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Research Article

Relationship between acute kidney injury and chest diseases in critically ill patients

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Abstract

Background: Acute kidney injury (AKI) is a common consequence in patients who have acute respiratory insult, in many studies reported incidence rates of up to 35%. The combination of AKI with ARDS guarantees worse consequences, including higher mortality. The risk factors that increase the risk of AKI in these patients need to be identified. Understanding these factors could aid physicians in better managing these conditions, ultimately reducing mortality. **Aim:** The aim of this study is to identify the incidence and risk factors of AKI development in patients with respiratory insults admitted to critical care units. **Method:** This retrospective cohort study was conducted in the ICU of Minia University Hospital from August 2021 to December 2022. It included all patients admitted to the ICU with respiratory diseases during the study period who met the inclusion criteria. Out of 140 patients admitted with respiratory diseases, 54 met the inclusion criteria. These were further classified into two groups: 24 patients who developed AKI and 30 patients who did not develop AKI. **Results:** The incidence of AKI among the studied patients with respiratory diseases was 44.4%. Logistic regression analysis revealed that hypertension (OR 3.7), diabetes (OR 2.7), BMI (OR 2.03), and mechanical ventilation (OR 1.3) were significant predictors of AKI development in these patients**. Conclusion:** Hypertension, diabetes, high BMI, and mechanical ventilation are significant predictors of AKI in patients with respiratory diseases. These findings underscore the importance of monitoring and managing these risk factors to mitigate the development of AKI in critical care settings.

Keywords: Acute kidney injury (AKI)- Respiratory disease -Intensive care unit (ICU)-Risk factors-Mechanical ventilation-Body Mass Index (BMI)

Introduction

The interplay between the lungs and kidneys has been a significant focus in critically ill patients [(1)]. Both organ injuries and dysfunctions are common and linked to considerable morbidity and mortality[(2)].Up to 20% of hospital admissions and 57% of ICU patients experience acute kidney damage (AKI), a common complication with significant death rates. Roughly 13% of these patients require renal replacement treatment (RRT)[(3)]

Hemodynamic, neurohormonal, and inflammatory consequences pose a risk of acute kidney injury (AKI) in patients with acute respiratory failure or acute respiratory distress syndrome (ARF/ARDS), especially those requiring invasive mechanical ventilation.[(4)]. 44.3% of ARDS patients experienced AKI within two days of the start of ARDS and the need for mechanical ventilation, according to a multicenter ICU research[(5)]. Acute respiratory failure can result in renal injury via a number of

pathways: hypercapnia, which results in elevated $PaCO_2$ levels, can cause renal vasoconstriction and systemic vasodilation, while hypoxia can lower renal blood flow and glomerular filtration[6]. Moreover, systemic proinflammatory mediators linked to AKI are produced from damaged lungs[7].

While AKI is the most frequent complication in patients with acute respiratory distress syndrome (ARDS), it is important to identify the major risk factors for AKI in these individuals. Knowing these variables could help medical professionals treat these illnesses more effectively, which would ultimately lower[8].Therefore, this study aims to identify the incidence and risk factors of AKI development in patients with respiratory insults admitted to critical care units.

Method

Study Design

This retrospective cohort study was conducted in the critical care units of Minia University Hospital, a tertiary referral center in Minia, Egypt, from August 2021 to December 2022.

Study Population

The study included all patients admitted to the ICU with respiratory diseases at Minia University Hospital during the study period who met the inclusion criteria. Out of 140 patients admitted with respiratory diseases, 54 met the inclusion criteria ***(Figure 1)***.

Inclusion Criteria:

- Patients aged 18 years or older admitted with any respiratory diseases who developed AKI during their ICU stay**.**

Exclusion Criteria:

- Patients with diseases affecting both systems, such as collagen diseases.
- Patients admitted for other reasons, such as cerebrovascular stroke or decompensated liver cirrhosis.

Study Groups

- **Group I:** Patients with respiratory diseases who developed AKI during ICU admission (n = 24).
- **Group II**: Patients with respiratory insults without AKI (AKI-free) (n = 30).

Acute kidney injury (AKI) was defined according to the RIFLE criteria, which assess serum creatinine levels and/or urine output[9]. Patients who met the RIFLE criteria within 48 hours of admission were classified as having community-acquired AKI (CAAKI) and were excluded from the study. Those who developed AKI according to the RIFLE criteria after 48 hours of admission were classified as having hospital-acquired AKI (HAAKI) and were included in the study.

Data collection

Data was retrieved from patients' medical records and included:

I- Medical history and clinical examination:

- Age, gender, weight, and height.
- History of chronic chest disease
- Signs of respiratory failure as dyspnea, cyanosis, tachypnea
- Jugular venous pressure
- urine output, fluid balance charts
- Signs of chest infection as crepitations, wheezes
- Pulmonary congestion as dyspnea, cough, recurrent chest infections.
- Mechanical ventilation.

II- Laboratory investigations; including:

- Complete blood count (CBC).
- Serum creatinine and blood urea.
- Calculation of eGFR by CKD-EPI equation.
- Serum Sodium, potassium, calcium.
- Arterial blood gases (pH, PaO2, PaCO2, HCO3)
- Microbiology as blood, sputum, urine cultures according to clinical evaluation.
- If patient clinically suspected for covid-19, we add (covid-19 PCR swab, serum ferritin, LDH, D-dimer)

III- Imaging studies:

- Chest X-rays,
- Abdominal ultrasound

Ethical consideration

- Consent was obtained from the patients when it was possible.
- The institutional review board for medical research ethics approved this research.

Statistical analysis

Data were analyzed using the Statistical Package for Social Science Program (SPSS 27 for Windows). Descriptive statistical measures for qualitative categorical variables were frequency and percentage, and for quantitative data were mean ± standard deviation. Chi squared test $\chi 2$ was used to examine the association between groups. The multivariate logistic regression was used to to determine the predictor and risk factors for developing AKI in admitted patients with respiratory insult. Statistical significance was set at a p-value of less than 0.05.

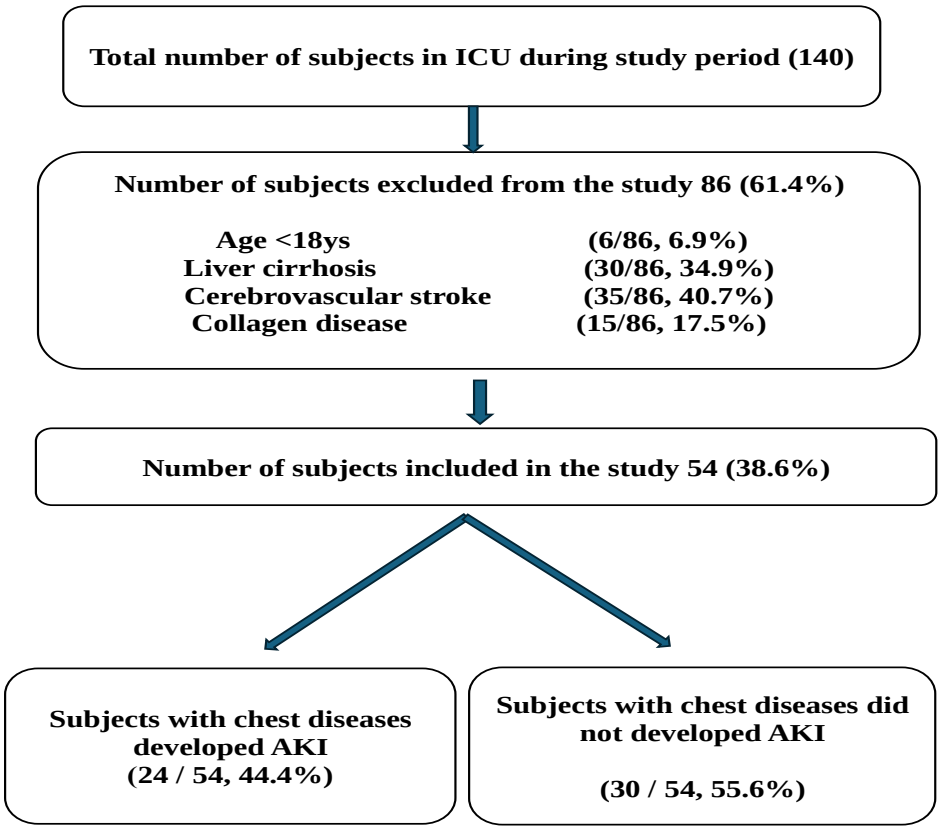

Figure 1: Flowchart Describing Study Subjects

Results

This study included 54 patients admitted to Minia University ICU with respiratory diseases. The patients were divided into two groups: 24 (44.4%) who developed AKI and 30 (55.6%) who did not develop AKI. There was no significant difference between the groups in terms of age and gender. However, there was a significantly higher prevalence of hypertension, diabetes, and chronic kidney disease in the group that developed AKI. No significant difference was observed between the groups regarding the history of chronic chest diseases (Table 1).

In the clinical examination, the body mass index (BMI) was significantly higher in the AKI group (28.2 ± 2.6) compared to the non-AKI group (25.5 ± 1.4). However, there were no significant differences between the groups in terms of respiratory rate, urine output per 24h, and jugular venous pressure (Table 1).

The comparison between the study groups revealed significant differences in C-reactive protein, creatinine, urea, GFR, arterial blood pH, PaO_2, $PaCO_2$, serum HCO_3, and serum Ca levels. However, no significant differences were found in hemoglobin, WBC count, serum Na, and serum K levels (Table 2).

In the abdominal ultrasound, 10 cases (41.7%) in the AKI group had diseased kidneys, showing no significant difference compared to the non-AKI group, which had 9 cases (30%). Similarly, chest X-ray findings were very similar between the two groups, with no significant differences observed (Table 3).

In our logistic regression analysis, aimed at identifying risk factors associated with the development of AKI in ICU patients with respiratory diseases, we found significant associations with several variables.

Hypertension emerged as a significant predictor, with the odds of developing AKI being approximately 3.7 times higher in hypertensive patients compared to non-hypertensive patients (OR 3.7 [95% CI 0.7–20], p = 0.04). Additionally, a history of diabetes was significantly associated with AKI occurrence, with diabetic patients being about 2.7 times more likely to develop AKI (OR 2.7 [95% CI 0.5–12.3], p = 0.031).

Body Mass Index (BMI) also proved to be a significant predictor; each one-unit increase in BMI was associated with 2.03 times increase in the odds of developing AKI. Furthermore, the need for mechanical ventilation significantly predicted AKI development, with an odds ratio of 1.3 (95% CI 1.1–8.1, p = 0.04). However, chronic kidney disease did not show a significant association with AKI occurrence in this analysis (Table 4).

Table 1: Comparison between demographic data, history of chronic diseases, clinical examination between study groups

Variables	Chest disease developed AKI N=24	Chest disease without AKI N=30	p- value
Demographic data			
Age			
Min-Max	18-90	19-65	0.5
Mean ± SD	47.1 ± 20.7	43.4 ± 15.5	
Gender			
Male	11 (45.8%)	15 (50%)	0.8
Females	13 (54.2%)	15 (50%)	
History of chronic diseases			
Hypertension			
No	6 (25%)	21 (70%)	<0.001*
Yes	18 (75%)	9 (30%)	
Diabetes Mellitus			
No	8 (33.3%)	21(70%)	0.01*
Yes	16 (66.7%)	9 (30%)	
Chronic chest diseases			
No	21 (87.5%)	24 (80%)	0.5
Yes	3 (12.5%)	6 (20%)	
Chronic kidney diseases			
No	9 (37.5%)	22 (73.3%)	0.02*
Yes	15 (62.5%)	8 (26.7%)	
Clinical Examination			
Body Mass Index (BMI: kg/m2)			
Min-Max	23.4-35.3	23.6-28.3	<0.001*
Mean ± SD	28.2 ± 2.6	25.5 ±1.4	
Respirator rate			
Min-Max	19-32	23-30	0.5
Mean ± SD	27.2 ± 3.5	26.7 ± 2.4	
Urine output / 24h			
Min-Max	700-2000	800-2000	0.3
Mean ± SD	1383.3 ± 300.2	1480 ± 366.2	
Jugular venous pressure (JVP)			
Min-Max	6-20	7-16	0.1
Mean ± SD	11.33 ±3.5	10.4 ± 2.9	
Mechanical ventilation			
Yes	14 (58.3%)	6 (20%)	0.004*
No	10 (41.7%)	24 (80%)	

*Significant

Table 2: Comparison between study groups in laboratory investigation on admission

laboratory investigation	Chest disease developed AKI N=24		Chest disease without AKI N=30		p- value
	Mean	SD	Mean	SD	
Hemoglobin (g/dl)	11.2	1.8	11	1.١	0.6
WBCs (counts/mm)	13.9	6.9	12.5	2.9	0.3
C-reactive protein (mg/dl)	49.8	45	27	28.7	0.03*
Creatinine (mg/dl)	2.2	0.7	1.2	0.4	<0.001*
Urea (mg/dl)	101.5	40.8	60.4	32.6	<0.001*
GFR (ml/min/1.73m2)	35.2	15.4	74.5	29.4	<0.001*
Arterial blood pH	7.٤	0.04	7.3	0.04	<0.001*
PaO2: FiO2	59.7	7.7	70.2	9.١	<0.001*
PaCO2 (mmHg)	34.9	8.2	40.6	8.7	0.02*
Serum HCO3 (mmol/L)	19.4	3.9	21.7	1.8	0.01*
Serum Na (mmol/L)	138.7	4.4	137.7	3.2	0.3
Serum K (mEq/L)	4.3	0.5	4.4	0.4	0.5
Serum Ca (mg/dl)	1.1	0.1	0.9	0.1	<0.001*

*Significant

N.B: PaO_2, partial pressure of oxygen in arterial blood. AKI, acute kidney injury; eGFR, estimated glomerular filtration rate

Table 3: Comparison between study groups in imaging

Variables	Chest disease developed AKI N=24	Chest disease without AKI N=30	p- value
Abdominal Us			
Normal	14 (58.3%)	21(70%)	0.4
Diseased kidney	10 (41.7%)	9 (30%)	
Chest X ray			
Consolidation	13 (54.2%)	18 (60%)	
GGO	8 (33.3%)	6 (20%)	0.6
Effusion	2 (8.3%)	3 (10%)	
Infarction	1 (4.2%)	3 (10%)	

Table 4: Risk factors for acute kidney injury in patients with chest diseases admitted in ICU

Risk factors	B	Odds Ratio	P- value	95% confidence interval	
				Lower	Upper
Hypertension	1.7	3.7	0.04*	0.7	20
BMI (kg/m2)	0.7	2.03	0.03*	1.4	2.9
Diabetes Mellitus	0.9	2.7	0.02*	0.5	12.3
Mechanical ventilation	0.3	1.3	0.04*	1.1	8.1
Chronic kidney diseases	1.3	3.8	0.1	0.8	18.1
Constant	-2.5	-	0.003	-	-

*Significant

Discussion

Acute kidney injury (AKI) is a common consequence in patients have acute respiratory distress syndrome (ARDS), in many studies reported incidence rates of up to 35%. The combination of AKI with ARDS guarantees worse consequences, including higher mortality and longer hospital stays [10].

In this study, we evaluated lung-kidney interactions in 54 patients admitted to critical care units with respiratory diseases. Among these patients, 24 (44.4%) developed AKI. This finding aligns with the study by Shebl et al., which reported that 38.3% of patients ARDS developed AKI [8], and the study by Darmon et al., which found that 44.3% of ARDS patients developed[5] .

Several risk factors can predispose patients with respiratory diseases to AKI. The most significant ones include advanced age, sepsis, , and the presence of comorbidities such as hypertension, diabetes mellitus, heart disease, chronic kidney disease, and liver diseases[11].

In this study the significant predictors of AKI development in patients with respiratory diseases were hypertension, diabetes, mechanical ventilation, and high BMI.

Our results indicated that diabetes was a significant predictor of AKI development in our study population, with diabetic patients being approximately three times more likely to develop AKI. This finding aligns with Magboul et al., who identified diabetes mellitus as one of the most frequent comorbidities in patients who developed AKI and a significant predictor of AKI (OR 2.6) [12]. Similarly, Mo et al., reported that the risk of AKI in diabetic patients was nearly twice that of non-diabetics (OR 1.76)[13].

Diabetic nephropathy involves both glomerular and microvascular changes. The microvascular injury component of DM is due to excess blood glucotoxicity, which leads to microinfarcts, a decreased number of nephrons, and a reduction in renal functional reserve. Additionally, diabetic hyperglycemia induces secondary metabolic pathway formations, such as non-enzymatic glycation, which causes disturbances in the production of extracellular matrix components leading to glomerular occlusion, and the polyol pathway, which produces sorbitol as a metabolite. In large quantities, sorbitol leads to hyperosmotic stress and subsequent cellular damage [14].

In this study, hypertensive patients were significantly more prevalent in the AKI group, with the odds of developing AKI being 3.7 times higher in hypertensive patients. This finding is slightly higher than the results reported by Magboul et al., where the odds ratio was 2.4[12], and by Mo et al., with an odds ratio of 1.6[13]. The increased risk in our study may be due to the compounding effects of chest diseases, which can exacerbate the severity and impact of hypertension. The link between hypertension and renal injury may be caused by endothelial injury, leading to the formation of atheromatous plaques. These plaques narrow the vessel lumen, reducing renal blood flow and impairing the self-regulatory mechanisms of the renin–angiotensin–aldosterone system (RAAS) [14].

This study demonstrated that patients with a higher BMI had a significantly increased risk of developing AKI, with each one-unit increase in BMI was associated with 2.03 times increase in the odds of developing AKI. This finding is consistent with the study by Danziger et al., which reported a 10% increase in the risk of developing AKI in ICU patients for every 5-unit increase in BMI(15). Similarly, Ju et al., found that a high BMI is associated with the development of AKI in patients with respiratory diseases and severe illness [16].

Several factors explain the relationship between obesity and AKI. Obesity can significantly alter renal hemodynamics leading to increased renal plasma flow and glomerular filtration rate, which lead to a high filtration rate, making the kidneys more susceptible to damage [17]. Moreover, ICU patients with obesity face a higher risk of intra-abdominal hypertension, which can lead to kidney dysfunction due to a combination of venous congestion and poor arterial perfusion[18]. Increased secretion of cytokines and hormones from adipocytes in obese patients may also contribute to inflammation and endothelial cell activation, making the kidneys more vulnerable to injury[19].

This study found that patients who developed AKI had significantly lower PaO2/FiO2 ratios, consistent with the findings of Shebl et al.,[8]. Also, Husain et al., explained that hypoxemia (oxygen saturation 83–87%) can reduce renal blood flow and decrease glomerular filtration[6] (Figure 2).

In this study, acidosis was more prevalent in the AKI group which was consistent with Shebl et al., finding[8]. This can be attributed to the fact that acidosis and blood gas disturbances are common features of acute pulmonary impairment and can impair renal function, although the mechanisms remain unresolved. Acidosis reflects hemodynamic instability, respiratory issues, and tissue oxygenation deficits [20]. A study by Vaia et al., demonstrated that metabolic acidosis is associated with an increased risk of doubling serum creatinine levels and higher all-cause mortality compared to normal status. Conversely, Hamlin et al., indicated that hypercapnia and its vasodilatory effects reduce systemic vascular resistance and systemic blood pressure, leading to neurohormonal activation and the retention of salt and water, although this response can vary [21].

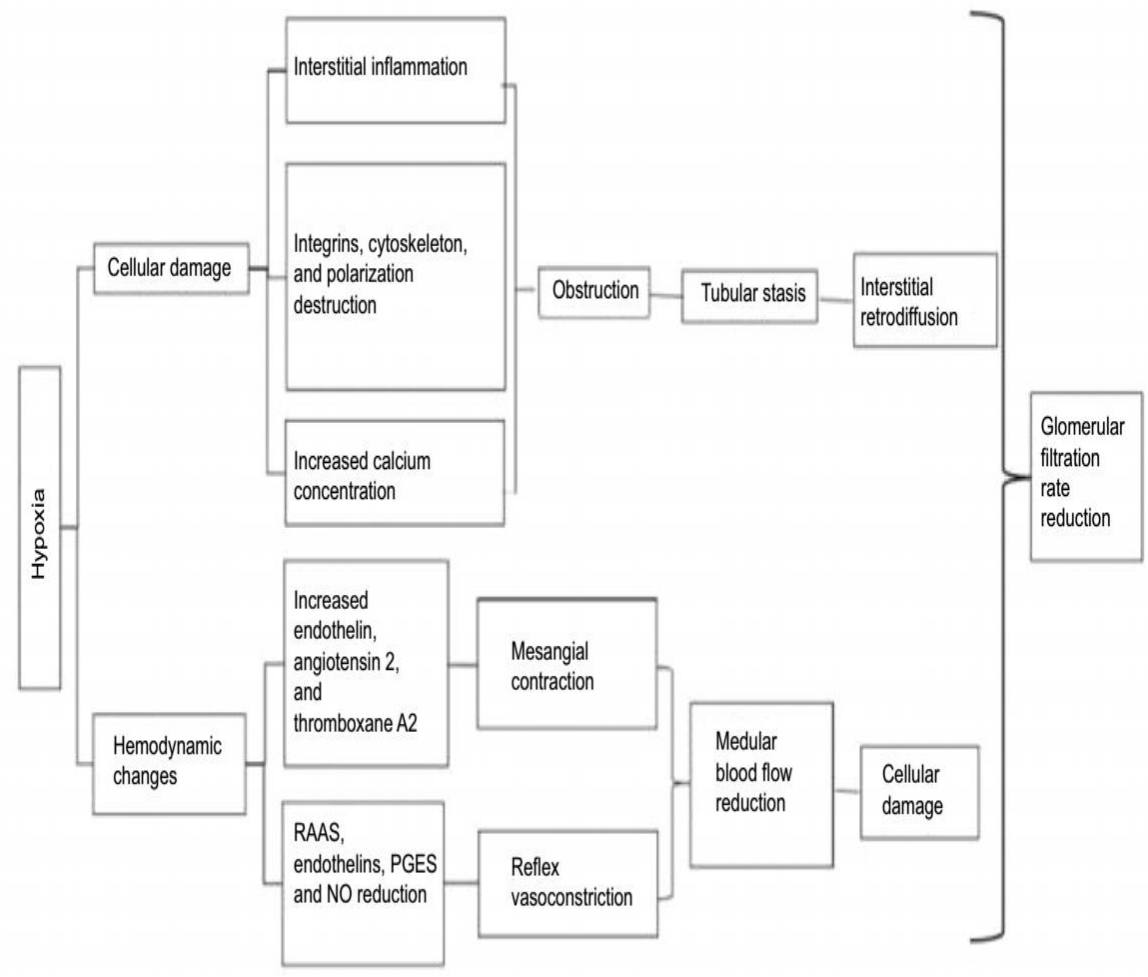

Figure 2: Hypoxia and AKI [22]

Our findings revealed that the need for mechanical ventilation significantly predicts the development of AKI. This aligns with Anumas et al., who identified mechanical ventilation as

an independent variable for AKI development [23]. Mechanical ventilation has several drawbacks that may adversely affect kidney function. Positive-pressure ventilation can stimulate the renin-angiotensin-aldosterone system (RAAS) and alter hemodynamic status, leading to decreased renal blood flow[24].

In our study, we did not find a statistically significant relationship between age and AKI development, contrary to previous study which reported that patients in the AKI group were significantly older [25]. The elderly are more prone to AKI due to kidney senility and a higher frequency of comorbidities, leading them to undergo several medical procedures, which are also risk factors for AKI [26]. As age increases, there is a higher rate of cellular apoptosis in the kidneys, resulting in fewer functional nephrons. This contributes to a reduction in glomerular filtration rate (GFR) and creatinine clearance ratio, which decreases renal functional reserve and makes the kidneys more susceptible to AKI [27].

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