ORIGINAL ARTICLE

Utility of Clinical Variables for Deciding Palliative Care in Paraquat Poisoning: A Retrospective Study

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Abstract

Background: Patients with paraquat poisoning (PP) have a mortality rate comparable to that of advanced malignancies, yet palliative care is seldom considered in these patients. This audit aimed to identify triggers for early palliative care referral in critically ill patients with PP.

Methods: Medical records of patients with PP were audited. Predictors of mortality within 48 hours of hospitalization and 24 hours of intensive care unit (ICU) admission were considered as triggers for palliative care referral.

Results: Among 108 patients, 84 complete records were analyzed, and 53 out of 84 (63.1%) expired. Within 48 hours after hospitalization, the lowest oxygen partial pressure in arterial blood to a fraction of inspired oxygen [the ratio of partial pressure of oxygen in arterial blood (PaO_2) to the fraction of inspiratory oxygen concentration (FiO_2) (PaO_2/FiO_2)] was the independent predictor of mortality, cut-off ≤ 197; the area under the curve (AUC), 0.924; sensitivity, 97%; specificity, 78%; p <0.001; and 95% confidence interval (CI): 0.878–0.978. Kaplan–Meier survival plot showed that the mean survival time of patients with the lowest PaO_2/FiO_2, ≤197, was 4.64 days vs 17.20 days with PaO_2/FiO_2 >197 (log–rank p < 0.001). Sequential organ failure assessment (SOFA) score within 24 hours of ICU admission had a cut-off ≥9; AUC, 0.980; p < 0.001; 95% CI: 0.955–1.000; 91% sensitivity; and 90% specificity for mortality prediction. Out of the total of 84 patients with PP analyzed, there were 11 patients admitted to the high dependency units (13.1%) and 73 patients admitted to the ICU (86.9%). Out of the total of 84 patients of PP in whom data was analyzed, 53 (63.1%) patients required ventilator support. All the 53 patients who required ventilator support due to worsening hypoxemia, eventually expired.

Conclusion: The lowest PaO_2/FiO_2 ≤ 197 within 48 hours of hospitalization, SOFA score ≥9 within 24 hours of ICU admission or need for mechanical ventilation are predictors of mortality in PP patients, who might benefit from early palliative care.

Keywords: Mortality, Palliative care, Paraquat poisoning, Predictors, Referral triggers.

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Highlights

Early palliative care in paraquat poisoning (PP) is quintessential. Parameters like poor oxygenation, multiorgan dysfunction with sequential organ failure assessment (SOFA) score ≥9 within 24 hours of intensive care unit (ICU) admission, or the need for mechanical ventilation may serve as triggers for early palliative care referrals and may obviate the need for serum paraquat concentrations.

Introduction

Mortality in patients with PP often correlates with its volume and concentration, which can be as high as 100%.[1,2] In comparison, mortality in these patients is higher than in advanced metastatic carcinoma.[3] Moreover, the time from onset of illness to death in PP is significantly shorter compared to terminal malignancies, necessitating the identification of triggers for early palliative care consideration.[4] Although plasma paraquat concentration can reliably predict mortality, its estimation facilities are often unavailable.[5,6] Widely available, point-of-care testing of arterial blood gases (ABG) in cases of critical illnesses could predict outcomes and may also be helpful in patients with PP.[7]

Lung involvement is common in PP, and alveoli can have 20 times the concentration of paraquat compared to plasma.[6] At present, there are no standardized methods for predicting the outcomes in patients with PP.[8] However, a recent study showed that decreased consciousness level with (Glasgow coma scale <15), high neutrophil-to-lymphocyte ratio (>18), alanine aminotransferase (>40 IU/L), and creatinine (>1.24 mg/dL) apart from high paraquat plasma concentrations at admission (>11.5 gm/mL) were identified as independent predictors of in-hospital mortality in patients with acute PP.[8] Previous literature also revealed that liver and renal dysfunction, serum anion gap above 25.5 mmoL/L, and

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computerized tomography of the thorax were predictors of outcomes in PP.[9,10]

We aimed to explore parameters correlating with the mortality in patients with PP in the first 48 hours of hospitalization and the utility of the SOFA score as a predictor of mortality within 24 hours of ICU admission. This may obviate the need for serum paraquat concentration which may be unavailable at many centers. The predictors of mortality can serve as triggers for palliative care referral in patients with PP. Although there is some empirical evidence on mortality prediction in patients with PP, it has never been considered a factor for early palliative care, making this audit a novel area of research inquiry.

- Primary objective: Determination of parameters correlating with mortality in patients with PP in the first 48 hours of hospitalization, which may then serve as early triggers for palliative care referral.
- Secondary objective: Determine the utility of the multiorgan dysfunction SOFA score as a predictor of mortality within 24 hours of ICU admission with a cut-off value for an early trigger for palliative care referral.

Methods

Study Design

It is a single-center retrospective audit. Case records of 108 patients with PP from 1 January 2018 to 28 November 2021 were audited.

Participants and Setting

Patients with documented history of paraquat toxicity were included in this audit, who were admitted to a medical college hospital.

The study is being reported in accordance with the strengthening of the reporting of observational (STROBE) studies in Epidemiology guidelines.

Inclusion Criteria

Patients of either gender belonging to any age-group, who were admitted with PP based on the history of consumption of paraquat.

Exclusion Criteria

- Patients who also had any history of trauma after PP.
- Patients who requested discharge were not included in the mortality analysis.

Outcome

Mortality at the end of hospital stay.

Instruments

The following details of the patients were extracted from the medical records: Age, gender, amount of paraquat (PQ) consumed, days from consumption of PQ to hospital admission, vital parameters on admission to the emergency department (ED) such as heart rate, respiratory rate (RR), oxygen saturation (SpO_2), systolic blood pressure (SBP), Glasgow coma score (GCS), and predominant symptoms on presentation. The number of patients with therapeutic modalities such as hemoperfusion (HP), *N*-acetyl cysteine (NAC) therapy, hemodialysis (HD), and corticosteroids administered was noted. The incidence of ICU admission, need for ventilator support, either noninvasive ventilation (NIV) or invasive mechanical ventilation (IMV), length of stay (LOS) in hospital, length of ICU stay, and mortality were recorded.

The trends of the clinical variables from the time of hospital admission till 48 hours of hospitalization were recorded, and the worst values of the variables were noted. In patients who expired within 24 hours of hospitalization, the worst values of clinical variables within the time frame of 24 hours were recorded.

Arterial blood gases parameters {the lowest [the ratio of partial pressure of oxygen in arterial blood (PaO_2) to the fraction of inspiratory oxygen concentration (FiO_2) (PaO_2/FiO_2) ratio]}, the lowest bicarbonate, and the highest lactate). The serum laboratory investigations were noted for the worst values within 48 hours of hospitalization—lowest hemoglobin level, lowest sodium level, lowest potassium level, highest white blood cell (WBC) count, lowest platelet count, the highest serum urea, highest creatinine, highest aspartate transaminase (AST), highest alanine transaminase (ALT), and highest total bilirubin levels. The maximum (worst) SOFA score within 24 hours of ICU admission was recorded. Out of 108 medical records, a total of 84 records were analyzed as complete information was available for all variables of interest. The continuous variables of the patients who were discharged against the medical advice were analyzed as a separate subgroup.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS), version 28.0 (IBM, Armonk, NY, USA) was used for the statistical analysis. For the continuous variables with parametric distribution, mean and standard deviation (SD) were calculated, whereas median and interquartile range (IQR) were calculated for the variables with nonparametric distribution. Comparison of the variables between the mortality and survival groups was done using the independent Student's *t*-test (continuous parametric variables) and Mann–Whitney *U* test (continuous nonparametric values). The categorical variables were compared using the Pearson Chi-square test to compare survivors and nonsurvivors. The variables identified as significant ($p < 0.05$) after the Independent Student's *t*-test and the Mann–Whitney *U* test between the mortality and the survival groups were considered for univariate analysis for the prediction of mortality (except the variable "dose of paraquat consumed" as it was unreliable, and the concentration of paraquat was also unknown). The variables significantly differing while comparing the mortality and survival groups were considered for the univariate analysis. The univariate analysis's variables with $p < 0.1$ were subjected to multivariable logistic regression (MLR) to predict mortality. The variables with *p*-value < 0.05 in the MLR were considered independent predictors of mortality, and the odds ratio (OR) and the adjusted OR were calculated. The receiver operating characteristic (ROC) curve was plotted to determine the area under the curve (AUC), the cut-off value, sensitivity, specificity, and 95% confidence interval (CI) to predict mortality. The Cox regression analysis for mortality prediction was done for the significant variable after MLR, and the cut-off of specific variables was used to determine the hazard ratio (HR). The Kaplan–Meier survival plot was plotted for the cut-off value of the independent mortality predictor variable, and the log–rank (Mantel–Cox) $p < 0.05$ was considered significant.

The utility of the maximum (worst) SOFA score to predict mortality within 24 hours of ICU admission was considered. The difference in SOFA scores between the mortality and survival

groups was made, along with univariate analysis, ROC, cut-off value to predict mortality, Cox regression using the maximum SOFA score, and the Kaplan–Meier survival plot for the cut-off maximum SOFA score. A relationship map was developed between the maximum SOFA score and mortality.

Results

Figure 1 provides a flowchart for the audit methodology. Out of 108 patients with documented PP, 84 complete case records were included for analysis. Twenty-four patients were discharged against medical advice (DAMA). Their outcomes were not known and not included in the complete analysis.

Baseline demographic data and various parameters assessed in the ICU are provided in Table 1. Of 84 patients, 73 needed ICU admission, and 53 required mechanical ventilation. All the 53 patients needing mechanical ventilation had expired.

The mean ± SD and median (IQR) of the worst values of the different variables of the 84 patients within 48 hours of hospitalization are depicted in Table 2. The mean ± SD of the SOFA scores of the 73 ICU patients within 24 hours of ICU admission was 9.41 ± 3.37. The mean ± SD and median (IQR) of the worst values of the variables in the subgroup of patients DAMA showed that the mean AST, ALT, total bilirubin, and creatinine levels were higher in these patients as compared to patients who continued to receive treatment in the hospital.

The lowest available values of hemoglobin, platelet count sodium, potassium, bicarbonate, and PaO_2/FiO_2 were compared between the survival and mortality groups (Table 3). The worst or the highest values of WBC count, urea, creatinine, lactate, total bilirubin, liver enzymes, dose of paraquat, and length of

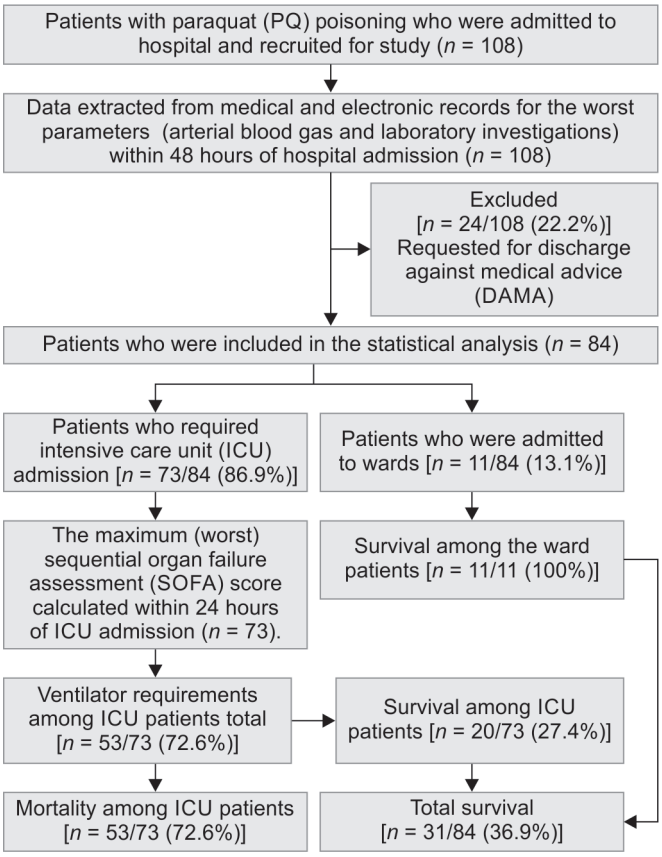

Fig. 1: Flowchart for the methodology of the audit

Table 1: Demographic, vital parameters on admission, and other study outcomes (*n* = 84)

Variable	*Values*
Age (mean ± SD)	30.32 ± 14.08
Gender (male)	54 (64.3%)
Heart rate (beats/minute) (mean ± SD)	90 ± 19
RR (per minute) (mean ± SD)	24 ± 8
SBP (mm Hg) (mean ± SD)	117 ± 23
GCS (mean ± SD)	13.7 ± 2
SpO_2 (%) (mean ± SD)	95 ± 5
Dose of paraquat consumed (mL) *(n* = 67) median (IQR)	50 (20–150)
Paraquat detected in the toxicology report in either gastric, blood, or urine sample *n* (%)	40 (47.6%)
The predominant symptom on admission – Vomiting *n* (%)	56 (66.7%)
Oral ulcers *n* (%)	18 (21.4%)
Days between PQ consumption and hospitalization median (IQR)	0 (0–1)
HP *n* (%)	45 (53.5%)
NAC therapy *n* (%)	65 (77.4%)
Hemodialysis *n* (%)	31 (37%)
Corticosteroids *n* (%)	35 (41.6%)
ICU admission required *n* (%)	73 (87%)
Ventilator support (NIV or IMV) *n* (%)	53 (63%)
Discharge against medical advice (DAMA) *n* (%)	24/108 (22%)*
LOS in hospital (days) median (IQR)	4.5 (2–11.75)
Mortality *n* (%)	53 (63%)

*The patients who went DAMA was *n* = 24, out of the total of *n* = 108 included patients. So, the denominator for DAMA patients to depict as a percentage was 108. For all the parameters (except DAMA) the denominator is 84 as the statistical analysis was done for the *n* = 84 patients who were hospitalized and had their outcomes (survival or mortality) recorded in the hospital. So, for statistical analysis of the clinical parameters and the predictors of mortality, 84 patients of PP were considered. GCS, Glasgow coma scale; HP, hemoperfusion; ICU, intensive care unit; LOS, length of stay; NAC, N-acetyl cysteine, RR, respiratory rate; SBP, systolic blood pressure; SpO_2, pulse oximetry saturation

hospital stay were compared between the two groups. The serum sodium level, bicarbonate level, and PaO_2/FiO_2 ratio were significantly lower in the mortality group as compared to the survivors (Table 3). The WBC count, creatinine level, total bilirubin, AST, ALT, and lactate were significantly higher in the mortality group as compared to the survivors (Table 3). The average dose of paraquat consumed was also significantly higher at 100 (50–200) mL in the mortality group vs 25 (12.5–50 mL) in the survival group ($p < 0.001$) (Tables 3 and 4). However, the exact concentration of the PP was unknown.

Univariate analysis and subsequent MLR analysis showed that the PaO_2/FiO_2 ratio within 48 hours of hospitalization was an independent early predictor of mortality ($p = 0.007$; adjusted OR: 0.983; 95% CI: 0.971–0.995). The Hosmer–Lemeshow test showed that the model was a good fit. The median (IQR) of the positive end-expiratory pressure (PEEP) values measured were 6 (5–8) cm H_2O.

The ROC curve of the lowest PaO_2/FiO_2 ratio within 48 hours of hospital stay to predict mortality had a cut-off value ≤ 197, with the AUC 0.924, $p < 0.001$, 95% CI: 0.870–0.978, 97% sensitivity, and 78% specificity as shown in Figure 2. The Cox regression for mortality was plotted using the lowest PaO_2/FiO_2 ratio within 48 hours of hospital stay, particularly cut-off ≤ 197. It showed $p = 0.03$, HR: 8.83, 95% CI: 1.194–65.39. The Kaplan–Meier survival plot showed that the mean days of survival in the patients with the lowest PaO_2/FiO_2 ratio within 48 hours of hospitalization was 4.64 days, as compared to 17.20 days in the patients with the lowest PaO_2/FiO_2 ratio >197 [log–rank (Mantel–Cox) $p < 0.001$] (Fig. 3). In the patients with the lowest PaO_2/FiO_2 ratio above 197, 16/46 (34.8%) died, whereas in the patients with the lowest PaO_2/FiO_2 ratio ≤197 at 48 hours of hospitalization, 37/38 (97.4%) died (Pearson Chi-square test, $p < 0.001$).

Among the 73 patients who were admitted to the ICU, there was a significant difference in the SOFA score within 24 hours of ICU admission between the mortality ($n = 53$) and survival ($n = 20$) patients. The patients who died had SOFA score of 11.08 ± 2.01 as compared to 5 ± 1.94 in those who survived ($p < 0.001$) (Table 5). Univariate analysis of the SOFA score to predict mortality showed an OR 3.24, $p < 0.001$, 95% CI:1.826–5.928 (Table 5). The AUC for the SOFA score on ICU admission to predict mortality had an AUC of 0.980, $p < 0.001$, 91% sensitivity, 90% specificity, 95% CI: 0.9555–1.000, cut-off score ≥ 9 (Fig. 4). The Kaplan–Meier survival plot of the patients with the SOFA score ≥ 9 had mean ICU survival days of 4.28 vs 15.5 days in patients with the SOFA score below 9 [log–rank (Mantel–Cox) $p < 0.001$] (Fig. 5).

In 50 patients with SOFA score ≥9, 48 patients (96%) died, whereas in the 23 patients with SOFA <9, 5 patients (21.7%) died (Pearson Chi-square $p < 0.001$, Phi and Cramer V value, 0.773). The relationship map was plotted between the SOFA score within 24 hours of ICU admission and mortality, which showed a strong relationship between the SOFA scores and mortality (Fig. 6).

Table 2: The worst values of the variables within the initial 48 hours of hospital admission ($n = 84$). The worst values include the lowest values of certain variables like hemoglobin and platelet count and the highest values of certain variables such as creatinine

Variable (worst values)	*Mean ± SD/median (IQR)*
Hemoglobin (lowest) (gm/dL)	13.69 ± 2.19
Sodium (lowest) (mEq/L)	137.67 ± 4.69
Potassium (lowest) (mEq/L)	3.67 ± 0.60
PaO_2/FiO_2 ratio (lowest)	207 (139.25–347)
Bicarbonate (lowest) (mEq/L)	16.38 ± 6.38
Lactate (highest) (mg/dL)	18 (11–79)
WBC (highest) (10^3/μL)	15.3 (11.55 ± 19.8)
Platelet (lowest) (10^3/μL)	205 (78–290)
Urea (highest) (mg/dL)	53.5 (31–99.5)
Creatinine (highest) (mg/dL)	2.96 (1.77–4.88)
AST (highest) (U/L)	55 (29.25–55)
ALT (highest) (U/L)	49.5 (19.25–49.5)
Total bilirubin (mg/dL)	1.32 (0.67–4.14)
SOFA score on the day of ICU admission ($n = 73$)	9.41 ± 3.37

ALT, alanine transaminase; AST, aspartate transaminase; SOFA, sequential organ failure assessment; WBC, white blood cells

Discussion

Worldwide, about 1,68,000 deaths every year are due to pesticide poisoning.[11] Paraquat is one of the most fatal poisons involving

Table 3: Comparison of variables between mortality and survival groups ($n = 84$) by 48 hours of hospital admission

Variables	*Mortality (n = 53)*	*Survival (n = 31)*	*p-value*
Hemoglobin (lowest) gm/dL	13.81 ± 2.26	13.49 ± 2.09	0.519**
Sodium (lowest) mEq/L	138.72 ± 5.18	135.87 ± 3.04	0.007**
Potassium (lowest) mEq/L	3.72 ± 0.69	3.58 ± 0.41	0.332**
Bicarbonate (lowest) mEq/L	13.81 ± 4.96	20.77 ± 2.44	<0.001**
PaO_2/FiO_2 (lowest)	172 (102–200)	380 (280–473)	<0.001*
WBC (highest) 10^3/μL	17.20 (13.9–23.6)	11.3 (9.2–13.9)	<0.001*
Platelet (lowest) 10^3/μL	222.5 (99.5–295.25)	198 (49–280)	0.566*
Urea (highest) 10^3/μL	55 (31.5–118)	49 (31–78)	0.335*
Creatinine (highest) mg/dL	3.68 (2.43–5.6)	1.87 (1–3.11)	<0.001*
Total bilirubin (highest) mg/dL	1.65 (0.78–5.16)	0.86 (0.51–1.43)	0.007*
AST (highest) U/L	138 (42.5–294.5)	29 (21–53)	<0.001*
ALT (highest) U/L	86 (24.5–241.5)	23 (13–47)	<0.001*
Lactate (highest) mg/dL	33 (14.5–107)	10.65 (8.75–16.37)	<0.001*
Dose of paraquat consumed ($n = 67$) mL	100 (50–200)	25 (12.5–50)	<0.001*
LOS (hospital) days	2 (2–4.5)	11 (7–15)	<0.001*

*Mann–Whitney *U* test; **Independent Student's *t*-test. ALT, alanine transaminase; AST, aspartate transaminase; LOS, length of stay; WBC, white blood cells

Table 4: Univariate analysis and MLR of the variables with worst values at 48 hours of hospital admission for mortality prediction ($n = 53$ patients)

	Univariate analysis			*MLR*		
Variables	*p-value*	*OR*	*95% CI*	*p-value*	*Adjusted OR*	*95% CI*
Sodium	0.009	1.15	1.036–1.288	0.864	1.025	0.771–1.364
PaO_2/FiO_2	**0.001**	**0.983**	**0.977–0.990**	**0.007**	**0.983**	**0.971–0.995**
Bicarbonate	<0.001	0.643	0.527–0.785	0.367	0.833	0.560–1.239
WBC	0.544	0.999	0.998–1.001			
Creatinine	<0.001	1.747	1.264–2.414	0.961	1.020	0.461–2.256
Total bilirubin	0.016	1.350	1.058–1.722	0.267	1.756	0.649–4.747
AST	0.003	1.016	1.006–1.027	0.424	1.007	0.989–1.026
ALT	0.006	1.008	1.002–1.014	0.441	0.993	0.977–1.010
Lactate	0.005	1.121	1.036–1.213	0.399	1.048	0.939–1.170

The values in bold represent the clinical variable which is significant for the prediction of mortality in paraquat poisoning patients after the multivariable logistic regression. ALT, alanine transaminase; AST, aspartate transaminase; WBC, white blood cells

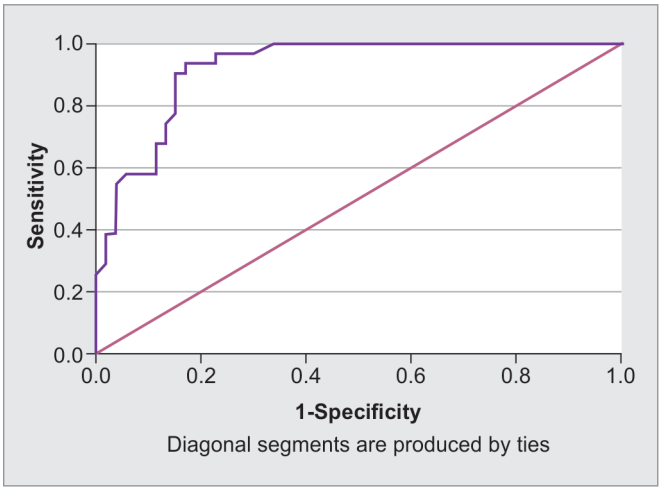

Fig. 2: ROC curve of the lowest PaO_2/FiO_2 (lowest value in 48 hours hospitalization) for predicting mortality. AUC: 0.924; $p < 0.001$; 95% CI: 0.870–0.978 using specific cut-off ≤197; 97% sensitivity and 78% specificity

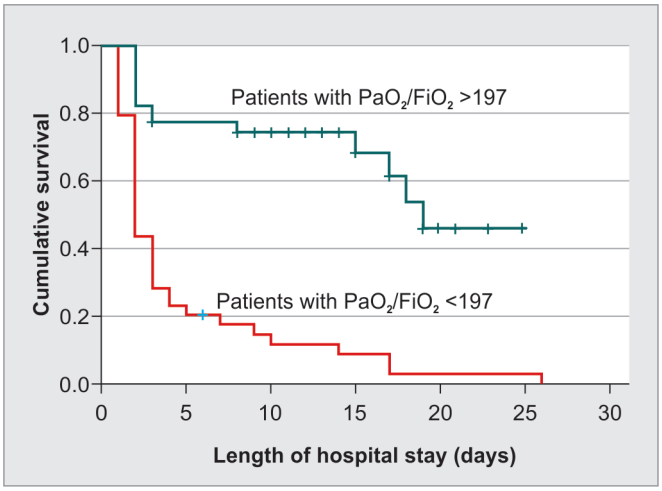

Fig. 3: Kaplan–Meier survival plot of the patients for the lowest PaO_2/FiO_2 in 48 hours ≤197 vs the lowest PaO_2/FiO_2 in 48 hours being >197. Green line: Survival function of PP patients with PaO_2/FiO_2 in 48 hours being >197; Red line: Survival function of PP patients with PaO_2/FiO_2 in 48 hours being ≤197

the lungs, liver, and kidneys.[6,9,12] The severity of symptoms after PP can be classified into mild, moderate, and severe based on the amount of paraquat consumed.[6] Consumption of about 30 mg/kg of paraquat leads to moderate poisoning, and above 40 mg/kg leads to fulminant poisoning, with progression to acute respiratory distress syndrome (ARDS) within 24 hours of PP and mortality within hours to a few days.[6,13]

Predictors of mortality in patients with PP, like neutrophil-lymphocyte ratio, glomerular filtration rate, paraquat concentration in plasma and urine, serum creatinine, and liver enzyme levels have been established.[9,14–18] Arterial blood lactate, volume of lung opacities, liberal oxygen therapy, and pneumomediastinum were other predictors of mortality.[19–22] Certain scores, like the acute PP mortality (APPM) score, reliably predict outcomes but necessitate estimating paraquat levels in urine.[23]

Our study found that the worst PaO_2/FiO_2 ≤197 mm Hg at 48 hours of hospitalization was an independent predictor of mortality. Our results were similar to that of Fengjun J et al., who found that PaO_2 of 64.07 ± 13.04 mm Hg was significantly lower in the mortality group as compared to the PaO_2 of 75.40 ± 13.27 mm Hg in the survival group.[24] However, we could determine a more specific PaO_2/FiO_2 ratio as compared to only the PaO_2 values without the FiO_2 values. The PaO_2/FiO_2 ratio better determines the severity of oxygenation abnormality than just the PaO_2, as it indicates the pulmonary shunt fraction.[25] The PaO_2/FiO_2 ≤200 indicates a shunt fraction of about 16–26%, as against a normal of <5%.[25] In critically ill patients, a PaO_2/FiO_2 ratio below 200 significantly increases the probability of mortality, which is similar to our findings.[26]

Among the patients who were admitted to the ICU, as compared to previous literature, we obtained a much higher cut-off value of SOFA score (≥9 vs 3) and a much higher AUC of the ROC (0.980 vs 0.776) for the prediction of mortality.[24] This could be because we considered the highest 24-hour SOFA score, per recommendations for the "daily maximum SOFA score" calculation.[27] Furthermore, PP leads to pulmonary, renal, hepatic dysfunction, and encephalopathy with multiple organ dysfunction syndrome (MODS), all of which can be objectively scored using SOFA.[27,28]

In ICU, all the patients who received ventilator support (invasive or noninvasive) died. Our findings were similar to the previous literature, where the authors found that patients with severe hypoxemia requiring ventilator support had higher mortality.[21] This could be attributed to the reactive oxygen species-induced lung damage.[29–32]

Table 5: The SOFA score (worst in 24 hours of ICU admission) for *n* = 73 patients admitted to ICU

Variable	*Mortality (n = 53)*	*Survival (n = 20)*	*p-value*
SOFA score	11.08 ± 2.018	5 ± 1.94	<0.001
Univariate analysis for mortality prediction			
Variable	*p*-value	OR	95% CI
SOFA score	<0.001	3.29	1.826–5.928
ROC curve characteristics for mortality prediction			
Cut-off SOFA score ≥9	$p < 0.001$	AUC: 0.980	95% CI: 0.955–1.000
91% sensitivity			
90% specificity			
Cox regression analysis for mortality			
SOFA score	$p < 0.001$	OR	95% CI
		1.317	1.182–1.468
SOFA score ≥9	$p < 0.001$	OR	95% CI
		7.287	2.866–18.52
Chi-square test for association of SOFA score ≥ 9 with mortality			
SOFA score ≥9	Expired 48/50 (96%)	Chi-square $p < 0.001$	
SOFA score <9	Expired 5/23 (21.7%)	Phi and Cramer V value: 0.773	

AUC, area under curve; CI, confidence interval; OR, odd's ratio; ROC, receiver operating characteristic; SOFA, sequential organ failure assessment

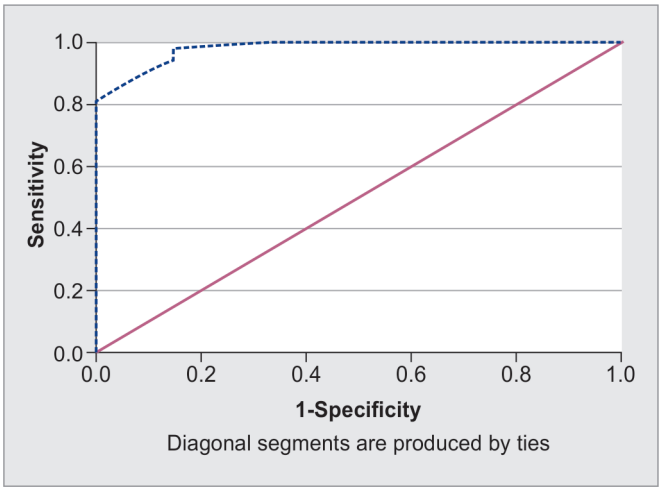

Fig. 4: ROC curve of the SOFA score (worst in 24 hours of ICU admission) for mortality prediction. Cut-off SOFA score ≥9; AUC: 0.980: $p < 0.001$; 95% CI: 0.955–1.000; 91% sensitivity; and 90% specificity for mortality prediction

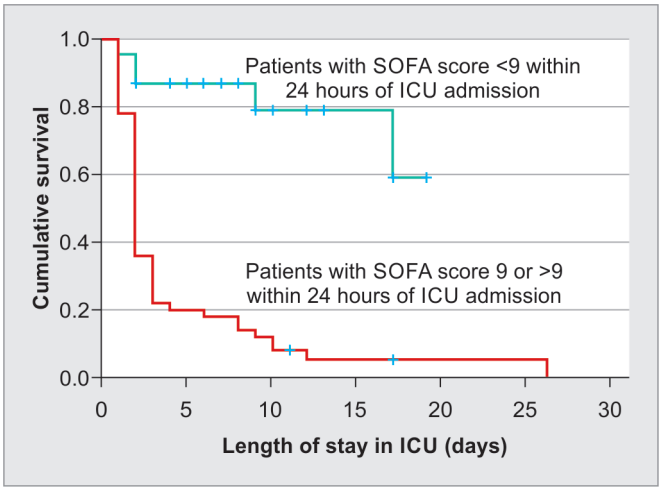

Fig. 5: Kaplan–Meier survival plot for the SOFA score ≥9 within 24 hours of ICU admission vs the SOFA score <9 within 24 hours of ICU admission. Green line: Survival function of PP patients with the SOFA score below 9 within 24 hours of ICU admission. Red line: Survival function of PP patients with the SOFA score ≥ 9 within 24 hours of ICU admission

PP, paraquat poisoning

The PaO_2/FiO_2 ratio, SOFA score, and the need for ventilator support are objective parameters available at most healthcare centers. It obviates the need for more expensive investigations such as lung imaging or paraquat concentration to predict outcomes reliably. It assumes significance because paraquat poison leads to maximum lung damage (reflected in the PaO_2/FiO_2 ratio and thereby needs ventilation) and causes MODS (which is best reflected in the SOFA score). These indicators can then serve as reliable triggers for palliative care in PP. Also, PP patients are one of the appropriate patient categories who should be referred to prompt palliative care to avoid futile treatments and health-related suffering.[33] It is often challenging to communicate to families of patients with PP even when there are triggers of palliative care as patients are often young and have an acute deterioration in condition.[33] Even the survivors of PP develop restrictive lung disorders due to pulmonary fibrosis and require prolonged care.[34] Thus, palliative care is of paramount importance not only amongst those with predictors of mortality after aggressive treatment but also among the survivors of PP.[33] Advanced palliative care planning and discussion with the stakeholders are beneficial for patients and relatives to ensure end-of-life care, the futility of treatment, a better understanding of the disease on the part of relatives, and prior acceptance of outcomes.[35–40]

Furthermore, it is essential to comprehend the role of ICU care outcomes in prediction models, specifically in the end-of-life decision-making process.[41] Regarding this aspect, our study identified the SOFA score and the need for ventilator support in the ICU as the triggers for planning for palliative care. The evaluation of SOFA-based models in predicting outcomes in the ICU has been validated.[42]

Our study had specific strengths. We could identify that high-priced investigations like paraquat levels may not be needed to

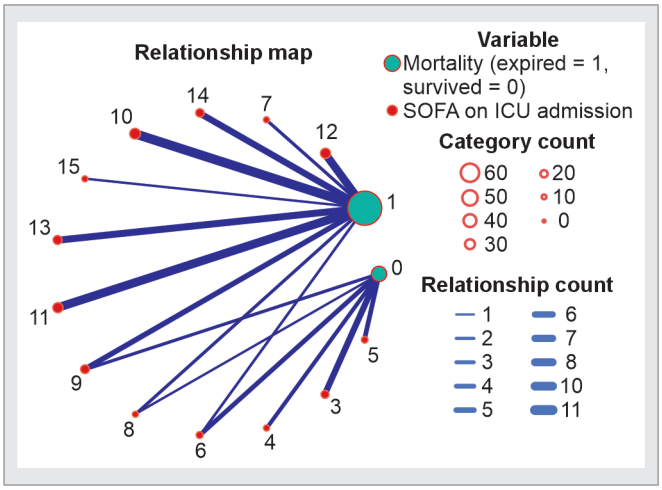

Fig. 6: The relationship map of the SOFA scores within 24 hours of ICU admission and mortality in the PQ poisoning patients. Green dot 1 represents expired patients; Green dot 0 represents survived patients; Red dots represent the SOFA scores within 24 hours of ICU admission; Blue lines represent the strength of association between the SOFA score and mortality, the thicker the line, the higher is the strength of association

PQ, paraquat

predict outcomes in patients with PP. Instead, oxygenation level and multiorgan dysfunction assessment could reliably predict mortality. The need for ventilation was proven to be a trigger for palliative care.

However, the study had few limitations. It was a single-center study with a smaller sample size. Also, it was a retrospective study design. Since we did not have the serum paraquat level estimation, it could not be used with oxygenation parameters to determine an appropriate trigger for referral. Due to the paucity of various parameters, other scores like the acute physiology and chronic health evaluation [acute physiology and chronic health (APACHE II) and APACHE III] could not be evaluated for mortality prediction. Patients of PP need palliative care if they have the predictors of mortality. It may ensure appropriate care of PP patients and optimal utilization of ICU resources.

Conclusion

The PaO_2/FiO_2 ratio ≤197, SOFA score ≥9, and the need for ventilatory support are predictors of mortality in patients with PP and could be considered as triggers for palliative care referral.

Clinical Significance

The study is relevant in cases of PP, which has a high mortality rate, and many young patients are affected. Especially in health-care set-ups where the paraquat serum concentration estimation is unavailable to predict mortality, clinicians can use the poor oxygenation cut-off value and the multiorgan dysfunction sequential organ failure score cut-off value as triggers for early palliative care referral.

Ethical Approval

Institutional Ethics Committee approval was sought prior to the commencement of the audit (IEC KMC/KH 33/2022).

Authors' Contributions

Shwethapriya R: Conceptualization, methodology, investigation, writing—review and editing, and supervision.

Sagar Maddani Shanmukhappa: Methodology and supervision.

Souvik Chaudhuri: Methodology, formal analysis, investigation, data curation, and writing the original draft.

Margiben Bhatt: Writing—review and editing.

Shubhada Karanth: Writing—review and editing.

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