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Original Article

Incidence and Risk Factors for Adverse Events During Intubation among Critically Ill Patients in Nigeria.

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Abstract

Background: Owing to the background physiologic derangements in critically ill patients, the risk of peri-intubation adverse events is higher than is seen in the operating room. Despite the burden of the problem, very little local data exists in Nigeria and sub-Saharan Africa. The objective of this study was to determine the incidence and risk factors for peri-intubation adverse events in the intensive care unit (ICU).

Methodology: This was a prospective, observational, multi-centre study involving critically ill adults requiring endotracheal intubation in the ICU between February and September 2024. The primary outcome measure was the incidence of peri-intubation adverse events (hypotension, hypoxia, cardiac arrest, and aspiration of gastric content) within 30 minutes of intubation. The secondary outcome measures included risk factors for these adverse events and their correlation with the length of ICU stay and 30-day in-hospital mortality. Data were analysed using SPSS version 25.

Results: Fifty-one intubations involving 50 patients were included. Respiratory failure and neurological impairment were the major reasons for intubation (49.0% and 35.3%, respectively). The incidences of adverse events were hypotension (60%), severe hypoxia (32.6%), cardiac arrest (13.7%) and aspiration pneumonitis (17.8%). At least one adverse event was recorded in 74.8% of the intubations. We identified multiple intubation attempts as central to the occurrence of most adverse events. The probability of survival was higher in those with an adverse event, but it was not statistically significant.

Conclusion: Adverse events following intubation are common among critically ill patients in Nigeria. While hypotension was the most common complication, severe hypoxaemia emerged as the most lethal. Further research is needed on this subject.

Keywords: Critically ill, ICU, Intubation practices, Peri-intubation adverse events, Physiologically difficult airway.

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Introduction

The term 'physiologically difficult airway' has been used to describe tracheal intubation in critically ill patients.[1–4] It is characterised by physiologic alterations that place the patient at an increased risk for cardiovascular collapse and other complications during tracheal intubation and transition to positive pressure ventilation.[3] Physiological derangements can occur due to acute illness, pre-existing disease, the effects of anaesthetic agents, and positive-pressure ventilation.[3] In 2011, the Fourth National Audit Project (NAP4) in the UK reported that 25% of major airway complications within the hospital occur in the emergency department (ED) or intensive care unit (ICU).[3,5] Sixty-one per cent (61%) of airway management episodes in the ICU, as compared to 14% during anaesthetic care, led to complications that result in death or brain injury.[3] Frequently reported adverse events include cardiovascular collapse, i.e. hypotension, hypoxemia, cardiac arrest and aspiration pneumonitis.[3–7]

The INTUBE study, an international, multi-centre, prospective cohort study that recruited 2964 patients, reported that 45.2% of patients experienced at least one peri-intubation major adverse event (MAE), with cardiovascular instability being the most common. The overall ICU mortality was 32.8%, but among those who had a MAE, mortality was 40.7% as against 26.3% in those without adverse events.[4] There is a paucity of literature on intubation practices and outcomes among critically ill patients in Nigeria and many other African nations. Mbanjumucyo et al.[7] in a prospective cohort study of patients intubated at the ED of a tertiary hospital in Kigali, Rwanda, in 2017, reported that one-third of patients experienced complications during intubation. These complications include hypoxia (23.1%), aspiration (6.7%) and cardiac arrest (3.6%).

These findings suggest that physiological derangements are associated with increased post-intubation complications. Therefore, it is essential to evaluate patients with a physiologically difficult airway and have strategies to mitigate these adverse events.[8,9] Local research into effective preventive strategies is vital. However, it is first necessary to identify current practices. Our primary outcome measure was to determine the incidence of peri-intubation adverse events (hypotension, severe hypoxaemia, cardiac arrest and pulmonary aspiration) while the secondary outcome measures were to identify risk factors for these events and their relation to in-hospital mortality and length of ICU stay.

Materials and Methods

Study Design

This was a prospective exploratory cohort study of adult patients intubated in the ICU of the three participating institutions between February and September 2024. The participating hospitals were the University College Hospital, Ibadan; Federal Teaching Hospital, Katsina; and the University of Nigeria Teaching Hospital, Enugu. These units run an open ICU overseen by the Anaesthesia department. Ethical approval was obtained from the University of Ibadan/University College Hospital Health Research Ethics Committee with a review number – UI/EC/23/0727 on the 30th of January 2024. The need for consent was waived due to the study's observational nature.

Study population and sampling technique

Adult patients aged 18 years and above admitted to the ICU and requiring endotracheal intubation were included. We excluded patients under 18 years, intubations outside the ICU, patients in cardiac arrest at the time of intubation, endotracheal intubation performed as part of resuscitative measures, and patients being intubated electively for a procedure. Being an exploratory study, we did not have a predetermined sample size but employed a convenience sampling technique aimed at recruiting eligible patients over the study period. We could not obtain data on the total number of intubations performed during this period, as this was not routinely recorded in these hospitals.

Data collection and outcome measures
The patient's data were collected using a pre-piloted, standardised pr[10]oforma adapted from the INTUBE study.[4] The collected data included intubation details, peri-intubation adverse events, ICU outcomes, ICU length of stay, and 30-day post-intubation outcomes. The primary outcome measure was the incidence of peri-intubation adverse events (hypotension, severe hypoxaemia, cardiac arrest and pulmonary aspiration). These were defined as follows:

Hypotension: Systolic blood pressure less than 90 mmHg or mean arterial pressure less than 60 mmHg OR a new requirement for or an increase of vasopressors or fluid bolus within 30 minutes of induction of anaesthesia to maintain target blood pressure.

Severe hypoxaemia: SpO_2 less than 80% within 30 minutes of induction of anaesthesia.

Cardiac arrest: Absence of cardiac activity or a need for cardiopulmonary resuscitation.

Pulmonary aspiration: Inhalation of oropharyngeal or gastric contents into the larynx and the respiratory tract within 30 minutes after intubation, according to clinical and/or radiographic findings.
These definitions were based on those used in the INTUBE study.[4] The shock index refers to the heart rate divided by the systolic blood pressure with a value > 1.0 indicating a severe derangement.[10]
Secondary outcome measures included the risk factors for these adverse events, the length of ICU stay and in-hospital mortality censored at 30 days.

Data analysis
Data were recorded and analysed using IBM Statistical Product and Service Solutions (SPSS) version 25 (SPSS Inc., Chicago, Illinois, USA). Categorical variables were presented as frequencies and percentages. Continuous variables were represented using mean ± standard deviation. The data are presented in tables and graphs as deemed appropriate. A test of associations for categorical variables was done using the Chi-square test.

Survival probabilities were estimated using the Kaplan-Meier method. Patients who remained alive at the end of the 30-day observation period or were discharged from the hospital before day 30 were treated as right-censored. The log-rank test was utilised to compare survival distributions between the adverse event and no adverse event groups. Binary outcomes were reported as proportions with 95% Clopper-Pearson exact confidence intervals. For risk factor analysis, Odds Ratios (OR) with 95% confidence intervals were calculated. In cases with zero cell counts, the Haldane-Anscombe correction was applied to obtain stable OR estimates. Missing data were excluded from the analysis in relation to the respective section. The level of statistical significance was set at $p < 0.05$.
Discrepancies in denominators for specific sub-analyses are attributed to missing data for those variables, and percentages are reported as 'valid percent' based on the available data for that parameter.

Results

Study population
Data were collected from fifty-one intubation episodes involving 50 patients. The study cohort was predominantly male (60%) and middle-aged (mean 47.3 ± 19.4 years). Nearly 70% of patients presented with a GCS ≤ 8, and the majority (82%) were admitted primarily for ventilatory support. The most frequent admitting diagnoses (44%) were neurological (Head Injury/Stroke) and Sepsis. The patient and clinical characteristics are summarised in Table 1.

Table 1: Patient and Clinical Characteristics

Variable	No. (%)
Age in years (Mean ± SD)	47.3 ± 19.4
Gender (n= 50)	
Female	20 (40)
Male	30 (60)
Indication for ICU admission (n = 50)	
Ventilatory support	41 (82)
Cardiovascular support	9 (18)
Post-operative care	3 (6)
Other organ support	1 (2)
Co-morbidities (n = 50)	
Hypertension	26 (52)
Diabetes	8 (16)
Asthma	3 (6)
Obesity	4 (8)
Renal failure	7 (14)
Malignancy	2 (4)
Heart failure	2 (4)
Other pulmonary disease	1 (2)
Route of admission (n= 49)	
Emergency department	21 (42.9)
HDU	2 (4.1)
Operating theatre	6 (12.2)
PACU	1 (2)
Ward	19 (38.8)
Medical specialty (n = 48)	
Cardiothoracic Surgery	1 (2.1)
General Surgery	2 (4.2)
Internal Medicine	17 (35.4)
Neurosurgery	22 (45.8)
Obstetrics	3 (6.3)

Orthopaedics	3 (6.3)
GCS before intubation (n = 49)	
≤ 8	34 (69.4)
9-12	7 (14.3)
13-14	5 (10.2)
15	3 (6.1)

Variation in denominators (n) is due to missing data for specific variables.

Intubation characteristics

Nearly half (49%) of all intubations were performed due to respiratory failure. Fourteen patients (28%) had experienced at least one prior intubation during their admission, with respiratory failure as the most frequent reason for re-intubation. Intubation was needed without delay in 58% of cases. All patients underwent preoxygenation, and only 16% received apneic oxygenation. Propofol was the most commonly used induction agent, and a muscle relaxant (suxamethonium) was employed in 90.2% of the intubations. Anaesthetists of different cadres performed intubations and were successful on the first attempt in only 68% of cases. Table 2 summarises the intubation characteristics.

Table 2: Intubation characteristics

Variable	No. (%)
Indications for intubation (n = 51)	
Airway obstruction	3 (5.9)
Cardiovascular instability	4 (7.8)
Neurological impairment	18 (35.3)
Respiratory failure	25 (49.0)
Others	1 (2.0)
Previous intubation in this admission	14 (28.0)
Reasons for re-intubation (n = 14)	
Failed extubation	2 (14.3)
Neurological impairment	1 (7.1)
Others	1 (7.1)
Respiratory failure	8 (57.1)
Self extubation	1 (7.1)
Tube blockage/dislodgement	1 (7.1)
Degree of urgency of endotracheal intubation (n = 50)	
Intubation required in < 1hour	14 (28.0)
Intubation required in ≥ 1hour	7 (14.0)

Intubation is required without any delay	29 (58.0)
Fluid boluses within 30 min before induction (n =47)	21 (41.2)
Vasopressor requirement within 30 min before induction (n =47)	11 (21.6)
Induction agent (n= 45)	
Ketamine	13 (28.9
Ketofol	7 (15.6)
Midazolam	6 (13.3)
Propofol	19 (42.2)
Use of a muscle relaxant (suxamethonium)	46 (90.2)
Type of intubation (n = 51)	
Nasotracheal	1 (2.0
Orotracheal	50 (98.0)
Laryngoscopy grade (n = 43)	
I	15 (34.9)
II	17 (39.5)
III	8 (18.6)
IV	3 (6.9)
Grade of the intubating anaesthetist (n = 51)	
Consultant	4 (7.8)
Registrar	11 (21.6)
Senior registrar	36 (70.6)
Number of attempts at intubation (n = 50)	
1	34 (68.0)
2	13 (26.0)
3	2 (4.0)
More than 3	1 (2.0)
Time of intubation (n = 35)	
Daytime (8:00 to 18:00)	17 (48.6)
Night time (18:01 to 7:59)	18 (51.4)
Intubating aids (n=43)	
Stylet	27 (62.8)

Bougie	19 (44.2)
Videolaryngoscope	1 (2.3)
McCoy laryngoscope	5 (11.6)

Variation in denominators (n) is due to missing data for specific variables.

Adverse events

Adverse events occurred in 38 of the 51 intubation episodes (74.5%). The most frequent complication was hypotension (60.0%), followed by severe hypoxaemia (32.6%), pulmonary aspiration (17.8%), and cardiac arrest (13.7%). Univariate analysis identified several modifiable risk factors for these adverse events. Patients who had a fluid bolus or vasopressor administered before intubation, had multiple intubation attempts, had baseline systolic blood pressure < 90 mmHg, or were intubated with ketamine were more likely to be hypotensive (p = 0.07, 0.033, 0.02, 0.031 and 0.004, respectively). The risk of hypotension was also positively correlated with the baseline shock index (p < 0.001). The incidence of severe hypoxaemia was slightly higher in intubations without delay (42.3%), with increasing laryngoscopy grade (36.0%) and multiple intubation attempts (37.5%), but these differences were not statistically significant (p = 0.354, 0.871, and 0.462, respectively). The need for vasopressor before intubation, multiple intubation attempts, and baseline systolic blood pressure < 90 mmHg were significantly associated with cardiac arrest (p = 0.042, 0.003 and 0.039, respectively). Table 3 summarises the peri-intubation adverse events and the outcome of ICU stay. The univariate analysis of associations with adverse events is shown in Supplementary Tables 1-5.

Table 3: Peri-intubation adverse events and Outcome

Adverse events	**No. (%)**	**95% CI (%)**
Hypotension (n = 50)	30 (60.0)	45.2 – 73.6
Severe hypoxia (n = 43)	14 (32.6)	19.1 – 48.5
Cardiac arrest (n =51)	7 (13.7)	5.7 – 26.3
Aspiration pneumonitis (n = 45)	8 (17.8)	8.0 – 32.1
Other adverse events (n = 50)	5 (10.0)	
Dental injuries	2 (4.0)	
Bronchospasm	1 (2.0)	
Airway bleeding	2 (4.0)	
30-day (post-intubation) outcome (n = 45)		**NA**
Alive	14 (31.1)	
Dead	25 (55.6)	
Discharged before 30 days	6 (13.3)	
If alive, location at 30 days (n = 14)		**NA**
Discharged home	1 (7.1)	
HDU	2 (14.3)	

ICU	2 (14.3)	
Ward	9 (64.3)	
Median length of ICU stay in days (Range)	8.5 (0-50)	**NA**

Variation in denominators (n) is due to missing data for specific variables.
NA – Not applicable
CI: Confidence Interval

Outcome data at 30 days were available for 45 patients. Of these, 25 (55.6%) had died, 14 (31.1%) remained hospitalised, and 6 (13.3%) had been discharged. The median length of ICU stay was 8.5 days (range: 0–50). The length of stay was shorter among those with an adverse event, but the difference was not significant (Supplementary Table 6).

The relationship between specific adverse events and mortality is detailed in Table 4. Severe hypoxaemia was the only adverse event significantly associated with mortality (p=0.030); notably, all patients in this subgroup died within 30 days (95% CI: 70.1–100.0%). Although mortality rates were high following cardiac arrest (83.3%) and hypotension (60.9%), these differences did not reach statistical significance (p=0.391 and p=0.614, respectively).

Table 4: Relationship between adverse events and in-hospital mortality

Adverse Event	Total n	Dead n (%)	95% CI (%)	p-value
Hypotension	23	14 (60.9)	40.8 – 77.8	0.614
Severe hypoxaemia	9	9 (100.0)	70.1 – 100.0	0.030*
Cardiac arrest	6	5 (83.3)	43.6 – 97.0	0.391
Pulmonary aspiration	6	3 (50.0)	18.8 – 81.2	0.641
Other immediate adverse events	3	2 (66.7)	20.8 – 93.9	1.000

Total refers to those participants who had both adverse events and outcome data captured.
CI: Confidence Interval
*: Statistically significant

Figure 1 compares the 30-day survival curves of patients with and without adverse events. Although the probability of survival was higher among those without adverse events, a log-rank test showed no statistically significant difference (p = 0.15).

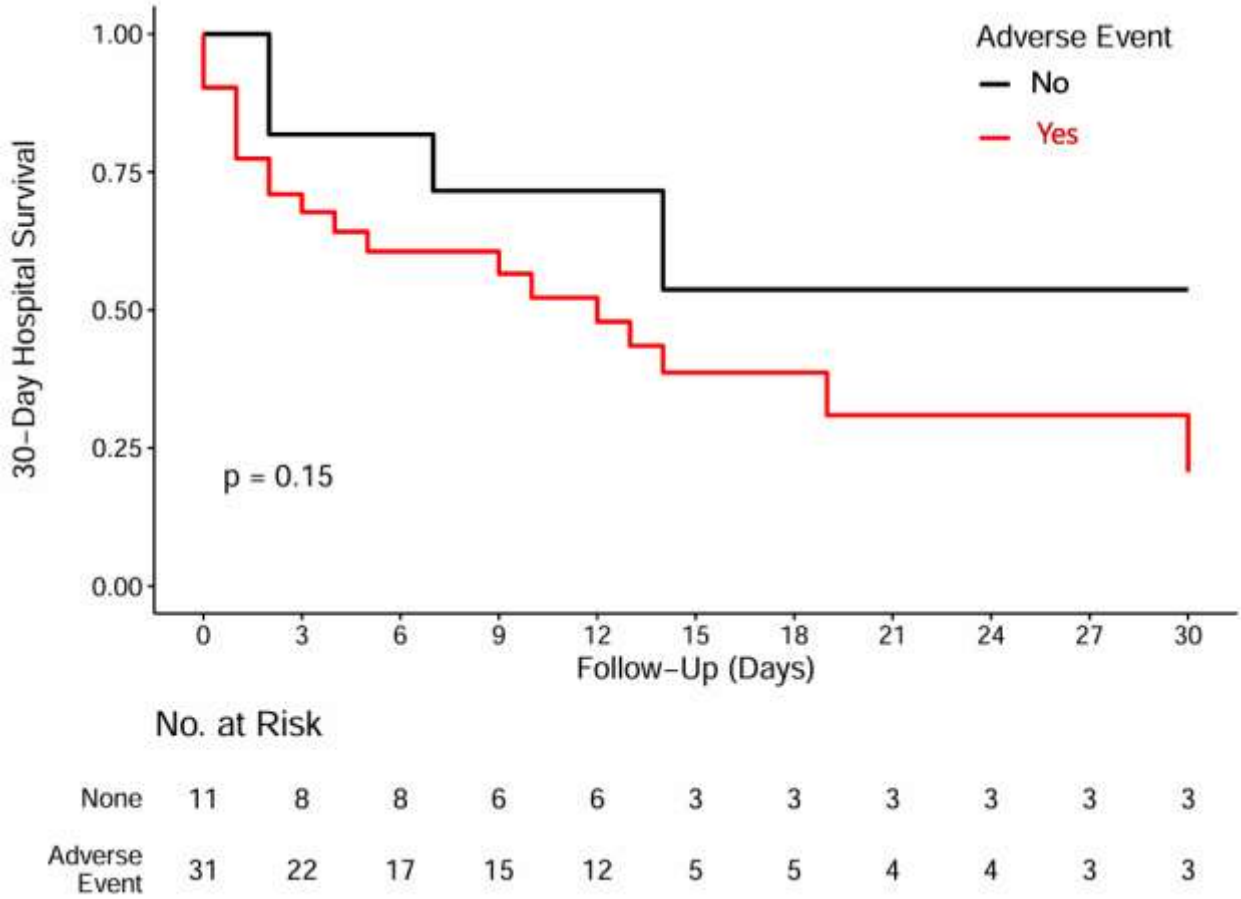

Figure 1: Kaplan Meier Plot of the probability of 30-day hospital survival.

Discussion

This study examined the incidence and risk factors for adverse events following endotracheal intubation in critically ill patients, and their association with in-hospital mortality and length of ICU stay. The main findings were a high incidence of peri-intubation adverse events, with 74.8% of intubations associated with at least one adverse event. There was a non-statistically significant trend toward an association between adverse events and in-hospital mortality.

As in previous studies, hypotension was the most commonly observed adverse event in the present study. However, the incidence (60%) was higher than in previous studies (18-42.6%).[4,5,11] The lower incidence reported in these studies may be due to the differences in the definition of hypotension and the choice of induction agent. Propofol, the most common induction agent in our study, is a known cardiac depressant. The need for a fluid bolus or vasopressor before intubation and induction with ketamine posed a risk factor for hypotension. The patients who required these interventions were likely haemodynamically unstable before the intubation and thus had a greater physiologic derangement compared to those who did not.

Price et al, in a retrospective observational study among trauma victims, also noted that the administration of crystalloids before intubation was significantly associated with hypotension post-intubation.[12] A secondary analysis of two multicentre studies by Fuchita et al.[13] and that of the INTUBE study by Russotto et al.[14] noted that prophylactic administration of fluid boluses or vasopressors did not reduce the incidence of cardiovascular collapse. Ketamine is considered relatively cardio-stable and recommended for endotracheal intubation in the haemodynamically unstable patient. Unfortunately, due to the depleted catecholamine reserve, its weak negative inotropic and vasodilatory effect may obscure its

sympathomimetic effect in these patients.[12] The incidence of hypotension was also noted to be higher in those who had more than one attempt at intubation.

Severe hypoxia was the second most common peri-intubation adverse event, occurring in a third of the patients. The incidence increased with increasing laryngoscopy grade and intubation attempts, but this was not statistically significant. Cardiac arrest is a rare complication of intubation occurring mainly in the critically ill. We reported a higher incidence of peri-intubation cardiac arrest (13.7%) than reported in the literature.[15–17] Vasopressor requirement before intubation and multiple intubation attempts were associated with its occurrence. Previously reported risk factors include pre-induction hypotension and hypoxemia, multiple intubation attempts, shock index ≥ 1.0, intubation within 1 hour of a nursing shift change, age > 75 years, body mass index > 25 kg/m^2, administering vasopressors before intubation, and use of muscle relaxants.[15–18] Pulmonary aspiration is another frequent and devastating complication of endotracheal intubation in the ICU.[19] Unfortunately, few studies have examined its incidence and possible risk factors. In this study, the incidence was slightly higher among those without a nasogastric tube in place before induction and among those who had more than one intubation attempt. However, these differences were not statistically significant.

The higher incidence of peri-intubation adverse events in the ICU when compared to the operating theatre is linked to the fact that critically ill patients often present in extremis, with marked physiological derangements and limited cardiopulmonary reserve. In addition, these intubations are frequently emergencies with less control and preparation.[3,11] Anaesthetic induction agents, muscle relaxants and positive pressure ventilation have also been implicated.[3,12] This high incidence of peri-intubation adverse events has also been reported among trauma victims who share similar characteristics to the ICU patients.[4,12] Numerous risk factors have been noted in the literature, with some contradictions on many of these. Price et al.[12] noted that it was impossible to identify determinants of post-intubation adverse events and recognised clinician intuition as superior to any combination of physiological variables for predicting hypotension.

It is generally believed that the occurrence of an adverse event increases not only the risk of mortality but also the length of ICU stay.[11,20] The median (range) length of ICU stay was 8.5 (0-50) days, and there was no significant difference between those with or without an adverse event. This lack of association might be due to our study being underpowered, and the higher mortality rate in those with an adverse event inadvertently shortened the length of stay. The 30-day in-hospital mortality rate was 55.6%. The probability of survival was lower in those with an adverse event. This was a clinically meaningful trend that likely lacked statistical significance due to the study being underpowered.

Our study revealed that multiple attempts at intubation were a central factor in many adverse events. Our first-pass success rate was only 68%, which is far below the recommended benchmark of ≥ 80%.[21,22] A similar study by Admas et al. in Ethiopia reported a first-pass success rate of 64.3%.[21] Every additional attempt at laryngoscopy dramatically heightened the risk of adverse events. The jump in incidence of cardiac arrest from 2.9% (1st attempt) to 46.2% (2nd attempt) is staggering. Russoto et al.[4] and De Jong et al.[23] also identified multiple intubation attempts as a risk factor for adverse events in the peri-intubation period and recommended the routine use of a videolaryngoscope. Videolaryngoscopes are, however, not readily available in many low-middle-income countries and may account for these poor figures.[21] In our study, a videolaryngoscope was used in only one intubation. Having a structured training on emergency intubation, adoption of an intubation algorithm and encouraging the routine use of intubation aids may also improve first-pass success rate.[2,3,6] It is also expedient that intubations in the critically ill be performed by the most experienced personnel.

Another striking finding of this study was the 100% mortality rate observed among patients who experienced severe peri-intubation hypoxaemia (p=0.030). This underscores a critical vulnerability in the management of critically ill patients in our setting. While hypotension was more prevalent, it did not carry

the same definitive mortality risk as oxygenation failure. This may suggest that the physiological insult of severe hypoxaemia in an already compromised patient may be irreversible. Implementing preventive strategies is thus paramount. This may include employing pre-oxygenation, apneic oxygenation and strategies to improve first-pass success rate. Only 16% of patients in this study received apneic oxygenation. This simple, low-cost intervention could potentially widen the safe apnea time during intubation.

Strengths

This study has several strengths. Firstly, it was a prospective, multicentre study. It provides valuable data on intubation practices among critically ill patients in Nigeria, which have not been previously reported. Data collection was standardised with clear definitions of terms. We aligned definitions with our studies to allow comparison and collected detailed information on intubation characteristics.

Limitations

The primary limitation of the study is its underpowered design, given the limited sample size. This may account for the lack of significant association between many of the variables. Similarly, due to the limited sample size, it was not possible to perform a multivariate analysis, and therefore, any associations should be interpreted with caution. Despite the investigators' efforts, the follow-up was incomplete, and sections of the proforma were left unrecorded. The use of a convenience sampling technique also introduced a risk of selection bias. This highlights the challenges of performing prospective research in this emergency setting without established data governance processes. Furthermore, we did not collect data on illness severity as it wasn't a routine practice at these institutions.

Recommendations

1. Clinicians should employ strategies to improve first-attempt intubation success rates, as multiple intubation attempts appear to be central to poor outcomes. Findings from the INTUBE study recommend the routine use of a videolaryngoscope.[8]
2. Intubating critically ill patients early before haemodynamic deterioration might also be a reasonable decision, as doing so when they are already in extremis is associated with poor outcomes even when preventive measures are instituted.
3. Among the critically ill, the routine use of pre-oxygenation and apneic oxygenation may increase the safe apnea time.
4. Caution in the use of ketamine in catecholamine-depleted patients. Doses should be significantly reduced (low and slow).

Conclusion

Peri-intubation adverse events are common in Nigeria and may exceed previously reported rates. While hypotension was the most common complication, severe hypoxaemia emerged as the most lethal, carrying a 100% mortality rate in this cohort.

Our findings highlight a "vicious cycle" where baseline physiological exhaustion predisposes patients to hemodynamic collapse. Although the small sample size limited the statistical significance of the overall survival curves, the clear clinical trend suggests that the first minutes of airway management are a primary determinant of 30-day hospital survival. There is a need to improve data collection on these events, conduct larger research on intubation practices, and identify specific interventions to improve intubation outcomes in critically ill patients.

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