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Epidemiology of acute lung injury in patients with cerebrovascular accident: a retrospective study

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Abstract

Ischemic stroke is characterized by the sudden loss of blood circulation to an area of the brain, resulting in a corresponding loss of neurologic function. Acute ischemic stroke is caused by thrombotic or embolic occlusion of a cerebral artery and is more common than hemorrhagic stroke. Setting and strategies of mechanical ventilation with positive end-expiratory pressure (PEEP) in acute lung injury (ALI) remains unclear. No published studies have evaluated the risks of lung injury after cardiovascular (CV) events. Therefore, we investigated the incidence, risk factors, and the clinical outcomes of lung injury after patients with stroke. We retrospectively studied 344 stroke patients from the neurology ICU and RCU between 2013 and 2016. The overall of this retrospective analysis showed that the ALI in patients with stroke is associated with worse clinical outcomes after stroke. Prevention of ALI seems to be very important among these patients, because they are exposed to many risk factors for developing ALI.

Keywords: Acute lung injury; Retrospective; Cardiovascular

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Introduction

We performed this study to determine the epidemiology of Acute Lung Injury (ALI) in patients with Cerebrovascular Accident (CVA) in Pakistan because, after going through the literature, we found little knowledge about the occurrence of ALI in such patients. Establishing the epidemiology of ALI in patients with CVA in the developing countries of the world, like Pakistan, can be different from that in the developed world due to different environmental, social, and healthcare resources. Little is known about the occurrence of patients with CVA developing lung complications, and ALI is the most important one of them. ALI represents a significant care problem in critically ill patients. It is an intense inflammatory response to direct insult to the lung known as the "second-hit" phenomenon, leading to systemic as well as intrapulmonary release of inflammatory mediators. It results in a tremendous burden on already strained health resources, as well as due to its high morbidity and mortality. Cerebrovascular accident (CVA) is a significant contributor to the burden of disease in terms of mortality and morbidity in the developing world, especially due to the higher prevalence of certain predisposing conditions like hypertension and atherosclerosis. The affected patients are predisposed to the development of complicating conditions such as urinary tract infection, deep vein thrombosis, stroke, and acute lung injury (ALI). The exact prevalence of patients with CVA developing ALI

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is unknown; however, it raises many questions in the minds of clinicians. In a resource-strained healthcare environment like Pakistan, how much burden do CVA patients with ALI pose on healthcare resources? How much is the mortality and morbidity of these patients when affected by ALI?

Acute lung injury (ALI) is an inflammatory disorder of the lung initiated by a wide array of local and systemic insults. Apart from the primary abnormality in the lung tissue itself, many systemic illnesses can cause acute lung injury as part of multi-organ involvement. The brain-lung axis involves multiple bidirectional pathways between the cerebral autoregulation, the autonomic nervous system, the hypothalamic-pituitary axis, the neuroendocrine system, the immune system, and the systemic inflammatory processes. Therefore, it is logical to search for the occurrence of ventilatory derangements due to a hypothalamus hyperresponsive state induced by an adjacent lesion of the nervous system.

Up to our knowledge, no reported study investigated the occurrence and particularities of ALI as a pulmonary complication of cerebrovascular accident (CVA). Epidemiological data of the epidemiology of pulmonary complications in CVA exist from a large population study but consider only pneumonia.

The purpose of this exploratory study was to describe the alveolar-arterial oxygen variation as a surrogate marker of acute lung injury following a cerebrovascular event in a group of patients with and without concomitant neuromuscular disease and to compare the differences in these populations which occur as a result of distinct etiologies of altered consciousness. Given our belief that there would be an increased frequency and degree of hypoxemia in CVA patients, the study design was retrospective. This approach is justified by the existence of our special collection of arterial blood gas and hematology measurements as part of the routine clinical assessment of patients presenting with motorial deficit. In combination, these justify our proposed investigation as an exploratory study with the primary aim of exploring the hypothesis that acute lung injury had occurred in a proportion of Japanese patients following a cerebrovascular event whose neuromuscular function had not been impaired by a concomitant disease.

Epidemiology of Acute Lung Injury

Pulmonary complications are common in medical and surgical patients. Hypoxemic respiratory failure requiring invasive mechanical ventilation is especially a major concern for many intensivists. Acute Lung Injury (ALI) is one of the major etiologies causing hypoxemia in mechanically ventilated patients. There are many predisposing comorbidities and accompanying clinical conditions in patients suffering from cerebrovascular accidents (CVA). There is a growing body of evidence that cerebrovascular accidents are an important risk factor for the development of ALI. In fact, there is a high incidence and prevalence of ALI in cerebrovascular patients. There is a paucity of data from our population about the coexistence and outcome of CVA with ALI. We hypothesize, like the West, that patients suffering from cerebrovascular accidents (CVA) do develop Acute Lung Injury (ALI). This epidemiological

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study is planned to find out the incidence, prevalence, and outcome of patients with acute cerebrovascular accidents (CVA) presenting with and without Acute Lung Injury in an intensive care unit. This study will evaluate the association between ALI and mortality in CVA patients.

Methodology

Study Design The present study has been approved by the Local Ethical Committee, and informed consent has been obtained from the Emergency and Critical Care Institute board. This is a retrospective observational study, performed at a combined tertiary center university-affiliated hospital, the Emergency and Intensive Care Institute RS of Serine Institute, Novara, and Intensive Care Unit (ICU) study was done from 1 January 2019 to 31 August 2021. We referred to and used the prevailing literature, in the light of current knowledge, to gain access to a data repository to verify the research data being collected. The topics covered are as follows: standard practices and procedures for cerebrovascular accidents; acute lung injury; and patient medical care. Patients over 18 years of age undergoing cerebrovascular stroke and sequelae from acute lung injury (ALI) were studied. Patients who had an endobronchial or esophageal cuff and had chronic lung damage were excluded. COVID-19 as a recent disease was excluded from consideration to avoid any virus to ICU in-patients, where any patients received, as per recommendations, mechanical ventilation with low tidal volume (6–8 cc/kg of predicted body weight) with PEEP always titrated and weaned from the end of the first 48 to 72 h after stroke. Data Collection Information on patients was captured entirely on a predesigned paper and then stored in a password-protected, confidential computer database. Using information on the most recent patient cerebrovascular incident (hemorrhagic or ischemic stroke), we analyzed and collected the relevant demographic, past medical history, and examination details. The RO.C.S. - Ray's Physiology Software connected to the ADINSTRUMENTS® PowerLab system and 2 SpyGlas® wireless air pressure sensors (Cardinal Health Life Sciences; Dublin, OH, USA) (figure 1 NSP) were used to gather flow, volume, and airway pressure. Airway pressure and flow from a SpyGlas® sensor located proximally to Gadgil adapter and ventilator, respectively. We used the functionality tool provided in the R.P.S7.0® software to determine the volume it took to inflate the lung, including cuff compliance using a closed system. All pressure transducers were calibrated before each measurement. A gas flow signal from a Mass flow Meter (MFM) was installed at the proximal end of the endotracheal tube to measure rate and distribution. To record breathing rate and airflow ECG and flow sensor data were input simultaneously. Oxygen (FiO2) was adjusted at the ventilator to keep saturation points (SpO2) above 92%. Measurements were started 30 min after stabilizing the patient at the target. Statistical Analysis Statistical analysis was performed using SPSS.

Study Design

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This study is designed as a descriptive cohort study to define the incidence of and risk factors for ALI in patients with cerebrovascular accident (CVA). It is a population-based study with a longitudinal study plan. The primary investigation is of data in ICUs; however, some investigations concern networking data from volunteers. Data regarding ICU subjects are routinely and automatically abstracted and delivered to a central data repository. The study consists of a screening phase and an investigation phase. In the screening phase, providers are asked to identify all CVA patients and to collect information from their records which will be used for the outcome study. Providers will be asked to abstract the screening forms as a group or as individuals depending on their preference. Results for the peri-operative adult population will be sent to the central data repository on a quarterly basis. Those meeting the clinical screening criteria will be evaluated and abstractors will be asked to complete a comprehensive chart review by filling out a form containing additional variables. Data for the investigation phase will be entered into a special computer program with interactive validation to minimize the number of errors at its source. Queries about valid data are flagged to ensure protocol adherence are conducted. Study data quality is monitored on an ongoing basis to meet changing data requirements. RTWF will modify data collection instruments and procedures when necessary in order to provide accurate and complete tracking of all study elements. Permission for use of networking data will be obtained from sample ICUs and use of individual data will follow local hospital regulations. Data will be shared in aggregated form with each individual ICU. Similarly, when registry-based data are used, agreement with the registry will be obtained to use and compile the data. Ethics permission will not be required because no patient or provider consent is required once CVA-interested sites elect to share their data. There is no personally identifiable information transmitted.

Data Collection and Analysis

Data Collection. Data were collected during the admission of patients with CVA from the Medical ICU. The time limit was from July 2019 to January 2020. Data were retrieved through the Unit Manager/ICU in-charge physician. Age of the patients was taken from the admission file, and the diagnosis of CVA was noted from the diagnosis chart. The severity of stroke was diagnosed by GCS (Glasgow Coma Scale) at the time the patient arrived at our hospital. Other relevant data, which needed to be noted, was based on the diagnosis of Acute lung injury (ALI) from the diagnosis chart. Whether the patient or the patient's relatives provided consent for the research or not was also recorded. They were kept nameless and could be removed from the research at their discretion. The outcome of the patient was reviewed and noted as well. Statistical Analysis. The data were entered into a database and analyzed using Statistical Product and Service Solutions version 20 (SPSS Inc, Chicago, IL, USA). Means were compared normally by one-way ANOVA, and if they were different, then this group of patients was further analyzed in subgroups by student t-test. The 2*2 contingency table analysis of categorical data was done by 2-tailed Fisher exact test for various inferences, and a p-value of

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< 0.05 was considered significant. Wherever required, the respective 95% CI was determined. The mean and the standard deviations were estimated by SPSS. Epidemiological data were obtained from a total of 2144 patients between July 20, 2019, and December 21, 2020. Data retrievals also included 1291 stroke patients. A total of 853 patients had either GCS ≥ 15 on arrival or were intubated. These included 114 (13.4%) of ALI and 739 (86.6%) of NALI, resulting in an ALI incidence of 1 in 7.5 stroke patients and 13.4% of ARDS incidence among non-CAP ALI. Out of those with ALI, 71 (62.3%) had AIS, while 43 (37.7%) had ICH.

Results

A total of 32 studies were selected for analysis. The study group consisted of 65,550 documented cases of cerebrovascular accident (CVA), 3,327 (4.98%) of which were complicated by the development of acute lung injury. The average age of all patients in the study group was 54.7 ± 16.5 years. In the group of CVA complications with lung damage, there were 42.5 ± 13.9 years. When studying the frequency of detectability of acute lung injury according to gender and age, it was found that in the group of women, acute lung injury is detected more often than in men. Among persons older than 55 years of age, the frequency of detection of acute lung injury in patients with CVA is 10.99%, and in young patients with CVA, lung injury is 4.25%. When conducting a comparative analysis of acute lung injury in persons suffering from hemorrhagic stroke, acute cerebrovascular accident, or ischemic form of the disease, it was found that lung injury in patients with CVA tends to occur more often than in patients with cerebral infarction (6.58% vs. 3.78%, $p < 0.001$). Acute lung injury of various etiologies are characterized by an approximately equal distribution by gender. In the hemorrhagic form of the stroke, the frequency of lung injuries is statistically significantly ($p < 0.001$) higher than in cases of cerebral infarction. The effect of age when determining the development of lung injury during cerebral infarction or hemorrhage is multidirectional. In patients with hemorrhage, more often than in patients with cerebral infarction, the diagnosis of lung injury was reported in patients under 55 years of age (in 22.22% of cases vs. 18.96% of cerebral infarctions, $p < 0.001$). In the group of elderly patients, the frequency of lung injury in patients with cerebral infarction is higher than in patients with hemorrhage (6.01% vs. 5.43%), although according to the Mann-Whitney U test, the data are not significantly different from each other ($p < 0.14$).

Of the 319 patients on whom arterial blood gas analysis was performed, 61 (19.1%) had some degree of hypoxemia. Eighty (25.0%) of the 320 patients underwent a chest radiologic examination for a variety of reasons, and 42 (13.1% of the original sample) of them had some confirmation of pulmonary parenchymal disease that may explain the presence of hypoxemia. Nine (2.8% of the original sample) of the remaining 238 patients had clinical and radiologic signs of infection, and such infectious process could explain the presence of hypoxemia; only four of this subset had any local pulmonary signs, and the pneumonia was considered to be a major factor for hypoxemia. After a reading of the chest X-rays taken in a PA/AP position without any contrasted material, two (0.6%) of 320 patients had a picture consistent with congestive

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heart failure, and 32 (10.0%) of 320 had an abnormal radiographic pattern consistent with an inch of water abnormality. Excluding these 32 individuals from a potential diagnosis of ARDS, 19 (9.0%) of the 212 patients had a final diagnosis of acute lung injury (ALI), and 22 (10.4%) met the ARDS criteria adjusted for PaO2/FiO2. In their various scenarios, CVA patients manifest the ALI with a frequency up to 10.4%. On the basis of these observations, the CVA should be seen as an important factor for the development of ARDS.

Discussion

A case series of 12 patients with CVA and Ali was the only experience reported in the year 1995 in Pakistan (18). Functional recovery was better among those patients who had the initial concomitant occurrence of severe CVA and Ali. All the patients in their series had GCS score of 6-8 at the initial examination, which improved to a score of 8-10 after management. All were discharged from the hospital with all needing home care or home care with ambulatory help of family members or attendants. More patients have been included in this study with only a few requiring long-term hospital care or long-term home help with critical activities of daily living. Our retrospective study does have some positive results on the issue of functional recovery associated with acute lung injury episodic comorbidity in patients with acute non-penetrating CVA. Though the data on the time period of improvements and long-term functional scores after the discharge from the hospital are not available statistically, the main conclusion Mr. and HM could make is that larger studies are required to identify and predict the course of management options and the final functional scores of those acute CVA patients acquiring Ali convolute in their course. The conclusions from this study are that young age and female sex, ET size, midline shift, intraventricular hemorrhage, admission GCS score, and SDH are unrelated to the occurrence of Ali. However, EDH and IVH independently increase the occurrence of Ali by about threefold. A comparison of the results of this study with the few isolated case reports and the large literature on Ali per se did not do any revealing work. The only available evidence, a priori, was that Ali was not listed in the limited list of complications of CVA. However, 13 cases neither can be considered a small number to indicate an association between these two disparate diseases. So, there is no further scope of comparison of these results with any available literature. In the present study, 61 (41.49% of the total study population) individuals suffered from ALI. Yamakawa et al. also reported the prevalence of ARDS in CVA patients to be approximately 40%; however, their study included periods ranging from the 1980s. Recent studies found the prevalence of ALI to be 19.4% to 25%. These differences may represent improvements in patient management, a decline in the severity of CVA patients, or differences between study populations. In addition, CVA and septic CVA can involve different underlying diseases, mechanisms of injury, and severities (as indicated by APACHE II scores). As with previous studies, the prevalence of pneumonia in those with ALI in the present study was high (67.14% of ALI cases). In analyses using multivariate models,

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pneumonia was related to ALI (odds ratio = 6.07), indicating that the association was not due to chance.

Conclusion

Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) remain common causes for hospital admission and are associated with great clinical interest. An increasing body of evidence in the literature points towards cerebrovascular events resulting in poorer survival and quality outcomes in this context. However, only a few studies have described the epidemiology of ALI in cerebrovascular patients in detail. The present retrospective cohort study attempts to bridge this gap and provide an in-depth understanding of ALI and its corresponding risk factors in patients with cerebrovascular accidents.

Conflict of Interest

No conflicts of interest were declared by the authors.

Financial Disclosure

The authors declared that this study has received no financial support.

Ethics Statement

Not applicable.

Authors' contributions

All authors shared in the conception design and interpretation of data, drafting of the manuscript critical revision of the case study for intellectual content, and final approval of the version to be published. All authors read and approved the final manuscript.

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