

https://dspace.org/

RSV Bronchiolitis in 2018: a descriptive study of children admitted to two Johannesburg Tertiary Hospitals

Cleak, Tannah Storm

2022

https://hdl.handle.net/10539/34457

Downloaded from a DSpace repository. https://dspace.org/

RSV BRONCHIOLITIS IN 2018:
A DESCRIPTIVE STUDY OF CHILDREN ADMITTED TO TWO JOHANNESBURG TERTIARY HOSPITALS

Tannah Storm Cleak
Student number: 304291

A Research Report submitted to the Faculty of Health Sciences, University of Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in the Discipline of Paediatrics.

Johannesburg, 20 December 2021



Declaration

I, Tannah Storm Cleak, declare that this research report is my own, unaided work. It is being submitted for the degree of Master of Medicine in the department of Paediatrics and Child Health, Faculty of Health Sciences, at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other university.

Dr T S Cleak

Signature: _____

Date: 20. 12. 2021

Dedication

I dedicate this work to my family and Stephan Broich, I am eternally greatly for all of you.

Abstract

RSV Bronchiolitis in 2018: A Descriptive Study of Children Admitted to two Johannesburg Tertiary Hospitals

TS Cleak[1], MBChB, FCPaed (SA), DCH (SA), DipHIVMan (SA); **DE Ballot**[1], MBBCh (Wits), FCPaed (SA), PhD; **NM Moshesh**[2], MBChB, FCPaed (SA), Cert Crit Care (Paeds); **L Chirwa**[2], MBChB, FC Paed (SA), Cert Neonatology; **T Thomas**[3],MBBCh, FCPath Micro, DTM&H, DipHIVMan (SA); MMed (Micro); **DA White**[1], MBBCh, FC Paed (SA), MMed (Paed), Dip Allergy (SA), Cert Pulmonology (SA) Paed.

[1]*Charlotte Maxeke Johannesburg Academic Hospital, Department of Paediatrics and Child Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg South Africa*

[2] *Nelson Mandela Children's Hospital*

[3] *Infection Control Services Laboratory, Department of Microbiology, National Health Laboratory Services*

Corresponding author: TS Cleak (tannahcleak@gmail.com)

Background. Respiratory Syncytial Virus (RSV) is the most common cause of severe bronchiolitis in children worldwide.

Objectives. To describe clinical characteristics and outcomes of children hospitalized with bronchiolitis and to compare those with respiratory syncytial virus (RSV) bronchiolitis to children with other viral causes of bronchiolitis.

Methods. A retrospective study of children admitted with virally screened bronchiolitis to Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and Nelson Mandela Children's Hospital (NMCH) from 01 February to 31 August 2018 was conducted, where RSV positive and negative children were compared.

Results. A total of 131 children admitted with bronchiolitis from CMJAH and NMCH were compared in this study, 58 from CMJAH and 73 from NMCH. These children were identified by the National Health Laboratory Service as having undergone respiratory viral multiplex molecular assay analysis and hospital charts were retrospectively reviewed. In the sample group, 65 (49.6%) children had RSV in comparison to 66 (50.4%) children without RSV. Children with RSV consisted of 55 (42%) children with RSV only and 10 (7.6%) children with RSV in combination with another respiratory virus. Rhinovirus was the second most common virus detected in this cohort of children (n=17, 12.9%) followed by adenovirus (n= 12, 9.2%) and coronavirus (n=9, 6.9%). A statistically significant risk factor noted in children requiring hospitalisation for RSV bronchiolitis was an age of less than six months (p-value <0.001).

Conclusions. Bronchiolitis is a common disease in children. Respiratory syncytial virus is the most common cause of severe bronchiolitis in hospitalised infants less than six months of age.

Acknowledgements

I wish to express my sincere appreciation and gratitude to, Professor Debbie White and Professor Daynia Ballot for their guidance and knowledge in this research endeavour. I am grateful to Karren le Roux and her team of medical biological scientists at Infection Control for processing the initial data necessary for my study. A special thank you to Rose Bandini for her advice regarding the statistical analyses.

Table of Contents

Declaration i
Dedication ii
Abstract iii
Acknowledgements iv
List of Abbreviations vi
List of Figures vii
List of Tables viii
Chapter One – Submissible Paper 1
1.1 Background 1
1.2 Methods 2
1.3 Results 4
1.4 Discussion 9
1.5 Conclusion 11
1.6 Study Limitations 12
References 13
Chapter Two – Author Guidelines 15
Chapter Three – Approved Protocol 34

Appendices
Appendix A: Ethics Certificate 53
Appendix B: Turnitin Certificate 54

List of Abbreviations

CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
CMV	Conventional mode of Ventilation
CPAP	Continuous Positive Airway Pressure
CPR	Cardiopulmonary Resuscitation
CRP	C-reactive Protein
CSF	Cerebrospinal Fluid
CT	Computed Tomography
ECHO	Echocardiogram
ECMO	Extracorpeal Membrane Oxygenation
ELISA	Enzyme Linked Immunosorbent Assay
HFOV	High Frequency Oscillatory Ventilation
$HFNO_2$	High Flow Nasal Oxygen
HIV	Human Immunodeficiency Virus
ICU	Intensive Care Unit
IPPV	Intermittent Positive Pressure Ventilation
MRI	Magnetic Resonance Imaging
NHLS	National Health Laboratory Service
NIV	Non-invasive ventilation
NMCH	Nelson Mandela Children's Hospital
NPO_2	Nasal Prong Oxygen
PCR	Polymerase Chain Reaction
PHPT	Pulmonary hypertension
PICU	Paediatric Intensive Care Unit
RSV	Respiratory Syncytial Virus

List of Figures

Figure 1: Children with bronchiolitis included in this analysis 4

Figure 2: A Bar graph demonstrating the epidemiology of Respiratory Viruses from February 2018 to August 2018 9

List of Tables

Table 1: Viral Multiplex PCR results of children admitted with bronchiolitis 5

Table 2: Comparison of risk factors for children with and without RSV infection 6

Table 3: Comparison of complications, outcomes and oxygen therapy for children with and without RSV infection 8

1. Chapter One – Submissible Format

1.1 Background

Bronchiolitis is a lower respiratory tract infection caused by many viruses, primarily affecting children younger than two years.[1,2] In South Africa, the overall prevalence of respiratory viruses in children with a lower respiratory tract infection and under the age of five was 78%.[3] Respiratory viruses causing bronchiolitis include rhinovirus, respiratory syncytial virus (RSV), adenovirus, parainfluenza virus, influenza virus, human metapneumovirus, bocavirus, coronavirus and measles virus.[1,2] Respiratory syncytial virus is the most common cause of severe bronchiolitis.[1,2,4,5] RSV is estimated to account between 40 and 90% for all children requiring hospitalisation with bronchiolitis.[4,5] The increasing burden of RSV, particularly in infants, has been well documented worldwide.[4,5]

Several well-described risk factors have been associated with severe RSV infection.[5] Risk factors include prematurity, chronic lung disease, congenital lung malformations, haemodynamically significant congenital heart defects, neuromuscular disease, infancy (particularly infants less than six months of age), male gender, immune compromise and lack of breastfeeding.[2,6,7] Environmental risk factors attributing to severe illness include tobacco smoke exposure, overcrowding and day-care attendance.[2,7] It is possible for children to suffer from severe re-infections with RSV despite having humoral immunity from previous infections.[8] RSV infection rates are highest in the autumn and early winter months in South Africa, generally lasting four months.[1]

Signs and symptoms for all viral causes of bronchiolitis, including RSV, are non-specific and consist of nasal congestion, rhinorrhoea, cough, irritability, poor feeding and low-grade fever.[6,8,9] Bronchiolitis is a clinically diagnosed lower respiratory tract infection characterised by bilateral wheezing, hyperinflation and tachypnoea, it is generally preceded by the above mentioned upper respiratory prodrome symptoms.[7] Children with moderate and severe cases bronchiolitis are more likely to be caused by RSV rather than any of the other respiratory viruses.[1,2,4,5]. Suspected complications should undergo further investigation, such as chest radiographs.[10] There may be a role for routine viral screening for surveillance and understanding the possible contributing role of co-infection with multiple viruses.[11,12]

Management for all cases of bronchiolitis, mild to severe, remains supportive. [13,14] Treatment goals include managing hypoxia, pyrexia and optimising nutrition.[13,14]

This study aimed to determine and compare clinical characteristics, risk factors, co-infections and outcomes for children admitted with RSV positive and RSV negative bronchiolitis at two state tertiary hospital centres in Johannesburg with the necessary equipment, facilities and staff to care for moderately and severely ill children.

1.2 Methods

This study was a retrospective, descriptive analysis of children younger than two years admitted to Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) and Nelson Mandela Children's Hospital (NMCH) with virally screened bronchiolitis from 1 February 2018 to 31 August 2018. Children with RSV positive bronchiolitis were compared to those children with RSV negative bronchiolitis.

Study Sites

CMJAH is a tertiary hospital incorporated into the academic circuit of the health science programme at the University of the Witwatersrand. The 220-bed paediatric service caters for all paediatric medical and surgical subspecialties. There are 14 beds available in the mixed paediatric and neonatal intensive care. CMJAH serves a large population including many referring clinics and hospitals. These include Bertha Gxowa Hospital, South Rand Hospital, Edenvale Hospital, Tambo Memorial Hospital, Pholosong Hospital and Far East Rand Hospital.

NMCH, a new tertiary facility in close proximity to CMJAH, opened three years ago. The hospital has both a paediatric and neonatal ICU, admitting up to 16 patients each. Paediatric cardiology and renal patients also receive care at NMCH.

Data Collection

Nasopharyngeal swab or tracheal aspirate specimens were submitted to the National Health Laboratory service (NHLS) for viral multiplex molecular assay analysis for patients admitted

with respiratory tract infections. Multiplex molecular assays detect viral nucleic acids.[15] Multiplex polymerase chain reaction (PCR)-based respiratory viral panels performed at NHLS at CMJAH tested for influenza virus, adenovirus and RSV. The NHLS outsourced full respiratory panel PCR testing on specimens from NMCH to Lancet Laboratories. The full respiratory panel tested for: adenovirus, bocavirus, coronavirus, enterovirus, influenza virus, metapneumovirus, mycoplasma pneumonia, parainfluenza, parechovirus, RSV and rhinovirus. The NHLS infection control specialists supplied lists of individuals who had undergone viral testing for bronchiolitis during the study period. These lists were reviewed and patients older than two years and from other hospitals were excluded. Hospital records of those children who were admitted with an initial diagnosis of bronchiolitis and met the specified study criteria, were reviewed. The severity of bronchiolitis was determined by the initial treating physician at the time of admission. While children from both CMJAH and NMCH's paediatric general ward and intensive care units were included in this study, all had been assessed as having either moderate or severe bronchiolitis.

Clinical, demographic, serological and radiological data were captured according to a pre-designed data collection sheet. The references ranges provided by the NHLS were used to categorise the children's results.[16] Survivors were those children who were discharged home or transferred from CMJAH or NMCH back to their base hospitals.

Statistical Analysis

An MS Excel (Microsoft, USA) spreadsheet was used to enter the data which was then imported into a statistical software package SPSS version 25 (IBM, USA). Frequencies and percentages were used to describe categorical variables. Means and standard deviations were used to describe normally distributed, continuous variables. Chi-square test and T-test were used to compare categorical and continuous variables, respectively. A p-value of <0.05 was considered significant.

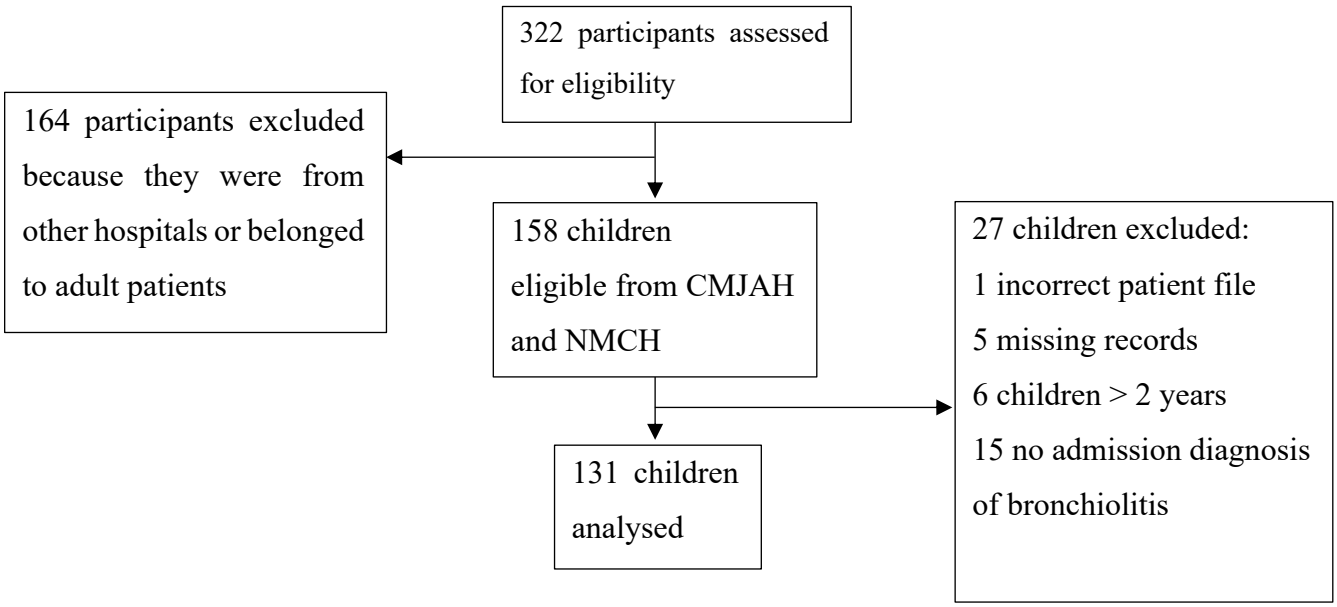
Ethics

The Human Research Ethics Committee of the University of the Witwatersrand, Johannesburg granted ethics approval for the study (clearance certificate number M190505).

1.3 Results

During the study period, 322 participants had viral specimens submitted for testing. A total of 191 participants were excluded from further analysis, 164 participants were either adult patients or from hospitals not included in this study and remaining 27 were excluded for other reasons (see Fig. 1). The remaining cohort included 131 children, 58 from CMJAH and 73 from NMCH. It is not known the total number of children who were admitted with bronchiolitis or who underwent swabbing during the study period was not known.

Figure 1: Children with bronchiolitis included in this analysis.



The most common virus isolated in children admitted with bronchiolitis to CMJAH and NMCH was RSV (n=65, 49.6%). Rhinovirus was the second most common virus detected in children (n=17, 12.9%) followed by adenovirus (n= 12, 9.2%) and coronavirus (n=9, 6.9%). There were 17 (12.9%) children who cultured more than one respiratory virus. Table 1 demonstrates the children's viral multiplex-PCR results.

Table 1. Viral Multiplex PCR (N=131) results of children admitted with bronchiolitis.

Participants with RSV	*n (%)*	Participants without RSV	*n (%)*
RSV	55 (42)	No virus present	25 (19.1)
RSV and Rhinovirus	3 (2.3)	Rhinovirus	13 (9.9)
RSV and Adenovirus	2 (1.5)	Adenovirus	5 (3.8)
RSV and Bocavirus	1 (0.8)	Influenza A virus	5 (3.8)
RSV and Coronavirus	1 (0.8)	Coronavirus	4 (3.1)
RSV and Influenza A virus	1 (0.8)	Human Metapneumovirus	3 (2.3)
RSV, Bocavirus and Coronavirus	1 (0.8)	Parainfluenza	2 (1.5)
RSV, Coronavirus and Parainfluenza	1 (0.8)	Enterovirus	2 (1.5)
		Influenza B virus	1 (0.8)
		Adenovirus and Parainfluenza	3 (2.3)
		Adenovirus and Coronavirus	1 (0.8)
		Adenovirus and Influenza B	1 (0.8)
		Rhinovirus and Coronavirus	1 (0.8)
Total	**65 (49.6)**	**Total**	**66 (50.4)**

The majority of children in this study were aged six months and younger (n=74, 56.5%), with more than half of these children having RSV positive bronchiolitis (n=47/75, 62.7%). The remaining children consisted of 45 (34.3%) between the ages of 7 to 11 months and 12 (9.1%) older than one year. Only 42 (32%) children were born prematurely, i.e. than 37 weeks gestation, with the majority of these children (n=24/42, 57,1%) having RSV positive bronchiolitis. However, prematurity was not a statistically significant risk factor for children having RSV positive bronchiolitis compared to children with non-RSV bronchiolitis. Children in this study were predominantly not exposed to HIV at birth (n=81, 61,8%). Only three children with HIV exposure were confirmed to be HIV positive with further testing. HIV did not demonstrate any statistical difference in children presenting with RSV positive bronchiolitis. There was not enough data for the following risk factors: feeding choice, other immunodeficiency states, siblings attending crèche or tobacco smoke exposure to compare and comment on in the context of this study. Table 2 compares other risk factors between RSV

positive and negative bronchiolitis participants. The only statistically significant risk factor for RSV bronchiolitis was an age of less than six months (p-value <0.001).

Table 2. Comparison of risk factors for children with and without RSV infection

Risk Factor	**RSV Positive** *N 65, n (%)*	**RSV Negative** *N (66), n (%)*	**p-value**
HIV Exposed	29 (44.6)	21 (31.8)	0.09
HIV Unexposed	36 (55.4)	45 (68.2)	
HIV PCR Positive	2 (3)	1 (1.5)	0.49
HIV ELISA/PCR Negative	63 (97)	65 (98.5)	
Premature	24 (36.9)	18 (27.3)	0.16
Congenital Heart Disease*	9 (13.8)	18 (27.3)	0.053
Chronic Lung Disease†	26 (40)	22 (33.3)	0.27
<6 months in age	47 (72.3)	27 (40.9)	**<0.001**

* Congenital heart disease with increased blood flow, consisting of: ventricular septal defects, atrial septal defects, atrioventricular septal defects and patent ductus arteriosus.

† Chronic lung disease was predominantly secondary to bronchopulmonary dysplasia (n=21/48), when specified in the respective children's hospital records, however, the remaining children's records did not specify the underlying cause for their chronic lung disease.

There was no statistically significant difference between both laboratory and radiological investigations performed on RSV positive and RSV negative children with bronchiolitis. A multivariable regression analysis showed that none of the above listed risk factors were found to be dependently associated with RSV, as evidenced by a p-value of greater than 0.05 for each variable. The majority of initial chest radiographs for children with RSV positive bronchiolitis were hyperinflated with infiltrates (n=33/65, 50.7%). Children with RSV negative bronchiolitis generally had infiltrates only on their chest radiographs (n=38/66, 57.6%). There were eight positive admission blood cultures for children with RSV and seven for children without RSV bronchiolitis. No clinically significant organisms were cultured for children with RSV bronchiolitis. While, two children without RSV grew Staphylococcus aureus and one Escherichia coli, the remaining cultures were clinically insignificant.

Complications, outcomes, oxygen therapy and length of admission is summarised in Table 3. A total of 103 (78.6%) children required admission to CMJAH and NMCH's ICU facilities for invasive methods of ventilation, during the study, 54 children with RSV and 49 without RSV. The remaining 28 (21.4%) children were cared for in the general wards. More than half of children from this study were investigated for nosocomial sepsis, 49 with RSV bronchiolitis and 43 without RSV. There were 11 children with RSV and 15 without RSV who had evidence of nosocomial sepsis on blood cultures. Children with RSV cultured the following organisms: one *Acinetobacter baumannii*, one *Candida albicans*, one *Escherichia coli*, two *Klebsiella pneumoniae*, two *Staphylococcus aureus* and four clinically insignificant organisms (*Coagulase negative staphylococcus)*. Children without RSV cultured the following organisms: one *Acinetobacter baumannii*, one *Candida albicans*, one *Escherichia coli*, one *Methicillin-resistant staphylococcus aureus*, one *Pseudomonas aeruginosa*, two *Staphylococcus aureus* and eight clinically insignificant organisms. Seven children experienced seizures during their admissions and underwent neuroimaging. Four of these children had features in keeping with hypoxic brain injury, three of whom had RSV positive bronchiolitis and one child without RSV. The three remaining children had normal neuroimaging. Seventeen children died in this study: three children had no virus isolated, seven children did not have RSV, and the remaining seven children had RSV. Three of the seven children with RSV who died had RSV in combination with another virus. However, there were no statistical differences demonstrated for outcomes or complications for either group of children.

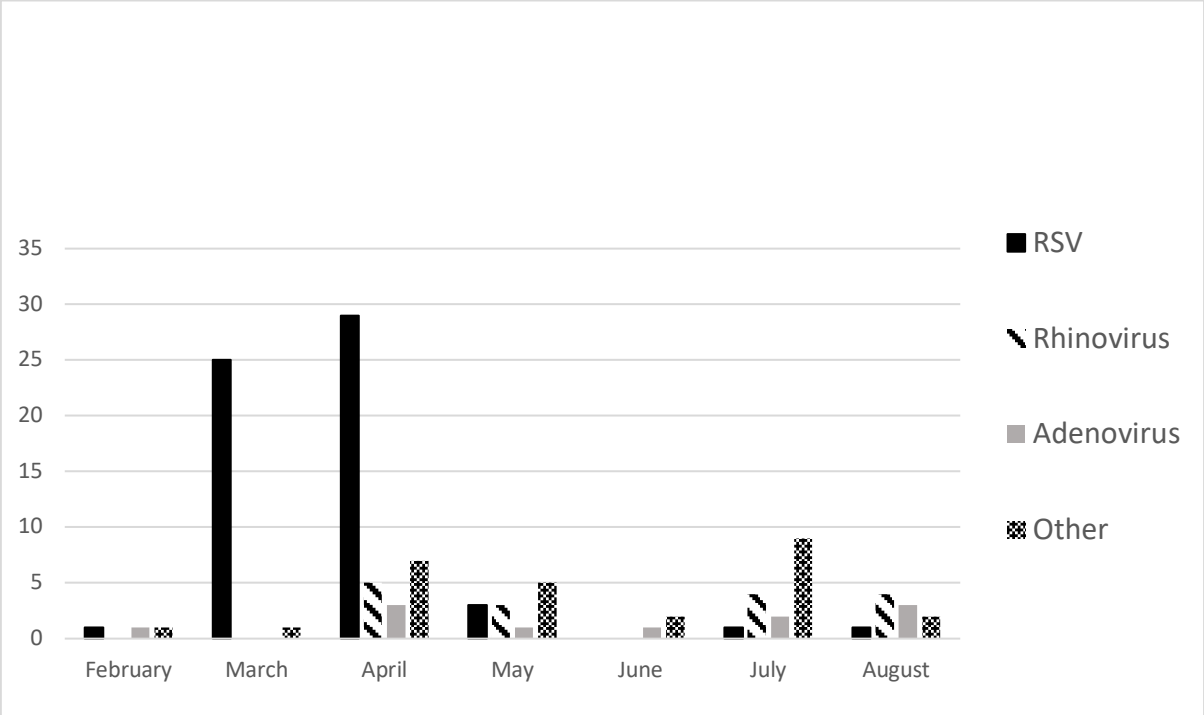
Table 3. Comparison of complications, outcomes and oxygen therapy for children with and without RSV infection

Complications and Outcomes		**RSV Positive** *n/N (%)*	**RSV Negative** *n/N (%)*	**p-Value**
Nosocomial Sepsis		49/65 (75.4)	43/66 (65.2)	0.18
Apnoea		35/65 (53.4)	30/66 (45.5)	0.38
Cardiopulmonary Resuscitation		9/65 (13.8)	14/66 (21.2)	0.35
Hypotension requiring inotropes		9/65 (13.8)	18/66 (27.3)	0.8
Seizures		5/65 (7.7)	2/66 (3)	0.27
Pulmonary Hypertension		3/65 (4.6)	7/66 (10.6)	0.61
Myocarditis		4/65 (6.2)	5/66 (7.6)	0.78
Ventilation Acquired Pneumonia		13/65 (20)	11/66 (16.7)	0.78
Outcomes	**Death**	7/65 (5.3)	10/66 (7.6)	0.64
	Discharge	58/65 (44.3)	56/66 (42.3)	
Days on oxygen	NPO_2	216/883 (24.5)	264/844 (31.3)	0.67
	$HFNO_2$	106/883 (12)	138/844 (16.4)	
	CPAP	16/883 (1.8)	4/844 (0.4)	
	CMV	429/883 (48.6)	319/844 (37.8)	
	HFOV	116/883 (13.1)	86/844 (10.2)	
	ECMO	0/883 (0)	33/844 (3.9)	
Length of admission (days)		945 (52)	873 (48)	0.27

In this study, children stayed at CMJAH and NMCH for an average of 14.5 days (s=10.3 days), admissions to ICU averaged 10.1 days (s=8.1 days). Children required oxygen therapy for approximately 13.4 days (s= 9.7days).

Children with RSV bronchiolitis were predominantly admitted in March and April of 2018, with some later admissions in July and August as shown in Figure 2. Rhinovirus was the second most common virus found from April to August.

Figure 2: A Bar graph demonstrating the epidemiology of Respiratory Viruses from February 2018 to August 2018.



Other: Human metapneumovirus, Coronavirus, Bocavirus, Parainfluenza virus, Influenza A, Influenza B and Enterovirus.

1.4 Discussion

This present study, conducted at two large academic referral centres in Johannesburg, South Africa, demonstrated that RSV was the most common virus detected in children hospitalised with moderate and severe bronchiolitis in the season of 2018 (n=65, 49.6%). In the present study, it was demonstrated that RSV was the most common virus detected in children hospitalised with severe bronchiolitis in the season of 2018 (n=65, 49.6% Table 1). Seventeen children had more than one virus identified on their respective viral swabs but the implications, i.e. determining if one specifically or the combination of all the viruses determined the severity of illness, duration of illness and subsequent outcomes for those respective children, cannot be determined in the context of this study. The next most common viruses identified in this study were adenovirus (n= 12, 9.2%) and coronavirus (n=9, 6.9%). The nine children with coronavirus all survived to discharge. These children had coronaviruses other than the newly identified SARS-CoV-2 in 2020 , responsible for the COVID-19 pandemic. The clinical presentation of children admitted with bronchiolitis with coronavirus were all respiratory in

nature with a well-documented prodrome of upper respiratory tract infection symptoms followed by unproductive coughing and tachypnoea. None of them had any of the following documented at the time of their presentations or preceding their arrival to hospital: erythematous maculopapular rash, conjunctivitis, gastrointestinal symptoms, myalgia, severe headache or confusion or loss of taste or smell, however, some of these symptoms would be difficult to illicit in a toddler.

Children with RSV presented mostly in March and April, with fewer RSV cases from May to August of 2018 (Figure 2). This is keeping with the seasonality described for RSV in Gauteng, with a peak around Autumn.[1,2] However, this specific seasonality of RSV may remarkably differ in the forthcoming years in view of the Covid-19 pandemic and our global fight to curb the infection rate. This international goal has caused our general behaviour to be modified through the implementation various levels of lockdown by each country, the mandatory wearing of face masks, better hand hygiene practices and many more individuals, including parents, working from home with fewer younger children needing to go to day-care. All of these factors contributed to an almost non-existent RSV season in 2020. However, in America during their summer months of 2021 they experienced unprecedented high levels of RSV, this was out of keeping with their typical winter season of RSV. This new pattern raises the concern that there may be a possibility of differing seasons of RSV in the not too distant future.

A number of well described risk factors have been associated with increased frequency and severity of RSV bronchiolitis.[5] In this study, infants under six months of age were more likely to be admitted with RSV positive bronchiolitis compared to other viruses ($p < 0,001$). More children with RSV bronchiolitis were premature and had chronic lung disease in comparison to RSV negative children, but these factors were not statistically significant in this study, which was unexpected when reviewing the data in comparison to other local and international studies. HIV-infected children are more likely to have pneumonia rather than bronchiolitis and HIV has been postulated to possibly be protective against RSV.[2] This was not the case in our study as more participants with RSV bronchiolitis were HIV exposed or positive, although this did not reach statistical significance. There was not enough data available to comment on impact of environmental risk factors on the children from this study.

Initial investigations, including haematological and radiological studies, yielded no statistical differences between children who were RSV positive or negative. This is in keeping with

current literature that bronchiolitis should be diagnosed clinically, assessing the disease severity from history and examination findings.[9] There may be some value in performing routine viral screening for all children presenting with bronchiolitis as it would contribute to epidemiological data as well as to cohort children with specific viruses. However, routine viral testing may not be viable in resource limited setting, especially as treatment for children with bronchiolitis remains supportive regardless of the infecting organism. However, in light of the Covid-19 pandemic, other treatment modalities have been tried and tested in the management of children admitted with coronavirus, which supports routine viral screening for children admitted with any presentation of respiratory illness.

The majority of children in this study required admission to CMJAH and NMCH's intensive care units (n=103, 78.6%). More than half of these children (n=54/103, 52.4%) had RSV bronchiolitis. This finding is comparable to other studies that have been conducted globally with regard to the large number of children of children needing hospitalisation for moderate or severe bronchiolitis having confirmed RSV. [4]

More children from the RSV positive group were investigated for nosocomial sepsis in comparison to the RSV negative group of children. This may be due to the fact that children with RSV were admitted for longer than children who did not have RSV, but this was not found to be statistically significant. Almost all the children admitted with bronchiolitis were discharged (n=114, 87.0%) home or back to their base hospital, despite the large number of children needing ICU admission and care. A total of 17 children demised, 10 (7.6%) from the RSV negative group of children and seven (5.3%) from the RSV positive group. It is difficult to compare this finding to international mortality estimations as the total number of cases of bronchiolitis and all possible causative organisms were not known in this study.

Conclusion

In keeping with international literature, RSV was the commonest virus isolated in this cohort of hospitalised children (65/131, 49.6%) with bronchiolitis.[1,2,4,5] The majority of children were under 6 months of age (75/131, 57.3%) and infants less than six months of age were more likely to have RSV confirmed bronchiolitis than those without (p-value <0.001). Respiratory syncytial virus cases peaked around Autumn in 2018, in keeping with the described local

seasonality of RSV.[1] Despite requiring hospitalisation, 114 of the 131 children in this study survived to discharge.

Study Limitations

As this was a retrospective study reviewing only the files of children screened for bronchiolitis the true prevalence of RSV bronchiolitis cannot be determined from this analysis. Not all data was available from participants' files, which limited accurate comparisons between children with and without RSV. Another limitation is that the number viruses screened for at each hospital was not standardised.

Author contributions. TSC: protocol, data collection, write-up, this article was submitted in fulfilment of the degree of Masters of Medicine in the discipline of Paediatrics at the University of the Witwatersrand; TT: supplied the NHLS raw data, review and advice; NMM and LC review and advice; DEB and DAW: oversight, advice and editing.
Funding. None.
Conflict of Interests. None.

References

1. White DA, Madhi SA, Jeena P, et al. Acute viral bronchiolitis in South Africa: Viral aetiology and clinical epidemiology. S Afr Med J. 2016;106(5):443-445. http://dx.doi.org/10.7196/SAMJ.2016.v106i5.10444
2. Dearden CX, Jeevarathnum AC, Havinga J, Green RJ. The epidemiology of respiratory syncytial virus: A retrospective review from Steve Biko Academic Hospital 2013-2016. AJTCCM. 2018;24(1):30-35. https://doi.org/10.7196/ajtccm.2017.v24i1.163
3. Cohen C, Walaza S, Moyes J, et al. Epidemiology of Viral-associated Acute Lower Respiratory Tract Infection Among Children <5Years of Age in High HIV Prevalence Setting, South Africa, 2009-2012. Pediatr Infect Dis. 2015;34(1):66-72. https://doi.org/10.1097/inf.0000000000000478
4. Walsh EE, Englund JA. Respiratory Syncytial Virus. In Benett JE, Blaser MJ, Dolin R, editors. Mandell, Douglas, and Bennett's Principle sand Practice of Infectious Diseases. Ninth Revised Edition. Philadelphia, United States: Elsevier – Health Sciences division; 2019. p. 2093 -2103. https://dx.doi.org/10.1016%2FB978-1-4557-4801-3.00160-0
5. Giovanni MD. RSV infections: State of the art. Cleve Clin J Med. 2015;82(1):s13-s18. https://doi.org/10.3949/ccjm.82.s1.03
6. Meissner HC. Viral Bronchiolitis in Children. N Eng J Med. 2016;374(1):62-72. https://doi.org/10.1056/nejmra1413456
7. Chávez-Bueno S, Mejías A, Jafri HS, Ramilo O. Respiratory Syncytial Virus: Old and New Approaches. Pediatr Ann. 2005;34(1):62-68. https://doi.org/10.3928/0090-4481-20050101-14
8. White DA, Zar HJ, Mahdi SA, et al. Acute viral bronchiolitis in South Africa: Diagnostic flow. S Afr Med J. 2016;106(4):328-329. http://dx.doi.org/10.7196/SAMJ.2016.v106i4.10704
9. Ralston SL, Lieberthal AS, Meissner HC, et al. Clinical Practice Guideline: The Diagnosis, Management and Prevention of Bronchiolitis. Pediatr Ann.2014;134:e1474-e1502. https://doi.org/10.1542/peds.2014-2742
10. Hervás D, Reina J, Yañez A, del Valle JM, Figuerola J. Hervás JA. Epidemiology of hospitalization for acute bronchiolitis in children: differences between RSV and non-RSV bronchiolitis. Eur J Clin Microbiol Infect Dis. 2012;31(8):1975-1981. https://doi.org/10.1007/s10096-011-1529-y
11. Heikkinen T, Marttila J, Salmi AA, Russkanen O. Nasal Swab versus Nasopharyngeal

Aspirate for Isolation of Respiratory Viruses. J Clin Microbiol. 2002;40(11): 4337-4339. https://doi.org/10.1128/jcm.40.11.4337-4339.2002

12. Pretorius MA, Mahdi SA, Cohen C, Naidoo D, Groome M, Moyes J. Respiratory Viral Coinfections identified by 10-Plex Real-Time Reverse-Transcription Polymerase Chain Reaction Assay in Patients Hospitalized with Severe Respiratory Illness – South Africa, 2009-2010. J Infect Dis. 2012;206(1):s159-s169. https://doi.org/10.1093/infdis/jis538
13. Zar HJ, Mahdi SA, White DA, et al. Acute viral bronchiolitis in South Africa: Strategies for management and prevention. S Afr Med J. 2016;106(4):330-332. http://dx.doi.org/10.7196/SAMJ.2016.v106i4.10437
14. Morrow BM, Feldman C, Green RJ. Acute viral bronchiolitis in South Africa: Intensive care management for severe disease. S Afr Med J. 2016;106(5):446-448. http://dx.doi.org/10.7196%2FSAMJ.2016.v106i5.10436
15. Brennan-Krohn T. Making Sense of Respiratory Viral Panel Results. ASM, 2020. https://asm.org/Articles/2020/March/Making-Sense-of-Respiratory-Viral-Panel-Results (accessed 22th July 2021). https://asm.org/Articles/2020/March/Making-Sense-of-Respiratory-Viral-Panel-Results
16. Schmidt BM, Tameris M, Geldenhuys H, et al. Comparison of haematology and biochemistry parameters in healthy South African infants with laboratory reference intervals. TM & IH. 2018; 23(1):63-68. https://doi.org/10.1111/tmi.13009

Chapter Two – Author Guidelines

Author Guidelines: SAJCH

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

To submit a manuscript, please proceed to the *SAJCH* Editorial Manager website: Editorial Manager

There is currently a backlog of articles in production. Authors submitting new articles should note that the earliest date for publication will be in the second quarter of 2022.

To access and submit an article already in production, please see the SAJCH author guidelines here.

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).

Article Processing Charges

All articles published in the South African Journal of Child Health are open access and freely available online upon publication. This is made possible by applying a business model to offset the costs of peer review management, copyediting, design and production, by charging an article-processing charge (APC) of R3 275.40 (ex Vat) for all articles published. The charge applies only to Research articles submitted after 1 Jan 2019. The APC is standard and does not vary based on length, colour, figures, or other elements.

When submitting a Research article to the SAJCH, the submitting author must agree to pay the APC should the article be accepted for publication. The APC is payable when your manuscript is editorially accepted and before production commences for publication. The submitting author will be notified that payment is due and given details on the available methods of payment. Prompt payment is advised; the article will not enter into production until payment is received.

Queries can be directed to claudian@hmpg.co.za.

Please refer to the section on 'Sponsored Supplements' regarding the publication of supplements, where a charge is applicable. Queries can be directed to dianes@hmpg.co.za or claudian@hmpg.co.za

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.

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. Please 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.

Clinical trials

Since 1st December 2005, all clinical trials conducted in South Africa have been required to be registered in the South African National Clinical Trials Register. The *SAJCH* therefore requires that clinical trials be registered in the relevant public trials registry at or before the time of first patient enrollment as a condition for publication. The trial registry name and registration number must be included in the manuscript.

Protection of rights to privacy

Patient

Information that would enable identification of individual patients 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. We further recommend that the published article is disseminated not only to the involved researchers but also to the patients/participants from whom the data was drawn. Refer to Protection of Research Participants. The signed consent form 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 *SAJCH*.

Copyright notice

Copyright remains in the Author's name. The work is licensed under a Creative Commons Attribution - Non-commercial Works License. Authors are required to complete and sign an Author Agreement form that outlines Author and Publisher rights and terms of publication. The Agreement form should be uploaded along with other submissions files and any submission will be considered incomplete without it *[forthcoming]*.

Material submitted for publication in the *SAJCH* 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 *SAJCH* 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.

Privacy statement

The *SAJCH* is committed to protecting the privacy of its website and submission system users. The names, personal particulars and email addresses entered in the website or submission system will not be made available to any third party without the user's permission or due process. By registering to use the website or submission system, users consent to receive communication from the *SAJCH* or its publisher HMPG on matters relating 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 that it is not appropriate to use self-reported or investigator-assigned racial or ethnic categories for genetic studies.

Continuing Professional Development (CPD)

SAJCH is an HPCSA-accredited service provider of CPD materials. Principal authors can earn up to 15 CPD continuing education units (CEUs) for publishing an article; co-authors are eligible to earn up to 5 CEUs; and reviewers of articles can earn 3 CEUs. Each month, *SAJCH* also publishes a CPD-accredited questionnaire relating to the academic content of the journal. Successful completion of the questionnaire with a pass rate of 70% will earn the reader 3 CEUs. Administration of our CPD programme is managed by Medical Practice Consulting. To complete questionnaires and obtain certificates, please visit MRP Consulting

Manuscript preparation

Preparing an article for anonymous review

To ensure a fair and unbiased review process, all submissions are to include an anonymised version of the manuscript. The exceptions to this requirement are Editorials, Correspondence, Book reviews and Obituary submissions.

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)'.
- Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dL).
- Litres is denoted with an uppercase L e.g. 'mL' for millilitres).
- Units should be preceded by a space (except for % and ºC), e.g. '40 kg' and '20 cm' but '50%' and '19ºC'.
- Please be sure to insert proper symbols e.g. µ not u for micro, a not a for alpha, b not B for beta, etc.
- 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.

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.

SAJCH is a Journal on child health, therefore for articles involving genetics, it is the responsibility of authors to apply the following:

- Please ensure that all genes are in italics, and proteins/enzymes/hormones arenot.

- Ensure that all genes are presented in the correct case e.g. TP53 not Tp53.

** NB: Copyeditors cannot be expected to pick up and correct errors wrt the above, although they will raise queries where concerned.

- Define all genes, proteins and related shorthand terms at first mention, e.g. '188del11' can be glossed as 'an 11 bp deletion at nucleotide 188.'

- Use the latest approved gene or protein symbol as appropriate:

- Human Gene Mapping Workshop (HGMW): genetic notations and symbols
- HUGO Gene Nomenclature Committee: approved gene symbols and nomenclature
- OMIM: Online Mendelian Inheritance in Man (MIM) nomenclature and instructions
- Bennet et al. Standardized human pedigree nomenclature: Update and assessment of the recommendations of the National Society of Genetic Counselors. J Genet Counsel 2008;17:424-433: standard human pedigree nomenclature.

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 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 clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. 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, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

- May include up to 3 illustrations or tables.
- A max of 20 - 25references

Structured abstract

- This should be no more than 250words, with the following recommended 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 intervention, primary and secondary outcomes, 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, include recommendations for further study/actions.
    - 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 include case reports, side effects of drugs and brief or negative research findings.

Guideline word limit: 1500 words

- Abstract: unstructured, of about 100-150 words
- May include only one illustration or table
- A maximum of 6 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

Review articlesshould always be discussed with the Editor prior to submission.

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 precis 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 and MP number (used for CPD points); 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 SAJCH 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.
- Scans/photos showing a specific feature e.g. *Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumour. (H&E stain).* –include an arrow to show the tumour.
- 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.
- Large tables will generally not be accepted for publication in their entirety. Please consider shortening and using the text to highlight specific important sections, or offer a large table as an addendum to the publication, but available in full on request from the author.
- 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.

Do not: Use [Enter] within a row to make ‘new rows’:

Rather: Each row of data must have its own proper row.

Do not: use separate columns for *n* and %:

Rather: Combine into one column, *n* (%).

Do not: have overlapping categories, e.g.

Rather: Use <> symbols or numbers that don't overlap.

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. http://dx/doi.org/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 *SAJCH* 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 [forthcoming]
    - Manuscript
    - 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 the Editor-in-Chief 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 either one or two reviewers selected on the basis of their expertise in the field. A double blind review process is followed at SAJCH.

Authors are expected to receive feedback from reviewers and an editorial decision within approximately 6 weeks of submission. 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.

Production process

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 anerratum 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 *SAJCH* are immediately available to all users of these databases, guaranteed a global and African audience:

- DOAJ
- AIM
- AJOL
- Crossref
- Sabinet
- Scielo
- EBSCO
- EMBASE
- Web of Science

Sponsored supplements

Contact claudian@hmpg.co.za for information on submitting ad hoc/commissioned supplements, including guidelines, conference/congress abstracts, Festschrifts, etc.

Copyright Notice

Copyright of published material remains in the Authors' name. This allows authors to use their work for their own non-commercial purposes without seeking permission from the Publisher, subject to properly acknowledging the Journal as the original place of publication.

Authors are free to copy, print and distribute their articles, in full or in part, for teaching activities, and to deposit or include their work in their own personal or institutional database or on-line website. Authors are requested to inform the Journal/Publishers of their desire/intention to include their work in a thesis or dissertation or to republish their work in any derivative form (but not for commercial use).

Material submitted for publication in the *SAJCH* 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

The *SAJCH* is committed to protecting the privacy of the users of this journal website. The names, personal particulars and email addresses entered in this website will be used only for the stated purposes of this journal and will not be made available to third parties without the user's permission or due process. Users consent to receive communication from the *SAJCH* for the stated purposes of the journal. Queries with regard to privacy may be directed to publishing@hmpg.co.za.

Chapter Three: Approved Protocol

RSV BRONCHIOLITIS IN 2018:

A DESCRIPTIVE STUDY OF CHILDREN ADMITTED TO TWO JOHANNESBURG TERTIARY HOSPITALS

Tannah Storm Cleak MBChB (UKZN)

Student Number:
304291

DEGREE: MASTERS OF MEDICINE IN THE DISCIPLINE OF PAEDIATRICS

RESEARCH PROTOCOL 2018

Supervisor:
Prof. D.A. White
MBChB, FC Paed (SA), MMed (Paed), Dip Allergy (SA), Cert Pulmonology (SA) Paed, PhD

Co-supervisor:
Prof. D. Ballot
MBChB, FC Paed (SA), PhD

Justification for study

Respiratory syncytial virus (RSV) is a common cause of moderate and severe bronchiolitis in infants. There are a number of risk factors associated with RSV infection; of these prematurity poses the greatest risk. Moderate and severe RSV bronchiolitis is associated with high morbidity and mortality rates. No effective vaccine or cure has been developed to prevent or treat RSV infection. The only form of prevention available currently is Palivizumab, a form of passive immunoprophylaxis. Palivizumab is costly and therefore strict guidelines for administration exist. However, in view of the number of cases of moderate and severe RSV bronchiolitis treated at Charlotte Maxeke Johannesburg Academic Hospital and Nelson Mandela Children's Hospital in 2018 the cost of prevention may be warranted not only in the best interests of high-risk patients but for cost effectiveness too.

List of Abbreviations

CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
CPAP	Continuous Positive Airway Pressure
CPR	Cardiopulmonary Resuscitation
CRP	C-reactive Protein
CSF	Cerebrospinal Fluid
CT	Computed Tomography
ECHO	Echocardiogram
ECMO	Extracorpeal Membrane Oxygenation
ELISA	Enzyme Linked Immunosorbent Assay
HFOV	High Frequency Oscillatory Ventilation
$HFNPO_2$	High Flow Nasal Prong Oxygen
HIV	Human Immunodeficiency Virus
IPPV	Intermittent Positive Pressure Ventilation
MRI	Magnetic Resonance Imaging
NICU	Neonatal Intensive Care Unit
NIV	Non-invasive ventilation
NMCH	Nelson Mandela Children's Hospital
NPO_2	Nasal Prong Oxygen
PCR	Polymerase Chain Reaction
PHPT	Pulmonary hypertension
PICU	Paediatric Intensive Care Unit
RSV	Respiratory Syncytial Virus

Glossary

Bronchiolitis: Bronchiolitis is a viral-induced lower respiratory tract infection that occurs predominantly in children younger than two years of age, particularly infants.

Bronchopulmonary Dysplasia (BPD) or Chronic lung disease (CLD): Is as a result of prolonged oxygen therapy in infants of 36 weeks postmenstrual age plus a total duration of 28 days of supplemental oxygen.

Congenital heart disease: Defect in the heart's structure and function present from birth.

Intermittent Positive Pressure Ventilation (IPPV): A form of manual or mechanical ventilation providing a breath sequence independent to the patient's inspiratory pattern.

Neuromuscular disease: A broad term encompassing all diseases affecting the muscles, nerves or neuromuscular junctions all resulting in impaired function of muscles.

Non-invasive Ventilation: is ventilatory support without the use of an artificial airway in the form of an endotracheal tube. Examples of which are continuous positive airway pressure (CPAP) and high flow nasal prong oxygen (HFOV).

Pulmonary hypertension: Hypertension in the pulmonary circuit, may be primary or secondary to pulmonary or cardiac disease.

Table of Contents

1.0 Introduction 39
1.1 Background 39
1.2 Rationale 43
2.0 Study Aims and Objectives 43
2.1 Principal Aim 43
2.2 Study Objectives 44
3.0 Methodology 44
3.1 Study Design 44
3.2 Study Population and Sampling 44
3.3 Data Collection and Handling 44
4.0 Data 45
4.1 Sample Size 45
4.2 Data Analysis 45
5.0 Ethics and Confidentially 45
6.0 Timeline 45
7.0 Costs and Funding 46
8.0 Limitations 46
9.0 Authorship 47
10.0 References 48
Appendix A 49

1.0 Introduction

1.1 Background Information

Definition

Bronchiolitis is a viral-induced lower respiratory tract infection that occurs predominantly in children younger than two years of age, particularly infants. [1]

Causative Organisms of Bronchiolitis

Bronchiolitis is caused by a number of different viruses, all leading to a similar clinical syndrome. [2] In South Africa, the overall prevalence of respiratory viruses in children presenting with a lower respiratory tract infection was 78%.[3] Causative viruses include respiratory syncytial virus (RSV), rhinovirus, adenovirus, parainfluenza virus, influenza virus, human metapneumovirus, bocavirus, coronavirus and measles virus.[1,2]

Respiratory syncytial virus causes approximately 60% of all lower respiratory tract infections in pre-school aged children worldwide.[4] Respiratory syncytial virus affects infants 2-3 times more than children younger than five years.[1] Moderate and severe cases of bronchiolitis are most commonly caused by RSV.[1]

Pathophysiology

Respiratory syncytial virus, a pneumovirus, is composed of a single strand of ribonucleic acid (RNA) surrounded by an 11-protein nucleocapsid and lipid envelope.[4] Respiratory syncytial virus derives its name from the syncytia formed during the invasion of the host's respiratory epithelium.[4] Respiratory syncytial virus is part of the paramyxoviridae family and is subdivided into two major subsets RSV-A and RSV-B.[1,4] These are further classified into several genotypes according to variations of the surface fusion glycoprotein G.[1,4]

Respiratory syncytial virus is acquired either through the inspiration of large virus-containing respiratory droplets or contamination of the nasal or conjunctival mucosa.[5] Viral replication takes place in the nasal epithelium with progression to the ciliated epithelial cells of the lower respiratory tract.[5] Virus invasion induces the host's innate immune response causing an influx of numerous inflammatory cells resulting in oedema of the cells, increased mucosal secretions, sloughing of necrotic tissue and reduction of ciliary movement, all of which contributes to bronchiolar narrowing.[5,6] Humoral immunity is also activated during the course of the infection to produce memory cells, however, these appear to be ineffective as evidenced by

subsequent re-infections.[6] Immune responses to RSV infection are exaggerated and this too contributes to the pathogenesis of the illness.[5,6] Respiratory syncytial virus appears to elude or impede host immune systems, but this is not completely understood and is further confounded by the fact that there is no antigenic change of RSV's surface glycoproteins.[5,6]

Seasonality of RSV

Specific RSV seasons are well documented around the world, with outbreaks lasting approximately four months.[1] In temperate climates, epidemics occur during winter months while in more tropical regions the incidence is higher during the hot, rainy seasons.[1] The cause of this temporal course of RSV, in comparison to other viruses, is not completely understood; but the geographical location and associated climate factors are thought to contribute to outbreaks.[1,2] In South Africa, RSV season varies marginally from province to province.[1] In Gauteng, RSV onset is in February and lasts until June.[1]

Risk Factors for developing RSV

A number of well-described risk factors have been associated with severe RSV infection. Risk factors include prematurity, chronic lung disease, congenital lung malformations, haemodynamically significant congenital heart defects, neuromuscular disease, infancy (particularly those younger than six months), male gender, immune compromise and lack of breastfeeding.[2,5,7] Environmental risk factors attributing to severe illness include tobacco smoke exposure, siblings living in the same household, overcrowding and day-care attendance.[2,7]

The most significant predictor associated with severe RSV infection is prematurity, with susceptibility increasing as the gestational age decreases.[5] The absence of transplacental transference of maternal immunoglobulins, which only occurs in the third trimester, may explain prematurity as a risk factor.[4] Chronological age is also an important predictor of severe disease as a large portion of hospitalizations occur in infants less than five months.[5] Infection in this age group coincides with the natural reduction of circulating immunoglobulins, as they are progressively removed by the infant's liver.[4] Immunodeficient states, including malignancy and primary immunodeficiency, have been noted to contribute to increased risk, however, in some studies conducted in South Africa, it is postulated that human immunodeficiency virus (HIV) may be protective against RSV infection, the reasons for this is not known.[2]

Clinical Course of RSV Bronchiolitis

Clinical features of bronchiolitis manifest after 4-6 days post inoculation with RSV.[5] Symptoms of RSV infection are non-specific and may consist of nasal congestion, rhinorrhoea, cough, irritability, poor feeding and low-grade fever.[5,7,8] Two days later, as a consequence of the airway inflammation and air trapping, tachypnoea, wheezing and hyperinflation develop.[7] Bronchiolitis is usually self-limiting but may progress to become severe as evidenced clinically by nasal flaring, intercostal or subcostal recessions, grunting and hypoxia.[7,8] Severe bronchiolitis usually results in hypoxia requiring hospitalisation for supplemental oxygen therapy and may even require intermittent positive pressure ventilation.

Investigations for Bronchiolitis

All patients presenting with bronchiolitis require measurement of their peripheral oxygen saturation levels in order to determine the presence of hypoxia.[7] Saturation levels of less than 92% at sea level and 90% inland indicate the need for supplemental oxygen. Other investigations, such as chest radiographs and blood studies, are generally not warranted unless severe illness or complications are suspected.[7] However, it has been recommended in a retrospective study conducted from 1995-2006, that chest radiographs be performed routinely on all hospitalized children with bronchiolitis.[9] Chest radiographs may demonstrate radiological features of Mycobacterium tuberculosis, possible congenital malformations, lung complications or be used for prognostication.[9]

Viral testing using nasopharyngeal aspirates and nasal swabs does not change routine management of bronchiolitis but may help tailor therapy, inform surveillance and measure frequency of disease.[4,7] The detection rates of viruses using nasopharyngeal aspirates versus nasal swabs are comparable for most viruses including rhinovirus, influenza type A or B, Parainfluenza virus 1, 2 or 3, adenovirus, enterovirus and herpes simplex virus.[10] However, nasopharyngeal aspirates have a higher RSV detection rate in comparison to nasal swabs.[10] In a study on the prevalence of viruses in patients hospitalised with pneumonia, viral detection rates using multiplex real-time polymerase chain reaction assay were found to be highest in patients between 2 and 4 years (83,9%) followed by those between 0 and 1 years (76,5%).[11] 17% were co-infected with other viruses, the following combinations of viruses, in order of frequency, were found in specimens tested using the 10-plex real-time reverse-transcription polymerase chain reaction assay: rhinovirus and adenovirus (24,9%), rhinovirus and RSV (22,4%), and RSV and adenovirus (14,8%).[11]

Other bacterial coinfections should be considered in complicated cases of bronchiolitis.[1] However, it may be difficult to isolate bacterial agents as blood culture yield rates are only between 3 and 18%.[1] C-reactive protein (CRP) of more than 40mg/dl has been described as a possible screening tool to differentiate between bacterial and viral infections.[4]

Management of Respiratory Syncytial Virus Bronchiolitis

Management of bronchiolitis is supportive.[11] No other adjunctive therapy, other than supplemental oxygen for hypoxia, has been shown to have any clinical benefit.[8,12] The following therapies including short-acting bronchodilator therapy, ipratropium bromide, systemic or inhaled corticosteroids, chest physiotherapy and antibiotics have been shown to have no effect on reducing hospital admissions after outpatient treatment, duration of admission or in time to full recovery at home.[8,12]

A small portion of children admitted with bronchiolitis will have severe disease needing ventilatory support.[13] An estimated 20% of admissions to paediatric intensive care units (PICU) in South Africa have positive respiratory viral isolates, particularly RSV.[13] Treatment in PICU remains supportive and is directed at managing hypoxia with either invasive or non-invasive methods, fluids and antipyretics.[13]

Prevention of Respiratory Syncytial Virus Bronchiolitis

There is no effective vaccine or antiviral available against RSV infection.[12] Passive immunoprophylaxis is the only form of prevention against RSV infection currently, an example of which is palivizumab, an intramuscular monoclonal antibody.[11] A course of five 15mg/kg intramuscular injections of Palivizumab one month apart for five months is required to treat a susceptible individual. In order to prevent one hospitalization of RSV disease in a premature infant or children with chronic lung disease or congenital heart defects between 16 and 23 need to be treated with Palivizumab.[11] A Palivizumab course costs approximately R55 000 and is hence, unaffordable in resource-limited settings. The duration of Palivizumab courses also contributes further limitation to administration in susceptible individuals.

Parents and carers, therefore, need to be counselled on other preventative measures such as hand hygiene and reducing environmental risk factors.[6]

Mortality

RSV has a case fatality rate globally of approximately 6.6%.[2] The incidence of severe RSV associated illness is found to be similar in both developing and developed countries, however, case mortality rates are higher in developing countries.[1]

1.2 Rationale

Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) is a large tertiary hospital incorporated into the academic circuit of the health science programme offered at the University of the Witwatersrand. The 220-bed paediatric service caters for all paediatric medical and surgical subspecialties. There are 14 beds available in the mixed paediatric and neonatal intensive care. Charlotte Maxeke Johannesburg Academic Hospital serves a large population including many referring clinics and hospitals. These include Natalspruit Hospital, South Rand Hospital, Edenvale Hospital, Tambo Memorial Hospital, Pholosong Hospital and Far East Rand Hospital.

Nelson Mandela Children's Hospital (NMCH), a brand new tertiary facility, has begun admitting and managing patients in their paediatric and neonatal intensive care facilities as part of their opening phase this year. NMCH will have the capacity to admit 48 patients to their PICU and NICU facilities but these units currently admit between 14 and 16 patients.

Microbiological services of the National Health Laboratory Service, provided to both CMJAH and NMCH, uses the multiplex real-time reverse-transcription polymerase chain reaction assays to process nasopharyngeal specimens for respiratory viruses.

In view of the above, CMJAH and NMCH's have been selected to describe the course of paediatric RSV infections and compare to current literature

2.0 Study Aims and Objectives:

2.1 Principal Aim

To determine the profile of paediatric patients diagnosed with bronchiolitis presenting to Charlotte Maxeke Johannesburg Academic Hospital and Nelson Mandela Children's Hospital from 01 February to 31 August 2018 and compare the profile of RSV positive to RSV negative patients.

2.2 Study Objectives

i. To describe characteristics and basic clinical information of all paediatric patients screened for bronchiolitis

ii. To compare RSV positive and negative patients in terms of risk factors, co-infections, complications and outcomes

3.0 Methodology

3.1 Study Design

A retrospective descriptive study of children admitted to Charlotte Maxeke Johannesburg Academic Hospital and Nelson Mandela Children's Hospital between 1 February and 31 August 2018, who were screened for bronchiolitis, comparing RSV positive and RSV negative patients.

3.2 Study Population and Sampling

i. Inclusion Criteria

-Any child <2 years admitted with bronchiolitis and screened using either a nasopharyngeal aspirate or nasal swab. This will be obtained from infection control records.

ii. Exclusion Criteria

-A patient treated for bronchiolitis with missing or indeterminate results.

3.3 Data collection and Handling

Files will be obtained from the record departments at CMJAH and NMCH according to the list of patients provided by the infection control team, for each hospital, who were screened for viral causes of bronchiolitis. Data will be entered onto a prepared data collection sheet (Appendix A). Each participant will be allocated a data collection number in sequential and rising order. The author will only know the participant's data collection number. Data will be entered into an Excel spreadsheet.

4.0 Data

4.1 Sample Size

A total number of approximately 110 patients were tested for bronchiolitis at Charlotte Maxeke Johannesburg Academic Hospital and Nelson Mandela Children's Hospital during the study time period.

4.2 Data Analysis

Data will be captured using Microsoft Excel spreadsheets. Statistical analysis will be carried out using means and standard deviations for continuous variables with a normal distribution. Categorical variables will be described using frequency and percentages. Medians, ranges and interquartile percentages will be used for ordinal variables not having a normal distribution. Comparisons will be carried out with the aid of chi-square tables for categorical variables and Student t-test for continuous variables. SPSS version 25 will be employed to analyze data.

5.0 Ethics and Confidentiality

Ethical clearance will be obtained from the Human Research Ethics Committee, University of Witwatersrand. Permission will be obtained from the respective chief executive officers at Charlotte Maxeke Johannesburg Academic Hospital and Nelson Mandela Children's Hospital. The study will be registered on the National Health Research Database. Furthermore, in view of it being a retrospective descriptive study with data obtained from existing records and the maintenance of patient confidentiality, consent will not be required from patients, parents or primary caregivers involved.

6.0 Timeline

Table 1. Timeline

	Sep 2018	Oct 2018	Jan 2019	Feb 2019	Mar 2019	Jun 2019	Jul 2019	Sep 2019	Oct 2019	Nov 2019	Nov 2019	Dec 2019
Literature Review												
Preparation of Protocol												

Protocol Assessment												
Ethics Approval												
Post Graduate Approval												
Data Collection												
Data Analysis												
Writing up of Research Report												
Supervisor Review												
Writing up of Paper												

7.0 Costs and Funding

Costs involved would include stationery, photocopying, printing and binding as well as the purchase of software from the University ofWitwatersrand (namely statistical and referencing packages). All costs incurred will be borne by the principal investigator. Costs are expected to total to the amount of R3000.

8.0 Limitations

In view of this study being a retrospective audit, it relies on both on the confirmed diagnosis of RSV and the existing records obtained during the period of analysis. Patients who have incomplete records may weaken the study. Assessing the presence of pulmonary hypertension will be limited to those patients who had echocardiograms undertaken, as this is not a routine investigation in children with bronchiolitis this data will be limited.

9.0 Authorship

Table 2. Authorship Table

Name	**Department/ Institution**	**Involvement**	**Contribution to Study**
Dr T. Cleak	Department of Paediatrics, University of Witwatersrand, CMJAH	Principle Investigator First Author	Principle Investigator
Prof D. White	Department of Paediatrics, University of Witwatersrand, CMJAH	Co-supervisor, Co-author	Co-supervisor
Prof D. Ballot	Department of Paediatrics, University of Witwatersrand, CMJAH	Co-supervisor, Co-author	Co-supervisor
Dr P. Moshesh	Department of Paediatrics, University of Witwatersrand, NMCH	Collaborator, Co-author	Patient data collection
Dr P. Chirwa	Department of Paediatrics, University of Witwatersrand, NMCH	Collaborator, Co-author	Patient data collection
Dr T. Thomas	Infection control Lab (NHLS) Department of Clinical Microbiology and Infectious Diseases University of Witwatersrand, CMJAH	Collaborator, Co-author	Patient data collection

10.0 References

1. White DA, Madhi SA, Jeena P, Zar HJ, Morrow BM, Masekela R, et al. Acute viral bronchiolitis in South Africa: Viral aetiology and clinical epidemiology. S Afr Med J. 2016;106(5):443-445.
2. Dearden CX, Jeevarathnum AC, Havinga J, Green RJ. The epidemiology of respiratory syncytial virus: A retrospective review from Steve Biko Academic Hospital 2013-2016. AJTCCM. 2018;24(1):30-35.
3. Cohen C, Walaza S, Moyes J, Groome M, Tempia S, Pretorius M, et al. Epidemiology of Viral-associated Acute Lower Respiratory Tract Infection Among Children <5Years of Age in High HIV Prevalence Setting, South Africa, 2009-2012. Pediatr Infect Dis. 2015;34(1):66-72.
4. Giovanni MD. RSV infections: State of the art. Cleve Clin J Med. 2015;82(1):s13-s18.
5. Meissner HC. Viral Bronchiolitis in Children. N Eng J Med. 2016;374(1):62-72.
6. Chávez-Bueno S, Mejías A, Jafri HS, Ramilo O. Respiratory Syncytial Virus: Old and New Approaches. Pediatr Ann. 2005;34(1):62-68.
7. White DA, Zar HJ, Mahdi SA, Jeena P, Morrow B, Masekela R, et al. Acute viral bronchiolitis in South Africa: Diagnostic flow. S Afr Med J. 2016;106(4):328-329.
8. Ralston SL, Lieberthal AS, Meissner HC, Alverson BK, Baley JE, Gadomski AM, et al. Clinical Practice Guideline: The Diagnosis, Management and Prevention of Bronchiolitis. Pediatr Ann.2014;134:e1474-e1502.
9. Hervás D, Reina J, Yañez A, del Valle JM, Figuerola J. Hervás JA. Epidemiology of hospitalization for acute bronchiolitis in children: differences between RSV and non-RSV bronchiolitis. Eur J Clin Microbiol Infect Dis. 2012;31(8):1975-1981.
10. Heikkinen T, Marttila J, Salmi AA, Russkanen O. Nasal Swab versus Nasopharyngeal

Aspirate for Isolation of Respiratory Viruses. J Clin Microbiol. 2002;40(11): 4337-4339.

11. Pretorius MA, Mahdi SA, Cohen C, Naidoo D, Groome M, Moyes J. Respiratory Viral Coinfections identified by 10-Plex Real-Time Reverse-Transcription Polymerase Chain Reaction Assay in Patients Hospitalized with Severe Respiratory Illness – South Africa, 2009-2010. J Infect Dis. 2012;206(1):s159-s169.
12. Zar HJ, Mahdi SA, White DA, Masekela R, Risenga S, Lewis H, et al. Acute viral bronchiolitis in South Africa: Strategies for management and prevention. S Afr Med J. 2016;106(4):330-332.
13. Morrow BM, Feldman C, Green RJ. Acute viral bronchiolitis in South Africa: Intensive care management for severe disease. S Afr Med J. 2016;106(5):446-448.

Appendix A

Study Identifier number: _____

Data Collection Sheet

Age: _____

Date of admission: _____

Date of discharge/death: _____

Length of stay: _____ days

Outcome: Discharge: ☐☐

Death: ☐

☐

HIV: Unexposed: ☐ Exposed: ☐

HIV PCR/ELISA Result: Positive: ☐ Negative: ☐

Risk Factors for RSV:

Ex-premature: Yes: ☐ No: ☐☐

Gestational Age: _____ weeks

Congenital heart disease: Yes: ☐ No: ☐

Congenital lung disease: Yes: ☐ No: ☐

Neuromuscular disease: Yes: ☐ No: ☐

Age <6months: Yes: ☐ No: ☐

Exclusive Formula Feeding: Yes: ☐ No: ☐

Immune compromise: Yes: ☐ No: ☐

(Malignancy, primary immunodeficiency)

Siblings in household: Yes: ☐ No: ☐

Age of siblings: _____

Attending day-care: Yes: ☐ No: ☐

Exposure to tobacco smoke: Yes: ☐ No: ☐

Unknown: Yes: ☐ No: ☐

Investigation:

Nasopharyngeal specimen: RSV: Yes: ☐ No: ☐

Indeterminant: Yes: ☐ No: ☐

If RSV negative; what virus was found:

Virus:_____

Initial Chest Radiograph:

Hyperinflation:	Yes:	□	No:	□
Patchy infiltrates:	Yes:	□	No:	□
Pneumothorax:	Yes:	□	No:	□
Atelectasis:	Yes:	□	No:	□
Other:	Yes:	□	No:	□

Describe:_____

Serology:

Admission:

Haemoglobin: _____

Platelets: _____

White cell count: _____

Lymphocytes (%): _____

Neutrophil (%): _____

CRP: _____

Blood culture:

Initial: Positive: □ Negative: □

Organism:_____

Subsequent: Positive: □ Negative: □

Organism:_____

CSF:

Cell count: Normal: □ Abnormal: □

Culture: Positive: □ Negative: □

Organism:_____

CT Scan: Yes: □ No: □

Findings:_____

_____

MRI Scan: Yes: □ No: □

Findings:_____

_____

ECHO: Yes: □ No: □

PHPT: Yes: □ No: □

Cardiac anomaly: Yes: □ No: □

Findings:_____

_____

Supplemental oxygen: Yes: □ No: □□ Number of days:_____

Ventilation

NIV: CPAP: Yes: □ No: □ Number of days:_____

HFNP$O_{2:}$ Yes: □ No: □ Number of days:_____

IPPV: CMV: Yes: □ No: □ Number of days:_____

HFOV: Yes: □ No: □ Number of days:_____

ECMO: Yes: □ No: □ Number of days:_____

Complications:

Nosocomial sepsis: Yes: □ No: □

Apnoea: Yes: □ No: □

CPR: Yes: □ No: □

Number of episodes:_____

Hypotension needing Inotrope support: Yes: □ No: □

Seizures: Yes: □ No: □

Pulmonology Hypertension: Yes: □ No: □

Other: Yes: □ No: □

Details:_____

Appendix A: Ethics

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Tannah Storm Cleak

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M190505

NAME: (Principal Investigator)	Dr Tannah Storm Cleak
DEPARTMENT:	Paediatrics Charlotte Maxeke Johannesburg Academic Hospital: Paediatric and Neonatal Intensive Care Unit, General Paediatric Wards, Nelson Mandela Children's Hospital: Paediatric and Neonatal Intensive Care Units
PROJECT TITLE:	RSV Bronchiolitis in 2018: A descriptive study of children admitted to two Johannesburg tertiary hospitals
DATE CONSIDERED:	31/05/2019
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof Debbie White and Prof Daynia Ballot
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	03/09/2019

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 Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. 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 resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **May** and will therefore be due in the month of **May** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix B: Turnitin Report

00100697:Tannah_Cleak.docx

ORIGINALITY REPORT

6%	5%	5%	3%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	www.samj.org.za Internet Source	2%
2	Zeina Naja, Danielle Fayad, Sarah Khafaja, Sarah Chamseddine, Ghassan Dbaibo, Rima Hanna-Wakim. "Bronchiolitis Admissions in a Lebanese Tertiary Medical Center: A 10 Years' Experience", Frontiers in Pediatrics, 2019 Publication	1%
3	Refiloe Keketso Mopeli, Debbie White, Daynia Ballot. "An audit of primary medical conditions in children admitted to the paediatric intensive care unit of Charlotte Maxeke Johannesburg Academic Hospital", South African Journal of Child Health, 2016 Publication	1%
4	Submitted to University of Witwatersrand Student Paper	1%
5	www.sarinet.org Internet Source	1%
6	journals.plos.org Internet Source	1%

7	academic.oup.com Internet Source	1 %

Exclude quotes	On	Exclude matches	< 1%
Exclude bibliography	On		