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Acquired subglottic stenosis in children younger than 1 year in a resource-restricted hospital in South Africa

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Background. Subglottic stenosis (SGS) is a congenital or acquired condition and is the most common site of airway narrowing in children. The pathogenesis of SGS includes subglottic mucosal pressure necrosis, leading to mucosal ulceration, perichondritis and mature scar formation. Acquired SGS accounts for 90% of laryngotracheal stenosis in children.
Objectives. To describe the associated disease factors, management and outcomes of infants with acquired SGS in a middle-income country.
Methods. A retrospective, descriptive study was performed between January 2018 and August 2022, including all infants aged ≤1 year who had bronchoscopically confirmed SGS. Data regarding demographics, intubation and invasive ventilation, various disease parameters, findings at bronchoscopy and short-term outcomes were collected. Descriptive statistical analysis was performed. Ethical approval was provided by Stellenbosch University.
Results. During the research period, 44 infants were diagnosed with acquired SGS, of whom 29 were included in the study. Most infants were born at term and underwent diagnostic bronchoscopy at a mean chronological age of <2 months. All infants were intubated and ventilated at birth, for a variety of diagnoses. Bronchoscopy showed grade 2 or worse stenosis in the majority, and most infants were managed successfully with balloon dilatation. An inappropriately sized endotracheal tube was used in 52% of infants, one-third of infants required multiple invasive ventilation periods, and one-third experienced unexpected extubation episodes.
Conclusion. In a resource-limited setting, SGS often develops as a result of preventable causes, with the majority of children being successfully treated with endoscopic procedures.

Keywords. Subglottic stenosis, bronchoscopy, stridor, HIV exposed, balloon dilatation.

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Study synopsis
What the study adds. The characteristics and management of subglottic stenosis (SGS) in infants aged ≤1 year are described in this retrospective study done at Tygerberg Hospital, South Africa. This is the first report of acquired SGS in infants aged ≤1 year from a resource-limited setting. Potential preventable risk factors were identified, specifically looking at the tertiary referral setting. The most common factor was use of an endotracheal tube (ETT) of the incorrect size. A few possible novel associations were also identified, that require further investigation. Balloon dilatation was noted to be an effective treatment option, and is feasible for use in resource-limited settings.
Implications of the findings. The findings of this study highlight the importance of having correct intubation practices in place to reduce the risk of acquired SGS. Training, supervision and correct documentation of airway management will contribute to a reduction in intubation attempts and unplanned extubations, and improve knowledge on the correct size of ETT to be used. The findings also support the effectiveness of balloon dilatation as a treatment option in a resource-limited setting.

The subglottis, extending from below the vocal cords to the lower border of the cricoid cartilage, is entirely cartilaginous, making it susceptible to stenosis (Fig. 1).

Subglottic stenosis (SGS) can either be congenital or acquired, with acquired SGS accounting for 90% of paediatric laryngotracheal stenosis.[1,2]

SGS is defined as a lumen of <4 mm in a term infant and <3 mm in a preterm infant.[1,3] It occurs mainly as a result of mucosal ulceration and the subsequent formation of mature scar tissue following mucosal pressure necrosis. Most commonly, mucosal pressure necrosis is due to endotracheal intubation.[4,5]

Acquired SGS is more common than congenital SGS, but with a

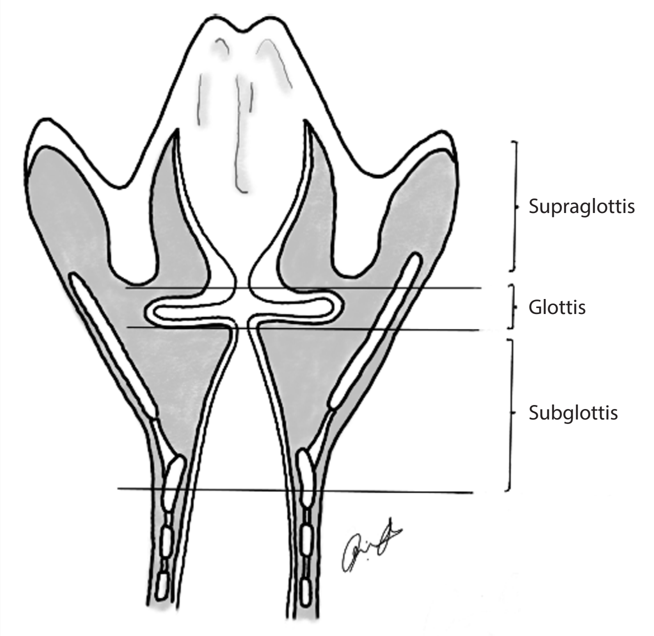

Fig. 1. Anatomy of the larynx.

variable prevalence.[6,7] In the past, acquired SGS was less frequent, with the most common cause being laryngeal infections such as diphtheria, with necrosis being due to endotoxin-induced mucosal damage.[8] This has now decreased significantly owing to the introduction of diphtheria vaccinations. Endotracheal intubation has now become the most common cause of acquired SGS.[1,6]

In an Australian study of 50 infants and children, the prevalence of acquired SGS was 0.93%.[6] This study also supported previous literature indicating an association between the size of the endotracheal tube (ETT) and the development of SGS.[8-11] Various factors have been associated with SGS. Some variables have been confirmed (level of sedation and gastrooesophageal reflux), while others have less evidence of association (age, weight, gender, duration of intubation, multiple intubations, traumatic intubation, tube size, absence of air leak, and infection).[12]

Bronchoscopy can be used for diagnosis and management in SGS. It remains the gold standard for grading airway obstruction severity.[1] SGS management is via a variety of endoscopic or open surgical procedures. Endoscopic management can be used as a primary treatment modality or as an adjuvant treatment before and after surgery.[1]

There is a paucity of data on acquired SGS in South Africa (SA) and other low- and middle-income countries (LMICs), despite the clinical relevance of the condition. These regions report high birth and preterm birth rates, yet awareness and recognition of airway complications such as SGS remain limited. Furthermore, initial management of affected neonates and infants often occurs at lower-tier healthcare facilities, frequently by less experienced medical personnel, which may delay diagnosis and contribute to suboptimal outcomes.

Most of the current literature is based on data from high-resource countries and their outcomes. The aim of this study was to describe the characteristics and management of infants ≤1 year of age diagnosed with SGS at Tygerberg Hospital, an academic referral hospital in Western Cape Province, SA, a middle-income country.

The Health Research Ethics Committee (HREC) of the Faculty of Medicine and Health Sciences at Stellenbosch University, Cape Town, SA, granted consent for this research (ref. no. S21/11/239).

Methods

A retrospective, descriptive study was conducted between January 2018 and August 2022, including all infants aged ≤1 year with bronchoscopy-confirmed SGS admitted to the neonatal and paediatric intensive care units at Tygerberg Hospital.

Tygerberg Hospital is a tertiary care facility with 132 neonatal beds. It serves as a referral centre for complicated and high-risk pregnancies, as well as for neonates requiring ventilation, increased non-invasive respiratory support or surgical intervention. The hospital has ~8 000 annual births, but is responsible for tertiary-level maternity services for an area delivering ~50 000 infants annually.

Infants were identified from an existing paediatric and neonatal bronchoscopy database, a bronchoscopy theatre book, and an existing ear, nose and throat surgical intervention database. Children who were diagnosed with SGS after the age of 1 year, infants with congenital SGS or other congenital airway abnormalities, amd infants with missing critical data regarding intubation were excluded. Collected information included demographic data and illness data (including sepsis and respiratory disease), intubation data (intubation, endotracheal intubation attempts, size of ETT, any episodes of unexpected extubation) and any mechanical ventilation data (number and duration of episodes of invasive ventilation). Bronchoscopy data were also collected.

An unplanned extubation is defined as the unintentional dislodgement of an ETT in a patient receiving invasive mechanical ventilation.

The appropriateness of the size of the ETT was determined using the Cincinnati airway card app (developed by the Division of Pediatric Otolaryngology, Cincinnati Children's Hospital, USA).[13] This app facilitates calculation of the Myer-Cotton grading. Myer and Cotton developed a score that helps to objectively assess the grading using ETT sizes.[14] Sepsis was defined as culture-positive sepsis, on blood culture, cerebrospinal fluid or urine, within 2 weeks of intubation as per previous studies.[6,15]

Normal intubation practice at Tygerberg Hospital is to intubate infants weighing <4 kg with an uncuffed ETT, with the predominant route being nasopharyngeal. Older, larger infants are intubated orally with a cuffed ETT. Bronchoscopy is standard practice for all infants with prolonged stridor, those who have more than two episodes of failed extubation attempts due to upper airway obstruction, or those with persistent stridor post ventilatory support. Both flexible and rigid bronchoscopy are performed under anaesthesia. SGS is graded using the Myer-Cotton classification.[4,14] The Myer-Cotton classification is based on the degree (%) of stenosis; it is the most widely recognised classification, and is the one used at Tygerberg Hospital. Computed tomography (CT) scans were done in selected patients where surgical planning was needed or if vascular or pulmonary anomalies were suspected.

Research was allowed to be performed using a waiver of informed consent, as approved by the HREC of Stellenbosch University. The research was performed in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

Data were described using means and standard deviations or medians and interquartile ranges, depending on normality of data. Categorical data were described using numbers and percentages.

Stata 18 (StataCorp, USA) was used for statistical analysis.

Results

Sixty-four cases of confirmed SGS were identified between 2018 and 2022, of which 44 were in infants aged ≤1 year. Five infants were excluded owing to missing data and 10 infants were excluded owing to a diagnosis of congenital SGS (Fig. 2). The final study cohort was 29 infants. The proportion of patients with acquired SGS aged ≤1 year, relative to all children with SGS in the time period, was 45%.

Demographic characteristics are shown in Table 1. Most infants were born at term gestational age and transferred to Tygerberg Hospital from other medical institutions. One-third of the infants were HIV exposed but uninfected (HEU). Of those who were HEU, 20% were small for gestational age and 20% were premature with very low birthweight or extremely low birthweight. The mean chronological age at admission for bronchoscopy was <2 months, and 52% of the infants were underweight for age at the time of bronchoscopy.

Indications for intubation varied, including stridor (41%; *n*=12), pneumonia (24%; *n*=7) and other causes (34%; *n*=10). Of the 12 intubations for stridor, 9 were due to previous intubation for neonatal reasons (respiratory distress syndrome *n*=3, meconium aspiration syndrome *n*=2, congenital pulmonary airway malformation *n*=1, hydrops fetalis *n*=1, bilateral vocal cord palsy *n*=1 and laryngeal web/cyst *n*=1). One infant had a retropharyngeal abscess, and there were 2 cases of croup. Other causes for intubation included necrotising fasciitis, organophosphate poisoning, post-cardiac surgery sepsis, viral encephalitis, necrotising enterocolitis, lower respiratory tract infection, pulmonary haemorrhage, severe dehydration, and prematurity.

All infants were intubated and ventilated within the first month of life. A larger than age-appropriate ETT was used to intubate 52% (*n*=15) of the infants.

Most infants were successfully intubated at the first attempt (52%). One-third of the infants had failed extubation episodes, and one-third experienced unexpected extubations (Table 2). The mean duration of invasive ventilation was <10 days, and that of non-invasive ventilation was <14 days. Most infants developed post-extubation stridor, and most received corticosteroids (Table 2). Sepsis within the first 2 weeks of intubation was noted in fewer than half of the study cohort.

At bronchoscopy, two-thirds of the infants had grade 2 or worse stenosis (Table 3). Most infants required intervention, of whom most were managed with balloon dilatation only (65%; *n*=19), balloon dilatation and surgical management (14%; *n*=4), and surgical management only (7%; *n*=2), with only 4 (14%) never requiring any endoscopic intervention. More than one session of balloon dilatation was required in 57% (*n*=13/23) of the infants. Surgical intervention consisted of placement of a tracheostomy or performance of a cricoid split with thyroid alar graft augmentation procedure. A tracheostomy was placed as an emergency procedure in 2 infants with severe SGS and bilateral vocal cord paralysis with side-to-side narrowing on a subsequent scope post intubation, and in 2 infants after failed endoscopic dilatation. Tracheostomy placement occurred at a mean age of 8 months (Table 3).

Six infants underwent CT scans for clinical management as well as surgical planning. Three cases showed significant parenchymal changes, 2 showed subglottic narrowing, and 1 showed vascular compression.

Discussion

Limited studies have looked at infants ≤1 year of age with acquired SGS in LMICs. Infants with acquired SGS showed a high prevalence of prematurity, underweight for age, emergency intubations, unexpected extubations, repeated intubations, multiple intubation attempts, and sepsis.

The incidence of acquired SGS has been stated to be 1 - 8% and up to 4.5 per 100 000 live births.[16,17] The present study was unable to determine an incidence owing to the large number of infants transferred to the referral centre from other medical institutions. The proportion of patients with aquired SGS aged ≤1 year relative to all children with SGS in the time period was 45%, lower than in a Serbian paediatric study (68.4%).[18] The present study showed a high prevalence (34%) of HEU infants with SGS. This is a novel finding. as HIV has not previously been shown to be associated with acquired SGS. However, the HIV exposure rate in Western Cape is 19 - 31%,[19,20] which may explain the prevalence in the present study.

In the present study, nearly half the cohort was premature. This is lower than in Argentinian (67%) and US cohorts (66%),[21,22] but higher than the figure in a European paediatric cohort (25%).[18]

Unplanned extubations can be decreased by improved staff awareness of the problem. It has been shown that having two licensed professionals involved when performing any procedure on an intubated patient can reduce the number of unplanned extubations.[23]

A study has shown that four episodes of unplanned extubations and documentation of trauma during intubation attempts have been associated with an increased risk of acquired SGS.[24] Another study showed a 3.5-fold increase in the risk of SGS with more than five intubation attempts.[6]

Multiple intubation attempts occurred less frequently (24%) in the present study compared with the 55% found in another study.[24]

The duration of invasive ventilation has also been associated with an increased risk of SGS. It has been shown that for every additional 5 days' duration of intubation, the risk of SGS increased by 50.3%.[25] It has also been shown that even a 24-hour mechanical ventilation period could trigger stridor and lead to the onset of SGS.[26] The mean duration of invasive ventilation in the present study (<10 days) was shorter than in various other studies (20 - 65 days).[6,21] The discrepancy in duration could be due to the small sample size in the present study, as well as the inclusion of more immature infants in some studies.

An association between ETT size and the subsequent development of SGS has been shown in multiple studies.[9-11,27] A formula to guide the selection of an ETT of appropriate size for neonatal intubations based on gestational age was proposed by Sherman *et al*.[11] and Sherman and Nelson.[28] An ETT size/gestational age of <0.1 has been shown to significantly decrease the prevalence of SGS in neonates. The present study showed that an ETT of incorrect size was used in

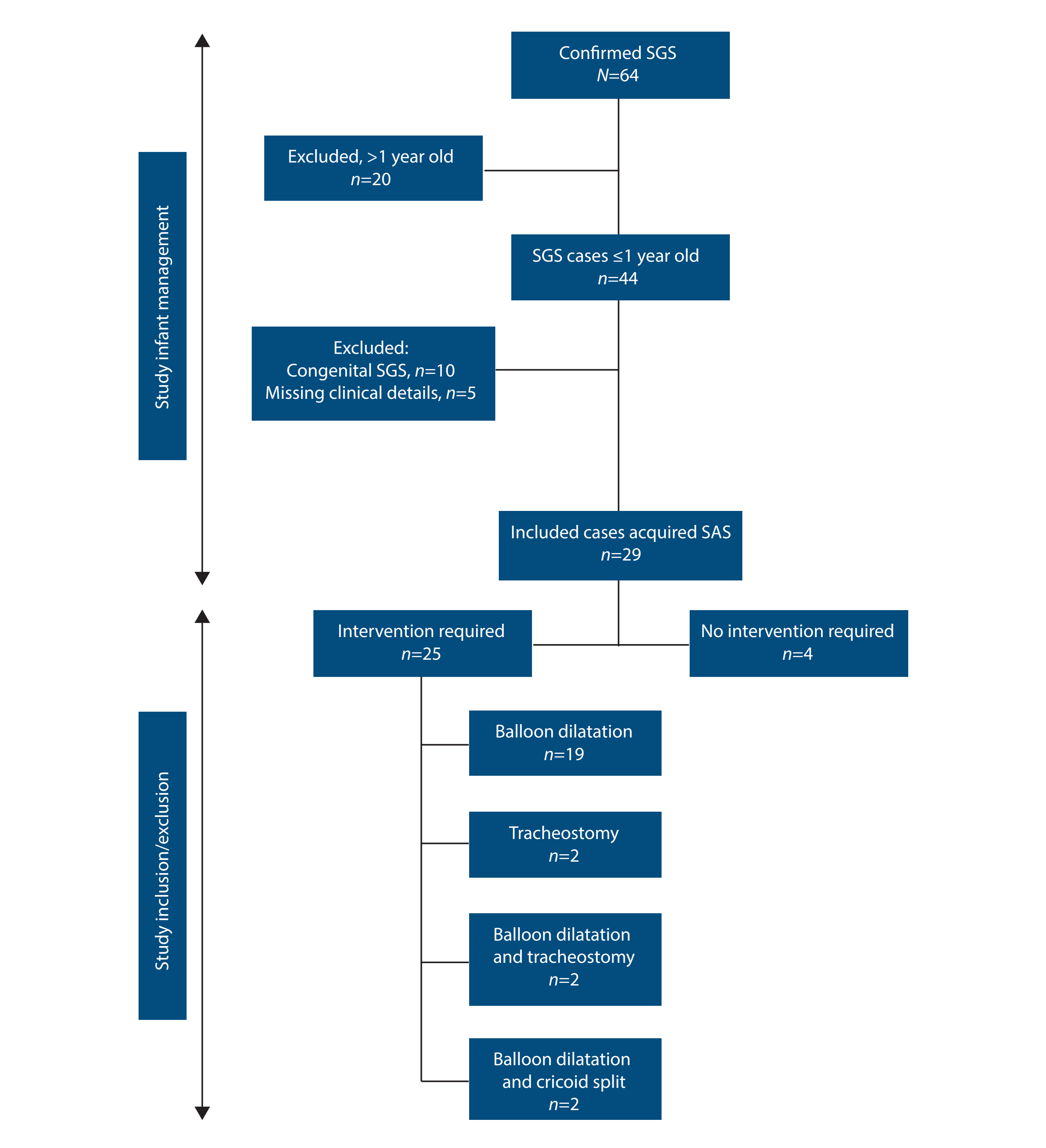

Fig. 2. Inclusion and management of infants with acquired SGS. (SGS = subglottic stenosis.)

just over half of the infants, similar to an Australian study (57%).[6] An oversized ETT has been shown to increase the risk of SGS 6-fold.[6]

Emergency intubation was performed in most of the infants in the present study. Few studies are available showing outcomes for emergency v. elective intubations in neonates and infants.[29-31] Non-elective intubations have been shown to be associated with an increased prevalence of post-extubation stridor.[32] It is therefore biologically plausible that rushed emergency intubations may lead to more traumatic intubations, resulting in a higher risk of SGS. Successful first-attempt intubations may be enhanced by the use of an appropriately sized ETT, video laryngoscopy and sufficient training. Video laryngoscopy has been shown to improve intubation success and has been endorsed by the British and European anaesthetic associations for use in neonates and children.[33]

Unplanned extubation is a known risk factor for acquired SGS. This complication can be prevented by ensuring that the ETT is

Table 1. Demographic characteristics (*N*=29)

Variable	*n* (%)*
Birth demographics	
Male	15 (52)
Gestational age at birth (weeks), mean (SD)	35.7 (4.8)
Premature (<37 weeks' gestational age at birth)	13 (45)
HEU	10 (34)
Birthweight	
Normal	13 (45)
LBW	5 (17)
VLBW	8 (28)
Unknown	3 (10)
Demographics at time of bronchoscopy	
Born at Tygerberg Hospital	9 (31)
Age at first scope (months), median (IQR)	1.2 (0.3 - 7.1)
Weight at first scope (kg), mean (SD)	4.6 (2.7)
UWFA at admission	15 (52)
Reason for admission	
Stridor (incl. post-extubation stridor)	12 (41)
Pneumonia	7 (24)
Other	10 (34)

SD = standard deviation; IQR = interquartile range; HEU = HIV exposed but uninfected;
LBW = low birthweight; VLBW = very low birthweight;
UWFA = underweight for age (*z*-score <–2) on the World Health Organization growth chart for children and according to Fenton and Kim[41] for neonates.
*Except where otherwise indicated.

Table 2. Intubation and ventilation characteristics (*N*=29)

Variable	*n* (%)*
Type of intubation	
Elective	3 (10)
Emergency	26 (90)
Age at intubation (months), median (IQR)	0.8 (0.1 - 1.7)
Total duration of intubation (days), mean (SD)	9.9 (7.0)
Intubation attempts	
Single	15 (52)
Multiple	7 (24)
Unknown	7 (24)
Unexpected extubations	
None	15 (52)
Multiple	9 (31)
Unknown	5 (17)
Inappropriate ETT size†	15 (52)
Type of ventilation	
Conventional	24 (83)
High-frequency ventilation	5 (17)
Duration of non-invasive ventilation (days), mean (SD)	12.9 (11.9)
Post-extubation stridor	24 (83)
Use of steroids for stridor	25 (86)
Sepsis episodes within 2 weeks of intubation	
None	15 (52)
Single episode	8 (28)
Multiple (≥2) episodes	6 (20)

IQR = interquartile range; SD = standard deviation; ETT = endotracheal tube.
*Except where otherwise indicated.
†According to the Cincinnati scale.[13]

properly secured and remains in place, particularly during patient movement or transport – especially from referral hospitals. The number of intubation attempts should be accurately documented in the clinical notes; this information was notably lacking in the present study. It is essential that medical personnel are trained to select the correct ETT size. The Cincinnati airway card app[13] is an easily accessible reference. Regular training and skills refreshers in neonatal intubation should be mandatory for all medical staff to ensure competence and consistency in practice.

The definition of stridor has been described differently in various studies, leading to different prevalences of stridor post extubation.[34,35] Most infants in the present study developed post-extubation stridor. Depending on definitions and inter-rater variability, the incidence of post-extubation stridor is 7 - 41%.[26,29,36] The prevalence in the present study remains higher than that described in these studies.

In the early 20th century, infection remained the primary cause of SGS.[8] However, in the late 20th century, trauma became the primary cause of SGS in infants and children.[8] Few studies have described the association between sepsis and SGS. Respiratory failure due to viral infections has been associated with SGS.[37] Respiratory tract infections may increase the risk of bacterial colonisation in the subglottic space. Bacteria then colonise the damaged subglottis, resulting in focal infection and granulation formation.[5,38] The present study showed that almost half of the patients had one or more episodes of infection within the first 2 weeks of intubation. More research is needed into the correlation between infection and the development of SGS.

The present study showed that one-third of the infants had grade 3 or higher SGS. This is lower than in Turkish (54%)[3] and Canadian studies (68%),[6] but higher than in Saudi Arabian (20%)[4] and Singaporean studies (16.7%).[17] The reason remains unknown and more research is needed. The grade of SGS is associated with the need for treatment, whereby infants with grade 1 SGS may be able to be observed, and grades 2, 3 and 4 will require intervention.[6]

Studies have reported that endoscopic balloon dilatation is successful in 90 - 95% of patients with acquired SGS over a short-term follow-up.[39,40] The present study showed an 82% success rate of balloon dilatation as the only management, with a failure rate of 17%. The lower rate compared with the literature may be due to later diagnosis, a different patient population and a high rate of HIV exposure, with well-established fibrosis by the time dilatation is attempted. The number of dilatations required in this study is in line with international literature, showing that multiple dilatations are often required in infants and children with SGS.[4,39]

This study has several limitations. It was a retrospective study performed in an academic referral centre, which restricts the generalisability of the findings. Various datapoints were also missing, which may have influenced the interpretation of the data. The background HIV and sepsis rate of the research centre must be borne in mind when interpreting the association between these parameters

Table 3. Interventions for subglottic stenosis (*N*=29)

Variable	*n* (%)*
Age at scope (months), median (IQR)	1.8 (1 - 6)
Subglottic stenosis grading†	
Grade 1 (<50%)	4 (14)
Grade 2 (51 - 70%)	10 (34)
Grade 3 (71 - 90%)	9 (31)
Grade 4 (91 - 100%)	0
Unknown	6 (21)
Intervention, *n* (%)	
None	4 (14)
Endoscopic (dilatation)	23 (79)
Endoscopic only	19 (65)
Endoscopic and surgical	4 (14)
Surgical	6 (21)
Tracheostomy	4 (14)
Cricoid split	2 (7)
Age at tracheostomy (months), mean (SD)	8 (5)
Number of dilatation sessions	
Single	10/23 (43)
Multiple	13/23 (57)
Number of bronchoscopies, median (IQR)	3 (2 - 4)
CT	6 (21)
Age at CT (months), median (IQR)	4.8 (0.3 - 10)

IQR = interquartile range; SD = standard deviation; CT = computed tomography.
*Except where otherwise indicated.
†Myer-Cotton scale.[14]

and acquired SGS. The level of training and experience of the staff performing intubations was not recorded in this study; however, these factors are likely to vary significantly and are critical in determining the success and safety of the procedure. This study was performed at a tertiary hospital on a selective group of predominantly critically ill infants, which may influence the findings. More research is needed into the association between these parameters and SGS.

Conclusions

This is the first report of acquired SGS in infants aged ≤1 year from a resource-limited setting. The prevalence was similar to that reported in some international literature. Many associated factors were similar to those found in international literature – prematurity, inappropriate ETT size, post-extubation stridor, multiple intubation attempts, and unexpected extubations. HIV and sepsis within 14 days of intubation may be novel findings, but require more research. Most infants were successfully treated with balloon dilatation, showing the feasibility of this management in a resource-limited setting.

Data availability. The datasets generated and analysed during the present study are available from the corresponding author (TK) on reasonable request. Any restrictions or additional information regarding data access can be discussed with the corresponding author.

Declaration. The research for this study was done in partial fulfilment of the requirements for TK's MMed (Paed) degree at Stellenbosch University. PG is a member of the editorial board.

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Conflicts of interest. None.

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