A retrospective review of all children admitted with acute severe asthma to the paediatric intensive care unit, Red Cross War Memorial Children's Hospital between 2009-2019.

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Abbreviations

ASA	Acute severe asthma
BiPAP	Bi level positive airway pressure
HFNC	High flow nasal cannula
HFOV	High frequency oscillatory ventilation
HELIOX	Helium-oxygen mixture
IQR	Interquartile range
LOS	Length of stay
LV	Length of ventilation
NHLS	National Health Laboratory Service
NIV	Non-invasive ventilation
NPA	Nasopharyngeal aspirate
PCAC	Pressure control assist control
PICU	Paediatric intensive care unit
PIM score	Paediatric index of mortality score
PRVC	Pressure regulated volume control
RCWMCH	Red Cross War Memorial Children's Hospital
RSV	Respiratory syncytial Virus
SD	Standard Deviation
TA	Tracheal Aspirate
VC-SIMV	Volume control synchronised intermittent mandatory ventilation

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Publication-ready manuscript

The following manuscript has been prepared for submission to The Southern African Journal of Critical Care. The journal's aims and scope, as well as author guidelines are given in Appendix A.

A retrospective review of all children admitted with acute severe asthma to the paediatric intensive care unit, Red Cross War Memorial Children's Hospital between 2009-2019.

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Abstract

Background and Aim

Asthma is one of the commonest chronic conditions of childhood and affects children worldwide. The majority of children who experience an acute exacerbation of asthma do not require admission to a paediatric intensive care unit (PICU). There is limited data on the admission rates, treatment modalities and length of PICU stay, for children who have acute severe asthma (ASA) in a South African context. In this study, we aim to describe the patient profiles and treatment of all children admitted to the PICU with ASA.

Method

We conducted a retrospective audit of all children admitted with ASA to the paediatric intensive care unit at Red Cross War Memorial Children's Hospital in Cape Town, South Africa between 01 January 2009 - 31 December 2019.

Results

There were 14592 PICU admissions over the 11-year period, of which 180 admissions (1,2%) were for acute severe asthma. There were 96 male (53,3%) admissions and the median, interquartile range (IQR) age on admission was 67 (37 – 93) months. Nearly all the patients received nebulisations, steroids, and magnesium sulphate before PICU admission. Half of the patients were loaded with IV salbutamol (n=96; 53,3%) and about a third (n=61; 34%) received a salbutamol infusion before admission to PICU. Similar proportions received nebulisations and steroids in PICU, 34 patients (19%) received magnesium sulphate again in PICU and a total of 130 patients (72,2%) received a salbutamol infusion. Most children received non-invasive respiratory support (n=167; 90,3%), and 18 children (9,7%) required mechanical ventilation for a median (IQR) of 3 (2 – 4) days. The median PICU stay was 1 (IQR 1 – 2) days and median hospital stay was 4 (IQR 3 – 6) days. No children died.

Conclusion

There has been an increasing number of children admitted to PICU with ASA over the 11-year period. There has been increased utilization of non-invasive ventilation (NIV) strategies, mainly HFNC and the duration of PICU support is short.

Introduction

Asthma is one of the commonest chronic conditions of childhood and affects children worldwide. Asthma is characterised by chronic airway inflammation and respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough which varies in time and intensity, together with variable expiratory airflow obstruction[1,2]

Asthma is said to affect 339 million people based on the most recent global report[3]. Asthma prevalence worldwide, measured by symptoms was 11,5% and 14,1% in children aged 6-7 years and 13-14 years [4]. Black African children had a prevalence of 15,3% in children aged 13-14 years[4]. In South Africa the prevalence increased between 1995 -2002 from 16% to 20,3% in children aged 13-14 years[4,5].

Acute severe asthma can be defined as severe asthma that is unresponsive to repeated courses of beta-2 agonist therapy such as inhaled salbutamol[6,7]. It is a medical emergency that requires immediate identification and management. There are good evidence-based asthma guidelines for the management of acute exacerbations and[2] children with acute severe asthma (ASA) have a relatively good outcome with a low mortality rate.[8][9] However, these patients often have a higher rate of readmission, increased chance of requiring PICU in the future and increased risk of mortality.[10–12]

The majority of children with ASA do not require PICU admission.[13,14] However, a small percentage of patients will require escalation of support, closer monitoring, and aggressive treatment plans. Reports show an increasing number of children requiring admission to PICU in several countries.[8,9,14] There is limited data to guide the management of children with ASA in PICU,[8,9] resulting in considerable variation in management strategies in different units.

There is limited data on the admission rates, treatment modalities and length of PICU stay, for children who have ASA in a South African context. This data could be utilised to update current management protocols, assist in medical training, and ultimately improve outcomes in patients with ASA. The aim of this study is to describe the patient profiles and treatment of all children admitted to the PICU with ASA over an 11- year period.

Methods

Study design

We conducted a retrospective audit of all children admitted with ASA to the paediatric intensive care unit at Red Cross War Memorial Children's Hospital (RCWMCH), Western Cape, South Africa between 01 January 2009- 31 December 2019.

Study setting

Red Cross War Memorial Children's Hospital is a Tertiary referral hospital in the Western Cape and is affiliated with the University of Cape Town. It serves the Western Sub-district of the Cape Metropole and serves a diverse population of low- to middle-income status. Medical practitioners employed in the Paediatric Department include interns, medical officers, registrars, registered specialists, and subspecialists. The RCWMCH PICU is a 22 bed multi-disciplinary unit, offering a vast number of interventions ranging from non-invasive ventilation to invasive ventilation. The unit admits approximately 1300 children annually. Approximately 60% of these admissions are for acute medical conditions.

Study population

The management of acute asthma exacerbations at RCWMCH consists of inhaled or nebulised beta-2 agonist, nebulised ipratropium bromide, corticosteroids, and intravenous magnesium sulphate. If there is no response, an intravenous dose of salbutamol is given over 10 minutes. If further escalation of management is needed, a salbutamol infusion is commenced and the patients are referred for further management in PICU.[15]

We included all children who were admitted to the RCWMCH PICU for ASA during the stipulated time frame.

Data collection

The main PICU electronic database was accessed and reviewed to identify patients admitted with ASA. The folder numbers and patient names were used to obtain the patient records from the PICU electronic database, electronic consultant database and hardcopy medical records at RCWMCH. These records were reviewed for study eligibility and included patients were allocated individual study numbers to ensure their anonymity. The desired demographic, clinical data, and details regarding the pre PICU care, PICU admission, hospital stay, and survival were extracted into a pre-designed excel spreadsheet. Results of investigations for

blood cultures, nasopharyngeal and tracheal aspirates were accessed through the National Health Laboratory Service (NHLS).

Data analysis

Statistical analysis was done using Microsoft Excel and Stata 11, StataCorp. 2009, College Station, TX: StatCorp LP. Numerical data was summarised as medians (interquartile ranges) and categorical data was summarised using counts and percentages. No inferential statistics were used.

Ethical considerations

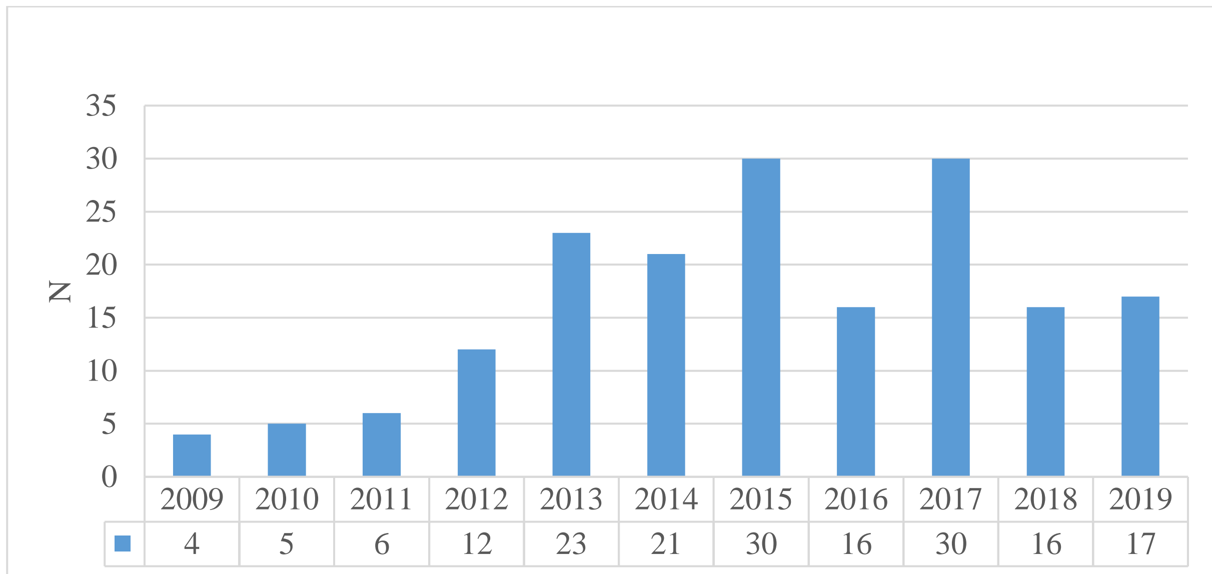
Ethics approval was obtained from the Human Research Ethics Committee of the Faculty of Health Sciences at University of Cape Town (ref. no. 082/2021). We obtained approval from hospital management to conduct the study at RCWMCH. The study is registered with The National Health Research Database. We were granted a waiver of informed consent.

Results

There were 14592 PICU admissions over the 11-year period, 233 admissions were identified as having a diagnosis code of asthma, only 187 admissions were identified as being admitted with ASA and all records were complete. One patient with hyper IgE syndrome had seven admissions and was excluded. This resulted in 180 admissions (1,2%) for ASA and no asthma related deaths were observed.

During the study period, 11 patients (6,1%) had more than one admission. Figure 1 illustrates the number of admissions for each year during the study period.

Figure 1: Number of admissions to PICU 2009-2019 (n = 180)



n= number of patients

The patient characteristics are summarised in Table 1. About half of the cohort were between 25 and 72 months old (57,3%) and the median age was 67 months (IQR 37-93). Almost two thirds of the patients weighed between 10 and 20 kilograms (61,1%) and the median weight was 17kg (IQR 14-25). Ninety percent of children had an appropriate weight for age, whilst 6,7% were underweight for age. Approximately half of the patients admitted were known asthmatics. Only 38,7% of known asthmatic children were adherent on treatment.

Table 1: Demographic and clinical characteristics (n=180)

Variable	n (%)
Gender	
Male	96 (53,3)
Age in months	
0-24	15 (8,3)
25-72	103 (57,3)
73-120	44 (24,4)
121-192	18 (10)
Weight (kilogram), median (IQR)	17 (14-25)
Nutritional status	
Appropriate weight for age	162 (90)
Underweight for age	12 (6,7)
Overweight for age	6 (3,3)
Diagnosis status	
Newly diagnosed asthmatic	83 (46,1)
Known asthmatic	97 (53,9)
Compliance	
Compliant	37 (20,6)
Non-compliant	60 (33,3)
Not applicable	83 (46,1)
PICU admission days, median (IQR)	1 (1-2)
Hospital admission days, median (IQR)	4 (3-6)

Medical intervention of the ASA episode before and during the PICU admission is shown in Table 2. Nearly all the patients received nebulisations, steroids, and magnesium sulphate before PICU admission. Half of the patients were loaded with intravenous (IV) salbutamol (n=96; 53,3%) and about a third (n=61; 33,8%) were started on a salbutamol infusion before admission to PICU. Similar proportions received nebulisations and steroids in ICU, magnesium sulphate was given again to 34 patients in PICU and a total of 130 patients (72,2%) received a salbutamol infusion.

The median PICU LOS for children was 1 day and median hospital LOS 4 days.

Table 2: Medical intervention of ASA before and during ICU

Intervention	Pre-ICU n, (%)	ICU n, (%)
MDI	1 (0,6)	0 (0)
Nebulisations	177 (98,3)	166 (92,2)
Salbutamol Load	96 (53,3)	4 (2,2)
Salbutamol Infusion	61 (33,8)	130 (72,2)
Methylxanthine	1 (0,6)	7 (3,8)
Steroids	176 (97,8)	175 (97,2)
Magnesium	155 (86,1)	34 (18,8)
Other: Adrenaline IM	1 (0,6)	0
Other: Adrenaline IV	1 (0,6)	0
Ketamine	0	2 (1,1)

Abbreviations: ICU- intensive care unit, IM- intramuscular, IV-intravenous, MDI- metered-dose inhaler

Patients admitted to PICU with ASA had a median hospital admission of 4 days (IQR 3-6) and a median PICU admission of 1 day (IQR 1-2). All patients required respiratory support and Figure 2 summarises the various modes per year. Most patients required non-invasive respiratory support (n=167; 90,3%), most of whom received high flow nasal cannula (HFNC) (n=92; 51,1%). Table 3 shows the type of respiratory support over the study period.

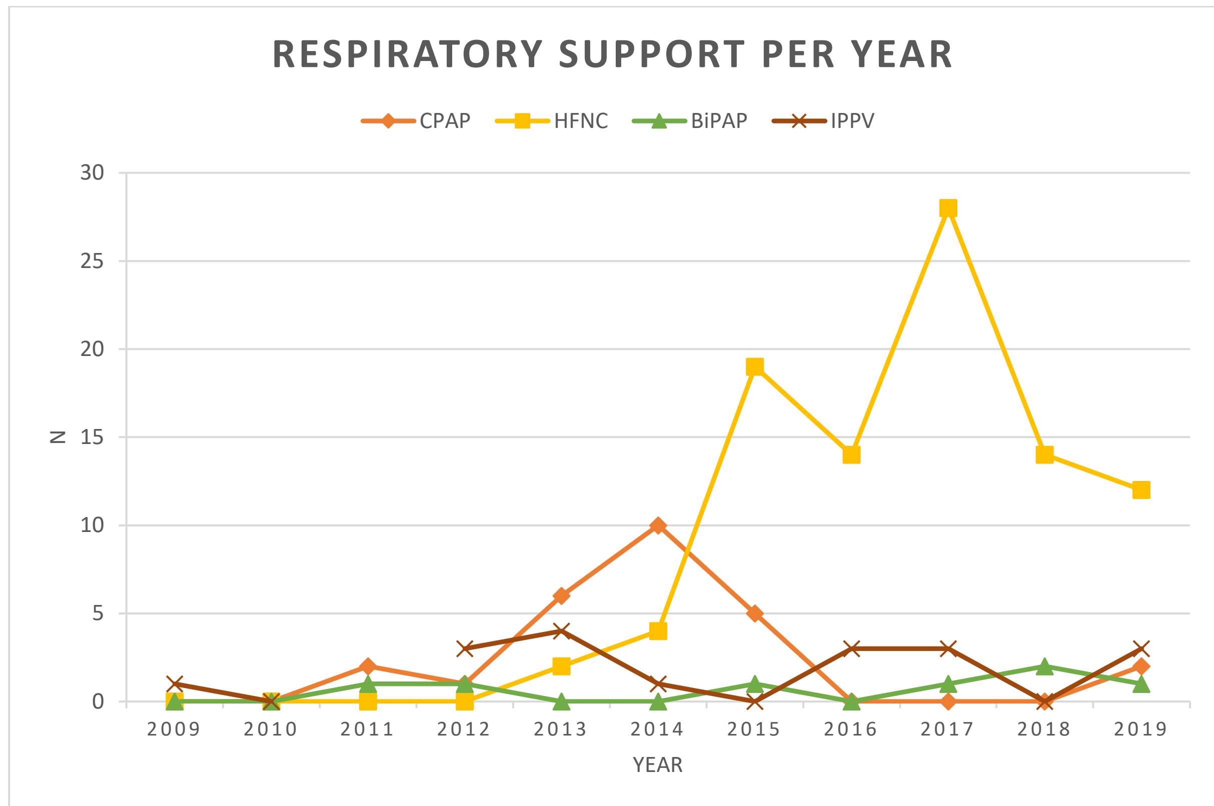
Eighteen patients required mechanical ventilation of which 14 were intubated prior to PICU admission and 4 during their PICU admission. Two patients required high frequency oscillatory ventilation (HFOV). The median length of ventilation was 3 days (IQR 2-4).

Table 3: Respiratory Support

Respiratory Support	Pre-ICU n	ICU n
Nasal Prongs	79	42
HFNC	71	92
CPAP	22	26
BiPAP	0	7
Mechanical Ventilation	14	18

Abbreviations: BiPAP: bi level airway pressure, CPAP: continuous positive airway pressure, HFNC: high flow nasal cannula

Figure 2 Respiratory support per year



Abbreviations: BiPAP: Bilevel positive airway pressure, CPAP: continuous positive airway pressure, HFNC: high flow nasal cannula, IPPV: intermittent positive pressure ventilation

Blood cultures were conducted on 58 children, with the majority showing no growth and two positives for skin commensal organisms. Nasopharyngeal aspirates were obtained from 57 patients, and the commonest organisms isolated were Rhinovirus (66,6%), Adenovirus (17,5%) and Parainfluenza (8,8%). Of the 18 patients who were intubated, 8 had tracheal aspirates done and the most common organism isolated was Rhinovirus (75%). All one hundred and eighty-one patients received antibiotics during their admission in PICU.

Discussion

Our 11-tear review of children admitted to the PICU with ASA shows an increasing trend in admissions and increasing use of non-invasive ventilatory support. Recent reports show an increasing number of children requiring admission to PICU in several countries worldwide[9].

According to Masekela et al, living within a rural setting is a protective factor for the development of asthma [4]. RCWMCH is based in the Cape Metropole where there is increased exposure to pollution, house dust mites, mould, tobacco smoke and viral respiratory pathogens. These are prominent risk factors for the development of asthma [4]. The more densely packed urban areas serve as a hub for various respiratory viral infections. Urban

migration continues to increase in South Africa[16]. As individuals seek economic empowerment, the number of people migrating to urban areas have increased thus increasing exposure to the above risk factors, the development of asthma and possibly contributing to the increase in hospital admissions with ASA.

Patterns of asthma prevalence are not only dependent on geographical location, economic status and respiratory irritant exposure, but are also influenced by sex and age.[17]. A higher incidence and rate of hospital admission has been described in prepubertal males when compared to females of the same age. [17] The sex distribution of those admitted to PICU in our study was almost equal, and the median age of our study population was 5,6 years (67 months). This contrasts to other studies where the median age was 6,8 years (81,6 months) and 3,1 years (37,2 months) respectively. [8][13]This disparity could be accounted for by the difference in socioeconomic backgrounds, genetic influences and the presence or absence of other risk factors for the development and presentation of asthma.

Studies show a PICU readmission rate of 6-16,6% following the index admission[10,18], our study showed 11 patients (6,1%) required readmission during the period. Risk factors known to be associated with repeated admission include prolonged length of stay, chronic comorbidities, and previous ASA admission[19]. Unfortunately, our study did not specifically investigate the risk factors for readmission, but this may be an interesting sub analysis that may be done in the future.

Engelkes et al demonstrated that good adherence was associated with less severe asthma exacerbations[20]. Half of the RCWMCH study population were newly diagnosed asthmatics. However, of those known with asthma, about two thirds were non-compliant. This also demonstrated that poor adherence is associated with more severe ASA.

Red Cross War Memorial Children's Hospital and its referring health care facilities use identical protocols and guidelines when managing ASA prior to PICU admission. Beta 2 agonists are the mainstay of our ASA guidelines pre-PICU. We found that 98,3% of patients received nebulized beta 2 agonists prior to PICU admission and this is in keeping with international studies showing that beta 2 agonists are deemed safe and effective in the initial management of ASA.[13]

About two thirds of patients admitted to PICU received a salbutamol infusion. Hon et al. showed that salbutamol infusion is effective and safe in the management of ASA in most children who would otherwise require invasive respiratory support methods[13].

Magnesium results in bronchial smooth muscle relaxation by inhibiting calcium uptake. Cheuk et all and Ozdemir et al, showed that intravenous magnesium sulphate provides additional benefits in ASA, by improving pulmonary function.[21,22] We found that 155 (86,1%) patients received intravenous magnesium sulphate and most doses were given in the emergency unit as a slow infusion.

Methylxanthines have fallen out of vogue as a result of their narrow therapeutic index and side effect profile[23]. During our study period 8 patients received methylxanthines for ASA. The use of methylxanthines is not advocated according to American guidelines[24]. However, in patients that are considered unresponsive the British Thoracic Society and Scottish Intercollegiate Guidelines Network recommend that aminophylline may be considered.[9,25].

We do not use Helium-oxygen mixtures (Heliox) in our PICU. Evidence for the use of Heliox for ASA in paediatrics is sparse[26] and according to Lew et al, the prescription of Heliox has declined over the last decade.[27]

There has been an increase in the use of non-invasive ventilatory support in children in PICU with respiratory distress and severe pneumonia[28]. The benefit from CPAP and HFNC is that it potentially reduces the inspiratory work of breathing and stents the airway open, allowing more effective exhalation[28]. However, the use of CPAP and HFNC in children with ASA is controversial, as they potentially have high intrinsic PEEP.

In 2013, we instituted HFNC at RCWMCH and it is by the far the commonest respiratory support mode used over the study period. HFNC delivers a gas mixture at flow levels equal or above the inspiratory demands of the patient.[29] It is postulated the mechanism of action include wash out of the dead space in the nasopharyngeal area, it provides adequate flow to overcome the airway resistance, provides a distending pressure and warm humidified gas, which together improves compliance of the lungs.[29].

A few studies have showed HFNC to be effective in emergency units, paediatric wards and PICU's. In an observational study by Pilar et al, 40% of patients needed stepping-up of respiratory support from HFNC to bi-level positive airway pressure (BiPAP) [30]. The same study showed that those who required escalation had a 3 fold higher median LOS [30]. Interestingly, there was no difference between the two cohorts regarding need for invasive ventilation [30].

In a French retrospective observational study of 69 patients, 39 (53%) were managed with HFNC, 1 patient required escalation of care, and another was stopped due to the development

of a pneumothorax. [31]. High flow nasal cannula was thus deemed a feasible treatment modality for ASA in the critical care setting [31].

Eighteen children (10%) required intubation and mechanical ventilation. Of note, 14 children were intubated prior to PICU admission. Our study did not investigate whether the patients were intubated at RCWMCH or in the periphery. There was no difference in median length of ventilation between those children intubated before or during PICU admission The proportion of children with ASA needing mechanical ventilation was similar to the findings of Newth et al. [8] Newth et al showed a 69% shorter length of ventilation with patient intubated prior to PICU admission and attributed this to the differences in pre-PICU care where no clear single ASA guideline was followed and some patients were intubated too early [8]. In our context, a single ASA guideline is used and may explain why no difference was seen.

Shein et al. noted that there is no superior mode of invasive mechanical ventilation for the management of ASA [6]. At RCWMCH pressure control ventilation was by far the most common mode used as opposed to volume controlled synchronized intermittent mandatory ventilation (VC-SIMV) or pressure regulated volume control ventilation (PRVC) demonstrated in Shein's study. [6] High frequency oscillatory ventilation has been safely used as rescue mode of ventilation for children with ASA[32,33] but data is limited and only two of our patients required HFOV.

Viral infections are known to be associated with asthma exacerbations, particularly Rhinovirus, Parainfluenza and Respiratory syncytial virus (RSV)[34]. Almost half of our study population either had a nasopharyngeal aspirate (NPA) or tracheal aspirate (TA) if they were intubated. Our study unsurprisingly found similar results with Rhinovirus, Adenovirus and Parainfluenza being the most common organisms isolated.

No mortalities due to ASA were reported during our study period. Newth et al. described eleven deaths (4%) associated with ASA over a five-year period[8]. Of note, ten of these deaths experienced cardiac arrest prior to admission to PICU.[8]

Our study demonstrated a median PICU LOS of 1 day (IQR 1-2) and a median hospital LOS of 4 days (IQR 3-6) this is comparable with international studies as described by Miksa and Al-Eyadhy[35,36].

Limitations

This is a single centre retrospective study, and the data is dependent on record keeping, thoroughness of the attending physician and the investigators' ability to interpret the records. Outcomes of children with ASA in our well-resourced facility is not generalizable to other institutions using different ASA protocols and varying resources. We were unable to look at paediatric index of mortality scores (PIM) as there was a change from PIM2 to PIM3 during the study period.

Conclusion

Our study shows that annual ASA admissions to the PICU have increased over the study period. Despite the increase in admissions, the outcomes are comparable to international standards, with children only requiring a short PICU admission. We have seen an overall increase in the use of NIV respiratory support, mainly HFNC.

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Author Contributions

Equal Contributions

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None

Conflict of interest

The authors declare that they have no competing interests.

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Appendix A – Journal guidelines

Southern African Journal of Critical Care Submission Guidelines

Author Guidelines

Author Guidelines

Please take the time to familiarise yourself with the policies and processes below. If you still have any questions, please do not hesitate to ask our editorial staff (tel.: +27 (0)21 532 1281, email: submissions@hmpg.co.za).

Scope of the Journal.

This Journal publishes scientific articles related to multidisciplinary critical and intensive medical care and the emergency care of critically ill humans.

To submit a manuscript, please proceed to the *SAJCC* Editorial Manager website: www.editorialmanager.com/sajcc

Please view the Author Tutorial for guidance on how to submit on Editorial Manager.

Authorship

Named authors must consent to publication. Authorship should be based on: (*i*) substantial contribution to conceptualisation, design, analysis and interpretation of data; (*ii*) drafting or critical revision of important scientific content; or (*iii*) approval of the version to be published. These conditions must all be met for an individual to be included as an author (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org)

If authors' names are added or deleted after submission of an article, or the order of the names is changed, all authors must agree to this in writing.

Please note that co-authors will be requested to verify their contribution upon submission. Non-verification may lead to delays in the processing of submissions. Author contributions should be listed/described in the manuscript.

Conflicts of interest

Conflicts of interest can derive from any kind of relationship or association that may influence authors' or reviewers' opinions about the subject matter of a paper. The existence of a conflict – whether actual, perceived or potential – does not preclude publication of an article. However, we aim to ensure that, in such cases, readers have all the information they need to enable them to make an informed assessment about a publication's message and conclusions. We require that both authors and reviewers declare all sources of support for their research, any personal or financial relationships (including honoraria, speaking fees, gifts received, etc) with relevant individuals or organisations connected to the topic of the paper, and any association with a product or subject that may constitute a real, perceived or potential conflict of interest. If you are unsure whether a specific relationship constitutes a conflict, please contact the editorial team for advice. If a conflict remains undisclosed and is later brought to the attention of the editorial team, it will be considered a serious issue prompting an investigation with the possibility of retraction.

Research ethics committee approval

Authors must provide evidence of Research Ethics Committee approval of the research where relevant. Ensure the correct, full ethics committee name and reference number is included in the manuscript an accompanying documentation. A copy of the ethics approval letter must be uploaded as a supplementary file.

If the study was carried out using data from provincial healthcare facilities, or required active data collection through facility visits or staff interviews, approval should be sought from the relevant provincial authorities. For South African authors, please refer to the guidelines for submission to the National Health Research Database. Research involving human subjects must be conducted according to the principles outlined in the Declaration of Helsinki (2013), and should include a statement on independent ethical review. Where appropriate, a statement must be made that informed consent was taken from human participants, and/or whether the need for informed consent was waived.

Please also refer to the National Department of Health's guideline on Ethics in Health research: principles, processes and structures to ensure that the appropriate requirements for conducting research have been met, and that the HPCSA's General Ethical Guidelines for Health Researchers have been adhered to.

Protection of rights to privacy

Research Participants

Information that would enable identification of individual research participants should not be published in written descriptions, photographs, radiographs and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) has given informed written consent for publication and distribution. Refer to Protection of Research Participants. The signed consent form for case reports should be submitted with the manuscript to enable verification by the editorial team.

Other individuals

Any individual who is identifiable in an image must provide written agreement that the image may be used in that context in the *SAJCC.*

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Material submitted for publication in the *SAJCC* is accepted provided it has not been published or submitted for publication elsewhere. Please inform the editorial team if the main findings of your paper have been presented at a conference and published in abstract form, to avoid copyright infringement. The *SAJCC* does not hold itself responsible for statements made by the authors. The corresponding author should also indicate if the research forms part of a postgraduate short report, dissertation or thesis.

Previously published images

If an image/figure has been previously published, permission to reproduce or alter it must be obtained by the authors from the original publisher and the figure legend must give full credit to the original source. This credit should be accompanied by a letter indicating that permission to reproduce the image has been granted to the author/s. This letter should be uploaded as a supplementary file during submission.

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to the journal or associated publications. Queries with regard to privacy may be directed to publishing@hmpg.co.za.

Ethnic/race classification

Use of racial or ethnicity classifications in research is fraught with problems. If you choose to use a research design that involves classification of participants based on race or ethnicity, or discuss issues with reference to such classifications, please ensure that you include a detailed rationale for doing so, ensure that the categories you describe are carefully defined, and that socioeconomic, cultural and lifestyle variables that may underlie perceived racial disparities are appropriately controlled for. Please also clearly specify whether race or ethnicity is classified as reported by the patient (self-identifying) or as perceived by the investigators. Please note thatit is not appropriate to use self-reported or investigator-assigned racial or ethnic categories for genetic studies.

Manuscript preparation

Preparing an article for anonymous review

To ensure a fair and unbiased review process, submissions may include an anonymized version of the manuscript.

Submitting a manuscript that needs additional blinding can slow down your review process, so please be sure to follow these simple guidelines as much as possible:

- An anonymous version should not contain any author, affiliation or particular institutional details that will enable identification.
- Please remove title page, acknowledgements, contact details, funding grants to a named person, and any running headers of author names.
- Mask self-citations by referring to your own work in third person.

General article format/layout

Submitted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction prior to being sent for review, which will delay publication.

General:

- Manuscripts must be written in UK English (this includes spelling).
- The manuscript must be in Microsoft Word or RTF document format. Text must be 1.5 line spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes). Pages and lines should be numbered consecutively.
- Please make your article concise, even if it is below the word limit.
- Qualifications, ***full*** affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
- Medical drugs should be referred to by their generic name although the trade name may be used in brackets in the text once if unique.

If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

Preparation notes by article type

Research

Guideline word limit: 3 000 words (excluding abstract and bibliography)

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The title of the manuscript should concisely describe the study but should not include the outcome. The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. At the end of the introduction clearly state the aim or objective of the study. The primary and secondary outcomes should be specified.

In the Methods section describe in sufficient detail so that others would be able to replicate the study should they need to. Sections of the methods that have been described in previous publications need only be referenced. The statistical methods should be described. Where appropriate, sample size calculations should be included to demonstrate that the study is not underpowered.

Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

The discussion should be confined to an interpretation of your results with respect to your stated aim and if applicable, a comparison to the results of similar studies. The strengths and weaknesses of your study should be discussed.

The conclusion should be confined to an interpretation of the results of the study and a recommendation if applicable.

- May include up to 6 illustrations or tables.
- References should only include the most recent and relevant articles. A maximum of 30 references is advised.

Structured abstract

- This should be no more than 250 words, with the following headings:
    - **Background:** why the study is being done and how it relates to other published work.
    - **Objectives:** what the study intends to find out
    - **Methods:** must include study design, number of participants, description of the research tools/instruments, any specific analyses that were done on the data.
    - **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
    - **Conclusion:** must be supported by the data, and be aligned with the conclusion in the main text.
    - Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors. It should be able to be intelligible to the reader without referral to the main body of the article.
    - Do not include any references in the abstracts.

Here is an example of a good abstract.

***Scientific letters*/short reports**

These are shorter length, scholarly research articles of no more than 1500 words, and include case reports.
Guideline word limit: 1500 words

- Abstract: Structured, maximum 250 words, with the following headings: Background, Objectives, Methods, Results, and Conclusion.
- May include only one illustration or table
- A maximum of 15 references

Editorials

Guideline word limit: 1 000 words
These opinion or comment articles are usually commissioned but we are happy to consider and peer review unsolicited editorials. Editorials should be accessible and interesting to readers without specialist knowledge of the subject under discussion and should have an element of topicality (why is a comment on this issue relevant now?) There should be a clear message to the piece, supported by evidence.
Please make clear the type of evidence that supports each key statement, e.g.:

- expert opinion
- personal clinical experience
- observational studies
- trials
- systematic reviews.

Review articles

Narrative review articles should always be discussed with the Editor prior to submission. (Structured reviews or meta-analyses' need not be).

Guideline word limit: 4 000 words
These are welcome, but should be either commissioned or discussed with the Editor before submission. A review article should provide a clear, up-to-date account of the topic and be aimed at non-specialist hospital doctors and general practitioners. They should be aligned to practice in South and/or sub-Saharan Africa and not a précis of reviews published in the international literature
Please ensure that your article includes:

- Abstract: unstructured, of about 100-150 words, explaining the review and why it is important
- Methods: Outline the sources and selection methods, including search strategy and keywords used for identifying references from online bibliographic databases. Discuss the quality of evidence.
- When writing: clarify the evidence you used for key statements and the strength of the evidence. Do not present statements or opinions without such evidence, or if you have to, say that there is little or no evidence and that this is opinion. Avoid specialist jargon and abbreviations, and provide advice specific to southern Africa.
- Personal details: Please supply your qualifications, position and affiliations address, telephone number and fax number, and your e-mail address; and a short personal profile (50 words) and a few words about your current fields of interest.

Correspondence (Letters to the Editor)

Guideline word limit: 400 words

Letters to the editor should relate either to a paper or article published by the SAJCC or to a topical issue of particular relevance to the journal's readership

- May include only one illustration or table
- Must include a correspondence address.

Obituaries

Guideline word limit: 400 words

Should be offered within the first year of the practitioner's death, and may be accompanied by a photograph.

Illustrations/photos/scans

- If illustrations submitted have been published elsewhere, the author(s) should provide evidence of consent to republication obtained from the copyright holder.
- Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'.
- Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).
- All images must be of high enough resolution/quality for print.
- All illustrations (graphs, diagrams, charts, etc.) must be in PDF form.
- Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g. 0; 1.0; 2.0; 3.0; 4.0 etc.
- Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

- Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.
- Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.
- Number each table in Arabic numerals (Table 1, Table 2, etc.) consecutively as they are referred to in the text.
- Tables must be cell-based (i.e. not constructed with text boxes or tabs) and editable.
- Ensure each table has a concise title and column headings, and include units where necessary.
- Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

References

NB: *Only complete, correctly formatted reference lists in Vancouver style will be accepted. If reference manager software is used, the reference list and citations in text are to be unformatted to plain text before submitting.*

- Authors must verify references from original sources.

- Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6]
- All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).
- Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.
- Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.
- Volume and issue numbers should be given.
- First and last page, in full, should be given e.g.: 1215-1217 **not** 1215-17.
- Wherever possible, references must be accompanied by a digital object identifier (DOI) link). Authors are encouraged to use the DOI lookup service offered by CrossRef:
    - On the Crossref homepage, paste the article title into the 'Metadata search' box.
    - Look for the correct, matching article in the list of results.
    - Click Actions > Cite
    - Alongside 'url =' copy the URL between { }.
    - Provide as follows, e.g.: https://doi.org/10.7196/07294.937.98x

Some examples:

- *Journal references:* Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. Stat Med 1998;289(1):350-355. DOI:10.1000/hgjr.182
- *Book references:* Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101.
- *Chapter/section in a book:* Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.
- *Internet references:* World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: WHO, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).
- Legal references
- Government Gazettes:

National Department of Health, South Africa. National Policy for Health Act, 1990 (Act No. 116 of 1990). Free primary health care services. Government Gazette No. 17507:1514. 1996.

In this example, 17507 is the Gazette Number. This is followed by :1514 - this is the notice number in this Gazette.

- Provincial Gazettes:

Gauteng Province, South Africa; Department of Agriculture, Conservation, Environment and Land Affairs. Publication of the Gauteng health care waste management draft regulations. Gauteng Provincial Gazette No. 373:3003, 2003.

- Acts:

South Africa. National Health Act No. 61 of 2003.

- Regulations to an Act:

South Africa. National Health Act of 2003. Regulations: Rendering of clinical forensic medicine services. Government Gazette No. 35099, 2012. (Published under Government Notice R176).

- Bills:

South Africa. Traditional Health Practitioners Bill, No. B66B-2003, 2006.

- Green/white papers:

South Africa. Department of Health Green Paper: National Health Insurance in South Africa. 2011.

- Case law:

Rex v Jopp and Another 1949 (4) SA 11 (N)
Rex v Jopp and Another: Name of the parties concerned
1949: Date of decision (or when the case was heard)
(4): Volume number
SA: SA Law Reports
11: Page or section number
(N): In this case Natal - where the case was heard. Similarly, (C) woud indicate Cape, (G) Gauteng, and so on.
NOTE: no . after the v

- *Other references (e.g. reports) should follow the same format:* Author(s). Title. Publisher place: Publisher name, year; pages.
- Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'.
- Unpublished observations and personal communications in the text must **not** appear in the reference list. The full name of the source person must be provided for personal communications e.g. '...(Prof. Michael Jones, personal communication)'.

From submission to acceptance

Submission and peer-review

To submit an article:

- Please ensure that you have prepared your manuscript in line with the SAJCC requirements.
- All submissions should be submitted via Editorial Manager
- The following are required for your submission to be complete:
    - Anonymous manuscript (unless otherwise stated)
    - Author Agreement form
    - Manuscript
    - Ethics Approval form (for research articles)
    - Any supplementary files: figures, datasets, patient consent form, permissions for published images, etc.
    - Once the submission has been successfully processed on Editorial Manager, it will undergo a technical check by the Editorial Office before it will be assigned to an editor who will handle the review process. If the author guidelines have not been appropriately followed, the manuscript may be sent back to the author for correcting.

Peer Review Process

All manuscripts are reviewed initially by two of the editors and only those that meet the scientific and editorial standards of the journal, and fit within the aims and scope of the

journal, will be sent for external peer review. Each manuscript is reviewed by two reviewers selected on the basis of their expertise in the field.

A double blind review process is followed at SAJCC. The time period of the entire review process may vary however depending upon the quality of the manuscript submitted, reviewers' responses and the time taken by the authors to submit the revised manuscript.

Manuscripts from review may be accepted, rejected or returned to the author for revision or resubmission for review. Authors will be directed to submit revised manuscripts within two months of receiving the editor's decision, and are requested to submit a point by point response to the reviewers' comments. Manuscripts which authors are requested to revise and resubmit will be sent for a second round of peer review, often to the original set of reviewers. All final decisions on a manuscript are at the Editor's discretion

Article Processing Charges

There is currently no article-processing charge (APC), also known as page fees, for the publication of manuscripts. The publication costs are supported by the Critical Care Society of Southern Africa and advertisements in the print version.

Please refer to the section on 'Sponsored Supplements' regarding the publication of supplements, where a charge is currently applicable.

Production process

The following process should usually take between 4 - 6 weeks:

1. An accepted manuscript is passed to a Managing Editor to assign to a copyeditor (CE).
2. The CE copyedits in Word, working on house style, format, spelling/grammar/punctuation, sense and consistency, and preparation for typesetting.
3. If the CE has an author queries, he/she will contact the corresponding author and send them the copyedited Word doc, asking them to solve the queries by means of track changes or comment boxes.
4. The authors are typically asked to respond within 1-3 days. Any comments/changes must be clearly indicated e.g. by means of track changes. Do not work in the original manuscript - work in the copyedited file sent to you and make your changes clear.
5. The CE will finalise the article and then it will be typeset.
6. Once typeset, the CE will send a PDF of the file to the authors to complete their final check, while simultaneously sending to the 2nd-eye proofreader.
7. The authors are typically asked to complete their final check and sign-off within 1-2 days. No major additional changes can be accommodated at this point.
8. The CE implements the authors' and proofreader's mark-ups, finalises the file, and prepares it for the upcoming issue.

Changing contact details or authorship

Please notify the Editorial Department of any contact detail changes, including email, to facilitate communication.

Errata and retractions

Errata

Should you become aware of an error or inaccuracy in yours or someone else's contribution after it has been published, please inform us as soon as possible via an email to publishing@hmpg.co.za,including the following details:

- Journal, volume and issue in which published
- Article title and authors
- Description of error and details of where it appears in the published article

- Full detail of proposed correction and rationale

We will investigate the issue and provide feedback. If appropriate, we will correct the web version immediately, and will publish an erratum in the next issue. All investigations will be conducted in accordance with guidelines provided by the Committee on Publication Ethics (COPE).

Retractions

Retraction of an article is the prerogative of either the original authors or the editorial team of HMPG. Should you wish to withdraw your article before publication, we need a signed statement from all the authors.

Should you wish to retract your published article, all authors have to agree in writing before publication of the retraction.

Send an email to publishing@hmpg.co.za, including the following details:

- Journal, volume and issue to which article was submitted/in which article was published
- Article title and authors
- Description of reason for withdrawal/retraction.

We will make a decision on a case-by-case basis upon review by the editorial committee in line with international best practices. Comprehensive feedback will be communicated with the authors with regard to the process. In case where there is any suspected fraud or professional misconduct, we will follow due process as recommended by the Committee on Publication Ethics (COPE), and in liaison with any relevant institutions.

When a retraction is published, it will be linked to the original article.

Indexing

Published articles are covered by the following major indexing services. As such articles published in the *SAJCC* are immediately available to all users of these databases, guaranteed a global and African audience:

- DOAJ
- AIM
- AJOL
- Scopus
- EBSCO
- EMBASE
- Crossref
- Sabinet
- Scielo

Sponsored supplements

Contact the editor for information on submitting ad hoc/commissioned supplements, including guidelines, conference/congress abstracts, Festschrifts, etc.

Submission Preparation Checklist

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

1. The submission has not been previously published, nor is it before another journal for consideration.
2. The text complies with the stylistic and bibliographic requirements in **Author Guidelines**.
3. The manuscript is in Microsoft Word format. The text is single-spaced, in 12-point Times New Roman font, and contains no unnecessary formatting.
4. Illustrations/figures are high resolution/quality (not compressed) and in an acceptable format (Jpeg). These must be submitted as 'supplementary files' (not in the manuscript).
5. For illustrations/figures or tables that have been published elsewhere, the author has obtained written consent to republication from the copyright holder.
6. Where possible, references are accompanied by a digital object identifier (DOI) and PubMed ID (PMID)/PubMed Central ID (PMCID).
7. An abstract has been included where applicable.
8. The research was approved by a Research Ethics Committee (if applicable)
9. Any conflict of interest (or competing interests) is indicated by the author(s).

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Material submitted for publication in the *SAJCC* is accepted provided it has not been published or submitted for publication elsewhere. Please inform the editorial team if the main findings of your paper have been presented at a conference and published in abstract form, to avoid copyright infringement.

Privacy Statement

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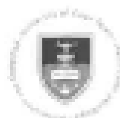
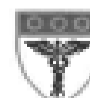
Appendix B – Ethics approval



UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee



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Website: www.health.uct.ac.za/fhs/research/humanethics/forms

16 February 2021

HREC REF: 082/2021

Dr S Salie
Division of Paediatrics and Child Health
PICU Red Cross War Memorial Children's Hospital
Rondebosch
Email: Shamiel.salie@uct.ac.za
Student: SLXMOE005@myuct.ac.za

Dear Dr Salie

PROJECT TITLE: A RETROSPECTIVE REVIEW OF ALL CHILDREN ADMITTED WITH ACUTE SEVERE ASTHMA TO THE PICU, RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL, BETWEEN 2009-2019 MMED CANDIDATE-DR MOEGAMAD SALIE

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020 & 06 July 2020.

Approval is granted for one year until the 28 February 2022.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Dr Moegamad Salie will also be involved in this study.

Please quote the HREC REF 082/2021 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

HREC/REF 082/2021sa

Appendix C – Data Collection Sheet

DATA SHEET

Demographics

Folder No:	
Sex:	
Age (months):	
Weight on admission (kilograms):	
Date of Birth	
Date of hospital admission:	
Date of ICU admission:	
Date of ICU Discharge:	
Date of Hospital Discharge:	
Co-morbidities: (TB/ cardiac lesion):	
Newly Diagnosed Asthma	
Known Asthma	
Compliant: yes no unknown	
Chronic Medications	
Nutritional status:	
PIM2 score PIM3 score:	
RVD status: (positive/negative):	

Interventions (Ward/Medreg/Referral Centre)

Medications required

Inhaled B2 Agonist MDI	
Inhaled B2 Agonist Nebulisation	
Intravenous Salbutamol Load	
Intravenous Salbutamol Infusion	
Methylxanthine	
Intravenous Magnesium Sulphate	
Corticosteroids	
Antibiotics	
Other	

Ventilatory Requirments

Nasal Prongs

HFNC	
CPAP	
NIV (BIPAP)	
Invasive Ventilation	
Ventilation Mode	
Length of Ventilation (hrs)	
Inline Nebulisation	

Interventions (PICU)

Medications required

Inhaled B2 Agonist Nebulisation	
Inhaled B2 Agonist MDI	
Intravenous Salbutamol Load	
Intravenous Salbutamol Infusion	
Methylxanthine	
Intravenous Magnesium Sulphate	
Corticosteroids	
Antibiotics	
Other	

Ventilatory Requirments

HFNC	
CPAP	
NIV (BIPAP)	
Invasive Ventilation	
Ventilation Mode	
Length of Ventilation (hrs)	
Inline Nebulisation	
Paralysis	
Post extubation support (CPAP/HFNC/NPO_2/RA)	

Investigations

Blood cultures	
Nasopharyngeal Aspirates	
Tracheal Aspirate	
Other	

Death in ICU:(date if yes):	
Length of ICU admission (days):	
Death in Ward:(date if yes):	
Length of hospital admission (days):	
Survival to discharge: (yes/no)	