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A DESCRIPTIVE STUDY OF CHILDREN ADMITTED WITH ACUTE SEVERE ASTHMA TO A TERTIARY HOSPITAL IN JOHANNESBURG, SOUTH AFRICA

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ABSTRACT

The prevalence of asthma is high and the incidence is increasing significantly in Africa. Cases of severe exacerbations of asthma are managed as inpatients and are often used as indicators of asthma care. There is a paucity of data regarding hospitalised paediatric asthma cases in low- and middle-income countries (LMICs). This retrospective study describes the clinical presentation of children admitted to Charlotte Maxeke Johannesburg Academic Hospital in Johannesburg, South Africa, with asthma, and the association, if any, with intensive care unit (ICU) admission. Medical records between the years 2015 and 2020 were reviewed, revealing 134 admissions, with eight children being admitted to the ICU. The median age was four years (IQR 3,7) and the median duration of stay was four days (IQR 4,6). 66% of the children admitted were aged 1–5 years; 52.5% of the admissions were male. Allergic rhinitis was the most common associated comorbidity, at 42.4%. Most children presented with subcostal retractions (88.8%) and hypoxia (74.2%). Two children died from asthma complications. Children who had a known asthma diagnosis at the time of admission were more likely to have been readmitted than those who did not have a prior asthma diagnosis (p = < 0.001). Previous asthma hospitalisation was associated with ICU admission (p = 0.041). Most admissions occurred during the summer months. The trend in hospitalised asthma cases declined over the study period and paediatric asthma mortalities were rare. Further studies are needed to assess risk factors for paediatric asthma hospitalisation, especially in LMICs.

Keywords: hospitalised paediatric asthma case, acute severe asthma, asthma exacerbation, allergic rhinitis

INTRODUCTION

Asthma is a heterogeneous disease characterised by chronic airway inflammation, enhanced bronchial hyperactivity and reversible airway obstruction. The main symptoms include coughing, wheezing, breathlessness, chest tightness and sputum production. Results from the Global Asthma Report indicate that South Africa has experienced an increase in the prevalence of paediatric asthma in rural and urban areas, including an increase in severe symptoms.[1] Similar results were published in the ISAAC studies of phases 1 and 3.[2–5] A recent time trend cross-sectional survey in the region showed that the prevalence of asthma in adolescents is increasing, with the children demonstrating frequent attacks of wheezing.[6] The increasing prevalence can lead to regular visits to emergency departments and the hospitalisation of the asthmatic children. Children showing signs of severe, life-threatening or near-fatal asthma should be admitted for further care.[7] To the best of our knowledge, there is a significant paucity of data, especially in LMICs, regarding the hospitalisation of paediatric asthma patients. Information relating to factors affecting admissions, admission trends, standards of care and mortality rates can be used to reduce the disease burden in sub-Saharan Africa. The study aimed to describe the clinical profile of children hospitalised with an acute exacerbation of asthma and the associations with ICU admission.

STUDY MATERIALS

STUDY SETTING

The study was conducted at the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), one of the tertiary academic hospitals affiliated to the University of the Witwatersrand, South Africa, an LMIC. The hospital has a 220-bed paediatric service including paediatric medical and surgical subspecialties. Fourteen beds are available in the mixed paediatric and neonatal ICU, where critically ill asthmatics needing ventilation are admitted.

STUDY DESIGN

A retrospective study was conducted on the medical records of children admitted with a diagnosis of severe acute exacerbation of asthma in the wards and in the ICU between March 2015 and April 2020.

STUDY POPULATION

We reviewed the medical records of children aged 1–14 years who had been admitted with a diagnosis of a severe

TABLE I: DEMOGRAPHIC CHARACTERISTICS OF CHILDREN HOSPITALISED WITH ASTHMA

VARIABLE	FREQUENCY (n)	PERCENTAGE (%)
Gender (*n* = 118)		
Female	56	47.5
Male	62	52.5
Age in years (*n* = 118)		
1–5	75	63.6
> 5	43	36.4
HIV status (*n* = 118)		
Negative	100	84.7
Positive	4	3.4
Test not documented	14	11.9
Nutritional status z score (*n* = 115)		
Wasted < –2	24	20.9
Normal ≥ –2 to ≤ 2	81	70.4
Overweight ≥ 2	10	8.7
Known asthmatic (*n* = 118)		
No	54	45.8
Yes	64	54.2
On follow-up for asthma (*n* = 118)		
No	68	57.6
Yes	50	42.4
Previous admission to hospital (*n* = 118)		
No	68	57.6
Yes	50	42.4
Previous ICU admission (*n* = 50)		
No	44	88.0
Yes	6	12.0

acute exacerbation of asthma in the general paediatric ward and ICU between March 2015 and April 2020. Children aged below one year and those with a known cause of wheezing in their admission course other than asthma were excluded – for example, those diagnosed with cystic fibrosis, primary ciliary dyskinesia, inhaled foreign body, vascular rings, congenital heart disease, bronchiectasis or pulmonary tuberculosis.

METHODS

DATA COLLECTION

All the electronic medical records of children admitted with asthma and fitting the inclusion criteria were extracted. The keywords searched were asthma, acute severe asthma, asthma attack and asthma exacerbation. Although the data of some patients were missing, they were not excluded from the final analysis.

VARIABLES

The patients' demographic characteristics, including age, sex, race, HIV status and nutrition status, were documented. The nutrition status was stratified using the WHO format of either body mass index (BMI) if > 5 years of age or weight for height/length Z scores (WHZ) if < 5 years of age. This included wasted (< –2 standard deviation), normal (> –2 < 2 standard deviation) and overweight (> 2 standard deviation). The patients' living conditions (house or informal dwelling) and patient exposure to household cigarette smoke, previous admissions to the ICU or ward, history of atopy and associated asthma comorbidities, such as eczema, allergic rhinitis (AR) and allergic conjunctivitis, were recorded.

The South African Weather System (SAWS) defines the weather seasons as either summer, autumn, winter or spring. These seasons were synchronised with the patients' admission dates. Clinical signs were recorded and patients were categorised into different levels of severity of asthma exacerbation according to the GINA and the British Thoracic Society guidelines.[7,8] These categories were: life-threatening asthma, severe asthma or moderate asthma exacerbation. The need for ICU was defined according to clinical signs of a silent chest, central cyanosis, confusion or drowsiness, oxygen saturation less than 92%, peak expiratory flow rate less than 33% of the predicted and a clinically exhausted child. On admission, arterial blood gases were analysed using the reference ranges for the ABL800 blood gas machine found in the hospital. The acid-base disorders were defined as normal acid-base with the pH 7.35–7.45, $HC0_3$ 22–28 mmHg, PCO_2 35–45 mmHg (4.7–6.0 kPa); respiratory acidosis pH < 7.350 with a $PaCO_2$ > 45 mmHg (> 6.0 kPA); metabolic acidosis pH < 7.350 with HCO_3 < 22 mmHg; and respiratory alkalosis pH > 7.450 with HCO_3 > 28 mmHg. The clinical outcome of either death or having been discharged alive was also documented.

SAMPLE SIZE

Consecutive sampling method covering the duration of the study.

DATA ANALYSIS

Data were analysed using STATA version 16.1. Categorical data were summarised using frequencies and percentages. The mean and standard deviation were used to analyse normally distributed quantitative or continuous data. For skewed data, the median and inter-quartile ranges were used. Statistical testing was done using the Chi-square test for categorical variables and the student's t-test for the continuous variables. A *p*-value of < 0.05 was used as the significant level for this study. Bivariate analysis was used to assess the associations between variables and outcome measures.

RESULTS

The records of a total of 134 patients with a primary diagnosis of asthma that fit the inclusion criteria were extracted for this study. The total number of children admitted was 118 because 16 of them were re-hospitalised during the study period. Only eight children were admitted to the ICU; two children died from asthma during the period under review.

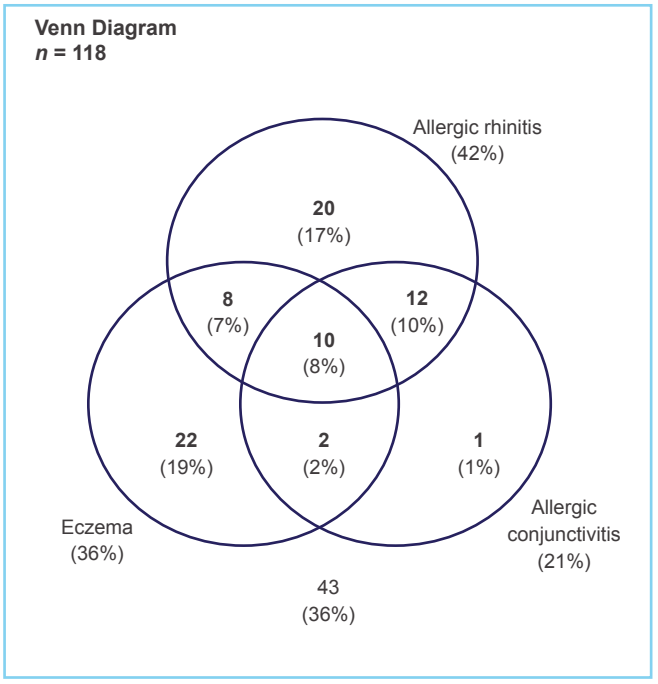


Figure 1: Comorbidities associated with asthma
*The most prevalent comorbidity was AR (*n *= 50/118 (42%)), whereas only 21% of the children had asthma and allergic conjunctivitis. Ten (8%) children had all the three conditions concurrently. Forty-three (36%) children had asthma and only one other comorbidity.*

DEMOGRAPHIC CHARACTERISTICS

At 62/118 (52.5%), most of the admissions were male. The median age of the cohort was four years (IQR 3,7) and the median duration of stay was four days (IQR 4,6). Their full nutrition status was documented in 115/134 (85.8%) of the medical records. Most of the participants had a normal z-score for weight for height (*n* = 81/115 (70.4%)), whereas 24/115 (20.9%) children were wasted and 10/115 (8.7%) were overweight. Table I summarises the demographic characteristics of the participants.

SOCIO-ECONOMIC CHARACTERISTICS

Most of the participants lived in houses with good amenities 113/118 (95.8%) and had not been exposed to household cigarette smoke 107/118 (90.7%).

ASTHMA COMORBIDITIES

Allergic rhinitis (AR) was the most common comorbidity associated with asthma, as shown in Figure 1.

ASTHMA ADMISSION TRENDS

Most admissions cumulatively occurred during summer – *n* = 44/134 (32.8%) – as illustrated in Figure 2. Both first-time admissions (*n* = 68/118, 57.6%) and readmission cases (*n* = 50/118, 42.4%) showed a downward trend over the five years of the study, as shown in Figure 3.

ANALYSIS OF RE-ADMISSION CASES

The odds of a male asthmatic child being re-admitted was 1.46 times greater than that of a female child, though this was statistically insignificant (*p* = 0.309). The children with a known asthma diagnosis were 20.1 times more likely to be rehospitalised than those with no history of asthma (*p* = < 0.001). There was no association between AR and cigarette exposure with readmission cases.

DESCRIPTION OF CLINICAL SIGNS OF CHILDREN ADMITTED WITH ASTHMA

The most common clinical sign recorded was accessory respiratory muscle use – for example, subcostal or suprasternal retractions: *n* = 119/134 (88.8%). Hypoxia, that is, oxygen saturation of less than 92%, was prevalent in 74.2% (*n* = 98/132), with a median oxygen saturation of 88% of the overall admission cases. The mean respiratory rate was 45 breaths per minute with a standard deviation (SD) of 13.5. The mean pulse rate was 148 beats per minute with an SD of 24.4. No child had bradycardia on admission. Most of the children were admitted with signs of severe acute asthma (*n* = 123/134, 91.8%). Of the ten children admitted with signs of life-threatening asthma (*n* = 10/134, 7,5%), only two (20%) were admitted to the ICU for mechanical ventilation.

ARTERIAL BLOOD GAS ANALYSIS

Metabolic acidosis and respiratory alkalosis were the most common acid-base disorders, at 33/63 (52.4%) and 15/63 (23.8%), respectively.

INITIAL EMERGENCY TREATMENT PROVIDED

Oxygen therapy was prescribed and administered in 84.3% (*n* = 113/134) of the children. The dominant delivery method was the low-flow oxygen by nasal prongs (78.8% (*n* = 89/113)), whereas only three children (2.7%) used a high-flow nasal catheter (HFNC). Corticosteroids were prescribed in 126/134 (94.0%) of the cases, with oral prednisolone being the commonest choice (123/126 (98.0%)). Of the 134 children, all but one patient received nebulised salbutamol on admission day, the exceptional child receiving only nebulised ipratropium bromide.

ANALYSIS OF ICU ADMISSION CASES

Eight of the 134 admissions required intensive care, all of them being ventilated. Five were boys; six had previously been admitted to a ward for asthma; and two had had a previous ICU admission. Two were newly diagnosed asthma cases.

There was an association between previous asthma hospitalisation and current asthma ICU admission: *p* = 0.04. Both intravenous magnesium sulphate and intravenous salbutamol were associated with ICU admission, as summarised in Table II.

BIVARIATE ANALYSIS OF THE ICU ADMISSIONS

The males were 1.55 times more likely to be admitted into the ICU than the females, though this was statistically insignificant: *p* = 0.56 (OR: 1.55, 95% CI 0.35–6.80). The children with a known history of asthma were 2.69 times more likely to be admitted into the ICU for further care than those without a previous asthma history: *p* = 0.238 (OR: 2.69, 95% CI 0.52–13.91). Those who had had a previous hospitalisation for asthma had a higher likelihood of ICU admission (OR: 4.86, 95% CI 0.94–24.19), although this was statistically insignificant: *p* = 0.06.

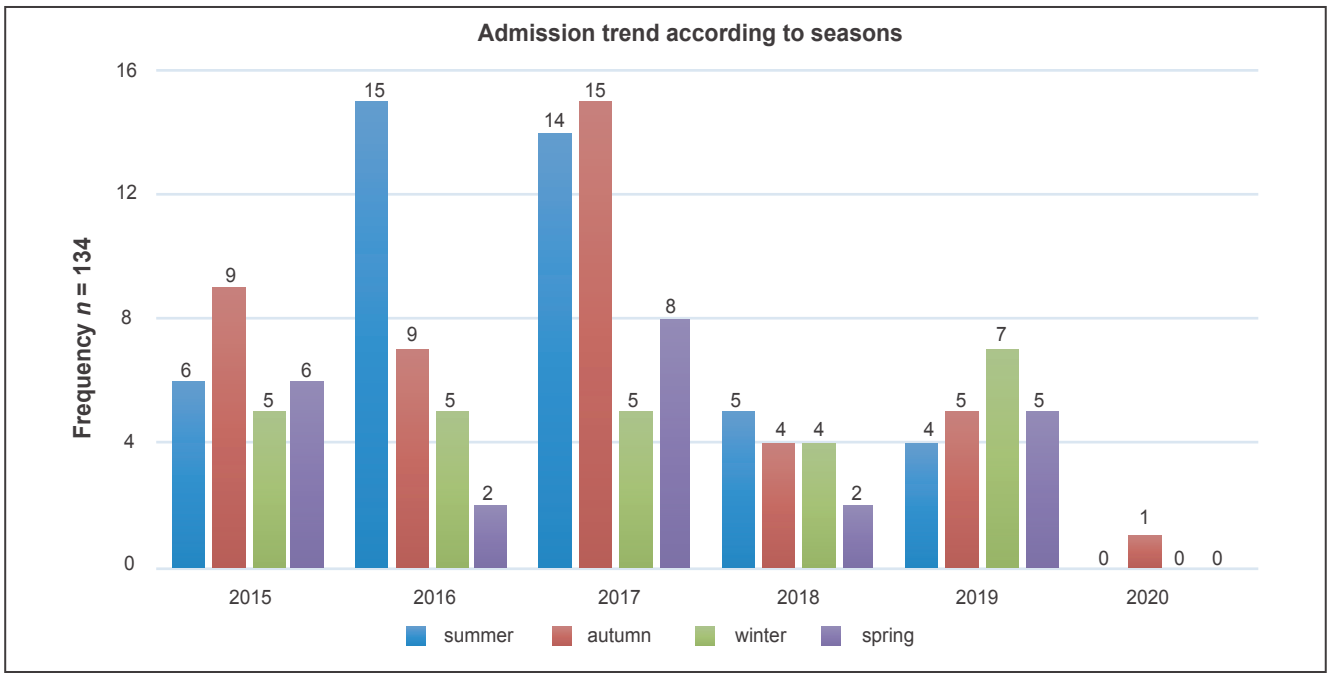


Figure 2: Illustration of asthma admission trends according to seasons and the admission year

The children with the inability to complete a sentence were 6.67 times more likely to be admitted to ICU than those who could: $p = 0.039$. The children who received IV magnesium sulphate: $p = < 0.001$ (OR: 24.58, 95% CI 4.96–121.82) or IV salbutamol: $p = < 0.001$ (OR: 13.67, 95% CI 1.91–97.80) were more likely to be admitted into the ICU than those who had never received these medications.

MORTALITY CASES ASSOCIATED WITH ASTHMA

Only two deaths were associated with asthma during the study period. Table III summarises the mortality cases.

DISCUSSION

A WHO report and data from some European countries show a declining trend in paediatric asthma admissions, mainly attributed to increased inhaled corticosteroids.[10–13] Our findings indicated a peak in 2017, followed by a declining trend in first-time and re-admission cases. We hypothesise that the change could be due to timely patient referral to the hospital respiratory clinic and improved care and follow-up from the specialists.

Asthmatic children become hospitalised due to poor symptom control or first-time presentation of the disease. They often have severe signs and symptoms of acute asthma, life-threatening or near-fatal signs that necessitate admission to either the high care area or the PICU.[14,15] Asthma management strategies demand accurate assessment of the children before treatment is initiated.[14,15] The evaluation can be clinical features, lung function tests and pulse oximetry.[16] According to the South African and GINA guidelines, our study revealed that the majority of the children were appropriately hospitalised in line with the severity of the illness.[7,17] Most of the children were admitted with signs and symptoms of severe acute asthma (n = 123/134, 91.8%). Ten children had life-threatening asthma, but only two of them were admitted to the PICU. The other eight children received emergency care, their symptoms resolving while they were in the high care area.

Our results revealed that 62% of children were under five years of age, which are consistent with other studies which indicate that almost 80% of asthma cases start before the age of six years.[18,19] This age group has different phenotypic expressions of asthma, much narrower airways prone to inflammation and various conditions that mimic the disease.[20–22] Males had more admissions and re-admissions than females, although this was statistically insignificant in our study ($p = 0.309$). Two extensive population studies in Finland and the United States had similar results.[21,22] The gender preference is unknown, but it is postulated that younger males have a smaller airway diameter than lung volume, which predisposes them to lower respiratory tract events.[20–22]

Previous studies have indicated that a child with a previous asthma-related admission has a higher chance of re-admission. The greater the number of previous admissions, the higher the chances of re-admission.[23] Chen et al (2003) found that a lifetime history of admission was strongly associated with a 4.36-fold higher hospitalisation rate.[24] Our results showed that 42.4% of the children had had one or more previous asthma-related hospitalisations. We hypothesise that re-admission of the known asthmatic child can be due to a lack of:

- access to care and appropriate treatment;
- adherence to the medication;
- regular follow-up; or
- adequate understanding of asthma education in the child and caregivers.

Despite careful attention having been paid to dealing with these factors, some children still have frequent exacerbations. A study by Teague et al (2018) found that children with severe asthma

TABLE II: DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF CHILDREN ADMITTED TO THE ICU DUE TO ASTHMA

CHARACTERISTICS		TOTAL ADMISSION *n* (%)	NO ICU ADMISSION (%)	ICU ADMISSION *n* (%)	*P* VALUE
Gender (*n* = 118)	Female	56 (47.5)	53 (94.6)	3 (5.4)	0.559
	Male	62 (52.5)	57 (91.9)	5 (8.1)	
Age (*n* = 118)	1–5 years	75 (63.6)	70 (93.3)	5 (6.7)	0.949
	> 5 years	43 (36.4)	40 (93.0)	3 (7.0)	
Known asthmatic (*n* = 118)	No	54 (45.8)	52 (96.3)	2 (3.7)	0.222
	Yes	64 (54.2)	58 (90.3)	6 (9.4)	
Previous hospital admission (*n* = 118)	No	70 (59.3)	68 (57.6)	2 (1.7)	**0.041**
	Yes	48 (40.7)	42 (35.4)	6 (5.1)	
Previous ICU admission (*n* = 50)	No	44 (88.0)	38 (90.5)	6 (75.0)	0.217
	Yes	6 (12.0)	4 (9.5)	2 (25.0)	
AR (*n* = 118)	No	68 (57.6)	63 (92.7)	5 (7.3)	0.773
	Yes	50 (42.4)	47 (94.0)	3 (6.0)	
Unable to speak	No	126 (94.0)	120 (95.2)	6 (75.0)	**0.019**
	Yes	8 (6.0)	6 (4.8)	2 (25.0)	
Clinical exhaustion	No	113 (95.8)	107 (97.3)	6 (75.0)	**0.003**
	Yes	5 (4.2)	3 (2.7)	2 (25.0)	
Confusion/drowsiness	No	129 (96.3)	123 (97.6)	6 (75.0)	**0.001**
	Yes	5 (3.7)	3 (2.4)	2 (25.0)	
Silent chest	No	133 (99.3)	125 (99.2)	8 (100.0)	0.800
	Yes	1 (0.7)	1 (0.8)	0 (0.0)	
Life-threatening asthma (*n* = 10)	No	124 (92.5)	118 (93.7)	6 (75.0)	**0.052**
	Yes	10 (7.5)	8 (6.3)	2 (25.0)	
Metabolic acidosis (*n* = 60)	No	30 (47.6)	28 (48.3)	2 (40.0)	0.722
	Yes	33 (52.4)	30 (51.7)	3 (60.0)	
Respiratory acidosis	No	61 (96.8)	57 (98.3)	4 (80.0)	**0.025**
	Yes	2 (3.2)	1 (1.7)	1 (20.0)	
IV salbutamol	No	129 (96.3)	123 (97.6)	6 (75.0)	**0.001**
	Yes	5 (3.7)	3 (2.4)	2 (25.0)	
IV magnesium sulphate	No	121 (90.3)	118 (93.7)	3 (37.5)	**< 0.001**
	Yes	13 (9.7)	8 (6.4)	5 (62.5)	

experienced frequent exacerbations and required higher doses of controller medication and prednisolone compared to those with non-severe asthma; they identified them as having 'severe treatment resistant asthma'.[25] This group of children can contribute significantly to hospitalisations and re-admissions as a result of asthma exacerbation. This study did not identify phenotypes of asthma in our cohort of children and further research is therefore needed to understand this category of child in our setting.

Exposure to environmental tobacco smoke is a widely known risk factor for asthma exacerbations and the development of severe or uncontrolled asthma, leading to increased chances of hospitalisation.[26,27] Our study did not find this association (p = 0.67). Published studies for weather season and asthma admissions rates have indicated mixed results.[28–30] Most of our admissions occurred during the summer–autumn period. We can extrapolate the peaks due to dispersed aeroallergens, especially from grass pollen, during summer storms in Gauteng

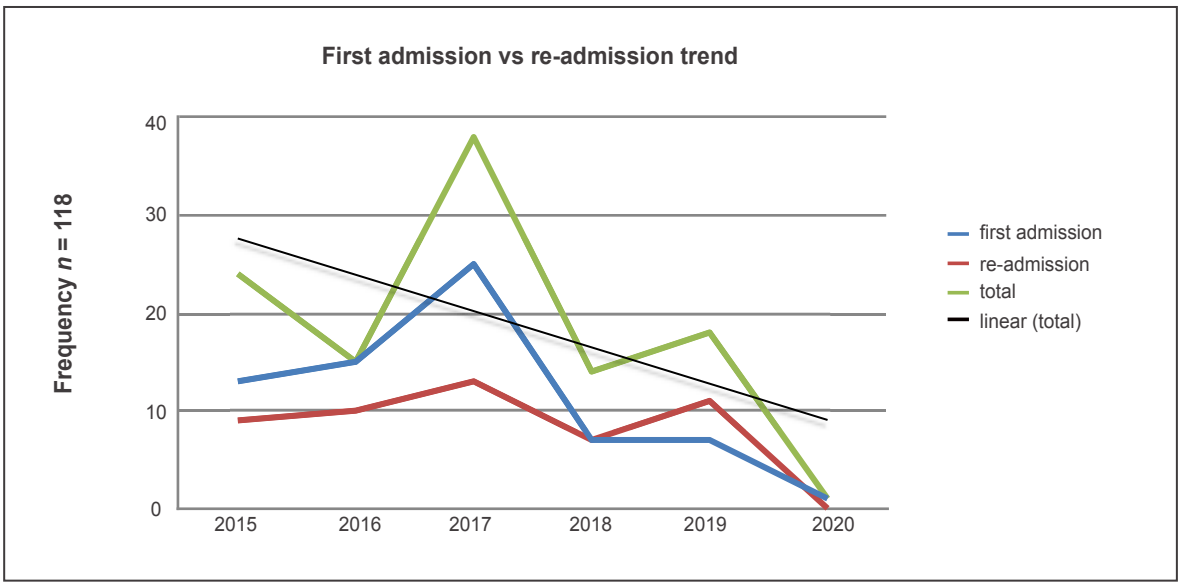


Figure 3: Comparison of first-time admission and re-admission cases

province, as documented by Berman.[31] Further research is needed to compare the specific allergens to the weather season period, as this was beyond the scope of our study.

AR is prevalent in up to 100% of allergic asthmatic patients with the manifestation of uncontrolled symptoms and increased risk for exacerbations.[32,33] Sazonov in Norway found that children with AR were 1.72 times more likely to have asthma-related re-admissions than those without it.[33] Our analysis showed that 42.4% of the admissions had AR, but there was no association with rehospitalisation and ICU admission.

Although it is not a routine test in asthma exacerbations, arterial blood gas analysis provides an objective assessment of severe to life-threatening asthma's not responding to treatment.[34] Hyperventilation leads to hypoxia and hypocarbia, with eventual respiratory muscle fatigue. The median $PaCO_2$ in our study was 31 mmHg with an IQR of 26.8–36.6, whereas the median PaO_2 was 89.6 mmHg (11.9 kPa) with an IQR of 64.5-124. The most common acid-base disturbance was metabolic acidosis (52.4%), which we can speculate to be secondary to hypoxia. Similarly to a study in Singapore, our study revealed an association between respiratory acidosis and ICU admission (p = 0.025).[35] On bivariate analysis, however, the association was statistically insignificant (p = 0.078).

The South African guidelines for first-line asthma exacerbation management were adhered to, with more than 90% of the children receiving oxygen, systemic steroids and inhaled bronchodilators. The non-responders received parenteral bronchodilators.[17] There was an association between IV salbutamol (p = 0.001), IV magnesium sulphate (p = < 0.001) and ICU admission, as summarised in Table III. Children who received IV salbutamol were 13.67 times more likely to be admitted to the ICU than those who did not, whereas those who received IV magnesium sulphate were 24.58 times more likely to be admitted to the ICU.

PICU asthma admission is reported to be uncommon.[36] Earlier reports in South Africa revealed that PICU asthma admissions were on the decline in a retrospective study conducted over 17 years.[16] In our study, only eight (6.0%) children were admitted for invasive ventilation during the study period. Children with life-threatening signs of asthma were 4.97 times more likely to be admitted to the PICU than children without these signs (p = 0.007). These signs included an inability to complete a sentence, confusion or drowsiness and clinical exhaustion. This indicates that the clinicians were able to discern the clinical signs accurately and institute the correct management.

Our analysis revealed that the children with previous asthma-related hospitalisation were 4.86 times likely to be admitted to the PICU with an acute asthma exacerbation, though this was statistically insignificant (p = 0.06). A similar result from a prospective multicentre study in the Netherlands showed no statistical significance between prior hospitalisation and PICU admission (p = 0.107).37 In contrast, Van den Bosch and Kam-Lun Hon found an association between a previous asthma admission and PICU admission.[38,39] Further studies are necessary to analyse the association, but clinicians should be aware of the risk involved and plan comprehensive preventive measures for a child discharged after an asthma hospitalisation.

Paediatric asthma-related deaths are rare and on a declining trend.[40,41] The Global Asthma Report ranks South Africa 5th in asthma-related mortality.[10] This is despite early reports showing that the region has declining mortality due to improved health services.[16] Zar et al mentioned that most of the deaths were adult cases, with the paediatric population having a 3% mortality rate.[16] In Brazil, the asthma mortality rate in children aged 5–19 ranged from 0.04 to 0.39 per 100 000 people.[42] In Ireland, the mortality was low, with no apparent trend.[43] Our mortality rate in the study period was 1.69%, indicating that paediatric asthma deaths are uncommon, possibly due to improved quality of care and early identification of the critically ill asthmatic child.

Our study had the limitation of missing data. Owing to a widespread lack of documentation on inhaler compliance, we

TABLE III: A SUMMARY OF THE ASTHMA MORTALITY CASES

CHARACTERISTICS	CASE 1	CASE 2
Gender, age (years), HIV status	Female, 2 years, Negative	Male, 13 years, Positive
Duration of stay	12 days	2 days
Known asthmatic **and on** follow-up	Yes	Yes
Previous hospital admission, previous ICU admission	Yes, No	Yes, No
Associated comorbidities	Nephrotic syndrome, hypothyroidism	None
Asthma severity on admission	Life-threatening asthma	Acute severe asthma
Admitted to ICU	No	Yes

could not assess whether the known asthmatics were compliant with their medication before hospitalisation. A lack of adherence to inhaler therapy is one of the main risk factors for poor asthma control, but it was omitted in the analysis. Our findings may not be generalisable but they may prompt other studies relating to acute asthma care in other facilities in the region.

Despite the limitations, this study describes an essential aspect of acute asthma in the paediatric population, focusing as it does on early patient assessment, awareness of the need for ICU care, guideline adherence and the importance of follow-up care.

CONCLUSION

Overall, this study showed a declining trend in paediatric acute asthma hospitalisation in our healthcare setting, with a notably rare mortality. Children with a known asthma diagnosis are at high risk for re-admission with an acute exacerbation and the clinical signs need to be recognised. Children with previous asthma hospitalisations are at a higher risk of re-admission with severe symptoms necessitating intensive care management. There is therefore a dire need for these groups of children to undergo meticulous monitoring and to attend comprehensive follow-up clinics, which should include personalised action plans to avoid rehospitalisation. This study highlights the overall good clinical outcome of acute asthma with appropriate care.

CONFLICT OF INTEREST

There is no conflict of interest and no funding for this research.
This article has been peer reviewed.

ETHICS

This study was approved by the University of the Witwatersrand Human Research Ethics Committee (medical) (Ref: M200406).

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