

## Endotracheal intubation in critically ill patients, practices, complications and factors associated with post intubation hypotension: a study in National Hospital Sri Lanka

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### Context

Intubation in critical care setting is common and associated complication rates are high, up to 40%. Complication rates differ from intensive care unit (ICU) to ICU as their guidelines and practices are different. Post induction hypotension (PIH) is associated with increased mortality, morbidity and length of ICU stay.

### Objectives

Primary objective was to describe the practices, common induction agents, neuromuscular blocking agents used for intubation and to identify the common complications following intubation in critically ill patients in National Hospital Sri Lanka (NHSL). The secondary objective was to identify factors associated with post intubation hypotension in critically ill patients.

### Methodology

Descriptive cross-sectional study design with analytical component. Critically ill patients who were subjected to intubation outside theatre were the target population. Study was conducted in all ICUs, A&Es and ward settings in NHSL. Data entered to IBM SPSS 20 version. Basic descriptive statistical analysis was done, and data was summarized using frequency percentages. In the analytical component, univariate analysis was performed on variables to find statistically significant risk-factors for development of PIH. Statistically significant risk-factors were subjected to multivariate analysis. Statistical associations were studied using regression co-efficient and chi-square test. P value <0.05 was taken as significant.

### Results

Data from 150 intubations were analysed. Pre intubation cardiovascular (52%) and respiratory support (60%) was high. Majority (60%) of intubations of critically ill was performed during daytime and in the ICUs (68%). Commonly used induction agent was midazolam (58%) and neuromuscular blocking agent (NMB) was suxamethonium (84%). Supplemental fentanyl was used in 76% of cases. No failed intubation was recorded and 68% of time intubation was successful in the first attempt. Mechanical complications were low (6%) each for oesophageal intubation and aspiration and regurgitation. Post intubation hypoxaemia was common (50%). PIH was calculated as 26% according to definition (New or increased requirement of vasopressors within 60mins of intubation). After multivariate analysis, propofol induction (OR 17.38, P value = 0.000), post intubation hypoxaemia (OR 3.3, P value = 0.033), post intubation mechanical complications (OR 3.8, P value = 0.000), suxamethonium (OR 0.09, p value = 0.003), pre intubation airway support (OR 0.012, P value = 0.000), pre intubation cardiovascular support (OR 0.025, P value = 0.000, have shown association with PIH).

### Conclusion

There is high success rate of intubation without any failed intubation during the study period in critically ill patients in NHSL. There is higher percentage (84%) of involvement of formally trained doctors in the process of intubating critically ill. More than half of intubations are directly

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supervised by a senior doctor. Adherence to preoxygenation was high as 98% however inadequate usage of difficult airway trolley (88%) and capnography (68%) was observed. Even though the mechanical complication rates of intubations are low, there is high rates of post intubation hypoxia and hypotension. Usage of propofol as induction agent, post intubation hypoxaemia and mechanical complications were identified as significant risk factors for PIH. Pre intubation airway support, cardiovascular support and usage of suxamethonium had shown protective effect towards the development of PIH.

**Keywords:** Intubation; critically ill; practices; post intubation complications; post intubation hypotension; associated factors

## Introduction

Intubation is a common occurrence in the intensive care setting.<sup>1</sup> This is quite different and difficult when compared with an intubation of a patient in theatre for elective procedures due to presence of hypoxaemia, hypotension, confusion, agitation with low GCS. Critically ill patients are unable to tolerate induction agents and neuromuscular blocking medications as they have cardiac depressing effects and induces apnoea in already hypotensive and hypoxic patients.<sup>2</sup> Complications depends not only on patient factors but also on the experience and competence of intubating doctor and dose and choice of induction and neuromuscular blocking agents.<sup>3,4</sup>

Complication rates are known to be as high as 40% and NAP4 study in UK showed one in four major airway event occurs in either intensive care units (ICU) or emergency department.<sup>4</sup> Different ICUs have different complication rates as their emergency airway management differs from each other.<sup>2</sup> Complications that commonly result from intubation in the critically ill include hypoxaemia, aspiration, hypotension, and cardiac arrest.

Though the information regarding airway complications are robust, the details on the haemodynamic compromise is limited. Post intubation hypotension (PIH) has shown to increase in ICU mortality, length of stay and in-hospital mortality.<sup>5,6,7</sup> Identified risk factors for PIH were pre-intubation shock index, chronic kidney disease, intubation for acute respiratory failure, advanced age, intubation complications and usage of neuromuscular blockers. They were independently associated with the development of PIH.<sup>5,6,8,9,10</sup>

There are no studies done on this topic in NHSL and there is no documented guidance on the induction or NMB agents. Primary aim of this study was to describe the practices, common

induction and NMB agents used for intubation in the critically ill patients in NHSL. Secondary aim was to identify the complications and factors associated with post intubation hypotension in this group.

## Subjects and Methods

This is a descriptive cross-sectional study with an analytical component. Institutional ethical committee approval was obtained, and patient consent was not considered as it is only documentation and analysis of existing practice. The critically ill patients (patients needing ICU care) who were subjected to intubation outside theatre were the target population.

Sample size for the study was calculated based on the following formula (Lowanga and Lames how 1991).  $N = Z^2 * p(1-p)/d^2$ , N = sample size, Z = Z value (corresponding to confidence level) P = Anticipated population proportion d = Absolute precision required for the estimate to fall within given percentage points of true proportion D = Design effect Considering a precision of (d) = 0.07, and expected prevalence of (p) = 0.2 (put the reference of hypotension prevalence), confidence level 95% and design effect 1.2 a minimum sample size of 150.

Critically ill adult patients (> 18yrs) who were intubated in non-theatre environments was included in the study while pregnant and post-partum patients were excluded. Data collection form was used and was filled by the doctor who had intubated the patient, after the intubation. Patients who fit the inclusion criteria were recruited for the study until the sample size (150) was reached.

There was no universal definition for post intubation hypotension. Few cohort studies have investigated this matter and found that immediate (within 60 minutes) post intubation requirement of vasopressors was the best predictor for in hospital mortality and ninety day mortality.<sup>7,10</sup>

Therefore for this study, new or increased vasopressor requirement within 60 minutes of post intubation was taken as definition of post intubation hypotension.

### Statistical analysis

Data was entered to IBM SPSS 20 version. Basic descriptive statistical analysis done. The data were summarized using frequency percentages. In the analytical component, univariate analysis was performed on the variables to identify statistically significant risk factors for development of PIH. Some variables were made binary variables to get reasonable numbers for analysis without harming the accuracy of data. Patients were stratified to two groups depending whether they developed PIH or not. Risk factors that show a significant association for PIH were then subjected to multivariable logistic regression model. Statistical associations were studied using regression co-efficient and chi-square test. P value <0.05 was taken as significant.

### Results

Highest percentage of patients (42%) were in the 46 to 60yr age group. Female to male ratio in this sample was 58% to 42%.

Primary pre intubation disease distribution of the study population was trauma (30%), respiratory failure (20%), cardiac failure (18%), cardiorespiratory (14%), shock (14%) and sepsis (8%). 36% of patients had hypoxia, defined by saturation less than 88% while 30% were hypotensive. 58% of intubated patients had Glasgow Coma Scale of less than 12 before intubation.

Majority (60%) of intubations took place at daytime and 68% of critically ill patients had undergone this procedure in ICUs. Twenty four percent of study sample was assessed to have difficult intubation, but only 10% of patients needed third attempt at intubation.

70% of the time urgency of intubation was recorded as immediate. Adherence to pre-oxygenation was good (98%). Availability of difficult intubation trolley and capnography for intubation was poor, 88% and 68% respectively.

Data on preparation and procedure of intubation documented in Table 1.

**Table 1:** Preparation and procedure

Procedure	Number	Percentage
Assessed difficult face mask ventilation	33	22%
Actual difficult bag and mask ventilation	6	4%
Intubation on first attempt	102	68%
Intubation on second attempt	33	22%
Intubation on third attempt	15	10%
Failed intubation	0	0%
Assessed difficult intubation	36	24%
Procedure	Number	%
Laryngoscopy view at first attempt (Cormack-Lehane)		
1	51	34%
2	69	46%
3	27	18%
4	3	2%
Time of intubation		
Day	90	60%
Night	60	40%
Location of intubation		
ICU	102	68%
Resuscitation room	21	14%
Ward	18	12%
ETU	9	6%
Urgency of intubation		
Immediate	72	48
Urgent	51	34
Semi elective	24	16
Elective	3	2

The most common reason for intubation was clinical deterioration (80%). Other reasons were change in existing ET tube (8%), failed extubation and accidental extubation each accounting for 6%.

Medication used for intubation is shown in Table 2. Induction agents were used in all intubations and most used agent was midazolam (58%). NMB agent usage was recorded as 98%. Atracurium was used in 14% of patients.

**Table2:** Medications used for intubation

Name of the medication	Number	Percentage
Induction agent	150	100%
Propofol	51	34%
Non Propofol induction		
Ketamine	21	14%
Midazolam	78	58%
Neuromuscular blocking agent (NMB)	147	98%
Suxamethonium	126	84%
Atracurium	21	14%
None	3	2%
Opioid		
Fentanyl	114	76%
None	36	24%

More than three quarter (84%) of intubations were performed by trained anaesthetists and 78 out of 150 intubations were done under senior supervision.

Immediate complications (within 60 minutes) of intubation are shown in Table 3. Half of the patients developed hypoxia (SpO2 <88%) with 6% developing very severe hypoxia.

46% patients developed post intubation low systolic blood pressure (< 90mmHg). Thirty-nine patients (26%) required new or increased need of vasopressor support following intubation (PIH). Rest of the patients responded to fluid boluses. Mechanical complications were relatively rare.

**Table 3:** Immediate complications of intubation

Complication	Number	Percentage
Hypoxia	75	50%
SpO2 <88% (mild)	57	38%
SpO2 <80% (moderate)	9	6%
SpO2<70% (severe)	9	6%
Hypotension (SBP <90mmHg)	69	46%
Post intubation (new or increased) vasopressor need	39	26%
Cardiac arrest	4	2%
Cardiac arrhythmia	18	12%
Mechanical complications		
Oesophageal intubation	9	6%
Regurgitation and aspiration	9	6%

**Table 4:** Univariate analysis on post intubation hypotension

	Total 150	Stable N-113	Unstable N-39	P value
Age (>60)	42 (28%)	24 (16%)	18 (12%)	0.47
Gender (female) N (%)	63(42%)	21(14%)	42 (28%)	0.738
Pre intubation				
Oxygen saturation (<88%) N (%)	75(50%)	42(28%)	33(22%)	.071
Systolic Blood pressure < 90mmHg N (%)	45(30%)	9(6%)	36(24%)	.000*
Mean arterial blood pressure< 65mmHg N (%)	51 (34%)	15(10%)	36 (24%)	.002*
GCS before intubation (<8) N (%)	27 (18%)	18 (12%)	9(6%)	.105
Airway support before intubation N (%)	24(18%)	3(4%)	21(14%)	.000*
Respiratory support before intubation N (%)	75 (50%)	51(34%)	24 (16%)	.478
CVS Support before intubation N (%)	78 (52%)	24 (16%)	54 (36%)	.000*
q SOFA (score 3)	54(36%)	15 (10%)	39 (26%)	.000*
Reason for intubation				
Patient newly admitted to ICU N (%)	42 (28%)	33 (22%)	9 (6%)	.594
Patient deterioration N (%)	78 (52%)	51 (34%)	27 (18%)	.456
Failed trial of extubation N (%)	9(6%)	6 (4%)	3 (2%)	.346
Propofol induction N (%)	51(34%)	15(11%)	36(23%)	.000*
Non propofol induction N (%)	99(66%)	98(86%)	3(7%)	.478
Neuromuscular blockers				
Suxamethonium N (%)	126(84%)	78 (52%)	48(32%)	.829
Atracurium N (%)	21 (14%)	15 (10%)	6(4%)	.667
Opioid				
Usage of Fentanyl	114(76%)	81(54%)	33 (22%)	.398
Post intubation hypoxia SpO2<88% N (%)	75(50%)	12 (8%)	63(42%)	.004*
Development of mechanical complication N(%)	18(12%)	3(2%)	15(10%)	.005*
Lack of supervision during intubation N (%)	72(48%)	24(16%)	48(32%)	.001*

N- Number, Stable- not developed PIH according to study definition, Unstable-developed PIH according to study definition.

Patients were stratified to two groups depending on whether they developed PIH or not. Univariate analysis was performed on collected variables. Some variables were made binary variables, for example, age, systolic blood pressure (SBP), oxygen saturation, mean arterial pressure (MAP), GCS, induction agents, NMB, development of mechanical complications (oesophageal intubation and regurgitation and aspiration) to get reasonable numbers for analysis without harming the accuracy of data.

Pre intubation hypotension (MAP<65 mmHg, SBP< 90mmHg), airway support before intubation, cardiovascular support before intubation, higher qSOFA score, usage of propofol, mechanical complication of intubation, post intubation hypoxia and lack of intubation supervision shows significant association for PIH.

Multivariate analysis was applied on the above significant associations, after adjusting to age and illness severity by qSOFA score. Significant factors are shown in Table 5. When controlled for the other variables the chances of developing PIH among patients who had propofol was 17.38 times higher than having other induction agents like midazolam and ketamine and this is statistically significant.

**Table 5:** Factors associated with development of post intubation hypotension multivariate analysis

Variable	P value	Odds ratio	95% CI
Usage of induction agent (propofol)	0.000	17.38	4.18-72.30
Usage of neuromuscular blocker	0.003	0.097	0.021-0.459
Cardiovascular support before intubation	0.000	0.038	0.005-0.134
Airway support before intubation	0.000	0.012	0.001-0.114
Mechanical complication during intubation	0.000	3.82	0.603-22.41
Post intubation hypoxia (<88%)	0.033	3.31	1.099-9.989

Other significant associations in this study shown in Table 6. Post intubation mechanical complications were significantly associated with place of intubation, number of laryngoscopy attempts, grade of laryngoscopy view and degree of training of intubator.

**Table 6:** Significant associations- univariate analysis

Association	P value
Pre intubation hypoxia * development of post intubation hypoxia	0.004
Post intubation mechanical complications	
Place of intubation	0.03
Number of laryngoscopic attempts	0.04
Higher laryngoscopic view	0.006
Training of intubating doctor	0.003

## Discussion

Success rate of intubation in this study was 100% and the complication rates are comparable with published reports from the developed world. This study has covered all ICUs in NHSL including A&E, catheter care laboratory and medical and surgical wards. Even though the success rates were high there was significant room for improvement.

Preoxygenation is an essential part in rapid sequence induction for intubation to improve the safe period of apnoea specially in critically ill patients. In this study 36% of patients were hypoxaemic before intubation and all patients had oxygen therapy before intubation as either face mask oxygen or non-invasive ventilation. Practice of preoxygenation was good in this study (98%). In literature the rates of preoxygenation varied from 80% to 95%.<sup>2,4,8</sup> Application of cricoid pressure is controversial as no proven benefit. It was 66% in this sample and clearly lower than the other studies, which was above 80%.<sup>2,3</sup> It was difficult to ascertain the reasons for it, as it wasn't analysed. Overall, the adherence to evidence-based practices is satisfactory in this study sample.

Usage of capnography and the availability of difficult intubation equipment is an integral part in intubation of critically ill. It is emphasized by NAP4 and guidelines provided by College of Anaesthesiologists and Intensivists of Sri Lanka. Availability of difficult airway trolley during the intubation was 88% and capnography use was 68%. Multicentre study in Scotland found their adherence with capnography in critically ill was only 54%.<sup>2</sup> Reason behind non-usage may be the lack of equipment in certain settings in NHSL. This is clearly needed to be addressed to reduce the complication rates associated with emergency intubation.

Commonly used induction agent in study sample was midazolam (58%) which is clearly higher than in the developed world. Usage of propofol was low at 32% and is almost half the frequency of usage in other studies.<sup>2,4</sup> Only opioid used in this setting was fentanyl, while alfentanil, fentanyl and remifentanyl was recorded in other studies.<sup>2,4</sup> Suxamethonium was used almost exclusively in NHSL (84%), the other NMB agent was atracurium. Rocuronium was the commonest in the literature. Since practices and availability of drugs is quite different in Asian and European countries this difference cannot be compared.

Intubation at first attempt was 68% and only 10% of patients needed a third attempt for intubation. Other studies have found first attempt success rates 90% to 63% and around 12% needing three or more attempts.<sup>2,4,8,9</sup> It is clearly encouraging as only few patients needed a third attempt at intubation and there were no failed intubations.

Common complications are two streamed, physiological and mechanical. Percentages of hypoxia (50%), cardiac arrest (2%) were comparable to literature, with relatively lower rates of moderate to severe hypoxia 2%-4%.<sup>8,9</sup>

However, incidence of post intubation hypoxia in this sample was higher than the study done in France, where they had a clear protocol for intubation of critically ill and practiced preoxygenation with positive pressure ventilation.<sup>1</sup> In this study, adherence to preoxygenation was quite good, but there was a significant association between pre intubation hypoxia and development of post intubation hypoxia.

Mechanical complications were only (6%) in this study, which is agreeing with the multi-centre study in Scotland. However, in other literature reported incidence was 1.3 to 9.7%.<sup>1,2-4,16</sup> There was clear association between mechanical complications and place of intubation, higher incidence was found in out of ICU intubations. Other significant factors that showed an association were number of intubation attempts, grade 4 laryngoscopy view and level of training of intubator. Thus, the low rate in this study may be reflecting the fact that higher percentage intubation was done by doctors with formal anaesthesia training (84%), most of the intubations were performed in the ICUs (68%)

and rates of first attempt intubations were high as 68. PIH is a common incident in intubation in critically ill. It was 26% according to study definition in this study and is comparable with studies done in other parts of the world, which used the same definition for post intubation hypotension.<sup>7,10</sup> Post intubation hypotension is associated with increased mortality and morbidity in ICUs.<sup>1,5,6,12,15,16,17</sup> Associated factors differ from each study as there is no universal definition for PIH. Study populations and study settings were differ between studies making comparison impossible.<sup>1,5,6,12,15,16,17</sup> On univariate analysis of this sample, pre intubation low SBP, low MAP, higher qSOFA score, pre intubation airway support, cardiovascular support, propofol induction, post intubation hypotension, mechanical complications during intubation and degree of supervision were significantly associated with PIH.

When controlled for other variables the odds of having PIH among post-intubation hypoxaemic patients was 3.314 times higher than the odds of having PIH among non-hypoxaemic patients and this was statistically significant. The chances of developing PIH in patients who developed mechanical complication was 3.82 times higher than that of patients who did not develop mechanical complication ( $P < 0.001$ ).

Similarly, propofol induction increased the odds of developing hypotension. The odds ratio was 17.38 compared to the other agents. In this study the agents that were being compared were ketamine and midazolam.

A study done in USA (sample size 147), documented three risk factors for PIH following multivariate analysis, those were pre intubation hypotension, administration of neuromuscular blockers and intubation complications.<sup>10</sup> In the same study there was no significant association of PIH and induction agent. They suggested that if it were a bigger sample size, there might be a significant association between induction agent and hypotension.<sup>10</sup> Multicentred cohort done in Canada failed to identify a significant association between propofol and PIH even though it was used in 68% of patients in their sample.<sup>17</sup>

This difference in findings may be due to differences in the population as well as the practices in two different regions of the world. The per kilogram dose of propofol may influence

this finding, but the doses were not analysed in this study.

Interestingly pre intubation airway support, cardiovascular support and usage of suxamethonium show significant protective effect towards the development of post intubation hypotension. When patient already had resuscitation with fluid, supportive inotropes and airway support before the intubation this might reduce the deleterious effect of induction agent and laryngoscopy stimulation. Retrospective cohort study done on this topic found that diagnosis of sepsis has protective effect for post intubation hypotension, their data demonstrated that this cohort of patients received more intravenous fluids than the other patients before emergency intubation.<sup>10</sup>

In the above-mentioned study, researchers found a significant association between PIH and usage of NMB during intubation. This study shows a total controversy to that finding. In Sri Lanka emergency intubations are mainly done using suxamethonium as rocuronium is not freely available. Only other commonly used NMB is atracurium. Thus, this result may reflect the effect between those two NMB agents. Thus, controversy may be a reflect of different agent being used in two different settings.

### Conclusion

There is high success rate of intubation with no recorded failed intubation during the study period in critically ill patients in NHSL. There is higher percentage (84%) of involvement of formally trained doctor in the process of intubating critically ill and more than half of intubations are directly supervised by a senior doctor during the procedure. Adherence to preoxygenation was as high as 98% but inadequate usage of difficult airway trolley (88%) and capnography (68%) was observed. Even though the mechanical complication rates of intubations are low, there is a high rate of post intubation hypoxia and hypotension. Identified significant associated factors for PIH were propofol induction, post intubation hypoxaemia and mechanical complications. Pre intubation airway and cardiovascular support and usage of suxamethonium had shown protective effect towards the development of PIH.

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