Associations of day of week and time of day of ICU admission with hospital mortality in Malawi

Meghan Prin¹ , Ruoyu Ji², Clement Kadyaudzu³, Guohua Li^{4,5} and Anthony Charles⁶

Abstract

This prospective cohort study evaluated the associations of day and time of admission to the Intensive Care Unit (ICU) with hospital mortality at a referral hospital in Malawi, a low-income country in sub-Saharan Africa. Patients admitted to the ICU during the day (08:00–16:00) were compared to those admitted at night (16:01–07:59); patients admitted on weekdays (Monday–Friday) were compared to admissions on weekends/holidays. The primary outcome was hospital mortality. Most patients were admitted during daytime (56%) and on weekdays (72%). There was no difference in mortality between night and day admissions (58% vs. 56%, $P = 0.8828$; hazard ratio [HR] = 1.09, 95% confidence interval [CI] = 0.82–1.44, $P = 0.5614$) or weekend/holiday versus weekday admissions (56% vs. 57%, $P = 0.9011$; HR = 0.87, 95% CI = 0.62–1.21, $P = 0.4133$). No interaction between time and day was found. These results may be affected by high overall hospital mortality.

Keywords

Outcomes, global health, Intensive Care Unit organisation

Introduction

Critically ill patients benefit from timely, quality intensive care medicine. Delays or deficiencies in care secondary to organisational factors have been associated with poor patient outcomes. These factors include the availability of dedicated intensive care specialist physicians (as opposed to general physicians),¹ ‘closed’ versus ‘open’ clinical management styles,^{2,3} and nursing staff patterns.⁴ Regardless of the specific operational organisation of an intensive care unit (ICU), some factors such as staffing and workload are expected to vary over the course of each day, week and season.

The timing of admission to the ICU (e.g. daytime versus night-time, weekend versus weekdays) has been evaluated in multiple studies,^{5–11} but not often in a low-income country or in the region of sub-Saharan Africa. Research that informs these questions has been cited as a path forward in global health critical care medicine.¹² Organisational factors affecting patient care are particularly important questions to address and optimise in the African region, because availability of ICU beds here is generally only 1 per million population or less¹³ and physician oversight in the ICU (generalist or

specialist) is rare. A recent meta-analysis demonstrated that an increased odds ratio for hospital mortality among weekend versus weekday ICU admissions was limited to North American studies, which suggests that this relationship may be modified by geographic setting and healthcare system.¹⁴ The aim of our study was to evaluate the association of time-of-day and day-of-

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week on hospital mortality among patients admitted to the ICU in a public referral hospital in Malawi.

Methods

This was a prospective, observational cohort study of patients admitted to the ICU of Kamuzu Central Hospital (KCH) in Lilongwe, Malawi, from September 2016 to July 2018. The timing of the study recruitment was based on funding limitations; no power calculations were undertaken. The study protocol was registered at researchregistry.com under protocol 4330. It was developed a priori and approved by the National Health Sciences Research Council of Malawi and the Institutional Review Boards of both American universities with which the study was affiliated, and the requirement for written informed consent was waived by all. The results are reported in line with the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) criteria.¹⁵

Malawi is a country in southern Africa with a population of 18 million people, a life expectancy of 63.8 years and a Human Development Index rank of 170 out of 187 countries.¹⁶ It is the fourth poorest country in sub-Saharan Africa.¹⁷ KCH is a referral hospital in the central region of Malawi with a catchment area of approximately 5 million. The ICU at KCH is a five-bed unit which offers a 1:1 nurse-to-patient ratio during the day and a 1:2 or higher nurse-to-patient ratio at night. Resources include continuous non-invasive vital sign monitoring, mechanical ventilation with a titratable fraction of inhaled oxygen, and intravenous medication infusions. Haemodialysis is available within the hospital campus. Clinical care in the ICU is directed by clinical officers in Anaesthesiology; exactly one clinical officer is on duty in the ICU at all times to oversee patient care. Although physicians from other services (e.g. Surgery, Obstetrics) consult on ICU patients, no physicians are on staff in this unit and no staff members have consultant-level expertise in intensive care medicine.

The data were collected prospectively by study staff trained in ICU data abstraction. Variables collected included the day and time of ICU admission, vital signs and laboratory measurements at the time of ICU admission, treatments utilised in ICU (e.g. mechanical ventilation), the date of ICU discharge and the hospital discharge date. Laboratory data collected included only those commonly measured by local standards and available in the hospital laboratory. For this study, this included a complete blood count, electrolytes, point-of-care malaria status and point-of-care human immunodeficiency virus (HIV) status.

All adult patients admitted to the study ICU were eligible for inclusion. Exclusion criteria included age ≤ 15 years, readmission to ICU during the same

hospitalisation, and missing primary exposure and/or multiple key data points. We performed analyses with and without patients admitted to ICU for a reported severe head injury, because this group is known to have very high mortality.¹⁸ The analysis excluding patients with severe head injury is included in the Supplemental Materials.

The cohort was divided into groups based on the time of ICU admission. We split each day based on shift hours at the study hospital (i.e. daytime [DT] hours are a period of more nurses with a 1:1 nurse-to-patient ratio, while the night-time [NT] hours generally have less staff). DT was defined as 08:00–16:00 and NT as 16:01–07:59 the next day. The days of the week were then grouped as weekdays (Monday–Friday) or weekends (Saturday, Sunday and public holidays as listed in Appendix A). This yielded the following

Figure 1. Flow diagram for cohort.

Table 1. Clinical characteristics and hospital course for study cohort, stratified by time of day of ICU admission.

Variable	Total	Daytime	Night-time	P value
Total ICU admissions	377	210 (55.7)	167 (44.3)	
Age (years)	31 (23–41)	32 (23–42)	30 (23–39)	0.3086*
Sex				0.3317 [†]
Female	196 (52.0)	104 (49.5)	92 (55.1)	
Male	181 (48.0)	106 (50.5)	75 (44.9)	
Hospital course preceding ICU admission				
Time in hospital before ICU (days)	1 (0–2)	1 (0–2.75)	1 (0–1)	0.02896*
Hospital location before ICU admission				0.1971 [†]
Emergency room	71 (18.8)	39 (18.6)	32 (19.2)	
HDU	91 (24.1)	59 (28.1)	32 (19.2)	
Operating room	180 (47.7)	91 (43.3)	89 (53.3)	
Outside hospital	12 (3.2)	6 (2.9)	6 (3.6)	
Ward	23 (6.1)	15 (7.1)	8 (4.8)	
Recent surgery in hospital course	238 (63.1)	122 (58.1)	116 (69.5)	0.03041 [†]
Cardiac arrest before ICU	45 (11.9)	26 (12.4)	19 (11.4)	0.8897 [†]
ICU admitting service				0.0004517 [†]
General surgery	234 (62.1)	130 (61.9)	104 (62.3)	
OBGyn	98 (26.0)	44 (21.0)	54 (32.3)	
Medicine	45 (11.9)	36 (17.1)	9 (5.4)	
Vital signs and assessments at admission to ICU				
Total MEWS	7 (5–8)	6 (5–8)	7 (5–8)	0.4391*
Heart rate (bpm)	117 (98–134)	115 (96–132)	119 (100.25–136.75)	0.2488*
Respiratory rate	19 (14–25)	19 (14–25)	18.5 (14–25)	0.7166*
MAP [§] (mmHg)	88.77 (72.27–104.86)	91.25 (74.09–106.01)	86.46 (71.03–104.53)	0.2798*
Temperature (°C)	36 (34.7–37)	36 (35–37)	36 (34–37)	0.2772*
Pulse oximetry value	97 (93–99)	97 (91–99)	98 (95–99)	0.05561*
Altered mental status	313 (83.7)	176 (84.2)	137 (83.0)	0.8683 [†]
Infection suspected	207 (54.9)	131 (62.4)	76 (45.5)	0.00155 [†]
HIV-positive	41 (12.9)	24 (13.6)	17 (12.1)	0.8378 [†]
Malaria	33 (11.5)	25 (15.2)	8 (6.5)	0.03643 [†]
Clinical course in ICU				
Provision of mechanical ventilation	364 (96.6)	203 (96.7)	161 (96.4)	~1 [†]
Length of mechanical ventilation (days)	2 (1–6)	3 (1–6)	2 (1–5)	0.589*
Length of stay in ICU (days)	3 (1–6)	3 (1–7)	3 (1–5)	0.3588*
ICU mortality	191 (50.7)	104 (49.5)	87 (52.1)	0.6947 [†]
Hospital mortality	214 (56.8)	118 (56.2)	96 (57.5)	0.8828 [†]

Values are given as n (%) or median (IQR).

*Wilcoxon rank-sum test (non-parametric equivalent for two-sample t test) for comparisons of continuous variables.

[†]Chi-squared test for homogeneity/independence of categorical variables: Assumptions: (i) independent groups; (ii) no expected cell counts are 0 and no more than 20% of cells have an expected count < 5.

[§]MAP is calculated using the following equation: $0.66 \times (\text{diastolic BP}) + 0.33 \times (\text{systolic BP})$.

BP, blood pressure; bpm, beats per minute; ICU, Intensive Care Unit; IQR, interquartile range; HDU, high-dependency unit; HIV, human immunodeficiency virus; MAP, mean arterial pressure; MEWS, Modified Early Warning Score; OBGyn, Obstetrics and Gynaecology.

non-exclusive groups for comparison: patients admitted at night; patients admitted during the day; patients admitted on weekdays; and patients admitted on weekends or public holidays. We sought to test two hypotheses: (1) hospital mortality differs between weekday versus weekend/public holiday ICU admissions; and

(2) hospital mortality differs between DT versus NT ICU admissions. Given our anticipated limited sample size, we did not seek to compare patients on a more granular level.

We summarised the clinical traits of the entire cohort and then compared the groups. We performed

univariate analyses to identify potential confounders of the relationship between timing of admission to the ICU and hospital mortality. Potential confounders were identified using a *P* value cut-off of 0.2. Special consideration was given to confounders identified a priori: severity of illness based on the Malawi Intensive Care Mortality Evaluation (MIME) model¹⁹ (age, sex, admitting service, systolic pressure at ICU admission, altered mental status at ICU admission and fever during the ICU course); the number of hospital days before ICU admission; and cardiopulmonary resuscitation before ICU admission. The primary outcome was hospital mortality.

We conducted survival analyses for the primary outcome following the example of Arulkumaran et al.⁵: (1) an unadjusted model of weekday versus weekend/public holiday, which used weekday as the reference; (2) an unadjusted model of time-of-day, which used DT as the reference, as well as an assessment of the interaction between time-of-day and day-of-week (see Supplementary Analyses). The estimated Kaplan–Meier survival curves were compared using the log-rank test, with right-censoring at hospital discharge. We then performed multivariable survival analyses. For the adjusted models, we built Cox proportional hazard regression models. The regression models initially included variables from our univariate analyses: time and day of admission to the ICU; age; sex;

admitting service; systolic blood pressure; heart rate; respiratory rate; altered mental status or suspicion of infection at ICU admission; fever during the ICU course; surgery within the index hospitalisation; and the length of hospital stay before admission to the ICU. We used backward selection to develop more parsimonious models based on these results. Finally, we plotted the adjusted Kaplan–Meier survival curves for hospital mortality. For every patient in the dataset, a prediction for hospital survival was made. Subpopulations of interest were balanced with respect to covariates to keep distributions similar in the whole dataset. The balancing was performed in the following way: (1) for each subpopulation, a logistic regression model was created to model the odds of being in the subpopulation given the other covariates; (2) reverse probabilities of belonging to a specific subpopulation were used as weights in the Cox model; (3) the Cox model was refitted with weights; and (4) expected survival curves were calculated for each subpopulation based on a refitted weighted model. The predictions were averaged for subpopulations after rebalancing.

Continuous data are presented as medians with interquartile ranges (IQR), categorical data as number and proportion of the total. Model output is described with hazard ratios (HR) and 95% confidence intervals (CI). Statistical significance was set at 0.05. Statistical analyses were conducted using R version 3.5.1.

Figure 2. Histogram of ICU admissions stratified by time of ICU admission. ICU, intensive care unit.

Results

During the study period, 499 patients were admitted to the study ICU and 377 met the inclusion criteria (Figure 1). The multivariable analyses included 346 patients after accounting for missing data. The cohort was 52% female (median age = 31 years; IQR = 23–41 years) (Table 1). Patients were admitted with multiple admission diagnoses; the most common were respiratory failure, severe head injury, postoperative monitoring and haemorrhagic shock (Supplementary materials, Tables S1–S2). The proportion of patients admitted during DT versus NT for each day of the week is summarised in Figure 2.

Time of day

There were 210 (55.7%) DT admission versus 167 (44.3%) NT admissions. Patients admitted during DT were more likely to have a clinically suspected infection (62.4% vs. 45.5%, $P=0.0015$), while patients admitted at NT were more likely to have had surgery preceding admission to the ICU (69.5% vs. 58.1%, $P=0.0304$). There were no other differences between the groups. Hospital mortality for DT admissions was 56.2% versus 57.5% for NT admissions ($P=0.8828$) (Table 1). In the univariate survival analysis, there was no difference in the hospital mortality for patients admitted to the ICU during the DT versus the NT ($P=0.650$) (Figure 3) and these results were unchanged in the multivariable Cox proportional hazards model (HR = 1.09, 95% CI = 0.82–1.45, $P=0.5614$; Figure 5 and Table S4 in Supplementary Materials) and in the supplementary analyses excluding patients with head injuries (Supplementary Materials). No significant interaction between day of the week and time of day was found (Supplementary Materials).

Figure 3. Unadjusted Kaplan–Meier curve for survival of day-time vs. night-time ICU admissions. ICU, intensive care unit.

Day of the week

There were 273 (72.4%) weekday admissions versus 104 (27.6%) weekend or public holiday admissions. Weekday admissions were more often general surgery patients (63.7% vs. 57.7%) or medicine (13.6% vs. 7.7%) and weekend/holiday admissions were more often obstetrics patients (34.6% vs. 22.7%). There were no other major differences. Hospital mortality was 57.1% for weekday admissions versus 55.8% for weekend or public holiday admissions ($P=0.9011$) (Table 2). In the univariate survival analysis, there was no difference in the hospital survival for patients admitted to ICU during the week versus the weekend or public holidays ($P=0.95$) (Figure 4); these results were unchanged in the multivariable Cox proportional hazards model (HR = 0.87, 95% CI = 0.62–1.21, $P=0.4133$; Figure 6 and Table S6 in Supplementary Materials) and in the supplementary analyses excluding patients with head injuries (Supplementary Materials).

Figure 4. Unadjusted Kaplan–Meier curve for survival of weekday vs. weekend/holiday ICU admissions. ICU, intensive care unit.

Figure 5. Adjusted Kaplan–Meier curve for survival of daytime vs. night-time ICU admissions. ICU, intensive care unit.

Table 2. Clinical characteristics and hospital course for study cohort, stratified by day of the week of ICU admission.

Variable	Total	Weekday	Weekend/ holiday	P value
Total ICU admissions	377	273 (72.4)	104 (27.6)	
Age (years)	31 (23–41)	31 (23–42)	33 (23–40)	0.7526*
Sex				0.138 [†]
Female	196 (52.0)	135 (49.5)	61 (58.7)	
Male	181 (48.0)	138 (50.5)	43 (41.3)	
Hospital course preceding ICU admission				
Time in hospital before ICU (days)	1 (0–2)	1 (0–2)	1 (0–1)	0.1509*
Hospital location before ICU admission				0.751 [‡]
Emergency room	71 (18.8)	53 (19.4)	18 (17.3)	
HDU	91 (24.1)	65 (23.8)	26 (25.0)	
Operating room	180 (47.7)	132 (48.4)	48 (46.2)	
Outside hospital	12 (3.2)	9 (3.3)	3 (2.9)	
Ward	23 (6.1)	14 (5.1)	9 (8.7)	
Recent surgery in hospital course	238 (63.1)	171 (62.6)	67 (64.4)	0.8401 [†]
Cardiac arrest before ICU	45 (11.9)	33 (12.1)	12 (11.5)	~1 [†]
ICU admitting service				0.0348 [†]
General surgery	234 (62.1)	174 (63.7)	60 (57.7)	
OBGyn	98 (26.0)	62 (22.7)	36 (34.6)	
Medicine	45 (11.9)	37 (13.6)	8 (7.7)	
Vital signs and assessments at admission to ICU				
Total MEWS	7 (5–8)	7 (5–8)	7 (5–9)	0.5418*
Heart rate (bpm)	117 (98–134)	116 (95.75–132)	119 (104.25–142.75)	0.03543*
Respiratory rate	19 (14–25)	18 (14–24)	20 (15–28.5)	0.1055*
MAP [§] (mmHg)	88.77 (72.27–104.86)	88.77 (71.28–106.18)	91.25 (73.10–103.04)	0.8528*
Temperature (°C)	36 (34.7–37)	36 (34.68–37)	36 (34.7–37)	0.4449*
Pulse oximetry value	97 (93–99)	97 (92–99)	98 (94.75–99)	0.6192*
Altered mental status	313 (83.7)	230 (84.6)	83 (81.4)	0.5581 [†]
Infection suspected	207 (54.9)	145 (53.1)	62 (59.6)	0.3086 [†]
HIV-positive	41 (12.9)	26 (11.3)	15 (17.2)	0.2232 [†]
Malaria	33 (11.5)	23 (10.8)	10 (13.2)	0.7397 [†]
Clinical course in ICU				
Provision of mechanical ventilation	364 (96.6)	265 (97.1)	99 (95.2)	0.3584 [‡]
Length of mechanical ventilation (days)	2 (1–6)	2 (1–6)	2 (1–6)	0.8018*
Length of stay in ICU (days)	3 (1–6)	3 (1–6)	3 (1–7)	0.908*
ICU mortality	191 (50.7)	137 (50.2)	54 (51.9)	0.8518 [†]
Hospital mortality	214 (56.8)	156 (57.1)	58 (55.8)	0.9011 [†]

Values are given as n (%) or median (IQR).

*Wilcoxon rank-sum test (non-parametric equivalent for two-sample t test) for comparisons of continuous variables.

[†]Chi-squared test for homogeneity/independence of categorical variables: Assumptions: (i) independent groups; (ii) no expected cell counts are 0 and no more than 20% of cells have an expected count < 5.

[‡]Fisher's exact test for count data in hybrid model: For tables larger than 2 × 2, in hybrid model, asymptotic Chi-squared probabilities are only used if the "Cochran conditions" (i.e. no expected cell counts are 0 and no more than 20% of cells have an expected count < 5) are satisfied, otherwise the exact calculation is used. (In the r × c case with r > 2 or c > 2, if tables are too large for the exact test, Fisher's exact test for count data with simulated P value [based on 2000 replicates] can be used as well.)

[§]MAP is calculated using the following equation: 0.66 × (diastolic BP) + 0.33 × (systolic BP).

BP, blood pressure; bpm, beats per minute; ICU, Intensive Care Unit; IQR, interquartile range; HDU, high-dependency unit; HIV, human immunodeficiency virus; MAP, mean arterial pressure; MEWS, Modified Early Warning Score; OBGyn, Obstetrics and Gynaecology.

Figure 6. Adjusted Kaplan–Meier curve for survival of weekday vs. weekend/holiday ICU admissions. ICU, intensive care unit.

Discussion

Our study demonstrates that day of the week and time of day admission to the ICU have no association with hospital mortality in a critically ill cohort at a referral hospital in Malawi. While our findings regarding DT versus NT are consistent with studies from high-income nations,^{5,14} we did not find evidence of the ‘weekend effect’ which has been demonstrated in high-income settings.^{14,20} This may be attributable to the high overall hospital mortality in this cohort, although we cannot rule out the possibility of a type 2 error given our relatively small sample size. Low-income countries face infrastructural challenges in the provision of healthcare, and studies such as ours which evaluate the effects of different organisational strategies may contribute to improved care delivery. A major strength of this study is the granularity of data collected within a region in which data collection is known to be difficult, and our findings contribute to the literature gap in characterising the processes of critical care services and outcomes in sub-Saharan Africa.

An important distinction between this study cohort and those from high-income settings is the overall hospital mortality. Hospital mortality in this study was 56.8% compared to overall crude hospital mortality generally <20% in the studies included in the above referenced systematic review.¹⁴ This high hospital mortality for critically ill patients in Malawi has been described in our previous work¹⁹ and reflects the context of critical care medicine in this region. In an ICU setting with no physician oversight and supply shortages, differences between DT/NT or weekday/weekend staffing models may be less pronounced. Furthermore, our study cohort was predominantly surgical (63.1%). Intraoperative patients who develop critical illness are moving from one high-intensity setting (operating theatre) to another (ICU), regardless of the time of the day or the day of the week. Our results may have differed if

this study focused exclusively on patients who developed critical illness and were admitted to ICU from general wards and/or the emergency ward, where staffing patterns may have higher variance.

Nevertheless, our study provides an opportunity to evaluate how critically ill patients may be triaged in a setting of extreme scarcity. With only 1.7 ICU beds per million population in Malawi, ICU care must be reserved for those who are most likely to benefit²¹ and staffing models must be optimised based on what is known about ICU admission patterns. Our study found some differences in the clinical characteristics for patients admitted at different times. Off-hours (weekends, holidays and NT) admissions were more likely to be obstetric patients. This may indicate the higher incidence of obstetric emergencies in the off-hours. Given that obstetric utilisation of ICU beds in Malawi is nearly one in four,²² hospital and ICU management personnel may plan, for example, to preferentially staff the ICU with obstetric specialists in the off-hours. We recognise that staffing in low-income areas is often too short for this type of customisation and do not mean to oversimplify these issues; these data are meant to inform hospital resource allocation as it improves.

Identification of infrastructural factors affecting patient outcomes is an important component of quality improvement. Nevertheless, this study has several limitations. First, our study was conducted at a single site in a relatively small ICU, which limited the sample size. Second, we measured the time of admission to the ICU but not the time at which patients were recommended for admission. Variations in the delay between ICU referral and admission could have affected the clinical presentation at ICU admission. We conducted multivariable adjustment using a model with discrimination for ICU and hospital mortality in Malawi¹⁹ to adjust for these clinical differences. We were also unable to differentiate between altered mental status at ICU admission secondary to disease pathology and altered mental status secondary to the residual effects of anaesthesia in this predominantly surgical population. Finally we assumed that the relevant staffing models for weekdays, weekends and the time of day were consistent throughout the study period.

Conclusion

Our prospective cohort study demonstrates that the majority of ICU admissions at a referral hospital in Malawi occur from Monday to Friday and during DT working hours. We found high overall hospital mortality, but no difference in crude or adjusted hospital mortality based on the timing of ICU admission. These results may be affected by the high overall

hospital mortality and resource restrictions in Malawi. Nevertheless, they provide an initial assessment of ICU admission patterns and may inform staffing models.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received the following financial support for the research, authorship, and/or publication of this article: This study was supported in part by the NIH Fogarty International Center Postdoctoral Research Fellowship to MP. The contents of the manuscript are solely the responsibility of the authors and do not necessarily reflect the official views of the funding agencies.

Supplemental material

Supplemental material for this article is available online.

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