



Etiology, Clinical Profile and Outcome of Acute Respiratory Failure in Adults in Kashmir Valley (North India): A Hospital Based Prospective Study

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Abstract

Background: A prospective study to evaluate the etiological factors, clinical features, treatment modalities and outcome of acute respiratory failure in adults (> 18 years age) in Kashmir valley north India is important to understand the epidemiological trends and the detailed disease manifestations. **Methods:** We conducted a hospital based prospective study which was conducted over a period of one and half year, initiated in January 2018 and concluded in 2019 in tertiary care hospital. 100 patients above the age of 18 years with acute respiratory failure were actively enrolled. Acute respiratory failure was identified by the defined criteria, in any patient presenting with respiratory arrest / respiratory failure/respiratory distress with $SPO_2 \leq 92\%$, breathlessness of <2 weeks duration and altered respiratory pattern. The patients who fulfilled at least one of the following criteria of respiratory failure were included in the study. (I) Arterial $PaO_2 < 70$ mmHg, (II) Peripheral O_2 saturation $\leq 92\%$ breathing in room air (III) Arterial $PaCO_2 \geq 45$ mmHg (IV) $PH \leq 7.35$ with signs and symptoms of respiratory distress. **Results:** Of the total of 100 patients included in the study, the mean age of the cohort was $55 \text{ SD} \pm 19$ years. The cause of respiratory failure were COPD with acute exacerbation (45%), sepsis with MODS (20%), acute O.P. poisoning (12%), massive ICH (4%), acute liver failure with respiratory failure (3%), ARDS (3%), acute opioid poisoning with respiratory failure (3%), acute LVF (2%), PTE (2%), anaphylaxis (2%), acute M.I. (1%), myasthenia crisis (2%) strangulation with asphyxia (1%) and fat embolism (1%). Type-2 respiratory failure was found in 45% while type-1 respiratory failure was found in 55% patients. 55% patients needed invasive ventilation; 26% patients needed NIV. While 19% patients needed high flow oxygen with nasal cannula. **Conclusion:** Commonest cause of acute respiratory failure in adults is COPD with acute exacerbation (45%) followed by sepsis with MODS (20%). Type 2 respiratory failure accounted for 45% while type 1 accounted for 55% of acute respiratory failure in adults. In our study, COPD is the leading cause of death in acute respiratory failure followed by sepsis with MODS.

Introduction

Acute respiratory failure is defined as disruption in the function of respiratory system that acutely impairs the delivery of adequate O_2 or removal of CO_2 from pulmonary capillary bed or both. It has varied etiology and related manifestations and has high mortality in all age groups especially the old age. The diagnosis of respiratory failure is made on fulfilling the criteria that is respiratory distress with any of the following: arterial $PaO_2 \leq 70$ mmHg, arterial $PCO_2 \geq 45$, arterial $pH \leq 7.35$, peripheral O_2 saturation $< 92\%$. Careful assessment of history, complete physical examination and evaluation of lab parameters give clear diagnosis of respiratory failure. Acute Respiratory Failure (ARF) is one of the major causes of consultation of elderly patients in emergency departments (EDs) and is the key symptom of most cardiac and respiratory diseases, such as Cardiogenic Pulmonary Edema (CPE), and exacerbation of

Chronic Respiratory Disease (CRD) including Chronic Obstructive Pulmonary Disease (COPD), Community Acquired Pneumonia (CAP) and Pulmonary Embolism (PE), which are associated with a high morbidity and mortality [1,2]. There is little knowledge of the presentation, clinical characteristics and outcomes of ARF in elderly patients.

The respiratory system can be said to consist of two parts: the lung, i.e. the gas exchanging organ, and the pump that ventilates the lung [3]. Respiratory failure is classified as type-1 respiratory failure or type-2 respiratory failure (Martin, 1977). Type-1 respiratory failure is defined by a PaO_2 of < 60 mmHg with a normal or low $PaCO_2$. Type-2 respiratory failure is defined by a PaO_2 of < 60 mmHg and a $PaCO_2$ of > 45 mmHg [4]. Respiratory failure classified as acute, acute on chronic or chronic [4]. This distinction is important in deciding on whether the patient needs to be treated in Intensive Care Unit (ICU) or can be managed in

general medical ward and most appropriate treatment strategy, particularly in type 2 respiratory failure.

In elderly patients differentiating cardiogenic pulmonary edema (CPE) from respiratory causes is difficult for several reasons. Cardiac and respiratory diseases frequently coexist. Atypical presentation such as wheezing in cardiogenic pulmonary edema or lack of infectious signs in pneumonia is confusing [5]. In eldest patients autopsy studies have demonstrated that the main causes of death were CPE, CAP and PTE which are frequently underestimated [6]. There is little knowledge of presentation, clinical characteristic and outcome of acute respiratory failure in elderly. Furthermore, two studies suggested that prognosis was improved when early diagnosis and treatment were accurate [7].

The objective of this study was therefore to determine the cause of ARF (Acute Respiratory Failure) in >18 years age (especially elderly), the accuracy of initial diagnosis suspected by emergency physician, the impact of the initial diagnosis and treatment and the variables associated with in hospital death.

Material and Methods

A prospective study was conducted over a period of one and half years from January 2018 to August 2019 in the age group of ≥18 years admitted in A.E. ward of SKIMS Medical College Bemina Srinagar Kashmir (a 350 bedded tertiary care hospital)

The patient included in the study fulfilled at least one of the following criteria

- a) Arterial PaO₂ ≤ 70
- b) Peripheral O₂ saturation ≤ 92% at room air
- c) Arterial partial pressure of CO₂ (PaCO₂) ≥ 45 mmHg.
- d) Arterial pH ≤ 7.35
- e) Respiratory arrest with history of dyspnoea of <2 weeks (defined by feeling shortness of breath).

All patients included in the study were above 18 years of age. For every patient standard medical care included medical history, physical examination like respiratory rate, use of accessory muscles of respiration, paradoxical abdominal respiration, ABG analysis, ECG, CXR, baseline blood chemistry, CBC.

Table 1: We included 100 patients with ARF; their main characteristics are summarized.

Diagnosis	Number of patients	Death	Death percentage with groups
Pulmonary Edema	1	0	0%
Liver Failure	3	2	66.6%
Laryngeal Cause	1	0	0%
Fat Embolism	1	0	0%
COPD	45	15	33.0%
Acute Organo phosphorus Poisoning	12	0	0%
Acute Respiratory Distress Syndrome	3	2	66%
Acute Opioid Posion	3	0	0%
Intra Cranial Hermorrhage	4	3	75.0%
Anaphylaxis	2	1	50%
Left Ventricular Failure	2	1	50%
Myasthenia Crisis	1	0	0%
Strangulation	1	1	100%
Myocardial Infarction	1	1	100%
Sepsis With MODS	20	8	40.0%

At clinical presentation all patients were attended by a senior consultant. Based on the suspected diagnosis, emergency treatment and admissions were decided by senior emergency physician in accordance with the normal practice and recommendations for less than 8 hours in the emergency department before admission into medical ward/ ICU. Performance of HRCT chest was encouraged whenever possible. The HRCT was read by a radiologist. Results of various other investigations decided by physician in charge were also recorded. USG of chest, lower limb USG, CECT chest, Echo, CTPA, BNP, CRP were done wherever required. The length of hospitalisation, admission in ICU, and in hospital mortality during the stay was also recorded. Final diagnosis was determined by two senior experts (General medicinal internist and Emergency senior physician) from detailed history, examination, and investigations available.

The use of validated criteria, response to the diuretics or vasodilators, results of Echocardiography, Doppler, BNP, NT pro BNP and other cardiac tests were specially analysed for cardiogenic pulmonary edema (CPE). Results of PFT, thoracic HRCT, response to bronchodilators or steroids or antibiotics were specially analysed for PTE as recommended.

Emergency physicians were asked for their diagnosis just before patient was leaving emergency room for medical ward/ ICU.

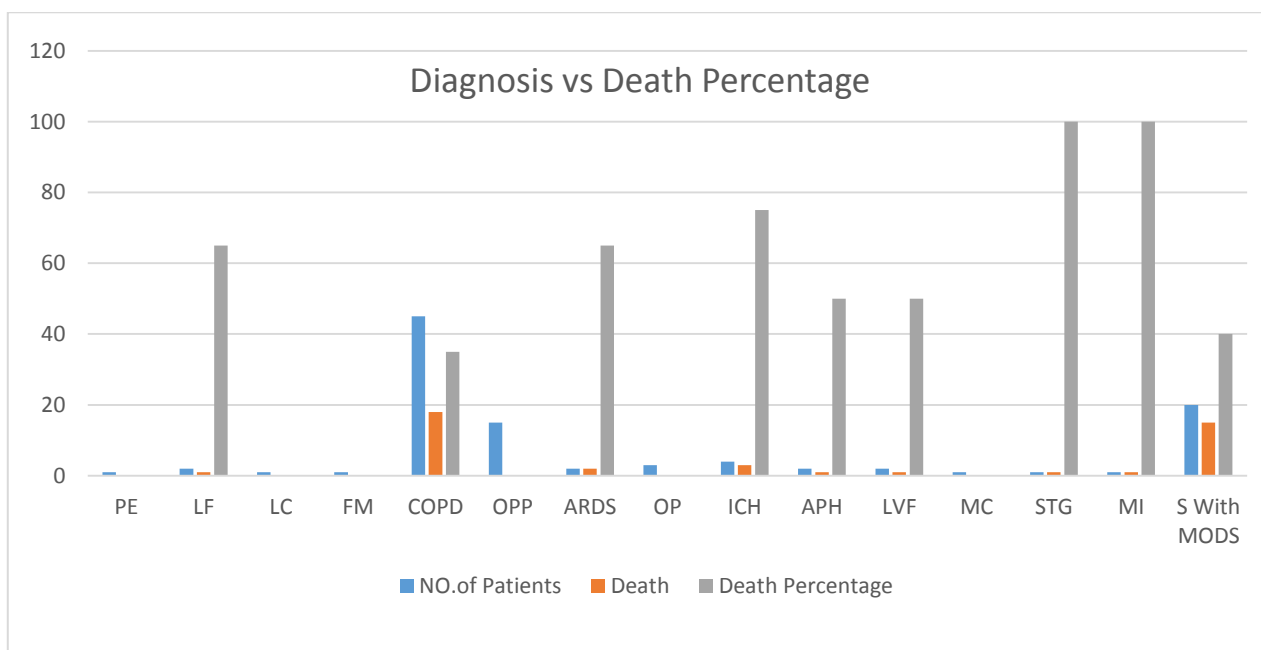
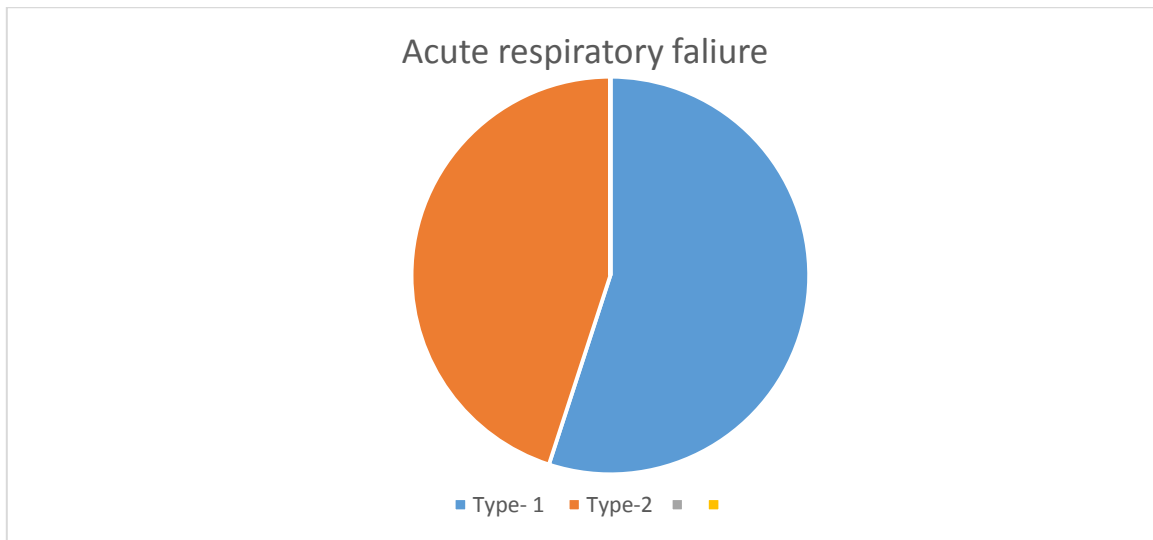
Exclusion criteria were as below:

- 1. Children <18 years.
- 2. RTA with head trauma. (traumatic cause of respiratory failure)

Statistical methodology

The statistical software programme SPSS-20 was used. A shapiro-wilk's test (p>0.05) (Shapiro and wilk, 1965; razali and wah, 2011), Kolmogorov-smirnov and a visual inspection of histogram, normal Q-Q plots and box for both control and experimental groups were tested with skewness and akurtotic values also calculated (Cramer, 1988; Cramer and howit, 2004; doane and seward, 2011). Significance was tested at p value (p<0.05) and data was presented as mean standard deviation of three individual reading.

Results



Discussion

In our study 100 patients studies showed 15 major causes of acute respiratory failure. The study showed it was COPD that resulted acute respiratory failure in majority of patients. COPD resulted in the death of 15 patients out of 45. COPD was followed by sepsis with MODS with 8 death reported in 20 patients admitted. Sepsis with MODS was followed by acute organo phosphorus poisoning. No death was recorded in acute organophosphorus poisoning patients. The acute respiratory failure was also reported in the patients diagnosed with liver failure, ARDS and in opioid poison. Mortality was observed in cases of liver failure and ARDS. In case of ICH out of 4, 3 patients died and the reason was due to co morbid conditions like diabetes mellitus, hypertension and sepsis. In case of pulmonary edema, laryngeal cause, fat metabolism, strangulation and myocardial infarction single patients were reported in each case, but death was reported only in strangulation and MI diagnosed patients.

In this prospective study, which evaluated acute respiratory failure in elderly patients, the in-hospital mortality was 34%. We observed that predictive variables of mortality were the following: initial inappropriate treatment, hypercapnia at least 45 mmHg, clearance of creatinine 50 ml/minute or less, clinical signs of acute ventilator failure, and elevated BNP or NT-pro BNP levels.

Inappropriate initial treatment occurred in one-third of case, and the in-hospital mortality was doubled than that of patients with appropriate treatment. Both the incidence and prevalence of heart failure, COPD, and CAP are increasing with age [5,8]. Previous studies have reported that COPD with AE is one of the main causes of hospitalization in elderly patients and has a high mortality rate [1,4,7,& 8]. This was confirmed in our study. However, we also showed that almost more than half of the patients had more than two causes of ARF.

Our study demonstrated an in-hospital mortality of 34 % (95% CI 13 to 19), with a higher mortality in patients in COPD (45%). In a multivariate analysis, we observed that three predictive variables of mortality were easily evaluated in emergency room: hypercapnia at least 45mmHg and clinical signs of acute ventilator failure. Thus, physicians should focus more on these criteria to evaluate the severity of illness in patients with ARF. We also confirmed that elevated BNP or NT-pro BNP levels should also be considered prognostic variables [9]. Thus, their measurements should be developed in the emergency room, because rapid measurement of BNP in the ED improved the evaluation and treatment of patients with dyspnea especially in the elderly [10]. In our study the sensitivity of diagnostic performance of the emergency physician varied from 0.86 for CAP to 0.76 for AE of COPD which was quite similar to that in another study [9]. Several

reasons explain the difficulties in assessing the causes of ARF in elderly patients. For CPE, typical presenting symptoms are frequent, such as cardiac asthma presenting an obstructive airways disease or fatigue or leg swelling [11]. Furthermore, classical radiological signs of CPE are sometimes confusing. In cases of CA, up to 50% of elderly patients have attenuated respiratory symptoms and non-respiratory symptoms such as confusion or falls, and over one third have no systemic signs of infection [5].

We confirmed that under treatment of causes of ARF was associated with higher morbidity and mortality with a close odds ratio for improved survival 92.83 (95% CI 1.48 to 4.41), $p < 0.002$. Again, age, sex, previous quality of life, respiratory rate, initial severity of hypoxemia, and admission to ICU were not significantly associated with mortality. Our study has several limitations. Our study was monocentric but included consecutively a small cohort middle aged dyspnoeic patient. Our results, especially the diagnostic performance of emergency physicians and outcomes, could have been modified if the study had taken place in other medical department (a respiratory unit or ICU, for example) or in other country where the medical care of patient is different, weather with cardiologist and pulmonologist in the assessment of the patients in the ED and hospital admission, or if Doppler echocardiography or natriuretic peptides levels are available 24 hours a day, or if non-invasive ventilation was performed in the ED. As one of inclusion criteria was an acute dyspnea (a subject symptom), it means that patients should have expressed their shortness of breath, which might have excluded some patients with severe neurological diseases but who had ARF. This might have explained the good health-related quality of life and the relatively low rate of institutionalized patients in our study population. Nevertheless, the incidences of neurological diseases and other coexisting non-cardiovascular diseases in our patients were like those observed previously [10]. Some argue that ARF is usually identified by a PaO₂ below 60 mmHg and/or a PaCO₂ above 45 mmHg (irrespective of the degree of respiratory acidosis), and we agree that these usual criteria are stricter than ours. Thus, we used a different cut off point to select ARF from that which is usually considered, with mild hypoxemia (70 mmHg or less). However, some previous studies have already other criteria in selecting patients for randomized clinical trials in non-invasive ventilation [12], with the use of clinical inclusion criteria (such as polypnea at least 25 per minute or contraction of the accessory muscles of respiration), not only gas exchange impairment. Moreover, it should be noted that we studied elderly patients in whom the capacity to face a respiratory distress is markedly reduced because of the ageing process and /or frequently associated chronic disease. In fact, we believe that our definition was enough. The method is used in our study to diagnose the cause of ARF requires comment. As in most EDs, Doppler echocardiography is not immediately available and performed in any case is rarely performed in elderly patients in clinical practice [13]. Thus, we encouraged, as soon as possible after stabilization, the use of several non-invasive investigations including HRTC without contrast iodine medium, Doppler echocardiography, and PFTs. Furthermore, to determine the final diagnosis, the experts also had the result of BNP or NT-pro BNP levels performed blind at admission, within the framework of a published study [14]. For an evident ethical reason, these investigations. Because the agreement between experts was above 85%, we suggest that the final diagnosis by experts was appropriate. Unfortunately, because it is rarely feasible in our country we did not perform an autopsy, which should be considered as the definitive diagnostic in deceased patients [6]. In our study, the rate of patients with an initial appropriate treatment

(32%) was higher than the rate of patients with an initial, missed diagnosis (14%). It should be noted that we recorded the initial treatment administered during the first hours in emergency room, whereas the diagnosis of the emergency physician was with the patient left the ED. A noticeable delay occurred between these two records, particularly in patients admitted our observation before being set to another department, usually within less than 24 hours. Although inappropriate treatment in the ED was the main factor associated with increasing mortality, we cannot demonstrate a link of causality between inappropriate initial treatment and outcomes. Thus, because our study was observational, we can only suggest that early appropriate treatment could improve prognosis, and that further studied are merited to confirm that hypothesis. Nevertheless, a prospective randomized controlled study in elderly patients suggested the rapid measurement of BNP in the ED reduced the time to discharge and the total treatment cost and seemed to reduce 30-day mortality (9a,9b).

Ethics approval and consent to participate

The study was conducted in line with the Declaration of Helsinki

List of abbreviations

ARF: Acute Respiratory Failure.
EDs: Emergency Departments.
CPE: Cardiogenic Pulmonary Edema.
CRD: Chronic Respiratory Disease.
COPD: Chronic Obstructive Pulmonary Disease.
CAP: Community Acquired Pneumonia.
PE: Pulmonary Embolism
ICU: Intensive Care Unit.
PFT: Pulmonary Function Test.
HRCT: High Resolution Computed Tomography.
ABG: Arterial Blood Gas.
ECG: Electrocardiogram.
CBC: Complete Blood Count
CXR: Chest X ray

Data Availability

Further data is made available by the authors on request to the corresponding author

Conflicts of Interest

The author(s) declare that there is no conflict of interest regarding the publication of this paper

Funding Statement

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Authors' contributions

Each author contributed equally for the research work done for the preparation of this manuscript

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