKI was 52%
g. The proportion of Stage 1 AKI patients requiring NRM was 10.2%, CPAP was 4.4% and MV was 0% at the end of the study.
h. The proportion of Stage 2 AKI patients requiring NRM was 1.7%,CPAP was 11.1% and MV was 25% at the end of the study.
i. The proportion of Stage 3 AKI patients requiring NRM was 3.4%,CPAP was 17.8% and MV was 25% at the end of the study.
j. Hence, it can be stated that as the AKI stage worsens the patient's oxygen requirement also increases. AKI indicated adverse outcome of the patients and is an important indicator of severity of COVID disease, faster progression, increased oxygen requirement and poor prognosis of the patient.

## LIMITATIONS

1. The study population were studied for only a period of 6 months during the first wave of entire pandemic.
2. Number of critically ill patients in the ICU is only a representative sample. The exact number of patients who had AKI in ICU was beyond the purview of the study.

## ANNEXURE I -BIBLIOGRAPHY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# ANNEXURE II- STUDY PROFORMA

## DEMOGRAPHIC DETAILS:

Name:
Age:

Gender:

Address:

Occupation:

Contact number:

Travel History:

History of contact with COVID19 positive patient:

Place of contact with COVID19 positive patient:

## CO-MORBIDITIES:

Hypertension:

Diabetes:

Coronary Artery Disease:

Chronic Obstructive lung disease:

Chronic Kidney Disease:

## DETAILS OF CHRONIC KIDNEY DISEASE:

Cause of CKD:

Any RRT:

If yes, details and duration of RRT:

Malignancy:

Immunosuppression:

## HABITS:

Smoking:

Alcohol consumption:

**PRESENTING SYMPTOMS: (Yes or No)**

Fever:

Cough:

Fatigue:

Diarrhea:

Anosmia:

Myalgia:

Time from onset of illness to hospitalization:

**RADIOLOGICAL FINDINGS:**

Chest X-ray or CT- Chest:

Unilateral or Bilateral finding:

No significant abnormality: Ultrasound Abdomen and Pelvis:

Table 1: Laboratory findings at admission,48 hours after admission and at discharge.

| Laboratory findings | At admission | 48 hours after admission | At discharge |
|---|---|---|---|
| Lymphocyte count (x $10^9$) | | | |
| Hemoglobin (g/dL) | | | |
| Platelet count (x$10^{9)}$ | | | |
| Random blood glucose (mg/dL) | | | |
| Serum Urea (mg/dL) | | | |
| Serum Creatinine (mg/dL) | | | |
| Serum electrolytes (in mEq/dL)<br>Sodium<br>Potassium | | | |

| | | | |
|---|---|---|---|
| Chloride<br>Bicarbonate | | | |
| Serum AST/ALT (U/L) | | | |
| Serum Alkaline phosphatase (U/L) | | | |
| Serum total bilirubin (mg/dL) | | | |
| Serum albumin (mg/dL) | | | |
| Urine protein/albumin | | | |
| Urine sugar | | | |
| Urine Pus cells | | | |

**OXYGEN REQUIREMENT: ( Yes/No):**

| MODE | At admission | After 48 hours | After one week |
|---|---|---|---|
| Nasal prongs/face mask | | | |
| Non-Rebreathing Mask | | | |
| Continuous Positive Airway Pressure | | | |
| Mechanical Ventilation | | | |

# ANNEXURE III- ETHICAL COMMITTEE CERTIFICATE

**GOVERNMENT STANLEY MEDICAL COLLEGE & HOSPITAL,CHENNAI_-01**

**INSTITUTIONAL ETHICS COMMITTEE**

| | |
|---|---|
| TITLE OF THE WORK | :"A DESCRIPTIVE STUDY TO ESTIMATE THE PREVALENCE OF ACUTE KIDNEY INJURY AND IT'S CORRELATION WITH SEVERITY OF ILLNESS AMONG CRITICALLY ILL **COVID 19** PATIENTS" |
| PRINCIPAL INVESTIGATOR | : DR.KIRUTHIKA SUBRAMANIYAN, |
| DESIGNATION | : PG IN GENERAL MEDICINE , |
| DEPARTMENT | : DEPARTMENT OF GENERAL MEDICINE, GOVT. STANLEY MEDICAL COLLEGE. |

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 03.11.2020 at the Council Hall, Stanley Medical College, Chennai-1 at 10am.

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

MEMBER SECRETARY, 8/1/20.
IEC, SMC, CHENNAI

# ANNEXURE IV-INFORMED CONSENT

TITLE: **"A CROSS SECTIONAL STUDY TO ESTIMATE THE PREVALENCE OF ACUTE KIDNEY INJURY AND IT'S CORRELATION WITH SEVERITY OF ILLNESS AMONG CRITICALLY ILL COVID 19 PATIENTS"**

**Place of study: Govt. Stanley Hospital, Chennai**

The content of the information sheet dated _____ that was provided have been read carefully by me/explained in detail to me, in a language that I comprehend and fully understood the contents. I confirm that I have had the opportunity to ask questions.

The nature and purpose of the study and its potential risks/benefits and expected duration of the study and other relevant details of the study have been explained to me in detail.

I understand that my participant is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal right being affected.

I agree to take part in the above study

_____

(Signature/Left thumb impression)

Name of the Participant: _____

Son/Daughter/Spouse of _____

Complete postal address: _____

This is to certify that the above consent has been obtained in my presence.

_____ Date:

Signature of the principal investigator Place:

1)Witness – 1 2) Witness – 2

_____ _____

Signature: Signature:

Name: Name:

Address: Address:

# INFORMED CONSENT

## தகவல் தொடர்பு ஒப்புதல் படிவம்

**“A CROSS SECTIONAL STUDY TO ESTIMATE THE PREVALENCE OF ACUTE KIDNEY INJURY AND IT’S CORRELATION WITH SEVERITY OF ILLNESS AMONG CRITICALLY ILL COVID 19 PATIENTS”**

நான்தகவல்நகலில்கொடுக்கபட்டுள்ளமுழுவிவரங்களையும்கவனமாகப் படித்தேன்/
ஆய்வின்முழுவிவரங்களையும்தமிழில்எனக்குவிளக்கமாகஎடுத்துக்குறப் பட்டது.

நான் இந்தஆய்வின்விவரங்களைமுழுமையாகபுரிந்துகொண்டேன்.

மேலும்,
நான்எந்தஒருவேளையிலும்ஆய்வில்இருந்துதிரும்பமுடியும்என்றும், அதன்பின்னர்நான்வழக்கம்போல்மருத்துவச்சிகிச்சைப்பெறமுடியும்என் றும்புரிந்துக்கொள்கிறேன்.

நான்ஆய்வில்பங்குகொள்ளபணம்எதையும்பெறமுடியாதுஎன்றுஅரிந்துள் ளேன்.

நான்இந்தஆய்வில்பங்குஎடுப்பதன்மூலம்நான்என்னசெய்ய போகிறேன்என்றுதெரியும்.

நான்இந்தஆய்வில்என்முழுஒத்துழைப்பையும்கொடுப்பேன்என்றுஉறுதி யளிக்கின்றேன்.

ஆய்வில்பங்கேற்பவர்பெயர்: சாட்சி:

பெயர்மற்றும்முகவரி: பெயர்மற்றும்முகவரி:

கையொப்பம்/விரல்ரேகை
கையொப்பம்/விரல்ரேகை

ஆராய்ச்சியாளராக

கையொப்பம்மற்றும்தேதி

## ANNEXURE V-MASTERCHART