Prevalence and predictors of laryngotracheal stenosis at Chris Hani Baragwanath Academic Hospital

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, in partial fulfilment of the requirements for the degree of Master of Medicine.

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Dedication

Dedicated to my parents Mmanakana Tselapedi and Omphemetse Tselapedi who worked to pave the road of success. My husband Allan-Roy Sekeitto who has since the beginning of the journey has been my side. My family Kgosi Tselapedi, Motlotleng Tselapedi, Agnes Ikatekit and Ignatius Odongo who kept me focused on the bigger picture.

Declaration

I *Boipelo Tselapedi-Sekeitto* declare that this Research Report is my own, unaided word. It is being submitted for the Degree of Master of Medicine in the branch of Otorhinolaryngology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

Signed: ……..... .....

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This dissertation is submitted as a final copy with my approval as the University's Academic and Clinical Supervisor.

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My loving husband Allan-Roy Sekeitto, thank you for your guidance and walking this path with me.

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List of Abbreviations

CEO	Chief Executive Officer
CHBAH	Chris Hani Baragwanath Academic Hospital
CT	Computed tomography
ED	Emergency Department
ENT	Ear Nose and Throat
ETT	Endotracheal intubation
HREC	Human Research Ethic Committee
ICU	Intensive Care Unit
LTS	Laryngotracheal stenosis
MVA	Motor vehicle accident

Abstract

Objective: The purpose of the research was to determine the prevalence and predictors of laryngotracheal stenosis at Chris Hani Baragwanath Academic Hospital.

Method: The research design was a retrospective cross-sectional study of 955 patients admitted into the ear, nose and throat department at Chris Hani Baragwanath Academic Hospital from 2010-2016. Demographic information, medical and surgical history, and clinical findings were examined. Inclusion criteria included 100 patients who were managed for laryngotracheal stenosis secondary to prolonged intubation. Patients with laryngotracheal stenosis from other causes such as caustic ingestion, congenital laryngotracheal stenosis, idiopathic laryngotracheal stenosis, and malignancy related laryngotracheal stenosis were excluded. Demographic data was analysed using descriptive statistics, while hypotheses were tested using multiple regression models.

Results: Out of 955 patients, 100 had been diagnosed with laryngotracheal stenosis, indicating a 10.47% prevalence rate. Patients who were diagnosed were mainly from the 26-30 age group, constituting 31%, followed by the 16-20 age group (21%), less than 1-years (19%), and the 21-25 age group (14%). The study showed that 65% men and 35% female were diagnosed with laryngotracheal stenosis. Severity levels among the studied population indicated that all patients fell under Myers-Cotton 1 to 3, with the majority in Myers-cotton 3 (85%). Multiple regression models indicated that maturity level, patient sex, indication for intubation and the intubating discipline, had no significant influence on the grades of laryngotracheal stenosis.

Conclusion: The research highlights the high prevalence rates of laryngotracheal stenosis. In order to reduce the high prevalence, this study recommends close adherence to guidelines regarding cuff pressure monitoring and selection of appropriate sized endotracheal tubes.

CHAPTER 1

1. Introduction and literature review

1.1 Background

Laryngotracheal stenosis (LTS) is a narrowing of the airway that may be congenital or acquired, involving the larynx and trachea up to the mainstem bronchi. Patients with this condition can develop severe morbidity and it may result in mortality if not correctly managed. The airway narrowing may affect the glottis, subglottis, and/or trachea.[1]

Furthermore, tracheal stenosis is defined as narrowing of the trachea. The diagnosis on computed tomography (CT) is confirmed when there is more than 10% narrowing of the tracheal lumen on trans-axial sections or coronal and sagittal reconstruction views.[2,3]

The incidence of tracheal stenosis varies from 1 % to 10%. This variation may be related to standard of care and the index of suspicion or availability of diagnostic tools of the condition.

The aetiology of LTS may differ by region since standard of care of intubated patients may vary based on the skills and protocol being adopted in each region. A survey was conducted among 100 professional nurses in six adult cardiac care units in the public and private healthcare sectors in the Nelson Mandela Metropole, Eastern Cape, South Africa. Approximately half of the respondents monitored cuff pressures 6-8 hourly, while a third monitored in 2-3 hourly intervals and the remainder only when prompted by a cuff leak. It was concluded that the majority of health professionals do not follow a standardised approach to cuff pressure monitoring.[4] In a study conducted at Chris Hani Baragwanath Academic Hospital's (CHBAH) Intensive Care Unit (ICU) with 75 nurses and a 51% response rate, 72% of the respondents reported measuring cuff pressure at least once per 12-hour shift. A majority of respondents (94%) knew at least one complication of abnormal cuff pressure. The study concluded that there is need to develop nursing guideline together with in-service training to improve compliance with cuff pressure monitoring.[5]

Thus, an evidence-based clinical protocol is necessary in our environment to standardise care and therefore reduce the incidence of tracheal stenosis and its associated complications. The severity of LTS may be related to sociodemographic factors (such as age, genetic predisposition on account of race,) clinical morbidities (such as diabetes mellitus, obesity) and

the management and monitoring of the patients by the attending physicians and nurses. However, little is currently known about the common causes of LTS in our environment. Furthermore, factors that may be associated with severe forms of LTS have not been well elucidated in our environment. This study was thus done to determine the prevalence and evaluate the predictors of the severity or grades of LTS among patients at the CHBAH.

1.2 Literature review

1.2.1 Aetiology

LTS is an uncommon but life-threatening complication arising from tracheotomy, endotracheal intubation, blunt or penetrating trauma, benign or malignant neoplasms, infectious aetiologies, and connective tissue disorders (Table 1.1). [3]

Endotracheal intubation is the most common aetiology. [3] The known risk factors for tracheal stenosis include endotracheal intubation longer than 10 days, high cuff pressures (greater than 30 mm Hg), excessive mobility of the tube, concurrent infection, large bore tubes, and traumatic or repeated intubations. [3]

Table 1.1: Causes of LTS

Acquired
Trauma
External laryngotracheal injury
Blunt neck trauma
Penetrating wound of the larynx
Internal laryngotracheal injury
Prolonged endotracheal intubation
Tracheotomy
Surgical procedure
Irradiation therapy
Endotracheal burn
Thermal
Chemical
Chronic Inflammatory Disease
Bacterial diphtheria
Syphilis
Fungal histoplasmosis
Tuberculosis
Leprosy

Sarcoidosis
Scleroma
Benign Neoplasms
Intrinsic
Papillomas
Chondromas
Minor salivary gland
Neural
Extrinsic
Thyroid
Thymus
Malignant Neoplasms
Intrinsic
Squamous cell carcinoma
Minor salivary gland
Sarcomas
Lymphoma
Extrinsic
Thyroid
Collagen Vascular Diseases
Wegener's granulomatosis
Relapsing polychondritis
Other

Clinical manifestations

The common clinical manifestations of LTS are dyspnoea on exertion, shortness of breath, and respiratory failure. The relationship between the degree of stenosis and the severity of the symptoms varies according to the patient's level of activity, fitness, pulmonary reserve, onset, and progression of the stenosis.[3]

1.2.2 Classification of Stenosis

There are multiple classification systems that are used for airway stenosis; these are based on function or location of the stenotic section. The common classifications include the Myers-Cotton Classification; Lano classification and McCaffrey classification as shown in Table 1.2 below.

Table 1.2 The Classification and Staging System for laryngotracheal stenosis

Myers-Cotton Classification: circumferential stenosis limited to tracheal region[6]	
Grade I	Obstruction of 0%-50% of the lumen
Grade II	Obstruction of 51%-70% of the lumen
Grade III	Obstruction of 71%-99% of the lumen
Grade IV	No detectable lumen; obstruction of 100% of the lumen

Lano classification[7]

I	One subsite involvement
I	Two subsite involvement
III	Three subsite involvement
	Subsites defined as glottis, subglottis and trachea

McCaffrey classification[8]

I	Subglottis or trachea < 1cm
II	Subglottis > 1cm
III	Subglottis and trachea >1cm
IV	Any lesion involving glottis

1.2.3 Pathogenesis

The pathogenesis of LTS is related to the host's inflammatory response to the initial injury. Intubation and tracheotomy may cause an inflammatory host response leading to compromise of the mucosal blood supply, ulceration, necrosis of the epithelium and perichondrium. The concomitant local infection further compromises the trachea. The inflammatory cascade results in the formation of granulation tissue, loss of cartilaginous support, and fibrosis that can lead to significant stenosis.[3] The tracheal wound healing can be divided into different sequences.[9] The secondary healing of the ulceration produces granulation tissue and subsequent fibrous scar formation. The exuberant granulation tissue usually resolves without any further sequelae. However, some lesions become fibrotic with a firm and avascular scar. The next stage is the accumulation of submucosal fibrous tissue which reduces the tracheal lumen diameter. The final stage is marked by further contraction of the scar tissue causing additional distortion of the subglottic and tracheal airway.[10]

1.2.4 Paediatric Subglottic Stenosis

Benjamin et. al and Martin et al noted the pathophysiology of post-intubation acute laryngeal lesions. The lesions were noted at greatest point of contact with the endotracheal tube (ETT). Common sites were noted to be from the arytenoid cartilages medially, posterior portion of the glottis and the inner mucosa in the subglottic area. The pressure of the ETT at the aforementioned sites resulted in ischaemia and lead to the sequence of developing acute laryngeal lesions.[11]

Benjamin et. al classified acute laryngeal lesions into five groups:[12]

1. Early nonspecific alterations
2. Oedema
3. Granulation tissue
4. Ulceration
5. Miscellaneous

Fan et al. classified acute laryngeal lesions into the following:

1. Normal to mild (inter-arytenoid region ulceration, vocal fold granuloma)
2. Moderate pseudomembranes, bulky granulomas
3. Severe (subglottic stenosis, subglottic membrane, tracheal stenosis, vocal fold paralysis) [13]

1.2.5 Incidence and Prevalence of Subglottic Stenosis in Paediatrics

In Chicago, Walner et al, studied the incidence of subglottic stenosis in intubated neonates. Between the 1970s and 1980s, the incidence of neonatal subglottis stenosis was noted to range between 0.9% to 8.3%. Studies have shown a downward trend after the 1990s to a prevalence of less than 0.63% due to better techniques of handling neonatal ventilatory support.[14] A study by Denise et. al included all children under the age of 5 that were intubated in the Paediatrics Intensive Care unit of the Hospital de Clinicas de Porto Algera. Post extubation, all subjects were followed up and fibre-optic laryngoscopy was performed. It was noted that 16 out of 142 children developed subglottic stenosis, which represented an incidence of 11.3% of subglottic stenosis.[15] Cordeiro et al. prospectively studied the prevalence of subglottic stenosis in the neonatal intensive care unit and Paediatric Intensive Care unit of the hospital University of Sao Paulo. The prevalence of subglottic stenosis was noted to be 10%.[16]

1.2.6 Incidence and Prevalence of Laryngotracheal Stenosis in the Adult Population

Nouraie et al studied the incidence of LTS between 2004 and 2006. The study was done at two tertiary hospitals in London. It was noted that there was an incidence of 4.9% cases per million per year of LTS.[17]

Yekaterina and colleagues studied the risk factors associated with tracheal stenosis in 179 patients. The matched cohort was made up of 74 patients with tracheal stenosis and 105 patients in the control group. The incidence was higher amongst patients who had risk factors such as previous tracheostomy, carcinoma of the larynx, previous intubation for more than 48 hours and were intubated for non-airway surgery.[18]

Sarper and colleagues noted that the incidence of postintubation stenosis can be reduced by the use of large-volume, low-pressure cuffs, careful placement of the stoma, avoidance of large apertures, elimination of heavy and prying ventilatory connecting equipment and meticulous care of the tracheostomy. [19]

Several studies have reported on prevalence of LTS in adult patients. There has been a higher prevalence of tracheal stenosis in patients post tracheostomy as compared to endotracheal intubation. [20]. John et al reported the prevalence of 19% after endotracheal intubation and a higher prevalence of 65% amongst the post tracheostomy group.[20]

Several studies have been done on the prevalence of LTS post tracheostomy. Harley et. al reported a 2.37% prevalence rate of LTS while Andrews et al reported a prevalence rate of 17.5%. [21,22]. Stoeckel et al's study revealed 85% prevalence of tracheal stenosis after tracheotomy. Lindholm et al reported 36% prevalence of tracheal stenosis post tracheotomy, and 1% prevalence after endotracheal intubation. [23]

William and colleagues studied the risk of tracheal stenosis following open or percutaneous tracheostomy. Neither of the two techniques was superior to the other in relation to prevention of tracheal stenosis. The literature illustrates numerous exacerbating factors such as trauma and inflammation at the ETT cuff site, excess granulation tissue around the tracheal stoma site or over a fractured cartilage, high tracheostomy site, prolonged intubation, traumatic intubation, or previous intubation or tracheostomy. It is therefore concluded that prolonged intubation with an inflated tracheal cuff increases the risk for tracheal stenosis. [24]

Shin reported patients with post-tracheostomy tracheal stenosis had more complicated stenosis, poorer general condition and a lower success rate for airway prosthesis removal than those with post-intubation tracheal stenosis. [25]

A study by Susan and colleagues also noted different tracheal stenosis patterns in relation to endotracheal intubation and tracheotomy. The post endotracheal intubation stenosis is located at the site of ETT cuff, whilst post tracheostomy stenosis is noted at the tracheal stoma site. [26]**.** Tracheostomy patients tend to have longer duration with tracheostomy as compared to endotracheal intubation patients which was the main variable risk factor. Most of the stenosis were noted at the tracheal stoma site.[20]

While several studies were focusing on aetiologies and management of tracheal stenosis, Hans-J. Welkoborsky and colleagues were focused on microscopic examination of iatrogenic subglottic tracheal stenosis, to observe its histological origin. Eighteen patients underwent open tracheal or laryngotracheal resection for iatrogenic subglottic tracheal stenosis. The morphological characteristics were investigated for each tissue layer, including the pars membranacea, adventitia, the outer surface of the perichondrium, cartilage, the inner surface of the perichondrium, submucosa, and mucosa. Each tissue layer was evaluated independently and compared to the other layers. The results showed the most severe pathologic observations occurring in the outer perichondrium and adventia with only minor changes in the inner tissue layers.[10]

The outer perichondrium and adventia are the greatest distance from the site of injury. This study supports the theory that the depth of the airway injury is more critical to the development of iatrogenic subglottic tracheal stenosis than is the extent or length of the injury. [10]

1.3 Problem Statement

LTS, when it occurs, is a life-threatening condition that must be promptly identified, and appropriate treatment offered. This condition can be prevented with minimising some iatrogenic risk factors. However, the prevalence and common risk factors of the disease is not well known at the CHBAH. Since endotracheal intubation is a risk factor for LTS, it is noted that intubation by less skilled and inexperienced physician can cause LTS. This study will investigate any difference in intra hospital and inter hospital rate. Results from this study may highlight the need for retraining of physicians that practise at peripheral hospitals, in

endotracheal intubation skills. This study therefore aims to determine the prevalence and associated predictors of the severity of LTS at CHBAH to improve care.

1.4 Research question

What is the prevalence and the factors affecting the severity of laryngotracheal stenosis at CHBAH?

1.5 Study Aim

To determine the prevalence and risk factors of the severity of laryngotracheal stenosis at CHBAH from 1 January 2010 to 31 December 2016,

The research sought to achieve the following objectives:

- To determine the prevalence of laryngotracheal stenosis from 2010-2016.
- To describe the demographic characteristic of the patient population with laryngotracheal stenosis from 2010-2016.
- To determine the prevalence of laryngotracheal stenosis by grades or severity among the studied population.
- To evaluate the predictors of the severity of laryngotracheal stenosis.

CHAPTER 2

2. Methodology

2.1 Study Design

This study was a retrospective cross-sectional study of patients with LTS from 2010 - 2016.

2.2 Study Population

The study population consists of all patients who presented to the Ear Nose and Throat (ENT) department at CHBAH with benign LTS following endotracheal intubation or tracheostomy, from 1 January 2010 to 31 December 2016. CHBAH is a tertiary referral centre. The patients seen at the ENT department were either referrals from external health facilities or from internal departments at CHBAH where the patient had undergone the intubation.

2.3 Selection Criteria

Inclusion Criteria

All patients who presented to the ENT department with a diagnosis of LTS, as recorded in the ENT Operating Theatre register, or the ENT ward admission register, were eligible for inclusion in the study.

The operating theatre register was used as a primary reference to identify eligible patients. These include patients who have had diagnostic laryngoscopy, as well as those who have had a tracheal resection or crico-tracheal resection with an end-to-end anastomosis. The ward admission register was used as a secondary reference to identify patients whose theatre record was unclear or lacking detail (e.g. incorrectly spelt names, missing or partial hospital numbers).

Exclusion Criteria

1. Patients with LTS from other causes such as:
    - Caustic ingestion
    - Congenital LTS
    - Idiopathic LTS

- Malignancy related LTS
- Patients with incomplete records, will be excluded from the study

2.4 Data Collection

Initially, the following documents were sourced: ENT operating theatre registers, and ENT ward admission registers for the period between 2010 and 2016.

Using the inclusion and exclusion criteria, each patient's data was carefully extracted into a Microsoft Excel spreadsheet. Patients identified exclusively from the secondary reference were cross checked against their recorded clinical findings and were included in the study population. Patients that lacked sufficient information, were excluded from the study population.

From each patient record, the following data was extracted (see Appendix A):

- Patient demographics: age and sex
- Reason for intubation
- Category of the person who intubated in terms of the team of professionals who handled the patient
- Findings at direct laryngoscopy

2.5 Data Analysis

Prior to data analysis, an analysis plan was developed. The purpose of the analysis plan was to guide the analysis process so that precise answers were obtained that specifically relate to the variables under consideration. Data analysis was conducted in both Microsoft Excel and the "R" software. Microsoft Excel was used for descriptive statistical analysis while "R" for used for regression modelling.

The summary of the analysis performed is summarised in Table 2.1 below:

Table 2.1: Summary of the Analysis Performed

Research Objective	Purpose of the analysis	Type of analysis conducted	Variables analysed
To determine the prevalence of LTS from 2010-2016	To determine the number and proportions of patients who had	Descriptive statistical analysis: numeric and analysis of proportions	• Patients diagnosed with LTS out of all patients who presented at the ENT

Research Objective	Purpose of the analysis	Type of analysis conducted	Variables analysed
	been diagnosed with LTS		department with benign LTS
To describe the demographic characteristic of the patient population with LTS from 2010-2016	To show the demographic characteristics by number and proportions of patients who had been diagnosed with LTS	Descriptive statistical analysis: numeric and analysis of proportions	• Patient age (categorical variable) • Patient gender (categorical variable) • Patient maturity: adult versus children (categorical variable)
To determine the prevalence of LTS by grades among studied population	To highlight by number and proportions, the patients who had been diagnosed with LTS based	Descriptive statistical analysis: numeric and analysis of proportions	• Patient age (categorical variable) • Patient gender (categorical variable) Patient maturity: adult versus children (categorical variable) Versus grading based on the Myers-Cotton Classification
To evaluate the predictors of the LTS	To highlight the predictors (factors that contribute to severity) of LTS	Multinomial logistic regression modelling was chosen because we had more than three nominal categorical variables. To facilitate regression analysis, the following variables were divided into two groups: • The team responsible for endotracheal intubation was divided into trauma and the non-trauma group • The trauma population group included vehicle accidents, assault and stab injuries • The non-trauma population group ranged from medical conditions such as status asthmaticus, organophosphate poisoning, elective surgical procedures	The following hypothesis were tested: *Hypothesis 1:* The level of maturity (whether the patient was a child or an adult) is a significant predictor of LTS *Hypothesis 2:* The gender of the patient (male or female) is a significant predictor of LTS *Hypothesis 3:* The indication for intubation (elective procedure or emergency) is a significant predictor for LTS *Hypothesis 4:* The intubating discipline (trauma or non-trauma) is significant predictor for LTS. p-values were computed for each hypothesis to denote its contribution to the severity of LTS, using a confidence interval (CI) of 95%.

Research Objective	Purpose of the analysis	Type of analysis conducted	Variables analysed
		The nature of injuries as to whether they were penetrating, blunt or involving neck region were not analysed.	

Patients with missing information were excluded from the analysis.

2.6 Ethical Considerations

An ethical clearance application was submitted to the "Human Research Ethic Committee" (HREC) of the University of Witwatersrand and was approved with clearance certificate no. M180475 (see Appendix B). Permission was given by the Chief Executive Officer (CEO) of CHBAH (see Appendix C) to conduct the study. Patient confidentiality was maintained as the names of the patients were not recorded. Only codes were used. The data was saved in a password protected computer. The study only commenced after obtaining ethical clearance from HREC.

CHAPTER 3

3. Results

3.1 Research Question

The study sought to answer the following research question:

What is the prevalence and predictors of laryngotracheal stenosis at CHBAH?

The results of the study are presented in accordance with the research objectives as explained here below:

Objective 1

The first objective sought to determine the prevalence of LTS from 2010-2016.

In this study, prevalence is defined as a measure of the burden of disease in a population in a given location and at a particular time, as represented in a count of the number of people affected. [27] Over the period between 2010 and 2016, a total of 955 patients were admitted and recorded in the registers. Indication of admission of these patients ranged between emergencies and elective admissions. For purposes of analyses, only patients that were diagnosed with LTS by either the ENT specialist in training or a qualified ENT specialist, with full hospital records were included in the study. Figure 3.1 below shows the prevalence over the 7-year period.

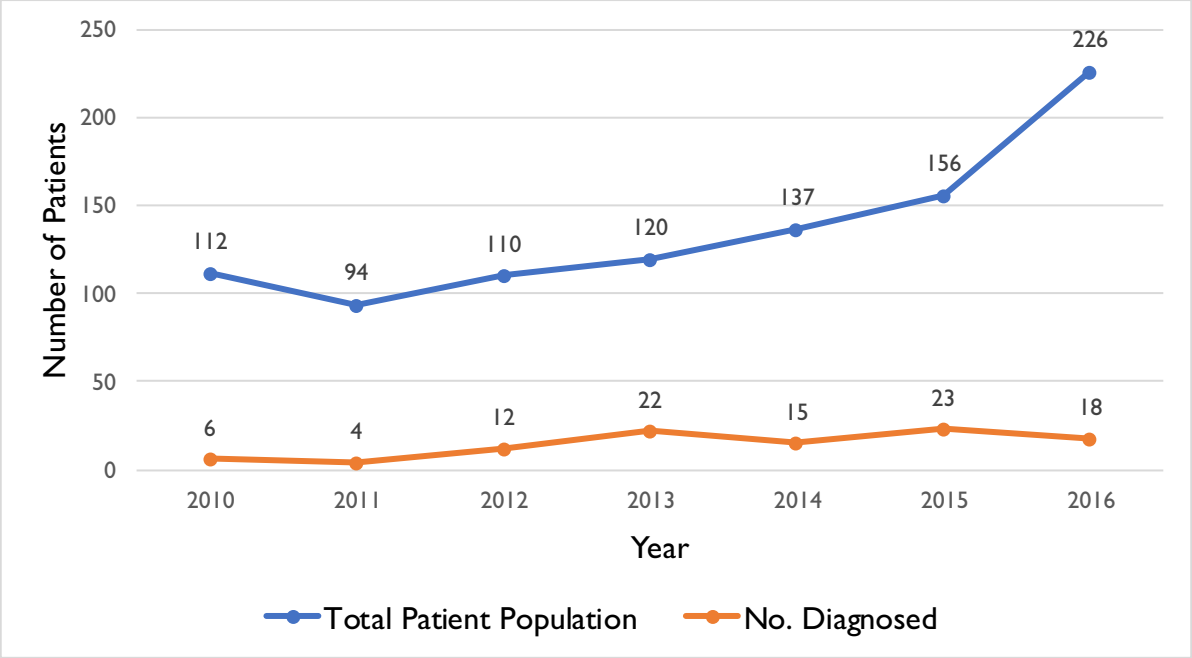

Figure 3.1: Prevalence of LTS from 2010-2016

According to Figure 3.1 above, after a slight drop between 2010 and 2011, there was a steady rise in patient admission into the ENT department up to 2016. The reasons that explain this steady rise are outside the scope of this study. In total, some 100 patients were diagnosed with LTS over the 7-year period, showing a prevalence rate of 10.47%. Considering year on year, there was a steady rise in the number of patients diagnosed with LTS between 2011 and 2013, rising from 4 to 22 (signifying a growth in prevalence from 2% to 6%). The number of patients diagnosed dropped in 2014 to 15 before rising again to 23 in 2015 and then dropping slightly in 2016 to 18.

Objective 2

The second objective sought to describe the demographic characteristic of the patient population with LTS from 2010-2016. Figures 3.2 to 3.4 below show these demographic features of the patients.

Patient Age: patient age was categorised into the following age group bins; < 1 year, 1-5 years, 6-10 years, 11-15 years, 16-20 years, 21-25 years, 26-30 years, and > 30 years. The proportion of the patients within these age group bins was then determined as shown in Figure 3.2 below.

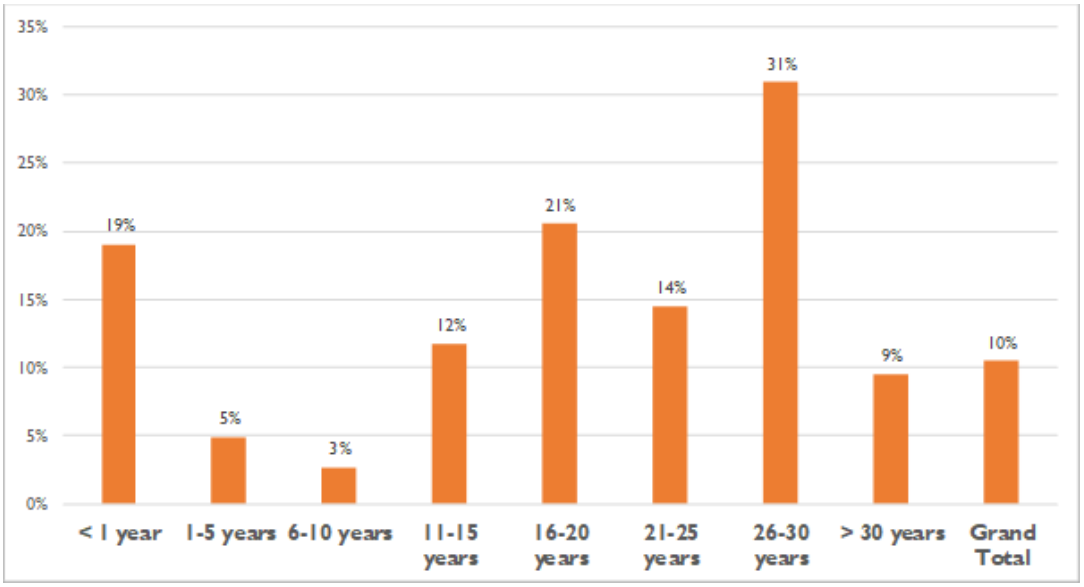

Figure 3.3: Proportion of LTS patients by age

From Figure 3.2 above, it appears that the most affected age group bin is the 26-30 years who constituted 31% of patients diagnosed with LTS. The next affected age groups which constituted more than 10% of the patients were the 16-20 years (21%), followed by less than 1-year (19%), 21-25 years (14%), and the 11-15 years (12%) age group. The least affected age group were the 6-10 years with only 3% of the patient population.

Patient Gender: overall, the proportion of patients of patients diagnosed with LTS were 65% male and 35% female. The distribution of patient gender over the years is shown on Figure 3.3 below.

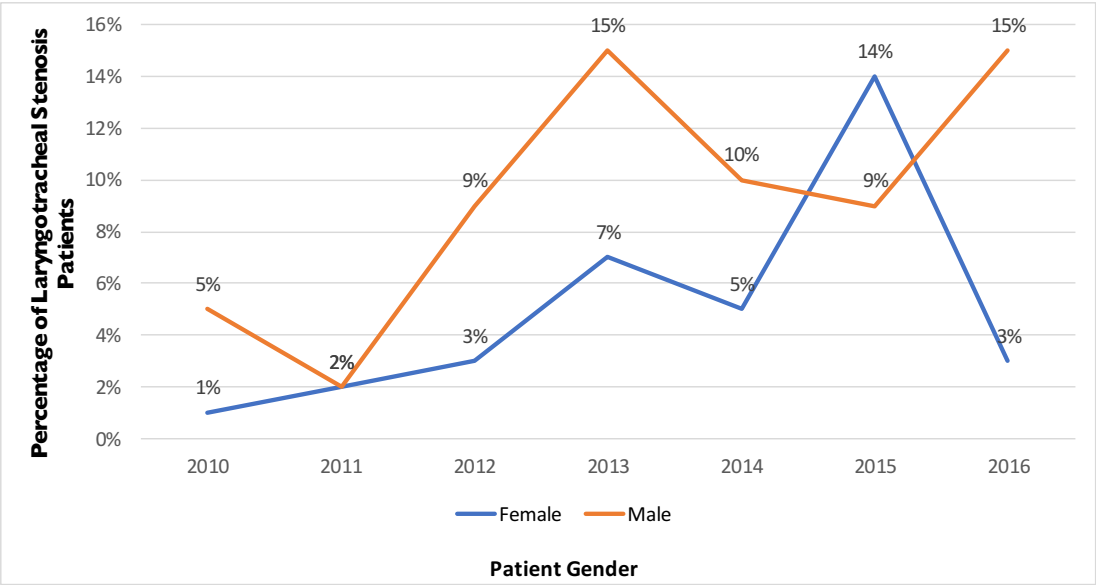

Figure 3.4: Gender Distribution of LTS Patients Year on Year

From Figure 3.3 above, it can be seen that there was a steady growth in the number of both male and female patients between 2011 and 2013. For females, the rate of diagnosis rose from 1% to 7%, before dropping to 5% in 2014, and rising significantly to 14% in 2014. For males, it started as high as 5% in 2010, slightly dropped in 2011 and then grew steadily up to 15% in 2013. In between 2014 and 2015, the female patient population exceeded that of their male counterparts, which was then dropping, before it saw a steady rise to 15% in 2016. Remarkably, while the male patient population was rising between 2014 and 2016, the female counterparts were experiencing a very steady fall up to only 3% by 2016.

Age and Gender Distribution of Patients: the graph that combines both age and gender distribution of patients is shown in Figure 3.4 below.

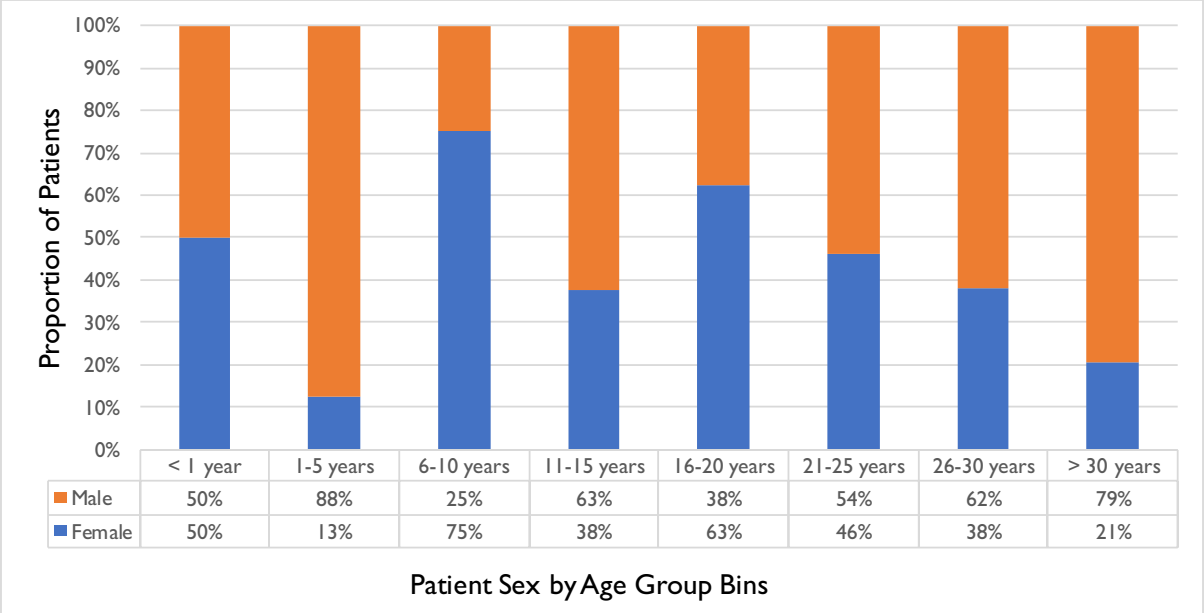

Figure 3.4: LTS Patients by Sex and Age Groups

According to Figure 3.4 above, it can be seen that female patients were predominant between the age groups of 6-10 years (75%) and 16-20 years (63%). The lowest female patient populations were between the age groups of 1-5years (13%) and greater than 30 (21%). The male patient population dominated the rest of the age groups.

Objective 3

The third research objective sought to determine the prevalence of LTS by grades or severity among the studied population.

The total number of patients with LTS were categorised according to Myers-Cotton classification as shown in Table 3.1 below.

Table 3.1: Myers-Cotton Classification: Circumferential stenosis limited to tracheal region[6]

Grade I	**Obstruction of 0%-50% of the lumen**
Grade II	Obstruction of 51%-70% of the lumen
Grade III	Obstruction of 71%-99% of the lumen
Grade IV	No detectable lumen; obstruction of 100% of the lumen

Based on this classification, all patients fell under Myers 1 to 3 as indicated in Figure 3.5 below. The majority of patients fell under severity level 3 (85%).

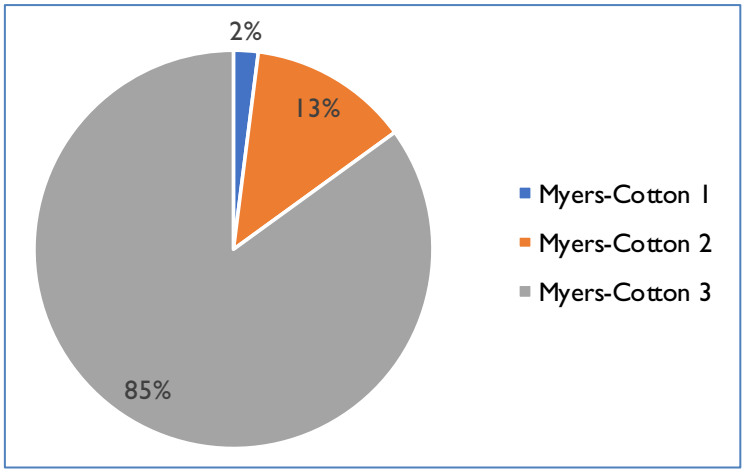

Figure 3.5: Classification of LTS patients by severity level

Figure 3.6 below shows severity level by gender of the patients.

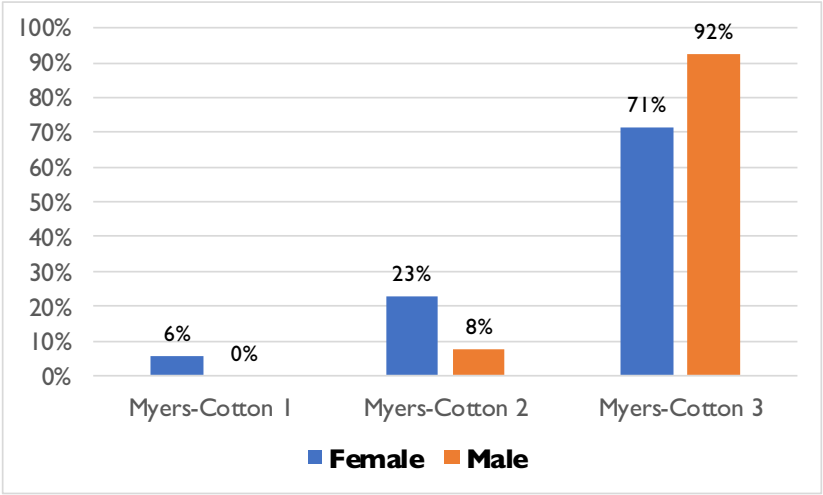

Figure 3.6: Severity Level of Gender of the Patients

Figure 3.6 above shows that female patients fell into all the three severity levels. However, the majority of both sexes experienced high severity levels, with 92% of males and 71% of females reaching Myers-Cotton 3.

Objective 4

This objective sought to determine the predictors of the severity of LTS.

The analyses conducted under this objective included evaluation of several variables which included the team responsible for endotracheal intubation and the reason for intubation. Both parameters were divided into 2 categories; the trauma and the non-trauma population group. The trauma population group included vehicle accidents, assault and stab injuries. The non-

trauma population group ranged from medical conditions such as status asthmaticus, organophosphate poisoning, elective surgical procedures. The nature of injuries as to whether they were penetrating, blunt or involving neck region were not analysed.

The summary of the team who intubated the LTS patients is given in Table 3.2 below:

Table 3.2: Proportion of Patients Incubated by the Specific Teams

Team Who Incubated	Proportion of Patients Incubated by Gender		Total
	Female	Male	
Anaesthetist	4%	3%	7%
Burns Unit	6%	10%	16%
Charlotte Maxete Johannesburg Academic Hospital Emergency Department (ED)	0%	1%	1%
Eastern cape ICU	0%	1%	1%
Hellen Joseph Hospital ED	1%	0%	1%
Klerksdorp ICU	0%	1%	1%
Medical Casualty	10%	8%	18%
Natal spruit ICU	0%	1%	1%
Neonatal ICU	2%	1%	3%
Paediatric ICU	0%	1%	1%
Trauma team	11%	38%	49%
Zimbabwe ICU	1%	0%	1%
Total	35%	65%	100%

It can be seen from Table 3.2 above that the majority of patients were intubated by the trauma team (49%), the medical casualty team (18%) and the Burns Unit (16%), together constituting 83% of the patient population. More males than females were intubated by the trauma team (38% versus 11%), and the burns unit (6% versus 10%); whereas more females than males were intubated by the medical causality unit (10% versus 8%).

Patients had various reasons for intubation, which are summarised in Table 3.3 below.

Table 3.3: Reasons for Intubation by Patient Gender

Reasons for Intubation	Proportion of Patients Incubated by Gender		Total
	Female	Male	
Motor vehicle accident (MVA)	12%	31%	43%
Blunt assault	1%	2%	3%
Status asthmaticus	3%	4%	7%
Burns injuries	6%	12%	18%
Chronic lung disease	1%	1%	2%
Near drowning	0%	2%	2%
Croup	0%	1%	1%
Gunshot	0%	3%	3%
Gynaecological procedure	3%	1%	4%
Organophosphate	4%	5%	9%
Paranasal surgery	1%	0%	1%
Patent ductus arteriosus	1%	0%	1%
Septic shock	3%	0%	3%
Sigmoid volvulus	0%	1%	1%
Stab wounds	0%	2%	2%
Grand Total	**35%**	**65%**	**100%**

According to the above table, the two main reasons for intubation were MVA accounting for 43% of the patient population and burns, accounting for 18%. More males than females were intubated for the same reasons.

In order to achieve the fourth research objective, multiple regression models were run to identify factors that influence or predict grading of LTS among the studied population. The following hypotheses were tested as predictors for severity:

- Hypothesis 1: The level of maturity (whether the patient was a child or an adult) is a significant predictor for severity of LTS
- Hypothesis 2: The gender of the patient (male or female) is a significant predictor for severity of LTS
- Hypothesis 3: The indication for intubation (elective procedure or emergency) is a significant predictor for severity of LTS

- Hypothesis 4: The intubating discipline (trauma or non-trauma) is a significant predictor for severity of LTS

Table 3.4 below summarises the results of the regression analysis:

Table 3.4: Regression Results for the four hypotheses

Variable	p-values
Level of maturity	0.58945
Gender	0.05584
Indication for intubation	0.07209
Intubating discipline	0.48363

Based on Table 3.4 above all the four hypotheses were proven false as they were not supported by the tests. All the variables were not significant enough to predict the severity levels of LTS as all the p-values were more than 0.05. The last factor, however, has far less significance than the other variables. However, there was evidence that the gender of the patient and the indication for intubation improved the p-values. However, improvement in the p-values did not reach significant levels. Regression analysis was repeated for the two factors that improved the p-values: gender of the patient and the indication for intubation. The results are as follows – Table 3.5 below:

Table 3.5: Regression Results for two variables

Variable	p-values
Gender	0.05233
Indication for intubation	0.07217

Table 3.5 above shows that the two variables gender of the patient and indication for intubation on their own were still not able to predict the levels of severity of LTS as their p-values were greater than 0.05.

CHAPTER 4

4. Discussion

The study sought to establish the prevalence and risk factors that affect the severity of LTS at CHBAH between January 01, 2010 and December 31, 2016. In particular, the study sought to fulfil the following research objectives:

- To determine the prevalence of LTS from 2010-2016
- To describe the demographic characteristic of the patient population with LTS from 2010-2016
- To determine the prevalence of LTS by grades or severity among the studied population
- To determine the predictors of the severity of LTS.

In this chapter, an attempt is made to put the results of the study into perspective and to locate them within the literature from previous studies.

4.1 Summary and Implications of Study Findings

Objective 1: To determine the prevalence of LTS from 2010-2016

The results of the study indicate that over the 7-year period between 2010 and 2016, some 100 patients were diagnosed with LTS, showing a prevalence rate of 10.47%. These figures seem to coincide with the steady rise in patients admissions into the ENT department. The results, however, seem to project a higher level of prevalence than has been documented in previous similar findings.

Prince et al. [28] and Webb et al.[29] indicate that the prevalence of LTS decreased substantially to about 1% after introduction of low-pressure cuff endotracheal tubes (ETTs). Similar conclusions on low prevalence rates were arrived at by Zias et al.[30] who conducted a retrospective chart review of 31 patients with post endotracheal intubation and post tracheostomy stenosis of all patients who were referred to the department of pulmonary and critical care at Lahey clinic, Burlington, Massachusetts. Gillespie et al.[31] reveal that a 2% incidence of LTS has been observed among patients who are intubated for less than 6 days, whereas the incidence increases to 12% among patients who are intubated for more than 10

days. They further explain that another study of 280 patients examined by endoscopy fewer than 6 months after an ICU admission found evidence of LTS in 7% of patients.

Objective 2: To describe the demographic characteristic of the patient population with laryngotracheal stenosis from 2010-2016

In a follow-up study of 100 patients evaluated for long-term symptoms and complications for tracheal stenosis at East Texas Medical Center, no differences in age, gender, days intubated before tracheostomy, days of tracheal cannulation, or perioperative complications were identified when patients with CT evidence of tracheal stenosis were compared with patients with no CT evidence of tracheal stenosis (Norwood, et al.[32]). According to Yaghchi and Sandhu[33] LTS can affect all age groups although the pathophysiology, management and long-term results vary between adult and paediatric patients. In children 95% of stenoses are post-intubation with the majority of others being congenital. In adults about 50% are due to ICU ventilation with the other causes being vasculitis, idiopathic, trauma, mucous membrane pemphigoid and sarcoidosis. Similarly, Alexander et al[34] found that the age at presentation differed significantly by strata (p=0.002) with those in the traumatic group being significantly younger than all others (34.4 years, CI 23.5 – 45.3).

Although there were more males (65% males compared to 35% females) diagnosed with LTS, this seemed to mirror larger male than female admissions rather than prevalence data, which seems to agree with previous studies.

Studies conducted by Mc Caffery et and Mehtal et al. reveal a predominance of females with tracheal stenosis, postulating that oestrogens increase the levels of transforming growth factor β1 promoting extracellular matrix production, including the deposition of type I and III collagens and finally fibrosis. The gender influence on the prevalence of LTS has attracted greater debate. A predominance of female with tracheal stenosis has been reported in two series by McCaffrey et al. and Mehta et al. respectively. Female predominance is also reported in cases of idiopathic subglottic stenosis. [35,36]

Objective 3: To determine the prevalence of laryngotracheal stenosis by grades among the studied population

The results indicate that all patients fell under Myers-Cotton 1 to 3, with the majority falling under Myers-cotton 3 (85%). Female patients fell into all the three severity levels. However,

the majority of both sexes experienced high grade disease, with 92% of males and 71% of females reaching Myers-Cotton 3.

Severe tracheal stenosis prevalence should be very low [7-9%] especially since the introduction of large volume, low pressure ETT cuffs, the careful placement of the tracheostomy stoma, avoidance of large apertures, elimination of heavy ventilatory connecting equipment, and meticulous care of the tracheostomy [37-39]. The challenge at CHBAH is that there is poor cuff pressure monitoring of ETT cuffs, which perhaps is one of the reasons why patients end up with LTS.[5] A study by Norwood et al. who followed 48 patients for 30 months after percutaneous tracheostomy using tracheal CT scans found that only 1 patient (2%) developed severe tracheal stenosis, while mild to moderate stenosis was detected in 29.3% patients. Norwood et al. concluded that although their department had a large referral network, their findings did not necessarily reflect the true prevalence of the condition [32].

Study findings reveal that most patients are involved in trauma (49%). Indication for intubation are divided into 2 groups, trauma group and non-trauma group. The study, however, does not show a significant effect on the indication for intubation. Findings from previous studies, however, present different reasons for intubation. According to Norwood, et al. and John, et al., several factors seem to contribute to severity of LTS including high tracheostomy site, prolonged intubation period, traumatic intubation, history of previous intubation or previous tracheostomy, excessive corticosteroid steroid usage, advanced age, female and oestrogen effect, severe respiratory failure, severe reflux disease, autoimmune diseases (Wegener's granulomatosis, sarcoidosis and others), obstructive sleep apnea, and radiation therapy for oropharyngeal laryngeal cancer. [20,32]

Objective 4: To determine the predictors of the severity of laryngotracheal stenosis

In this study, multiple regression models were run to identify factors that influence or predict levels of LTS among the studied population. These factors included: level of maturity; gender of the patient (male or female); indication for intubation (elective procedure or emergency); and the intubating discipline (trauma or non-trauma). Based on the data that was analysed, none of the variables were seen to have significant effect on the severity levels of LTS. From previous studies, it appears that intubation, congenital factors and injury, contribute to severity of LTS as explained below.

After analysing patient data between 1997 and 2005 and identifying 74 patients with LTS, Koshkareva et al.[40] found that the risk factors included prolonged intubation, tracheostomy, previous non-airway surgery, and irradiation for oropharyngeal and laryngeal tumours. According to Reiss and Tibboel[41] LTS is a congenital or acquired narrowing of the airway that may affect the glottis, subglottis, or trachea. Among children, severe symptoms can be seen either by multiple episodes of croup or croup that fails to respond to medical management or requires endotracheal intubation. Willging et al.[42] opine that acquired LTS is more common, occurring after manipulation or injury to the airway or resulting from prolonged or traumatic intubation, hypopharyngeal stenosis, secondary to trauma or caustic agent inhalation or ingestion, vocal fold paralysis as a result of surgical intervention, and tracheal stenosis following intubation. Jardine et al.[43] observe that LTS is most commonly seen as a complication of prolonged endotracheal intubation. Injury most commonly occurs in the larynx at the level of the cricoid cartilage. Laryngeal intubation injury appears to result from an interaction of several elements, including individual susceptibility, movement of the ETT, size of the ETT, presence of infection, and duration of intubation.

4.2 Limitations of the Study

This research has highlighted the characteristics of the patients who have been diagnosed with LTS between the period 2010 and 2016 and also indicated grading of LTS and reasons for intubation. However, the study was limited in its scope and did not include other important variables such as patients' co-morbidities, number of days ventilated (whether the patient has endotracheal intubation or tracheostomy), length of intubation, and their body mass index. With the limited scope, it is not possible with certainty, to draw firm conclusions on the prevention or management of LTS among children or adults.

4.3 Conclusion

The research highlights the high prevalence rates of laryngotracheal stenosis. In order to reduce the high prevalence, this study recommends close adherence to guidelines regarding cuff pressure monitoring and selection of appropriate sized ETTs.

4.4 Recommendations

Based on the results from this study the following recommendations are made:

Preventing the high prevalence rates of LTS: In order to reduce the high prevalence, this study recommends close monitoring of compliance to advanced trauma life support protocols among the intubating teams.

Expand the scope of the study: it is recommended that the scope of the study should be extended to better understand both the demographic and behavioural characteristics of the patients against treatment outcomes so as to obtain a deeper insight on how LTS can be better prevented and/or managed. Increasing the study scope will also enable expansion of analytical techniques that will reveal better insights.

Follow up on studied patients: It is recommended that the patients whose details were analysed should be identified and followed up to better understand how their condition was managed. This will enable better analysis of treatment outcomes.

Expand the scope to include other hospitals: it is advised that this study should be extended to other similar hospitals to better understand patient characteristics and how they are managed. This will form a basis for further studies that will explore the prevention or management of LTS among the different patient populations and other contextual factors.

CHAPTER 5

5. Summary

The study established a high prevalence rate of LTS over a seven-year period (2010-2016) which was at 10.47%, with the most affected age group being the 26-30 (31%).

Factors including level of maturity; gender of the patient (male or female); indication for intubation (elective procedure or emergency); and the intubating discipline (trauma or non-trauma) had no significant influence on the grades of LTS.

This research offers important insights on the characteristics of the patients who have been diagnosed with LTS over the years. It is therefore highly recommended that there is close adherence to guidelines regarding cuff pressure monitoring and selection of appropriate sized ETTs.

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Appendix A: Data Collection Sheet

Title: Prevalence and predictors of laryngotracheal stenosis at Chris Hani Baragwanath Academic Hospital

Code:

Age:

Sex:

Who intubated:

Clinical findings:

Findings at direct laryngoscopy/ tracheal resection:

Appendix B: Ethics Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr B Tselapedi

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M180475

NAME: (Principal Investigator)	Dr B Tselapedi
DEPARTMENT:	School of Clinical Medicine Department of Otorhinolaryngology Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Prevalence and predictors of laryngotracheal stenosis at Chris Hani Baragwanath Academic Hospital
DATE CONSIDERED:	04/05/2018
DECISION:	Approved unconditionally
CONDITIONS:	Study title change noted on 01/08/2019
SUPERVISOR:	Dr Y Atiya
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	11/05/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. I **agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **April** and will therefore reports and re-certification will be due early in the month of **April** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

04/06/2018
Date

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES

Appendix C: Letter of Permission

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE
CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 29 March 2018

TITLE OF PROJECT: Prevalence and predictors of laryngotracheal stenosis at Chris Hani Baragwanath Academic Hospital

UNIVERSITY: Witwatersrand

Principal Investigator: B Tselapedi

Department: ENT

Supervisor (If relevant): Y Atiya

Permission Head Department (where research conducted): Yes

Date of start of proposed study: March 2018
Date of completion of data collection: Dec 2020

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Hospital. The CEO /management of Chris Hani Baragwanath Hospital is accordingly informed and the study is subject to:-

- Permission having been granted by the Human Research Ethics Committee of the University of the Witwatersrand.
- the Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- the MAC will be informed of any serious adverse events as soon as they occur
- permission is granted for the duration of the Ethics Committee approval.

.....
Recommended
(On behalf of the MAC)
Date: 29 March 2018

.....
Approved/Not Approved
Hospital Management
Date: 04/5/18