AN AUDIT OF PRIMARY MEDICAL CONDITIONS IN CHILDREN ADMITTED TO THE PAEDIATRIC INTENSIVE CARE UNIT OF CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in particular fulfillment of the requirements for the degree of Masters in Medicine (MMed).

Johannesburg, 2017.

DECLARATION

I Refiloe Keketso Mopeli declare that this Research Report is my own, unaided work. It is being submitted for the Degree of Masters in Medicine at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

6th day of January 2017 in _____

Abstract

Objective: There is approximately one paediatric intensive care unit (PICU) bed per 22800 children in South Africa, making it a very limitedresource. Our objectives were to determine the spectrum of medical conditions in children admitted to a PICU, their outcomes, and to compare the number and outcomes of HIV exposed/infected children versus HIV unexposed children.

Design and setting: This was a retrospective chart review of children older than 28 days of life, admitted to Charlotte MaxekeJohannesburg Academic Hospital (CMJAH) PICU for medical conditions from 1st January 2013 to 31st July 2014.

Results: There were 883 admissions; 518(59%) were neonates, 234(26.5%) were surgical patients leaving a final sample of131(14.8%) children with medical conditions. The median age of children admitted was 3.8 months. Forty four/131(34%) childrenwere HIV exposed. Sixteen/131(12.2%) had a positive HIV PCR result. Lower respiratory tract infections (LRTI) accounted for two thirds of all admissions at 84/131(64.1%) and were significantly more common in HIV exposed children (p=0.0005). Thirty two/131(24.4%) patients died. HIV exposed children stayed 3 days longer (p=0.015), were ventilated for 4 more days (p=0.012) and were three times more likely to require high frequency oscillatory ventilation (p=0.0005) than HIV unexposed children. Mortality was similar between these two groups. Children confirmed HIV PCR positive had significantly longer duration of ICU stay (p=0.03) and ventilation (p=0.006) than those who were exposed but uninfected.

Conclusion: There were883 childrenadmitted in 19 months to CMJAH PICU. Fifteen percent of admissions were for medical conditions, two thirds of which were for LRTI. One third of the children were HIV exposed and had similar outcomes to their unaffected counterparts, although their duration of ventilation and length of stay were longer.

ACKNOWLEDGEMENTS

The hospital management of Charlotte Maxeke Johannesburg Academic Hospital.

The staff of the PaediatricIntenive Care Unit of Charlotte Maxeke Johannesburg Academic Hospital.

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LIST OF ABBREVIATIONS

SA: South Africa

LRTI:lower respiratory tract infection

PICU:paediatric intensive care unit

PRISM:paediatric risk of mortality

PIM:paediatric index of mortality

CMJAH: Charlotte Maxeke Johannesburg Academic hospital

HIV:human immunodeficiency virus

HAART: highly active antiretroviral therapy

PCP: pneumocystis jirovecii pneumonia

CMV:cytomegalovirus

ELISA:enzyme-linked immunosorbent assay

PCR:polymerase chain reaction

rRT-PCR: real-time reverse transcription polymerase chain reaction

TB: tuberculosis

REDCAP: research electronic data capture tools

CPAP: continuous positive airway pressure

IPPV:intermittent positive pressure ventilation

HFOV: high frequency oscillatory ventilation

URT: upper respiratory tract infection

CNS: central nervous system

GIT: gastrointestinal tract

RSV: respiratory syncytial virus

PMTCT: prevention of mother to child transmission

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An audit of primary medical conditions in children admitted to the paediatric intensive care unit of Charlotte Maxeke Johannesburg Academic Hospital

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Conclusion: There were883 childrenadmitted in 19 months to CMJAH PICU. Fifteen percent of admissions were for medical conditions, two thirds of which were for LRTI. One third of the children were HIV exposed and had similar outcomes to their unaffected counterparts, although their duration of ventilation and length of stay were longer.

Keywords: children; intensive care; paediatrics; HIV; pneumonia

Introduction

Background

South Africa (SA) is a low to middle income country with an estimated population of 18.6 million children.[1] The under 5 mortality rate was estimated to be 41 per 1000 live births in 2015, with lower respiratory tract infections (LRTIs) causing 16.9% of those deaths.[2] Many of these children may have benefitted from admission into a Paediatric Intensive Care Unit (PICU) where mechanical ventilation could have been offered to them. However, there are not enough PICU beds in S.A to cater for the needs of the sickest children.

A South African national audit of critical care resources done in 2005 found that only 815 of 4618 ICU beds were assigned to paediatric and neonatal patients, and these are often shared. There is a paucity of data on the breakdown of allocated paediatric versus neonatal beds.Most hospitals were found to be admitting children to combined medical and surgical units.[3] There is thus approximately one paediatric ICU bed per 22800(18.6 million/815) children.

In this South African setting with limited resources, decisions have to be made as to how best to allocate these resources. Some PICUs have developed and implemented explicit policies for the use of PICU resources, thus providing a 'reasonable' process for equitable utilization of limited resources; however SA does not have national or provincial guidelines for admitting patients to ICU.[4, 5]

Various scoring systems have been developed to allow for assessment of the quality of care in PICUs, e.g. PRISM III, PIM2, PEMOD, PELOD, TISS and SOFA scores.[6]Wells et al found the PRISM score to have a poor discriminatory function over a 6 year period (1989-1994) in a South African ICU.[7] Subsequent to that a study done at the Red Cross War Memorial Children's Hospital in 2007 found that the PIM and PIM2 scores demonstrated good overall discrimination, therefore validating their use in S.A.[8] There is not much data on admission trends and outcomes in South African PICUs which could be used to possibly develop our own scoring systems.This study could add to that pool of knowledge in terms of assessing quality of care in PICUs.

Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) is a tertiary teaching and referral center that provides health care services to the people of Gauteng Province as well as to neighbouring provinces. The 220 bed paediatric service caters for all paediatric and paediatric surgical subspecialties. There are 15 beds in the PICU which are in high demand. The consultant staff in the PICU consists of four neonatologists and one paediatric pulmonologist. There are no dedicated paediatric intensivists. A retrospective review was done from 1993 to 1994 by Ballot et al which included all patients above 3 months age of age admitted to the PICU. They found that patients with the highest mortality rates were those with complicated infectious illnesses,

near drowning, gastroenteritis, and cardiomyopathy.[9] An audit of this nature at CMJAH PICU has not been done for several years.

Impact of Human Immunodeficiency Virus (HIV) on PICU Admissions

SA is faced with one of the highest rates of HIV infection worldwide. The Joint United Nations Programme on HIV/AIDS estimated that in 2013 there were 360000 children from 0 to 14 years of age living with HIV in SA.[10]In the pre-highly active anti-retroviral therapy(HAART) era,HIV infected children with co-infections such as pneumocystis jirovecii pneumonia (PCP) had worse outcomes than other patients admitted to PICU and were therefore not routinely ventilated. Admitting HIV infected children with severe pneumonia to a PICU in a setting of scarce resources created several ethical dilemmas for paediatricians.[11]Many times the first suspicion of HIV in infected children is after they have been admitted to PICU.[12]

More information is needed as to whether there are differences in comorbidities and outcomes of HIV exposed and HIV infected children admitted to PICU and if these differences should be considered when making decisions for PICU bed allocations. A retrospective chart review by Rabie et al at Tygerberg Children's Hospital, to determine the prevalence and outcome of HIV-infected patients in PICU, showed a median length of stay for HIV infected children of 6 days which was significantly longer than for the non HIV infected children of 3 days (p=0.0001).[5]Cost differentials for HIV infected and uninfected children admitted for the management of pneumonia in a public setting were determined by Kitchin et al who found that the length of stay for HIV infected children was 5.7 days longer among admissions to the PICU, and that the cost of admission for HIV infected children was significantly higher. They also found that the number of deaths of HIV infected children was 28.1 % higher than uninfected children.[13]However; it has been shown that early initiation of HAART can improve outcomes of HIV infected children in PICU.[11]

Acute respiratory failure due to LRTI is a major cause for admission in HIV exposed and infected children.Rabie et al found that 76% of HIV infected children admitted to the PICU were admitted for acute respiratory failure and 33% of admissions had a confirmed diagnosis of PCP.[5]Another review found that cytomegalovirus (CMV) infection had affected nearly 90% of HIV exposed children.[14]

Study Aim

This study aimed to describe the disease spectrum and outcome of children admitted for medical conditions to PICU at CMJAH.

Study Objectives

This study was a retrospective review to determine the following:

1. The spectrum of medical conditions among children admitted to PICU
2. The short term outcomes of children admitted to the PICU
3. The number and outcomes of HIV exposed or infected children admitted compared with HIV unexposed children.

Subjects and Methods

This study was conducted in the PICU of CMJAH, areferral hospital in Gauteng, South Africa. The records of children admitted to the PICU from 1st January 2013 to 31st July 2014 were reviewed.Admission to the PICU at the time of the study was primarily based onthe need for ventilation, but occasionally patients requiring intensive observation were admitted.The study included children over 28 days of life admitted to PICU for medical conditions. All surgical and trauma admissions were excluded.If a child had a medical condition but subsequently required surgery they were excluded. Children with confirmed HIV infection would not be routinely readmitted to the PICU. The records were reviewed for demographics, admission diagnosis, HIV status, duration of ICU stay and ventilation, and survival to discharge from PICU. Some children had multiple diagnoses and each one was counted.

The definitions used for the conditions have been listed in Table 1. All children admitted with a medical condition were routinely tested for HIV with an enzyme linked-immunosorbent assay (ELISA) test. Those with a positive ELISA were further tested with an HIV polymerase chain reaction (PCR) test for confirmation of their HIV status. Blood specimens were taken under sterile conditions for bacterial culture in all patients. Children with acute LRTIs were only screened for respiratory pathogens if clinically indicated, at the discretion of the attending physician and may have included any of the following: tracheal aspirates for multiplex real-time reverse-transcription polymerase chain reaction (rRT-PCR) assay for respiratory viruses, microscopy and culture, pertussis PCR, gene Xpert for tuberculosis (TB) and/or PCP immunofluorescence. Children were managed according to standard treatment protocols at the discretion of the attending physician. Empiric antibiotics for bacterial pneumonia were intravenous Ampicillin and Gentamicin. Children with suspectedPCP and CMV pneumonia were treated as a syndrome as the two are not easy to differentiate clinically; therefore children were treated empirically with Trimethoprim-Sulphamethoxazole plus corticosteroids, and Ganciclovir while awaiting confirmatory results.

After reviewing the records for conditions and outcomes the children were then divided into two groups, HIV exposed and HIV unexposed. Comparisons were made between the two groups to find statistically significant differences in all the variables. The group of HIV exposed children was further divided into those that were HIV PCR positive and those that were HIV PCR negative. These two groups were also compared for any significant differences.

Data was managed using Research Electronic Data Capture tools (REDCAP), hosted by the University of the Witwatersrand.[15] Information was captured for each patient on discharge from PICU. De-identified data was then entered into Microsoft Excel. Cases were allocated a study number.

Table 1. Definitions

Medical condition	A life threatening disease not requiring surgical intervention.
Duration	Period of time calculated in days and not hours.
Upper respiratory tract infections	An infection affecting the respiratory tract above the level of the larynx including croup and retropharyngeal abscess.
Lower respiratory tract infection	An infection affecting the respiratory tract from below the larynx leading to cough, difficulty breathing, tachypnea or chest wall indrawing .
Clinical diagnosis of PCP	A lower respiratory tract infection accompanied by severe hypoxia, a clear chest on auscultation, and a ground-glass interstitial infiltrate on chest radiograph findings.
Neonates	Children less than 28 days old, including those who had been discharged and admitted from home.
Bacterial infection	Diagnosis made on the basis of a positive blood culture.
Cardiovascular conditions	Includes congenital cardiac lesions, myocarditis, shock(need for inotropes), cardiac failure, and arrhythmia.

Statistical Analysis

Categorical variables were described using percentages and frequencies. Continuous variables were described using median and range as the data was skew. Comparisons were made using the Chi squared test for categorical variables and the Mann Whitney U test for continuous variables. A p value <0.05 was used as the level of significance.

Ethical Considerations

Ethical approval was obtained from the University of the Witwatersrand Human Research Ethics Committee (Ethics Clearance Number M140363). Permission to review the patients' records was obtained from the clinical manager of CMJAH.

Results

Demographics

There were 883 PICU admissionsduring the 19 month study period. Five hundred and eighteen (59%) of these were neonates (<28 days) and 234(26.5%) were surgical patients. The remaining sample thus included 131 children (14.8%). The male:female ratio was 1:0.66. The median age of the patients admitted was 3.8 months with an interquartile range (IQR) of 14.3 months as represented in figure 1.

The median duration of ventilation was 4 days with an interquartile range of 6 days, while the median duration of stay was 5 days with an interquartile range of 7 days. There were 32/131 (24.4%) deaths in the PICU, and a further 8 (6%) children died in the hospital wards after discharge from PICU.

There were 129/131 children tested for HIV. Forty four/131 (33.5%) of the children were HIV exposed, 85/131 (65.9%) were unexposed, and two were unknown. The 2 children whose status was unknown were excluded from further analysis. Sixteen of 131 children (12.2%) were HIV infected with a positive HIV DNA PCR.

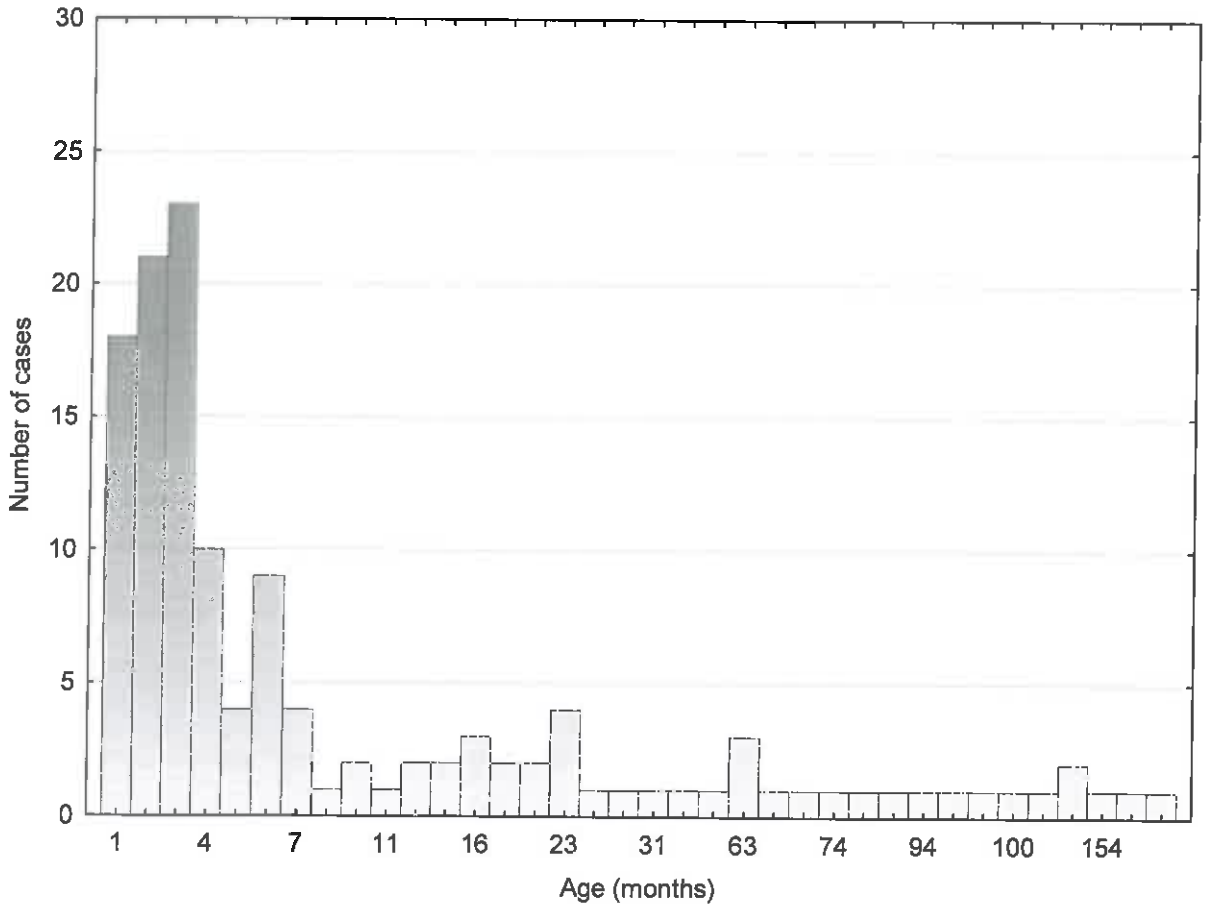

Figure 1. Histogram of the ages of the children admitted in months

Conditions of Children Admitted

The spectrum of medical conditions was wide with 84/131 (64.1%)having LRTIs, accounting for the majority of admissions. (See Figure 2)

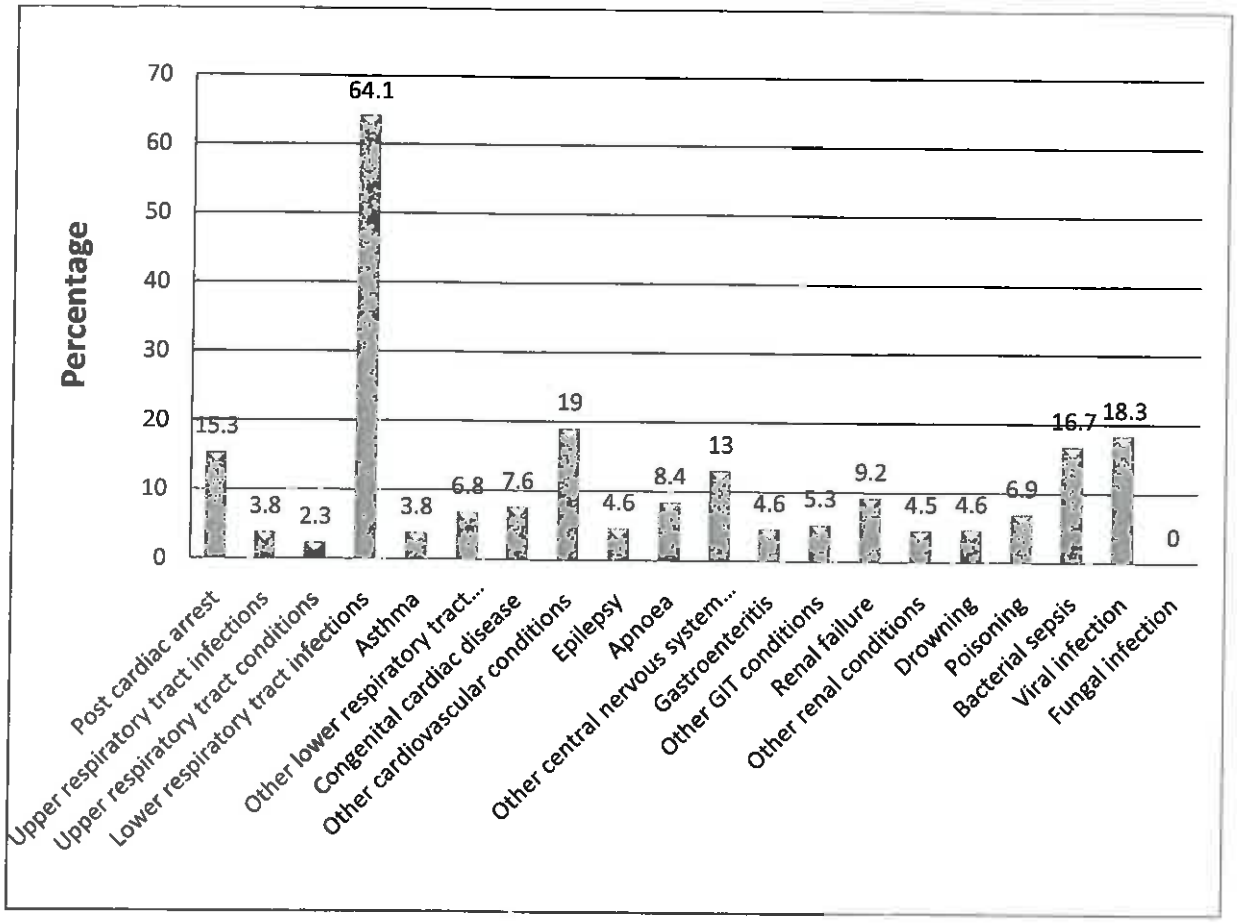

Figure 2. Admission diagnoses for children admitted with medical conditions to PICU from 1st January to 31st July 2014

Note: Some children had multiple admission diagnoses.

There were 122/131 childrenwho were intubated and ventilated, 1/131 child received continuous positive airway pressure (CPAP), and 8 children were not ventilated. Of those 122 children that were on intermittent positive pressure ventilation(IPPV), 14/122 (11.4%) were switched to high frequency oscillatory ventilation (HFOV). Twelve children needed inotropic support.

Pathogens

There were 22/131 (16.7%) positive bacterial cultures on blood specimens from the children. Coagulase negative staphylococcus (CNS) was the bacterial pathogen most frequently identified,

in 6/131 (4.6%) children. There is a possibility that these may have been contaminants howeverCNS is the commonest infection in this PICU.(See Table 2)

Viral pathogens were identified in 16/131 (12.2%) children.No fungi were isolated, and PCP was identified in only 3/131 (2.3%)tracheal aspirates by direct immunofluorescence assay.(See Tables 2 and 3)

Table 2. Infections of Children Admitted Confirmed on Blood Culture

Infections	**number**
Bacterial sepsis 22/131 (16.7%)	
-*Klebsiella pneumonia*	1 (0.8%)
-*ESBL Klebsiella*	2 (1.5%)
-*Staphylococcus aureus*	1 (0.8%)
-*Coagulase negative staphylococcus*	6 (4.6%)
-*Streptococcus viridans*	4 (3.1%)
-*Streptococcus pneumoniae*	1 (0.8%)
-*Acinetobacter baumannii*	1 (0.8%)
-*Escherichia.coli*	5 (3.8%)
-*Enterococcus faecalis*	2 (1.5%)
-*Enterobacter cloacae*	1 (0.8%)

Table 3. Infections of Children Admitted Confirmed on Tracheal Aspirate

Infections	**number**
Viral infection 16/131 (12.2%)	
-Adenovirus	4 (3.1%)
-Respiratory Syncitial Virus	9 (6.9%)
-Other viruses	3 (2.3%)
-Pneumocystis Jirovecii	3 (2.3%)
Fungal infection 0 (0%)	

Eight children had a clinical diagnosis of CMV made by the admitting doctors. These 8 patients were also found to be HIV positive on DNA PCR. The patients had their CMV viral loads quantified from a blood specimen by DNA PCR to support the diagnosis, and were empirically treated with Ganciclovir while awaiting viral load results. Only two patients had viral loads above 6000IU/ml while five were below the level of quantification and one was indeterminate. At the CMJAH PICU a viral load of greater than 4.0 log copies is considered indicative of active CMV infection and disease, therefore infection was not proven in the 8 children.

Comparison between HIV unexposed and HIV exposed children

Table 4 compares the demographics, medical conditions and outcomes of HIV exposed and unexposed children.44/131 (34.1%) of the children were HIV exposed. The median duration of stay for HIV exposed children of 8 days was significantly longer than for HIV unexposed children of 5 days, (p=0.015). Duration of ventilation was also 4 days longer for HIV exposed children, (p=0.012). More HIV exposed children were transitioned to HFOV 11/44 (25%) than unexposed children 3/85 (3.5%), (p=0.0005).

LTRIs accounted for over half of all admissions, regardless of HIV status but HIV exposed children were much more likely to be admitted with LRTI (90.9%) than HIV unexposed children (51.8%), (p=0.0005). There was no significant difference in the proportion of deaths between the two groups.

Table 4. Comparison of HIV Exposed Children with Unexposed Children

	HIV unexposed	HIV exposed	
Total admissions	85 (65.9%)	44 (34.1%)	2 unknown
Median age in months	6.3	2.7	p=0.0005
Died in PICU	19 (22.4%)	11 (25%)	p=0.73
Median PICU stay in days	5	8	p=0.015
Median days ventilated	4	8	p=0.012
Readmission	11 (12.9%)	0	p=0.013
IPPV	77 (90.6%)	42 (95.5%)	p=0.32
HFOV	3 (3.5%)	11 (25%)	p=0.0005
Inotropes	6 (7.1%)	5 (11.4%)	p=0.4
Respiratory tract conditions			
Upper respiratory tract conditions			
URT infections	4 (4.7%)	1 (2.3%)	p=0.394
Other URT conditions	1 (1.2%)	2 (4.5%)	p=0.21
Lower respiratory tract conditions			
LRT infections	44 (51.8%)	40 (90.9%)	p=0.0005
Asthma	5 (5.9%)	0	p=0.1
Pleural effusion	2 (2.4%)	0	p=0.3
Other LRT conditions	4 (4.7%)	0	p=0.25
Other systems			
Cardiovascular conditions	25 (29.4%)	9 (20.5%)	p=0.27
CNS conditions	23 (27.1%)	9 (20.5%)	p=0.41
GIT conditions	9 (10.6%)	3 (6.8%)	p=0.485
Renal conditions	16 (18.8%)	2 (4.5%)	p=0.027
Infections			
Bacterial sepsis	12 (14.1%)	10 (22.7%)	p=0.218
Viral infections	10 (11.8%)	6 (13.6%)	p=0.78
RSV	5 (5.9%)	4 (9.1%)	p=0.49
PCP infection	1 (1.2%)	2 (4.5%)	p=0.229

Some of the diagnoses of bacterial or viral pneumonia were made clinically by the admitting doctor before blood or tracheal aspirate samples could be collected and the children would therefore be treated empirically for those conditions. Taking a closer look at the LRTIs it was found that HIV exposed children were significantly more likely to present with bacterial pneumonia (45.5%) compared to HIV unexposed children (20.3%) (p=0.002). All ten children who had a clinical diagnosis of PCP were HIV exposed compared to 0 children in the HIV unexposed group, (p=0.0005). Eight of these children had Beta D glucan assays done. Five children had a BD glucan level greater than 500pg/ml, and the others were below that level. This supports but does not confirm the diagnosis made by the doctors clinically.

Comparison of HIV Polymerase chain reaction(PCR) positive and PCR negative children

Of the 44 children that were HIV exposed, one child did not get a PCR test done. Sixteen/43(37.2%) children were found to be HIV PCR positive. The mortality between the groups was not significantly different. Of significance was that HIV PCR positive children required more days of ventilation (p=0.006), were more likely to require HFOV (p=0.0005) and stayed longer in PICU (p=0.03) than HIV exposed PCR negative children. (See Table 5)

There were no significant differences with regards to the number and type of medical conditions found.

Table 5. Comparison of HIV PCR Positive and HIV PCR Negative Children

	HIV PCR negative	HIV PCR positive	
Total admissions	27 (62.7%)	16 (37.2%)	
Median age in months (IQR)	2.5 (1.9)	3.1 (1.2)	p=0.03
Died in PICU	5 (18.5%)	5 (31.3%)	p=0.33
Median PICU stay in days	5	11.5	p=0.03
Median days ventilated	4	11	p=0.006
IPPV	26 (96.3%)	15 (93.8%)	
HFOV	2 (7.4%)	9 (56.3%)	p=0.0005
Inotropes	2 (7.4%)	2 (12.5%)	p=0.58
Respiratory tract conditions			
URT conditions			
URT infections	1 (3.7%)	0	
Other URT conditions	1 (3.7%)	1 (6.3%)	
LRT conditions			
LRT infections	23 (85.2%)	16 (100%)	p=0.1
PCP	3 (11.1%)	7 (43.8%)	p=0.14
Other systems			
Cardiovascular conditions	6 (22.2%)	3 (18.8%)	p=0.78
CNS conditions	8 (29.6%)	1 (6.3%)	p=0.069
GIT conditions	3 (11.1%)	0	
Renal conditions	2 (7.4%)	0	
Infections			

Bacterial sepsis	6 (22.2%)	4 (25%)	p=0.66
Viral infection	5 (18.5%)	1 (0.06%)	p=0.39

Comparison of HIV unexposed and HIV exposed PCR negative children

The mediansof the duration of PICU stay and number of days ventilatedof the HIV unexposed children was same as that of the HIV exposed but PCR negative children. Statistical comparison showed no significant difference in these variables between these groups as shown in Table 6. The significant differences between these two groups were that the HIV exposed PCR negative children were younger than the HIV unexposed children at admission p=0.001, and had a higher percentage of lower respiratory tract infections.

Table 6. Comparison of HIV Unexposed and HIV Exposed PCR Negative Children

	HIV Unexposed	HIV PCR Negative	
Median PICU stay in days	5	5	p=0.33
Median days ventilated	4	4	p=0.43
Median age in months	6.3(24.5)	2.5(1.9)	p=0.001
LRT Infections	44(51.8)	23(85.2)	p=0.006

Discussion

This audit shows that the majority of admissions to the PICU at CMJAH are neonates, followed by post-surgical and trauma patients. Medical admissions comprised 15% of the total, with a median age of 3.8 months. More male than female children were admitted, a similar finding to other studies.[16] There were 34.1% HIV exposed children, while 12.2% were HIV PCR positive. We were unable to calculate how many children were denied beds due to their HIV status being positive as this information was unavailable. It's possible that there may have been a selection bias. All the children admitted were severely ill as 92% required conventional ventilation with 10% requiring transition to HFOV.

Median duration of stay was 5 days and 24.4% of children died in the PICU.The spectrum of conditions was wide, but the predominance of acute LRTI was not surprising asup to 40% of hospital admissions in South Africa are accounted for bycommunity acquired pneumonia.[17]This was quite different to results from 1994 in the study by Ballot et al which found only 9/117 (7.6%) children admitted with pneumonia in the CMJAH PICU and none of them died.[9]Respiratory viral pathogens were identified in 12.2% of admissions, with Respiratory syncytial virus (RSV) accounting for the highest number. RSV is known to be the commonest cause of moderate or severe bronchiolitis.[18]

Only three children had confirmed PCP infection on tracheal aspirate analysis. Two of the three were HIV exposed and one was HIV unexposed. PCP has been found in HIV unexposed children who have compromised immune systems for other reasons such as malnutrition.

Comparison between HIV exposed and HIV unexposed children

There was no significant difference in mortality rates between HIV exposed and unexposed patients. This is possibly due to the ventilation strategies and choice of antibiotics used in the PICU. HIV exposed children stayed 3 days longer in the PICU and were ventilated for 4 more days than HIV unexposed children. Length of stay may be linked to increased expense.

In the CMJAH PICU HFOV is used as a second line ventilation strategy, for children who remain in respiratory failure or whose condition deteriorates on conventional mechanical ventilation.A total of 25% of HIV exposed children were converted to HFOV compared to only 3.5% of unexposed children ($p=0.0005$). This is another indicator that HIV exposed children were generally sicker and required more support.

Almost all HIV exposed children suffered from a LRTI.A birth cohort study done in Paarl, SA, showed that exposure to HIV was a significant independent risk factor for severe pneumonia.This could be due to limited protection due to lower maternal antibodies.[19]

It was clear that bacterial pneumonia and PCP pneumonia were the predominant LRTIs affecting HIV exposed children. Kitchin suggested that the immune dysregulation that increases the risk for PCP in HIV infected children is also present in HIV exposed but uninfected children.[11]

Comparison between HIV PCR positive and PCR negative children

HIV infected childrenhad a higher mortality compared to those that were exposed but uninfected, but this difference was not statistically significant.HIV infected children had a significantly longer duration of ICU stay and duration of ventilation than exposed but uninfected patients. This finding is similar to that in other studies that found that HIV infected children had a longer length of hospital stay due to the increased severity of their LRTI.[20, 21]

A study done at the Steve Biko Academic Hospital PICU showed better survival to 1 year of age as compared to previous studies when HAART was initiated early in the course of the disease.[11] This highlights the importance of early testing and initiation of HAART for children as well as an effective prevention of mother to child transmission(PMTCT) programme in decreasing the burden of HIV.

Comparison between HIV unexposed and HIV exposed PCR negative children

Once the HIV PCR positive children were filtered out of the HIV exposed group, leaving the exposed but PCR negative children it became evident that the only significant differences between these children and those unexposed to HIV was their age at presentation and a higher

percentage of lower respiratory tract infections. This further supports that exposure to HIV should not be used as an exclusion criterion for intensive care.

It has been said that PCP occurs most frequently in HIV infected children, and can be the first clinical presentation of HIV infection.[22] We found 7 HIV infected children clinically diagnosed with PCP compared to 3 HIV exposed but uninfected children, (p=0.14). Only two children were proven sputum positive for PCP in this group; however this is not a sensitive method of diagnosis, even though microscopic visualisation is the gold standard.[23]

Study limitations include the fact that this is a retrospective study. Different clinicians may have used different criteria for the clinical diagnosis of some conditions. Some data was missing and there was no routine screening of patients for respiratory pathogens.It is difficult to know if some of the positive cultures such as the coagulase negative staphylococcus were contaminants. The exclusion of all neonates may have led to those with medical and not purely neonatal conditions, being missed.

Conclusion

The PICU admitted just short of 900 children in 19 months. The mortality rate of the children with medical conditions was 24.4%.The most frequent cause for admission was LRTI which is reflective of the high rates of pneumonia affecting South African children. Thirty four percent of childrenwere HIV exposed while 12.2% were HIV PCR positive. These children were mostly admitted for LRTIs with bacterial pneumonia and PCP being prominent causes.

Although the HIV exposed patients were more ill as proven by increased need for HFOV, longer duration of ventilation and PICU stay, they did not have a higher mortality. Their exclusion from PICU admission is no longer justified, especially in the era of HAART.

References

1. South African Human Rights Commission. South Africa's Children: A Review of Equity and Child Rights. South African Human Rights Commission/UNICEF, 2011.
2. WHO. Global Health Observatory Data. 2015. Available from: www.who.int/gho/child_health/mortality/causes/en (Accessed 2.08.2016 at 11:00)
3. Bhagwanjee S, Scribante J. National audit of critical care resources in South Africa - unit and bed distribution. S Afr Med J. 2007 Dec;97(12 Pt 3):1311-4.
4. Argent AC, Ahrens J, Morrow BM, Reynolds LG, Hatherill M, Salie S, et al. Pediatric Intensive Care in South Africa: An account of making optimum use of limited resources at the Red Cross War Memorial Children's Hospital. Pediatr Crit Care Med. 2014 Jan;15(1):7-14. doi: 10.1097/PCC.0000000000000029.

5. Rabie H, de Boer A, van den Bos S, Cotton MF, Kling S, Goussard P. Children with human immunodeficiency virus infection admitted to a paediatric intensive care unit in South Africa. J Trop Pediatr. 2007 Aug;53(4):270-3.
6. Rady HI, Mohamed SA, Mohssen SA, ElBaz M. Application of Diffferent Scoring Systems and their Value in Pediatric Intensive Care. Gaz Egypt Pediatr Assoc. 2014 Sep-Dec;62(3):59-64. doi: 10.1016/j.epag.2014.10.003.
7. Wells M, Riera-Fanego JF, Luyt DK, Dance M, Lipman J. Poor Discriminatory Performance of the Pediatric Risk of Mortality (PRISM) Score in a South African Intensive Care Unit. Crit Care Med. 1996 Sep;24(9):1507-13
8. Solomon LJ, Morrow BM, Argent AC. Paediatric Index of Mortality Scores: An Evaluation of Function in the Paediatric Intensive Care Unit of the Red Cross War Memorial Children's Hospital. S Afr J Crit Care. 2014 Aug;30(1):8-13. doi: 10.7196/SAJCC.166
9. Ballot DE, Davies VA, Rothberg AD, Ginsberg N. Selection of paediatric patients for intensive care. S Afr Med J. 1995 Nov;85(11 Suppl):1221-3, 6.
10. UNAIDS. HIV and AIDS estimates 2014 [cited 2014 10 September]. Available from: www.unaids.org/en/regionscountries/countries/southafrica. (Accessed 24.03.2016 at 21:20)
11. Kitchin OP, Masekela R, Becker P, Moodley T, Risenga SM, Green RJ. Outcome of human immunodeficiency virus-exposed and -infected children admitted to a pediatric intensive care unit for respiratory failure. Pediatr Crit Care Med. 2012 Sep;13(5):516-9. doi: 10. 1097/PCC.0b013e31824ea143.
12. Jeena PM, McNally LM, Stobie M, Coovadia HM, Adhikari MA, Petros AJ. Challenges in the provision of ICU services to HIV infected children in resource poor settings: a South African case study. J Med Ethics. 2005 Apr;31(4):226-30.
13. Kitchin OP, Wessels F, Masekela R, Becker P, Green RJ. Costs of admission for paediatric pneumonia in a setting of human immunodeficiency virus infection. Int J Tuberc Lung Dis. 2011 Dec;15(12):1702-7. doi: 10.5588/ijtld.11.0167.
14. Slyker JA, Lohman-Payne BL, John-Stewart GC, Maleche-Obimbo E, Emery S, Richardson B, et al. Acute cytomegalovirus infection in Kenyan HIV-infected infants. AIDS. 2009 Oct;23(16):2173-81. doi: 10. 1097/QAD.0b013e32833016e8.
15. Harris PA. Research Electronic Data Capture (REDCap)- A Metadata-driven metodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009 April;42(2):377-81. doi: 10.1016/j.jbi.2008.08.010.
16. Haque A, Bano S. Clinical profile and outcome in a paediatric intensive care unit in Pakistan. JColl Physicians Surg Pak. 2009 Aug;19(8):534-5. doi: 08.2009/JCPSP.534535.
17. Zar HJ, Jeena P, Argent A, Gie R, Madhi SA, Working Groups of the Paediatric Assembly of the South African Thoracic Society. Diagnosis and management of community-acquired pneumonia in childhood--South African Thoracic Society Guidelines. S Afr Med J. 2005 Dec;95(12 Pt 2):977-81, 984-90.
18. Green RJ, Zar HJ, Jeena PM, Madhi SA, Lewis H. South African guideline for the diagnosis, management and prevention of acute viral bronchiolitis in children. S Afr Med J. 2010 May;100(5):320, 322-5.

19. Le Roux DM, Myer L, Nicol MP, Zar HJ. Incidence and Severity of Childhood Pneumonia in the First Year of Life in a South African Birth Cohort: The Drakenstein Child Health Study. Lancet. 2015 Feb;3(2):95-103.
20. Zar HJ, Hanslo D, Tannenbaum E, Klein M, Argent A, Eley B, et al. Aetiology and outcome of pneumonia in human immunodeficiency virus-infected children hospitalized in South Africa. Acta Paediatr. 2001 Feb;90(2):119-25.
21. 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 <5 Years of Age in a High HIV Prevalence Setting, South Africa, 2009-2012. Pediatr Infect Dis J. 2015 Jan;34(1):66-72. doi: 10.1097/INF.0000000000000478.
22. Zar HJ. Pneumonia in HIV-infected and HIV-uninfected children in developing countries: epidemiology, clinical features, and management. Curr Opin Pulm Med. 2004 May;10(3):176-82.
23. Onishi A, Sugiyama D, Kogata Y, Saegusa J, Sugimoto T, Kawano S, et al. Diagnostic accuracy of serum 1,3-beta-D-glucan for pneumocystis jiroveci pneumonia, invasive candidiasis, and invasive aspergillosis: systematic review and meta-analysis. J Clin Microbiol. 2012 Jan;50(1):7-15. doi:10.1128/JCM.05267-11.

M140363

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M140363

NAME: (Principal Investigator) Dr Kekesto Mopeli

DEPARTMENT: Paediatrics
Charlotte Maxeke Johannesburg Academic Hospital

PROJECT TITLE: An Audit of Primary Medical Conditions in Children Admitted to Charlotte Maxeke Johannesburg Academic Hospital
(revised title)

DATE CONSIDERED: 28/03/2014

DECISION: Approved unconditionally

CONDITIONS:

SUPERVISOR: Dr D White

APPROVED BY:
Professor PE Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 06/06/2014

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 Secretary in Room 10004, 10th floor, Senate House University
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**

Principal Investigator Signature M140363Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES