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Acute Kidney Injury in Elderly Subjects Hospitalized for Pneumonia: Incidence and Predictors for In-Hospital Mortality

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ABSTRACT

Background: Pneumonia is a significant health problem, especially in elderly, where it is associated with higher mortality and morbidity. Similarly, acute kidney injury [AKI] had major impact in the overall outcome of hospitalized patients. The development of AKI in elderly with pneumonia suggested to have a worse outcome. However, previous results are heterogenous.

Aim of the work: The current work was designed to retrospectively estimate the incidence of AKI in hospitalized elderly subjects with pneumonia.

Patients and Methods: Files with complete data of 92 elderly patients hospitalized for pneumonia were checked for collection of data. The main outcomes were the development of acute kidney injury [primary outcome] and associated in hospital mortality [secondary outcome. The collected data included patient demographics, laboratory data and outcome.

Results: The incidence of AKI was 33.7%. The minimum age was 66 years, with slight increase of males than females. No significant differences were found for patient demographics or individual comorbid diseases. However, overall patients with morbidity were significantly higher in AKI than non-AKI groups [90.3% vs 68.9%, respectively, $p < 0.05$]. AKI was significantly associated with anemia, higher WBCs count, higher urea and creatinine. But with lower estimated glomerular filtration rate [eGFR]. The total rate of in hospital mortality was 27.2% with significant increase of mortality in AKI than non-AKI groups [41.9% vs 19.7%, respectively]. Mortality in AKI was associated with anemia, sepsis, hypertension, diabetes mellitus, ischemic heart disease and cerebrovascular accidents, higher serum urea and creatinine and lower eGFR. With multiple regression, ischemic heart disease and lower eGFR are the main predictors [associates] of mortality in AKI.

Conclusion: Elderly subjects with pneumonia had a higher incidence of Acute kidney injury. The presence of associated comorbid conditions [specifically ischemic heart diseases] and impaired renal functions were the main predictors of in-hospital mortality among those patients.

Keywords: Geriatrics; Pneumonia; Critically Ill; Mortality; Complications.

INTRODUCTION

Pneumonia is a serious condition, associated with significant morbidity and mortality, especially in elderly. In addition, its incidence is increased with age. The healthcare costs are increased due to hospitalization. In addition, it is one of the top 10 leading causes of death in USA for example. The highest mortality was reported among patients aged 70 or older [1-3]. In this age group, the clinical characteristics of pneumonia may differ from younger population. Asymptomatic or atypical presentations are more frequent in older adults. Atypical presentations include flaring up of chronic conditions [e.g., heart failure or COPD [Chronic obstructive pulmonary disease]]. Absent clinical manifestations like fever, hypoxemia, high white blood cell count, tachycardia or respiratory manifestations do not rule out the diagnosis of pneumonia in older population [4, 5].

The commonest atypical presentations include altered mental state, falls, altered consciousness, anorexia, general weakness, dehydration or urinary incontinence. These manifestations may prevent the proper diagnosis of pneumonia and thus affects the adequate and early treatment intervention. A previous study showed that unaltered vital signs like heart rate and temperature in older patients with suspected pneumonia delays diagnosis and antibiotic administration. This increases the likelihood of hospitalization with increased need for admission to intensive care and higher rate of complications [6].

Acute kidney injury [AKI] is a frequent complication of pneumonia. Its incidence ranged from 18 to 34% [7-11]. The coexistence of pneumonia and AKI had a worse outcome than patients with either AKI or pneumonia alone [12-15]. AKI is common in pneumonia regardless of the severity [up to 25% in mild and moderate cases]. The presence of AKI is associated with a significant increase of short- and long-term morbidity and mortality [16, 17].

However, the impact of AKI on in-hospital morbidity and mortality of pneumonia in geriatrics remains unclear. Thus, the current work was designed to examine the incidence of AKI in elderly patients hospitalized for pneumonia and compare outcome to patients with preserved kidney function.

PATIENTS AND METHODS

This study was performed in Al-Azhar University Hospitals [Cairo and Damietta]. The data of all patients admitted due to pneumonia between October 2021 and October 2023 was collected.

The inclusion criteria were patients aged 60 years or older with a diagnosis of pneumonia and preserved kidney function. The preserved kidney function was defined as an estimated glomerular filtration rate > 60 ml/min/1.73 square meter.

On the other side, the exclusion criteria were patients with impaired renal function, liver cell failure, cancer, and pressure sores. The complete health records were obtained for 92 patients. Then patients were categorized into two groups. Those with AKI developed during the first five days of admission and the second group, without AKI.

The collected data included patient demographic characteristics, pre-existing associated chronic medical diseases, the history of medications, data of laboratory workup and radiological investigations. The collected data was documented on an excel worksheet and transferred to statistical software package for analysis.

The diagnosis of Pneumonia [Figures 1-3] was based on the clinical profile and detection of new infiltrative inflammatory changes on the chest radiography performed at the time of admission. In addition, the AKI was diagnosed by the rise of serum creatinine concentration by 0.3 mg/dl or more during any time of the first 48 hours compared to values at admission or 1.5 or more times of the basal values [18].

The primary outcome was the development of AKI. The secondary outcomes include other complications or mortality during admission.

Data analysis: The mean ± standard deviation [mean ± SD] was calculated for continuous variables. On the other side, relative frequencies and percentages were calculated for categorical variables. Independent samples student and Chi square tests were used to compare between means and test association, respectively. When small frequencies were expected [< 5], the Fisher's Exact test was used to test association instead of Chi square. Linear regression analysis was performed to determine predictors of mortality in study groups. P value < 0.05 was considered significant. All analyses were performed using the statistical package for social science, version 23 [IBM®, Armonk, NY, USA].

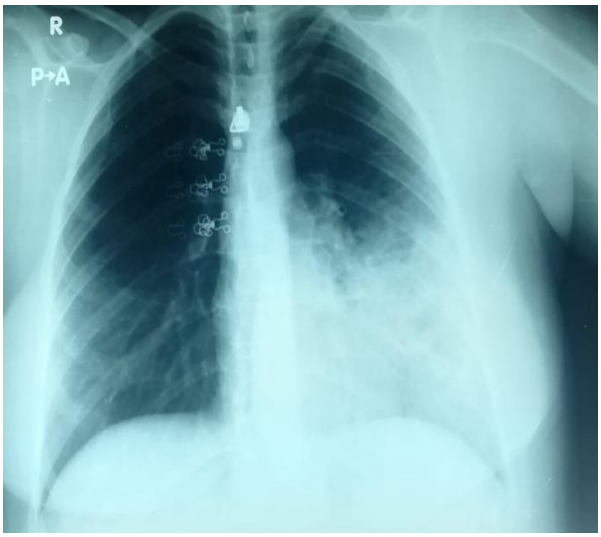

Figure [1]: Plain x-ray chest, PA view showing left sided pneumonia

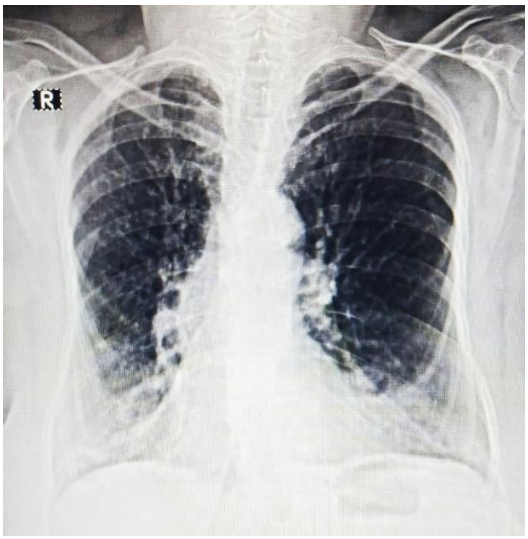

Figure [2]: Plain X-ray chest, PA view showing bilateral basal pneumonia

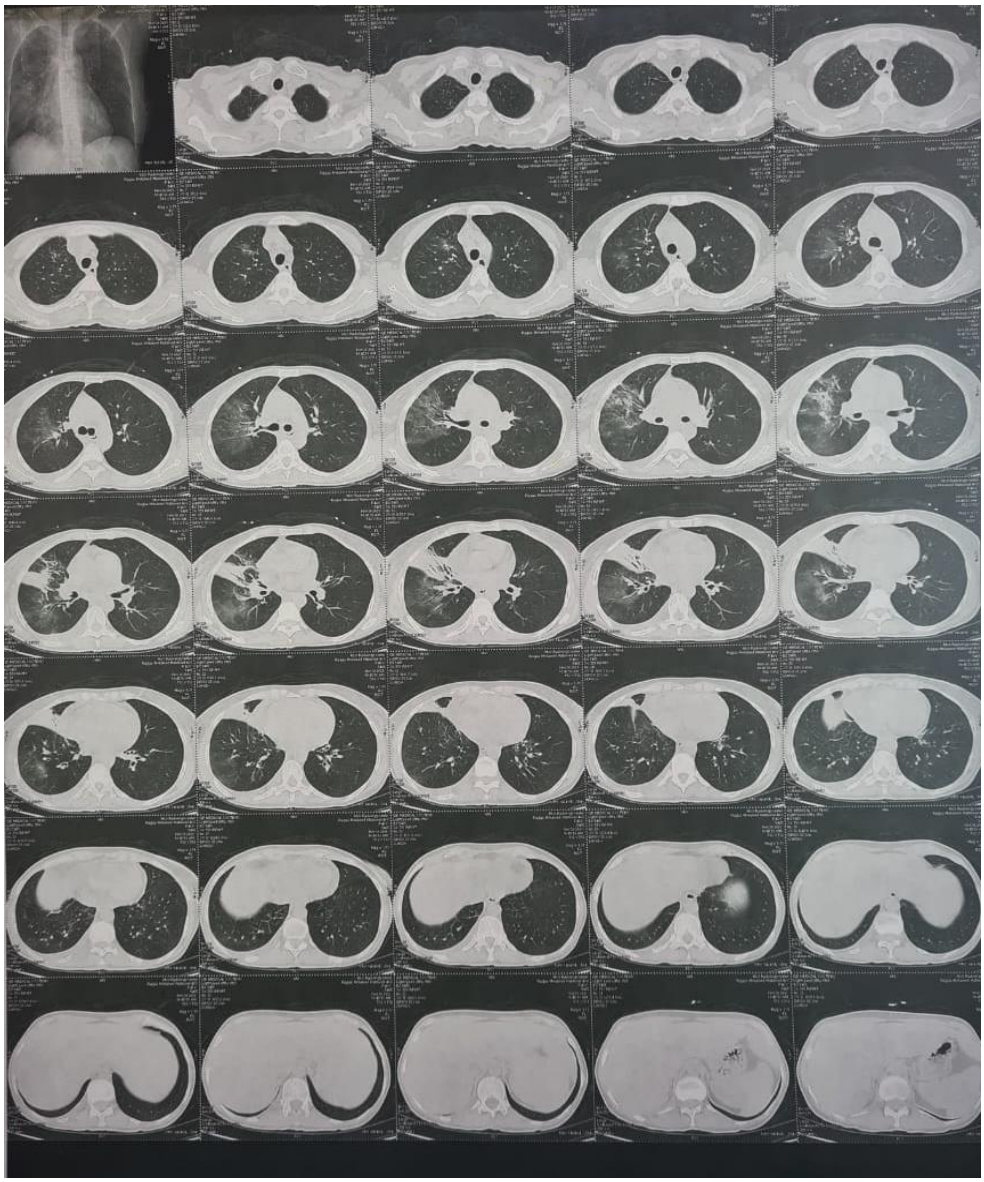

Figure [3]: CT chest showing Right sided pneumonia [middle lobe]

RESULTS

In the current work, data for 92 elderly subjects admitted for pneumonia were collected and documented. The AKI was developed in 31 subjects [33.7%], while others did not develop AKI. Patients age ranged between 66 and 88 years with no significant difference between those who developed AKI and those who not. There was slight increase male gender in both groups, with no significant difference [males represented 51.6% and 63.9% of AKI and non-AKI groups, respectively]. Both groups were comparable regarding associated comorbid conditions [chronic medical diseases]. However, when checking all cases with other morbid condition, the morbidity was significantly increased in AKI than non-AKI groups [90.3% vs. 68.9%, respectively] [Table 1].

Regarding results of laboratory work up at admission, the development of AKI was significantly associated with lower RBCs, lower hemoglobin, higher white blood cell count, higher serum creatinine, lower estimated GFR and higher blood urea nitrogen. However, there was no significant differences between groups regarding platelet count, fasting blood sugar, ALT and AST. [Table 2]. In addition, the overall rate of in hospital mortality was 27.2% with significant increase of mortality in AKI than non-AKI groups [41.9% vs 19.7%, respectively] [Table 2].

Mortality in AKI group was significantly associated with significant increase of hypertension, diabetes, ischemic heart disease and cerebro-vascular accidents. In addition, it is significantly associated with lower hemoglobin, higher WBCs count, higher fasting blood sugar, lower estimated GFR and higher values of serum urea and creatinine [Table 3].

To check for predictors of mortality in AKI groups, liner regression analysis was performed for significantly associated factors with mortality. This analysis revealed that, ischemic heart disease and estimated GFR are the main predictors of mortality in this group [Table 4]. On the other side, in those who do not develop AKI, the main predictors of mortality were higher white blood cell count and higher serum creatinine [Table 5].

Table [1]: Patient demographics and associated comorbid chronic medical diseases among the study groups

Variable	Measures	AKI [n=31]	No AKI [n=61]	Test	P
Age [years]	Mean ± SD	80.26 ± 4.23	78.89 ± 4.90	1.33	0.187
	Min.- Max	69-86	66-88		
Gender, n [%]	Male	16 [51.6%]	39 [63.9%]	1.30	0.25
	Female	15 [48.4%]	22 [36.1%]		
Hypertension, n [%]		16 [51.6%]	22 [36.1%]	2.05	0.15
Diabetes Mellitus, n [%]		12 [38.7%]	19 [31.1%]	0.53	0.47
Ischemic Heart disease, n [%]		12 [38.7%]	21 [34.4%]	0.16	0.69
Osteoporosis, n [%]		10 [32.3%]	13 [21.3%]	1.31	0.25
Cerebrovascular accident, n [%]		11 [35.5%]	14 [23.0%]	1.63	0.20
Other comorbid condition, n [%]		28 [90.3%]	42 [68.9%]	**5.20**	**0.022***

Table [2]: Laboratory workup at admission and in-hospital mortality among study groups

Variable	AKI [n=31]	No AKI [n=61]	Test	P
RBCs x 10^6/ml	3.98 ± 0.45	4.40 ± 0.47	4.18	**<0.001***
Hemoglobin [g/dl]	9.95 ± 0.85	10.79 ± 0.92	4.23	**<0.001***
WBCs x 10^3 / ml	12.76 ± 1.90	11.55 ± 1.62	3.19	**0.002***
Platelets x 10^3 / ml	274.71 ± 53.03	293.37 ± 65.40	1.37	0.17
Fasting blood sugar [mg/dl]	132.26 ± 32.96	121.89 ± 28.64	1.56	0.12
ALT [IU/L]	58.68 ± 16.88	58.29 ± 13.38	0.12	0.91
AST [IU/L]	52.71 ± 14.18	49.15 ± 12.18	1.25	0.22
Serum creatinine [mg/dl]	2.88 ± 0.84	0.99 ± 0.19	16.80	**<0.001***
Blood urea nitrogen	89.62 ± 24.81	31.34 ± 6.10	17.41	**<0.001***
Estimated GFR [ml/min/1.73 m^2]	20.71 ± 5.86	63.49 ± 10.89	20.37	**<0.001***
In hospital mortality [n, %]	13 [41.9%]	12 [19.7%]	5.15	**0.023***

Table [3]: Factors associated with mortality in pneumonia with AKI

Variable	Died [n=13]	Survived [n=18]	Test	P
Age [years	79.46 ± 4.68	80.83 ± 3.91	0.89	0.38
Sex [male] [n, %]	8 [61.5%]	8 [444.4%]	0.88	0.34
Hypertension [n, %]	12 [92.3%]	4 [22.2%]	14.84	**<0.001***
Diabetes [n, %]	8 [61.5%]	4 [22.2%]	4.92	**0.027***
Ischemic heart disease	11 [84.6%]	1 [5.6%]	19.88	**<0.001***
Osteoporosis	3 [23.1%]	7 [38.9%]	0.86	0.35
Cerebrovascular accident	9 [69.2%]	2 [11.1%]	11.14	**<0.001***
Other comorbid disease[s]	13 [100.0%]	15 [83.3%]	2.40	0.12
RBCs x 10^6/ml	3.87 ± 0.45	4.06 ± 0.44	1.16	0.256
Hemoglobin [mg/dl]	9.58 ± 0.53	10.21 ± 0.95	2.16	**0.039***
WBCs x 10^3/ml	14.16 ± 1.58	11.75 ± 1.43	4.45	**<0.001***
Platelets x 10^3/ml	268.77 ± 65.98	279.00 ± 42.95	0.52	0.61
Fasting blood sugar [mg/dl]	147.15 ± 31.74	121.50 ± 30.24	2.28	**0.030***
ALT[IU/L]	61.31 ± 12.11	56.78 ± 19.76	0.73	0.47
AST [IU/L]	55.00 ± 11.91	51.06 ± 15.74	0.76	0.45
eGFR [ml/min/1.73 m^2]	15.38 ± 3.55	24.56 ± 3.79	6.82	**<0.001***
Creatinine [mg/dl]	3.66 ± 0.69	2.32 ± 0.37	7.02	**<0.001***
BUN [mg/dl]	112.31 ± 20.06	73.22 ± 11.14	6.94	**<0.001***

Table [4]: Linear regression analysis to estimate predictors of mortality in AKI group

	Unstandardized Coefficients		Standardized Coefficients	Sig.
	B	Std. Error	Beta	
Hypertension	0.107	0.085	0.108	0.225
Diabetes	-0.100	0.307	-0.099	0.747
Ischemic heart disease	0.250	0.104	0.246	**0.026***
Cerebrovascular accident	0.008	0.090	0.008	0.927
Hemoglobin	-0.003	0.039	-0.005	0.938
WBCs	-0.019	0.026	-0.072	0.471
Fasting blood sugar	-0.002	0.004	-0.135	0.644
eGFR	0.038	0.014	0.483	**0.013***
Creatinine	-0.078	0.128	-0.136	0.548
BUN	-0.001	0.003	-0.054	0.750

Table [5]: Linear regression analysis to determine predictors of mortality in the group of non-AKI

	Unstandardized Coefficients		Standardized Coefficients	Sig.
	B	**Std. Error**	**Beta**	
Hypertension	0.019	0.072	0.024	0.787
Diabetes	-0.008	0.290	-0.009	0.978
Ischemic heart disease	0.051	0.077	0.061	0.511
Cerebrovascular accident	0.170	0.066	0.180	**0.012**
Hemoglobin	-0.029	0.034	-0.068	0.393
WBCs	-0.144	0.021	-0.581	**0.000**
Fasting blood sugar	-0.001	0.005	-0.050	0.882
eGFR	0.005	0.004	0.133	0.198
Creatinine	-1.084	0.368	-0.502	**0.005**
BUN	0.020	0.011	0.297	0.091

DISCUSSION

The current work revealed that; the AKI incidence is higher in elderly patients admitted for pneumonia. The incidence was 33.7%. This was associated with significantly higher mortality when compared to patients who did not develop AKI [41.9% vs. 19.7%, respectively]. The main predictors of mortality in AKI group were the presence of ischemic heart disease and reduced estimated GFR. On the other side, predictors of mortality in elderly patients with pneumonia

without development of AKI were higher white blood cells and higher creatinine. These results are comparable to those reported by **Lubart *et al.*** [19] who reported that, old patients who developed AKI after admission for community acquired pneumonia [CAP] experienced significantly higher mortality rate and worse in-hospital outcomes. In addition, the there was a significant relationship between reduced levels of estimated GFR and mortality. The highest mortality was reported in patients with estimated GFR lower than 30 ml/min/1.73 m^2. in addition, **Chen *et al.*** [11] reported higher rate of in-hospital mortality in AKI than non-AKI groups [23,5 % versus 4.9 %, respectively]. However, the incidence of mortality in their study is lower than the current one and this could be explained by the different inclusion criteria and the small sample size in the current work compared to their study. However, values of the current work are lower than those reported by **Chawla *et al.*** [12] who reported that, the mortality rate was 51.3% and 42.7% in patients admitted for pneumonia who developed AKI and those who do not developed AKI, respectively.

Latief *et al.* [20] reported a mortality rate of 27.6% in patients with pneumonia developed AKI. Like the current work, the patients with AKI in their study had significantly higher associated comorbid conditions [e.g., chronic kidney disease, ischemic heart disease, hyperuricemia, hyperbilirubinemia, significantly elevated creatinine and urea, and lower albumin, when compared to non-AKI group]. **Serov *et al.*** [21] reported that, the predisposing factors for development of AKI in patients with pneumonia are old age, diabetes mellitus, urinary tract infection and hemodynamic disorders.

Jain *et al.* [10] on the other side, reproved that, the risk factors associated with in-hospital mortality included male gender, obesity and hypertension. However, **Lin *et al.*** [22] reported elevated incidence of AKI in patients with pneumonia associated with other comorbid conditions [e.g., diabetes, hypertension, liver cirrhosis, congestive heart disease and cerebro-vascular accidents].

The relation between lung and kidney [lung-kidney crosstalk's] was recently examined especially in critically ill patients. However, the pathogenesis of pneumonia-induced AKI is still under-investigated, as reported by **Hepokoski *et al.*** [13]. However, it is suggested to be of multifactorial lung-kidney interactions. For example, ventilator-induced pneumonia and chronic obstructive pulmonary disease [COPD] stimulates inflammation of the endothelial lining of the lung and kidney [23, 24].

Huang *et al.* [25] suggested that, the acute sepsis associated with pneumonia is the initial stimulator of acute kidney injury in pneumococcal pneumoniae. They added, the immune response to infection and associated comorbid chronic disease may contribute to the renal insults. Furthermore, the renal hypoxemia and tissue hypoxia associated with pneumonia may contribute to the development of AKI in pneumonia [26-29]. **Mortensen *et al.*** [30] and **Coca *et al.*** [31] reported that the inappropriate use of antibiotics such as aminoglycosides and macrolides may contribute to the pathogenesis of AKI in pneumonia.

Interestingly and on the other side, the AKI my lead to worsening of respiratory functions by multiple mechanisms [e.g., uremic toxins, inflammation, oxidative stress and acid/base or electrolyte disturbances [32, 33].

In contradiction to the results of the current work, **Almutairi *et al.*** [34] reported that among mechanically ventilated patients with pneumonia, AKI is higher with increased stage of AKI. However, the higher mortality among AKI with CAP could not be attributed to the AKI along, but it appears to be due to multiorgan failure. The predictors of mortality were older age, the need for vasopressors, reduced level of consciousness, reduced PaO2/Fio2 ratio, lower platelet count, hyperbilirubinemia and lactic acidosis. Female sex was associated with reduced mortality. The cause of this contradiction mainly could be attributed the different inclusion criteria, as they included only patients who need mechanical ventilation. However, we included all patients, whether or not need mechanical ventilation.

In conclusion, elderly subjects admitted for pneumonia developed AKI in a considerable percentage. The presence of associated comorbid conditions [specifically, ischemic heart diseases] and impaired renal functions were the main predictors of in-hospital mortality among those patients.

The results of the current study must be explained with caution due to some limitations [e.g., the retrospective nature of the study with increased liability of bias] and small sample size which reduce the power of results. However, the data was collected from many centers, which

represent a strength point of the current work. Future large-scale studies are recommended.

Conflict of Interest: None.

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