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Predictors of In-ICU Mortality Among Older Patients with Healthcare-Associated Infection: A Cohort Study

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Abstract

Background: Deaths occur frequently in intensive care units (ICUs), especially in older adults, and healthcare-associated infections (HCAIs) can increase mortality risk in this age range. Identifying the underlying factors that lead to HCAI is crucial for preventing and mitigating the risk of premature deaths.

Objectives: This study aimed to identify predictors of in-ICU mortality among older adult patients with HCAI.

Methods: This prospective cohort study was conducted in two general hospitals in Tehran, Iran, where 461 individuals aged 60 years and older were meticulously observed over a 6-month in March 2021. Mortality was considered the outcome, and the Apache II questionnaire, the frailty index, and demographic information were completed. The data were analyzed using binary logistic regression with a significance level of $P < 0.05$.

Results: Older adult patients with HCAI had a 77% death rate out of 461 eligible individuals. Half of HCAIs were reported as ventilator-associated pneumonia. The most significant death percentages were observed in *Klebsiella* (37%) and *Acinetobacter* (21%). Ventilator-associated pneumonia (OR = 50.90, CI = 1.22 - 214.95), frailty status (OR = 45.94, CI = 17.51 - 120.52), COVID-19 (OR = 2.87, CI = 1.24 - 6.66), Apache-II (OR = 1.192, CI = 1.13 - 1.25) and length of hospital stays (OR = 1.05, CI = 1.02 - 1.07) significantly predicted mortality in older adult patients with HCAI.

Conclusions: The mortality of older adults with HCAI is affected by factors such as Ventilator-associated pneumonia, frailty, COVID-19, disease severity, and length of hospital stay. Identifying risk factors for mortality is helpful for treatment planning, resource allocation, and identifying at-risk patients.

Keywords: Health Care Associated Infection, Older adult, Death, Intensive Care Unit, Frailty

1. Background

Modern medicine aims to improve the survival rates of critically ill patients, especially in the intensive care unit (ICU), using technology and cutting-edge equipment (1). However, the ICU still has the most significant fatality rates among all hospital departments (2). In a retrospective cohort study between 2006 and 2015, the ICU mortality prevalence was reported to be between 20 and 50% (3). The mortality rate in the intensive care units of Middle Eastern countries has been, on average, 10% higher than the global average (4, 5). According to a 2019 meta-analysis study, Iranian ICU mortality rates were 29.8% (6).

Mortality in the ICU is a multifactorial phenomenon (7). Factors such as type of ICU, reason for hospitalization, age, comorbidities, occurrence of infections, and acute physiological changes during admission and treatment increase patients' mortality prognosis (8, 9). The older adults among the high-risk populations are more likely to die in the ICU (8, 10). Physiological changes that occur with increasing age put elderly patients at a higher risk of adverse outcomes such as cognitive impairment, delirium, functional decline, and infections during hospitalization, making them more vulnerable to premature mortality

(10).

One-third of those over 65 had an infection as their leading cause of death (11). Topelli et al. demonstrated that older adult patients still have lower survival rates than patients under 65 when they develop hospital infections, even after controlling for confounding factors like disease severity score, invasive procedures, and comorbidities (12).

Few studies have focused on the causes of death in older adult patients despite being among the high-risk groups for mortality when they have hospital-acquired infections. Boonomee et al. identified risk factors for mortality in older adult patients with bloodstream infections, including age, hospitalization within the previous three months, respiratory infections, systolic blood pressure less than 100mmHg, oxygen saturation, and low Glasgow Coma Scale score (13). This study included all bloodstream infections and did not specifically assess healthcare-associated infections. Other studies examining ventilator-associated pneumonia have found disease severity, comorbidities, and pneumonia severity as risk factors for mortality (14, 15). Serum albumin levels and organ infections are linked to death in older adult patients with surgical site infections (16). Peltz et al. also studied mortality in patients with bloodstream infections and likened the contributing factors to an iceberg, with some factors being ignored or receiving less attention (17). The ability to compare results to corroborate findings or identify discrepancies is constrained by the few dispersed and currently accessible reports.

Hospital-acquired infections present a challenge because the most common or high-risk factors for mortality can change periodically due to pathogen trends (18). Infection control practices and antibiotic usage can change the frequency of pathogens (19-21), emphasizing the necessity of periodic assessments of infections acquired in hospitals. Therefore, health policymakers, healthcare providers, and researchers need to clarify the pattern of mortality and their underlying causes to allocate their budget effectively for health interventions and research programs (22).

Each country should tailor their healthcare system to the needs of its population to provide the most effective care (10). Iran is one of the countries experiencing a transition to an aging population, and there is a shortage of information regarding the causes of hospital-acquired infection-related mortality among older adults.

2. Objectives

This study aims to identify the predictors of ICU mortality in older adult patients with hospital-acquired infections.

3. Methods

This prospective cohort study was conducted over a six-month follow-up period. Participants included all older adult patients hospitalized in the Rasool-e Akram and Firouzgar hospital ICUs who developed hospital-acquired infections from March to September 2021. Patient mortality was considered as the outcome of this study. The sample size for regression analyses could range from 5 to 10 cases per independent variable (23), which led to an estimated minimum sample size of 150 people. The inclusion criteria were age 60 or older and being diagnosed with a hospital-acquired infection within 48 hours of hospital admission. The targeted infections included pneumonia, bloodstream infection, surgical site infection, and urinary tract infection, diagnosed by the hospital infection control committee and selected from the registered infected patients in the infection control monitoring system of the Ministry of Health. The exclusion criteria included unwillingness to continue participating in the study or losing access to medical records.

The independent variables were the length of hospital stay, concurrent use of more than three antibiotics, polypharmacy, underlying disease, illness severity, frailty status, COVID-19, gender, and type of infection and microorganism. The Apache II questionnaire was used to measure the severity of illness in older adult patients, and the Groningen Frailty Index (GFI) was used to assess their frailty status. Both questionnaires have Iranian versions with validated reliability and validity in the Iranian older adult population (24-27).

The data were collected from patient records, laboratory, and clinical documents upon admission to the special care unit (with the assistance of a caregiver if the patient could not respond). The study obtained ethical approval from the University of Social Welfare and Rehabilitation Sciences with the ethics code IR.USWR.REC.1398.199. Informed consent forms were obtained from patients or their caregivers in cases where the patient could not provide consent (due to severe illness, cognitive impairment, or intubation). Based on the skewness and kurtosis test results, which were within the range of ± 1, the data are normally distributed. The data were analyzed using IBM Corp. released in 2019 and IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp. and *t*-test, chi-square test, binary logistic regression, and descriptive statistics (mean, frequency, and standard deviation). $P < 0.05$ was chosen as the significance threshold for studying the correlations between the variables.

4. Results

In this study, the predictors of in-ICU mortality among older patients were investigated with healthcare-associated infection and yielded several key findings. Out of 1115 older adult patients with nosocomial infection admitted to the intensive care unit of Rasool-e Akram and Firouzgar hospitals, 576 older adult patients were eligible for the study, and finally, 461 older adult patients were included based on the exclusion criteria.

The mean age of the participants was 73.07 (SD = 9.02) years. Nearly half of hospital-acquired infections (49.7%) were reported as ventilator-associated pneumonia. The most common microorganisms associated with hospital-acquired infections were *Klebsiella*, *Acinetobacter*, *Candida*, *E. coli*, *Enterococcus*, and *Staphylococcus*, respectively. More than half of the study participants (58.10%) had COVID-19 either during hospitalization or before being admitted to the hospital with the targeted infections (Table 1). A mortality rate of 77% was observed among older adult patients with HCAI. The mean APACHE-II score was 27.70 (SD = 10.33). The length of hospital stay ranged from 2 to 385 days.

Based on the descriptive results, the mean APACHE-II score was 14.01 (SD = 0.73) in discharged older adult patients and 24.43 (SD = 0.15) in deceased older adult patients. About 30.1% died among the patients with an APACHE-II score below 15, 50% died between 16 and 19, 75% died between 20 and 30, and 96.8% died with a score above 30. Approximately 96.8% of frail older adult patients died (Table 2).

The chi-square test showed a significant relationship ($P < 0.05$) between each of the variables of gender, COVID-19, type of infection, and frailty status with the mortality of older adult patients with hospital-acquired infections. However, no significant relationship ($P > 0.05$) was found between the variables of type of microorganism, polypharmacy, comorbidities, and concurrent use of more than three antibiotics with patient mortality. *Klebsiella* (37%) and *Acinetobacter* (21%) had the highest percentage of mortality among the types of microorganisms (Table 3).

The independent *t*-test did not show a significant relationship ($P = 0.505$) between age and mortality in older adult patients with hospital-acquired infections, but a significant relationship ($P < 0.001$) was found between the APACHE-II score and length of hospital stay with patient mortality (Table 4).

A binary logistic regression model was used to investigate the simultaneous relationship between the predictor variables and the mortality outcome in older adult patients with hospital-acquired infections. The predictor variables (gender, COVID-19, type of infection,

Table 1. Demographic Information of Study Participants

Variables and Category	No. (%)
Age	
Young old	268 (58.10)
Old	174 (37.70)
Old old	19 (4.10)
Gender	
Women	194 (42.10)
Men	267 (57.90)
Comorbidities	
Yes	272 (59.00)
No	189 (41.00)
Polypharmacy	
Yes	204 (44.30)
No	257 (55.7)
COVID-19	
Yes	332 (72.00)
No	129 (28.00)
Type of infection	
VAE-PVAP	268 (58.10)
PNEU-PNU1	193 (41.90)
PNEU-PNU2	195 (42.30)
LRI-LUNG	15 (3.30)
SST-ST	24 (5.20)
UTI-SUTI	1 (0.20)
BSI-LCBI	7 (1.50)
Extra	122 (26.50)
Type of microorganism	
Klebsiella	93 (20.20)
Candida	4 (0.80)
Pseudomonas	162 (35.10)
Acinetobacter	59 (12.80)
E. coli	43 (9.30)
Staphylococcus aureus	92 (20.00)
Coagulase-negative *Staphylococcus*	38 (8.20)
Enterococcus	12 (2.60)
Stenotrophomonas	4 (0.90)
Other	23 (5.00)

Abbreviations: VAE, ventilator-associated event; possible ventilator-associated pneumonia (PVAP). PNEU-PNU1, pneumonia clinically defined pneumonia; LRI-LUNG, lower respiratory system infection, other than pneumonia; SST-ST, surgical site infection soft tissue; UTI-SUTI, urinary tract infection (symptomatic urinary tract infection); BSI-LCBI, bloodstream infection (BSI): A laboratory confirmed bloodstream infection (LCBI).

Table 2. The Relationship Between APACHE-II and GFI Scores with Mortality Rate in Older Adult Patients Under Study [a]

Variables	Apache-II Score				GFI Score	
	< 15	16 - 19	20 - 30	> 30	No	Yes
Discharge	58	16	24	8	96	10
	54.70	15.10	22.60	7.50	90.60	9.40
Death	25	17	72	241	57	298
	7.0	4.80	20.30	67.90	16.10	83.90

[a] Values are presented as No. (%).

length of hospital stay, frailty status, and APACHE-II score) were selected based on a significance level of $P < 0.05$ in bivariate analyses. The results of the omnibus tests (chi-square = 327.70, $P < 0.001$) showed that the model had a good fit. The model's classification power was 93%, indicating that the predictor variables could predict mortality in older adult patients with hospital-acquired infections with 93% accuracy (Table 5).

The odds ratios showed that the APACHE-II score (OR = 1.192, CI = 1.13 - 1.25), length of hospital stay (OR = 1.05, CI = 1.02 - 1.07), COVID-19 (OR = 2.87, CI = 1.24 - 6.66), ventilator-associated pneumonia (OR = 50.90, CI = 1.22 - 214.95), and frailty status (OR = 45.94, CI = 17.51 - 120.52) significantly predicted mortality in older adult patients with hospital-acquired infections. The model under investigation explains approximately 51 to 77% of the variations in mortality among older adult individuals with infection based on the entered predictor variables (Table 5).

5. Discussion

Numerous factors contribute to mortality in older adult patients with healthcare-associated infections. There was a significant correlation between mortality in older adult patients with hospital-acquired infections and Ventilator-associated pneumonia, COVID-19, disease severity, and length of hospital stay.

Nearly 50% of deaths were due to ventilator-associated pneumonia, which also had a significant relationship with mortality in older adult patients and has been reported to have a high mortality rate among hospital-acquired infections in other studies (5, 28, 29). One study reported a three-fold higher mortality rate than other infections (30). The ventilator-associated events (VAEs) include mortality and prolonged hospitalization in the ICU and are used as indicators of quality in the ICU (31). Therefore, more attention should be paid to providing care and conducting specialized studies for this group of patients to identify risk factors and reduce mortality rates.

Frailty can be used as a predictor of mortality in older adult patients (32), even though some studies have shown that age is not considered a predictor of mortality in this age group, despite frailty being a significant risk factor (33, 34). This study identified frailty as a predictor variable, while age was not significantly related to the mortality rate, which contrasts with another study conducted in 10 Middle Eastern countries where age was recognized as a risk factor (5). Even in different research in the west of Iran, which included 8895 patients with hospital infections and a range of ages from 1 to 99, increasing age was found to be a risk factor for mortality (29). This difference might stem from the fact that all age groups were considered rather than specifically focusing on older adults.

HCAI with COVID-19 is another factor that significantly influences death rates. Other studies have also shown that COVID-19 significantly contributes to hospital-acquired infections (35). Furthermore, a high mortality rate has been reported due to COVID-19 (36). The unknown care and treatment methods during the first waves are among the influential factors, which led to undesirable efficacy for prioritizing patients in the ICUs (37).

The present study also reported a relationship between disease severity and mortality in older adult patients with hospital-acquired infections. This finding is consistent with other studies (38), and hospital-acquired infections put older adult patients at risk of mortality (8). Differences in statistical scores with Apache-II scores could be due to this issue. In this study, approximately 97% of older adult patients who scored above 30 died. Therefore, the Apache-II scoring system seems to be able to predict mortality in patients with hospital-acquired infections. The mortality rate obtained from the scoring method was higher than the standard level, and there was a significant difference between the received scores and the expected values. Patients with scores below 15 had a difference of around 15%, between 16 and 19 had a difference of about 20%, between 20 and 30 had a difference of about 40%, and above 30 had a difference of about 20% more than the standard values. These differences may direct attention to

Table 3. Investigating the Relationship Between Hospital-Acquired Infection Mortality in Older Adult Patients and Qualitative Predictive Mortality Variables [a]

Variables and Category	Discharge	Death	χ^2	P-Value
Gender			5.65	0.017
Women	34 (17.50)	160 (82.50)		
Men	72 (27.0)	195 (73.0)		
COVID-19			6.80	0.009
Yes	56 (29.0)	137 (71.0)		
No	50 (18.70)	218 (81.30)		
Type of infection			20.78	0.008
VAE-PVAP	31 (15.90)	164 (84.10)		
PNEU-PNU1	2 (13.30)	13 (86.70)		
PNEU-PNU2	9 (37.50)	15 (62.50)		
LRI-LUNG	0 (0)	1 (100.0)		
SST-ST	1 (14.30)	6 (85.70)		
UTI-SUTI	42 (34.40)	80 (65.60)		
BSI-LCBI	19 (20.40)	74 (79.60)		
Extra	2 (50.0)	2 (50.0)		
Type of microorganism			12.36	0.193
Klebsiella	32 (19.80)	130 (80.20)		
Candida	13 (22.0)	46 (78)		
Pseudomonas	12 (27.90)	31 (72.10)		
Acinetobacter	15 (16.30)	77 (83.70)		
E. coli	14 (36.80)	24 (63.20)		
Staphylococcus aureus	2 (16.70)	10 (83.30)		
Coagulase-negative *Staphylococcus*	2 (50.0)	2 (50.0)		
Enterococcus	7 (30.40)	16 (69.60)		
Stenotrophomonas	1 (50.0)	1 (50.0)		
Other	8 (30.80)	18 (69.20)		
Comorbidity			1.04	0.307
Yes	58 (21.30)	214 (78.70)		
No	48 (25.40)	141 (74.60)		
Utilization of antibiotics > 3			0.332	0.564
Yes	74 (22.30)	258 (77.70)		
No	32 (24.80)	97 (75.20)		
Polypharmacy			0	0.983
Yes	47 (23.0)	157 (77.0)		
No	59 (23.0)	198 (77.0)		
Frailty			204.37	0.001
Yes	10 (9.40)	96 (90.60)		
No	298 (83.90)	57 (16.10)		

Abbreviations: VAE, ventilator-associated event; possible ventilator-associated pneumonia (PVAP). PNEU-PNU1, pneumonia clinically defined pneumonia; LRI-LUNG, lower respiratory system infection, other than pneumonia; SST-ST, surgical site infection soft tissue; UTI-SUTI, urinary tract infection (symptomatic urinary tract infection); BSI-LCBI, bloodstream infection (BSI): A laboratory confirmed bloodstream infection (LCBI).

[a] Values are presented as No. (%).

Table 4. Comparison of Mortality in Older Adult Patients with Hospital-Acquired Infections by Age, Length of Hospital Stays, and APACHE-II Score

Variables and Category	Mean (SD)	Homogeneity of Variances Test		Means Equality Test	
		F	P-Value	T	P-Value
Age		2.7	0.102	0.66	0.505
Discharge	72.55 (8.43)				
Deceased	73.23 (9.40)				
Length of stay		14.41	0	4.7	0.001
Discharge	19.49 (10.58)				
Deceased	32.51 (48.54)				
Apache-II		11.98	0.001	11.62	0.001
Discharge	14.01 (7.57)				
Deceased	24.43 (9.64)				

Table 5. Logistic Regression Coefficients for Predicting Mortality in Older Adult Patients with Hospital-Acquired Infection Based on Predictive Variables

Variables	B	S.E.	P-Value	OR	95% CI for OR	
					Lower	Upper
GFI	3.827	0.492	< 0.001	45.940	17.511	120.521
Apache-II	0.176	0.026	0.001	1.192	1.133	1.255
COVID-19	1.057	0.429	0.014	2.877	1.242	6.666
Gender	- 0.622	0.428	0.146	0.537	0.232	1.241
LOS	0.047	0.012	< 0.001	1.048	1.023	1.074
Type of infection			0.091			
VAE-PVAP	3.930	1.901	0.039	50.904	1.225	2114.952
PNEU-PNU1	1.837	2.131	0.389	6.279	0.096	409.033
PNEU-PNU2	2.561	2.007	0.202	12.955	0.254	661.823
LRI-LUNG	23.669	40192.970	1.000	190184687	0.000	.
SST-ST	3.059	2.274	0.179	21.302	0.247	1836.045
UTI-SUTI	2.316	1.886	0.220	10.130	0.251	408.358
BSI-LCBI	3.482	1.908	0.068	32.514	0.773	1367.792
Extra	0.708	5.489	0.897	2.030	0.000	95351.600
Constant	- 9.118	2.189	< 0.001	0.000		
Hosmer and Lemeshow test = 1.55, P-value = 0.99						
Model chi-square = 327.70, P-value = 0.000						
Cox & Snell R square = 0.51, Nagelkerke R square = 0.77						

high-risk populations, including elderly individuals with hospital-acquired infections.

Another predictor factor for mortality is the length of hospital stay. A more extended hospital stay also puts patients with hospital-acquired infections at a higher mortality risk, consistent with other studies (5, 30, 39). The length of hospital stay is considered a risk factor for hospital-acquired infections (40). On the other hand, hospital-acquired infections require a more extended hospital stay to receive treatment, which puts older adult patients at risk of mortality (41). Considering the importance of the length of hospital stay, there should be an intelligent care system to transfer older adult patients to less invasive centers such as nursing homes or provide care at home based on the required level and intensity of healthcare.

The present study reported no significant relationship between gender and mortality. In contrast, in some

studies, the likelihood of mortality was higher in men (42); in other studies, women were identified as a risk factor (5, 39, 43). The diversity of participant samples in research may have produced varying and contradictory outcomes.

One of the study's limitations was the timing of the COVID-19 epidemic. The peaks of COVID-19 had differences, and studies have shown that the severity of COVID-19 and the causative agent differed in each peak (44, 45). Additionally, some intensive care units were allocated to COVID-19 patients, and the change in the use of these units may have affected the mortality rate. These limitations affected the relationship between the unit type and mortality.

Many clinical and laboratory findings are not covered by the Iranian Nosocomial Infection Surveillance System (INIS) due to limitations in data collection, which reduces the speed and generalizability of sample size.

5.1. Conclusions

According to this cohort study, factors such as disease severity, frailty, COVID-19, ventilator-associated pneumonia, and length of hospital stay affect the death of senior individuals who have contracted infections during their hospital stay. Identifying risk factors for treatment planning, resource allocation, and identifying at-risk individuals can be helpful and actively considered in decision-making. Frailty, disease severity, and COVID-19 are uncontrollable factors that influence hospital-acquired infections. Healthcare providers should carefully monitor these patients.

Controllable factors, such as length of hospital stay, can also be adjusted with focused control measures, such as recommending continuing care at home or outpatient centers. Additionally, medical devices like mechanical ventilators can significantly improve patient survival by reducing connection times and using sterile techniques, such as good hand hygiene by staff and adherence to hygiene standards during connections and throughout the entire care procedure. However, more targeted and specialized study on infections brought on by ventilator-related problems has to be conducted to improve patient survival.

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Footnotes

Authors' Contribution: F. R conceived and designed the evaluation and drafted the manuscript. F. M. Sh and R. F supervisor, conceived and designed the evaluation and drafted the manuscript. M. Sh. and Gh. Gh. performed parts of the statistical analysis and, revised the manuscript. All authors read and approved the final manuscript.

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