ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCE SCHOOL OF MEDICINE DEPARTEMENT OF ANESTHESIA

INCIDENCE AND RISK FACTORS OF POST EXTUBATION LARYNGEAL EDEMA AMONG INTUBATED PATIENTS AT TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA, IN 2023. A CROSS SECTIONAL STUDY.

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ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCE SCHOOL OF MEDICINE DEPARTEMENT OF ANESTHESIA

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Declaration

This thesis is my original work in partial fulfillment for the requirements of Master of Science Degree in anesthesia. I understand that plagiarism will not be tolerated and all directly quoted material has been appropriately referenced.

Name: --

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Submitted to Msc. Tutor, Department of anesthesia, Addis Ababa University.

Date of submission: --

This thesis work has been submitted for examination with my/our approval as Advisors and Tutors on the Master of Science degree in anesthesia.

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Acronyms and abbreviations

AOR Adjusted odd ratio

CP Cuff pressure

ENT Ear nose throat

ETT Endotracheal tubes

GA General Anesthesia

PLE Post Extubation Laryngeal edema

PES Post extubation stridor

IRB Institutional review board

ICU Intensive care units

IV Intravenous

PI Principal Investigator

SPSS Statistical package for social science

TASH Tikur Anbessa Specialized Hospital

SD Standard deviation

HVLP High volume low pressure

LVHP Low volume high pressure

LDI Long duration intubation

OSA Obstructive sleep apnea

PV P-Value

MV Mechanical ventilation

Abstract

Background: Post extubation laryngeal edema is the prominent complications of endotracheal intubation that require immediate diagnosis and intervention. It is the leading cause of airway obstruction that requires re-intubation. In spite of these there is no adequate information related to the exact incidence of post extubation laryngeal edema among studies.

Objective: To determine the incidence and risk factors of post-extubation laryngeal edema among intubated patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

Method: A cross sectional study was conducted at TASH from January 1, to March 30, 2023 by using well-structured questionnaires. Data entry was performed by Epi- info version 7.2.5 and the analysis was carried out by SPSS version 25.A descriptive statistics, bivariate and multivariate analysis was performed in which incidence and risk factors of post extubation laryngeal edema were determined at P-value < 0.05 and 95% CI.

Results: Out of 193 patients enrolled 31[16.1%; 95% CI; 12.1, 20%] had developed post extubation laryngeal edema. Increased duration of intubation (AOR=18.385;95%CI; 2.823, 119.743; PV=0.002),Increased number of attempt during intubation (AOR=17.921; 95% CI; 2.823, 134.342; PV=0.005),Age < 17 years(AOR=50.383; 95%; 5.966,425.492;PV < 0.0001) ,Age between 17- 65 years (AOR=5.585; 95% CI; 1.399,22.296; PV=0.015) were significant risk factors to develop post extubation laryngeal edema.

Conclusions: The overall incidence of post extubation laryngeal edema was 16.1%.Increased duration of intubation, increased number of attempt, and age of the patients were identified as significant risk factors to develop post extubation laryngeal edema. For these reason, clinicians and Tikur Anbessa Specialized Hospital should implement safest management strategies that significantly reduce the risks of post extubation laryngeal edema.

Key words: Post extubation laryngeal edema, Post extubation stridor, Incidence, risk factors

Introduction

1.1. Back ground

Endotracheal intubation is a vital medical procedure that frequently performed in both Operating Room and Intensive Care Unit. Performing this technique involves manipulation of different airway structures by laryngoscope, Video laryngoscope, fiber optics bronchoscope,aiway stylet,bouge,endotracheal tube and suction tips that could potentially injury the patients airway(1,2).

These injuries usually involve laryngeal apparatus, the pharynx, oral cavity and nasal cavity. Larynx is the most common site of injury followed by the pharynx and the esophagus. Soft tissue hematomas, lacerations, and arytenoid dislocation can also be traumatized from the initial act of intubation. Other injuries, such as laryngotracheal stenosis and vocal fold paralysis, can occur from tissue-endotracheal tube interactions, even if intubation was performed without direct tissue trauma(3,4).

Some of these injuries occur at the initial traumatic intubation technique, while others occur after initial tube placement or even after the removal of the tube(5).Tracheal tube that even placed for a shorter period can cause mucosal trauma, whilst prolonged intubation is mostly responsible for a range of pressure related necrosis of the sub mucosa, perichondrium and eventually cartilage. The arytenoid cartilages, vocal processes, cricoarytenoid joints, posterior glottis, vocal folds and subglottic are particularly vulnerable(6).

Respiratory complications is three fold increased after extubation of endotracheal tube than complications occurring during tracheal intubation and induction of anesthesia(4.6% vs. 12.6%).Among those complications post extubation laryngeal edema is the leading cause of upper airway obstruction after patients' extubation(7-10).

It arises from direct mechanical trauma to the larynx by manipulation during intubation or interaction initiated post technique that triggers serious inflammatory reaction that could contribute to laryngeal swelling. The cardinal presentation of relevant laryngeal swelling is post extubation inspiratory stridor that indicates significant airway lumen narrowing or obstruction. Decreased airway lumen increases air flow velocity that manifest as post extubation inspiratory stridor, a clinical marker of relevant post extubation laryngeal edema. Although, the exact quantitative relationship between lumen narrowing and clinical symptoms is unclear, the presence of respiratory distress and post extubation inspiratory stridor is thought to reflect a narrowing of the airway lumen to greater than 50 % of its diameter which is capable of causing upper airway obstruction that can progress to acute respiratory compromise necessitating emergency re- intubation (8-10).

According to some previous studies conducted, the incidence of post extubation laryngeal edema varies between 5.0 % to 54.4 %of extubated patients (10-12).

And also some studies report female gender, longer duration intubation, difficult intubation, large tube size, and absence of steroid treatment, increased intubation attempt, high cuff pressure, and difficult intubation as risk factors of post extubation laryngeal edema (8,9,13,14).

The majorities of post extubation laryngeal edema were mild to moderate and short lived. Unrecognized severe cases of post extubation laryngeal edema lead to fatal upper-airway obstruct that can progress to respiratory failure. Airway obstruction alerts the need for re-intubation, administration of intravenous/nebulized corticosteroids and nebulized epinephrine (15, 16).

1.2. Statement of the problem

The pathophysiologic process involving post extubation laryngeal edema includes trauma, pressure and ischemia or combination of these of process. Following these insult airway mucosa that are directly affected becomes engorged primarily due to trauma and inflammatory reactions triggered. Airway engorgement starts soon after endotracheal tube placement and clinically becomes evident after removal the tube. In about 80% of patients post extubation laryngeal edema become symptomatic within 30 minutes; while in about 50% of the cases symptoms develop in 5 minutes after extubation (16-20).

Almost two-third of symptomatic post extubation laryngeal edema requires re-intubation.Re-intubating patients who develop post extubation laryngeal edema increases the risk of extubation failure.Re-intubation by itself increases intensive care admission from operating room and intensive care morbidity and mortality by 43%.

The main cause of this morbidity and mortality in re-intubated post extubation laryngeal edema patient is increased hospital stay that increases patients risk to other intensive care related complications including hospital acquired infectious and non-infectious complications. The overall post extubation failure requiring re-intubation following post extubation laryngeal edema varies from 1.8% to 31.4% (13,19,20).

Despite early administration of steroid prophylaxis and advance in patient care the incidence of post extubation laryngeal edema among extubated patient is still high. According to some studies report the incidence of post extubation laryngeal edema varies between 5-54.5 %(14, 20-23).

A prospective observational conducted at South African tertiary children Hospital Intensive Care Unit in 2022 among pediatric intensive care unit patients had found extubation failure in 20% of extubated patients within 48 hours (24).

In Ethiopia a cross sectional study conducted at Tikur Anbessa Specialized Hospital in 2020 by Tadesse Tamire et al, among 310 pediatric patients undergoing major surgery reported tracheal intubation related adverse event in 36.5% of the patients extubated (25, 26).

Until designing this study the magnitude of post extubation laryngeal edema and its associated risk factors was not adequately investigated and reported clearly because of this post extubation laryngeal edema is poorly recognized in both intensive care and operating team. Beside this predictive technique and investigation such as beside cuff leak test before planned extubation, application laryngeal ultrasound is not practiced as part of planned extubation especially in intensive care unit patients who remain intubated for longer duration. Even though performing this test enable early detection and initiation of treatment (18-20, 22, 25, 27).

1.3. Importance of the study:

This study will alert anesthesia team, nursing, respiratory therapist and other physician involved in patients management after extubation to organize their resources to safely handle post extubation laryngeal edema complications by improving post-extubation patients monitoring, early diagnosis and commencement of early treatment.The study also improve coordination between varies health professionals to ensure the better patients outcome.

The study further encourages professionals to use novel diagnostic tools, such as laryngeal ultrasound, the cuff leak test, fiber optic bronchoscope into clinical practice to assist early diagnosis and treatment of post extubation laryngeal edema, in which intensive care patients are particularly benefited most (18, 27).

This study also adds current knowledge to practical and theoretical input for both clinical and academic activities purpose. The survey will motivate other researchers to conduct huge multicenter studies over long periods of time to address additional issues that remained unexplored by utilizing this study as input.

Above all, the study will be helpful for the development of post extubation guidelines that allow close monitoring, early diagnosis, and current treatment to minimize complication related to post extubation laryngeal edema.

The study also encourages health professionals to utilize recent strategies that enable safest practice to reduce post extubation laryngeal edema and its complication.

Chapter two: Literature review

2.1. Incidence of post extubation laryngeal edema

A clinical review conducted at Intensive Care Unit in 2009 by Bastian HJ Witter Kamp, et al. on post-extubation laryngeal edema and extubation failure in critically ill adult patients, had found clinically relevant post-extubation laryngeal edema in up to 30% of extubated patients. From which 4% of the patients need re-intubation (22).

A prospective study conducted at intensive care unit in 2010 by Jean Marc Tadie, et al. among 136 critically ill intensive care patients extubated after more than 24 hours of mechanical ventilation, detected laryngeal injuries in 73% of patients(27).

A systemic review and meta-analysis of 1 cross-sectional,3 cohort, 5 case series, and 12 randomized controlled trials review in 2018 by Martin B. Brodsky et al.among intensive care patients that were intubated for a mean intubation duration of 132 minutes at 95% CI: 106-159 minutes, and had found a high prevalence of laryngeal injury in 83% of the cases. The majority of these injuries were mild, although moderate to severe injuries were reported in 13-31% the patients (28).

According to a prospective, randomized, placebo-controlled, double-blind, multicenter trial, at critical care unit conducted in 1992, by Darmon Jean Y et al. among 700 intensive care patients reported the overall incidence of post extubation laryngeal edema requiring tracheal intubation and mechanical ventilation in 4.2%(29).

A prospective study conducted at pediatric surgical department in 1977 by Koka BV et al. among 7875 surgical children under the age of 17 to determine the incidence and contributing factors of post-intubation laryngeal edema reported overall incidence of 1%(30).

A prospective observational study conducted at Ramathibodi Hospital, Mahidol University, Bangkok, Thailand Intensive Care Units in 2013 by Dr.Yuda Sutherasan, et al.that enrolled a total of 101 patients admitted to the intensive care unit, to predict laryngeal edema after extubation by using ultrasound had found the prevalence of laryngeal edema in 16.8% of the patients (31).

According to prospective study conducted in intensive units in 2002 by Yann De Bast's, among intensive care patients to predict extubation failure of post extubation laryngeal edema in patients intubated for more than 12 hours by using cuff leak test had reported post extubation laryngeal edema in 11% the patients (32).

An observational study conducted at single center Yokohama Hospital intensive care unit Japan in 2020 by Mafumi Shinohara,et al. among adults over the age of 20 years to assess the risk factors associated and important clinical manifestations had reported laryngeal edema in 29 % diagnosis made by post extubation hoarseness and/or stridor(33).

2.2. Risk factors of post extubation laryngeal edema

Duration of intubation, high endotracheal tube cuff pressure, and number of attempt during difficult intubation as risk factors of post extubation laryngeal edema (18).

A placebo – controlled, double blind multi center trail conducted at intensive care unit, in 2007 by Bruno Francois, et al.among 761 adults intensive care units patients who were ventilated for more than 36 hours were extubated after receiving 20mg intravenous methylprednisolone (n=380) or placebo (381) 12 hours before extubation then every 4 hours until tube removal had found methylprednisolone significantly reduce the risk of post extubation laryngeal edema PV< 0.0001(20).

According to an observational study conducted at emergency medical /trauma center of Yokohama hospital, Japan in 2020 by Mafumi Shinohara,et al. that includes adults patients greater than 20 years of age intubated for emergency purpose at intensive care unit, result indicated female gender using endotracheal tube >7 mm (odd ratio, 2.65; 95% CI, 1.21-5.81),duration of intubation (odd ratio,1.18; 95% confidence interval, 1.05-1.32) and emergency intubation were associated with symptoms of post extubation laryngeal edema was post-extubation stridor and hoarseness (22,33).

A prospective study conducted at intensive care unit in 2015 by Milena Siciliano Nascimento,et al. among 136 intubated patients for mechanical ventilation with a mean age of 1.4 year (3 days -17 years) and a mean duration of mechanical ventilation of 73.5 hours, identified duration of mechanical ventilation as main risk factor for post extubation stridor. Mechanical ventilation for more than 72 hours was associated with an increased risk of stridor (odds ratio of 8.60; 95 % confidence interval of 2.98-24.82; p0.001)(34).

A case report from Otsu Red Cross Hospital, Japan in 2008 by Hiroki Daijo, et al.A 69 –year-old female patient who underwent transurethral ureter lithotripsy and who had previous history of head and neck surgery 7 years back had associated head down or prone positioned during neurosurgical procedures, pregnancy, fluid resuscitation, neck and airway injuries, inhalational injuries and burns, difficult intubation and self extubation as a risk factor of post extubation laryngeal edema (35).

2.3. Treatment of Post Extubation Laryngeal Edema

Most studies have strong evidence related to treatment of symptomatic post extubation laryngeal edema that includes early administration of intravenous methyl prednisolone 20- 40 mg at least 4 hours before extubation and adrenaline nebulization and re-intubation with smaller size tube. Then continuing methyl prednisolone and adrenaline nebulization for 24-48 hours after re-intubation (10, 13,16,36,37, 41).

2.4. Conceptual framework

Conceptual frame work of risk factors associated with post extubation laryngeal edema. Some of these risk factors are patients related, intubation related factors

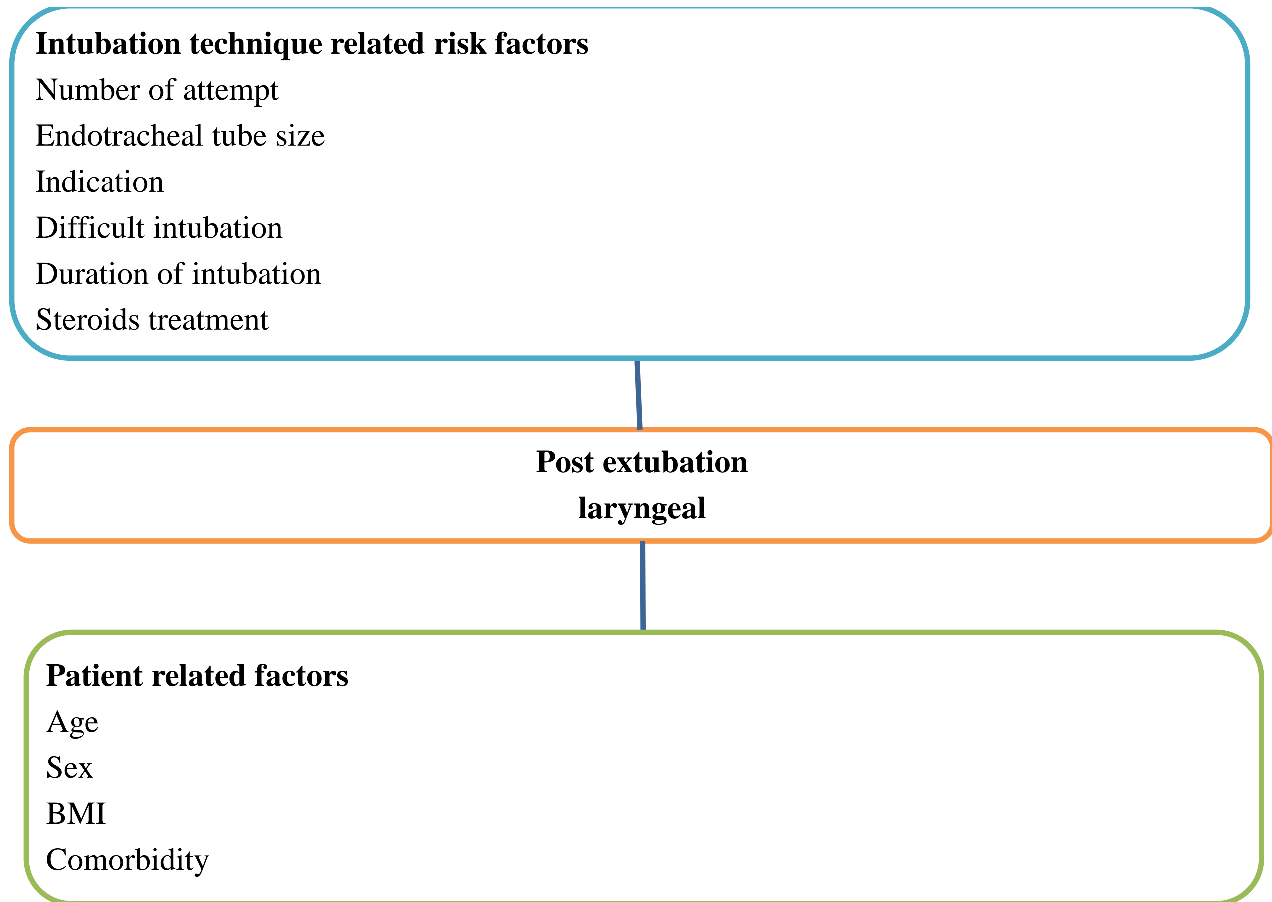

Figure 1: Conceptual frame work developed from previous study conducted to identify risk factors of post extubation laryngeal edema among patients intubated at Tikur Anbessa Specialized Hospital(20, 22, 42).

Three chapters: Objectives of the study

3. 1. General objective

- To determine the incidence and risk factors of post-extubation laryngeal edema among patients intubated at Tikur Anbessa Specialized Hospital, from January 1, to March 30, 2023.

3.2. Specific objective

- To report the incidence of post-extubation laryngeal edema among intubated patients at Tikur Anbessa Specialized Hospital.
- To identify the risk factors of post-extubation laryngeal edema among endotracheal intubated patients at Tikur Anbessa Specialized Hospital.

Chapter Four: Methodology

4.1. Study design

A cross-sectional study design, using survey questionnaires were conducted to determine the incidence and risk factors of post extubation laryngeal edema among intubated patients at Tikur Anbessa Specialized Hospital.

4.2. Time frames

The study was conducted from January 1, to March 30, 2023 GC.

4.3. Research area

The study was carried out at Tikur Anbessa Specialized Hospital, Addis Ababa University, College of Health Science, in Addis Ababa, Ethiopia. Tikur Anbessa Specialized Hospital is the largest teaching Hospital in Ethiopia. It was established in 1964 in Addis Ababa, Ethiopia.

In 1998, Tikur Anbessa Specialized Hospital becomes the largest Referral Hospital in Ethiopia. Tikur Anbessa Specialized Hospital was transferred from Federal Ministry of Health to University Teaching Hospital under Federal Ministry of Education.

Tikur Anbessa Specialized Hospital is currently the main teaching hospital for both clinical and preclinical training of most disciplines.

It also provides specialized clinical services that are not available in other public or private institutions in the country. Aside from these it also constantly involved in public services to improve communities' health in collaborative approach with other stakeholders.

4.4. Source population and study population

4.4.1. Source population

All patients admitted to Tikur Anbessa Specialized Hospital Intensive Care Unit and Operating Room from January 1, to March 30, 2023.

4.4.2. Study Population

All patients that underwent went endotracheal intubation at Tikur Anbessa Specialized Hospital Intensive Care Unit and Operating Room from January 1, to March 30, 2023.

4.5. Sample Size calculation and sampling procedure

4.5.1. Sample size determination

All patients extubated at Tikur Anbessa Specialized Hospital, Operating Room and Intensive Care Unit was included until a total number of patients desired to be included was determined by using single proportion Yamane formula by assuming percentage (p=0.5).

Minimum sample size required for accuracy will be determined by estimating the proportion considering that standard normal deviation set at 95% Confidence Interval and this value is obtained from corresponding z-score table, which is z=1.96 by substituting into the formula

n= Z^2P (1-P)/d^2 ➔z = standard normal value at 95% confidence interval

N= Sample size, d= desired degree of precision (5%), P= Percentage, NF= corrected sample size

N= Z^2P (1-P)/d^2= (1.96) (1.96) (0.5) (0.5)/ (0.05) (0.05) = 384

For contingency 10% of sample determine will be 384 x 0.1=38.4.Therefore, calculated sample size will be 384+38.4 = 422.4 Minimum of 384 required during the study period which is < 10000 population size Using sample size correction formula, a corrected sample size is calculated.

Nf (corrected sample) = n/1+ ((n-1)/N) =384/1+ (384-1)/422

= 384/1+383/422 = 384/1.9075 = 201 patients.

4.5.2. Sampling procedure

On average about 900 patients underwent elective intubation for elective surgeries, 91 intubations were performed at ICU and more than 200 emergency intubations were performed for emergency surgeries at Tikur Anbessa Specialized Hospital Intensive Care Unit and Operating Room during the study period from January 1, to March 30, 203.From these intubated patients 201 were selected by employing a convenience sampling technique.

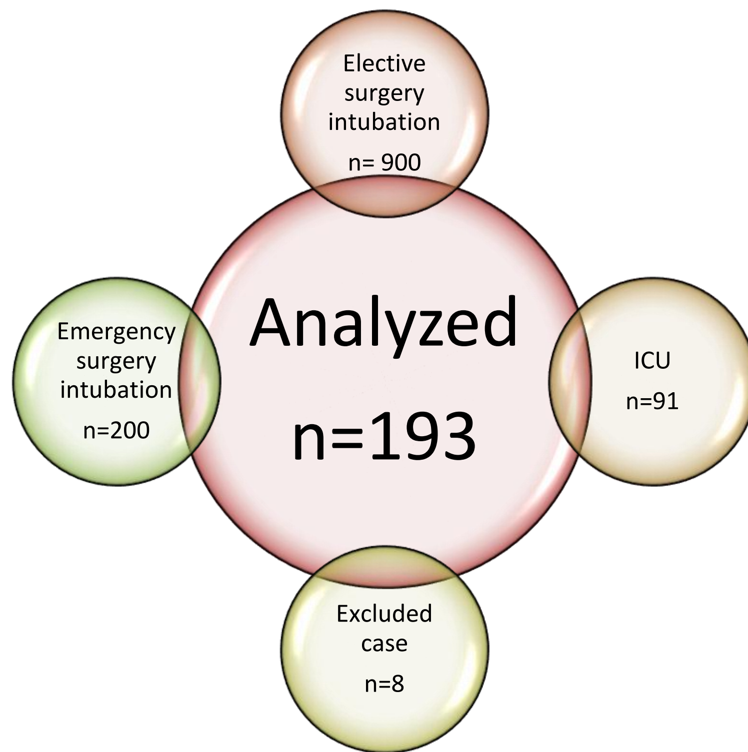

Figure 2: Sample selection flow diagram to determine the incidence and risk factors of post extubation laryngeal edema at Tikur Anbessa Specialized Hospital.

4.6. Eligibility Criteria

4.6.1. Inclusion criteria

- All patients intubated at Tikur Anbessa Specialized Hospital Intensive Care Unit and Operating Room.

4.6.2. Exclusion Criteria

- Previous airway obstruction
- Epiglottitis
- Obstructive sleep apnea
- Foreign body aspiration
- Bronchial asthma
- Chronic obstructive pulmonary disease
- Unconscious patients
- Large thyroid mass
- Nerve injury
- Laryngeal pathologies
- Craniofacial anomalies
- Genetic syndromes
- Head down position
- Fluid overload
- Pregnancy

4.7. Variables of the study

4.7.1. Dependent variable

- Post extubation laryngeal edema

4.7.2. Independent variables

4.7.2.1. Patient related factors

- Age
- Sex
- BMI
- Comorbidity

4.7.2.2. Technique related factors

- Number of attempt at intubation
- Difficult intubation
- Duration of intubation
- Endotracheal tube size
- Perioperative steroid

4.9. Procedures for gathering data

Data collection instruments

Data was collected by using well-structured, pre-tested, questionnaires. These questionnaires consist of three parts; questionnaires related to socio-demographic information, questionnaires related to diagnosis of post extubation laryngeal edema, and questionnaires related to risk factors assessment that were completed for every patients included in the study.

The content validating of these questionnaires were checked by seniors and adapted from deep analysis of relevant preliminary literatures (20.22, 42).

Assisted by these questionnaires patients were carefully observed in the first 1 – 4 hours until the patients were transferred to ward from PACU and in the first 24 hours of weaning from mechanical ventilation in ICU patients.

During observation of each patients all necessary information related to clinical presentation of post extubation laryngeal edema such as; inspiratory stridor, cyanosis, respiratory muscle retraction, and information related to risk factors such as duration of intubation, treatment with steroid,age,indication for intubation, difficult intubation, weight, height,pre-existing airway obstruction, tube size, and number of attempt at intubation was obtained by data collectors for each patients(4,20, 22).

Data collection periods

Data collection took three months that start from January 1, 2023 and ends on March 30, 2023. During these period data was collected from a total of 201 extubated patients at Tikur Anbessa Specialized Hospital Intensive Care Units, Recovery Room, and Operating Room.

Data collectors

Data collection were carried out by 2 Msc. Anesthesia Students, 2 Anesthesiology Residents, 3 PACU Nurses and 1 Physicians working at ICU, after adequate orientation was given by principal investigator related to questionaries' and post extubation laryngeal edema.

4.10. Data processing and analysis

After data coding, data entry was performed by using Epi-info version 7.2.5.After data was exported to SPSS version 25, data exploration, cleaning, editing, and recoding was carried out. Descriptive statistics were computed for variable such as age, BMI, Comorbidity, duration of intubation, number of attempt, indication of intubation, ETT size, difficult intubation technique, steroid treatment, and post extubation laryngeal edema at 95% confidence interval, while analytical statistics were computed for age, duration of intubation, number of attempt, comorbidity, steroid treatment, tube size, indication of intubation and difficult intubation to determine the risk factors post extubation laryngeal edema.

The effect of co-founder was also tried to be minimized during selection of participants in which some patients were restricted from the study and also by using binary logistic regression.

Binary logistic regression assumptions like multicollinearity was checked by using linear logistic regression in which significant multicollinearity was not diagnosed as indicated by multicollinearity diagnostic output of SPSS VIF<1.4 and tolerance >0.7 and Spearson correlation coefficient < 0.5, and also binary outcome of dependent variable, independent observation, no strong influential multivariate outliers were detected as shown by Maximum Mahalanobis' distance(MD) = 26.410 which is less than Chi-square critical value at 0.001 and df=10 is 29.59 and expected frequency for each categorical variables were checked and accepted.

Adequate model fitness to data was also insured by Hosmer and Lemeshow goodness of model fitness test indicated by p-value = 0.145 which is greater than 0.005 and small Chi-square value of 10.854.

The models explain about 34.7-59.2% variation in the post extubation laryngeal edema by variations in the predictors as shown by Cox and Snell R square and Nagelkerke R square. The remaining 40.8% variations in the post extubation laryngeal edema were due to random variability.

Bivariate analysis was under taken to identify important risk factors of post extubation laryngeal edema in which age, gender, BMI, indication, technique, number of attempt, duration of intubation were selected by including all variable having P-value < 0.25 then multivariate analysis was performed in which age of the patients, duration of intubation, number of attempt during intubation, indication of intubation and difficult intubation were identified as risk factors of post extubation laryngeal edema in which statistical significance were determined at p-value < 0.05 at 95 % Confidence interval.

These significant risk factors of post extubation laryngeal edema were like duration of intubation, number of attempt at intubation and age of the patients were reported by including AOR, 95% confidence interval and P-values and summarized by using either text in a tabular form.

4.11. Data quality control and management

One week prior to data collection, the questionnaires was pretested among 5% of total sampled study population at Saint Peter Specialized Hospital Intensive Care and Recovery Room.

Then appropriate data collectors were assigned and trained by principal investigator before the start of data collection and continuously supervised during data collection period by principal investigator.

All collected data was verified for accuracy and completeness, data entry was carried out by principal investigator followed by adequate data clerking before being subjected to analysis. Finally, data was appropriately saved in digital form to prevent information loss.

4.12. Dissemination plan

The result of the study will be presented to department of anesthesia as a partial fulfillment requirement for Msc in clinical anesthesia thesis.

The thesis will be communicated through annual students and staff research conference, including Annual National Conference of Ethiopia Anesthesia Association.At last the manuscript will be prepared and sent to highly impact full journals for peer-review to be published.

4.13. Operational definition

Post-extubation laryngeal edema: A decrease in the airway lumen diameter due to mucosal engorgement (20, 22,41, 42).

Minor post extubation laryngeal edema: Presence of stridor and signs of respiratory distress and **major post extubation laryngeal edema**: respiratory distress secondary to airway obstruction that require re intubation (22).

Post extubation stridor: High pitched inspiratory (whistling) within 24-48 hours of intubation that become evident within minutes to hours after extubation (20,22, 39,40).

Cuff pressure: The pressure that is applied by endotracheal tube cuff balloon against tracheal lumen after it is filled with fluid or air at 20-30 cm H_2O ,to achieve adequate seal of trachea(43).

Endotracheal intubation: Process of placing endotracheal tube into the trachea following clear indication (1).

Post Extubation: It is the period after removal of the tube from intubated patient at the end of the surgery or liberated from mechanical ventilation.

Cuff leak test: Positive cuff leak test if cuff leak volume (CLV) is less than 110 ml it indicates high possibility of post extubation laryngeal edema;

Negative cuff leak test if cuff leak volume is greater than 110 ml indicate low possibility of post extubation laryngeal edema (32).

Extubation failure: Inability to maintain spontaneous breathing after removal of endotracheal tube or tracheostomy tube; and the need for re-intubation within 24-72 hours (19, 20).

Appropriate endotracheal tube size: Adult female = 7, Adult male = 7.5, New born = 3-3.5, 6month to 1 year = 3.5 - 4.0, 2 - 8 years = (age (years)/4) +4

Chapter five: Ethical Reviews

This study was carried out by obtaining a permission letter from Addis Ababa University's Institutional Review Board given under protocol number: Anes/22/2022/2023 that was submitted to Tikur Anbessa Specialized Hospital on December, 13, 2022.

Before the start of data collection the participants were clearly explained about the purpose of the study in order to enable the patients understanding of the benefit of the study.

After patients adequate understanding of the purpose of the study informed consent was obtained that indicates their willingness to participate.

Patients’ autonomy and confidentiality was also highly ensured by keeping all information secrete and accepting their decision not to participate in the study.

Chapter Six: Result

A total of 201 patients were intubated during a study period from January 1 to March, 30, 2023. From these 193 intubated patients were analyzed to determine the incidence and risk factors of post extubation laryngeal edema. The ages SD of patients involved in the study were 0.605, while the SD for duration of intubation and number of attempt were 0.496 and 0.424 respectively. Out of 193 intubated patients for whom the final analysis were performed 31 patients had developed symptomatic post extubation laryngeal edema.

Table 1: Socio demographic characteristics of patients intubated at Tikur Anbessa Specialized Hospital from January to March, 2023(n=193).

Socio demographic characteristics		Frequency	Percent (%)
Sex of patients	Male	96	49.7
	Female	97	50.3
Age of the patients	< 17 Years	69	35.7
	17-65 Years	100	51.8
	>65 Years	24	12.4
Body mass index	<18.5	75	38.9
	18.5-24.9	90	46.6
	25-30	20	10.4
	>30	8	4.2
Comorbidity	Present	60	31.1
	Absent	133	68.9

6.1. The Incidence of Post Extubation Laryngeal Edema

The overall, incidence of post extubation laryngeal edema among intubated patients at Tikur Anbessa Specialized Hospital Intensive Care Unit and Operating Room from January 1, to March 30, 2023 was 16.1%; 95% CI; 12.1, 20.2%.

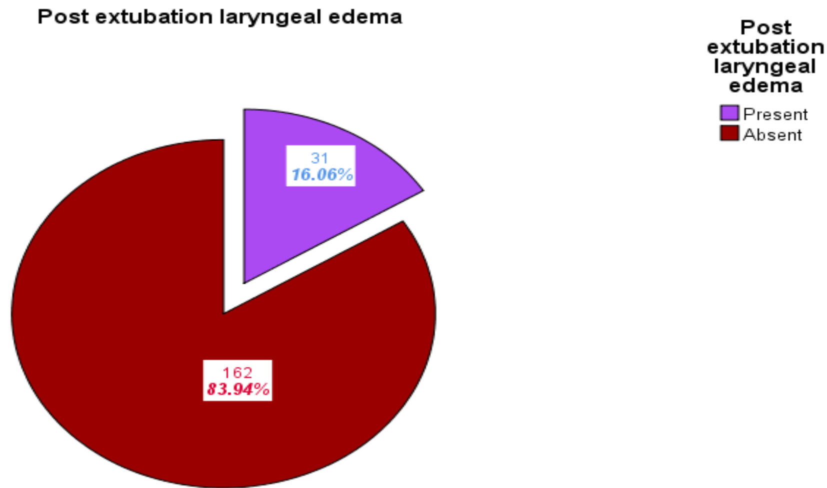

Figure 3: Post extubation laryngeal edema among extubated patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia from January 1, to March 30, 2023.

6.2. Result of Bivariate and Multivariate Analysis

Bivariate and multivariate logistic regression analysis was computed among 193 intubated patients to determine the risk factors of post extubation laryngeal edema.

During the bivariate analysis endotracheal tube size used for intubation and steroid treatment given were found to be statistically insignificant with p-value of 0.610 and 0.701 respectively. Age, gender, BMI, Comorbidity, indication of intubation, difficult intubation, number of attempt, and duration of intubation were fit to compute for multivariate analysis.

After computing multivariate analysis age of the patients, indication of intubation, difficult intubation, number of attempt during intubation, duration of intubation were identified as statistically significant risk factors of post extubation laryngeal edema.

Table 2: Bivariate and Multivariate analysis to identify risk factors of post extubation laryngeal edema at Tikur Anbessa Specialized Hospital from January,1 to March, ,30,2023(n=193

Variable	**Categories**	**Post extubation laryngeal edema**		**COR (95%CI)**	**AOR (95%CI)**	**P-Value**
		Present (%)	**Absent (%)**			
Age (years)	<17 Years	6(3.1%)	63(32.6%)	12.409(3.890,39.590)*	50.383(5.966,425.492)*	0.015
	17-65 years	12(6.2%)	88(45.6%)	8.667(3.175,23.659)*	5.585(1.399,22.296)*	< 0.0001

	>65 Years	13(6.7%)	11(5.7%)	1	1	
Indication	Intubation for patients undergoing surgeries	23(11.9%)	152(78.7%)	1	1	
	Intubation for mechanical ventilation in ICU	8(4.1%)	10(5.2%)	0.189(0.068,0.529)	0.080(0.014,0.448)	0.004
Intubation technique difficulty	Present	13(6.7%)	16(8.3%)	0.152(0.063,0.366)	0.040(0.008,0.199)	< 0.0001
	Absent	18(9.3%)	146(75.6%)	1	1	
Attempt at intubation	1 Attempt	29(15.02%)	119(61.7%)	1	1	
	>1 Attempt	2(1.04%)	43(22.3%)	5.239(1.199,22.896)	17.921(2.391,134.342)*	0.005
Duration of intubation	<3 Hours	25(12.95%)	86(45.6%)	1	1	
	>3Hours	6(3.11%)	76(39.4%)	3.682(1.434,9.454)	18.385(2.823,119.74	0.002

					3)*	
Sex of the patients	Male	10(5.2%)	86(44.6%)	1	1	
	Female	21(10.9%)	76(39.2%)	2.376(1.053,5.362)	2.671(0.819,8.712)*	0.103
Body mass index (kg/m2)	<18.5	13(6.7%)	62(32%)	1	1	
	18.5-24.9	15(7.8%)	75(38.9%)	1.048(0.464,2.369)	6.650(1.250,35.377)	0.026
	25-30	2(1%)	18(9.3%)	1.887(.389,9.148)	4.357(0.443,42.808)	0.207
	>30	1(0.5%)	7(3.6%)	1.468(.166,12.970)	22.120(0.292,1674.265)	0.161
Steroid treatment	Present	22(11.4%)	120(62.2%)	1	1	
	Absent	9(4.7%)	42(21.8%)	0.856(.365,2.005)		0.701
Endotracheal tube size	> = Appropriate size	12(6.2%)	55(28.5%)	0.814(0.368,1.798)		0.610
	<Appropriate size	19(9.8%)	107(55.4%)	1		

Chapter Seven: Discussion

According to this cross sectional study conducted at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, from January 1,to March 30,2023 among 193 intubated patients had found the overall incidence of post extubation laryngeal edema in16.1%;95%CI;12.1,20.2%.

This figure is consistent with a prospective observational study conducted at Ramathibodi Hospital, Bangkok, Thailand Intensive Care Units in 2013 by Yuda Sutherasan and his co-worker among 101 patients admitted to Intensive Care Unit to predict laryngeal edema after extubation by using ultrasound had reported similar incidence of post extubation laryngeal edema in 16.8% of the patients. The possible reason for this similarity in the incidence may be related both studies designed (31).

Another randomized controlled trial conducted at Chi Mei Medical Center, Tainan, Taiwan Intensive Care Units in 2011 by Kuo Chen Cheng, et al. among adult medical and surgical Intensive Care Unit, reported the incidence of post extubation laryngeal edema in 14.2% which is almost close to the incidence determined by this study. The probable cause of lower incidence of post extubation laryngeal compared to this study may be methyl prednisolone effect on post extubation laryngeal edema (16).

A multi-center trial conducted at Dupuytren teaching Hospital, Medical and Surgical Intensive Care Unit, France in 2007 by Francois and his co-author, had found the incidence of post extubation laryngeal edema in 22% among patient who didn't received methylprednisolone. The incidence is lower in my survey finding when compared to this study probably related to the effect of steroid treatment and differing detection method used by these studies (20).

Another clinical review conducted at Gelderse Vallei Hospital Intensive Care Unit, Netherlands in 2009 by Bastiaan HJ Wittekamp, et al. among intensive care patients on post extubation laryngeal edema and extubation failure, reported higher clinically relevant post extubation laryngeal edema in 30 % of extubated patients when compared to this study finding. The reason for this variation could due to extensive reviews of different studies that had used different definition and assessment methods of post extubation laryngeal edema (22).

A meta-analysis study conducted among intensive care units had reported higher overall incidence of post extubation laryngeal edema in 5-54%.The cause of this variation in the incidence report could be related to design, assessment tools used, study population difference that had been used by these studies (17, 20, 31, 32, 41).

A prospective study conducted at France Intensive Care Unit in 2010 by Jean Marc Tadie, et al. among 136 intubated patients for more than 24 hours by using Fiber optic bronchoscopy observed laryngeal injuries in 73% from these post extubation laryngeal edema was noted in 54% of the patients. Incidence report is higher because of better laryngeal edema detection method have been employed that can able to visual even milder injuries (27).

In which duration of intubation increases the risk of laryngeal injury by the odds of 1.11 times [odds ratio 1.11, 95% CI 1.02-1.21, P=0.02]. But according to this study finding increased duration of intubation to greater than 3 hours increases the risk of post extubation laryngeal edema by 18 times(AOR=18.385;95%CI;2.823,119.743;PV=0.002).The reason could be explained by as duration of intubation increased the insult is also extended(27).

Another risk factors identified by this survey was increased number of attempt to more than one during endotracheal intubation, that increases the risk of developing post extubation laryngeal edema by 18 times (AOR=18.501; 95% CI; 2.548, 134.328; P-value=0.004).A clinical review conducted at Netherlands Intensive Care Unit in 2015 by Pluijms A woulter also reported a number of attempts during difficult intubation as significant risk factors of post extubation laryngeal edema. The main explanation for this risk similarity could be related to extensive review of studies of similar design conducted for common purpose and other possible explanation could be as number of attempt increased injury to the airway also increased per attempt (18).

This study also indicated that the risk of developing post extubation laryngeal edema was increased by 50 times in patients whose age less than 17years (AOR=50.383; 95% CI; 5.966, 425.492; PV < 0.0001)and increased by more than 5 times in patients age between 17-65 years (AOR=5.585; 95% CI; 1.399,22.296; PV= 0.015).A retrospective review conducted at United States of America's Intensive Care Unit in 2016 by Jordan T Lilienstein,et al. among all Intubated Intensive Care trauma patients; also identified age <18 years (p-value=0.004),female gender (p-value=0.001),prolonged duration of intubation > 5days (p-value=0.001),and trauma (p-value = 0.013) as a significant risk factors of post extubation laryngeal edema. Pediatric age groups are more prone to post extubation laryngeal edema due to narrower, less developed, fragile airway passage that increases the risk of airway trauma and because of narrower, less developed and fragile pediatric airway that are prone to airway injuries (23).

Increased duration of intubation to greater than 3 hours increases the risk of post extubation laryngeal edema by 18 times (AOR=18.385; 95% CI; 0. 2.823, 119.743; PV = 0.002). Multicenter placebo controlled, double blind study conducted at France Intensive Care Unit in 1992 by Darmon JY, et al. among adult Intensive Care Unit patients reported longer duration of intubation >36 hours [p-value= 0.001], and female gender [p-value= 0.05] as risk factors of post extubation laryngeal edema. However, according to this study finding is not significant risk factor even though the odd of developing post extubation laryngeal edema is 2.7 times increased compared to male patients because female airway is thin.The possible reason for both studies similarity in their risk identified for post extubation laryngeal edema could be related to similar assessment technique employed and inclusion criteria used by these studies and for other reason explained in this study (29).

BMI between 18.5-24.9 kg/m2 is significant risk factor to develop post extubation laryngeal edema (AOR=6.65;95%CI(1.250,35.377);P=0.026).Possible reason could be because of large number of patients included belong to this group 46.6% of patients included in the study. The overall BMI is statistically insignificant risk factor for post extubation laryngeal edema.

Wider confidence interval during risk factors analysis indicates uncertainty in which range true population parameter could be found before inferring to population. The possible cause of this wider confidence interval especially in risk factors identified may be related to sampling error.

Chapter Eight: Strength and Limitations of Study

8.1. Strengths

- This study used relatively larger sample size (n= 193).
- This study determines the incidence of post extubation laryngeal edema with cost effective method of diagnosis.
- Incidence and risk factors of post extubation laryngeal edema was directly determined

8.2. Limitation

- No uniform guidelines were available for the assessment of post extubation laryngeal edema.
- Diagnostic tools like Cuff Leak Test, Laryngeal Ultrasound, CT scan, and Video Laryngoscope weren't applicable to assess the degree of post extubation laryngeal edema at Tikur Anbessa Specialized Hospital.
- Subjective bias among data collectors to diagnose post extubation laryngeal edema.
- Selection bias was introduced during data collection.
- The study's finding generalizability was limited since it was conducted in single center.

Chapter Nine: Conclusion and Recommendation

9.1 Concussions

In this study, the overall incidence of post extubation laryngeal edema among intubated Tikur Anbessa Specialized Hospital patients were 16.06 %. In addition to the incidence of post extubation laryngeal edema, the study also identified increased duration of intubation, increased number of attempt during intubation, and age of the patient as statistically significant risk factors of post extubation laryngeal edema.

9.2. Recommendations

Recommendation forwarded to health care professionals

This studies finding, alerts clinicians to give high emphasis during the entire technique of intubation in order to reduce the risk of post extubation laryngeal edema through utilizing the safest strategies in a collaborative approach.

In patients at high risk of intubation difficulties, in which increased number of attempt is expected; adequate planning is highly recommended.

Performing beside cuff leak test at least 1 hour before performing extubation is also highly recommended to detect the presence laryngeal edema especially in intensive care unit patients to improve patient management.

Adequate post extubation patient monitoring during the first hours of extubation is also highly advised to early detect post extubation laryngeal edema and to start treatment to prevent worsening.

Recommendation forwarded to stakeholder

Ministry of health, Tikur Anbessa Specialized Hospital expert in the area of this should work jointly to develop guidelines that will enable comprehensive patient management during endotracheal tube placement, after it's placement, during and after it's removal to facilitate early detection and management of post extubation laryngeal edema.

Recommendation forwarded to researcher

Further research will be required to extensively investigate post extubation laryngeal edema and its complication among Intensive Care Unit patients since this study didn't investigate deeply in this area due to limited resource.

Reference

1. Alvarado AC, Panakos P. Endotracheal Tube Intubation Techniques. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2022, StatPearls Publishing LLC.; 2022.

2. Rawicz M. [Indications for endotracheal intubation]. Med Wieku Rozwoj. 2008;12(4 Pt 1):851-6.

3. Tikka T, Hilmi OJ. Upper airway tract complications of endotracheal intubation. Br J Hosp Med (Lond). 2019;80(8):441-7.

4. Domino KB, Posner KL, Caplan RA, Cheney FW. Airway injury during anesthesia: a closed claims analysis. The Journal of the American Society of Anesthesiologists. 1999;91(6):1703-.

5. Martin LD, Mhyre JM, Shanks AM, Tremper KK, Kheterpal S. 3,423 emergency tracheal intubations at a university hospital: airway outcomes and complications. The Journal of the American Society of Anesthesiologists. 2011;114(1):42-8.

6. Benjamin B, Holinger LD. Laryngeal complications of endotracheal intubation. Annals of Otology, Rhinology & Laryngology. 2008;117(9_suppl):2-20.

7. Asai T, Koga K, Vaughan R. Respiratory complications associated with tracheal intubation and extubation. British journal of anaesthesia. 1998;80(6):767-75.

8. Colice GL, Stukel TA, Dain B. Laryngeal complications of prolonged intubation. Chest. 1989;96(4):877-84.

9. Epstein SK, Ciubotaru RL. Independent effects of etiology of failure and time to reintubation on outcome for patients failing extubation. American journal of respiratory and critical care medicine. 1998;158(2):489-93.

10. Kriner EJ, Shafazand S, Colice GL. The endotracheal tube cuff-leak test as a predictor for postextubation stridor. Respiratory care. 2005;50(12):1632-8.
11. De Bast Y, De Backer D, Moraine J-J, Lemaire M, Vandenborght C, Vincent J-L. The cuff leak test to predict failure of tracheal extubation for laryngeal edema. Intensive care medicine. 2002;28(9):1267-72.
12. Mackle T, Meaney J, Timon C. Tracheoesophageal compression associated with substernal goitre. Correlation of symptoms with cross-sectional imaging findings. The Journal of Laryngology & Otology. 2007;121(4):358-61.
13. Abbasi S, Moradi S, Talakoub R, Kashefi P, Koushki AM. Effect of nebulized budesonide in preventing postextubation complications in critically patients: A prospective, randomized, double-blind, placebo-controlled study. Adv Biomed Res. 2014;3:182.
14. Kastanos N, Estopá Miró R, Marín Perez A, Xaubet Mir A, Agustí-Vidal A. Laryngotracheal injury due to endotracheal intubation: incidence, evolution, and predisposing factors. A prospective long-term study. Crit Care Med. 1983;11(5):362-7.
15. Lee CH, Peng MJ, Wu CL. Dexamethasone to prevent postextubation airway obstruction in adults: a prospective, randomized, double-blind, placebo-controlled study. Crit Care. 2007;11(4):R72.
16. Cheng KC, Chen CM, Tan CK, Chen HM, Lu CL, Zhang H. Methylprednisolone reduces the rates of postextubation stridor and reintubation associated with attenuated cytokine responses in critically ill patients. Minerva Anestesiol. 2011;77(5):503-9.
17. Epstein SK, Ciubotaru RL. Independent effects of etiology of failure and time to reintubation on outcome for patients failing extubation. Am J Respir Crit Care Med. 1998;158(2):489-93.
18. Pluijms WA, van Mook WNKA, Wittekamp BHJ, Bergmans DCJJ. Postextubation laryngeal edema and stridor resulting in respiratory failure in critically ill adult patients: Updated review. Critical Care: BioMed Central Ltd.; 2015.
19. Mikaeili H, Yazdchi M, Tarzamni MK, Ansarin K, Ghasemzadeh M. Laryngeal ultrasonography versus cuff leak test in predicting postextubation stridor. Journal of cardiovascular and thoracic research. 2014;6(1):25-8.

20. François B, Bellissant E, Gissot V, Desachy A, Normand S, Boulain T, et al. 12-h pretreatment with methylprednisolone versus placebo for prevention of postextubation laryngeal oedema: a randomised double-blind trial. Lancet (London, England). 2007;369(9567):1083-9.
21. Seegobin RD, van Hasselt GL. Endotracheal cuff pressure and tracheal mucosal blood flow: endoscopic study of effects of four large volume cuffs. British medical journal (Clinical research ed). 1984;288(6422):965-8.
22. Wittekamp BHJ, van Mook WNKA, Tjan DHT, Zwaveling JH, Bergmans DCJJ. Clinical review: Post-extubation laryngeal edema and extubation failure in critically ill adult patients. Critical Care2009.
23. Lilienstein JT, Davis JW, Bilello JF, Dirks RC. Risk factors associated with post-extubation stridor in the trauma intensive care unit. American journal of surgery. 2016;212(3):379-83.
24. Salie S, Morrow B. Risk factors and outcomes of extubation failure in a South African tertiary pediatric intensive care unit. Southern African Journal of Critical Care. 2022; 38:26-32.
25. Tilahun L, Molla A, Ayele FY, Nega A, Dagnaw K. Time to recovery and its predictors among critically ill patients on mechanical ventilation from intensive care unit in Ethiopia: a retrospective follow up study. BMC Emerg Med. 2022 Jul 12;22(1):125. doi: 10.1186/s12873-022-00689-3. PMID: 35820844; PMCID: PMC9277794.
26. Tamire T, Garbessa B, Gebeyu G, Getachew L. Tracheal Intubation related adverse Events in Pediatrics Anesthesia in Ethiopia. Pediatric Anesthesia. 2021; 31.

27. Tadié JM, Behm E, Lecuyer L, Benhmamed R, Hans S, Brasnu D, et al. Post-intubation laryngeal injuries and extubation failure: a fiberoptic endoscopic study. Intensive Care Med. 2010;36(6):991-8

28. Brodsky MB, Levy MJ, Jedlanek E, Pandian V, Blackford B, Price C, et al. Laryngeal Injury and Upper Airway Symptoms After Oral Endotracheal Intubation With Mechanical Ventilation During Critical Care: A Systematic Review. Critical care medicine. 2018;46(12):2010-7.

29. Darmon J-Y, Rauss A, Dreyfuss D, Bleichner G, Elkharrat D, Schlemmer B, et al. Evaluation of Risk Factors for Laryngeal Edema after Tracheal Extubation in Adults and Its Prevention by Dexamethasone A Placebo-controlled, Double-blind, Multicenter Study. The Journal of the American Society of Anesthesiologists. 1992;77(2):245-51.

30. Koka BV, Jeon IS, Andre JM, MacKay I, Smith RM. Postintubation croup in children. Anesthesia and analgesia. 1977;56(4):501-5.

31. Sutherasan Y, Theerawit P, Hongphanut T, Kiatboonsri C, Kiatboonsri S. Predicting laryngeal edema in intubated patients by portable intensive care unit ultrasound. Journal of critical care. 2013 Oct 1;28(5):675-80.

32. De Bast Y, De Backer D, Moraine JJ, Lemaire M, Vandenborght C, Vincent JL. The cuff leak test to predict failure of tracheal extubation for laryngeal edema. Intensive care medicine. 2002 Sep;28(9):1267-72.

33. Shinohara M, Iwashita M, Abe T, Takeuchi I. Risk factors associated with symptoms of post-extubation upper airway obstruction in the emergency setting. Journal of International Medical Research. 2020;48(5).

34. Nascimento MSi, Prado C, Troster EJu, Valério N, Alith MBa, Almeida JFLod. Risk factors for post-extubation stridor in children: the role of orotracheal cannula. Einstein (São Paulo, Brazil). 2015;13(2):226-31.

35. Daijo H, Habara T, Katagawa T, Yoshikawa Y, Shinomura T. [Postextubation laryngeal edema seven years after undergoing neck dissection]. Masui. 2008 May;57(5):631-4. Japanese. PMID: 18516894.

36. Esteban A, Alia I, Gordo F, Fernandez R, Solsona JF, Vallverdu I, Macias S, Allegue JM, Blanco J, Carriedo D, Leon M. Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. American journal of respiratory and critical care medicine. 1997 Aug 1;156(2):459-65.

37. Wang C, Tsai Y, Huang C, Wu Y, Ye M, Chou H, Shu S, Lin M. The role of the cuff leak test in predicting the effects of corticosteroid treatment on postextubation stridor. Chang Gung medical journal. 2007 Jan 1;30(1):53.

38. American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice guidelines for management of the difficult airway: an updated report. Anesthesiology. 2003;98:1269-77.

39. Westley CR, Cotton EK, Brooks JG. Nebulized racemic epinephrine by IPPB for the treatment of croup: a double-blind study. American Journal of Diseases of Children. 1978;132(5):484-7.

40. Accuracy of stridor-based diagnosis of post-intubation subglottic stenosis in pediatric patients. J Pediatr (Rio J). 2020 Jan-Feb;96(1):39-45. doi: 10.1016/j.jped.2018.08.004. Epub 2018 Sep 21. PMID: 30243644; PMCID: PMC9432238.

41. AK AK, Cascella M. Post Intubation Laryngeal Edema. [Updated 2021 Jul 17]. In: Stat Pearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: **https://www.ncbi.nlm.nih.gov/books/NBK560809/**

42. Lange M, Badjatia N, Chang WT. Implementation of a Clinical Pathway to Reduce Rates of Postextubation Stridor. Critical care nurse. 2018;38(5):34-41.

43. Sengupta, p, Sesseler, D.I., Maglier, P.et al. Endotracheal tube cuff pressure.BMC Anesthesiol 4, 8(2004).http://doi.org/10.1186/1471-2253-4-8.

Annex One: Consent Form

Consent form of incidence and risk factors of post extubation laryngeal edema at Tikur Anbessa Specialized Hospital from January 1, to March 30, 2023.

Dear participant this proposal has been reviewed and approved by Addis Ababa University College of Health Science School of Medicine Institutional Review Boards Committee whose task is to ensure the research participants high protection. You are selected to be included in the study depending on the anesthesia and treatment you received.

Your participation in the study is highly important for the success of this study and also I want to assure you that all the information you provide will be kept confidential and used only for this study purpose.At the same time, data collection will be carried out based on your free will indicated by providing oral / written consent.

Participant name --Signature --------------------- Date ---------

Data collectors Name: -- Signature: -------------

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Annex two: Questionnaires to assess the incidence and risk factors of post extubation laryngeal edema among intubated patients at Tikur Anbessa Specialized Hospital from January 1, to March 30, 2023.

Dear data collectors this questionnaires were designed to assess the incidence and risk factors of post extubation laryngeal edema at Tikur Anbessa Specialized Hospital Post Anesthesia Care Unit, Intensive Care Unit, and Operating Room following extubation in conscious patients by observation in the first 1- 4 hours in the patients undergoing surgery before patients transferring to ward and in the first 24 hours after extubation in intensive care unit patients. These questionnaires contain three parts and each part must be completed for each patient after extubation as each part guides you.

Part one: Socio demographic characteristics questionnaires at Tikur Anbessa Specialized Hospital at Tikur Anbessa Specialized Hospital from January 1, to March 30, 2023.

101	Age (years) 1. <17 2. 17-65 3. >65
102	Gender: 1. Female 2. Male
103	BMI (kg/m2) ○ <18.5 ○ 18.5-24.9 ○ >30

Annex Three: Questionnaires

Part two: Questionnaires to diagnosis post extubation laryngeal edema at Tikur Anbessa Specialized Hospital from January 1 to March 30, 2023.

<table>
<tr><td>S.No</td><td colspan="4"></td></tr>
<tr><td rowspan="10">201</td><td rowspan="10">Post extubation Laryngeal edema</td><td rowspan="2">1. Stridor</td><td>○ Absent</td><td></td></tr>
<tr><td>○ Present</td><td></td></tr>
<tr><td rowspan="2">2.Level of consciousness</td><td>○ Normal</td><td></td></tr>
<tr><td>○ Disoriented</td><td></td></tr>
<tr><td rowspan="2">3.Cyanosis</td><td>○ Present</td><td rowspan="2"></td></tr>
<tr><td>○ Absent</td></tr>
<tr><td rowspan="2">4. Air entry</td><td>○ Normal</td><td rowspan="2"></td></tr>
<tr><td>○ Decreased /absent</td></tr>
<tr><td rowspan="2">5.Retraction</td><td>○ Present</td><td rowspan="2"></td></tr>
<tr><td>○ Absent</td></tr>
</table>

Questionnaires to diagnosis post extubation laryngeal edema among extubated patients at Tikur Anbessa Specialized Hospital, Addis Ababa Ethiopia, from January 1, to March 30, 2023.

<table>
<tr><td>S.No</td><td></td><td>Severity</td><td>Presentation</td><td>Code</td></tr>
<tr><td rowspan="4">202</td><td rowspan="4">Post extubation Laryngeal edema</td><td colspan="2">Minor laryngeal edema</td><td rowspan="2">1</td></tr>
<tr><td colspan="2">○ Occasional barking cough
○ No stridor at rest
○ Mild or no retractions
○ Frequent barking cough
○ Stridor at rest
○ Mild to moderate retraction
○ No or little distress or agitation</td></tr>
<tr><td colspan="2">Major laryngeal edema</td><td rowspan="2">2</td></tr>
<tr><td colspan="2">○ Frequent barking cough
○ Stridor at rest
○ Marked retraction
○ Significant distress, and agitation
○ Depressed conscious level,
○ Stridor at rest,
○ Severe retractions,
○ Poor air entry,
○ Cyanosis or pallor</td></tr>
</table>

Part three: Questionnaires to assess risk factor of post extubation laryngeal edema at Tikur Anbessa Specialized Hospital from January 1, to March, 30, 2023.

S.No			Code
301	Indication of endotracheal intubation?	○ Intubation in patients undergoing surgeries	1
		○ Intubation for mechanical ventilation of intensive care patients	2
302	Known co - morbidities?	○ Present If' present' (write……………………………………..)	1
		○ Absent	2
303	Difficult intubation?	○ Present ○ If 'present 'write the number of attempt (------------------)	1
		○ Absent	2
305	Does the patient receive steroid treatment during endotracheal intubation?	○ Yes	1
		○ No	2
306	Endotracheal tubes size used?	○ ≥ETT of appropriate size of age	1
		○ Cuffed ETT of < 0.5/1 of appropriate size	2
307	Duration of intubation?	○ < 3 Hours	1
		○ >3 Hours	2 3