RESEARCH ARTICLE

Predictors of in-hospital mortality in patients requiring transfer to the medical intensive care unit

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Abstract

Objective: To identify the factors associated with higher odds of in-hospital mortality among inpatients requiring transfer to the medical intensive care unit.

Method: The retrospective audit was conducted from April 1 to September 30, 2023, at The Aga Khan University Hospital, Karachi, Pakistan and comprised data from January 1, 2018, to December 31, 2022, of patients initially admitted to the general ward or high dependency unit in the Department of Medicine who required transfer to the medical intensive care unit during hospitalisation. Data was analysed using SPSS 23.

Results: Of the 601 patients with mean age 53.6±17.4 years, 373(62.1%) were males. Overall, 321(53.6%) of the patients expired while in the hospital. Patients whose transfer to the intensive care unit was initiated within 48 hours of admission had lower in-hospital mortality compared to those whose transfer was initiated beyond 48 hours of admission (p=0.004). Patients with a history of autoimmune disease or malignancy as co-morbid conditions, or a primary discharge diagnosis of sepsis had higher odds of in-hospital mortality (p<0.05).

Conclusions: In-hospital mortality in patients requiring transfer to the intensive care unit was found to be very high. Early transfer to intensive care unit could lead to improved survival rate.

Keywords: Critical care, Hospital medicine, Clinical deterioration, Sepsis, Autoimmune diseases.

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Introduction

Patients admitted to the hospital are triaged to different levels of care depending on the nature of their illness.[1] Patients with critical illness[2] are admitted directly to the intensive care unit (ICU) on presentation because they require the highest level of care. Besides, during hospitalisation, patients admitted to other parts of the hospital outside the ICU may develop clinical deterioration[3] for which they may need to be transferred to the ICU.[4]

A higher mortality rate and a longer length of hospital stay (LOS) are associated with patients who develop clinical deterioration, resulting in admission to the ICU.[5] Mortality rates for these patients have been reported to be as high as 50% in developing countries.[6] Studies from developed countries have shown relatively low mortality rates of 25.7%[5] and 36.8%.[7] A common cause of unplanned transfer to the ICU is respiratory failure or haemodynamic instability.[8]

The demand for critical care services is increasing globally,[9] while the provision of these services is a major challenge for developing countries due to resource constraints.[10] The lack of trained healthcare workers as well as logistical and financial constraints together contribute to this challenge.[11]

In contexts where critical care resources are limited, such as in developing countries, many patients who would have been directly transferred to the ICU in developed countries are shifted to the ward instead.[12] Hence, it is important to identify patient populations that are at higher risk of mortality and may need subsequent transfer to the ICU so that they may be prioritised for direct admission to the ICU, if resources allow, or be monitored more closely after admission outside the ICU due to resource limitations.

To the best of our knowledge, regional and national data on this topic is not available in the published literature. The current study was planned to fill the gap in literature by determining predictors of in-hospital mortality in patients requiring transfer to the ICU after initial admission to a ward or a high dependency unit (HDU) bed in a low- and middle-income-country (LMICs) setting.

Materials and Methods

The retrospective audit was conducted from April 1 to September 30, 2023, at a large tertiary care hospital in Karachi, and comprised data from January 1, 2018, to December 31, 2022, of patients initially admitted to the general ward or HDU in the Department of Medicine who required transfer to the medical ICU during hospitalisation.

The sample size was calculated using OpenEpi[13] software on the basis of an earlier study which mentioned the

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frequency of patients who required transfer to the ICU during hospitalisation to be 1.25%.[7] The sample size was calculated with a bound on error of 0.90 and 95% confidence interval (CI).

A list of patients who required transfer to the ICU was obtained from the admissions department of the university hospital, which is accredited with the Joint Commission International (JCI).[14] Data of patients aged <18 years and those directly admitted to the ICU from the emergency department (ED) was excluded. Approval was obtained from the institutional ethics review committee, which waived the condition for obtaining informed consent as the entire data was collected retrospectively without any interaction with the patients.

At the study site, HDUs are peripherally organised and speciality-specific. They operate separately from the centrally located ICU. The HDUs serve as a place to monitor patients who require higher levels of care that cannot be provided on a regular ward bed, such as those with respiratory failure requiring non-invasive mechanical ventilation (NIMV), but require less care than the standards of an ICU bed. As per institutional policy, patients in need of NIMV and those requiring vasopressor or ionotropic support are often managed in the HDU. The ICU is mostly reserved for patients who require IMV. This is due to the limited number of ICU beds available.

Data was collected by reviewing electronic health records. Variables collected included age, gender, comorbidities, location of admission, admitting diagnosis, principal and secondary diagnosis on discharge, LOS before transfer to the ICU, LOS after transfer to the ICU, total LOS, and outcome. The primary outcome of the study was in-hospital mortality. Primary discharge diagnosis was the condition that occasioned the need for hospitalisation. Secondary discharge diagnoses were conditions that coexisted at the time of admission, that developed subsequently, or that affected the treatment received and/or LOS. Admitting diagnoses and primary and secondary diagnoses on discharge were grouped into related speciality categories, such as infections, pulmonary diseases, cardiovascular diseases, etc.

Data was analysed using SPSS 23. The frequency and percentage of qualitative variables were determined. Normality of data was assessed using the Shapiro-Wilk test. Quantitative variables with normal and non-normal distributions were reported as mean±standard deviation (SD) and median with inter-quartile range (IQR), respectively. Chi-square test was used to determine the relationship between categorical variables, while the relationship between numerical and categorical values was determined using the independent sample t-test. Binary logistic regression analysis was performed. Univariate logistic regression was done to identify factors associated with in-hospital mortality. Variables with $p<0.25$ were included in the multivariable model. Multivariable logistic regression was performed using a backward stepwise selection procedure to identify independent factors associated with in-hospital mortality. P<0.05 at 95% CI was considered significant.

Results

Of the 2,031 patients, 601(29.6%) met the inclusion criteria. There were 373(62.1%) male patients, and the overall mean age was 53.6±17.4 years. The most common co-morbid condition was hypertension 300(49.9%), followed by diabetes mellitus 255(42.4%), and ischaemic heart disease/congestive heart failure 103(17.1%). The most common admitting diagnoses were infections 328(54.6%), followed by renal 87(14.5%) and neurological 74(12.3%) diseases. The most common primary diagnoses on discharge were infections 327(54.4%), followed by neurological 64(10.6%), and pulmonary 58(9.7%) diseases. The number of patients with a primary discharge diagnosis of sepsis was 150(25%) (Table 1).

The majority of patients were initially admitted to the HDU 516(85.9%) on admission, while 85(14.1%) were admitted

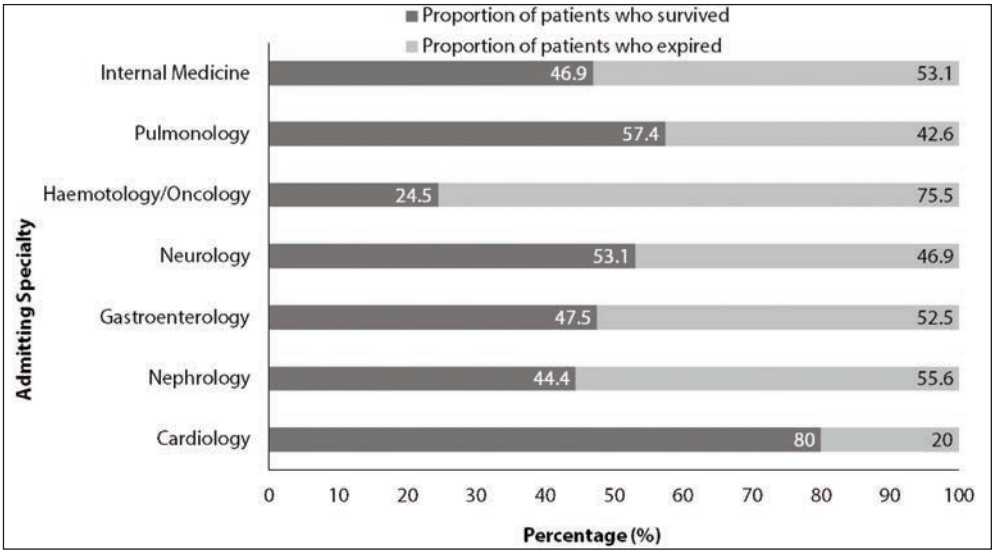

Figure-1: Proportion of patients transferred to the medical intensive care unit who survived and those who expired stratified by admitting specialty.

to the general ward. The admitting speciality with the largest number of patients was internal medicine 383(63.6%), followed by pulmonology 54(9%), haematology/oncology 53(8.8%), neurology 49(8.2%), gastroenterology 40(6.7%), nephrology 18(3%) and cardiology 5(0.8%). Sepsis as a primary diagnosis on discharge was most frequently present in patients admitted to haematology/oncology 27(50.9%), nephrology 6 (33.3%) and internal medicine 101(26.5%).

Table-1: Comparison of patients who expired during the hospital stay with those who survived.

Variable	Total (n=601)	Patients who expired during hospital stay (n=321)	Patients who survived (n=280)	*p* value
Age (years)	53.6±17.4	55.5±17.1	51.5±17.6	0.005
Gender				
Male	373 (62.1)	208 (64.8)	165 (58.9)	0.139
Female	228 (37.9)	113 35.2)	115 (41.1)	
Co-morbidities				
Hypertension	300 (49.9)	165 (51.4)	135 (48.2)	0.436
Diabetes Mellitus	255 (42.4)	130 (40.5)	125 (44.6)	0.305
Ischaemic Heart Disease/ Congestive Heart Failure	103 (17.1)	57 (17.8)	46 (16.4)	0.666
Chronic Kidney Disease	82 (13.6)	40 (12.5)	42 (15.0)	0.366
Chronic Pulmonary Disease	66 (11.0)	37 (11.5)	29 (10.4)	0.647
Malignancy	65 (10.8)	48 (15.0)	17 (6.1)	< 0.001
Chronic Liver Disease	37 (6.2)	18 (5.6)	19 (6.8)	0.549
Autoimmune Disease	29 (4.8)	23 (7.2)	6 (2.1)	0.004
History of cerebrovascular attack	20 (3.3)	8 (2.5)	12 (4.3)	0.221
Admitting diagnoses				
Infections	328 (54.6)	198 (61.7)	130 (46.4)	< 0.001
Renal disease	87 (14.5)	48 (15.0)	39 (13.9)	0.722
Neurological diseases	74 (13.3)	34 (10.6)	40 (14.3)	0.169
Haematological/Oncological disease	58 (9.7)	36 (11.2)	22 (7.9)	0.164
Cardiovascular disease	57 (9.5)	27 (8.4)	30 (10.7)	0.336
Primary Discharge Diagnoses				
Infections	327 (54.4)	205 (63.9)	122 (43.6)	< 0.001
Neurological disease	64 (10.6)	32 (10.0)	32 (11.4)	0.563
Pulmonary disease	58 (9.7)	29 (9.0)	29 (10.4)	0.584
Cardiovascular disease	46 (7.7)	18 (5.6)	28 (10.0)	0.043
Gastrointestinal disease	35 (5.8)	18 (5.6)	17 (6.1)	0.809
Secondary Discharge Diagnoses				
Infections	264 (43.9)	127 (39.6)	137 (48.9)	0.021
Renal disease	237 (39.4)	144 (44.9)	93 (33.2)	0.004
Pulmonary disease	86 (14.3)	52 (16.2)	34 (12.1)	0.157
Cardiovascular disease	80 (13.3)	41 (12.8)	39 (13.9)	0.677
Neurological disease	65 (10.8)	37 (11.5)	28 (10.0)	0.548

The median LOS was 11 days (IQR: 6-20 days). The median LOS before transfer to ICU was 3 days (IQR: 2-6 days), while the median LOS after transfer to ICU was 6 days (IQR: 3-13 days). The number of patients transferred to the ICU within 48 hours of admission was 288(47.9%). These patients had a shorter LOS 7 days (IQR: 5-13 days) compared to those whose transfer to the ICU was delayed beyond 48 hours 16 days (IQR: 10-25 days) (p<0.001).

The number of patients who expired during the hospital stay was 321(53.4%), while 231(38.4%) were discharged and 49(8.2%) left against medical advice (LAMA) or were transferred to an outside hospital. Out of the 29(4.8%) patients with a history of autoimmune disease, 23(79.3%) expired during the hospital stay. Out of the 65(10.8%) patients with a history of a malignancy, 48(73.8%) expired during the hospital stay. In-hospital mortality for the 150(25%) patients with a primary discharge diagnosis of sepsis was 112(74.7%). Patients whose transfer to the ICU was initiated within 48 hours of admission had lower in-hospital mortality 136(47.2%) compared to patients whose transfer to the ICU was initiated beyond 48 hours of admission 185(59.1%) (p=0.004). The proportion of patients who expired during the hospital stay and those who survived was stratified by admitting specialty (Figure-1).

Table-2: Independent factors associated with in-hospital mortality.

Variable	Adjusted Odds Ratio (95% CI)	*p* value
Age (years)	1.012 (1.002-1.023)	0.015
Comorbidities		
History of Malignancy		0.010
No	Reference	
Yes	2.264 (1.221–4.197)	
History of Autoimmune Disease		0.007
No	Reference	
Yes	3.634 (1.426–9.259)	
Primary Discharge Diagnosis		
Sepsis		< 0.001
No	Reference	
Yes	2.837 (1.850–4.352)	

The presence of a malignancy (p=0.010) or autoimmune disease (p=0.007) as co-morbid conditions was associated with higher odds of in-hospital mortality along with age (p=0.015) and sepsis as a primary discharge diagnosis (p<0.001) (Table 2).

Discussion

In the current study, more than half of the patients who required transfer to the ICU did not survive. Around three-fourths of patients with the presence of autoimmune disease or malignancy as co-morbid conditions, or a primary discharge diagnosis of sepsis expired during the hospital stay. Early transfer to the ICU within 48 hours of

admission resulted in lower in-hospital mortality, and a shorter LOS. The presence of malignancy or autoimmune disease as co-morbid conditions, age or sepsis as the primary discharge diagnosis were associated with higher odds of in-hospital mortality.

Similar to the current findings, a study in Brazil observed that half of the patients transferred from the intermediate care unit to the ICU expired.[6] In contrast, a study in the Unites States observed that the death rate for patients transferred from transitional care to the ICU was 25.7%.[5] A study done in Australia observed a mortality rate of 36.8% in patients with unplanned ICU admission.[7] Variability in mortality rates may reflect differences in quality of critical care services available in different countries.

The current study observed that a history of malignancy as a co-morbid condition was among the factors associated with a higher odds of in-hospital mortality among patients who required transfer to the ICU during hospitalisation, with around three-fourths of patients not surviving till discharge. Among patients with malignancies who required unplanned transfer to the ICU, those who develop complications directly related to the underlying cancer have a worse prognosis than those who develop complications not related to the primary disease, or drug-related adverse events.[15] In contrast to the very high mortality rate observed in patients with malignancy who required transfer to the ICU in the current study, a study in France observed a relatively lower hospital mortality rate of 37.9% in patients with haematological malignancy and 20% in patients with a solid malignancy.[16] Long-term follow-up of patients after discharge is also important as one-year survival has been shown to be only 33.2% in this patient population.[15] Therefore, patients with a history of malignancy must be closely monitored for clinical deterioration when admitted outside the ICU.

The presence of an autoimmune disease as a co-morbid condition was also associated with a higher odds of in-hospital mortality in the patients. Similar to patients with the presence of malignancy as a co-morbid condition, around three-fourths of patients with the presence of an autoimmune disease as a co-morbid condition expired during their hospital stay. The most common reason for admission to the ICU in patients with autoimmune disease is a flare-up of the autoimmune disease itself, followed by infections.[17] In a systematic review, mortality rates in patients with autoimmune disease admitted to the ICU ranged from 17% to 55% with the highest mortality observed in patients with systemic lupus erythematosus (SLE).[18] Hence, patients with a history of autoimmune disease must also be closely monitored for clinical deterioration when admitted outside the ICU, especially patients with SLE.

The current study observed that a primary discharge diagnosis of sepsis was present in one-fourth of patients, and it was associated with a higher odds of in-hospital mortality. Globally, sepsis is one of the leading causes of death and critical illness.[19] Sepsis-related ICU and hospital mortality rates vary from region to region, and range from 11.9% to 19.3% in Oceania versus 39.5% to 47.2% in Africa.[20] In the current study, around three-fourths of patients with a primary discharge diagnosis of sepsis expired during the hospital stay. In contrast, in a study in the US, in-hospital mortality was 25% in patients with sepsis who required transfer to the ICU.[21] The combination of modified Early Warning Score (MEWS) and blood lactate levels has been used to predict ICU transfer in patients with severe sepsis/septic shock.[22] Further studies from other centres to validate these findings should be conducted in patients admitted with sepsis outside the ICU, especially in LMICs considering the high burden of sepsis in such populations.

In the current study, patients transferred to the ICU within 48 hours of admission had a shorter LOS and lower in-hospital mortality than those who were transferred beyond 48 hours of admission. Delays in transfer to the ICU have been associated with increased in-hospital mortality.[23] Each one-hour increase in delay has been shown to be associated with an adjusted 3% increase in odds of mortality.[24] These findings highlight the importance of early warning scores (EWS) and rapid response systems that are designed as a safety net, and comprise an afferent arm and an efferent arm.[25] Multiple steps are involved in the afferent limb, including monitoring for abnormal physiological parameters and delivering a signal when a certain threshold is reached to activate the rapid response team (RRT).[26] Responders may include physicians and/or nurses, with the composition varying, depending on the institution's resources.[27]

To the best of our knowledge, the current study is the first from an LMIC to highlight patient populations with higher odds of in-hospital mortality amongst those transferred to the ICU. However, the study has limitations, including a relatively small sample size and a single-centre design. Considering the challenges associated with providing critical care services in LMIC's, further research is needed to identify methods for the early detection of clinical deterioration in high-risk patient populations to facilitate early transfer to the ICU, or, if possible, perform necessary interventions to prevent the need for transfer to the ICU.

Conclusion

In-hospital mortality in patients who required transfer to the medical ICU was very high. Patient populations at higher odds of in-hospital mortality included those with a history of malignancy or autoimmune disease as co-morbid

conditions, or those with a primary discharge diagnosis of sepsis. Early transfer within 48 hours of admission could lead to a shorter LOS and improved survival.

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References

1. Ganjali R, Golmakani R, Ebrahimi M, Eslami S, Bolvardi E. Accuracy of the Emergency Department Triage System using the Emergency Severity Index for Predicting Patient Outcome; A Single Center Experience. Bull Emerg Trauma 2020;8:115-20. doi: 10.30476/BEAT.2020.46452
2. Maslove DM, Tang B, Shankar-Hari M, Lawler PR, Angus DC, Baillie JK, et al. Redefining critical illness. Nat Med 2022;28:1141-8. doi: 10.1038/s41591-022-01843-x
3. Blythe R, Parsons R, White NM, Cook D, McPhail S. A scoping review of real-time automated clinical deterioration alerts and evidence of impacts on hospitalised patient outcomes. BMJ Qual Saf 2022;31:725-34. doi: 10.1136/bmjqs-2021-014527
4. Eddahchouri Y, Peelen RV, Koeneman M, van Veenendaal A, van Goor H, Bredie SJH, et al. The Effect of Continuous Versus Periodic Vital Sign Monitoring on Disease Severity of Patients with an Unplanned ICU Transfer. J Med Syst 2023;47:43. doi: 10.1007/s10916-023-01934-3
5. Escobar GJ, Greene JD, Gardner MN, Marelich GP, Quick B, Kipnis P. Intra-hospital transfers to a higher level of care: contribution to total hospital and intensive care unit (ICU) mortality and length of stay (LOS). J Hosp Med 2011;6:74-80. doi: 10.1002/jhm.817
6. Ramos JGR, Dos Santos GMN, Bispo MCC, de Almeida Matos RC, de Carvalho GMLS, Passos RDH, et al. Unplanned Transfers From Intermediate Care Units to Intensive Care Units: A Cohort Study. Am J Crit Care 2021;30:397-400. doi: 10.4037/ajcc2021453
7. Frost SA, Alexandrou E, Bogdanovski T, Salamonson Y, Parr MJ, Hillman KM. Unplanned admission to intensive care after emergency hospitalisation: risk factors and development of a nomogram for individualising risk. Resuscitation 2009;80:224-30. doi: 10.1016/j.resuscitation.2008.10.030
8. Boerma LM, Reijners EPJ, Hessels RAPA, V Hooft MAA. Risk factors for unplanned transfer to the intensive care unit after emergency department admission. Am J Emerg Med 2017;35:1154-8. doi: 10.1016/j.ajem.2017.03.019
9. Crawford AM, Shiferaw AA, Ntambwe P, Milan AO, Khalid K, Rubio R, et al. Global critical care: a call to action. Crit Care 2023;27:28. doi: 10.1186/s13054-022-04296-3
10. Bartlett ES, Lim A, Kivlehan S, Losonczy LI, Murthy S, Lowsby R, et al. Critical care delivery across health care systems in low-income and low-middle-income country settings: A systematic review. J Glob Health 2023;13:04141. doi: 10.7189/jogh.13.04141
11. Kovacevic P, Meyer FJ, Gajic O. Challenges, obstacles, and unknowns in implementing principles of modern intensive care medicine in low-resource settings: an insider's perspective. Intensive Care Med 2024;50:141-3. doi: 10.1007/s00134-023-07270-x
12. Dünser MW, Bataar O, Tsenddorj G, Lundeg G, Torgersen C, Romand JA, et al. Differences in critical care practice between an industrialized and a developing country. Wien Klin Wochenschr 2008;120:600-7. doi: 10.1007/s00508-008-1064-8
13. Dean AG, Sullivan KM, Soe MM. OpenEpi: Open Source Epidemiologic Statistics for Public Health, Version: 3.01. [Online] 2013 [Cited 2021 January 01]. Available from URL: https://www.openepi.com/Menu/OE_Menu.htm
14. Joint Comission International (JCI). Joint Commission International: A Global Leader for Healthcare Quality and Patient Safety. [Online] [Cited 2024 June 01]. Available from URL: https://www.jointcommissioninternational.org/.
15. Vigneron C, Charpentier J, Valade S, Alexandre J, Chelabi S, Palmieri LJ, et al. Patterns of ICU admissions and outcomes in patients with solid malignancies over the revolution of cancer treatment. Ann Intensive Care 2021;11:182. doi: 10.1186/s13613-021-00968-5
16. van der Zee EN, Termorshuizen F, Benoit DD, de Keizer NF, Bakker J, Kompanje EJO, et al. One-year Mortality of Cancer Patients with an Unplanned ICU Admission: A Cohort Analysis Between 2008 and 2017 in the Netherlands. J Intensive Care Med 2022;37:1165-73. doi: 10.1177/08850666211054369
17. Antón JM, Castro P, Espinosa G, Marcos M, Gandía M, Merchán R, et al. Mortality and long term survival prognostic factors of patients with systemic autoimmune diseases admitted to an intensive care unit: a retrospective study. Clin Exp Rheumatol 2012;30:338-44. Epub 2012 Jun 25
18. Quintero OL, Rojas-Villarraga A, Mantilla RD, Anaya JM. Autoimmune diseases in the intensive care unit. An update. Autoimmun Rev 2013;12:380-95. doi: 10.1016/j.autrev.2012.06.002.
19. Shibata J, Osawa I, Fukuchi K, Goto T. The Association Between Time From Emergency Department Visit to ICU Admission and Mortality in Patients With Sepsis. Crit Care Explor 2023;5:e0915. doi: 10.1097/CCE.0000000000000915
20. Vincent JL, Marshall JC, Namendys-Silva SA, François B, Martin-Loeches I, Lipman J, et al. Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. Lancet Respir Med 2014;2:380-6. doi: 10.1016/S2213-2600(14)70061-X
21. Wardi G, Wali AR, Villar J, Tolia V, Tomaszewski C, Sloane C, et al. Unexpected intensive care transfer of admitted patients with severe sepsis. J Intensive Care 2017;5:43. doi: 10.1186/s40560-017-0239-7
22. Yoo JW, Lee JR, Jung YK, Choi SH, Son JS, Kang BJ, et al. A combination of early warning score and lactate to predict intensive care unit transfer of inpatients with severe sepsis/septic shock. Korean J Intern Med 2015;30:471-7. doi: 10.3904/kjim.2015.30.4.471
23. Kiekkas P, Tzenalis A, Gklava V, Stefanopoulos N, Voyagis G, Aretha D. Delayed Admission to the Intensive Care Unit and Mortality of Critically Ill Adults: Systematic Review and Meta-analysis. Biomed Res Int 2022;2022:4083494. doi: 10.1155/2022/4083494
24. Churpek MM, Wendlandt B, Zadravecz FJ, Adhikari R, Winslow C, Edelson DP. Association between intensive care unit transfer delay and hospital mortality: A multicenter investigation. J Hosp Med 2016;11:757-62. doi: 10.1002/jhm.2630
25. Shiell A, Fry M, Elliott D, Elliott R. Exploration of a rapid response team model of care: A descriptive dual methods study. Intensive Crit Care Nurs 2022;73:103294. doi: 10.1016/j.iccn.2022.103294
26. Piasecki RJ, Himmelfarb CRD, Gleason KT, Justice RM, Hunt EA. The associations between rapid response systems and their components with patient outcomes: A scoping review. Int J Nurs Stud Adv 2023;5:100134. doi: 10.1016/j.ijnsa.2023.100134
27. Song MJ, Lee YJ. Strategies for successful implementation and permanent maintenance of a rapid response system. Korean J Intern Med 2021;36:1031-9. doi: 10.3904/kjim.2020.693

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HJ: Concept and Preparation of original draft.
MA: Proposal writing, data collection and literature review.
AA: Concept, methodology and project administration.
SA: Formal analysis.
SAA: Supervision, interpretation of analysis, critical review, revision and editing.
MT: Design, proforma, methodology, critical review, revision and editing.
All authors agreed to be accountable for all aspects of the work.