# ACUTE RESPIRATORY FAILURE AT THE ACCIDENT AND EMERGENCY DEPARTMENT, KENYATTA NATIONAL AND REFERRAL HOSPITAL, NAIROBI, KENYA.

A dissertation submitted as part fulfillment of the requirements for the degree of Master of Medicine in Internal Medicine, University of Nairobi, by:

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University of Nairobi, 2009.

## DECLARATION.

I declare that this is my original work and has not been presented for a degree award elsewhere.

Signed.....

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## DEDICATION:

To my loving wife Naomi, who stood with me all the way.

To my lovely children (Bera, Geoffrey and Pauline) for giving me a reason to aspire.

To my parents and siblings for constant encouragement.

To God Almighty for making it all possible.

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To many others whose diverse input made the completion of this study possible.

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## ABBREVIATIONS:

ABG.....Arterial Blood Gases.

ALI.....Acute Lung Injury.

A&E.....Accident and Emergency

ARDS.....Acute Respiratory Distress Syndrome

ARF.....Acute Respiratory Failure

AVM.....Arterio-Venous Malformation

CNS.....Central Nervous System

COPD..... Chronic Obstructive Pulmonary Disease

CXR.....Chest X-Ray

ECG..... Electrocardiogram

$FEV_1$.....Forced Expiratory Volume in one second.

$FiO_2$..... Fraction of inspired Oxygen

HIV..... Human Immunodeficiency Virus

HRCT..... High Resolution Computer Tomography Scan

ICU..... Intensive Care Unit.

JVP..... Jugular Venous Pressure

KNH..... Kenyatta National Hospital

MI..... Myocardial Infarction

MS..... Mitral Stenosis

PEFR..... Peak Expiratory Flow Rate

PI .....Principal Investigator

PTB..... Pulmonary tuberculosis

PTE..... Pulmonary Thromboembolism

V/Q..... Ventilation/Perfusion ratio.

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# 1.0: ABSTRACT:


***Background:***

Acute respiratory failure (ARF) is a common presentation at the Accident and Emergency (A&E) department. Delay or failure to identify ARF can result in significant morbidity and mortality. Advances in assisted respiratory support and oxygen therapy for patients in ARF have had a positive impact on overall prognosis. The burden of ARF at the Kenyatta National Hospital (KNH) Accident and Emergency (A&E) department is unknown. Outcome in both short and long-terms in and out of hospital is unknown, too.

***Objective:***

The main objective of this study was to determine the prevalence of acute respiratory failure, identify the causes and document the outcome up to two weeks in hospital in patients presenting with acute dyspnoea to the A&E department of KNH.

***Methods:***

In this prospective descriptive study, all patients aged 13years or more, presenting to the A&E department, KNH with acute dyspnoea were screened for clinical as well as laboratory evidence of ARF by pulse oximetry and baseline arterial blood gas analysis (ABG). A chest radiograph was taken in all patients. Other tests were done as clinically indicated and all findings documented. The primary clinical diagnosis associated with the ARF was determined and documented. Patients were followed up by alternate day ABG till death/recovery or till the fourteenth day of hospitalization, whichever came earlier. The outcome was documented.

***Outcome Measures:***

Outcome events were either full recovery from ARF, persisting respiratory failure (acute evolving into chronic) or death. The time duration to each outcome was documented.

***Results:***

Thirteen thousand and three patients age $\geq$ 13 years were seen at the Accident and Emergency department during the study period. Two hundred and eighty six of them presented in acute dyspnoea, and 83 were in ARF. The period prevalence of ARF was 0.6% (95% CI, 0.47-0.73),

with 29.02% (95% CI, 28.2-29.8) of all acutely dyspnoeic patients in ARF. Majority of patients (65.1%) were male. M: F ~ 2:1. Most patients were young, with peak age as 31-40 years of age. Most patients presented with symptoms of ≤ 2 days in duration, which was significantly associated with an adverse outcome (OR 4.135, p-value 0.003). Acute trauma was the commonest cause of ARF. Central causes of ARF were significantly associated with an adverse outcome. 65.1% 0f all patients in ARF died within eight days of presentation. Most deaths occurred in the A&E department while awaiting ICU admission.

***Conclusion:***

Acute respiratory failure is common among patients presenting in acute dyspnoea, affecting younger patients. Trauma is the commonest cause of ARF. ARF is associated with a high mortality rate. Patients presenting in ARF due to central disorders and those with symptoms of ≤ 2 days in duration are at the highest risk of mortality.

## 2.0: LITERATURE REVIEW.

### 2.1: Introduction:

The respiratory system consists anatomically of the lungs as the gas exchanging organ and a pump that ventilates them. The pump consists of the respiratory muscles, namely, the diaphragm and the external intercostal muscles.

Air accesses the gas exchange units (alveoli) via a conduction system consisting of the upper and lower airways. The upper airway is made up by the nose, mouth, pharynx and the trachea. The lower airway is made up of the generations of the bronchial tree from the primary bronchi, all the way to the terminal bronchioles. [1]

The gas exchange unit consists of the respiratory bronchioles, the alveolar ducts and the alveoli. It is across the membrane of this unit that oxygen is transferred by diffusion to arterial blood, and carbon dioxide diffuses from blood to the alveoli and is expired. This gas exchange by diffusion is driven by the concentration gradient of gases between the pulmonary circulation and the alveolar sacs.

Normally, the alveoli have a higher content of oxygen than the pulmonary venous circulation, while carbon dioxide concentration is higher in the pulmonary venous circulation. This scenario may undergo fundamental disruption in disease. [2]

Spontaneous respiration is the result of rhythmic discharge of motor neurons that innervate the respiratory muscles. This discharge is totally dependent on nerve impulses from the brain; hence, transection of the spinal cord above the origin of the phrenic nerve abolishes breathing. [1, 2]

The rhythmic discharges from the brain that produce spontaneous respiration are in turn regulated by alternations in arterial oxygen, carbon dioxide and hydrogen ion concentrations (chemical control), sensed in the pons, medulla, carotid and aortic bodies.

This chemical control of breathing is supplemented by non-chemical influences that are either voluntary or involuntary. The voluntary control system is located in the cerebral cortex and sends

impulses to the respiratory motor neurons via the corticospinal tracts. The autonomic system is driven by a group of pacemaker cells in the medulla. Impulses from these cells activate motor neurons in the cervical and thoracic spinal cord that innervate inspiratory muscles. Those in the cervical cord activate the diaphragm via the phrenic nerves, and those in the thoracic spinal cord activate the external intercostals muscles, internal intercostals muscles and other expiratory muscles. [1, 2]

The pulmonary circulation is equally important in respiratory function. The venous component delivers carbon dioxide to the lungs from the body, while the arterial component takes up oxygen from the alveoli and transports it to the rest of the body. The function of pulmonary circulation is in turn dependent on cardiac function and pulmonary vascular resistance. [1, 2]

Any disease process that affects the function of any of these components of the respiratory system can potentially lead to respiratory failure. Disorders affecting the higher centers that control respiration, the upper airway, the pump or the gas exchange units form the bulk of etiology of acute respiratory failure. [1, 2]

## 2.2: Definition of acute respiratory failure:

**Acute respiratory failure** (ARF) is characterized by inability to maintain adequate oxygenation; or ventilation that develops over a short period of time. The time period is hours to days, not exceeding two weeks. [3]

The oxygenation criteria defining ARF are: oxygen saturations ($SaO_2$) of less than or equal to 92% by pulse oximetry and hypoxemia ($PaO_2 \leq 60$mmHg or $\leq 8$KPa) on arterial blood gas (ABG) analysis. [3] The ventilation criteria for ARF are hypercapnia ($PaCO_2 \geq 45$mmHg or $\geq 6$ KPa) or an increase of more than 10mmHg over the baseline $PaCO_2$ on ABG. [3] The acid-base dysregulation criteria defining ARF is the presence of respiratory acidosis ($pH \leq 7.35$). These oxygenation, ventilation and acid base abnormalities occur while the patient is breathing room air. [3]

Acute respiratory failure is a life threatening condition, and its early diagnosis and management is important in the survival of the acutely ill patient. Patients in ARF are severely ill and often require respiratory support. The primary cause of ARF must also be sought and managed in order to improve the prognosis.

## 2.3: Epidemiology of acute respiratory failure.

The exact incidence/prevalence of ARF in the outpatient emergency setting is unknown. This is largely attributable to the fact that ARF is a syndrome, rather than a single clinical diagnosis. In the USA, the incidence of ARF is estimated at 360,000 cases per year, with mortality rates of 30-40%. **[5, 23]**

From a multinational study conducted in Germany, Sweden, Denmark and Iceland, the incidence was estimated at 77.6-88.8 per 100,000 population per year, with 40% mortality. These are, however estimates from ICU settings. **[6, 7]**

The incidence of ARF due to acute lung injury in USA was noted to increase with age, from 16 per 100,000 person years for the 15-19 year age group to 306 per 100,000 person years for people between 75 and 85 years of age. It is estimated that there are 190,600 cases of ALI, associated with 74500 deaths and 3.6 million hospital days annually in the USA. Between 1999 and 2000 ***Gordon et al*** in a study of 1113 adult subjects on mechanical ventilation for acute lung injury found a mortality of 38.5%. Mortality increased with age from 24% for patients of 15-19 years of age to 60% for patients over 58 years of age ($p<0.001$). **[54]**

ARF is a common diagnosis among medical patients admitted to ICUs, and carries a high mortality. It is however noteworthy that this mortality is significantly dependent on other co-morbidities, usually leading to multiple organ failure. **[5, 6, 7, 8, 9]** Both the incidence of and the mortality from ARF increase exponentially with age and in the presence of other co-morbid conditions. **[10]**

Recent advances in mechanical ventilation and airway management, coupled with better diagnostic technology have improved the prognosis of patients with ARF. **[10]**

Epidemiologic data on ARF in the outpatient setting is lacking throughout the world. The incidence, prevalence and outcome of ARF in our setting have not been studied, yet conditions that could potentially result in ARF are prevalent at the A&E Department of KNH.

## 2.4: Classification of acute respiratory failure:

Acute respiratory failure (ARF) can be classified based on pathophysiologic derangements into: [2, 3, 4, 31]

### 2. 4.1: Acute hypoxemic respiratory failure:

Acute hypoxemic ARF is also called type 1 ARF. It is characterized by decreased $PaO_2$ and a normal or low $PaCO_2$. Type 1 ARF is the result of ventilation/perfusion mismatch. Oxygen delivery to the alveoli and subsequent diffusion into pulmonary arterial system is inadequate, and oxygenation of hemoglobin in arterial blood is suboptimal.

Hypoxemia is commonly the result of; **shunt** that occurs when areas of lung are perfused but not ventilated leading to hypoxemia that does not correct with increasing the fraction of inspired oxygen ($FiO_2$); **ventilation/perfusion** (V/Q) **mismatch**: uncommonly due to **a diffusion block** resulting from marked thickening of the interstitial space between the alveolar space and the capillary; **low $FiO_2$** ; or **hypoventilation** in patients with decreased respiratory drive, including neuromuscular disease, narcotic drug overdose or sleep apnea.

The distinction between V/Q mismatch and shunt can be made by assessing the response of oxygen supplementation or calculating the shunt fraction following inhalation of 100% oxygen.

### 2. 4.2: Acute hypercapnic ARF.

Hypercapnic ARF is also called type 2 ARF. At a constant rate of $CO_2$ production, $PaCO_2$ is determined by the level of alveolar ventilation. A decrease in alveolar ventilation can result from a decrease in the overall (minute) ventilation or an increase in the proportion of dead space ventilation.

A decrease in minute ventilation is observed primarily in the setting of neuromuscular disorders and CNS depression, and results in the inability to effectively eliminate carbon dioxide, hence hypercapnia.

The consequences of hypercapnia are hypoxemia, acidemia, tachycardia, decreased blood pressure, decreased work of breathing and changes in cerebral vascular autoregulation. In pure hypercapnic ARF, any existent hypoxemia is easily corrected with oxygen therapy.

### 2.4. 3. Mixed type ARF.

In this form of ARF both hypoxemia and hypercapnia occur on ABG.

## 2.5: Etiology and Pathophysiology of ARF.

Acute respiratory failure can result from disease process that affect any part of the different components of the respiratory system, either singly or in combination. Therefore, ARF could arise from dysfunction of the controller (CNS), Pump (respiratory musculature), Airways, Alveolar compartment or the pulmonary vasculature. **[2, 23, 25, 27]**

### 2.5.1: Dysfunction in the central control of respiration:

Central apnea as a cause of ARF is rather rare. It can be an enormous diagnostic challenge in the very ill patient, or in the intubated patient. Careful history and observation of the rate and pattern of respiration does give strong indications of controller dysfunction. The most frequent cause of controller dysfunction is the presence of medications that impair respiratory drive, many of which also impair the level of consciousness.

A history of use of respiratory depressants or an impaired level of consciousness prior to the administration of medication to facilitate intubation strongly suggests the possibility of controller dysfunction. **[2, 26]**

Clinically, the minimally sedated patient with a defect in regulating respiratory drive typically presents with either significant hypercapnia, or hypoxemia or both. Such a patient demonstrates no elevation in respiratory rate, and no use of accessory muscles of respiration. This is explained by impaired ventilation as well as impaired carbon dioxide clearance in the patient with impaired

central respiratory dysfunction. As a result, oxygen entry to the alveoli as well as carbon dioxide transfer out of the alveoli (i.e. Inspiration and expiration) are both impaired. **[2, 23]**

In pure controller failure, as occurs in opiate overdosage, the degree of hypoxemia is directly proportional to the degree of hypercapnia. This can be calculated from measured arterial blood gases (ABG). **[2, 25]**

In outpatient settings, formal testing of controller function can be done by determining if the respiratory rate increases to at least 25 breaths per minute when the patient inhales a mixture of 5% carbon dioxide and 15% oxygen ( the $CO_2$ challenge test) and measuring the pressure generated 0.1 seconds after the start of inhalation ( the $P_{0.1}$ test). **[2, 24]**

Common causes of central nervous system disorders leading to ARF include: ***Drugs*** such as the sedatives, hypnotics, opioids, and anesthetic agents; ***Brain stem respiratory center disorders*** including trauma, stroke, tumors, hypothyroidism: ***intracranial hypertension; CNS infections; Hypothermia post-operatively*** and ***chronic obstructive or interstitial lung disease.*** **[2, 24, 26, 27]**

**2.5.2: Respiratory muscle dysfunction:**

Pump dysfunction is a more common cause of ARF in both outpatient and Intensive Care Unit settings. In outpatient (non-intubated), pump failure manifests with tachypnoea, and reduced excursions of the intercostals muscles and diaphragm. The patient may have paradoxical respiratory motions and overt signs of fatigue. **[2, 11, 12]**

Failure of the respiratory muscles leads to impairment of inspiration, which is an active process. The result is a marked reduction in alveolar ventilation and severe hypoxemia. Carbon dioxide production in the body tissues is increased as a result of anaerobic respiration as well as reduced carbon dioxide elimination via the respiratory system. Hypercapnia is therefore not unexpected. **[2, 11, 12]**

Common causes of pump failure include:

***Chest wall, diaphragm, and pleural disorders*** such as Rib fracture, Flail chest, Pneumothorax, Pleural effusion, massive ascitis, abdominal distention and abdominal compartment syndrome **[12, 13, 14, 15, 27]**;

***Primary neuromuscular disease*** such as Guillain-Barre syndrome, myasthenia gravis, poliomyelitis, polymyositis, and myopathy **[11, 16, 27]**;

***Drug or Toxin- induced*** such as botulism, organophosphates, aminoglycosides, neuromuscular blocking agents, steroids, and snake venom **[17, 27, 57, 58]**

***Metabolic abnormalities*** such as ***hypothyroidism***, hypophosphatemia, and hypokalemia. **[18, 27]**;

***Spinal cord and nerve root disorders*** such as spinal cord injury, phrenic nerve injury/dysfunction, paraneoplastic syndrome, and polyradiculopathy of critical illness. **[19, 20, 27]**

**2.5.3: Airway dysfunction:**

Airway obstruction or narrowing from whatever etiology is the commonest cause of airway dysfunction with consequent ARF. **[2, 21, 27]**

Careful history and physical examination usually suffices in diagnosing airway dysfunction. Stridor suggests the presence of large airway or laryngeal obstruction. Detection of wheezing/ronchi on auscultation is diagnostic of bronchospasm. Coarse breath sounds or ronchi during the inspiratory phase of respiration indicates obstruction of large airways, frequently from retained secretions. High pitched wheezing during expiration indicates obstruction of the small airways and is commonly associated with bronchospasm. **[2, 21, 22]**

In cases of severe airflow obstruction, wheezing may be reduced because airflow is minimal. In these cases, the obstruction may be manifest as dynamic hyperinflation or intrinsic positive end expiratory pressure (auto-PEEP), and detected by persistent faint wheezing that continues throughout expiration to the point of initiation of the subsequent inspiration. **[2, 28, 29]** Because airway obstruction impairs both ventilation and carbon dioxide elimination, most cases of severe airway obstruction results in a combination of hypoxia and hypercapnia. **[29]**

Diagnostic tests for airway obstruction include pulmonary function testing, functional response to bronchodilators, chest radiography, bronchoscopy, C.T imaging and occasionally lung biopsy. **[28, 29]**

Common causes of airway dysfunction include: ***asthma, acute exacerbations of chronic bronchitis or emphysema, bronchiolitis, obstruction of pharynx, larynx, trachea, mainstem bronchus, or lobar bronchus by edema, mucus, mass, or foreign body.*** **[2, 27, 31]**

**ARF in asthma**

The pathophysiologic hallmark of asthma is a reduction in airway diameter brought about by contraction of smooth muscle, vascular congestion, edema of the bronchial wall, and thick, tenacious secretions. The net result is an increase in airway resistance, a decrease in Forced Expiratory Volumes (FEV) and flow rates, hyperinflation of the lungs and thorax, increased work of breathing, alterations in respiratory muscle function, changes in elastic recoil, abnormal distribution of both ventilation and pulmonary blood flow with V/Q mismatch, culminating in altered arterial blood gas concentrations.

Thus, although asthma is considered to be primarily a disease of airways, virtually all aspects of pulmonary function are compromised during an acute attack. In addition, in severely symptomatic patients, there frequently is electrocardiographic evidence of right ventricular strain acutely, and hypertrophy in the long term with eventual pulmonary hypertension. When an acutely ill patient presents for therapy, the $FEV_1$, or PEFR is typically <40% of predicted. In keeping with the alterations in mechanics, the associated air trapping is substantial. In acutely ill patients, residual volume frequently approaches 400% of normal, while functional residual capacity doubles. **[2, 28, 30, 31]**

Hypoxia is a universal finding in acute asthmatic attacks owing to a precipitous decrease in ventilation, but frank ARF is relatively uncommon, being observed in 10-15% of patients presenting for therapy in the USA. **[29]**

Most patients with mild to moderately severe asthma have hypocapnia and respiratory alkalosis. **[28, 32]** Severe asthmatic attacks are associated with hypercapnia and respiratory acidosis. **[29]**

In acutely ill patients, the finding of a normal $PaCO_2$ tends to be associated with quite severe levels of airway obstruction. Consequently, when found in a symptomatic individual, it should be viewed as representing impending respiratory failure, and the patient should be treated accordingly. **[2, 29]**

Equally, the presence of metabolic acidosis in the setting of acute asthma signifies severe obstruction. **[2, 29]**

Cyanosis is a very late sign of ARF in acute asthma. **[2]** All acutely ill asthmatic patients with suspected alveolar hypoventilation must have ABG measurements, alongside lung volumes and airflow measurements. **[29]**

**ARF in acute exacerbation of COPD.**

Patients with COPD have very limited respiratory reserve owing to chronic obstruction, reduced elastic recoil and altered pulmonary circulation due to the often elevated pulmonary vascular pressure. This, therefore results in altered ventilation/ perfusion matching. Indeed many of these patients have a variable degree of chronic respiratory failure. **[33, 36]**

Acute exacerbations worsen the obstruction owing to further bronchoconstriction and mucus secretion with plugging of airways. This leads to deterioration in air flows, and severely impairs pulmonary function. Pulmonary infection is a frequent cause of exacerbations of COPD. Sepsis increases oxygen demand by raising metabolic rate. Carbon dioxide production is increased. Consequently, a concomitant increase in respiration is inevitable. In these patients with an already limited functional respiratory reserve, less than adequate adaptation often culminates in Acute on chronic respiratory failure. **[34, 35]**

When $FEV_1$ drops<50%, $PaO_2$ begins to decline; and PaCO2 elevation is observed with $FEV_1$<25% of predicted. **[34]**

Pulmonary hypertension severe enough to cause cor-pulmonale and RVF due to COPD occurs only in patients with marked decrease in $FEV_1$ (<25% of predicted), together with chronic

hypoxemia ($PaO_2$<55mmHg), and is exacerbated by increase in oxygen demand as occurs with infection, exercise as well as change in altitude. **[2, 34, 35]**

Non-uniform ventilation and V/Q mismatching are characteristic of COPD, reflecting the heterogeneous nature of the disease process within the airways and the lung parenchyma. V/Q mismatching accounts for essentially all the reduction in $PaO_2$ that occurs in COPD. Shunting is minimal. This finding explains the effectiveness of modest elevations of inspired oxygen in treating COPD, and therefore the need to consider problems other than COPD when hypoxemia is difficult to correct with modest levels of supplemental oxygen in the patient with COPD. **[2, 34, 37]**

Patients with acute exacerbations are diagnosed on history. They are typically patients known to have stable COPD but with acute onset of dyspnoea and other features of acute deterioration in respiratory function. Indeed, the patient may even come in frank respiratory failure. ABG assessment, chest imaging, Full blood count as well as sputum microscopy, culture and sensitivity are the usual tools for evaluating such patients. In contrast to its utility in the management of exacerbations of asthma, measurement of pulmonary function has not been demonstrated to be helpful in the diagnosis or management of exacerbations of COPD. **[2, 34]**

Typically, acute exacerbations of COPD are characterized by a combination of hypoxemia and hypercapnia. **[2, 34]**

**ARF in acute upper airway obstruction:**

Upper airway obstruction is a medical emergency. Complete airway obstruction abolishes ventilation, leading to death in a short period of time due to the resultant acute hypoxemia. **[38]**

In the unconscious patient, obstruction is often due to occlusion by the tongue or soft tissues of the pharynx. **[38]** Obstruction due to a foreign body lodged in the upper airway calls for immediate removal of it, or emergency establishment of alternative airway, e.g. tracheostomy. Forceful diaphragmatic thrust can facilitate removal of the foreign body. Occasionally, removal may require laryngoscopy and removal with forceps. **[38]**

**2.5.4: Alveolar compartment dysfunction**:

The alveolar compartment is the exact site for gaseous exchange. It is across the alveolo-capillary space that oxygen diffuses from the alveolar sac into the pulmonary arterial circulation while carbon dioxide diffuses from pulmonary veins into the alveoli. Any pathologic process that interferes with this space impairs respiration. [1, 2] This compartment can be assessed at the bedside, in addition to gas exchange measurements. Findings on physical examination that are suggestive of consolidation, such as bronchial breath sounds, dullness to percussion, and egophony, establish a diagnosis of alveolar compartment dysfunction. [2]

Lung stiffness as reflected in static respiratory system compliance can be assessed by measuring the distending pressure required to inflate the lung once inspiratory flow has ceased. This is calculated by measuring the end-inspiratory plateau pressure and dividing the inspiratory volume by end-inspiratory plateau pressure minus whatever level of PEEP is being applied. Normal value of static respiratory system compliance is 35 to 50ml/cm$H_2O$. Values <30 during conventional tidal volume inflation indicate increased stiffness of the lung, chest wall or both. Such increase in stiffness compromises ventilation. [2]

The chest radiograph is also very important in diagnosing alveolar compartment dysfunction. Radiographic densities consistent with airspace disease point to alveolar infection, injury, or flooding, and, together with a reduced lung compliance and reduced arterial oxygen level, favour a diagnosis of alveolar compartment dysfunction. [2]

ABG show a combination of hypoxemia and hypercapnia. [2]

Common causes of alveolar compartment dysfunction include:

***Pulmonary edema***

Increased hydrostatic pressure as occurs in acute left ventricular failure (e.g. MI, heart failure), acute mitral regurgitation, left atrial outflow obstruction (e.g. in MS), volume overload states, resulting in cardiogenic pulmonary edema. Increased pulmonary capillary permeability as occurs in Acute Respiratory Distress Syndrome (ARDS) and Acute Lung Injury (ALI) also result in pulmonary edema. Pulmonary edema of unclear etiology occurs as neurogenic pulmonary

edema, with negative pressure (Inspiratory airway obstruction), with reexpansion following management of lung collapse, and has been seen in association with the use of tocolytics in obstetric practice. **[2, 31]**

*Parenchymal lung disorders*

Parenchymal lung pathology such as pneumonia, interstitial lung disease, diffuse alveolar hemorrhage syndromes, aspiration and lung contusion also result in dysfunction of the alveolar compartment. **[2, 31]**

**ARF in acute pulmonary oedema.**

Acute pulmonary edema can be cardiogenic or non- cardiogenic. However, irrespective of the primary etiology the pathophysiologic mechanisms resulting in ARF are very similar. Pulmonary edema occurs due to an imbalance in Starling forces, resulting in fluid accumulation in the interstitium and alveoli. It results from alterations in the delicate balance between the plasma oncotic pressure (normal=25mmHg), pulmonary capillary hydrostatic pressure (normal=7-12mmHg), altered permeability of the connective tissue cellular barriers to fluid and plasma proteins and altered pulmonary lymphatic system function. **[39, 40, 41]**

In pulmonary edema, the ability of the lymphatics to drain excess interstitial fluid is exceeded, leading to accumulation of fluid in the interstitial space that surrounds the respiratory bronchioles, the alveoli and lung vasculature. Eventual flooding of the alveoli occurs after disruption of the tight junctions of the alveolar membranes. **[39, 40, 41]**

Fluid accumulation in the interstitium expands the alveola-capillary barrier, impairing gas exchange. **[39, 40, 41]**

Gravity exerts important influence on the fluid mechanics of the lung, with fluid accumulating at the lung bases, and a consequent decrease in perfusion due to redistribution of blood towards the apices of the lungs. **[42]**

Clinically, the patient is dyspnoeic, tachypnoeic, orthopnoeic, tachycardic, may have low or a high blood pressure, and has a cough productive of frothy pinkish sputum. The patient has excessive use of respiratory muscles.

Auscultation findings include bilateral rales with or without wheezes. [39] ABG analysis reveals a combination of hypoxia and hypercapnia proportional to the severity of the pulmonary edema. [40]

Chest radiographic findings include Kerley B lines, butterfly pattern haziness with central shadows and clear peripheries with or without cardiac enlargement. [2, 39, 40, 41]

ECG and Echocardiography are useful when cardiogenic pulmonary edema is suspected. [2, 41]

**ARF in Tuberculosis:**

Patients with PTB occasionally present with ARF, during which the CXR most commonly shows bilateral small nodular lesions mixed with consolidation or ground-glass opacities. HRCT demonstrates findings of milliary or bronchogenic disseminated tuberculosis, with diffuse areas of ground glass attenuation. [43]

ARF caused by PTB necessitating mechanical ventilation has a high mortality rate and poor prognosis, particularly in patients with TB destroyed lungs, high APACHE-II scores and sepsis. [44] ARF is more common in milliary TB than it is in TB bronchopneumonia, and has a worse prognosis. ARF in tuberculosis is of the mixed type. [45]

**ARF in severe pneumonia.**

Severe pneumonia causes ARF by inducing an intense inflammatory reaction, whose consequences greatly impair alveolar function.

In the initial stage of infection (Stage of congestion) acute inflammation leads to marked vascular congestion and alveolar edema. These changes impair gas exchange and result in both hypoxemia and hypercapnia through interference with the alveolar-capillary transfer of oxygen

and carbon dioxide. In the red hepatization stage the lung becomes firm and stiff, with a marked loss of compliance, and hence a significant reduction in ventilation. A decline in ventilation leads to carbon dioxide retention and decreased oxygen delivery to arterial blood.

As the pneumonia resolves increased secretions interfere with alveolar and airway function, reducing oxygen delivery to the alveoli as well as carbon dioxide clearance. The severity of ARF resulting from pneumonia is in proportion with the severity and extent of lung involvement. **[2, 31]**

**ARF in ARDS:**

Acute respiratory distress syndrome was first described by *Ashbaugh et al*, in 1967. **[46]**

In 1994, a definition of ARDS was recommended by the American Consensus Conference committee, a definition recognizing that the severity of pulmonary injury varies, and is simple to use. ARDS was defined as $PaO_2/FiO_2 < 200$ in the presence of bilateral alveolar infiltrates on the CXR. The cardiac silhouette appears normal, and the capillary wedge pressure, obtained by pulmonary arterial catheterization, is normal (<18mmHg) - as opposed to a rise in LVF. A $Pao_2/FiO_2 < 300$ but >200mmHg with bilateral infiltrates indicates ALI, a precursor to ARDS. **[5]**

Diffuse severe inflammation of the lung parenchyma and mechanical stress are implicated as the main pathophysiologic processes responsible for lung dysfunction. Diffuse inflammation of the lung parenchyma occurs, mediated via cytokines and other inflammatory mediators secreted by local epithelial and endothelial cells in response to diverse lung insults. Neutrophils and T-lymphocytes quickly migrate to the inflamed lung parenchyma and contribute in the amplification of the phenomenon. Histology reveals diffuse alveolar damage and hyaline membrane formation in alveolar walls. **[47, 48, 49]**

As a result of inflammation, endothelial dysfunction occurs; fluid extravasates from the capillaries into the interstitium. Lymphatic drainage is overwhelmed. Dysfunction of type II pneumocytes may occur and lead to reduced surfactant production with consequent atelectasis. **[47, 49]**

Resulting pulmonary edema increases the thickness of the alveola-capillary space, increasing the distance oxygen and carbon dioxide must diffuse for efficient gaseous exchange. The result is hypoxemia, hypercapnia, increased work of breathing, and eventual fibrosis of the air space. Further edema with reduced surfactant production leads to atelectasis and / or alveolar flooding; hence loss of aeration. This contributes to the right to left shunt in ARDS. As the alveoli contain progressively less gas , more blood flows via them without being oxygenated, resulting in massive intrapulmonary shunting, hence poor/no response to 100% oxygen therapy. **[47, 48, 49]**

The pathophysiologic consequences of ARDS therefore include: decreased lung compliance, decreased lung volumes, large intrapulmonary shunting, and decreased residual volume with consequent V/Q irregularity and pulmonary hypertension due to a three to five-fold increase in pulmonary vascular resistance hence right ventricular strain. **[48, 49, 50]**

Mechanical stress on the already inflamed lung results in further loss of aeration. Stress of mechanical ventilation, an inevitable component of ARDS treatment (high PEEP) leads to barotrauma. **[51]**

Mortality is high, and is usually due to barotrauma, pulmonary embolism (PE), pulmonary fibrosis, ventilator associated pneumonia and eventual multiple organ failure. **[50]**

Common risk factors for ARDS include sepsis, aspiration of gastric contents, shock, infection, lung contusion, non-thoracic trauma, toxic inhalation, near drowning, and multiple blood transfusions. **[45, 48, 50]**

### 2.5.5: <u>Pulmonary vascular dysfunction:</u>

This consists of pulmonary capillary network, intimately associated with the membrane system, but distinct both in structure and with respect to the types of diseases that can alter its normal function. Common causes of dysfunction include acute thromboembolism, air embolism, amniotic fluid embolism, pulmonary hypertension, arterio-venous malformations (AVM), and intracardiac shunts. **[2, 31]**

There are no specific bedside diagnostic tests for pulmonary vascular dysfunction, but features of right heart dysfunction such as elevated JVP, a pronounced or delayed pulmonic component of the second heart sound, a right sided parasternal heave, a right sided third heart sound, or o murmur of tricuspid valve regurgitation strongly suggest this diagnosis. In the absence of these signs, it can be suggested by exclusion in cases where abnormal gas exists in the apparent absence of controller, airway, pump, or alveolar compartment dysfunction. **[2, 31]**

**Acute severe pulmonary embolus** from whatever cause decreases perfusion to the areas supplied by the vasculature involved. This V/Q mismatch leads to impaired gas exchange due to increase in the alveolar dead space and significant right-to-left shunt. Vascular obstruction with acute elaboration of neurohumoral agents from platelets, such as serotonin, greatly elevates pulmonary vascular resistance. Reflex stimulation of irritant receptors leads to alveolar hyperventilation, while constriction of airways distal to the bronchi results in increased airway resistance. Lung edema due to inflammation, lung hemorrhages and loss of surfactant due to impaired function of type II pneumocytes together result in decreased lung compliance, and ultimate alteration in air flow dynamics. **[2, 31]**

**Acute pulmonary hypertension** results in right ventricular strain and may manifest as frank right ventricular failure. Clinically, the patient has exertional dyspnoea, and hypoxemia, along with other features of right sided heart failure detailed above. **[2, 31]**

**Arterio-Venous Malformations (AVM)** or **intracardiac shunt** manifests with hypoxemia that is refractory to oxygen therapy. **[2, 31]**

Investigations for pulmonary vascular dysfunction include ABG, Ventilation-Perfusion scanning, CT pulmonary embolism study, Echocardiography, right heart catheterization, and HRCT. **[2, 31, 51, 52]**

## 2.6: Outcome of acute respiratory failure:

The incidence and outcome of ARF depend on dysfunction in other organs. As a result, reported mortality in patients with ARF is derived from a mixed group of patients with different degrees

of multi-organ failure. Patients with multi-organ failure have as high as 75% mortality, compared to ~ 21.8% mortality in single organ failure. Hence, the high overall mortality from ARF is caused by dysfunction in other organs. [9]

*Allan et al (2004)* found an overall in-hospital mortality of 38.6%, with most deaths occurring before day 25 after admission to hospital. [53] *Luhr et al (1999)* reported an ICU based 90-day mortality from ARF of 41%. [7] *Gordon et al (2001)* reported an in-hospital mortality of 38.5% for ALI/ARDS related ARF. [54]

Mortality following acute exacerbations of COPD ranges between 2.5%-30%, with a median hospital stay of 9 days (5-15). In-hospital death was reported to be 11%; and the 60-day mortality being 20%. [55, 56]

Death rates are higher for older patients who suffer acute exacerbations of COPD. *Seneff et al* reported 24% hospital mortality. They concluded that the determinants of poor outcomes from ARF were: age, severity of respiratory and non-respiratory organ system dysfunction, hospital stay before ICU admission. Development of non-respiratory organ system dysfunction was the major predictor of hospital mortality. [10]

## 3.0: STUDY JUSTIFICATION:

Acute respiratory failure is a syndrome of diverse etiology. Most of the conditions that could potentially lead to ARF are prevalent diagnoses at KNH. The prevalence of ARF is unknown in our setting, yet such information is essential to enhance quality of care and reduction of mortality in the accident and emergency department.

ARF carries high morbidity and mortality globally. The exact mortality statistics attributable to ARF is unknown in our setting.

Early diagnosis and intervention is key to reducing mortality and advances in respiratory support have impacted positively on outcomes. Therefore, increased surveillance for ARF is essential in the A&E department. This study estimates the magnitude of ARF among patients presenting with

acute dyspnoea to the KNH A&E department, and put forth a case for greater index of suspicion while evaluating such patients.

The short-term prognosis of ARF is unknown in our setting, and this study informs on this important issue.

This study forms a baseline survey of the magnitude of ARF, associated clinical etiologies as well as the short term outcomes at KNH, and will serve to inform strategies to identify and manage ARF at the A&E department.

## 4.0: RESEARCH QUESTION:

What are the prevalence, etiology and short-term outcome of ARF among acutely dyspnoeic patients presenting to the A&E department of KNH?

## 5.0: OBJECTIVES:

### 5.1: Broad Objective:

To determine the prevalence of acute respiratory failure and associated etiologies among acutely dyspnoeic patients presenting to the Accident and Emergency department of KNH and the associated two week in-hospital outcome.

### 5.2: Specific Objectives:

1. To determine the three- month period prevalence of acute respiratory failure among acutely dyspnoeic patients presenting to the Accident & Emergency department of KNH.

2. To document the etiology of ARF.

3. To determine the type of ARF.

4. To establish the outcome of ARF within the first two weeks of hospitalization.

5. To correlate age, gender, duration of respiratory symptoms, etiology and type of ARF with outcome.

## 6.0: METHODOLOGY:

### 6.1: Study design:

A single-centre prospective descriptive study.

### 6.2: Study sites:

**KNH Accident and Emergency department.**

At the Accident and Emergency department, patients were first seen at the emergency observation desk, and triaged on the basis of presence or absence of acute dyspnoea. Acutely dyspnoeic patients were immediately taken into the acute/resuscitation room, for immediate determination of $SaO_2$, ABG analysis and appropriate emergency management.

**KNH Intensive Care Unit.**

The Intensive Care Unit is the primary admission unit for patients in ARF who survive beyond the A&E department acute room, hence was the next study and follow-up site for these patients.

**KNH adult in-patient wards**

Patients admitted to the ICU in ARF, once stable were discharged to the appropriate adult in-patient wards, from where the P.I followed them up till full recovery, death or day fourteen in hospital, whichever came earlier.

### 6.3: Study population:

All patients aged 13 or more years of age presenting with acute dyspnoea to the A&E department of KNH. The rationale for choice of this age is that the A&E department at the KNH attends to patients aged $\geq$ 13years. Patients aged < 13 years are routinely seen at the Pediatric Filter Clinic. Age for patients aged less <18 years was determined, to the nearest year, based on information given by the care giver/parent. For patients aged > 18 years, information from the

patient/caregiver with confirmation from the national identity card, where available, was used to determine age to the nearest year.

## 6.4: Patient selection:

### 6.4.1: Inclusion criteria:

1. Patients aged 13 years or more presenting to the A&E department, and meet the defining criteria of ARF.
2. Informed written consent/assent.

### 6.4.2: Exclusion criteria:

1. All patients who decline consent/assent.
2. All patients with dyspnoea of more than two weeks in duration.
3. All patients aged less than 13 years.

### 6.4.3: Sampling technique:

Consecutive sampling was applied.

### 6.4.4: Screening criteria:

Patient screening was done on the basis of a subjective criterion defined by the patient, on the presence of breathlessness, feeling of shortness of breath, experience of air hunger or an increased effort of breathing; **and/or** $SaO_2 \leq 92\%$ on pulse oximetry.

## 6.5: Case definition:

**Acute respiratory failure:**

ARF was defined as acute dyspnoea (< two weeks in duration) with any one or more of the following ABG abnormalities: $PaO_2 \leq 60$mmHg ($\leq$ 8KPa); $PaCO_2 \geq 45$mmHg ($\geq$ 6 KPa) and a pH$\leq$ 7.35 while breathing room air.

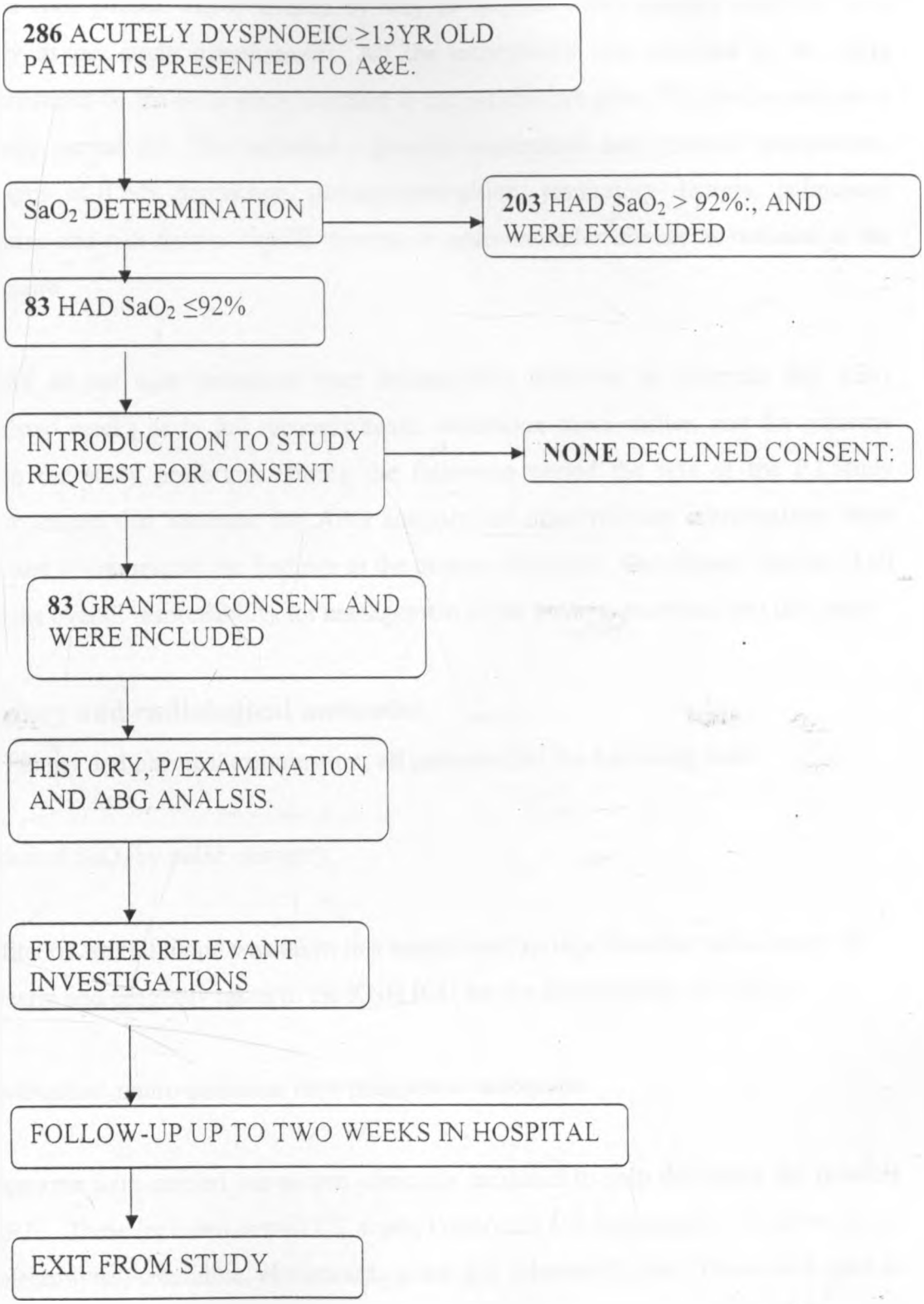
## 6.6: Screening and Recruitment of cases:

All patients aged $\geq$13years presenting at the emergency triage desk of the A&E department, KNH, with acute dyspnoea were identified and referred to the PI or a trained study assistant to be

screened for ARF as per definition, throughout the study period. Notices were placed strategically at the A&E triage desk and acute room, requesting duty staff to inform the PI/study assistant whenever patients meeting the study inclusion criteria were seen. The PI/study assistant then determined the $SaO_2$ on all acutely dyspnoeic patients by pulse oximetry, readily available at the acute room in the A&E department. The P.I (who is resident in the hospital) and the study assistants ensured twenty four hour availability on a rotational basis; hence no delays occurred between the presentation of patients and the determination of ABG. In all cases, ABG were determined within fifteen minutes of patient presentation. The P.I/study assistants participated in immediate resuscitation care of these very ill patients in collaboration with the primary care givers at the A&E department. Initiation of active management of the patients was prompt, without waiting for arterial blood gas analysis.

Patients meeting the inclusion criteria ($SaO_2 \leq 92\%$) or their care givers were then approached, rapport established, the details of the study explained in lay terms and request for consent/assent sought, as management of the patient continued. Once written consent/assent was granted, the questionnaire was administered and appropriate investigations carried out as outlined under laboratory and radiological methods section below.

## 6.6.1: CASE SCREENING AND RECRUITMENT FLOW CHART.



## 7.0: DATA COLLECTION:

### 7.1: Clinical Methods:

Once recruited each patient was evaluated by way of baseline ABG analysis followed by a medical history as per study questionnaire. All the information was recorded in the study proforma administered by the PI or study assistant to the patient/care giver. Physical examination was subsequently carried out. This included a general examination and systemic examination, looking for signs of CNS depression, airway obstruction, respiratory distress, pulmonary infection, features and risk factors for PE, trauma or neuromuscular disease as outlined in the study questionnaire.

Patients in ARF as per case definition were subsequently followed by alternate day ABG analysis up to two weeks or to full recovery/death, whichever came earlier, and the outcome documented on the study proforma. During the follow-up period the role of the P.I/Study assistant was to ensure that alternate day ABG analysis and other relevant investigations were actually done, and communicate the findings to the primary doctor(s). The primary doctors at all times retained the overall responsibility for management of the patients recruited into this study

### 7.2: Laboratory and radiological methods:

In addition to history and physical examination, **all patients** had the following done:

1. Determination of $SaO_2$ by pulse oximetry.

2. One milliliter of arterial blood was taken in a heparinized syringe from the radial artery of either forearm and promptly taken to the KNH ICU lab for determination of ABG.

3. A postero-anterior/ antero-posterior view plain chest radiograph.

Other investigations were carried out as was clinically indicated to help determine the possible etiology of ARF. These included cranial CT scans, Pulmonary CT angiography, complete blood count, urea, electrolytes, creatinine, electrocardiogram and echocardiogram. These were used to determine/confirm the etiology of ARF.

### 7.3: Outcome measures:

At the end of two weeks stay in hospital, the outcome of each patient was documented, as follows:

1. Full recovery from acute respiratory failure.
2. Persisting respiratory failure, and hence classified as sub-acute to chronic ARF.
3. Death.

Duration from presentation to each outcome was also documented.

## 8.0: DATA MANAGEMENT AND STATISTICAL ANALYSIS.

All data in this study was collected by the PI and study assistants and entered into data entry sheets, with weekly data cleaning and verification to ensure completeness and accuracy of the information. The clean verified data was then entered into a Microsoft Office Excel database by the PI. Upon completion of the study, data was analyzed using the Statistical Package for Social Sciences (SPSS) for windows, version 15.0.

Descriptive statistics were used to summarize all the variables into means and proportions. The continuous variables such as age, $SaO_2$, $PaO_2$, $PaCO_2$, pH, duration of illness and duration from admission to death/recovery were summarized into means and these means were compared using the student's t-test.

Categorical variables such as sex, type of ARF and occupation were summarized into proportions; and Chi-square test used to compare two proportions.

The association between hypoxemia, hypercapnia, acidosis and duration of illness before presentation to the A & E with outcomes was made by regression analysis.

Period prevalence was the number of patients with ARF as a percentage of the total number of eligible patients presenting to A&E department over the study period.

Differences were considered significant when the p-value was equal to/less than 0.05 (95% CI).

## 9.0: ETHICAL CONSIDERATIONS.

1. Informed consent/assent was obtained from all patients/caregivers before enrolment into this study.

2. The initiation/continuation of acute treatment of these very ill patients was not delayed or unduly hampered by the activities of this study. Indeed, the P.I and Study assistant participated in the emergency care of these patients.

3. Patients were free to withdraw consent any time during the study period without being discriminated in any way; or being denied appropriate care.

4. All information gathered from patients during this study was kept confidential.

5. Study results were communicated to the primary health care providers to facilitate quality management of the patients.

6. The study results were discussed with the patient whenever possible.

7. Only after approval from the Department of Medicine (UON), and the KNH Ethics and Research Committee was this study be carried out.

# 10.0: RESULTS.

Thirteen thousand and three patients aged ≥ 13 years of age were seen at the KNH A&E department during the study period, 286 (2.2%) of whom were acutely dyspnoeic. 83 patients were in ARF by the screening and definition criteria, therefore giving a period prevalence of 0.6% ( 95% CI, 0.47-0.73)

## 10.1: BASELINE CHARACTERISTICS OF THE STUDY POPULATION.

### 10.1.1: GENDER:

There were 54 male patients (65.1%) and 29 female patients (34.9%) in ARF, therefore the gender ratio (M: F) was ~ 2:1.

### 10.1.2: EMPLOYMENT STATUS:

**Table 1: Employment status of patients in ARF:**

| Employment status | FREQUENCY n=83 | PERCENTAGE (%) |
|---|---|---|
| Formal employment | 11 | 13.2 |
| Informal employment | 34 | 41.0 |
| Unemployed | 38 | 45.8 |

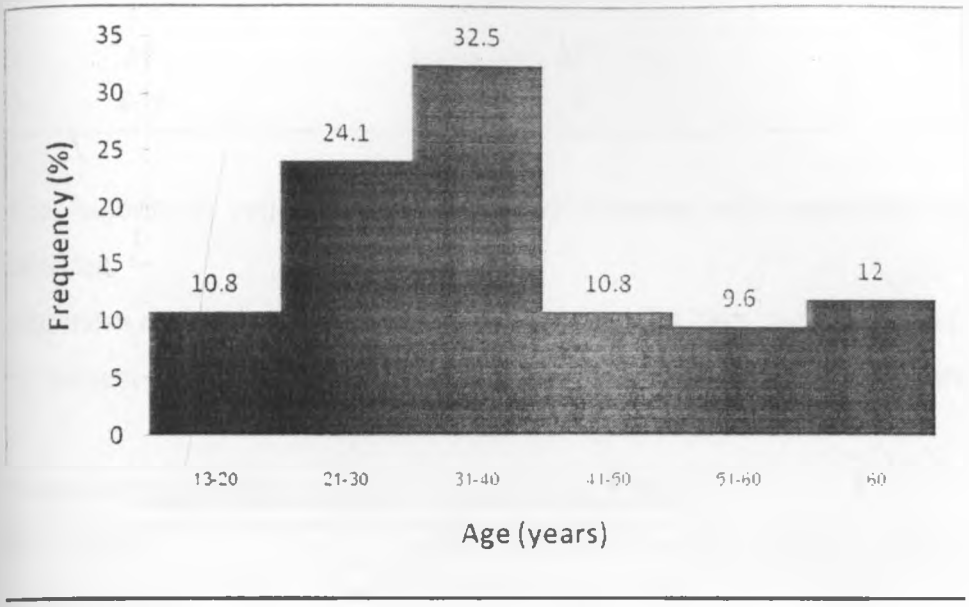
45.8% of the patients were unemployed.

All patients enrolled in this study were low income earners.

Patients in informal employment were either small scale business people or in casual employment.

### 10.1.3: AGE

**Figure 1: Distribution of patients in ARF by age.**




The peak age of the patients was 31-40 years, as seen in figure 1 above. The mean age was 39.86 years ±17.30. The median age was 38 years (minimum=14years, maximum =95 years).

### 10.2: CLINICAL CHARACTERSTICS OF PATIENTS IN ARF.

### 10.2.1: HISTORY:

**Table 2: Chief complaints of patients in ARF:**

| COMPLAINT | FREQUENCY: n=83 | PERCENTAGE, % |
|---|---|---|
| Cough | 49 | 59.0 |
| Depressed consciousness | 47 | 56.6 |
| Hemoptysis | 29 | 34.9 |
| Orthopnoea/PND | 16 | 19.3 |
| Calf pain/swelling | 2 | 2.4 |

All the patients recruited into this study were acutely dyspnoeic as per inclusion criteria. Other common presenting complaints were cough (59%), depressed level of consciousness (56.6%) and hemoptysis (34.9%) in that order.

**Table 3: Grouped data on duration of respiratory complaints in patients in ARF.**

| DURATION IN DAYS | FREQUENCY, n=83 | PERCENT, % |
|---|---|---|
| ≤2 | 47 | 56.6 |
| 3-7 | 27 | 32.5 |
| 8-10 | 9 | 10.9 |

The majority of patients in ARF (89.1%) presented with respiratory complaints of ≤ 1 week duration.

The mean duration of respiratory complaints was 3.4 days, with a range of 1 - 10 days.

No patient in ARF presented with respiratory complaints of > 10 days duration.

**Table 4: Past medical history of patients in ARF:**

| FINDING | FREQUENCY. n=83 | PERCENTAGE (%) |
|---|---|---|
| Hypertension | 18 | 21.7 |
| Cigarette smoking | 14 | 16.9 |
| Diabetes mellitus | 7 | 8.4 |
| Chronic/Recurrent lung disease | 3 | 3.6 |

21.7% and 16.9% of patient had a past history of hypertension and cigarette smoking respectively. Other co-morbidities were as shown on table 4, above.

**Table 5: Current medical history of patients in ARF:**

| FINDING | FREQUENCY: n=83 | PERCENTAGE: % |
|---|---|---|
| Acute trauma | 22 | 26.5 |
| Cardiac disease | 6 | 7.2 |
| Heavy alcohol consumption in last 24 hours | 6 | 7.2 |
| Renal failure | 3 | 3.6 |
| Use of CNS depressants < two weeks prior | 2 | 2.4 |
| DVT/predisposition to DVT | 2 | 2.4 |
| Myasthenia gravis | 1 | 1.2 |

26.5% of patients had acute trauma; 16 with severe head trauma and 6 with chest trauma.

Fifteen (18.1%) of the patients in ARF had oxygen therapy at presentation, 14 by face mask and 1 by endotracheal tube. These were patients referred to KNH from other health facilities.

### 10.2.2: PHYSICAL EXAMINATION FINDINGS.

**Table 6: Physical examination findings of patients in ARF:**

| FINDING | FREQUENCY: n=83 | PERCENT, % |
|---|---|---|
| Use of accessory respiratory muscles | 70 | 84.3 |
| Tachypnoea | 62 | 74.7 |
| Cyanosis | 56 | 67.5 |
| Depressed CNS function | 45 | 54.2 |
| Hypotension | 36 | 43.4 |
| Fever | 30 | 36.1 |
| Slow respiratory rate | 21 | 25.3 |
| Hypertension | 19 | 22.9 |
| Edema | 17 | 20.5 |
| Heart failure | 11 | 13.3 |
| Acute airway obstruction | 6 | 7.2 |
| Paradoxical abdominal respiration | 2 | 2.4 |
| Signs of neuromuscular dysfunction/paralysis | 1 | 1.2 |

The commonest examination findings of the patients in this study were: Use of accessory muscles of respiration, in 70 (84.3%); Tachypnoea, in 62 (74.7%); Cyanosis (central), in 56 (67.5%) and Depressed CNS function in 45 (54.2%). Some patients had more than one sign.

### 10.2.3: CHEST RADIOGRAPH FINDINGS:

**Table 7: Chest radiograph findings of patients in ARF:**

| FEATURE | FREQUENCY, n=83 | PERCENT , % |
|---|---|---|
| Normal | 19 | 22.9 |
| Consolidation | 16 | 19.3 |
| Pulmonary edema | 15 | 18.1 |
| Cardiomegally | 14 | 16.9 |
| ARDS/ALI | 13 | 15.7 |
| Hemo/Pneumothorax | 6 | 7.2 |
| Fractured ribs | 4 | 4.8 |

22.9% (19) of the patients had normal chest radiograph. Abnormal findings are summarized in the table above. Common chest radiograph changes during follow-up were ARDS (10); consolidation (4) and pulmonary edema (3).

### 10.2.4: BASELINE ARTERIAL BLOOD GAS ANALYSIS:

**Table 8: Baseline arterial blood gas analysis of patients in ARF:**

| | n | Mean | Median | Std deviation | Minimum | Maximum | Percentiles | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | 25th | 50th | 75th |
| $SaO_2$, % | 83 | 77.64 | 78.00 | 8.062 | 43 | 90 | 75 | 78 | 84 |
| $PaO_2$, KPa | 83 | 5.30 | 4.85 | 1.192 | 3.04 | 7.82 | 4.25 | 4.85 | 6.33 |
| $PaCO_2$, KPa | 83 | 7.71 | 7.86 | 2.005 | 3.26 | 13.32 | 6.98 | 7.86 | 9.19 |
| pH | 83 | 7.258 | 7.282 | 0.118 | 6.964 | 7.570 | 7.184 | 7.282 | 7.324 |

The ARF patients in this study were markedly hypoxemic, hypercapnic and acidotic.

### 10.3: ETIOLOGY OF ACUTE RESPIRATORY FAILURE:

**Table 9: Etiology of ARF in the study population:**

| AETIOLOGY OF ARF | FREQUENCY, n=83 | PERCENT, % |
|---|---|---|
| Central disorders | 25 | 30.1 |
| Pneumonia | 16 | 19.3 |
| Acute pulmonary edema | 15 | 18.1 |
| Chest trauma | 7 | 8.4 |
| Sepsis | 7 | 8.4 |
| Upper airway obstruction | 6 | 7.2 |
| Pulmonary vascular dysfunction | 3 | 3.6 |
| ( P.E & Amniotic fluid Embolism) | | |
| Respiratory muscle dysfunction | 3 | 3.6 |
| Acute obstructive lower airway disease | 1 | 1.2 |

Central disorders leading to ARF included acute head trauma in 16 patients, CVA in 6 patients, meningitis in 2 patients and hypoxic brain injury in 1 patient. Of those with respiratory muscle dysfunction, 2 had organophosphate poisoning, and 1 had myasthenia gravis. Upper airway obstruction was present in 3 patients with inhalational burns, 2 patients with Ludwig's angina and in 1 patient with acute bleed into a thyroid carcinoma. Six patients with acute chest trauma

had rib fractures with hemo/pneumothorax. Eight patients had acute cardiogenic pulmonary edema while 7 had acute nephrogenic pulmonary edema. Of the patients with pulmonary vascular dysfunction, 2 had features of PTE and 1 had amniotic fluid embolism secondary to abruptio placenta.

## 10.4: CLASSIFICATION OF ACUTE RESPIRATORY FAILURE:

**Table 10: Types of ARF in the study population.**

| TYPE OF ARF | FREQUENCY, n=83 | PERCENT. % |
|---|---|---|
| Type I | 17 | 20.5 |
| Type III | 66 | 79.5 |

The majority of patients, 66 (79.5%) had type III ARF. None of the patients seen in this study had a purely hypercapnic (type II) ARF.

## 10.5: OUTCOME OF PATIENTS IN ACUTE RESPIRATORY FAILURE:

**Table 11: Outcomes of patients in ARF within 14 days of hospitalization.**

| OUTCOME | FREQUENCY, n=83 | PERCENT, % |
|---|---|---|
| Full recovery | 27 | 32.5 |
| Death | 54 | 65.1 |
| Still in respiratory failure | 2 | 2.4 |

54 (65.1%) of the patients in this study died within two weeks of admission. The mean duration from admission to death was 2.26 days (range: <1day to 8 days).

33 (39.8%) of the patients admitted to ICU in ARF developed additional complications during follow up. ARDS was reported in ten patients; acute renal failure in three; shock in twelve; pneumonia in four and sepsis in four.

29 (34.9%) of patients survived to day 14 post admission, with 27 (32.5%) recovering fully from ARF within a mean of4.54 days (range: 1day to 10 days).

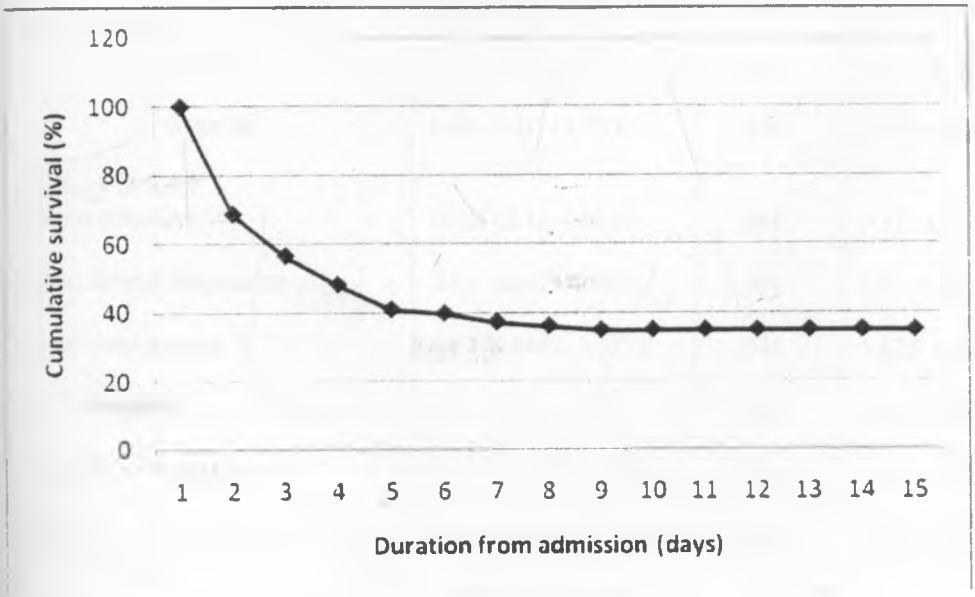
Only two patients (2.4%) were still in respiratory failure beyond 14 days of hospitalization.

**Table 12: Sites of death for patients in ARF:**

| SITE | FREQUENCY, n=54 | PERCENT, % |
|---|---|---|
| A&E resuscitation room | 27 | 50.0 |
| ICU | 25 | 46.3 |
| Medical wards | 2 | 3.7 |

Most patients died in the A&E resuscitation room while awaiting admission to ICU. Admission to ICU was not immediate for most patients, with delays up to 48 hours, subject to availability of bed space in the ICU.

**Figure 2. Survival curve of patients in ARF.**




51.8% (36) of all patients in ARF died within the first two days of presenting to the A&E department. No deaths were reported in patients surviving beyond 8 days after presentation.

**Table 13: UNIVARIATE ANALYSIS: Odds ratio for death and recovery from ARF according to baseline characteristics, type and etiology of ARF.**

| Variable | | Death from ARF | | Recovery from ARF | |
|---|---|---|---|---|---|
| | | OR (95% CI) | p-value | OR (95% CI) | p-value |
| **Age (Years)** | 13-30 | 1.670 (.626 – 4.455) | .303 | .541 (.196 – 1.491) | .232 |
| | 31-50 | .913 (.368 – 2.267) | .845 | 1.067 (.423– 2.691) | .891 |
| | >50 | .597 (.206 – 1.731) | .339 | 1.937 (.663 – 5.66) | .223 |
| **Gender** | Male | 1.93 (.757 – 4.922) | .166 | .545 (.211 - 1.408) | .207 |
| | Female | | | | |
| **Dur. of resp.complaints(days)** | | | | | |
| | ≤ 2 | 4.135 (1.59 – 10.77) | **.003** | .237 (.089 - .629) | **.003** |
| | 3-7 | .267 (.101 - .704) | **.006** | 3.56 (1.34 – 9.464) | **.009** |
| | >7 | .64 (.157 – 2.587) | .526 | 1.77 (.436 – 7.222) | .419 |
| **Type of ARF** | | | | | |
| | Type I | .714 (.239 – 2.131) | .545 | 1.169 (.38 – 3.588) | .785 |
| | Type III | 1.40 (.41 – 4.73) | .840 | 1.40 (.469 – 4.177) | .785 |
| **Etiology of ARF** | | | | | |
| Central disorders | | 10.02 (2.16 – 46.45) | **.001** | .115 (.025 - .533) | **.002** |
| Upper airway obstruction | | .24 (.041 - 1.402) | .091 | 4.7 (.803 – 27.46) | .064 |
| Acute chest trauma | | .69 (.144 – 3.333) | .646 | 1.625 (.337– 7.84) | .542 |
| Acute Pneumonia | | .33 (.09 – 1.15) | .078 | 1.83 (.598 – 5.59) | .286 |
| Acute pulmonary edema | | .547 (.176 – 1.700) | .293 | 2.10 (.67 – 6.57) | .197 |
| Sepsis | | .693 (.144 – 3.333) | .646 | 1.63 (.337 – 7.835) | .542 |

On Univariate analysis:
Patients with respiratory complaints ≤ 2 days were significantly more likely to die from ARF (OR 4.14; p-value=.003). Patients with respiratory complaints 3-7 days in duration were significantly more likely to survive (OR 3.56; p-value= .018) Patients with ARF due to central disorders were significantly more likely to die (OR 10.0; p-value=.001)

**Table 14: MULTIVARIATE ANALYSIS : Odds ratios for death and recovery from ARF according to baseline characteristics, type and etiology of ARF.**

| Variable. | | Death from ARF | | Recovery from ARF | |
|---|---|---|---|---|---|
| | | OR (95% CI) | p-value | OR (95% CI) | p-value |
| **Age (years)** | 13-30 | 1.802 (.396 – 8.194) | .446 | .396 (.086 – 1.82) | .234 |
| | 31-50 | 1.822 (.441 – 7.525) | .407 | .472 (.116 – 1.91) | .293 |
| | >50 | | .673 | | .045 |
| **Gender:** | Male | 1.149 (.342 – 3.857) | .823 | 1.039 (.305 – 3.54) | .952 |
| | Female | | | | |
| **Dur. of resp. complaints (days)** | | | | | |
| | ≤ 2 | 1.898 (.288 – 12.524) | .506 | .348 (.50 – 2.404) | .285 |
| | 3-7 | .724 (.131 – 3.998) | .711 | 1.067 (.196 – 5.815) | .940 |
| | >7 | | .472 | | .362 |
| **Type of ARF** | | | | | |
| | Type I | | | | |
| | Type III | .86 (.200 – 3.701) | .840 | 1.171 (.267 – 5.141) | .834 |
| **Etiology of ARF** | | | | | |
| Central disorders | | 1.229 (.074 – 20.303) | .885 | .968 (.052 – 18.032) | .983 |
| Upper airway obstruction | | .075 (.004 – 1.377) | .081 | 16.604 (.791-348.60) | .70 |
| Acute chest trauma | | .127 (.007 – 2.452) | .172 | 9.48 (.43 – 209.22) | .154 |
| Acute pneumonia | | .133 (.011 – 1.646) | .116 | 4.422 (.327 – 59.76) | .263 |
| Acute pulmonary edema | | .226 (.017 – 3.062) | .264 | 4.83 (.33 – 70.626) | .250 |
| Sepsis | | .346 (.023 – 5.298) | .446 | 3.067 (.186 – 50.48) | .433 |

On multi-variate analysis, however, none of the variables analyzed in the table above were significantly independently predictive of outcome.

## 11.0: DISCUSSION:

Acute respiratory failure is a common medical emergency associated with a high mortality rate globally. Most population based studies in developed countries give an incidence of 77.6-88.8 per 100,000 population per year. [7] There is no published data on the prevalence of ARF in outpatient setting. In this study the prevalence of ARF was 0.6% (95% CI, 0.47-0.73), a figure much higher than that found by *Luhr* et al in a multinational European study. Remarkable, too, is that one out of every three to four patients presenting in acute dyspnoea were in ARF. The higher prevalence of ARF in this study could be explained by the large numbers of acute trauma patients and the referral status of the study site. KNH receives very ill patients referred from other hospitals, and the probability of such patients being in ARF is high.

ARF occurs in equal prevalence in both male and female patients as was illustrated in a study by *Behrendt* et al and *Vincent* et al, both in an ICU setting in American studies **[23, 25].** In this study, however, 65% of patients in ARF were male for an uncertain reason. It is notable, though, that most patients in ARF due to acute trauma were male (M: F=15:1).

Unlike other studies that have found no association of ARF with poverty, this study found that all the patients in ARF were low income earners. This is not a true association between poverty and ARF, but rather a reflection of the socioeconomic status of the clientele that patronize KNH, a public referral health institution. Patients of higher income preferentially seek treatment in relatively costly private hospitals, and were therefore not enrolled in this study.

In developed countries, ARF is commoner in elderly patients. *Behrendt* et al in an American ICU based study found an increased incidence of ARF with increasing age. The mean age for patients in ARF in that study was 63 years **[23]**. This study, however, found that ARF occurred in younger patients, with a mean age of 39.86 ± 17.30 years. This is attributable to a higher prevalence of trauma as a cause of ARF in the setting of our study **[7, 8, 10]**. Kenya is a developing country with a predominantly young population, unlike the developed countries where the elderly make a significantly large proportion of the population.

The commonest signs of ARF included the use of accessory muscles of respiration, tachypnoea, central cyanosis, and depressed central nervous system function. Hypotensive patients were also found to be much more likely in ARF. This is similar to the findings of *Luhr* et al and led to their conclusion that the morbidity and mortality from ARF were significantly dependent on other co-morbidities.

Acute respiratory failure may occur in patients without primary pulmonary pathology. This is particularly so in patients with disorders of central control of respiration. This explains why 22% of patients in this study had normal chest radiographs. Most of these patients had severe acute head trauma, while others had CVA, meningitis, sepsis, respiratory muscle dysfunction and upper airway obstruction.

The morbidity and outcome of patients in ARF is related to the severity of hypoxemia, hypercapnia and acidosis, as was found in an ICU based German study by *Lewandowski* et al **[6].** In this study, patients in ARF were invariably hypoxemic. Most of them were hypercapnic and acidotic. All patients that presented while on oxygen therapy were in ARF. This is most likely due to inadequate oxygen delivery to the alveoli or impaired oxygen diffusion across the alveolo-capillary barrier for diverse reasons related to the primary pathologies, or inappropriate oxygen delivery techniques.

ICU based studies in the west as well as population based incidence studies report commonest etiologies of ARF as COPD, asthma, ARDS/ALI and pulmonary infections **[4, 6, 7, 10, 28, 33].** These statistics exclude trauma, which is managed admitted and managed in specialist surgical units, while this study does not. Consequently, this study found central disorders secondary to acute head trauma to be the commonest cause of ARF. Most of these cases were a result of automobile accidents. Unlike what has been reported in studies from developed countries, ARF due to acute pulmonary edema was also common in this study. This finding possibly reflects inadequacy of care for these patients (in renal and cardiac failure) due to poverty. Most patients presenting in decompensated cardiac and/or renal failure could not afford to sustain appropriate long-term therapy. To virtually all these patients, drugs for heart failure and renal replacement therapy were not affordable.

Acute respiratory failure is a result of inadequate oxygenation and/or ventilation. Often these disorders occur in combination; hence most patients in ARF have a combination of hypoxemia and hypercapnia **[3, 4, 31].** This study found that the majority of patients in ARF had co-existent hypoxemia and hypercapnia (type III ARF). Why no patient was in type II ARF is uncertain, but this form of ARF is relatively uncommon. This observation could be due to the relatively small numbers of patients recruited in this study. A study covering a longer period of time and involving a larger number of patients in ARF is likely to identify some cases of type II ARF.

Globally, acute respiratory failure is associated with a high mortality rate. Different investigators report mortality rates in the 21.8% - 75% range, depending on the etiology of ARF and the setting of the study **[8, 9, 23, 54].** *Seneff* et al **[10],** *Flaaten* et al **[9],** *Luhr* et al **[7]** and *Allan* et al **[53]** identified the determinants of mortality from ARF as severity of respiratory and non-respiratory organ dysfunction, delay in admission to ICU, advanced age and development of multi-organ involvement/complications. The mortality rate in our study was 65.1%, a rate within the range reported from similar studies in different settings. This study did not find an increase in mortality with increasing age. Most of our patients were young. There was a higher mortality among male patients, who were also the majority, and among whom acute trauma was most prevalent. There is no known gender bias on adverse outcome of ARF.

In this study, there was a definite delay in admission of patients to ICU, which explains why 50% of all patients died at the A&E department. This finding is consistent with findings of similar studies quoted above. Limited bed-space in the ICU was the reason for delayed admission of patients in ARF.

Severe hypoxemia, hypercapnia and acidosis as shown by baseline ABG analysis pointed to severe respiratory dysfunction, which further explains the high mortality rate found in this study. Most patients died within two days of presentation (mean duration 2.8 days); no deaths occurred after the seventh day post-admission. *Allan* et al in an American study found that most deaths from ARF occurred before day 25 after admission to hospital **[53].**

Multi-organ complications developed in a number of our patients after admission. These complications included pneumonia, ARDS, sepsis and acute renal failure. Invariably, all patients that developed multi-organ complications died. This finding is consistent with the findings of *Seneff* et al **[10]**.

On univariate analysis, significant predictors of an adverse outcome were central disorders and duration of respiratory complaints $\leq 2$ days. It is possible that patients who presented within 2 days of onset of dyspnoea were more ill. In deed all trauma patients were in this category. It appears that the more rapidly progressive the dyspnoea the more likely it was to have an adverse outcome

On multivariate analysis, however, none of the variables considered was significantly independently related to outcome. This could be explained by the relatively small numbers of cases of ARF in this study; the consideration of only two main dependent variables (outcomes) and the stringent p-value applied, and the findings from similar studies that most deaths for patients in ARF are attributable to multiple organ dysfunction/failure rather than a single etiology. **[9, 10]** Advanced age was not predictive of an adverse outcome in this study. Most of our patients were younger and the etiologies of ARF identified in this study were not age dependent. This was a significant departure from finding in studies from developed countries.

## 12.0: CONCLUSIONS:

1. ARF is common among patients presenting with acute dyspnoea.

2. Most patients in ARF are younger than has been reported elsewhere.

3. Trauma is the most common cause of ARF.

4. ARF results in very high mortality (65.1%), often the result of delayed ICU admission as well as multi-organ failure/complications.

5. Patients presenting in ARF due to central disorders and those with respiratory complaints of ≤ 2 days in duration are significantly more likely to have an adverse outcome.

## 13.0: RECOMMENDATIONS:

1. Make pulse oximetry and arterial blood gas analysis standard baseline assessment tools for acutely dyspnoeic patients in our A&E setting.

2. Improved acute respiratory care in the form of ensuring availability of mechanical ventilators and improved A&E staff training will go a long way to improving outcomes of ARF.

3. Prompt admission to ICU of all patients in ARF will help reduce mortality. This may call for an increase in bed capacity of the ICU.

4. Closer surveillance for multi-organ failure in patients admitted in ARF to minimize mortality.

5. A similar study over a longer period of time, with larger numbers of patients to address possible seasonal variations of ARF.

## 14.0: LIMITATIONS OF THE STUDY:

1. This study was based in the A&E department of a national referral hospital to which very ill patients were referred. The results of this study may not be generalizable to the A&E settings in other public and private hospitals.

2. Identification of the etiology and subsequent classification of ARF was based on history, physical examination and baseline lab and radiological investigations. Post-mortems were not carried out, and it is possible that some diagnoses were missed, leading to misclassification of the etiology of ARF. CXR were reported by one radiologist, hence possible introduction of interpreter dependent bias.

3. This study was carried out over a period of three consecutive months, and does not address possible seasonal variations in the prevalence of ARF.

## 15.0: APPENDICES:

## APPENDIX 1: STUDY PROFORMA:

**Demographic data.**

Age ……

Occupation: Employed=1;
Self employed=2
Unemployed =3.

Gender …… (M=1; F= 2)

Serial number……

**History.**

Chief complaints: Dyspnoea……Yes=1 No=2.

Orthopnoea/PND……. Yes=1 No=2

Depressed consciousness …….. Yes=1 No=2.

Hemoptysis……. Yes=1 No=2.

Calf pain/swelling…… Yes=1 No=2.

Cough…… Yes=1 No=2.

Duration of respiratory complaints (days) ……..

History of acute trauma..... (Yes=1; No=2). Site of Trauma……

History of cigarette smoking…… (Yes=1; No=2)

History of chronic/ recurrent Chest ailment …… (Yes=1; No=2) Specify……..

History of cardiac disease..... (Yes=1; No=2) Specify.....

History of use of CNS depressant drugs less than two weeks prior..... (Yes=1; No=2)

Specify .....

History of DVT or recent symptoms of DVT or predisposing factors ..... (Yes=1; No=2)

History of neuromuscular disease..... (Yes=1; No=2) Specify diagnosis.....

History of CNS malignancy..... (Yes=1; No=2)

History of heavy alcohol consumption in last 24 hours..... (Yes=1; No=2)

History of Diabetes mellitus..... (Yes=1; No=2)

History of hypertension..... (Yes=1; No=2)

History of known renal failure..... (Yes=1; No=2)

History of oxygen therapy prior to and up to time of presentation..... (Yes=1; No=2)

**Physical examination:**

Cyanosed..... (Yes=1; No=2)

Respiratory rate ..... Low=1; Normal=2; High=3.

Blood pressure: Systolic..... Diastolic..... (Low=1; Normal=2; High=3)

Edema..... (Yes=1; No=2)

Fever..... (Yes=1; No=2)

Findings of heart failure on Cardiovascular exam..... (Yes=1; No=2)

Use of accessory muscles of respiration..... (Yes=1; No=2)

Paradoxical abdominal respiration..... (Yes=1; No=2)

Finding of depressed CNS function..... (Yes=1; No=2)

Signs of neuromuscular dysfunction/paralysis..... (Yes=1; No=2)

Acute airway obstruction..... (Yes=1; No=2)

Other significant findings.....

.....

**Clinical impression/Diagnosis** .....( 1=Central disorders; 2= Respiratory muscle dysfunction; 3= Upper airway obstruction; 4=Acute obstructive airway disease; 5=Chest trauma; 6= Pneumonia; 7=Acute pulmonary edema; 8= Septicemia; 9= Pulmonary vascular dysfunction)

**Investigation Findings:**

**$SaO_2$** =.....%

**ABG:** $PaO_2$ =.....mmHg.

$PaCO_2$ = .....mmHg.

pH = ……..

**CXR FEATURES:** ARDS/ALI…… (Yes=1; No=2)

TB …… (Yes=1; No=2)

Consolidation…… (Yes=1; No=2)

Pulmonary edema…… (Yes=1; No=2)

Cardiomegally…… (Yes=1; No=2)

Fracture Ribs…… (Yes=1; No=2)

Haemo/pneumothorax…… (Yes=1; No=2)

**Other investigations:**

| INVESTIGATION | FINDING(S) |
|---|---|
| | |
| | |
| | |
| | |

**Outcome at 2weeks in hospital:**

Death….. (Yes=1; No=2) Specify number of days from admission……

Still in ARF…….. (Yes=1; No=2)

Full recovery from ARF… (Yes=1; No=2) Duration (days) to recovery from admission……

## APPENDIX 2A: CONSENT EXPLANATION FORM:

I am **Dr Mativa Boniface Mutunga**, a medical doctor in postgraduate training at the University of Nairobi. As part of my training, I am required to carry out a postgraduate research project. My project is on respiratory failure among patients coming to the A&E Department with difficulty in breathing. I am required to recruit patients with this condition into this study, and I have identified you as a potential recruit.

However, before recruiting you to participate I request to give you the details of this research work. Acute respiratory failure is a condition developing in less than two weeks in which the patient is unable to oxygenate body tissues and to eliminate carbon dioxide adequately from the body. The diagnosis of ARF involves the estimation of oxygen saturation in the body, first by attaching a pulse oximeter to your finger and subsequently taking one milliliter of blood from an artery in your forearm for analysis of arterial oxygen, carbon dioxide and pH. It will also involve tests such as a chest X-ray, full blood count, kidney function tests, ECG/Echocardiogram to assess your heart, among other tests, depending on the suspected cause of respiratory failure in you after careful examination.

In carrying out these tests, pain/discomfort will be felt while drawing blood, some questions asked may cause you distress emotionally and psychologically. This questions and/or procedures are, however, essential in establishing a diagnosis of ARF, and will guide the type of treatment that is most fitting for you.

No test that is not necessary for your management will be carried out. The follow-up for purposes of this study will be harmonized with regular follow-up in the wards. Participation in this study, therefore does not add any costs to your treatment.

While carrying out this study, all effort shall be made to ensure that no delay of or interference with your treatment occurs.

By participating in this study, you will directly benefit from speedy, exhaustive investigation, closely supervised treatment, elaborate education and feed back at every stage of your treatment, as well as wider consultation, discussion and collaboration between myself and your primary doctor. Except for inevitable pain/discomfort during diagnostic procedures, no harm will be visited upon you.

Your participation will yield information that will increase knowledge and skill in diagnosing and treating patients in ARF in future in our setting.

You are now free to ask any questions for clarification.

All information relating to your illness will be kept absolutely confidential. Your routine care provider and you will be informed of my findings at all stages of this study.

You will **not be paid** to take part in this study.

If you decline to take part in this study, you will not be discriminated in any way, and will still get complete and quality care.

You will be free to withdraw from the study and time, and this will not influence your access to and quality of your care.

I however request and encourage you to remain in the study to the end, for your benefit and that of other patients in future.

My contact is: Tel. 0733345644; and P.O Box 2552-00202, Nairobi.

You may also contact the Ethics Committee through: Prof. A. N. Guantai; Tel. 020-2726300 ext. 44355.

Thank you for your co-operation and participation.

**APPENDIX 2B: INVESTIGATOR'S STATEMENT:**

As the Principal investigator, I confirm that I have adequately explained to this patient/caregiver all the details of this study, and given them the opportunity to ask questions, which have been adequately answered.

Signed: .....

Date: .....

**APPENDIX 3: CONSENT FORM.**

Name.....

Age.....

Serial number.....

I, named above, after a well understood explanation from Dr. Mativa Boniface Mutunga, and having sought and obtained all clarification, do willingly accept to take part in the study he is conducting on prevalence, associations and outcomes of acute respiratory failure. I further accept to have all necessary tests done on me, all of which have been explained to me.
The benefits of my participation have been clearly explained, and I have understood well.

I understand that I am free to join or not to join in this study, and will either way be accorded the best possible medical care. I know that I may withdraw from the study any time I so wish without jeopardizing access to and quality of care accorded me.

With this understanding, I, on my own free will accept to take part in this study.

Sign.....

Relationship to patient.....

Dated.....

Contact:1. Dr. Mativa Boniface .M; Tel: 0733-345644; P.O Box, 2552-0202, Nairobi.
2. ECRC c/o Prof. A.N. Guantai; Tel. 020-2726300 ext.44355.

**APPENDIX 4: IDHINI YA KUSHIRIKISHWA KWA UTAFITI.**

Jina.....

Umri.....

Nambari.....

Mimi, mwenye jina lililoko hapo juu, baada ya kuelezewa vyema na Dkt. Mativa Boniface Mutunga, kwa hiari yangu nakubali kuhusishwa katika utafiti anaofanya kuhusu maradhi ya mapafu. Nakubali kufanyiwa uchunguzi wote kwa maabara, ambao nimeelezewa kwa kina.
Nakiri kwamba nimefafanuliwa kikamilifu manufaa ya kushiriki kwangu, na kuelewa barabara.

Naelewa kwamba niko huru kushiriki au kutoshiriki katika utafiti huu, na sitanyimwa haki yangu ya huduma ya matibabu kwa misingi ya uamuzi wangu.
Niko huru kujiondoa kwa utafiti huu wakati wowote pasi adhabu yoyote.

Nikielewa haya yote, na kwa hiari yangu, najitolea kushirikishwa kwa utafiti huu.

Saini.....

Uhusiano na mgonjwa.....

Tarehe.....

Anwani: 1. Dkt. Mativa Boniface .M. Simu: 0733-345644. S.L.P 2552-0202, Nairobi.
2. ECRC, c/o Prof. A.N.Guantai; Simu: 020-2726300 ext.44355.

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8th October 2008

Dr. Mativa B.M.
Dept. of clinical Medicine & Therapeutics
School of Medicine
University of Nairobi

Dear Dr Mativa

RESEARCH PROPOSAL: "ACUTE RESPIRATORY FAILURE AT THE ACCIDENT AND EMERGENCY DEPARTMENT, KENYATTA NATIONAL & REFERRAL HOSPITAL, NAIROBI, KENYA" (P187/07/2008)

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and approved your above revised research proposal for the period 8th October 2008 – 7th October 2009

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimen must also be obtained from KNH/UON-ERC for each batch.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

DR. L. MUCHIRI
AG. SECRETARY, KNH/UON-ERC

c.c. Prof. K.M.Bhatt, Chairperson, KNH-ERC
The Deputy Director CS, KNH
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