

## Importance of early transfer to higher levels of in-patient care – an experience from a lower-middle-income country

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### Abstract

**Objective:** To ascertain the frequency of hospitalised internal medicine patients requiring escalation to a higher level of care, and in-hospital mortality in such cases.

**Method:** The prospective, observational study was conducted from September 1 to October 15, 2021 at a tertiary care hospital in Karachi, and comprised adult patients of either gender admitted to the internal medicine general wards and high dependency units. Data was collected prospectively using a proforma. Data was analysed using SPSS 23.

**Results:** Of the 837 patients admitted, 617(73.7%) were included. There were 310(50.2%) females and 307(49.8%) males with mean age 52.2±18.8 years. The most common comorbidity was hypertension 288(46.7%). Of the 617 patients, 51(8.3%) required escalation to a higher level of care. Escalation to the intensive care unit and high dependency unit occurred in 19(37.3%) and 32(62.7%) patients, respectively. In-hospital mortality among patients who required escalation to the intensive care unit was 52.6%. In instances where the escalation was required within 48 hours of admission, in-hospital mortality was 8.3% (2/24), whereas, it was 40.7% (11/27) in cases when it was initiated beyond 48 hours of admission ( $p=0.010$ ). The median length of hospital stay was also significantly lower when the escalation was initiated within 48 hours of admission 5 days (interquartile range: 4-7 days) compared to when it was delayed 13 days (interquartile range: 6-19 days) ( $p<0.001$ ). The principal discharge diagnosis of sepsis was significantly associated with escalation to a higher level of care ( $p<0.001$ ) and in-hospital mortality ( $p<0.001$ ).

**Conclusions:** Initiation of escalation to higher levels of care within 48 hours of admission was found to be associated with reduced in-hospital mortality and length of hospital stay.

**Key Words:** Critical Illness, Intensive care units, Emergency medical service.

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### Introduction

After initial triage, patients presenting to the emergency department (ED) are hospitalised with a wide range of conditions.<sup>1</sup> Clinical deterioration in hospitalised patients necessitating escalation to a higher level of care can occur at any moment during hospitalisation, and results in excess mortality and length of hospital stay (LOS).<sup>2</sup>

In a multicentre study done in the United States, the frequency of patients who required transfer to higher levels of care was 5.4%.<sup>2</sup> Patients who required escalation to a higher level of care were older, had more acute physiological disturbance and a higher burden of pre-existing conditions.<sup>2</sup> ED admitting diagnoses associated with escalation of care to the intensive care unit (ICU) included sepsis and acute renal failure, while one-third of patients expired during hospital stay.<sup>3</sup> Compared to surgical patients, a higher frequency of escalation to a

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higher level of care and adverse outcomes has been observed in medical patients.<sup>4</sup>

Prior studies on patients requiring transfer to higher levels of care are from the developed countries.<sup>2-4</sup> To the best of our knowledge, no work on the subject has been published from a developing country. As the availability of high dependency unit (HDU) and ICU beds in developing countries is limited, the current study was planned to ascertain the frequency of hospitalised internal medicine patients who required escalation to a higher level of care, and in-hospital mortality in such cases.

### Materials and Methods

The prospective, observational study was conducted at the Department of Medicine at the Aga Khan University Hospital (AKUH), Karachi, from September 1 to October 15, 2021. Approval was obtained from the institutional ethical review committee, which waived the need for informed consent as data was collected prospectively by reviewing medical record files and electronic health records without any interaction with the patients or their attendants.

The sample size was calculated using OpenEpi<sup>5</sup> software with a bound on error of 2 and 95% confidence interval (CI) while keeping the frequency of patients requiring escalation of care after admission from the ED as 6.3%.<sup>6</sup> The sample was raised using consecutive sampling technique. Those included were adult patients of either gender admitted to the internal medicine general ward (GW) and HDU. Patients having Do Not Resuscitate (DNR) orders that did not allow for transfer to a higher level of care were excluded.

Data was collected prospectively using a proforma, noting age, gender, comorbidities, location of admission, code status, LOS, ED admitting diagnosis, principal diagnosis on discharge, requirement of escalation to a higher level of care, location of transfer, and outcome represented by discharge, in-hospital mortality, left against medical advice (LAMA) status or transferred to an outside facility.

Data was analysed using SPSS 23. Frequencies and percentages were calculated for qualitative variables. Data normality was assessed using Shapiro-Wilk test. Quantitative variables with normal and non-normal distributions were expressed as mean  $\pm$  standard deviation, and median with inter-quartile range (IQR), respectively. Chi-square test was used to determine the relationship between categorical variables. The relationship between numerical and categorical values was determined using the independent sample t-test.  $P < 0.05$  was taken as significant at 95% CI. Univariate logistic regression was used to identify factors associated with escalation to a higher level of care. 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 escalation to a higher level of care.  $P < 0.05$  at 95% CI was considered significant.

## Results

Of the 837 patients admitted, 617(73.7%) were included. There were 310(50.2%) females and 307(49.8%) males with mean age  $52.2 \pm 18.8$  years. The most common comorbidity was hypertension 288(46.7%), followed by diabetes mellitus (DM) 242(39.2%) and ischaemic heart disease (IHD)/congestive heart failure (CHF) 85(13.2%). The number of patients with Charlson Co-morbidity Index (CCI) score 0 was 228(37%), while 107(17.3%) had a score of  $>4$  (Table 1).

From the ED, 367(59.5%) patients were admitted to GW, and 250(40.5%) to HDU. Escalation to a higher level of care during hospitalisation occurred in 51(8.3%) patients.

**Table-1:** Demographic and clinical characteristics.

Variables	Total Study Population N = 617
Age (years)	52.2 $\pm$ 18.8
Gender	
Male	307 (50.2)
Female	310 (48.8)
Co-morbid conditions	
Diabetes Mellitus	242 (39.2)
Hypertension	288 (46.7)
Ischaemic Heart Disease/Congestive Heart Failure	85 (13.2)
Chronic Kidney Disease	38 (6.2)
History of Cerebrovascular Attack	27 (4.4)
Autoimmune Disease	23 (3.7)
Charlson Co-morbidity Index Score	
0	228 (37.0)
1-2	116 (18.8)
3-4	166 (26.9)
$>4$	107 (17.3)

The escalation occurred in 29(11.6%) HDU patients and 22(6%) GW patients ( $p=0.013$ ). Among patients needing a higher level of care, 32(62.7%) required transfer to HDU, while 19(37.3%) required transfer to ICU. Among patients transferred to the ICU, 17(89.5%) were admitted to the HDU from the ED on admission. Age was significantly different between patients who required escalation to a higher level of care and those who did not (Table 2).

Of the total study population, 564(91.4%) patients were discharged, while 37(6%) either used LAMA option or were transferred to another facility, and 16(2.6%) expired during the hospital stay. Among patients who expired after being transferred to a higher level of care, 10(76.9%) required transfer to ICU. Patients who required escalation had an in-hospital mortality of 25.5% (13/51) while it was 0.5% (3/566) for patients who did not ( $p < 0.001$ ).

Sepsis was the ED admitting diagnosis in 40(9.6%) of the 418 patients with an infection-related diagnosis on admission, while it was present in 52(14%) of the 372 patients with an infection-related principal diagnosis on discharge. Sepsis as a diagnosis on admission or principal diagnosis on discharge was significantly associated with escalation to a higher level of care ( $p = 0.005$  and  $< 0.001$  respectively). A principal discharge diagnosis of sepsis was also significantly associated with in-hospital mortality ( $p < 0.001$ ).

The median LOS was 3 days (IQR: 2-5 days). For patients who required escalation to a higher level of care, the median LOS was 7 days (IQR: 5-14 days), while for patients who did not, it was 3 days (IQR: 2-4 days) ( $p < 0.001$ ). Among patients who survived after being transferred to a

**Table-2:** Comparison of patients admitted to the general ward and HDUs on admission, and of those who required transfer to a higher level of care during hospitalisation with those who did not.

Variable	On Admission from the ED		p-value	During Hospitalisation		p-value
	Patients admitted to the HDU (N = 250)	Patients admitted to the GW (N = 367)		Patients who Required Transfer to a Higher Level of Care (N = 51)	Patients who Did Not Require Transfer to a Higher Level of Care (N = 566)	
Age (in years)	58.6 ± 17.3	47.8 ± 18.6	<0.001	58.9 ± 17.9	51.6 ± 18.8	0.008
Gender			0.376			0.100
Male	119 (47.6)	188 (51.2)		31 (60.8)	276 (48.8)	
Female	131 (52.4)	179 (48.8)		20 (39.2)	290 (51.2)	
Co-morbidities						
Diabetes Mellitus	134 (53.6)	108 (29.4)	<0.001	27 (52.9)	215 (38.0)	0.036
Hypertension	156 (62.4)	132 (40.0)	<0.001	25 (49.0)	263 (46.5)	0.726
Ischaemic Heart Disease/ Congestive Heart Failure	55 (22)	30 (8.2)	<0.001	13 (25.5)	72 (12.7)	0.011
Chronic Kidney Disease	23 (9.2)	15 (4.0)	0.01	4 (7.8)	34 (6.0)	0.544
History of Cerebrovascular Attack	13 (5.2)	14 (3.8)	0.409	6 (11.8)	21 (3.7)	0.007
Autoimmune Disease	14 (5.6)	9 (2.5)	0.043	6 (11.8)	17 (3.0)	0.002
Admitting Diagnoses						
Infections	152 (60.8)	266 (72.5)	0.002	31 (60.8)	387 (68.4)	0.267
Renal diseases	51 (20.4)	33 (9.0)	<0.001	12 (23.5)	72 (12.7)	0.031
Cardiovascular diseases	64 (25.6)	16 (4.4)	<0.001	6 (11.8)	74 (13.1)	0.79
Electrolyte Imbalance	49 (19.6)	29 (7.9)	<0.001	9 (17.6)	69 (12.2)	0.261
Neurological diseases	25 (10.0)	11 (3.0)	<0.001	2 (3.9)	34 (6.0)	0.759
Principal Discharge Diagnoses						
Infections	116 (46.4)	256 (69.8)	<0.001	28 (54.9)	344 (60.1)	0.411
Cardiovascular diseases	37 (14.8)	11 (3.0)	<0.001	7 (13.7)	41 (7.2)	0.098
Neurological diseases	23 (9.2)	13 (3.5)	0.003	1 (2.0)	35 (6.2)	0.349
Electrolyte Imbalance	21 (8.4)	11 (3.0)	0.003	1 (2.0)	31 (5.5)	0.505
Gastrointestinal diseases	12 (4.8)	19 (5.2)	0.833	4 (7.8)	27 (4.8)	0.313

HDU: High dependency unit, GW: General ward.

higher level of care, the median LOS before transfer was 2 days (IQR: 1-4 days) compared to 6 days (IQR: 3-8 days) for those who expired during the hospital stay (p=0.039). Among patients who required transfer to the ICU and survived, the median LOS before transfer was 2 days (IQR: 1-4 days), while it was 7 days (IQR: 4-8 days) for those who did not (p=0.010).

The number of patients who required escalation to a higher level of care within 48 hours of admission was 24(47.1%). In-hospital mortality for patients who required escalation within 48 hours of admission was 8.3% (2/24), while it was 40.7% (11/27) for those who were transferred beyond 48 hours of admission (p=0.010). The median LOS was 5 days (IQR: 4-7 days) when escalation was initiated within 48 hours of admission, whereas the median LOS was 13 days (IQR: 6-19 days) in cases where the escalation occurred beyond 48 hours of admission (p<0.001).

On multivariable regression analysis, the co-morbid conditions of IHD/CHF (adjusted odds ratio [aOR]: 2.267; 95%CI: 1.122-4.584; p=0.023), history of cerebrovascular

**Table-3:** Independent factors associated with transfer to a higher level of care on multivariable regression analysis

Variable	Adjusted Odds Ratio (95% CI)	p - value
Comorbidities		
<b>Ischaemic Heart Disease/Congestive Heart Failure</b>		0.023
No	1.0	
Yes	2.267 (1.122 – 4.584)	
<b>History of Cerebrovascular Attack</b>		0.014
No	1.0	
Yes	3.420 (1.278 – 9.149)	
<b>Autoimmune disease</b>		0.007
No	1.0	
Yes	4.055 (1.458 – 11.283)	
Principal Discharge Diagnosis		
<b>Sepsis</b>		0.005
No	1.0	
Yes	2.977 (1.382 – 6.415)	

attack (aOR: 3.420; 95% CI: 1.278-9.149; p=0.014), and autoimmune disease (aOR: 4.055; 95% CI: 1.458-11.283; p=0.007) were associated with higher odds of transfer to a higher level of care during hospitalisation along with sepsis as a principal discharge diagnosis (aOR: 2.977; 95% CI: 1.382-6.415; p=0.005) (Table 3).

## Discussion

Around every 10th patient admitted to the HDU in the current study required escalation to a higher level of care during the hospital stay, while more than half of the patients who required escalation of care to the ICU expired during the hospital stay. Patients with co-morbid conditions of autoimmune diseases, IHD/CHF, or history of cerebrovascular attack had higher odds of requiring transfer to a higher level of care along with those having sepsis as the principal discharge diagnosis. Patients who required escalation to a higher level of care within 48 hours of admission had lower in-hospital mortality and shorter LOS compared to those whose required escalation beyond 48 hours of admission.

The frequency of hospitalised patients who required escalation to a higher level of care was 5.4% in a multi-centre study from 19 acute care hospitals in the US.<sup>2</sup> Similarly, 6.3% of hospitalised patients required escalation to a higher level of care in another study.<sup>6</sup> The frequency of patients who required escalation to a higher level of care in the current study (8.3%) was higher, which may be because the study included only patients admitted to internal medicine, while the earlier studies<sup>2,6</sup> included both medical and surgical patients. In addition, both the studies<sup>2,6</sup> did not exclude patients with DNR orders.

In the current study, the frequency of patients admitted to HDU who required transfer to a higher level of care was 11.6%. This suggested that the burden of medical patients who required escalation to higher levels of care, especially those admitted to the HDU, was perhaps higher than previously thought. This difference might be due to the fact that critical care facilities in developing countries are limited, leading to admission of many patients to HDUs who should have been admitted in ICUs. Further studies from other centres, especially from developing countries, are needed to confirm these findings.

The current study observed that in-hospital mortality was highest in those patients who required escalation of care to the ICU. Sepsis and renal diseases were among the diagnoses on admission that were significantly associated with escalation of care to the ICU. Similarly, ED admitting diagnoses of sepsis and acute renal failure were significant risk factors for escalation to the ICU in an earlier study.<sup>3</sup> For these reasons, physicians should be vigilant once these patients are admitted to GW and HDU from the ED. When required, escalation to higher levels of care should be initiated early as delays in escalation for clinically deteriorating patients have been associated with increased in-hospital mortality.<sup>7</sup> The current study

supported this finding.

In the current study, more than half of the patients who required escalation of care to the ICU did not survive. This is higher than the 36% observed earlier.<sup>3</sup> It is also higher than the 21% and 25% observed among patients shifted from GW and transitional care unit (TCU) to ICU, respectively.<sup>2</sup> This may be because the current study was conducted only among internal medicine patients. This may also be because, due to limited resources, escalation of care to the ICU at AKUH is mostly reserved for patients who require invasive mechanical ventilation. Given the high mortality rates, future research should focus on identifying risk factors for in-hospital mortality in patients who require transfer to the ICU.

Clinical deterioration<sup>8</sup> resulting in escalation to a higher level of care may occur at any moment during hospitalisation. Early warning scores such as the Modified Early Warning Score (MEWS)<sup>9</sup> and National Early Warning Score (NEWS)<sup>10</sup> have been traditionally used to assist healthcare providers to identify patients at risk of clinical deterioration. Machine learning is now also being used with the Deep-learning-based Early Warning Score (DEWS) and MEWS++ as examples of machine learning models developed to predict clinical deterioration that have outperformed traditional early warning scores.<sup>11-12</sup> Further research is needed to establish the effectiveness of the use of these tools to detect patients who may benefit from early escalation to a higher level of care in patients admitted to hospitals in developing countries.

The major strengths of the current study were the inclusion of patients admitted only to internal medicine, and the prospective nature of data collection along with the exclusion of patients with DNR orders that barred escalation to a higher level of care. Limitations of the study include a relatively small sample size and a single-centre design which lowers the generalisability of the findings as all tertiary care hospitals in the country have different levels of care. The current findings may encourage other centres in the country to undertake similar studies.

## Conclusion

Initiation of escalation to higher levels of care within 48 hours of admission was found to be associated with reduced in-hospital mortality and length of hospital stay.

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**HJ:** Proposal writing, data collection, literature review, preparation of original draft.

**SAA:** Preparation of original draft.

**SA:** Formal analysis.

**MT:** Concept, methodology, revision and editing.

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